

HANDBOOK OF CHEMICAL RISK ASSESSMENT

Health Hazards to Humans,
Plants, and Animals

VOLUME 1

Metals



Ronald Eisler

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CHEMICAL RISK
ASSESSMENT

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VOLUME 1
Metals

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VOLUME 2
Organics

HANDBOOK OF
CHEMICAL RISK
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**Health Hazards to Humans,
Plants, and Animals**

VOLUME 3

**Metalloids, Radiation,
Cumulative Index to
Chemicals and Species**

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Preface

Risk assessment is an inexact science. Successful risk assessment practitioners rely heavily on extensive and well-documented databases. In the case of chemicals entering the environment as a result of human activities, these databases generally include the chemical's source and use; its physical, chemical, and metabolic properties; concentrations in field collections of abiotic materials and living organisms; deficiency effects, in the case of chemicals essential for life processes; lethal and sublethal effects, including effects on survival, growth, reproduction, metabolism, mutagenicity, teratogenicity, and carcinogenicity; proposed regulatory criteria for the protection of human health and sensitive natural resources; and recommendations for additional research when databases are incomplete. Of the hundreds of thousands of chemicals discharged into the environment yearly from agricultural, domestic, industrial, mining, manufacturing, municipal, and military operations, there is sufficient information on only a small number to attempt preliminary risk assessments.

The chemicals selected for inclusion in this handbook series were recommended by environmental specialists of the U.S. Fish and Wildlife Service and other resource managers responsible for protecting our fish, wildlife, and biological diversity. Their choices were based on real or potential impact of each contaminant on populations of free-living natural resources — including threatened and endangered species — and on insufficient knowledge on how best to mitigate damage effects. Each chapter selectively reviews and synthesizes the technical literature on a specific priority contaminant in the environment and its effects on notably terrestrial plants and invertebrates, aquatic plants and animals, avian and mammalian wildlife, and other natural resources. Early versions of individual chapters were published between 1985 and 1999 in the *Contaminant Hazard Reviews* series of the U.S. Department of the Interior. This series rapidly became an important reference tool for contaminant specialists, scientists, educational institutions, state and local governments, natural resources agencies, business and industry, and the general public. More than 105,000 copies of individual reports were distributed in response to specific requests before supplies became exhausted. The current offering is updated to reflect the burgeoning literature in this subject area. I authored the original versions and the updates while stationed at the Patuxent Wildlife Research Center; however, all interpretations are my own and do not necessarily reflect those of the U.S. government. Moreover, mention of trade names or commercial products is not an endorsement or recommendation for use by the U.S. government.

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HANDBOOK OF

CHEMICAL RISK

ASSESSMENT

Health Hazards to Humans,

Plants, and Animals

VOLUME 1

Metals

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CHAPTER 1

Cadmium

1.1 INTRODUCTION

There is no evidence that cadmium (Cd) is biologically essential or beneficial; on the contrary, it has been implicated as the cause of numerous human deaths and various deleterious effects in fish and wildlife. In sufficient concentration, it is toxic to all forms of life, including microorganisms, higher plants, animals, and man. It is a relatively rare metal, usually present in small amounts in zinc ores, and is commercially obtained as an industrial by-product of the production of zinc, copper, and lead. Major uses of cadmium are in electroplating, in pigment production, and in the manufacture of plastic stabilizers and batteries. Anthropogenic sources of cadmium include smelter fumes and dusts, the products of incineration of cadmium-bearing materials and fossil fuels, fertilizers, and municipal wastewater and sludge discharges; concentrations are most likely highest in the localized regions of smelters or in urban industrialized areas (Hammons et al. 1978; U.S. Environmental Protection Agency [USEPA] 1980; Nriagu 1980, 1981; Hutton 1983b; Eisler 1985; Scheuhammer 1987; U.S. Public Health Service [USPHS] 1993; Cooke and Johnson 1996). Industrial consumption of cadmium in the United States, estimated at 6000 metric tons in 1968, is increasing; projected use in the year 2000 is about 14,000 tons, primarily for electroplating of motor parts and in the manufacture of batteries. The cadmium load in soils and terrestrial biota in other industrialized countries also appears to be increasing and is of great concern in Scandinavia (Tjell et al. 1983), Germany (Markard 1983), and the United Kingdom (Hutton 1983a).

1.2 ENVIRONMENTAL CHEMISTRY

Cadmium, as cadmium oxide, is obtained mainly as a by-product during the processing of zinc-bearing ores and also from the refining of lead and copper from sulfide ores (USPHS 1993). In 1989, the United States produced 1.4 million kg of cadmium (usually 0.6 to 1.8 million kg) and imported an additional 2.7 million kg (usually 1.8 to 3.2 million kg). Cadmium is used mainly for the production of nickel–cadmium batteries (35%), in metal plating (30%), and for the manufacture of pigments (15%), plastics and synthetics (10%), and alloys and miscellaneous uses (10%) (USPHS 1993).

Cadmium is a silver-white, blue-tinged, lustrous metal that melts at 321°C and boils at 767°C. This divalent element has an atomic weight of 112.4, an atomic number of 48, and a density of 8.642 g/cm³. It is insoluble in water, although its chloride and sulfate salts are freely soluble (Windholz et al. 1976; USPHS 1993). The availability of cadmium to living organisms from their immediate physical and chemical environs depends on numerous factors, including adsorption and desorption rates of cadmium from terrigenous materials, pH, Eh, chemical speciation, and many

other modifiers. The few selected examples that follow demonstrate the complex behavior of cadmium in aquatic systems.

Microbial extracellular polymeric substances (EPS) — ubiquitous features in aquatic environments — actively participate in binding dissolved overlying and pore-water metals in sediments. Organic sediment coatings in the form of bacterial EPS equivalent to about 0.5% organic matter can adsorb cadmium under estuarine conditions (Schlekat et al. 1998). EPS aggregates rapidly sorbed up to 90% of cadmium from solution. Changes in pH affected cadmium sorption, with the proportion of freed Cd to sorbed Cd changing from 90% at pH 5 to 5% at pH 9; desorption was enhanced with increasing salinity (Schlekat et al. 1998).

Adsorption and desorption processes are likely to be major factors in controlling the concentration of cadmium in natural waters and tend to counteract changes in the concentration of cadmium ions in solution (Gardiner 1974). Adsorption and desorption rates of cadmium are rapid on mud solids and particles of clay, silica, humic material, and other naturally occurring solids. Concentration factors for river muds varied between 5000 and 500,000 and depended mainly on the type of solid, the particle size, the concentration of cadmium present, the duration of contact, and the concentration of complexing ligands; humic material appeared to be the main component of river mud responsible for adsorption (Gardiner 1974). Changes in physicochemical conditions, especially pH and redox potential, that occur during dredging and disposal of cadmium-polluted sediments may increase chemical mobility and, hence, bioavailability of sediment-bound cadmium (Khalid et al. 1981). For example, cadmium in Mississippi River sediments spiked with radiocadmium was transformed from potentially available organic forms to more mobile and readily available dissolved and exchangeable forms (i.e., increased bioavailability) under regimens of comparatively acidic pH and high oxidation (Khalid et al. 1981). The role of dissolved oxygen and aquatic plants on cadmium cycling was studied in Palestine Lake, a 92-ha eutrophic lake in Kosciusko County, Indiana, a long-term recipient of cadmium and other waste metals from an electroplating plant. The maximum recorded concentration of dissolved cadmium in the water column was 17.3 µg/L; for suspended particulates, it was 30.3 µg/L (Shephard et al. 1980). During anaerobic conditions in the lake's hypolimnion, a marked decrease in the dissolved fraction and a corresponding increase in the suspended fraction were noted. The dominant form of cadmium was free, readily bioavailable, cadmium ion, Cd²⁺; however, organic complexes of cadmium, which are comparatively nonbioavailable, made up a significant portion of the total dissolved cadmium. Cadmium levels in sediments of Palestine Lake ranged from 1.5 mg/L in an uncontaminated area of the lake to 805 mg/L near the outlet of a metal-bearing ditch that entered the lake (McIntosh et al. 1978). The dominant form of cadmium in sediments was as a carbonate. Levels of cadmium in water varied over time and between sites, but usually ranged from 0.5 to 2.5 µg/L. It is possible that significant amounts of cadmium are transferred from the sediments into rooted aquatic macrophytes and later released into the water after macrophyte death (natural or herbicide-induced), particularly in heavily contaminated systems. In Palestine Lake, cadmium levels in pondweed (*Potamogeton crispus*), a rooted aquatic macrophyte, were about 90 mg/kg dry weight; a maximum burden of 1.5 kg was retained by the population of *P. crispus* in the lake (McIntosh et al. 1978). Release of the total amount could raise water concentrations by a maximum of 1 µg/L. This amount was considered negligible in terms of the overall lake cadmium budgets; however, it might have limited local effects.

1.3 CONCENTRATIONS IN FIELD COLLECTIONS

Small amounts of cadmium enter the environment from the natural weathering of minerals, but most is released as a result of human activities such as mining, smelting, fuel combustion, disposal of metal-containing products, and application of phosphate fertilizers or sewage sludges (USPHS 1993). In 1988, an estimated 306,000 kg of cadmium entered the domestic environment as a result

Table 1.1 Cadmium Burdens and Residence Times in the Principal Global Reservoirs

Reservoir	Concentration	Total Cd in Reservoir, in Metric Tons	Residence Time
Atmosphere	0.00003 µg/m ³	1500	7 days
Oceans			
Dissolved	0.06 µg/kg	84,000,000	21,000 years
Suspended particulates (total)	1.0 mg/kg	1,400,000	—
Particulate organic matter	4.5 mg/kg	320,000	1.3 years
Freshwaters			
Dissolved	0.05 µg/kg	16,000	—
Sediments	0.16 mg/kg	100,000	3.6 years
Groundwater	0.1 µg/kg	400	—
Glaciers	0.005 µg/kg	82,000	—
Sediment pore waters	0.2 µg/kg	64,000,000	—
Swamps and marshes, biomass	0.6 mg/kg	3600	—
Biosphere			
Marine plants	2.0 mg/kg	400	18 days
Marine animals	4.0 mg/kg	12,000	—
Land plants	0.3 mg/kg	720,000	20 days
Land animals	0.3 mg/kg	6000	—
Freshwater biota	3.5 mg/kg	7000	3.5 years
Human biomass	50 mg/person	200	1–40 years
Terrestrial litter	0.6 mg/kg	1,300,000	42 years
Lithosphere (down to 45 km)	0.5 mg/kg	2.8 × 10 ¹³	1 billion years

Adapted from Nriagu, J.O. (ed.) 1980. *Cadmium in the Environment. Part I: Ecological Cycling*. John Wiley, NY. 682 pp.

of human activities, mostly from industrial releases that were subsequently applied to soils (USPHS 1993). Where cadmium is comparatively bioavailable, these values are very near those that have been shown to produce harmful effects in sensitive biological species, as will be discussed later.

Loading of cadmium in uncontaminated, nonbiological compartments extended over several orders of magnitude, with most of the cadmium in lithosphere and ocean reservoirs (Table 1.1; Korte 1983). Concentrations (µg/L or µg/kg) of cadmium reported in uncontaminated compartments ranged from 0.05 to 0.2 in freshwater, up to 0.05 in coastal seawater, from 0.01 to 0.1 in open-ocean seawater, 0.1 to 14 in stormwater runoff, up to 5000 in riverine and lake sediments, 30 to 1000 in marine sediments, 10 to 1000 in soils of nonvolcanic origin, as much as 142 in human dietary items, up to 4500 in soils of volcanic origin, 1 to 600 in igneous rock, up to 100,000 in phosphatic rock, and 0.001 to 0.005 µg/m³ in air (Korte 1983; USPHS 1993). Higher values are reported in abiotic materials and living organisms from cadmium-contaminated environments, being highest near cadmium-emitting industries such as smelters, municipal incinerators, and fossil fuel combustion facilities (Eisler 1985; USPHS 1993).

Cadmium, unlike synthetic compounds, is a naturally occurring element, and its presence has been detected in more than 1000 species of aquatic and terrestrial flora and fauna. Concentrations of cadmium in selected species of biota are shown in Table 1.2; more extensive documentation was presented by Hammons et al. (1978), NRCC (1979), Jenkins (1980), and Eisler (1981). At least six trends are evident from Table 1.2. First, marine biota generally contained significantly higher cadmium residues than their freshwater or terrestrial counterparts, probably because total cadmium levels are higher in seawater. Second, cadmium tends to concentrate in the viscera of vertebrates, especially the liver and kidneys. Third, concentrations of cadmium are higher in older organisms than in younger stages; this relationship is especially pronounced in carnivores and marine vertebrates (Eisler 1984). Fourth, higher concentrations reported for individuals of a single species collected at several locations are almost always associated with proximity to industrial and urbanized

areas or to point source discharges of cadmium-containing wastes. Fifth, background levels of cadmium in crops and other plants are usually <1.0 mg/kg (ppm). Little is known about the cadmium concentrations required to reduce plant yields; however, plants growing in cadmium-contaminated soils contain abnormally high residues that may be detrimental to plant growth and to animal and human consumers. Finally, it is apparent from [Table 1.2](#) that species analyzed, season of collection, ambient cadmium levels, and sex of organism all modify concentrations of cadmium in organisms. In freshwater isopods, for example, cadmium was stored mainly in the hepatopancreas; cadmium concentrations were higher in juveniles than in adults; and seasonal fluctuations accounted for as much as 79% of the within-population variability (van Hattum et al. 1996).

Cadmium tends to accumulate in avian tissues in the order of kidney, liver, brain, bone, and muscle, with the highest concentrations in older birds and those found closest to a point source of cadmium (Pedersen and Myklebust 1993; Ferns and Anderson 1994; Garcia-Fernandez et al. 1996). In Norwegian birds, cadmium in tissues is generally higher in adults than in juveniles, higher in winter than in other seasons, positively correlated with tissue copper burdens, and positively correlated with selective consumption of seeds of the willow (*Salix* sp., known to have a high level of cadmium) and insects living on the willow (Hogstad 1996). However, cadmium concentrations in kidneys of canvasback ducks (*Aythya valisineria*) foraging on the submerged plant *Vallisneria americana* do not seem to reflect dietary cadmium intake (Lovvorn and Gillingham 1996). Cadmium and other metals also tend to concentrate in feathers, and molting frequency is important in the depuration process (Pilstro et al. 1993). Most birds molt their body feathers once a year, but some — such as Franklin's gulls (*Larus pipixcan*) — molt twice. Therefore, they have a greater opportunity than other birds to rid the body of contaminants (Burger and Gochfeld 1996).

The relationship between reported tissue cadmium concentrations of “unstressed” populations and hazard to the organism or its consumer is not well documented. For example, cadmium in eggs of successful nests of Cooper’s hawks (*Accipiter cooperii*) collected in Arizona and New Mexico ranged from 0.015 to 0.24 mg/kg fresh weight (FW); concentrations were higher in eggs from unsuccessful nests (Snyder et al. 1973). Cadmium concentrations in the livers of breeding birds were higher in two declining colonies of puffins in St. Kilda and Clo Mor (12.9 to 22.3 mg/kg DW) than in colonies of puffins from other areas, or in livers of other seabirds examined (Parslow et al. 1972). However, the link to cadmium requires elucidation. Among marine teleosts, whole-body levels exceeding 5 mg/kg FW or 86 mg/kg ash weight (AW) in laboratory-stressed fish suggested that death would follow within 4 weeks (Eisler 1971). Marine bivalve molluscs occasionally contain more than 13 mg Cd/kg soft parts FW ([Table 1.2](#)), a level considered acutely toxic to humans (Zaroogian and Cheer 1976). However, many species of marine and terrestrial mammals frequently contained more than 20 mg Cd/kg FW in various tissues without apparent adverse effects to the organism ([Table 1.2](#); Taylor et al. 1989; Gamberg and Scheuhammer 1994). The significance of cadmium residues to organism health is further developed later.

In terrestrial mammals, cadmium tends to accumulate with increasing age in kidneys and livers of hares (Venalainen et al. 1996), moles and shrews (Talmage and Walton 1991), deer (Musante et al. 1993), and caribou (*Rangifer tarandus*) and muskox (*Ovibos moschatus*; Gamberg and Scheuhammer 1994). Concentration of cadmium in the kidneys of deer increased from <0.002 mg/kg DW at age zero to 10.5 at age 7 in males; in females, these values were 6.5 mg/kg DW at age 3, 12.5 at age 7, and 20 to 40 at age 8 (Musante et al. 1993). Cadmium concentrations were positively correlated with age in kidneys of caribou and muskox collected from the Canadian Yukon and Northwest Territories between 1985 and 1990. The highest cadmium concentration measured, 166 mg/kg DW, was in renal tissue of a 15-year-old caribou. Caribou diets rely heavily on lichens which accumulate cadmium to a greater extent than do sedges (muskox diet; Gamberg and Scheuhammer 1994). The mean kidney concentration of 467 mg Cd/kg DW of beavers from a cadmium-contaminated estuary in Germany is the greatest reported in free-ranging herbivores (Nolet et al. 1994).

Table 1.2 Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
MARINE		
Algae and Macrophytes		
Brown alga, <i>Ascophyllum nodosum</i> ; whole Norway locations		
Sorfjorden	6.0–15.0 DW	1
Eikhamrane	3.5–7.7 DW	2
Flak	<1.0 DW	2
Transferred from Eikhamrane to Flak, 120 days	<1.0–4.0 DW	2
Lofoten	<0.7 DW	3
Trondheimsfjord	<0.7–1.0 DW	3
Hardangerfjord	0.7–16.0 DW	3
United Kingdom locations		
Menai Straits	1.8 DW	4
Dulas Bay	1.5 DW	4
Bladder wrack, <i>Fucus vesiculosus</i> ; whole		
Sorfjorden, Norway	8.6–10.6 DW	1
Tamar estuary, U.K.	1.8–9.0 DW	5
Menai Straits, U.K.	2.1 DW	4
Dulas Bay, U.K.	1.8 DW	4
Irish Sea	1.4 DW	6
Severn estuary, U.K.	220.0 DW	7
Algae, <i>Ulva rigida</i> ; Venice, Italy; 1991–93	0.03–0.59 DW	65
Algae, <i>Ulva</i> spp.		
Goa, India	Max. 18.0 DW	65
Lebanon	Max. 2.3 DW	65
Hong Kong	Max. 0.7 DW	65
Black Sea	Max. 2.2 DW	65
Molluscs		
Sydney rock oyster, <i>Crassostrea commercialis</i>		
Soft parts	0.4–18.6 FW	8
Soft parts	0.1–1.0 FW	9
Pacific oyster, <i>Crassostrea gigas</i>		
Soft parts	0.2–2.1 FW	10, 11
Soft parts	0.0–30.7 FW	8
Soft parts	3.7–9.0 DW	12
Red abalone, <i>Haliotis rufescens</i>		
Gill	4.0–10.0 DW	13
Mantle	2.8–12.8 DW	13
Digestive gland	183–1163 DW	13
Foot	0.2–0.5 DW	13
Periwinkle, <i>Littorina littorea</i>		
Soft parts	0.9–1.5 DW	14
Soft parts	0.0–0.5 FW	15
Soft parts	210.0 DW	7
Squid, <i>Ommastrephes bartrami</i>		
Liver	81–782 DW	16, 17
Muscle	0.7 DW	16, 17
Gonad	0.4 DW	16, 17

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Common mussel, <i>Mytilus edulis</i> ; soft parts		
U.S. West Coast	2.3–10.5 DW	18
U.S. East Coast	0.6–6.2 DW	18
Port Phillip Bay, Australia	0.2–1.3 FW	19
Western Port Bay, Australia	Max. 18.2 FW	19
Scottish waters	0.1–2.0 FW	15
Looe estuary, U.K.	0.8–2.6 DW	20
Tasmania	5.5 FW	21
Corio Bay, Australia	2.0–63.0 DW	22
Mussel, <i>Mytilus edulis planulatus</i> ; soft parts		
Mean dry weight		
0.09 g	0.6 DW	23
0.39 g	0.8 DW	23
0.48 g	1.1 DW	23
0.69 g	1.3 DW	23
Scallop, <i>Pecten maximum</i>		
Soft parts	13.0–32.5 DW	24, 25
Muscle	1.9 DW	24
Gut and digestive gland	96.0 DW	24
Mantle and gills	3.2–17.0 DW	24
Gonad	2.5 DW	24
Shell	0.0 DW	24
Kidney	54–79 DW	25, 26
Kidney concretion	546.6 DW	27
Digestive gland	321.0 DW	25
Edible tissues	5.1–23.0 FW	15
Giant scallop, <i>Placopecten magellanicus</i>		
Muscle		
March	Max. 8.8 DW	28
Rest of year	<3.7 DW	28
Viscera		
March	104.1 DW max.	28
August	121.2 DW max.	28
February	161.8 DW max.	28
June	105.3 DW max.	28
Gonad	0.5–3.2 FW	29
Visceral mass	3.7–27.0 FW	29
Clam, <i>Scrobicula plana</i> ; digestive gland		
Gannel estuary, U.K.	39.8 DW	30
Camel estuary, U.K.	1.7 DW	30
Transferred from Camel to Gannel estuary for 352 days	5.6 DW	30
Transferred from Gannel to Camel estuary for 352 days	21.0 DW	30
Whelk, <i>Thais lapillus</i> ; soft parts	425.0 DW	7
Crustaceans		
Rock crab, <i>Cancer irroratus</i>		
Muscle	0.1–1.0 FW	31
Digestive gland	1.1–4.8 FW	31
Gills	0.7–2.7 FW	31
Brown shrimp, <i>Penaeus</i> sp.		
Muscle	0.2 DW	32
Exoskeleton	0.5 DW	32
Viscera	2.6 DW	32
Whole	<0.4 DW	33

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
American lobster, <i>Homarus americanus</i>		
Whole	0.5 FW; 5.3 AW	34
Meats	0.2 FW; 10 AW	34
Exoskeleton	0.6 FW; 4.1 AW	34
Gill	0.5 FW; 17 AW	34
Viscera	1.2 FW; 34 AW	34
Prawn, <i>Pandalus montagui</i>		
Tail	0.0 DW	35
Egg	0.1 DW	35
Carcass	0.3 DW	35
Hepatopancreas	6.4 DW	35
Whole	0.5 DW	35
Spiny lobster, <i>Panulirus interruptus</i>		
Muscle	0.3 FW	36
Hepatopancreas	5.6–29.3 FW	36
Grass shrimp, <i>Palaemonetes pugio</i> ; whole	1.4–6.2 DW	37
Annelids		
Marine worm, <i>Nephtys hombergi</i> ; whole; March vs. October	9 FW vs. 89 FW	38
Sandworm, <i>Nereis diversicolor</i> ; whole	0.1–3.6 DW	20, 30
Echinoderms		
Asteroid, <i>Echinus esculentus</i>		
Intestines	8.9 DW	39
Remaining tissues	<0.7 DW	39
Fishes		
Flounder, <i>Platichthys flesus</i> ; whole		
Barnstaple Bay, U.K.		
Age II	1.1 DW	40
Age III	1.4 DW	40
Age IV	1.6 DW	40
Age V	1.7 DW	40
Oldbury on Severn, U.K. (metals-contaminated area)		
Age II	4.0 DW	40
Age III	4.5 DW	40
Age IV	5.1 DW	40
Age V	5.2 DW	40
Yellowtail flounder, <i>Limanda limanda</i>		
Liver	0.4 DW	41
Skin	0.2 DW	41
Otoliths	0.2 DW	41
Gills	0.2 DW	41
Fin	0.2 DW	41
Muscle	0.1 DW	41
Backbone	0.05 DW	41
Blue marlin, <i>Makaira indica</i>		
Muscle	0.1–0.4 FW	9
Liver	0.2–83.0 FW	9
Striped bass, <i>Morone saxatilis</i>		
Muscle	0.03 FW	42
Liver	0.3 FW	42

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Atlantic cod, <i>Gadus morrhua</i>		
Roe	0.0–0.5 DW	43
Muscle	0.02 DW	44
Gonad	0.0–0.07 DW	44
Liver	0.09 DW	44
Bluefish, <i>Pomatomus saltatrix</i>		
Muscle	Max. 0.08 FW	45
Shorthorn sculpin, <i>Myoxocephalus scorpius</i>		
Muscle	1.4 DW	46
Liver	4.1 DW	46
Birds		
Adelie penguin, <i>Pygoscelis adeliae</i>		
Liver	90.0 DW	47
Lesser scaup, <i>Aythya affinis</i>		
Liver	0.6 FW	48
Kidney	2.3 FW	48
Dunlin, <i>Calidris alpina</i> ; 1979–82; Bristol Channel, England; kidneys; 5 sites		
Adult males	Usually <1.3 DW; Max. 13–60 DW	74
Adult females	Usually <1.3 DW; Max. 4–61 DW	74
Juveniles	Usually <0.8 DW; Max. 2–11 DW	74
Dunlin diet		
Annelid worms	2.4–24.5 DW	74
Clams	1.8–4.5 DW	74
New York Bight, 5 species, 1989		
Eggs	Max. 0.02 DW	73
Feathers, fledgling	0.03–0.57 DW	73
New Zealand estuaries, 5 spp.		
Liver	0.1–1.5 FW	49
Kidney	0.1–14.8 FW	49
Corpus Christi, Texas, 7 spp.		
Kidney	0.4–22.7 FW	50
Puffins, 2 spp. St. Kilda, Scotland		
Males		
Liver	14.6–29.4 DW	51
Kidney	67.0–133.0 DW	51
Females		
Liver	14.1–39.9 DW	51
Kidney	75.1–231.0 DW	51
Laughing gull, <i>Larus atricilla</i>		
Downy young		
Kidney	0.5 FW	52
Other tissues	<0.05 FW	52
Adults		
Muscle	0.1 FW	52
Heart	0.1 FW	52
Brain	0.5 FW	52
Bone	0.4 FW	52
Liver	0.6 FW	52
Kidney	5.0 FW	52

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Franklin's gull, <i>Larus pipixcan</i> ; Minnesota; 1994		
Breast feathers	0.5–0.6 DW	75
Eggs	0.04 DW	75
Diet (earthworms)	0.4 DW	75
Kittiwake, <i>Rissa tridactyla</i> ; nestlings; North Sea; 1992–94; age 1 day vs. age 21–40 days		
Feather	0.02 DW vs. 0.03 DW	91
Kidney	0.02 DW vs. 0.12 DW	91
Liver	0.01 DW vs. 0.03 DW	91
Common eider, <i>Somateria mollissima</i>		
Egg	1.0 DW	53
Muscle	2.0 DW	53
Liver	13.0 DW	53
Kidney	25.0 DW	53
Brown pelican, <i>Pelecanus occidentalis</i>		
Florida		
Liver	1.3–2.4 FW	54
Muscle	0.2–0.3 FW	54
California		
Liver	0.6–13.6 FW	54
Muscle	0.2–0.4 FW	54
Seabirds; liver	Usually 5–35 FW	89
Seabirds		
Liver, 11 species	8–71 DW	95
3 species, maximum values		
Brain, fat, bone, feather	<2 DW	95
Stomach, muscle, skin, eyeball, esophagus, trachea	2–10 DW	95
Intestine, liver, pancreas, spleen, gallbladder, gonad	23–39 DW	95
Kidney	180 DW	95
Common tern, <i>Sterna hirundo</i>		
Liver	3.8 FW	54
Kidney	21.3 FW	54
Mammals		
Northern fur seal, <i>Callorhinus ursinus</i>		
Kidney	0.1–15.6 FW	55
Liver	0.5–4.6 FW	55
Pilot whale, <i>Globicephala macrorhynchus</i>		
Blubber	0.4–0.8 FW	56
Liver	11.3–19.0 FW	56
Kidney	27.1–41.8 FW	56
Pilot whale, <i>Globicephala melas</i> ; Faroe Islands; 1986		
Erythrocytes	(0.8–699) FW	76
Kidney	86 (2–194) FW	76
Liver	77 (2–167) FW	76
Plasma	(0.6–238) FW	76
Marine mammals; 13 species; liver	Usually <8 FW; (not detectable –35) FW	77
Pacific walrus, <i>Odobenus rosmarus divergens</i>		
1981–84		
Kidney	46.5 FW; Max 99 FW	79
Liver	9.5 FW; Max. 50 FW	79
1991; Spring; Alaska; Bering Sea; diet		
Clam, <i>Mya</i> sp.	6.8 DW	78
Other food items	0.7–2.7 DW	78

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Baikal seal, <i>Phoca sibirica</i> ; Siberia; 1992; Immatures vs. adults		
Kidney	0.6 FW vs. 2.4 FW	96
Liver	0.07 FW vs. 0.35 FW	96
California sea lion, <i>Zalophus californianus</i>		
Liver	2.0–2.6 FW	57
Kidney	10.2 FW	57
Cerebellum	0.6 FW	57
Other tissues	<0.2 FW	57
Sea otter, <i>Enhydra lutris</i>		
Kidney	89.0–300.0 DW	54
Walrus, <i>Odobenus rosmarus divergens</i>		
Kidney	51.6 FW	54
Liver	7.7 FW	54
Muscle	0.3–0.7 FW	54
FRESHWATER		
Macrophytes		
Water lily, <i>Nuphar luteum</i>		
Whole	0.5–1.8 DW	54
Pondweed, <i>Potamogeton richardsoni</i>		
Leaf and stem	0.6–4.9 DW	54
Root	1.3–6.7 DW	54
Molluscs		
Clams, Illinois River		
Soft parts, 3 spp.	0.2–1.4 FW	58
Crustaceans		
Isopods, various species; the Netherlands		
1986, whole	Max. 0.21 DW	66
1987–89, whole	Max. 12.0 DW	66
River Dommel, 1987–89; contaminated (0.1–18 mg Cd/L)		
Hindgut	119 DW	66
Hepatopancreas	253 DW	66
Head, exoskeleton	3–6 DW	66
Annelids		
Whole, Illinois River	0.5–3.2 FW	58
Fish		
United States, Nationwide, 1976–1977; whole	0.07 FW (0.01–1.0)	59
Upper Clark Fork River, western Montana		
Muscle, 3 spp.	0.2–0.6 FW	58
Liver, 7 spp.	0.3–0.8 FW	58
Great Lakes		
Whole, 3 spp.	0.0–0.14 FW	58
Liver, 10 spp.	0.1–1.4 FW	58
Illinois River		
Whole, 10 spp.	<0.08 FW	58

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
New York State, various locations; whole		
Adirondacks region	0.02–0.05 FW	60
Hudson River	up to 0.14 FW	60
47 other areas	<0.02 FW	60
Spain, northern rivers; (Max. water 0.6 µg Cd/L; max. sediments 0.3 mg/kg DW); 2 species; adults; liver		
European eel, <i>Anguilla anguilla</i>	Max. 2.45 FW	67
Brown trout, <i>Salmo trutta</i>	Max. 2.05 FW	67
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Alaska; whole	<0.07 FW	54
Arizona; whole	<0.05 FW	54
White crappie, <i>Pomoxis annularis</i>		
Whole	0.0–0.3 FW	54
Sauger, <i>Stizostedion canadense</i>		
Whole	<0.05 FW	54
Walleye, <i>Stizostedion vitreum vitreum</i>		
Liver	0.2 FW	54
Whole	Max. 0.16 FW	54
Amphibians		
Bullfrog, <i>Rana catesbeiana</i> ; tadpoles; South Carolina; 1997		
With digestive tract		
Body	0.4 DW; 0.08 FW	93
Tail	0.2 DW; 0.03 FW	93
Whole	0.33 DW; 0.07 FW	93
Without digestive tract		
Body without gut	0.5 DW	93
Digestive tract	1.4 DW	93
Tail	0.1 DW	93
Whole	0.3 DW	93
Birds		
Waders and waterfowl that eat molluscs; liver	Usually 1–5 FW	89
Kenya; Lake Nakuru; 1990		
White pelican, <i>Pelecanus onocrotalus</i>		
Kidney	1.0 (0.1–2.4) FW	94
Liver	0.2 (0.1–0.5) FW	94
White-necked cormorant, <i>Phalacrocorax carbo</i> ; liver vs. kidney	0.05 FW vs. 0.25 FW	94
Lesser flamingo, <i>Phoeniconaias minor</i>		
Liver	0.35 FW	94
Kidney	1.3 (0.5–2.1) FW	94
TERRESTRIAL		
Plants		
Lettuce, <i>Lactuca sativa</i> , whole		
Cd in soil, mg/kg		
<2.5	2.8 DW	54
2.5	11.5 DW	54
10.0	27.1 DW	54

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Southern Norway; birch forest ecosystem		
Trees, leaves		
Birch, <i>Betula</i> sp.	0.28 DW	97
Mountain ash, <i>Sorbus aucuparia</i>	0.03 DW	97
Aspen, <i>Populus</i> sp.	1.53 DW	97
Grasses and sedges; shoots; 5 species	0.03–1.25	97
Soybean, <i>Glycine max</i> , plant top		
Cd in soil, mg/kg		
10	13.0 DW	54
50	24.0 DW	54
100	26.0 DW	54
Tobacco, <i>Nicotiana tabacum</i>	2.0 DW	54
Wheat, <i>Triticum aestivum</i> , grain		
Tons sewage sludge/hectare		
6.5	119.0 DW	54
58.0	257.0 DW	54
Control	<0.15 DW	54
Annelids		
Earthworms, whole, 4 spp.		
Distance from highway, meters		
3	12.6 DW	61
6.1	8.8 DW	61
12.2	8.3 DW	61
24.4	6.9 DW	61
48.8	7.1 DW	61
Control	3.0 DW	61
Birds		
Wood duck, <i>Aix sponsa</i> ; northern Idaho; 1986–87; kidneys; reference site vs. near mining and smelting complex		
	0.13 (0.1–1.0) FW vs. 4.8 (1–20) FW	68
Birds		
Idaho; 1987; kidneys		
Waterfowl	Max. 7.5 FW	69
Passerines	Max. 1.1 FW	69
Norway; 1992–95; liver; 5 spp.		
Juveniles	0.7 DW	70
Adults	1.3 DW	70
Spain; 32 species; 1993		
Brain		
Adults	Max. 0.36 FW	71
Immatures	Max. 0.05 FW	71
Nestlings	Max. 0.04 FW	71
Kidney		
Adults	0.2 FW; Max 18.2 FW	71
Immatures	0.15 FW; Max. 0.5 FW	71
Nestlings	0.2 FW; Max. 0.65 FW	71
Liver		
Adults	0.1 FW; Max. 2.9 FW	71
Immatures	0.06 FW; Max. 0.4 FW	71
Nestlings	0.07 FW; Max. 0.65 FW	71
Willow ptarmigan, <i>Lagopus lagopus</i> ; Norway; 1988–89		
Liver		
Age 2–3 months	0.1 FW	72
Age 10–23 months	2.1–5.2 FW	72

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Kidney		
Age 2–3 months	0.4 FW	72
Age 10–23 months	21.1–22.7 FW	72
Passerines and raptors; liver	Usually <1 FW	89
Ring-necked pheasant, <i>Phasianus colchicus</i>		
Liver	0.9 FW	54
Kidney	7.4 FW	54
American robin, <i>Turdus migratorius</i>		
Kidney	2.0 FW	54
Liver	0.6 FW	54
European starling, <i>Sturnus vulgaris</i>		
Whole, various U.S. locations		
Bakersfield, CA	0.24 FW	62
Lansing, MI	0.12 FW	62
Elkins, WV	0.12 FW	62
Farmington, NM	0.12 FW	62
Phoenix, AZ	0.11 FW	62
Other U.S. areas	<0.05 FW	62
Cooper's hawk, <i>Accipiter cooperii</i>		
Egg	0.12 (0.015–0.24 FW)	63
Mammals		
Moose, <i>Alces alces</i> ; New Hampshire; 1987		
Kidney	3.2–20.0 FW	80
Liver	0.6–9.1 FW	80
Short-tailed shrew, <i>Blarina brevicauda</i>		
Liver	1.3 FW	54
Whole	0.4 FW	54
Cow, <i>Bos bovis</i>		
Distance from smelter		
Liver		
0.8 km	0.9 FW	54
72.4 km	0.3 FW	54
Kidney		
0.8 km	3.7 FW	54
72.4 km	1.4 FW	54
Coyote, <i>Canis latrans</i>		
Kidney	0.4 FW	54
European beaver, <i>Castor fiber</i> ; Germany; from cadmium-contaminated estuary		
Diet	6.9 DW	81
Hair	0.14 DW (vs. 0.025 DW from reference site)	81
Kidney	55 DW	81
Elk, <i>Cervus</i> sp.		
Liver	1.5 DW	54
Kidney	8.1 DW	54
Muscle	0.6 DW	54
Porcupine, <i>Erethizon dorsatum</i>		
Heart	0.4 FW	54
Human, <i>Homo sapiens</i>		
Blood		
Nonsmokers	Max. 0.001 FW	82
Smokers	Max. 0.01 FW	82
Occupationally-exposed	Max. 0.05 FW	82
Acceptable	<0.01 FW	82

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Urine		
Acceptable vs. substantial exposure ($\mu\text{g Cd/g}$ creatinine)	<2 FW vs. 50 FW	82
European hare, <i>Lepus europeaeus</i> ; Finland; 1980–82 vs. 1992–93		
Industrial site		
Kidney	3.8 FW vs. 1.9 FW	83
Liver	0.3 FW vs. 0.2 FW	83
Muscle	0.008 FW vs. 0.003 FW	83
Reference site		
Kidney	1.5 FW vs. 0.6 FW	83
Liver	0.2 FW vs. 0.06 FW	83
Muscle	0.003 FW vs. 0.001 FW	83
Mountain hare, <i>Lepus timidus</i> ; Finland; 1980–82 vs. 1992–93		
Industrial site		
Kidney	11.1 FW vs. 10.7 FW	83
Liver	0.5 FW vs. 0.45 FW	83
Muscle	0.01 FW vs. 0.006 FW	83
Reference site		
Kidney	4.6 FW vs. 3.7 FW	83
Liver	0.4 FW vs. 0.2 FW	83
Muscle	0.01 FW vs. 0.005 FW	83
Meadow vole, <i>Microtus pennsylvanicus</i> ; Collected from fields near Oxford, Ohio, receiving sewage sludge for 4 years at yearly rate of 8960 kg sludge/ha		
Liver		
Adult males	0.8 FW	64
Adult females	3.1 FW	64
Subadult males	1.2 FW	64
Subadult females	1.1 FW	64
Kidney		
Adult males	6.3 FW	64
Adult females	19.1 FW	64
Subadult males	3.5 FW	64
Subadult females	6.2 FW	64
From control fields		
Liver		
Adult males	0.7 FW	64
Adult females	0.1 FW	64
Subadult males	0.1 FW	64
Subadult females	0.1 FW	64
Kidney		
Adult males	0.3 FW	64
Adult females	1.1 FW	64
Subadult males	0.3 FW	64
Subadult females	0.3 FW	64
Bats, <i>Myotis</i> spp.; near battery salvage plant; Florida; 1981–83		
Kidney	0.6 FW; Max. 2.9 FW	84
Liver	0.4 FW; Max. 0.85 FW	84
Guano	1.9–2.3 DW vs. 0.3 DW from reference site in Maryland	84
White-tailed deer, <i>Odocoileus virginianus</i>		
Kidney	0.7–11.7 FW	54
Muscle	0.0–0.3 FW	54
Liver	0.0–0.7 FW	54

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Deer mice, <i>Peromyscus maniculatus</i> ; Vancouver Island, British Columbia; near abandoned mine vs. reference site; 1994		
Soil	5.6 DW vs. 0.7 DW	87
Diet	2.7 DW vs. 0.8–1.1 DW	87
Bone	0.6 DW vs. 0.3–0.6 DW	87
Kidney	0.4 DW vs. 0.10.2 DW	87
Liver	0.7 DW vs. 0.2–0.4 DW	87
Reindeer, <i>Rangifer tarandus fennica</i> ; northwestern Russia; 1986–90		
Antlers	1.5 (0.8–4.6) DW	85
Bone	2.1 (0.5–6.2) DW	85
Teeth	1.9 (0.6–4.8) DW	85
Gray squirrel, <i>Sciurus carolinensis</i> ; kidney		
Urban area	15.9 FW	54
Rural	2.0–4.6 FW	54
Red squirrel, <i>Sciurus hudsonicus</i>		
Kidney	7.8–17.4 FW	54
Liver	0.7–2.0 FW	54
Eastern cottontail, <i>Sylvilagus floridanus</i>		
Liver	Max. 2.1 FW	54
Kidney	Max. 13.5 FW	54
Muscle	Max. 0.5 FW	54
Mexican free-tailed bat, <i>Tadarida brasiliensis</i> ; 1991; liver		
New Mexico; May vs. August		
Females	0.5 (0.2–1.3) FW vs. 0.8 (0.5–1.6) FW	86
Males	0.4 (0.3–0.7) FW vs. 0.9 (0.5–1.5) FW	86
Oklahoma; May vs. August		
Females	0.9 (0.5–1.5) FW vs. 1.2 (0.6–2.0) FW	86
Males	0.4 (Max. 1.0) FW vs. 0.2 (Max. 0.22) FW	86

INTEGRATED STUDIES

England; near copper-cadmium refinery vs. reference site		
Soil	15 DW vs. 1 DW	88
Creeping bent grass, <i>Agrostis stolonifera</i> , senescent leaf	10 DW vs. 1 DW	88
Earthworms, whole	107 DW vs. 15 DW	88
Wood lice, whole	231 DW vs. 15 DW	88
Spiders, whole	102 DW vs. 3 DW	88
Beetles, whole	15 DW vs. 1 DW	88
Field vole, <i>Microtus agrestis</i> ; kidney	89 DW vs. 2 DW	88
Common shrew, <i>Sorex araneus</i> ; kidney	253 DW vs. 21 DW	88
Greenland; 1975–91; marine animals		
Bivalve molluscs; 5 species; soft parts	0.4–3.3 FW	90
Crustaceans; 6 species; whole	<0.2–4.6 FW	90
Fishes; 10 species		
Muscle	Max. 0.05 FW	90
Liver	0.03–2.1 FW	90
Seabirds; 10 species		
Muscle	<0.02–0.7 FW	90
Liver	0.15–12.6 FW	90
Kidney	0.3–60.5 FW	90

Table 1.2 (continued) Cadmium Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg Cd/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (mg/kg or ppm)	References ^a
Seals; 3 species		
Muscle	<0.02–0.4 FW	90
Liver	1.9–36.6 FW	90
Kidney	9–110 FW	90
Whales; 4 species		
Muscle	Max. 0.1 FW	90
Liver	0.04–14.2 FW	90
Kidney	3–54 FW	90
Polar bear		
Kidney	Max. 18.6 FW	90
Liver	Max. 1.7 FW	90
Muscle	Max. 0.02 FW	90
Poland, 1993–96		
Soils		
Near Zn–Pb smelter	Max. 143 DW	98
Urban areas	Max. 10 DW	98
Agricultural		
Sandy	0.22 DW	98
Loamy	0.43 DW	98
Crop plants		
Cereal grains	0.06 DW	98
Potato tubers	0.11 DW	98
Grasses	0.12 DW	98
Taiwan, 1995–96		
Fish; 8 species; muscle	0.01–0.13 DW; Max. 0.46 DW	92
Shrimp; 2 species; muscle	0.05–0.14 DW	92
Pacific oyster, <i>Crassostrea gigas</i> ; soft parts	0.8 (0.2–2.9) DW	92

^a 1, Melhuus et al. 1978; 2, Myklestad et al. 1978; 3, Haug et al. 1974; 4, Foster 1976; 5, Bryan and Uysal 1978; 6, Preston et al. 1972; 7, Butterworth et al. 1972; 8, Ratkovsky et al. 1974; 9, Mackay et al. 1975; 10, Pringle et al. 1968; 11, Kopfler and Mayer 1967; 12, Watling and Watling 1976; 13, Anderlini 1974; 14, Leatherland and Burton 1974; 15, Topping 1973; 16, Martin and Flegal 1975; 17, Hamanaka et al. 1977; 18, Goldberg 1978; 19, Phillips 1976; 20, Bryan and Hummerstone 1973; 21, Eustace 1974; 22, Talbot et al. 1976; 23, Harris et al. 1979; 24, Segar et al. 1971; 25, Bryan 1973; 26, George et al. 1980; 27, Carmichael et al. 1979; 28, Reynolds 1979; 29, Greig et al. 1978; 30, Bryan and Hummerstone 1978; 31, Greig et al. 1977; 32, Horowitz and Presley 1976; 33, Sims and Presley 1976; 34, Eisler et al. 1972; 35, Ray et al. 1980; 36, Vattuone et al. 1976; 37, Pesch and Stewart 1980; 38, Rosenberg 1977; 39, Riley and Segar 1970; 40, Hardisty et al. 1974; 41, Westernhagen et al. 1980; 42, Heit 1979; 43, Julshamn and Braekkan 1978; 44, Julshamn and Braekkan 1975; 45, Bebbington et al. 1977; 46, Bohn and Fallis 1978; 47, Robertson et al. 1972; 48, White et al. 1979; 49, Turner et al. 1978; 50, White et al. 1980; 51, Bull et al. 1977; 52, Hulse et al. 1980; 53, Lande 1977; 54, Jenkins 1980; 55, Anas 1974; 56, Stoneburner 1978; 57, Buhler et al. 1975; 58, Hammon et al. 1978; 59, May and McKinney 1981; 60, Lovett et al. 1972; 61, Gish and Christensen 1973; 62, Martin and Nickerson 1973; 63, Snyder et al. 1973; 64, Maly and Barrett 1984; 65, Favero et al. 1996; 66, van Hattum et al. 1996; 67, Linde et al. 1996; 68, Blus et al. 1993; 69, Blus et al. 1995; 70, Hogstad, 1996; 71, Garcia-Fernandez et al. 1996; 72, Pedersen and Myklebust 1993; 73, Burger and Gochfeld 1993; 74, Ferns and Anderson 1994; 75, Burger and Gochfeld 1996; 76, Caurant and Amiard-Triquet 1995; 77, Mackay et al. 1996; 78, Miles and Hills 1994; 79, Taylor et al. 1989; 80, K.M. Klein, personal communication, 1988; 81, Nolet et al. 1994; 82, USPHS 1993; 83, Venalainen et al. 1996; 84, Clark et al. 1986; 85, Medveder 1995; 86, Thies and Gregory 1994; 87, Laurinolli and Bendell-Young 1996; 88, Cooke and Johnson 1996; 89, Furness 1996; 90, Dietz et al. 1996; 91, Wenzel et al. 1996; 92, Han et al. 1998; 93, Burger and Snodgrass 1998; 94, Kairu 1996; 95, Kim et al. 1998; 96, Watanabe et al. 1998; 97, Brekken and Steinnes 1999; 98, Kabata-Dendias and Stuczynski 1999.

1.4 LETHAL EFFECTS

The lethal effects of cadmium are thought to be caused by free cadmium ions, that is, cadmium not bound to metallothioneins or other proteins. Free cadmium ions may inactivate various metal-dependent enzymes; however, cadmium not bound to metallothionein may have the capacity to directly damage renal tubular membranes during uptake (USPHS 1993).

A substantial toxicological database for cadmium and freshwater biota demonstrates that ambient cadmium water concentrations exceeding 10 µg/L are associated with high mortality, reduced growth, inhibited reproduction, and other adverse effects. Inasmuch as one recommended drinking water criterion for human health protection is 10 µg Cd/L (USEPA 1980), it is noteworthy that several species of freshwater aquatic insects, crustaceans, and teleosts exhibited significant mortality at cadmium concentrations of 0.8 to 9.9 µg/L during exposures of 4 to 33 days. Mortality generally increased as exposure time increased, water hardness decreased, and organism age decreased (Table 1.3). Daphnids (*Daphnia magna*), for example, were more resistant to the biocidal properties of cadmium under conditions of increasing concentrations of dissolved organic materials and water hardness, especially Ca²⁺ (Penttinen et al. 1998). Prior exposure to elevated sublethal concentrations of waterborne cadmium protects a minnow (*Phoxinus phoxinus*) against subsequent exposure to a lethal waterborne dose of cadmium; this phenomenon was associated with reduced uptake of ¹⁰⁹Cd into the gills of a minnow when this species was challenged with a lethal dose of waterborne cadmium (Glynn and Olsson 1991). In the case of larval toads (*Bufo arenarum*) and northwestern salamanders (*Ambystoma gracile*), adverse effects on survival were documented at 250 to 468 µg Cd/L, with mortality greatest at elevated temperatures and early developmental stages (Ferrari et al. 1993; Herkovits and Coll 1993; Nebeker et al. 1994, 1995; Perez-Coll and Herkovits 1996).

Resistance to cadmium is higher in marine than in freshwater organisms and survival usually is higher at the lower temperatures and higher salinities for any given level of cadmium in the medium (Eisler 1985). Cadmium was fatal to 50% of nauplii of copepods (*Eurytemora affinis*) at 51 µg/L and 5 ppt salinity, and 83 to 213 µg/L at higher salinities. A similar pattern was evident for larvae of the sheepshead minnow (*Cyprinodon variegatus*); the free ion (Cd²⁺) accounted for 20% of total cadmium at 5 ppt, 8% at 15 ppt, and 4.5% at 25 ppt salinity (Hall et al. 1995). Decapod crustaceans are also sensitive in short-term tests; LC50 (96 h) values ranged from 320 to 420 µg/L for the grass shrimp (*Palaemonetes vulgaris*), the hermit crab (*Pagurus longicarpus*), and the sand shrimp (*Crangon crangon*) (Eisler 1971). Studies of longer duration demonstrated that survival of shrimp groups was low at >250 µg/L during 6 weeks of exposure and that hermit crab deaths were recorded at 60 µg/L after 6 weeks, although some survivors remained at 10 weeks when the studies ended (Pesch and Stewart 1980). In another study, an LC50 range of 14.8 to 19.5 µg Cd/L was reported for two species of mysid shrimp subjected to “lifetime” (i.e., 23 to 27 days) exposure to cadmium salts (Gentile et al. 1982). Studies with *Leptocheirus plumulosus*, an estuarine amphipod, showed that gravid females were more resistant than males or mature females to the biocidal properties of aqueous Cd²⁺; juveniles were more sensitive than adults; sensitivity was greatest among starved animals and immediately after molting; and field-collected animals were more sensitive to dissolved cadmium than laboratory animals, regardless of season of collection (McGee et al. 1998).

Birds are comparatively resistant to the biocidal properties of cadmium. Adult drake mallards (*Anas platyrhynchos*) fed up to 200 mg cadmium per kg diet for 90 days all survived with no loss of body weight (White and Finley 1978). Laying hens fed 200 mg Cd/kg diet also survived; egg production was suppressed at that concentration but not at lower concentrations (White and Finley 1978). Marine and terrestrial animals, including ducks, have been shown to be particularly abundant in a wildlife community associated with a marine sewer outfall (Brown et al. 1977). These animals were contaminated with high levels of cadmium, as well as zinc and copper, but were apparently protected from the deleterious effects of high metal body burdens by metallothioneins. Amounts

Table 1.3 Lethal Concentrations (LC) of Cadmium to Freshwater Biota during Various Exposure Intervals
 (Concentrations shown are in µg Cd/L (ppb) of medium fatal to 10% or 50% of test organisms)

Group, Taxon, or Life State	Water Hardness, (mg CaCO ₃ /L)	LC Values, (µg/L)	Exposure Interval	Reference ^a
INSECTS				
<i>Ephemerella</i> sp.	44–48	LC50, <3.0	28 d	1
<i>Tanytarsus dissimilis</i>	47	LC50, 3.8	10 d	2
CLADOCERANS				
<i>Daphnia magna</i>	51	LC50, 9.9	96 h	3
<i>Daphnia magna</i>	51	LC50, 5.0	21 d	4
<i>Daphnia magna</i>	"soft"	LC50, 0.7	20 d	5
<i>Simocephalus serrulatus</i>	11	LC50, 3.5–8.6	96 h	6
FISH				
Threespine stickleback, <i>Gasterosteus aculeatus</i>	—	LC50, 0.8	33 d	7
Striped bass, <i>Morone saxatilis</i>				
Larvae	70	LC50, 1.0	96 h	8
Fingerlings	70	LC50, 2.0	96 h	8
Chinook salmon, <i>Oncorhynchus tshawytscha</i>				
Swimup	23	LC10, 1.2	200 h	9
Swimup	23	LC50, 1.8	96 h	9
Parr	23	LC10, 1.3	200 h	9
Parr	23	LC50, 3.5	96 h	9
Smolt	23	LC10, 1.5	200 h	9
Juveniles	—	LC50, 0.6–1.6	96 h	10
Coho salmon, <i>Oncorhynchus kisutch</i>				
Juveniles	22	LC50, 2.0	217 h	11
Adults	22	LC50, 3.7	215 h	11
Rainbow trout, <i>Oncorhynchus mykiss</i>				
Swimup	23	LC10, 1.0	200 h	9
Swimup	23	LC50, 1.3	96 h	9
Parr	23	LC10, 0.7	200 h	9
Parr	23	LC50, 1.0	96 h	9
Smolt	23	LC10, 0.8	200 h	9
Age 2-months	82–132	LC50, 6.6	96 h	12
Age 2-months	31	LC50, 1.8	96 h	13
Age 2-months	—	LC50, 6–7	96 h	14,15
Adult	54	LC50, 5.2	17 d	11
Adult	—	LC50, 5–7	10 d	14
Guppy, <i>Poecilia reticulata</i> ; life cycle exposure beginning with 5-day-old juvenile	—	LC50, 500	73 d	17
Brook trout, <i>Salvelinus fontinalis</i>	330–350	LC50, 5000	8 d	17
	44	LC50, 4.1	96 h	16
	44	LC50, 2.4	96 h	16
AMPHIBIANS				
Columbia spotted frog, <i>Rana luteiventris</i> ; tadpoles	—	LC50, 15,800	96 h	18
Water frog, <i>Rana ridibunda</i> ; tadpoles	—	LC10, 400,000	96 h	19

^a 1, Spehar et al. 1978; 2, Anderson et al. 1980; 3, USEPA 1980; 4, Biesinger and Christian 1972; 5, Canton and Sloof 1982; 6, Giesy et al. 1977; 7, Pascoe and Mattey 1977; 8, Hughes 1973; 9, Chapman 1978; 10, Finlayson and Verree 1982; 11, Chapman and Stevens 1978; 12, Hale 1977; 13, Davies 1976; 14, Kumada et al. 1973; 15, Kumada et al. 1980; 16, Carroll et al. 1979; 17, Miliou et al. 1998; 18, Lefcort et al. 1998; 19, Vogiatzis and Loumbourdis 1998.

of these metal-binding proteinaceous metallothioneins and heavy metal loading appear to depend primarily on the degree of pollution and secondarily on the species of animal and its position in the food web. Ducks contained the highest levels of metallothioneins of all groups examined (Brown et al. 1977).

Mammals, like birds, are comparatively resistant to cadmium. The lowest oral dose, in mg/kg body weight of cadmium (as fluoroborate) producing death, was 250 in rats (*Rattus* sp.) and 150 (as cadmium fluoride) in guinea pigs (*Cavia* sp.; USEPA 1980). Exposure to high levels of cadmium by inhalation or orally are fatal in humans and other animals (USPHS 1993). Inhalation of a lethal dose of cadmium can occur without signs of acute distress during exposure, although high oral doses of cadmium sometimes induce vomiting in humans. Cause of death is pulmonary edema after inhalation exposure, and massive fluid imbalance and widespread gastrointestinal, liver, and other organ damage after oral exposure — due mainly to the destruction of lung cell membranes (inhalation) and gastrointestinal tract membranes (oral) at the point of entry (USPHS 1993). Suicidal doses in 2 humans are reported at 25 and at 1500 mg Cd/kg BW (USPHS 1993).

1.5 SUBLETHAL EFFECTS

Studies of 30 to 60 days' duration with three comparatively sensitive species of freshwater fishes demonstrated that concentrations of >1 and <3 μg Cd/L in water of low alkalinity caused reductions in growth, survival, and fecundity of brook trout (*Salvelinus fontinalis*), the most sensitive species tested (Table 1.3). Under conditions of increasing alkalinity, the maximum allowable cadmium concentration range for brook trout increased to >7 and <12 $\mu\text{g}/\text{L}$; a similar case was made for the walleye (*Stizostedion vitreum*; Table 1.3).

Among all species of freshwater biota examined, cadmium concentrations of 0.47 to 5.0 $\mu\text{g}/\text{L}$ were associated with decreases in standing crop, decreases in growth, inhibition of reproduction, immobilization, and population alterations (Table 1.4). Juvenile rainbow trout (*Oncorhynchus mykiss*) exposed to 1 or 5 μg Cd/L for 30 days showed reductions in liver size, glycogen content, growth rate, and plasma calcium with changes attributed in part to disrupted endocrine function (Ricard et al. 1998). Cadmium interactions with other metals and compounds are significant. For example, 4 μg Zn/L or 11 μg Se/L were effective in counteracting the decrease in oxygen uptake induced by ionic cadmium in *Channa punctatus*, freshwater teleost (Sastry and Shukla 1994). There is abundant technical literature documenting numerous sublethal effects at higher concentrations of cadmium salts. However, these were excluded if the effects were observed at >10.0 $\mu\text{g}/\text{L}$, a recommended criterion for drinking water. Delayed effects of cadmium intoxication, however, need to be considered. Studies with daphnids, amphipods, and fathead minnows indicate that exposure to cadmium concentrations as low as 370 $\mu\text{g}/\text{L}$ for as little as 30 minutes caused increasing immobility for up to 172 h after exposure (Brent and Herricks 1998).

For marine organisms, ambient cadmium concentrations between 0.5 and 10.0 $\mu\text{g}/\text{L}$ resulted in decreases in growth, respiratory disruption, molt inhibition, shortened life span of F1-generation crustaceans, altered enzyme levels, and abnormal muscular contractions. Effects, in general, were more pronounced at lower salinities and higher temperatures (Table 1.5). Marine algae accumulated more cadmium at lower salinities than at higher salinities; algae bound only free cadmium ions, and these are inversely related to the concentration of the suspended particulate matter (Favero et al. 1996). Adaptation to environmental cadmium stress is reported for mussels (*Mytilopsis sallei*) exposed to high (>50 μg Cd/L) sublethal concentrations for at least 96 h. The decrease in oxygen consumption and the increased metabolism of glycogen and carbohydrates during exposure to cadmium suggest that *M. sallei* might shift to anaerobic metabolism to counter the environmental cadmium stress (Devi 1996).

One of the more sensitive indicators of cadmium exposure is the inhibition of non-thionein hepatic metal binding proteins; inhibition was observed in juvenile bluegills (*Lepomis macrochirus*)

Table 1.4 Maximum Allowable Toxicant Concentrations (MATC) of Cadmium to Sensitive Species of Freshwater Teleosts

Organism and Exposure Period (days)	Water Alkalinity, (mg CaCO ₃ /L)	MATC, (µg Cd/L)
Brook trout, <i>Salvelinus fontinalis</i>		
60	30	>1-<3
60	177	>7-<12
Channel catfish, <i>Ictalurus punctatus</i>		
60	34	>11-<17
60	172	>12-<17
Walleye, <i>Stizostedion vitreum vitreum</i>		
30	33	>9-<25
30	172	>86.7

Adapted from Brungs, W.A., R.A. Carlson, W.B. Horning II, J.H. McCormick, R.L. Spehar, and J.D. Young. 1978. Effects of pollution on freshwater fish. *Jour. Water Pollut. Control Fed.* 50:1582-1637.

at concentrations as low as 0.8 µg Cd/L (Cope et al. 1994). Cadmium at elevated concentrations (100 µg/L) significantly inhibits the Na⁺/K⁺-ATPase activity in different tissues of rat, frog, rabbit, and trout, and also sometimes at concentrations as low as 16 µg/L in the case of gill basolateral membrane vesicle of European eels (*Anguilla anguilla*). Inhibition of ATPase activities may lead to severe perturbations of osmoregulation processes, causing disturbances in migration and perhaps the survival of feral eel populations (Lemaire-Gony and Mayer-Gostan 1994). In the scorpionfish (*Scorpaena guttata*), cadmium disrupts cytosol balance and inhibits copper–zinc–superoxide dismutase activity in the intestine (Bay et al. 1990; Brown et al. 1990), with important implications for detoxification. Dose-dependent induction of liver metallothionein proteins within 24 h were observed in juvenile winter flounders (*Pleuronectes americanus*) after subcutaneous injection of high doses of cadmium (5 to 20 mg Cd/kg BW), with RNA disruption reported at the highest dose (Jessen-Eller and Crivello 1998).

Sublethal effects in birds are similar to those in other species and include growth retardation, anemia, renal effects, and testicular damage (Hammons et al. 1978; Di Giulio et al. 1984; Blus et al. 1993). However, harmful damage effects were observed at higher concentrations when compared to aquatic biota. For example, Japanese quail (*Coturnix japonica*) fed 75 mg Cd/kg diet developed bone marrow hypoplasia, anemia, and hypertrophy of both heart ventricles at 6 weeks (Richardson et al. 1974). In zinc-deficient diets, effects were especially pronounced and included all of the signs mentioned plus testicular hypoplasia. A similar pattern was evident in cadmium-stressed quail on an iron-deficient diet. In all tests, 1% ascorbic acid in the diet prevented cadmium-induced effects in Japanese quail (Richardson et al. 1974). In studies with Japanese quail at environmentally relevant concentrations of 10 µg Cd/kg BW daily (for 4 days, administered per os), absorbed cadmium was transported in blood in a form that enhanced deposition in the kidney; less than 0.7% of the total administered dose was recovered from liver plus kidneys plus duodenum (Scheuhammer 1988).

In wood ducks (*Aix sponsa*) fed rations containing 10 mg Cd/kg, no renal effects were noted even though kidneys contained 62 mg Cd/kg FW. Renal damage was noted when wood ducks were fed diets containing 100 mg Cd/kg and their kidneys contained 132 mg Cd/kg FW (Blus et al. 1993). Adult male white leghorn chickens (*Gallus* sp.) given 2 mg CdSO₄ daily by intraperitoneal injection for 15 to 22 days, or a total dose of 60 mg of cadmium per chicken, developed anemia, an enlarged heart, myocardial infarction, and other abnormalities (Sturkie 1973). Testicular damage was observed in ring doves (*Streptopelia* sp.) 20 days after intramuscular injection of 6.6 mg Cd/kg body weight (BW) (Richardson et al. 1974); in domestic pigeons (*Columba livia*), however, testicular damage was observed after a single subcutaneous injection of only 0.5 mg/kg BW (Sarker and Mondal 1973), and cardiovascular disease developed after exposure to 600.0 µg/L in drinking water (Revis et al. 1981). In mallard ducklings fed 20 mg Cd/kg ration for 12 weeks, blood chemistry

Table 1.5 Sublethal Effects of Cadmium to Selected Species of Aquatic Biota

Medium, Taxonomic Group, Organism, and Other Variables	Cd, µg/L	Exposure Period	Effect	Reference ^a
FRESHWATER				
Algae				
<i>Asterionella formosa</i>	2.0	—	Decreased growth rate	1
Mollusca				
<i>Lymnaea stagnalis</i>	25.0	7 weeks	Inhibited reproduction	28
Arthropoda				
<i>Daphnia pulex</i>	1.0	20 weeks	Reduced reproduction	2
<i>Nephrops norvegicus</i>	1–25	18 days	Adult males had dose-dependent decrease in gill Na, K-ATPase activity; adult females had dose-dependent decrease in gill Mg-ATPase activity	26
<i>Daphnia galeata mendotae</i>	4.0	22 weeks	Reduced biomass	3
<i>Eucyclops agilis</i>	5.0	52 weeks	Population reduction	4
<i>Cambarus latimanus</i>	5.0	22 weeks	Increased mortality	5
<i>Daphnia magna</i>	2.6	21 days	Immobilization threshold	6
<i>Daphnia magna</i>	0.7	21 days	Decreased reproduction (50%)	6
<i>Daphnia magna</i>	0.17	21 days	No effect	6
<i>Daphnia magna</i>	0.37	20 days	No effect	7
<i>Daphnia magna</i>	4.7	20 days	Decreased reproduction (50%)	7
<i>Asellus aquaticus</i>	20–100	96 h	Reduced predation from the turbellarian <i>Dendrocoelum lacteum</i>	20
Annelida				
<i>Pristina</i> sp.	5.0	52 weeks	Population reduction	4
Miscellaneous mixed macro-invertebrates	5.0	52 weeks	Reduction in biomass and number of taxa	4
Fish				
Common carp, <i>Cyprinus carpio</i>	22.0	21 days	Skin histopathology beginning at 24 h and continuing through day 21; no deaths	21
<i>C. carpio</i>	560.0	8 days	Skin histopathology at 1 h; all dead by day 8	21
Tilapia, <i>Oreochromis mossambica</i>	22.0	96 h	LC 50 for 3-day-old larvae; survivors had cadmium accumulation rate of 4.9 ng/larva daily	22
<i>O. mossambica</i>	83.0	96 h	LC 50 for 1-day-old larvae; cadmium accumulation rate of 2.6 ng/larva daily	22
Rainbow trout, <i>Oncorhynchus mykiss</i>	1.8–3.4	—	Eggs taken from adults exposed for 90 weeks failed to develop to the fry stage	23
<i>O. mykiss</i>	5.5	90 weeks	No effect on adult growth or survival	23
Guppy, <i>Poecilia reticulata</i>	500	30 days	Growth reduction; RNA decrease	27
Brown trout, <i>Salmo trutta</i>	9.3–29.1	—	Oogenesis delayed in eggs taken from adults exposed for 90 weeks	23
<i>S. trutta</i>	29.1	54 weeks	LC 50 for adults	23
Brook trout, <i>Salvelinus fontinalis</i>	2.0	8 weeks	Disrupted lactic dehydrogenase activity and blood glucose levels	8
Atlantic salmon, <i>Salmo salar</i>	0.47	12 weeks	Alevin growth reduction	9
<i>Salmo salar</i>	2.0	60 days	Cranial pathology, reduced growth, death	10
<i>Salmo salar</i>	0.2	60 days	Normal growth and development	10

Table 1.5 (continued) Sublethal Effects of Cadmium to Selected Species of Aquatic Biota

Medium, Taxonomic Group, Organism, and Other Variables	Cd, µg/L	Exposure Period	Effect	Reference ^a
Medaka, <i>Oryzias latipes</i>	6.0	96 h	No effect	7
Amphibians				
Northwestern salamander, <i>Ambystoma gracile</i>	13.0	10 days	Limb regeneration normal; larvae	24
<i>A. gracile</i>	45.0	10 days	Limb regeneration inhibited; larvae	24
<i>A. gracile</i>	193.0	24 days	Inhibited larval growth	25
MARINE				
Algae				
<i>Phaeodactylum tricornutum</i>	10.0–25.0	—	Decreased growth	11
<i>Skeletonema costatum</i>	10.0–25.0	—	Decreased growth	12
Mollusca				
Mussel, <i>Mytilopsis salleri</i>	50.0	96 h	No deaths	19
<i>M. salleri</i>	710.0	96 h	LC 50	19
Arthropoda				
Crab, <i>Pontoporeia affinis</i>	6.5	265 days	Reduced F1 life span	13
Fiddler crab, <i>Uca pugilator</i>	1.0	—	Reduced respiration	14
Mysid shrimp, <i>Mysidopsis</i> spp.	10.0	23–27 days	Molt inhibition	15
<i>Mysidopsis</i> spp.	5.1	23–27 days	No effect	15
Coelenterata				
<i>Laomedea loveni</i>				
Salinity 10 ppt	3.0	7 days	EC-50, irreversible polyp retraction	16
Salinity 15 ppt	5.6	7 days	As above	16
Temperature 15°C	9.0	7 days	As above	16
Temperature 17°C	5.6	7 days	As above	16
Fish				
Striped bass, <i>Morone saxatilis</i>				
Juveniles	5.0	90 days	Enzyme disruption	17
Juveniles	0.5–5.0	30 days	Decreased oxygen consumption	17
Winter flounder, <i>Pleuronectes americanus</i>	5.0	60 days	Increased gill tissue respiration	18

^a 1, Conway 1978; 2, Bertram and Hart 1979; 3, Marshall 1978; 4, Giesy et al. 1979; 5, Thorp et al. 1979; 6, Biesinger and Christian 1972; 7, Canton and Sloof 1982; 8, Christiansen et al. 1977; 9, Rombough and Garside 1982; 10, Peterson et al. 1983; 11, Cossa 1976; 12, Berland et al. 1977; 13, Sundelin et al. 1983; 14, Vernberg et al. 1974; 15, Gentile et al. 1982; 16, Theede et al. 1979; 17, Dawson et al. 1977; 18, Calabrese et al. 1975; 19, Devi 1996; 20, Ham et al. 1995; 21, Iger et al. 1994; 22, Hwang et al. 1995; 23, Brown et al. 1994; 24, Nebeker et al. 1994; 25, Nebeker et al. 1995; 26, Canli and Stagg 1996; 27, Miliou et al. 1998; 28, Gomot 1998.

was altered and mild to severe kidney lesions developed (Cain et al. 1983). But mallard juveniles were unaffected when given diets containing 50 mg Cd/kg ration for 6 weeks (Di Giulio et al. 1984). Mallard juveniles fed diets containing 150 mg Cd/kg ration and higher for 6 weeks had elevated liver (>135 mg Cd/kg DW) and kidney (>335 mg Cd/kg DW) burdens, disrupted plasma fatty acid concentrations, and increased adrenal and kidney weights (Di Giulio et al. 1984). Altered avoidance behavior in the form of hyperresponsiveness was observed in young American black ducks (*Anas rubripes*) produced from parents fed 4 mg/kg dietary cadmium for about 4 months before egg laying; this behavioral effect was observed only at comparatively low dietary cadmium levels and is considered harmful to wild birds (Heinz and Haseltine 1983). Cadmium readily reacts with sulfhydryl groups and may compete, especially with zinc, for binding sites on proteins and, thus, may inhibit a variety of enzymatic reactions. The addition of zinc, iron, ascorbic acid, calcium, or selenium to diets ameliorated the effects of cadmium damage, whereas the addition of lead or mercury exacerbated them (Hammons et al. 1978).

In male rats (*Rattus* sp.) and mice (*Mus* sp.), acute oral exposure to near-fatal doses (7 to 14 mg Cd/kg BW daily for 90 to 120 days) can cause testicular atrophy and necrosis, and decreased fertility (USPHS 1993). Oral intake of cadmium disrupts calcium metabolism of laboratory and free-living rodents (Shore et al. 1995). Bank voles (*Clethrionomys glareolus*) on low-calcium diets given diets equivalent to 1.5 to 1.7 mg Cd/kg BW daily had significantly poorer calcium net gut absorption efficiency than animals fed cadmium-free diets and were in negative calcium balance. Cadmium-mediated impairment of calcium assimilation may be important in calcium-poor habitats (Shore et al. 1995), suggesting more research in this area. Among small laboratory mammals it appears that physiologically bound cadmium is more effective than CdCl₂ in producing metabolic iron irregularities. For example, in young mice fed oysters containing 1.8 mg Cd/kg ration for 28 days, hematocrit and hemoglobin values were depressed and other blood chemistry factors were altered (Siewicki et al. 1983). Diets containing intrinsic oyster cadmium at 1.8 mg/kg were more effective in producing hematopoietic alterations than were diets containing CdCl₂ at 3.6 mg/kg (Siewicki et al. 1983). Adequate dietary iron supplementation markedly reduced cadmium retention and cadmium-induced anemia in rats. Iron supply and the increased iron demand during growth of rats can be disturbed within one week by a daily cadmium intake as low as 0.7 to 1.3 mg Cd/kg BW (Schumann et al. 1996).

A study by Beyer et al. (1985) of metal contamination in wildlife from the vicinity of two zinc smelters in Palmerton, Pennsylvania, demonstrated the difficulties in interpretation of cadmium residues from biota in the presence of other potentially hazardous metal contaminants (Table 1.6). The soil litter horizon at Palmerton was heavily contaminated with lead (2700 mg/kg), zinc (24,000 mg/kg), copper (440 mg/kg), and cadmium (710 mg/kg). Invertebrates that fed on soil litter or soil organic matter, such as earthworms, slugs, and millipedes, were rare or absent in the vicinity of the smelters but not at more distant sampling sites (Table 1.6). Concentrations of all metals tended to be higher in these invertebrates than in other invertebrate groups collected. Amphibians and reptiles were also rare or absent at the Palmerton site, but not at more distant stations. Mean cadmium concentrations, in mg/kg dry weight, were highest in carrion insects (25), followed by fungi (9.8), leaves (8.1), shrews (7.3), moths (4.9), mice (2.6), songbirds (2.5), and berries (1.2). By contrast, average concentrations of lead, in mg/kg dry weight, were highest in shrews (110), followed by songbirds (56), leaves (21), mice (17), carrion insects (14), moths (4.3), berries (4), and fungi (3.7). Evidence for lead poisoning in shrews included high residues in kidney (280 mg/kg wet weight) and reduced blood enzyme levels. In addition, livers from two yellow-billed cuckoos (*Coccyzus americanus*) from Palmerton had lead concentrations of 18 and 25 mg/kg wet weight; however, they and other songbirds appeared to be healthy. Concentrations of zinc and copper tended to be highest in the same organisms that contained the highest concentrations of cadmium, emphasizing the importance of documenting organism body burdens of all suspected contaminants before significance is attributed to any single component. Beyer et al. (1985) demonstrated that only a small portion of all metals measured in the soil became incorporated into plant foliage and suggested that most of the metal contamination detected in biota came from aerial deposition.

Table 1.6 Cadmium Residues (mg/kg dry weight [ppm]) in Soil, Flora, and Fauna Collected near Two Zinc Smelters in Palmerton, Pennsylvania

Soil and Category of Plants and Animals	Direction and Distance of Areas from Smelter Emissions	
	Downwind (about 2.1 km)	Upwind (9.7 km)
Soil		
Upper litter layers	250–710	6–13
Upper mineral layers	3–35	1–3
Foliage	8.1	2.3
Acorns and berries	1.2	0.6
Fungi	9.8	2.2
Moths, 8 spp.	0.8–11.0	0.4–1.7
Caterpillars	3.3	0.8
Earthworms, 2 spp.	NF ^a	62–140
Slugs	NF	20
Millipedes	NF	2.1–4.5
Beetles	1.3	0.8
Flies, 2 spp.	29–44	NF
Hornets	NF	2.3
Centipedes	28	NF
Birds		
Carcasses, 9 spp.	—	1.2
Carcasses, 10 spp.	2.5	—
White-footed mouse, carcass	2.6	1.2
Short-tailed shrew, carcass	NF	4.8
Amphibians, 5 spp.	NF	1.4

^a NF = organism not found

Modified from Beyer, W.N., O.H. Pattee, L. Sileo, D.J. Hoffman, and B.M. Mulhern. 1985. Metal contamination in wildlife living near two zinc smelters. *Environ. Pollut.* 38 A:63–86.

The kidney is the critical organ in mammalian cadmium toxicity and is the first organ in which damage is observed or adverse functional changes start to occur. Cadmium concentrations in excess of 200 mg/kg FW kidney cortex results in renal dysfunction in about 10% of the exposed human population; a similar pattern is evident in mice, rats, and rabbits (Cooke and Johnson 1996). In male rats given a single intravenous injection of 0.15 mg metallothionein-bound Cd/kg BW, DNA fragmentation was seen in kidney 12 hours after injection; cycloheximide (3 mg/kg BW) inhibited Cd-induced DNA fragmentation, suggesting that protein synthesis is impaired (Ishido et al. 1998). In human tissues, there was a significant increase in cadmium burdens in 1980 when compared to the period 1897 to 1939. Cadmium content in the renal cortex portion of the kidney increased by a factor of 47 during this interval, and whole-body burden increased by a factor near 5 (Drasch 1983). The significance of this increase is not fully clear, but one study has suggested that cadmium and lead are associated with increased risk of heart-related death, even in light of known conventional causes of such fatalities (Voors et al. 1982). Similar data for wildlife are lacking, and this clearly indicates an area for additional research.

1.6 BIOACCUMULATION

Cadmium biomagnifies in terrestrial food chains and tends to accumulate in liver and kidneys of older apex organisms (Scheuhammer 1987). This process was documented in the chain of soil to vegetation to invertebrates to upper trophic level consumers, including roe deer (*Capreolus capreolus*), barn owls (*Tyto alba*), weasels (*Mystela nivalis*), and kestrels (*Falco tinnunculus*; Gorree

et al. 1995). Radishes (*Raphanus sativa*) accumulated cadmium from the soil in roots and shoots over a 75-day period; uptake was decreased markedly with liming or increased soil pH (Han and Lee 1996). However, centipedes (*Lithobius forficatus*) near a zinc smelter, with body burdens as high as 80 mg Cd/kg DW, on transfer to an uncontaminated site for 10 weeks lost all but 18 mg Cd/kg DW despite the very high cadmium diet provided (Descamps et al. 1996).

Biological half times of cadmium in humans is lengthy. Based on body burden and excretion data, cadmium may remain in the human body for 13 to 47 years. Although cadmium is excreted primarily in urine and feces, it tends to increase in concentration with the age of the organism and eventually acts as a cumulative poison (Hammons et al. 1978). These phenomena have not been documented adequately in wildlife species.

In marine mammals, cadmium was present in all liver and kidney samples analyzed (Taylor et al. 1989). Cadmium concentrations in livers of beluga whales (*Delphinapterus leucas*) were positively correlated with age, and in ringed seals (*Phoca hispida*) with length, increasing from <0.7 to 3.6 mg Cd/kg FW in belugas and <0.14 to 8.8 mg/kg FW in seals (Mackey et al. 1996). A similar case is made for kidney and liver tissues of the Baikal seal (*Phoca sibirica*; Watanabe et al. 1998). Pilot whales (*Globicephala melas*) contained higher concentrations of cadmium in the liver and kidney tissues than did other marine mammals, and this is attributed, in part, to the elevated cadmium (as much as 5.8 mg Cd/kg DW) content in squids (*Loligo forbesi*) — a major dietary item (Caurant and Amiard Triquet 1995). Similarly, elevated levels of cadmium in Pacific walruses (*Odobenus rosmarus divergens*) are considered related to elevated cadmium burdens in clams (*Mya* sp.), a major food item (Miles and Hills 1994). Also, uptake of cadmium from cadmium-contaminated prey by fish plays an important role in contaminated waters (Kraal et al. 1995).

Red-eared turtles (*Trachemys scripta*) given very high doses of cadmium (10 mg Cd/kg BW daily for 6 days) by intraperitoneal injection accumulated 42% of the cadmium body burden in liver, followed by kidney (20%), spleen (12%), heart (8%), gonads (8%), and shell (5%). Lesser amounts were measured in lung, muscle, brain, and blood (Thomas et al. 1994). Turtle metallothioneins, which are similar to those of other vertebrates, seemed to control the accumulation process. Frogs seem relatively resistant to cadmium. Adult female water frogs (*Rana ridibunda*) were held in solutions containing 200 mg Cd/L, as CdCl₂, for 30 days (Vogiatzis and Loumbourdis 1998). Cadmium accumulated in kidneys and livers in a time-dependent manner, and metallothionein and glutathione concentrations increased with increasing liver cadmium burdens. After 30 days, livers had 240 mg Cd/kg DW and kidneys 657 mg Cd/kg DW (Vogiatzis and Loumbourdis 1998).

Freshwater and marine aquatic organisms accumulate cadmium from water containing cadmium concentrations not previously considered hazardous to public health or to many species of aquatic life (USPHS 1993; Currie et al. 1998; Table 1.7). In American oysters (*Crassostrea virginica*), held for 40 weeks in flowing seawater containing 5.0 µg Cd/L, edible meats contained 13.6 mg Cd/kg fresh weight, a level considered to be an emetic threshold for human consumers (Zaroogian and Cheer 1976). These oysters retained virtually all accumulated cadmium (12.5 mg/kg) during a 16-week posttreatment immersion in clean seawater (Zaroogian 1979). Human emetic thresholds for cadmium in oysters were surpassed in 5 weeks at 25 µg/L and in only 2 weeks at 100 µg/L (Shuster and Pringle 1969). The emetic threshold for juvenile northwestern salamanders (*Ambystoma gracile*) is higher than that of humans; regurgitation occurred between 2458 and 5701 mg Cd/kg diet with no regurgitation at 982 mg Cd/kg diet and lower (Nebeker et al. 1995).

Two species of freshwater aquatic mosses (*Fontinalis dalecarlica*, *Platyhypnidium riparoides*) exposed to concentrations between 0.5 and 6.5 µg Cd/L for 28 days had accumulation factors as high as 137,000 and 158,000, respectively (Gagnon et al. 1998). Accumulations increased with increasing cadmium concentration and decreasing water hardness. Cadmium tended to persist in these mosses. During a depuration period of 28 days following the 28-day exposure, only 37 to 48% of the accumulated cadmium was eliminated (Gagnon et al. 1998).

Cadmium uptake from the medium by aquatic organisms usually increased with increasing water temperature in the range of 5 to 25°C; in the case of midge (*Chironomus riparius*) larvae,

Table 1.7 Bioconcentration of Cadmium from Ambient Medium by Selected Species of Aquatic Biota

Type of Medium, Taxonomic Group, and Organism	Ambient Concentration of Cd ($\mu\text{g/L}$)	Exposure Period, (weeks)	Bioconcentration Factor (whole organism)	References ^a
FRESHWATER				
<i>Aquatic mosses</i>				
<i>Fontinalis</i> sp.	6.5	4	158,000	9
<i>Platyhypnidium</i> sp.	6.5	4	137,000	9
<i>Insects</i>				
<i>Ephemerella</i> sp.	5.0	52	1630	1
<i>Pantala hymenea</i>	5.0	52	736	1
<i>Ischnura</i> sp.	5.0	52	1500	1
Family Pytiscidae	5.0	52	164	1
Family Chironomidae	5.0	52	2200	1
Family Ceratopogonidae	5.0	52	936	1
<i>Fish</i>				
<i>Oncorhynchus mykiss</i>	4.0	10	33	2
<i>Gambusia affinis</i>	0.02	8	4100	3
<i>Gambusia affinis</i>	5.0	26	7440	4
<i>Algae</i>				
<i>Chlorella vulgaris</i>	10.0	1.4	2550	5
MARINE				
<i>Molluscs</i>				
<i>AQUIPECTEN irradians</i>	10.0	3	131	6
<i>Crassostrea virginica</i>	10.0	3	116	6
<i>Crassostrea virginica</i>	5.0	40	2720	7
<i>Fish</i>				
<i>Fundulus heteroclitus</i>	10.0	3	15	6
<i>Crustaceans</i>				
<i>Homarus americanus</i>	10.0	3	21	6
<i>Pontoporeia affinis</i>	6.5	66	3500	8

^a 1, Giesy et al. 1979; 2, Kumada et al. 1980; 3, Williams and Giesy 1978; 4, Giesy et al. 1977; 5, Ferard et al. 1983; 6, Eisler et al. 1972; 7, Zaroogian and Cheer 1976; 8, Sundelin et al. 1983; 9, Gagnon et al. 1998.

about 60% of the increased uptake is due to increased respiration (Bervoets et al. 1996). However, mayfly (*Hexagenia rigida*) nymphs accumulated more cadmium at 15°C than at 25°C. In that study, more cadmium was bioavailable for uptake owing to the higher pH of 7.5 at 15°C vs. pH 5.0 at 25°C (Odin et al. 1996). In another study with *Hexagenia rigida* nymphs, cadmium accumulation from sediments containing 0 to 41 mg Cd/kg DW was higher with increasing exposure duration (0 to 60 days), increasing water temperature (12 to 24°C), and increasing sediment cadmium concentration (Andreou et al. 1998). Cadmium was accumulated by fish hepatoma cells to a greater degree than were other metals tested. Present in declining order of accumulation were: cadmium, nickel, copper, cobalt, zinc, and lead (Bruschweiler et al. 1996). There is considerable variation in the ability of teleost tissues to accumulate cadmium from the ambient medium. Cadmium accumulation

rates in larvae of tilapia (*Oreochromis mossambica*) increased with increasing larval development and were inversely related to LC50 (96 h) values (Hwang et al. 1995). Sequestering agents, such as EDTA, reduced by 34% the accumulation of cadmium from the medium (15 µg/L) by sac fry of the African tilapia (*Oreochromis niloticus*; Siriwardena et al. 1995). Among rainbow trout exposed for 2 weeks to 9 µg Cd/L, bioconcentration factors (BCF) were 260 for gill, 17 for liver, 26 for kidney, and zero for spleen and heart tissues (Roberts et al. 1979). At slightly higher ambient dissolved cadmium levels of 10 µg/L and exposure for 3 months, BCF values were substantially higher: 1740 for gill, 4900 for liver, 740 for kidney, 160 for spleen, and 100 for heart tissues (Roberts et al. 1979). The evidence for cadmium transfer through various trophic levels suggests that only the lower trophic levels exhibit biomagnification. In the freshwater food chain extending from the alga *Chlorella vulgaris*, to the cladoceran *Daphnia magna*, to the teleost *Leucospius delineatus*, it was demonstrated that algae held 10 days in water containing 10 µg Cd/L had 30 mg Cd/kg dry weight, up from 4.5 mg/kg at the start (Ferard et al. 1983). Cladocerans feeding on cadmium-loaded algae for 20 days contained 32 mg Cd/kg dry weight, up from 1.4 mg/kg at the start. However, fish fed cadmium-contaminated cladocerans for 4 days showed no change in body burdens.

Cadmium resistance has recently been documented in marine annelids (Wallace et al. 1998). Oligochaetes (*Limnodrilus hoffmeisteri*) from Foundry Cove, New York — a severely cadmium-contaminated site — were more tolerant of cadmium than conspecifics from a reference site, surviving twice as long in a 7-day acute toxicity bioassay (1.0 mg Cd/L) and with bioconcentration factors of 2020 vs. 577 for the controls (radiocadmium-109). The cadmium-resistant worms produced metal-rich granules and metallothioneins for cadmium storage and detoxification, whereas nonresistant worms only produced metallothioneins. Grass shrimp (*Palaemonetes pugio*) fed cadmium-resistant worms absorbed 21% of the ingested cadmium vs. 75% for shrimp fed nonresistant worms (Wallace et al. 1998).

In laboratory studies with chipping sparrows (*Spizella passerina*) fed radiocadmium-109 in their diets for 3 weeks, it was demonstrated that cadmium became localized in the liver and kidneys (Anderson and Van Hook 1973). During posttreatment on a radiocadmium-free diet, there was an initial rapid drop in radioactivity, and the remaining radiocadmium had an estimated biological half-life of 99 days (Anderson and Van Hook 1973). Marine killifish (*Fundulus heteroclitus*) containing radiocadmium-115m lost 90% of the accumulated radiocadmium during a 6-month posttreatment observation period; the liver usually contained 75 to 80% of the total body dose at any time (Eisler 1974). Mallards fed 200 mg Cd/kg diet for about 13 weeks all survived, but levels in liver and kidney were elevated at 110 and 134 mg/kg fresh weight, respectively (White and Finley 1978). Mallard ducklings fed only 20 mg Cd/kg in the diet for 12 weeks contained 42 mg Cd/kg liver (Cain et al. 1983).

The exact mechanism of acute cadmium poisoning is unknown, but, among teleosts, it depends in part on exposure period, concentration of dissolved and ionic cadmium in the medium, and water temperature and salinity. Under conditions of high cadmium concentration and short exposure, the gill seems to be the primary site of damage and accumulation; under conditions of prolonged exposure and low cadmium levels, the intestine, kidney, and possibly other tissues were measurably affected. Retention of cadmium by teleosts depends on tissue biomagnification potential, length of postexposure recovery period, and other factors. The significance of comparatively low concentrations of cadmium in tissues of fish, other aquatic organisms, and wildlife, and the implications for organism health, is not fully understood. Although numerous physical, chemical, and biological factors demonstrably modify uptake and retention of cadmium by fish and wildlife (Hammons et al. 1978; USEPA 1980; Eisler 1981, 1984, 1985; Scheuhammer 1987; USPHS 1993), the significance of relatively high cadmium residues to animal and plant health is difficult to interpret. There is some evidence, however, that life-threatening concentrations are 200 mg Cd/kg fresh weight in the renal cortex of the mammalian kidney (Hammons et al. 1978) and 5.0 mg/kg fresh weight whole body of estuarine teleosts (Eisler 1974).

1.7 TERATOGENESIS, MUTAGENESIS, AND CARCINOGENESIS

Teratogenic effects on animals appear to be greater for cadmium than for other metals, including lead, mercury, copper, indium, and arsenic (Ferm and Layton 1981). Among amphibians, frog embryos reared in 5000 to 7500 µg Cd/L showed nonclosure of the neural tube (Ferm and Layton 1981). In embryos of fathead minnows from adults reared in water containing 37 to 57 µg Cd/L, and from eggs transferred directly to such media, percent hatching was reduced, deformities were increased, and various blood clots developed (Pickering and Gast 1972). Embryos of the bluegill (*Lepomis macrochirus*) held in water at 80 µg Cd/L and higher showed edema, microcephalia, and malformed caudal fins (Eaton 1974). Eggs of a marine killifish (*Fundulus heteroclitus*) were little affected at up to 10,000 µg Cd/L (Weis and Weis 1977). Caudal and hindlimb abnormalities were observed in chickens following injection of eggs with 0.1 to 1.0 mg/kg egg of cadmium chloride; excess zinc appeared to have a protective effect (Ferm and Layton 1981). Rats subjected to >6 mg Cd per kg body weight daily during pregnancy produced fetuses with jaw defects, cleft palates, club feet, and pulmonary hyperplasia (Ferm and Layton 1981). Among hamsters (*Cricetus spp.*), cadmium administration was associated with embryonic tail defects; effects were synergized by salts of lead or mercury and antagonized by selenium (Ferm and Layton 1981). No conclusive evidence of cadmium teratogenesis in humans is available.

At high concentrations, cadmium is genotoxic to isolated cells (Shimada et al. 1998). From a variety of studies in which mice and bacteria were used as models, it appears likely that cadmium has mutagenic effects. Mice injected with 3 or 6 mg CdCl₂/kg body weight showed changes in chromosome number 12 h later. Similar changes were observed in hamsters at 1.5 to 3.0 mg/kg (Ferm and Layton 1981). Very high dosages (>100 mg/kg) produced chromosomal abnormalities in plant seeds. Also, CdCl₂ had a mutagenic effect on indicator strains of *Salmonella* bacteria. However, the evidence for these effects is still diffuse and often contradictory (Ferm and Layton 1981).

Laboratory studies with mice and rats have conclusively demonstrated that the injection of cadmium metal or salts causes malignancies (sarcoma) at the site of injection and testicular tumors. However, the simultaneous administration of zinc is protective against sarcoma and interstitial cell tumor development (USEPA 1980). In rats, no dose-related increases in tumors were found at maximum oral daily doses of 4.4 mg Cd/kg BW (USPHS 1993). Among humans, the available epidemiological evidence is not sufficient to conclude that cadmium is definitely implicated as a carcinogen (USEPA 1980; Nomiyama 1982), although cadmium exposure is associated with lung cancer in humans (Shimada et al. 1998).

1.8 RECOMMENDATIONS

Proposed limits for cadmium in water, diet, tissues, air, soils, and sewage sludge for the protection of human health, plants, and animals are shown in [Table 1.8](#). It is noteworthy that the current upper limit of 10.0 µg Cd/L in drinking water for human health protection is not sufficient to protect many species of freshwater biota against the biocidal properties of cadmium or against sublethal effects, such as reduced growth and inhibited reproduction. Ambient water-quality criteria formulated for protection of freshwater aquatic life state that, for total recoverable cadmium, the criterion, in µg/L, is the numerical value given by $e^{(1.05(\ln(\text{hardness})) - 8.53)}$ as a 24-h average, and the concentration, in µg/L, should never exceed the numerical value given by $e^{(1.05(\ln(\text{hardness})) - 3.73)}$. Thus, at water hardnesses of 50, 100, and 200 mg/L as CaCO₃, the criteria are 0.012, 0.025, and 0.051 µg Cd/L, respectively, and the concentration of total recoverable cadmium should never exceed 1.5, 3.0, and 6.3 µg/L, respectively. Unfortunately, data are accumulating that demonstrate that even these comparatively rigorous criteria are not sufficient to protect the most sensitive species of

Table 1.8 Proposed Cadmium Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Effective Concentration	Ref. ^a
AIR		
Human health protection^b		
Best case, ambient exposure		
	0.001 µg/m ³	1
Average case, ambient exposure	0.03 µg/m ³	1
Worst case		
Occupational exposure	100 µg/m ³	1
Cadmium dust	<200 µg/m ³	9
Cadmium fumes	<100 µg/m ³	9
Ambient exposure	0.4 µg/m ³	1
To prevent kidney damage, chronic inhalation	<0.2 µg/m ³	9
NOAEL; 8 h daily, 250 days/year, 70-year lifetime ^c	<1.6 µg/m ³	9
Threshold Limit Value		
Current	<50 µg/m ³	9
Proposed		
Total dust	10 µg/m ³	9
Respirable fraction	<2 µg/m ³	9
DIET		
Birds, nonmarine	<2 mg Cd/kg FW ration	14
Domestic herbivores	<0.5 mg Cd/kg DW ration	7
Mammals		
Adverse effects on reproduction or development	3.5–7.5 mg Cd/kg BW daily, and higher	12
Human health protection		
Chronic oral, USA ^d	<0.7 µg Cd/kg BW daily	9
Best case, USA	12 µg daily; 16 µg/kg diet daily	1
Average case, USA	30 µg daily; 40 µg/kg diet daily	1
Worst case, USA	75 µg daily; 100 µg/kg diet daily	1
Spain, edible fish tissues	<3 mg/kg FW	5
Weekly tolerable intake ^e	400–500 µg/adult or 7 µg Cd/kg BW	3
Taiwan, brown rice	<0.5 mg/kg rice	16
SEDIMENTS		
Freshwater aquatic life protection		
From Great Lakes for disposal into water	<1 mg Cd/kg DW	11
Marine aquatic life protection, Spain	<35.0 mg/kg DW	5
SEWAGE SLUDGE		
Crop protection		
For application to agricultural lands		
Florida		
Moderately contaminated	>5 kg Cd/surface ha	11
Prohibited	>100 mg Cd/kg DW	11
Illinois	<11 kg Cd/surface ha	11
Maryland		
Soils with low cation exchange capacity vs. high cation exchange capacity soils	5 vs. 10 kg Cd/surface ha	11
Massachusetts	<5 kg Cd/surface ha	11
Minnesota, Missouri, Oregon		
Cation exchange capacity of soil, in meq/100 g		
Low (<5)	5 kg Cd/surface ha	11
Medium (5–15)	10 kg Cd/surface ha	11
High (>15)	20 kg Cd/surface ha	11
New York	3.4–4.5 kg Cd/surface ha	11

Table 1.8 (continued) Proposed Cadmium Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Effective Concentration	Ref.^a
Vermont, maximum amounts allowed on various soils		
Loamy sand, or sandy loam	6 kg Cd/surface ha	11
Fine sandy loam, loam, or silt loam	11 kg Cd/surface ha	11
Clay loam, clay, silty clay	22 kg Cd/surface ha	11
Forest soil protection		
New York	<11 kg Cd/surface ha	11
SOILS		
Human health, crops, and livestock protection		
Canada		
Agriculture	1–6 mg Cd/kg DW	11
Residential/Parkland	<4 mg Cd/kg DW	11
Commercial/Industrial	<8 mg Cd/kg DW	11
Acidic soils (pH <6.5), Alberta, needs cleanup	>1 mg Cd/kg DW	11
Europe, after application of sewage sludge	1–3 mg Cd/kg	11
Japan	<9 mg Cd/kg DW	11
The Netherlands		
Background	<1 mg Cd/kg DW	11
Moderate contamination	50–<20.0 mg Cd/kg DW	11
Requires cleanup	>20 mg Cd/kg DW	11
Taiwan, agricultural soils	<10 mg Cd/kg DW	16
USA		
New Jersey	<3 mg Cd/kg DW	11
TISSUE CONCENTRATION		
Birds, nonmarine		
Indicative of increased environmental exposure		
Kidney	>8 mg/kg DW	2
Liver	>3 mg/kg DW	2
Significant renal tubular dysfunction	>100–200 mg/kg FW renal cortex; >400–800 mg/kg DW	2, 3
Some kidney necrosis	100–200 mg Cd/kg DW kidney	2
Adverse effects expected		
Liver	>40 mg/kg FW	14
Kidney	>100 mg/kg FW	14
Mammals		
Acceptable		
Kidney cortex	<150 mg/kg FW	13
Whole kidney	<100 mg/kg FW; <350 mg/kg DW	13
Adverse effects, kidney		
Cellular damage	Reported at 105 mg Cd/kg DW and higher	12
Significant damage	>200 mg Cd/kg FW renal cortex or >1000 mg Cd/kg DW	7
Human health		
Acceptable		
Blood	<10.0 µg/L	9
Kidney cortex	<200 mg/kg FW	13
Urine	<2 µg Cd/g creatinine	9
Indicative of substantial exposure		
Urine	>50.0 µg Cd/g creatinine	9

Table 1.8 (continued) Proposed Cadmium Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Effective Concentration	Ref. ^a
WATER		
Freshwater aquatic life protection		
At water hardness, in mg CaCO ₃ /L, of		
50	<1.5 µg/L	1
100	<3.0 µg/L	1
200	<6.3 µg/L	1
Chesapeake Bay; protection of 90% of species tested		
Acute		
Fish	<0.9 µg/L	15
All species	<5.1 µg/L	15
Benthos	<12.3 µg/L	15
Chronic		
All species ^b	<0.4 µg/L	15
Fish	<1.8 µg/L	15
Saltwater aquatic life protection		
Water, 24-h average	<4.5 µg/L	1
Water, maximum allowable concentration		
USA, acute	43.0 µg/L	6
USA	59.0 µg/L	1
UK, estuaries and coastal waters	<5.0 µg/L	4
Chesapeake Bay; protection of 90% of species tested		
Acute		
All species	<31.7 µg/L	15
Benthos	<23.3 µg/L	15
Fish	<163.0 µg/L	15
Chronic		
Benthos ^c	<0.25 µg/L	15
Human health protection, drinking water		
Canada ^d	<10.0 µg/L	8
Europe	<5.0 µg/L	10
International, goal	<5.0 µg/L	9
Spain	<7 µg/L	5
USA		
Best case	0.5 µg/L	1
Average case	1.3 µg/L	1
Worst case	10.0 µg/L	1
Current	5–10 µg/L	9
Recommended	<0.5 µg Cd/kg BW daily	9
Bottled water	<10 µg/L	9

^a 1, USEPA 1980; 2, Scheuhammer 1987; 3, Gamberg and Scheuhammer 1994; 4, Canli and Stagg 1996; 5, Linde et al. 1996; 6, Hall et al. 1995; 7, Nolet et al. 1994; 8, Ricard et al. 1998; 9, USPHS 1993; 10, Brown et al. 1994; 11, Beyer 1990; 12, Shore and Dounben 1994; 13, Cooke and Johnson 1996; 14, Furness 1996; 15, Hall et al. 1998; 16, Chen 1999.

^b Assumes consumption of 0.75 kg food per day by 70-kg adult

^c Includes uncertainty factor of 10.

^d Includes uncertainty factor of 3.

^e Assumes an absorption rate of 5% and a daily excretion rate of 0.005%.

^f Concentrations greater than 3.4 µg Cd/L are frequently encountered in the Chesapeake and Delaware Canal and infrequently greater than 1.4 µg Cd/L in other portions of the bay.

^g However, surface water levels in numerous Canadian lakes subjected only to atmospheric deposition within mining areas are often >1.0 µg Cd/L and may not be sufficiently low to prevent adverse physiological effects on early life stages of sensitive aquatic species.

freshwater insects, plants, crustaceans, and teleosts. It now appears that levels in excess of 3.0 µg Cd/L in freshwater are potentially hazardous to aquatic biota and that levels near 1.0 µg/L are cause for concern in waters of low alkalinity. Not listed in Table 1.8, but still recognized as proposed criteria (USEPA 1973), are the comparatively high levels of 10.0 µg Cd/L allowed for agricultural

use on all soils (except neutral and alkaline soils, which may be irrigated with water having levels as high as 50.0 µg Cd/L) and public water supplies for livestock purposes, which may not exceed 50.0 µg Cd/L.

The saltwater aquatic life protection criterion of 4.5 µg Cd/L seems adequate to prevent death, but will not prevent potentially deleterious physiological effects, including disrupted respiration in crustaceans and teleosts. Incidentally, at 5.0 µg Cd/L, the lowest concentration critically examined, oysters biomagnify ambient levels to concentrations hazardous to human consumers and possibly other animal consumers. The maximum allowable saltwater concentration (MAC) during a 24-h period was recommended as 59.0 µg/L ([Table 1.8](#)). However, death of various species of marine crustaceans was reported at 60.0 µg Cd/L after exposure for 6 weeks and at 14.8 to 19.5 µg/L after 23 to 27 days. Furthermore, a MAC of 59 µg Cd/L may be met with daily discharges of 59 µg/L for 2 h and no discharge of cadmium for the rest of the day. The effects of exposure of marine life to 59 µg/L of cadmium salts for 2 h daily for protracted periods have not yet been investigated. Accordingly, seawater concentrations in excess of 4.5 µg/L of total cadmium at any time should be considered potentially hazardous to marine life until additional data prove otherwise.

Food is recognized as the major source of cadmium in humans, except in comparatively rare cases of occupational air exposure. The recommended upper limit for cadmium in food is 75 µg/day ([Table 1.8](#)). On the basis of an absorption factor of 0.1 (USEPA 1980), a total of 7.5 µg Cd will be retained daily. A 70-kg adult ingests an estimated 0.75 kg of food daily, which suggests that human diets should not exceed 100 µg/kg. Regular weekly consumption by humans of kidney tissue (range 23 to 166 mg Cd/kg DW) from Arctic caribou (*Rangifer tarandus*) and from muskox (*Ovibos moschatus*) older than 1 year (2.4 to 12.4 mg Cd/kg DW kidney) will probably cause the World Health Organization provisional weekly tolerable intake of cadmium (400 µg) to be exceeded (Gamberg and Scheuhammer 1994). On cadmium-contaminated habitats, common shrews (*Sorex araneus*) may ingest more than 3.5 to 7.5 mg Cd/kg BW daily (associated with reproductive effects in laboratory animals) without apparent harm (Shore and Douben 1994). Large cadmium concentrations in body organs of shrews may reflect their ability to store cadmium in a nontoxic metallothionein-bound state. Adverse effects were, however, observed in feral rodents that consumed more than 3.5 mg Cd/kg BW daily, and this suggests a need to establish dose–residue–effect relationships for intakes and residues appropriate for feral organisms (Shore and Douben 1994).

Ducks, geese, and other species of wildlife, unlike adult humans, may consume 6 to 7% of their total body weight daily and may graze extensively on crops directly affected by sewage and other wastes containing high cadmium residues. Feeding studies with mallards indicated that diets containing 200 mg Cd/kg produced no obvious deleterious effects after 13 weeks. At the end of that study, however, kidney cadmium levels under those conditions were about 134 mg/kg fresh weight, a level near the 200 mg/kg fresh weight designated a “critical threshold” (and presumably life-threatening) for the renal cortex of the human kidney. Field observations on ducks and laboratory studies are not strictly comparable. Under field conditions, birds and other wildlife may consume food containing high cadmium levels, but it is almost certain that these diets also contain other potentially harmful contaminants, as well as metals or compounds that may ameliorate cadmium toxicity. The significance of foods containing complex mixtures of contaminants and their resultant toxicological interactions are imperfectly understood. Until other data become available, wildlife dietary levels exceeding 100 µg Cd/kg diet fresh weight on a sustained basis should be viewed with caution — as they are for humans.

Recommendations for cadmium in air and human health protection under the worst scenario ([Table 1.8](#)) assume that total daily air intake is 27.14 m³ for an adult human who spends about 6.3 h in occupational exposure to air containing 100 µg Cd/m³ (USEPA 1980). Under these conditions, a 70-kg adult would retain about 361 µg Cd/day, based on an absorption factor of 0.5 (USEPA 1980), and most of this cadmium would probably be translocated to the kidney; a critical threshold level of 200 mg Cd/kg in the kidney would be reached in about 1.52 years. It is not now known

whether respiration rates of wildlife, particularly birds, are comparable to those of humans, or whether cadmium absorption energetics are similar, or whether wildlife species that frequent point sources of air contaminated by high cadmium levels for protracted periods are at greater risk than humans. Evidence given by Beyer et al. (1985) demonstrated that flora and fauna in the vicinity of industrial smelters were affected by cadmium and its associated heavy metals. This strongly suggests that proposed recommendations for cadmium levels under occupational air exposure should be revised downward for wildlife protection.

Additional research on cadmium is recommended in three areas: (1) effects on cancer, genotoxicity, and reproductive toxicity under conditions of acute, intermediate, and chronic durations of exposure, and administered by way of diet, inhalation, and dermal routes of exposure; (2) emphasis on studies with pregnant animals; and (3) methods for reducing toxic effects (USPHS 1993). Finally, the issue of the significance of cadmium residues in various body parts requires resolution. At this time, it appears that cadmium residues in the vertebrate kidney or liver that exceed 10.0 mg/kg fresh weight or 2.0 mg/kg in whole-body fresh weight should be viewed as evidence of probable cadmium contamination. Elevated levels of 13.0 to 15.0 mg Cd/kg tissue fresh weight probably represent a significant hazard to animals of the higher trophic levels, and residues of 200.0 mg Cd/kg fresh weight kidney cortex or more than 5.0 mg Cd/kg whole animal fresh weight should be considered life-threatening.

1.9 SUMMARY

Cadmium contamination of the environment is especially severe in the vicinity of smelters and urban industrialized areas. There is no evidence that cadmium, a relatively rare heavy metal, is biologically essential or beneficial; on the contrary, cadmium is a known teratogen and carcinogen, a probable mutagen, and has been implicated as the cause of severe deleterious effects on fish and wildlife. The freshwater biota is the most sensitive group. Concentrations of 0.8 to 9.9 µg Cd/L (ppb) in water were lethal to several species of aquatic insects, crustaceans, and teleosts, and concentrations of 0.7 to 570 µg/L were associated with sublethal effects such as decreased growth, inhibited reproduction, and population alterations. These effects were most pronounced in waters of comparatively low alkalinity. Marine organisms were more resistant than freshwater biota. Decapod crustaceans, the most sensitive saltwater group, died at concentrations of cadmium in seawater ranging from 14.8 to 420 µg/L. Sublethal effects to marine animals recorded at concentrations of 0.5 to 10 µg Cd/L included decreased growth, respiratory disruption, altered enzyme levels, and abnormal muscular contractions; effects were usually most obvious at relatively low salinities and high temperatures. Freshwater and marine aquatic organisms accumulated measurable amounts of cadmium from water containing concentrations not previously considered hazardous to public health or to many species of aquatic life; i.e., 0.02 to 10 µg Cd/L.

Mammals and birds are comparatively resistant to the biocidal properties of cadmium. The lowest single oral doses producing death in rats and guinea pigs ranged from 150 to 250 mg Cd/kg body weight. Although mallards and chickens tolerated 200 mg Cd/kg diet for protracted periods, kidney cadmium exceeded 130 mg/kg fresh weight under this regimen, a concentration considered life-threatening to some organisms. Sublethal effects of cadmium in birds, which were similar to those in other animals, included growth retardation, anemia, and testicular damage. However, these effects were observed at higher concentrations than in aquatic biota. Although the evidence is incomplete, wildlife populations, especially migratory birds that feed on crops growing on fields fertilized with municipal sewage sludges, may be exposed to considerable risk of harmful effects from cadmium.

It is now conservatively estimated that adverse effects on fish or wildlife are either pronounced or probable when cadmium concentrations exceed 3 µg/L in freshwater, 4.5 µg/L in saltwater,

100 µg/kg in the diet, or 100 µg Cd/m³ in air. Cadmium residues in vertebrate kidney or liver that exceed 10 mg/kg fresh weight or 2 mg/kg whole-body fresh weight should be viewed as evidence of probable cadmium contamination; residues of 200 mg Cd/kg fresh weight kidney, or more than 5 mg/kg whole-animal fresh weight, are probably life-threatening to the organism.

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CHAPTER 2

Chromium

2.1 INTRODUCTION

Environmental effects of chromium (Cr) have been extensively reviewed (National Academy of Sciences [NAS] 1974; Steven et al. 1976; Snyder et al. 1977; Towill et al. 1978; Taylor and Parr 1978; Langard and Norseth 1979; Post and Campbell 1980; Hatherill 1981; Ecological Analysts 1981; Eisler 1986; Nriagu and Nieboer 1988; Outridge and Scheuhammer 1993; U.S. Public Health Service [USPHS] 1993). These authorities agree that chromium is used widely in domestic and industrial products and that some chemical forms, notably hexavalent chromium (Cr^{+6}), are toxic, and others, notably trivalent chromium (Cr^{+3}), are essential nutrients. In North America, thousands of tons of chromium ore and concentrates are imported annually for the production of stainless steels, chrome-plated metals, pigments for inks and paints, and a wide variety of chemicals. Reports from Europe, Scandinavia, Asia, and North America all emphasize the high incidence of lung cancer and other respiratory diseases among workers involved in the manufacture of chromates. Others document that land dumping of wastes from chromate production and electroplating operations has been responsible for groundwater contamination; that discharge of chromium wastes into streams and lakes has caused damage to aquatic ecosystems and accidental poisoning of livestock; and that large amounts of Cr^{+3} and Cr^{+6} are reintroduced into the environment as sewage and solid wastes by the disposal of consumer products containing chromium.

2.2 ENVIRONMENTAL CHEMISTRY

Chromium is the seventh most abundant element on earth with more than 2108 million tons of chromium metal, most of it residing in the core and mantle (Nriagu 1988). The annual world production of chromium is estimated at 9 million metric tons. Most of the ore, in the form of chromite ($\text{FeO}\text{Cr}_2\text{O}_3$), is produced by the Former Soviet Union and the Republic of South Africa. In the United States, trivalent chromium compounds are used as pigments and in leather tanning, and hexavalent chromium compounds are used principally in the ferrochrome and chemical industries (Langard and Norseth 1979; Nriagu 1988; Walsh et al. 1994). The combined production of chromium ferroalloys and chromium metal in the United States in 1988 was 119,645 metric tons from producers in West Virginia, South Carolina, New Jersey, Ohio, Kentucky, New York, Indiana, Utah, Pennsylvania, California, Texas, and North Carolina (USPHS 1993). Exports of chromium materials from the United States in 1988 was 39,887 tons, mostly to Mexico, Canada, the Netherlands, Japan, and Germany. In 1990, the United States produced 150,600 tons of sodium dichromate and 53,300 tons of chromic acid (USPHS 1993).

Although natural mobilization of chromium by weathering processes is estimated at 32,000 tons/year, the amounts of chromium added to the environment as a result of anthropogenic activities are far greater. New York City alone contributes about 440 tons of chromium annually to the environment (Steven et al. 1976). In the 1970s, major atmospheric emissions of chromium were from the chromium alloy and metal-producing industries, and lesser amounts came from coal combustion, municipal incinerators, cement production, cooling towers (Towill et al. 1978), use of chromium-containing phosphate fertilizers, and landfill dumping of chromium-contaminated sewage sludge and consumer products (Outridge and Scheuhammer 1993). In the United States in the 1990s, atmospheric chromium emissions from anthropogenic sources average 2800 tons per year, mostly from combustion of coal and oil (60%) and chrome-plating (24%) sources (USPHS 1993). Atmospheric emissions contribute 4 to 6 times more chromium to aquatic ecosystems than do liquid wastes (Ecological Analysts 1981). In aquatic environments, the major sources of chromium are the electroplating and metal-finishing industries and publicly owned treatment plants; relatively minor sources (other than localized contamination) are iron and steel foundries, inorganic chemical plants, tanneries, textile manufacturing, and runoff from urban and residential areas (Towill et al. 1978; Ecological Analysts 1981). Chromium in phosphates used as fertilizers may be an important source of chromium in soil, water, and some foods (Langard and Norseth 1979). In general, elevated chromium levels in biological or other samples have been positively correlated with increased industrial and other uses of the element — especially uses associated with plating and foundry applications, chemical manufacturing, and corrosion inhibition (Taylor and Parr 1978).

Chromium in the crystalline form is a steel-gray, lustrous, hard metal characterized by an atomic weight of 51.996, an atomic number of 24, a density of 7.14 g/cm³, a melting point of 1857°C, and a boiling point of 2672°C. Four chromium isotopes occur naturally: Cr-50 (4.3%), -52 (83.8%), -53 (9.6%), and -54 (2.4%), and seven are man-made. Elemental chromium is very stable but is not usually found pure in nature. Chromium can exist in oxidation states ranging from -2 to +6, but is most frequently found in the environment in the trivalent (+3) and hexavalent (+6) oxidation states. The +3 and +6 forms are the most important because the +2, +4, and +5 forms are unstable and are rapidly converted to +3, which in turn is oxidized to +6 (Towill et al. 1978; Langard and Norseth 1979; Ecological Analysts 1981; USPHS 1993).

Most compounds prepared from chromite ore contain chromium in the more stable +3 and +6 states. The chromium in essentially all environmentally important chromium compounds is in one of these two oxidation states. Chromium in biological materials is usually in the +3 form (Langard and Norseth 1979) and is the form that functions as an essential element in mammals by maintaining efficient glucose, lipid, and protein metabolism (Steven et al. 1976; Outridge and Scheuhammer 1993; USPHS 1993). In general, the toxicity of trivalent chromium to mammals is low because its membrane permeability is poor and it is noncorrosive; further, there is little tendency for Cr⁺³ to biomagnify in food chains in the inorganic form. However, organo-trivalent chromium compounds may have significantly different accumulation tendencies although little is known about these compounds (Steven et al. 1976). Hexavalent chromium is more toxic than the +3 form because its oxidizing potential is high and it easily penetrates biological membranes (Steven et al. 1976; Taylor and Parr 1978; Langard and Norseth 1979; Ecological Analysts 1981; USPHS 1993).

All toxic effects of Cr⁺⁶ seem to be related to the strong oxidizing action of chromates, and all biological interactions of chromates seem to result in reduction to the Cr⁺³ form and subsequent coordination to organic molecules (Langard and Norseth 1979). It is difficult to distinguish between the effects caused by Cr⁺⁶ and those caused by Cr⁺³ since Cr⁺⁶ is rapidly reduced to Cr⁺³ after penetration of biological membranes and in the gastric environment. However, whereas Cr⁺⁶ can be readily transported into cells, Cr⁺³ is unable to cross cell membranes. The reduction of Cr⁺⁶ to Cr⁺³ may be the most important mechanism for the toxicity of chromium (USPHS 1993).

Most of the Cr⁺⁶ found in nature is a result of domestic and industrial emissions (Steven et al. 1976). Interaction of +6 chromic oxide, dichromate, or chromate compounds with organic compounds can result in reduction to the comparatively less toxic trivalent form (Taylor and Parr 1978).

Chromium compounds interact synergistically or antagonistically with many chemicals. For example, potassium dichromate administered by subcutaneous injection potentiated the effects of mercuric chloride, citrinin, and hexachloro-1,3-butadiene on rat kidneys (USPHS 1993). Chromium effects were lessened by ascorbic acid and Vitamin E, and N-acetyl cysteine was effective in increasing urinary excretion of chromium in rats (USPHS 1993).

Little is known about the relationship between concentrations of total chromium in a given environment and biological effects on the organisms living there. Depending on the physical and chemical state of the chromium, the same element concentration has a wide variety of mobilities and reactivities and thus has different effects (Steven et al. 1976). Chromium toxicity to aquatic biota is significantly influenced by abiotic variables such as hardness, temperature, pH, and salinity of water; and biological factors such as species, life stage, and potential differences in sensitivities of local populations (Ecological Analysts 1981; Holdway 1988). In both freshwater and marine environments, hydrolysis and precipitation are the most important processes that determine the fate and effects of chromium, whereas adsorption and bioaccumulation are relatively minor (Ecological Analysts 1981; Mayer 1988). Both Cr^{+3} and Cr^{+6} can exist in water with little organic matter; Cr^{+6} is usually the major species in seawater (Towill et al. 1978; Mayer 1988). Under oxygenated conditions, Cr^{+6} is the dominant dissolved stable chromium species in aquatic systems. The hexavalent form exists as a component of a complex anion that varies with pH and Eh and may take the form of chromate (CrO_4^{2-}), hydrochromate (HCrO_4^{-1}), or dichromate ($\text{Cr}_2\text{O}_7^{2-}$), with dichromate predominating at acidic pH's. These ionic Cr^{+6} forms are highly soluble in water and thus mobile in the aquatic environment. All stable Cr^{+6} anionic compounds strongly oxidize organic matter on contact and yield oxidized organic matter and Cr^{+3} (Ecological Analysts 1981; Mayer 1988; Saleh et al. 1989; Outridge and Scheuhammer 1993). Trivalent chromium tends to form stable complexes with negatively charged inorganic or organic compounds, and thus is unlikely to be found uncomplexed in aqueous solution if anionic or particulate compounds (such as decaying plant or animal tissues, or silt or clay particles) are present (Steven et al. 1976; Pfeiffer et al. 1980; Ecological Analysts 1981). Precipitated Cr^{+3} hydroxides remain in the sediments under aerobic conditions. Under low pH and anoxic conditions, however, Cr^{+3} hydroxides may solubilize and remain as ionic Cr^{+3} unless oxidized to Cr^{+6} through mixing and aeration (Ecological Analysts 1981; Mayer 1988). Among estuarine sediments, chromium content tends to be highest in those of small grain size and high organic and iron content. Concentrations in European estuaries ranged from 3.9 mg/kg in intertidal sands to 162.0 mg/kg in anaerobic muds (Rehm et al. 1984). Adsorption of chromium by sediments is salinity-dependent; adsorption is greatest at salinities of 0.1 to 1.0‰ (Mayer and Schick 1981). Colloidal iron strongly scavenges Cr^{+3} from river water; flocculation of the colloids when they are mixed with seawater, coupled with lack of removal of the colloids to the sediments by gravitational settling or scavenging by suspended sediments, promotes the flux of Cr^{+3} through the estuary to the open ocean (Mayer et al. 1981).

The solubility and potential bioavailability of chromium waste added to soils through sewage sludge, animal manures, and industrial wastewater are modified by soil pH and organic complexing substances (James and Bartlett 1983a, 1983b; Bartlett and James 1988). Although soil pH can affect oxidation rates of Cr^{+6} to Cr^{+3} , organic complexes appear to play a more significant role. For example, organically complexed Cr^{+3} added to soils may remain soluble for at least a year, whereas the free Cr^{+3} metal ion in the absence of soluble complexing ligands quickly becomes adsorbed, or hydrolyzed and precipitated. The biological effects of organochromium compounds, which are not well documented, appear to be high-priority subjects for further research.

In groundwater, hexavalent chromium tends to be mobile due to the lack of solubility constraints and the low adsorption of Cr^{+6} anion species by metal oxides in neutral to alkaline waters (Calder 1988). Above pH 8.5, no Cr^{+6} adsorption occurs in groundwater; Cr^{+6} adsorption increases with decreasing pH. Trivalent chromium species tend to be relatively immobile in most groundwaters because of the precipitation of low-solubility Cr^{+3} compounds above pH 4 and high adsorption of the Cr^{+3} ion by soil clay below pH 4 (Calder 1988).

Data on the environmental cycling of chromium are lacking, and those on the biochemistry of chromium are incomplete and sparse (Towill et al. 1978); it is clear that these two subjects merit additional research. Furthermore, there is increasing concern about the uncertainties in the analysis of some types of biological and environmental samples (Towill et al. 1978; Taylor and Parr 1978). For example, collaborating laboratories have reported order-of-magnitude differences in persistence of chromium in standard bovine liver. Until more is learned about the reasons for these differences, caution should be exercised in interpreting past analytical results.

2.3 CONCENTRATIONS IN FIELD COLLECTIONS

Chromium concentrations in selected nonbiological materials are elevated in the vicinity of industrial operations and municipal waste treatment facilities where chromium is a significant component of wastes discharged into the environment ([Tables 2.1](#) and [2.2](#)). It is generally agreed that suspended particulates are a major source of transport in aquatic systems, that most chromium in soil and sediment is unavailable to living organisms, that Cr⁺⁶ in air and water is hazardous to fish and wildlife, and that the grossly elevated levels of chromium (especially inorganic fractions) in sludge components may have serious implications to wildlife when the sludge is applied to croplands (Eisler 1986). Severe groundwater contamination, i.e., 40 mg Cr/L, is reported in Nassau County, New York, from an aircraft plant that used chromium solutions for anodizing and plating metals (Calder 1988). Chromium contamination of shallow aquifers is also reported near Telluride, Colorado, from heavy-metal mining and milling wastes discharged into a leaky holding pond, and from chromium wastes from automotive, electroplating, and wood treatment industries in Michigan (Calder 1988). Hexavalent chromium added to or found in soils may be leached, reduced, adsorbed, precipitated, or taken up by a living organism (Bartlett and James 1988). Chromium-contaminated sediments may act as a toxicant source by releasing chromium to interstitial sediment pore waters; the acute toxicity of chromium and other metals in sediments has been correlated with pore water concentrations (Gendusa et al. 1993).

Certain plants grown on serpentine soils containing 1000 to 50,000 mg Cr/kg DW may contain 10 to 100 mg Cr/kg DW — levels that may be toxic to wildlife, although no reports of this phenomenon are known (Outridge and Scheuhammer 1993). Most plant and invertebrate species die before accumulating amounts of chromium that are toxic to predators (Outridge and Scheuhammer 1993). Some species of terrestrial plants have been proposed for the removal of chromate from waste waters (Kleiman and Cigliatti 1997). Terrestrial plants, such as wheat (*Triticum aestivum*), accumulate the greatest amount of chromium under conditions of sulfate deficiency or deprivation. Because sulfate is a strong inhibitor of chromate uptake in terrestrial plants, the presence of sulfates in the environment negates the usefulness of this approach (Kleiman and Cigliatti 1997).

Concentrations of chromium in representative species of plants and animals collected worldwide are shown in [Table 2.3](#). Additional data were given by Jenkins (1980) and Eisler (1981, 1986). Chromium concentrations in species of individual taxonomic groups tended to be elevated when collection localities were near electroplating plants, tanneries, oil drilling operations, sewage outfalls, drift cooling towers, dump sites, or other sources of chromium-containing wastes that were being discharged into the environment. Among marine algae and invertebrates, for example, comparatively high concentrations of chromium were recorded in algae, clams, and annelids from the vicinity of electroplating plants; in crabs collected near an ocean dump site receiving large quantities of metals; and in algae and echinoderms near urbanized areas in Puerto Rico. Grossly elevated levels of chromium were also noted ([Table 2.3](#)) in selected plasma fractions of tunicate blood, in the scales from a few species of teleosts, and in corals from chromium-rich areas containing high concentrations of scandium and titanium. However, these accumulations were not attributed to anthropogenic activities. Studies demonstrate that fish and sediments in Florida stormwater ponds

Table 2.1 Chromium Concentrations in Abiotic Materials

Sample (units in parentheses)	Concentration	Reference ^a
TERRESTRIAL (mg/kg dry weight)		
Earth's crust	100–300	1
Earth's crust	Mean, 125	2
Soils	Trace to 300	2, 3
Soils, USA	37 (1–2000)	14
Granite and limestones	10	3
Serpentine materials	1800	3
Marsh sediments		
Receiving fertilizers containing sewage sludge, for 7 years (total dose of 10,300 mg Cr/m ²)	2150–4750	4
Control areas	50–54	4
Sewage sludge		
Publicly owned treatment works		
USA	428	13
Missouri	86 (10–12,000)	13
AQUATIC		
Suspended particulates (mg/kg)		
Atlantic coastal streams	460	5
United States	37–2000	3
Brazil, electroplating plant		
Distance from discharge site (meters)		
0	2210–61,070	6
50	15,260	6
600	18,620	6
Sediments (mg/kg)		
Freshwater		
Maine, receiving tannery wastes	25,000	7
California	90–140	3
Wisconsin	1–49	3
Rhine River, Germany	Max. 1240	3
Brazil, electroplating plant, distance from discharge site (meters)		
0	1420–54,300	6
50	24,820	6
600	1700	6
Marine		
United Kingdom	30–52	8
Rhode Island, near electroplating plant	60–80	9
Maine, near tanneries	80–3000	10
Water (µg/L)		
Freshwater		
Rivers and lakes	10 (<1–30)	2, 14
Streams	0–112, mean 9.7	3
Drinking water, USA	1.8 (0.4–8.0)	14
Untreated industrial effluents	5,000,000	11
India, chromium-contaminated site		
Irrigation water	160,000–780,000	12
Reservoir water	25,000–100,000	12
Vicinity Brazilian electroplating plant		
Waste stream	1,290,000	6
At discharge	80,000	6

Table 2.1 (continued) Chromium Concentrations in Abiotic Materials

Sample (units in parentheses)	Concentration	Reference ^a
50 m downstream	54	6
600 m downstream	0.23	6
Seawater	0.3 (0.0–0.5)	3, 14
AIR ($\mu\text{g}/\text{m}^3$)		
Background level	0.001	11
Urban	0.01–0.03	14
Occupational exposure, chromate plants	1000	11
Rural areas	<0.01–0.01	2, 14
USA; 1977–84; 2106 sites	0.005–0.525 (averages highest in Steubenville, Ohio and Baltimore, Maryland); Max. 5.5 (Corpus Christi, Texas)	14

^a 1, Ecological Analysts 1981; 2, Langard and Norseth 1979; 3, Towill et al. 1978; 4, Giblin et al. 1980; 5, Turekian and Scott 1967; 6, Pfeiffer et al. 1980; 7, Duval et al. 1980; 8, Bryan et al. 1983; 9, Eisler et al. 1977; 10, Mayer et al. 1981; 11, Steven et al. 1976; 12, Venugopal and Reddy 1992a; 13, Beyer 1990; 14, U.S. Public Health Service (USPHS) 1993.

do not have elevated concentrations of chromium (Campbell 1995), that chromium does not biomagnify in marine food chains in an Egyptian bay heavily contaminated with chromium (Dahab et al. 1990), that chromium from sediments containing 717 mg Cr/kg DW in a New Jersey wetlands is not biologically available to biota in the immediate vicinity (Hall and Pulliam 1995), and that elevated chromium residues in biota from a Texas estuary are not reflective of residues of other heavy metals (Custer and Mitchell 1993). Many factors are known to modify chromium levels. In marine molluscs, as one example, chromium concentrations tended to increase with the age of the organism (Eisler et al. 1978), although uptake was significantly inhibited at high salinities (Olson and Harrel 1973). Accidental contamination of field samples by metal particles in the samples, rust from stainless hydrowire, or flaking paint from the hull of the collecting ship may also constitute significant sources of elevated chromium residues in aquatic environments (Martin and Knauer 1973).

Waterfowl from areas contaminated by mining wastes and which consumed diets rich in chromium had elevated chromium concentrations in tissues, especially in gonads, gallbladder, and pancreas (van Eeden and Schoonbee 1992; Table 2.3). Chromium burdens were highest in livers of seed-eating species of birds from Baja California (Mora and Anderson 1995). In feathers of passerine birds, chromium concentrations were lowest in species that ate mostly fruit and highest in older adults of long-lived species (Burger et al. 1993a). Bones of 24 species of birds collected from southwestern Russia in 1993–95 contained 0.3 to 14.7 mg Cr/kg DW. Concentrations were higher in conspecifics collected in urban areas than in rural areas, highest in sparrows and other seed-eating species, lowest in owls, highest in bones of terrestrial species, and lowest in those of aquatic species (Lebedeva 1997). Elevated concentrations of chromium were measured in brain, lung, kidney, and liver of rock doves (*Columba livia*) from Mexico City when compared to conspecifics collected from a rural area (Gonzalez et al. 1994). In terrestrial ecosystems, elevated chromium levels were reported in cotton rats and plants collected near drift cooling towers and in earthworms and plants from sludge-amended soils (Table 2.3). However, the high levels of chromium reported in the hair of pronghorns and elk (Table 2.3) require verification.

A source of concern is the accuracy and precision of chromium analyses in biological samples. One interlaboratory calibration study, involving 87 laboratories, showed that an oyster homogenate averaged 1.1 mg/kg dry weight, with a standard deviation of 0.5 mg/kg (Fukai et al. 1978). This means that about 67% of the laboratories reporting were in the range of 0.6 to 1.6 mg/kg and about 33% were outside this range. It seems clear that more rigorous and standardized sample preparation techniques and analyses for chromium are needed.

Table 2.2 Concentrations of Total Chromium and Cr⁺⁶ in Air, Water, Soil, and Sludge near Industrial Sites and Sewage Outfalls in the United States

Industry	Water							
	Air ($\mu\text{g}/\text{m}^3$)		Filtered (mg/L)		Particulates (mg/L)	Sediments (mg/kg)	Soil (mg/kg)	Sludge (mg/L) Inorganic/Organic
	Total	Cr ⁺⁶	Total	Cr ⁺⁶				
Chromium pigment producer	13.5	2.1	3.3	1.3	59.6	568.0	41.0	—/—
Chromium plating facility	1.1	—	0.6	0.6	0.14	1.2	36.9	—/—
Tanning operation	<0.2	—	2.3	0.1	10.8	14.8	—	—/—
Sewage treatment plant								
Receiving tannery wastes	<0.4	—	0.05	0.001	0.5	23.3	—	13,950/101
Not receiving tannery wastes	<0.2	—	0.04	<0.001	0.09	—	—	911/9

Adapted from Snyder, A.D., D.G. DeAngelis, E.C. Eimutus, D.M. Haile, J.C. Ochsner, R.B. Reznik, and H.D. Troy. 1977. Environmental monitoring near industrial sites: chromium. *U.S. Environ. Protection Agen. Rep.* 560/6-77-016. 56 pp. plus Appendices.

Table 2.3 Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
MARINE		
Algae and macrophytes		
Algae, whole		
Sea of Japan, 12 spp.	1.0-14.0 DW	1
United Kingdom, 11 sp.	2.8-30.0 DW	2
Algae and macrophytes, whole		
Puerto Rico, 18 spp.	0.4-110.0 DW	3
Knotted wrack, <i>Ascophyllum nodosum</i> , whole		
Norway	4.0 DW	4
Great Britain	1.1-10.0 DW	5, 6
Bladder wrack, <i>Fucus vesiculosus</i> , whole		
United Kingdom	2.6-4.5 DW	4, 5, 6
Phytoplankton, whole		
Narragansett Bay, RI	4.3-73.3 DW	7
Seaweeds, whole		
Japan, 44 spp.	0.1-2.5 DW	8
Korea, 20 spp.	0.7-7.4 DW	9
Marsh grasses, <i>Spartina</i> spp., whole		
Control areas	2.3-3.1 DW	10
From areas treated with sewage-amended sludge at 10,300 mg Cr/m ² over 7-year period	31.0-44.0 DW	10
Coelenterates		
Corals, 34 spp.		
Deep open ocean	0.8-3.0 DW	11
Shallow open ocean	2.0-35.0 DW	11
Shallow coastal zone	0.2-23.0 DW	11
Molluscs		
Red abalone, <i>Haliotis rufescens</i>		
Gill	0.6-4.0 DW	12
Mantle	0.0-12.6 DW	12
Digestive gland	2.0-13.2 DW	12
Foot	ND	12
Hardshell clam, <i>Mercenaria mercenaria</i>		
Soft parts	3.3-24.7 DW	7
Soft parts	0.2-5.8 FW	13
Soft parts	0.8 DW	14
Shell	0.4 DW	14
Periwinkle, <i>Littorina littorea</i>		
Soft parts, United Kingdom	<0.1-1.6 DW	15
Common mussel, <i>Mytilus edulis</i>		
Soft parts	0.9-2.7 DW	14, 16, 17, 18, 19
Soft parts	0.4-21.0 DW	20
Shell	0.1 DW	18
Shell	1.0-2.0 DW	4
Digestive gland	7.4 FW	21
Hepatopancreas	3.5-15.0 DW	22
Gonad	3.0 FW	21
Muscle	11.0 FW	21
Near leather tannery effluent vs. reference site; gills; Ireland; River Calligan; 1992-94		
	400-1000 DW vs. Max. 6.0 DW	85

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Clam, <i>Pitar morrhuanus</i>		
Soft parts	14.2 DW	23
Squid, unidentified		
Various tissues	3.1-5.4 DW	24
Crustaceans		
Edible tissues		
7 spp.	0.1-0.2 FW	25
9 spp.	0.2-0.3 FW	25
Crab, <i>Cancer irroratus</i>		
Flesh	<0.3-0.6 FW	26
Digestive gland	<0.5-1.2 FW	26
Gills	0.8-2.5 FW	26
Annelids		
Polychaete annelids		
Whole	8.1-14.7 DW	27
Whole	23.8-38.0 DW	7
Annelid worm, <i>Nereis diversicolor</i> , whole	0.6 DW	19
Echinoderms		
U.K., whole, 5 spp.	<0.5 DW	28
Puerto Rico, whole, 2 spp.	24.2-43.2 FW	3
Greece, whole, 7 spp.	0.5-13.0 DW	29
Sea cucumber, <i>Holothuria forskalii</i>		
Muscle	0.3 DW	16
Tunicates		
Tunicates, whole		
Greece, 2 spp.	5.5-6.6 DW; 0.2-1.1 FW	30
Tunicate, <i>Podoclavella moluccensis</i>		
Blood		
Plasma, whole	0.4 DW	31
Plasma fractions 9-12	940.0 DW	31
Cell residues	22.0 DW	31
Elasmobranchs		
Smooth dogfish, <i>Mustelus canis</i> , New York Bight		
Muscle	<0.3 FW	32
Liver	<0.8 FW	32
Fishes		
Arabian Gulf; 1992; following 1991 oil spill; gills; various species	5.5-7.5 DW	70
Israel; Mediterranean; 7 species; muscle	0.07-0.8 (0.06-3.7) DW	71
Morocco; Mediterranean Sea; edible portions of the 15 most frequently consumed species	(<0.01-1.8) FW	81
Various species, worldwide		
Gills, 7 spp.	<0.1-0.6 FW	33
Gonad, 7 spp.	<0.1-0.3 FW	33
Heart, 7 spp.	<0.1-0.8 FW	33
Kidney, 7 spp.	<0.1-0.3 FW	33

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Liver, 86 spp.	<0.1-0.4 FW	25, 33
Liver, 4 spp.	0.4-2.0 FW	25
Muscle, 196 spp.	<0.1-1.9 FW	25, 33, 34, 35, 36
Muscle, 31 spp.	0.2-7.3 DW	24, 35, 37
Otoliths, 8 spp.	2.5-6.9 DW	38
Scales, 6 spp.	0.6-97.0 DW	38
Skin, 8 spp.	3.1-8.1 DW	24
Spleen, 7 spp.	<0.1-4.8 FW	34
Vertebrae, 8 spp.	<0.1-1.2 FW	34
Viscera	<0.1-4.5 DW	24, 27
Whole, 17 spp.	<0.1-0.8 FW	25

Birds

Seabirds; Atlantic Canada; 1988 breeding season; liver

Herring gull, <i>Larus argentatus</i>	1.0-1.2 DW	64
Atlantic puffin, <i>Fratercula arctica</i>	1.5-4.3 DW	64
Leach's storm petrel, <i>Oceanodroma leucorhoa</i>	1.6-3.5 DW	64
Double-crested cormorant, <i>Phalacrocorax auritus</i>	0.9-3.6 DW	64

Mammals

Harbor seal, *Phoca groenlandica*

Kidney	0.2-0.6 FW	39
Heart	0.7-1.2 FW	39
Spleen	0.8-1.4 FW	39
Brain	1.0-2.8 FW	39
Blubber	<0.5 FW	39

Mammals; 1987-88; found dead; U.S. Atlantic coast; liver

Common dolphin, <i>Delphinus delphis</i> ; adult male	3.2 DW	66
White-sided dolphin, <i>Lagenorhynchus acutus</i> ; adult male	5.9 DW	66
Bottlenose dolphin, <i>Tursiops truncatus</i>		
Adult male	3.0 DW	66
Adult female	3.3 DW	66
Immature female	1.0 DW	66

Integrated Studies

Egypt; Mex Bay, Alexandria (receives about 504 kg of chromium salts daily)

Sediments	243 (42-752) DW	75
Algae, 2 species, whole	1.9-3.5 DW	75
Crustaceans, 2 species, whole	212-483 FW	75
Fish, 4 species; whole	64-151 FW	75

Spain; April–May 1990; Mediterranean Sea; edible portions

Molluscs, 6 species	0.06-0.39 FW	68
Crustaceans, 5 species	0.10-0.38 FW	68
Fishes, 8 species	0.01-0.47 FW	68

Texas; Laguna Madre; 1986–87

Sediments	4.7 (0.7-50.0) DW	73
Shoalgrass, <i>Halodule wrightii</i> ; rhizomes	13 (5-149) DW	73
Grass shrimp, <i>Palaeomonetes</i> sp.; whole	68 (15-463) DW	73
Brown shrimp, <i>Penaeus aztecus</i> ; whole	60 (8-130) DW	73
Blue crab, <i>Callinectes sapidus</i> ; whole less legs, carapace, and abdomen	1.4 (0.5-5.7) DW	73
Pinfish, <i>Lagodon rhomboides</i> ; whole	40 (3-1386) DW	73

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
New Jersey; Hackensack River wetlands vs. reference site; August–November 1991		
Surface waters ($\mu\text{g/L}$)	3.3 (2.3–11.0) vs. 5.1 (1.7–11.0)	74
Sediments	717 (153–11,760) DW vs. 80 (33–180) DW	74
Macrophyte, <i>Phragmites</i> sp.		
Roots	240 DW vs. 65 DW	74
Shoots	0.3 DW vs. 0.2 DW	74
Blue crab		
Hepatopancreas	5.2 (1.8–7.3) DW vs. 1.4 (0.8–1.8) DW	74
Muscle	0.45 DW vs. 0.54 DW	74
Killifish, <i>Fundulus</i> sp.; whole	3.4 (0.9–8.4) DW vs. 1.7 (1.1–2.4) DW	74

FRESHWATER

Molluscs

Zebra mussel, *Dreissena polymorpha*; soft parts; 1994; the Netherlands

Rhine River	0.6 FW	84
Meuse River	0.3 FW	84
Reference site	0.2 FW	84
Snails, 8–9 km below electroplating plant discharge		
Soft parts	450.0 DW	40

Amphibians

Anurans, Laurel, Maryland

Tadpoles, whole, 2 spp.	1.6–3.8 FW	41
Adults, whole, 3 spp.	1.8–5.4 FW	41

Bullfrog, *Rana catesbeiana*, tadpoles

South Carolina; 1997

With digestive tract		
Body	6.6 DW; 1.3 FW	86
Tail	1.3 DW; 0.2 FW	86
Whole	5.0 DW; 1.0 FW	86
Without digestive tract		
Body without gut	1.8 DW	86
Tail	1.0 DW	86
Digestive tract	27.2 DW	86
Whole	3.5 DW	86
Leopard frog, <i>Rana pipiens</i> , whole	0.5 FW	41

Fishes

Alewife, <i>Alosa pseudoharengus</i> , whole	1.1 FW	42
California; San Joaquin valley; September–November 1986; whole fish		
Common carp, <i>Cyprinus carpio</i>	(<0.1–1.5) DW	82
Mosquitofish, <i>Gambusia affinis</i>	(<0.1–3.8) DW	82
Bluegill, <i>Lepomis macrochirus</i>	(<0.05–2.1) DW	82
Largemouth bass, <i>Micropterus salmoides</i>	(<0.07–0.74) DW	82
Sacramento blackfish, <i>Orthodon microlepidotus</i>	(1.8–3.0) DW	82

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Central Florida; 1991–92; stormwater ponds vs. reference sites; whole fish		
Sediments	2.2 (0.7–3.1) FW vs. 4.3 (0.5–12.9) FW	69
Bluegill	0.53 FW vs. 0.49 FW	69
Redear sunfish, <i>Lepomis microlophus</i>	0.20 FW vs. 0.44 FW	69
Largemouth bass	0.11 FW vs. 0.66 FW	69
Pumpkinseed, <i>Lepomis gibbosus</i> , whole, Laurel, Maryland	5.7 FW	41
Rainbow trout, <i>Oncorhynchus mykiss</i> ; juveniles; Po River, Italy; caged groups exposed upstream and downstream of the (contaminated) Lambro confluence for 30 days		
Start		
Bone	0.7 DW	72
Gills	1.3 DW	72
Kidney	0.7 DW	72
Muscle	0.25 DW	72
Spleen	0.3 DW	72
Whole	18.7 FW	72
Upstream vs. Downstream		
Bone	0.5 DW vs. 0.6 DW	72
Gills	1.2 DW vs. 2.1 DW	72
Kidney	1.0 DW vs. 0.9 DW	72
Muscle	0.6 DW vs. 1.1 DW	72
Spleen	0.9 DW vs. 0.5 DW	72
Whole	21.0 FW vs. 23.0 FW	72
Lake trout, <i>Salvelinus namaycush</i>		
Lake Cayuga, New York, whole		
Ages 1–10 years	<0.013 FW	43
Age 11	0.032 FW	43
Age 12	0.09 FW	43
Eastern mudminnow, <i>Umbra pygmaea</i> , whole, Laurel, Maryland	0.9 FW	41
Fish		
Muscle, 12 spp.	0.03–1.1 FW	44

TERRESTRIAL

Plants

Big sagebrush, <i>Artemesia tridentata</i> , whole, Idaho		
Distance from phosphate plant		
Downwind 3 km	270.0–400.0 DW	45
Upwind 3 km	77.0–117.0 DW	45
Fescue, <i>Festuca arundinacea</i>		
Distance downwind from drift of cooling towers		
15 meters	342.0 DW	46
130 meters	15.0 DW	46
Control areas	0.6 DW	46
Tobacco, <i>Nicotiana tabacum</i>		
Kentucky		
Burley leaf	2.5 DW	47
Cigarette leaf	0.3–6.5 DW	47
Pipe leaf	2.8 DW	47
Cigar leaf	3.1–6.2 DW	47

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Rye, <i>Secale cerealis</i>		
United States		
Seed	0.05 FW	48
Whole	0.04 FW	48
Ontario, Canada, on sludge-amended soil		
Whole	2.2-3.3 DW	49
Corn, <i>Zea mays</i>		
Seed	0.25 DW	44
Kernel	0.02 FW	44
Oil	0.47 FW	44
Meal	0.06-0.13 DW	44
Grain	0.1 DW; 3.4 AW	44
Insects		
Termites, Rhodesia, 2 spp.		
Worker	1500.0 DW	44
Soldier	300.0 DW	44
Queen	20.0 DW	44
Annelids		
Earthworms, whole, 2 spp.	5.0-10.2 DW	44
Earthworm, <i>Eisenia foetida</i>		
From sewage treatment plant sludge containing 299-650 mg Cr/kg		
Whole less gut		
2 weeks' residence	1.0 DW	50
28 weeks' residence	13.0 DW	50
Grain fed worms	0.8 DW	50
Feeding on cattle manures	ND	50
Birds		
American black duck, <i>Anas rubripes</i>		
Egg	0.6 FW	51
Canvasback, <i>Aythya valisineria</i>		
Liver	0.02 FW	52
Rock dove, <i>Columba livia</i> ; Mexico City vs. Ixtlahuaca (reference site)		
Brain	Max. 5.3 DW vs. Max. 1.5 DW	79
Kidney	Max. 6.1 DW vs. Max. 1.2 DW	79
Liver	Max. 2.3 DW vs. 0.6 DW	79
Lung	Max. 3.3 DW vs. Max. 0.9 DW	79
Delaware Bay, Delaware and New Jersey, breast feathers, 1991-92		
Sanderling, <i>Calidris alba</i>	16.5 DW	59
Red knot, <i>Calidris canutus</i>	24.1 DW	59
Semipalmented sandpiper, <i>Calidris pusilus</i> , 1991 vs. 1992	26.3 DW vs. 14.5 DW	59
Redknobbed coot, <i>Fulica cristata</i> ; polluted (mining) wetland region; Transvaal, South Africa		
Brain	6.0 (1.8-9.7) DW	60
Fat	2.2 (0.5-7.3) DW	60
Feathers	12.5 (0.5-40.4) DW	60
Gallbladder	13.7 (6.0-20.0) DW	60

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Heart	3.6 (0.9–5.5) DW	60
Intestine	3.3 (1.0–7.3) DW	60
Kidneys	3.1 (0.6–5.8) DW	60
Liver	0.9 (0.3–1.7) DW	60
Lungs	1.9 (0.6–3.4) DW	60
Muscle	1.9 (0.3–3.0) DW	60
Ovary	17.0 (5.0–29.0) DW	60
Pancreas	8.8 (5.0–17.0) DW	60
Spleen	7.0 (2.0–13.0) DW	60
Stomach	3.3 (1.5–5.7) DW	60
Stomach contents	55.0 (13.0–96.0) DW	60
Testes	53.0 (30.0–75.0) DW	60
Vertebrae	5.4 (4.0–8.2) DW	60
Herring gull, <i>Larus argentatus</i> ; egg contents; Long Island, New York		
1989 vs. 1991	0.22 DW vs. 0.35 DW	61
1992 vs. 1993	0.34 DW vs. 0.91 DW	61
1994	0.23 DW	61
Lesser black-backed gull, <i>Larus fuscus</i>		
Muscle, liver, kidney, and egg	<1.0 DW	4
Mexicali Valley, Baja California, 1986		
Livers, 5 species	1.7–4.6 (1.0–7.2) FW	57
Franklin's gull, <i>Larus pipixcan</i> ; Agassiz National Wildlife Refuge, Minnesota; 1994		
Egg contents	3.1 DW	62
Feathers; females vs. males	1.9 DW vs. 2.1 DW	62
Diet (earthworms)	1.2 DW	62
New Guinea, 5 species		
Feathers	7.8–20.8 DW	58
Black-crowned night heron, <i>Nycticorax nycticorax</i> ; egg contents; east coast, USA; various locations	Max. 0.6 FW	63
Osprey, <i>Pandion haliaetus</i>		
Liver	<0.2 FW	54
Brown pelican, <i>Pelecanus occidentalis</i>		
Liver	<0.2 FW	54
Southwest Russia, 1993–95, bone		
13 species	0.3–1.0 DW	78
7 species	1.1–2.9 DW	78
4 species	6.5–14.7 DW	78
Common eider, <i>Somateria mollissima</i>		
Muscle, liver, kidney, and egg	<1.0 DW	4
Roseate tern, <i>Sterna dougallii</i> ; Long Island, New York; 1992; egg shell vs. egg contents	1.6 DW vs. 2.7 DW	63
Tree swallow, <i>Tachycineta bicolor</i> ; Hackensack River Basin, New Jersey; contaminated area		
Sediments	1098 DW	65
Eggs		
Embryos	6.5 DW	65
Shell	173.0 DW	65
Prefledglings		
Brain	211 (84–363) DW	65
Feather	26 (10–40) DW	65
Gizzard	84 (49–171) DW	65
Liver	101 (69–123) DW	65
Muscle	56 (24–79) DW	65

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Waterfowl		
Feathers, 4 spp.	<0.05 DW	55
Mammals		
Moose, <i>Alces alces</i>		
Sweden; liver; 1982 vs. 1992	0.21 (0.002–0.98) FW vs. 0.07 (0.002–1.7) FW	77
Pronghorn, <i>Antilocapra americana</i>		
Hair		
Idaho	1.9–640.0 DW	44
Wyoming	0.3–130.0 DW	44
Coyote, <i>Canis latrans</i>		
Hair	0.7–12.0 DW	44
Elk, <i>Cervus canadensis</i>		
Hair	1.9–570.0 DW	44
Human, <i>Homo sapiens</i> ; diet		
Vegetables		
Canned	0.23 FW	76
Fresh	0.03–0.14 FW	76
Frozen	0.23 FW	76
Fruits		
Canned	0.51 FW	76
Fresh	0.09–0.19 FW	76
Eggs, chicken	0.06–0.52 FW	76
Dairy products	0.1 FW	76
Whole fish	0.05–0.08 FW	76
Fish muscle	<0.1–0.16 FW	76
Seafoods	0.12–0.47 FW	76
Grains and cereals	0.04–0.22 FW	76
Sugar, refined	0.02 FW	76
Bighorn sheep, <i>Ovis canadensis</i>		
Hair	<0.1 DW	44
Cotton rat, <i>Sigmodon hispidus</i>		
Controls		
Bone	0.2 DW	46, 56
Pelt	0.1 DW	46, 56
Hair	0.4 DW	46, 56
GI tract	1.1 DW	46, 56
Whole	0.06 FW; 0.19 DW	46, 56
Collected 100–130 m from cooling tower drift		
Bone	0.5 DW	46, 56
Pelt	1.1 DW	46, 56
Hair	4.4 DW	46, 56
GI tract	1.0 DW	46, 56
Whole	0.12 FW; 0.40 DW	46, 56
Wild boar, <i>Sus scrofa</i> ; Russia; Minsk vs. Reserve (contaminated)		
Kidney	0.6 DW vs. 1.9 DW	80
Spleen	0.4 DW vs. 1.6 DW	80
Mole, <i>Talpa europaea</i> ; Finland; 1986–89; liver		
Adult	0.14 DW	67
Juvenile	0.22 DW	67
Brown bear, <i>Ursus arctos</i> ; Slovak Republic; 1988–90		
Fat	0.1 FW; Max. 0.6 FW	83

Table 2.3 (continued) Chromium Concentrations in Field Collections of Selected Species of Marine, Freshwater, and Terrestrial Plants and Animals (Values shown are in mg Cr/kg [ppm] whole organism or designated body part fresh weight [FW], dry weight [DW], or ash weight [AW]; ND = nondetectable.)

Ecosystem, Taxonomic Group Organism, Tissue, Location, and Other Variables (mg/kg)	Concentration (mg/kg)	Reference ^a
Kidney	0.1 FW; Max. 0.5 FW	83
Liver	0.1 FW; Max. 0.5 FW	83
Muscle	0.1 FW; Max. 0.6 FW	83
Western jumping mouse, <i>Zapus princeps</i>		
Hair	23.0-45.0 DW	44

^a 1, Gryzhankova et al. 1973; 2, Riley and Roth 1971; 3, Bernhard and Zattera 1975; 4, Lande 1977; 5, Foster 1976; 6, Bryan and Uysal 1978; 7, Phelps et al. 1975; 8, Ishibashi and Yamamoto 1960; 9, Pak et al. 1977; 10, Giblin et al. 1980; 11, Livingston and Thompson, 1971; 12, Anderlini 1974; 13, Shuster and Pringle 1968; 14, Segar et al. 1971; 15, Bryan et al. 1983; 16, Fukai 1965; 17, Graham 1972; 18, Bertine and Goldberg 1972; 19, Bryan and Hummerstone 1977; 20, Karbe et al. 1977; 21, Young and McDermott 1975; 22, Young et al. 1979; 23, Eisler et al. 1978; 24, Horowitz and Presley 1977; 25, Hall et al. 1978; 26, Greig et al. 1977; 27, Fukai and Broquet 1965; 28, Riley and Segar 1970; 29, Papadopoulou et al. 1976; 30, Papadopoulou and Kaniás 1977; 31, Hawkins et al. 1980; 32, Greig and Wenzloff 1977; 33, Brooks and Rumsey 1974; 34, Van As et al. 1973; 35, Plaskett and Potter 1979; 36, De Clerck et al. 1979; 37, Roth and Hornung 1977; 38, Papadopoulou and Kassimati 1977; 39, Duinker et al. 1979; 40, Duval et al. 1980; 41, Hall and Mulhern 1984; 42, Lucas et al. 1970; 43, Tong et al. 1974; 44, Jenkins 1980; 45, Gough and Severson 1976; 46, Taylor and Parr 1978; 47, Nadkarni and Ehrmann 1970; 48, Schroeder et al. 1962; 49, Bates et al. 1975; 50, Hartenstein et al. 1980; 51, Haseltine et al. 1980; 52, White et al. 1980; 53, Wiemeyer et al. 1980; 54, Blus et al. 1977; 55, Kelsall 1970; 56, Taylor et al. 1975; 57, Mora and Anderson 1995; 58, Burger et al. 1993a; 59, Burger et al. 1993b; 60, van Eeden and Schoonbee 1992; 61, Burger and Gochfeld 1995; 62, Burger and Gochfeld 1996; 63, Burger 1994; 64, Elliott et al. 1992; 65, Kraus 1989; 66, Kuehl et al. 1994; 67, Pankakoski et al. 1993; 68, Schuhmacher et al. 1992; 69, Campbell 1995; 70, Al-Yakoob et al. 1994; 71, Hornung and Ramelow 1987; 72, Camusso et al. 1995; 73, Custer and Mitchell 1993; 74, Hall and Pulliam 1995; 75, Dahab et al. 1990; 76, USPHS 1993; 77, Frank et al. 1994; 78, Lebedeva 1997; 79, Gonzalez et al. 1994; 80, Deryabina 1996; 81, El Hraiki et al. 1992; 82, Saiki et al. 1992; 83, Zilincar et al. 1992; 84, Hendricks et al. 1998; 85, Walsh and O'Halloran 1998; 86, Burger and Snodgrass 1988.

2.4 BENEFICIAL AND PROTECTIVE PROPERTIES

Hexavalent chromium has no known essential function. However, trivalent chromium in the form of a dinicotinic acid-glutathione complex is an essential cofactor for insulin production, forms complexes with protein, amino acids, and other organic acids, and is the most biologically stable form of chromium. Dietary trivalent chromium deficiency results in an inability to clear glucose from the blood and pathology similar to diabetes (Outridge and Scheuhammer 1993; USPHS 1993). Although trivalent chromium is an essential nutrient, exposure to high levels via inhalation, ingestion, or dermal contact may cause adverse health effects (USPHS 1993; Domingo 1994). In humans, other mammals, and turkeys (*Meleagris gallopavo*), trivalent chromium is essential for the normal metabolism of carbohydrates, insulin, and glucose (Langard and Norseth 1979; Shiao and Chan 1993) and for regulating carbohydrate metabolism in mammals (Preston et al. 1976; Onkelinx 1977; Gale 1978; Towill et al. 1978; Langard and Norseth 1979; Post and Campbell 1980; Outridge and Scheuhammer 1993; USPHS 1993). Chromium deficiency has been described in rats, guinea pigs, and squirrel monkeys; signs include reduced growth, decreased life span, elevated serum cholesterol, increased formation of aortic plaques, and signs resembling those of diabetes mellitus. Subjecting chromium-deficient animals to stress can exacerbate the signs (Preston et al. 1976). In humans, chromium deficiency has been suggested as a possible factor in the incidence of diabetes and atherosclerosis. Autopsy data from 31 areas of the world suggest that many Americans, but few non-Americans, were deficient in chromium. One characteristic feature of chromium levels in human tissues is that they decline with increasing age (Onkelinx 1977).

Chromium is beneficial but not essential to growth in higher plants. Residues in plants seldom exceed a few mg/kg, except in plants living on infertile serpentine soils containing high chromium

concentrations, or grown on soils amended with sewage sludge. Plants with elevated chromium residues show no toxic effects, although concentrations in excess of 1 mg/kg in the aqueous medium may inhibit germination of the seed and growth of roots and shoots (Towill et al. 1978).

Chromium has proved effective in counteracting the deleterious effects of cadmium in rats and of vanadium in chickens. High mortality rates and testicular atrophy occurred in rats subjected to an intraperitoneal injection of cadmium salts; however, pretreatment with chromium ameliorated these effects (Stacey et al. 1983). The Cr-Cd relationship is not simple. In some cases, cadmium is known to suppress adverse effects induced in Chinese hamster (*Cricetus* spp.) ovary cells by Cr⁺⁶ (Shimada et al. 1998). In southwestern Sweden, there was an 80% decline in chromium burdens in liver of the moose (*Alces alces*) between 1982 and 1992 from 0.21 to 0.07 mg Cr/kg FW (Frank et al. 1994). During this same period in this locale, moose experienced an unknown disease caused by a secondary copper deficiency due to elevated molybdenum levels as well as chromium deficiency and trace element imbalance (Frank et al. 1994). In chickens (*Gallus* sp.), 10 mg/kg of dietary chromium counteracted adverse effects on albumin metabolism and egg shell quality induced by 10 mg/kg of vanadium salts (Jensen and Maurice 1980). Additional research on the beneficial aspects of chromium in living resources appears warranted, especially where the organism is subjected to complex mixtures containing chromium and other potentially toxic heavy metals.

2.5 LETHAL EFFECTS

2.5.1 General

Biocidal properties of chromium salts to aquatic organisms are modified, sometimes by an order of magnitude or more, by a variety of biological and abiotic factors. These include the species, age, and developmental stage of the organism; the temperature, pH, salinity, and alkalinity of the medium; interaction effects of chromium with other contaminants; duration of exposure; and the chemical form of the chromium tested. For hexavalent chromium, LC50 (96 h) values for sensitive freshwater and marine species were between 445 and 2000 µg/L. For trivalent chromium, LC50 (96 h) concentrations were 2000 to 3200 µg/L for sensitive freshwater organisms and 3300 to 7500 µg/L for marine biota.

Among warm-blooded organisms, hexavalent chromium was fatal to dogs in 3 months at 100 mg/kg in their food and killed most mammalian experimental animals at injected doses of 1 to 5 mg Cr/kg body weight, but it had no measurable effect on chickens at dietary levels of 100 mg/kg over a 32-day period. Trivalent chromium compounds were generally less toxic than hexavalent chromium compounds, but significant differences may occur in uptake of anionic and cationic Cr⁺³ species, and this difference may affect survival.

2.5.2 Aquatic Organisms

Records of acute toxicities of hexavalent and trivalent chromium salts to representative species of aquatic life (Table 2.4) make it clear that Cr⁺⁶ is the more toxic to freshwater biota in comparatively soft and acidic waters, that younger life stages are more sensitive than older organisms, and that 96 h is insufficient to attain stable mortality patterns. Euryhaline species of estuarine algae tested show increasing resistance to Cr⁺⁶ at increasing salinities (Wong and Trevors 1988). There are at least five ionic species of hexavalent chromium, of which two — the hydrochromate ion and the chromate ion — are the predominant species and probably the agents that are toxic to freshwater life (Van der Putte et al. 1981b). However, water pH dramatically affects the concentration of each: as pH decreased from 7.8 to 6.5, the hydrochromate ion increased by a factor of about 3, and the chromate ion decreased by a factor of about 6.8 (Van der Putte et al. 1981b). To some species of freshwater fishes, Cr⁺⁶ was 50 to 200 times more toxic at pH 6.4 to 7.4 than at pH 7.8 to 8.0 (Wepener et al. 1992). Hexavalent chromium interacts with other metals in solution to produce additive

Table 2.4 Acute Toxicities of Hexavalent and Trivalent Chromium to Aquatic Life

Chemical Species, Ecosystem, Taxonomic Group, Organism, Modifiers, and Other Information	Concentration ($\mu\text{g/L}$)	Percent Dead	Duration of Test ^a	References ^b
HEXAVALENT CHROMIUM				
Freshwater				
Plants	2500–25,000	50	96 h	1
Rotifers				
<i>Philodina acuticornis</i>				
Water hardness, in mg CaCO_3/L				
25	3100	50	96 h	2
81	15,000	50	96 h	2
Molluscs				
Snail, <i>Physa heterostropha</i>				
Water hardness, in mg CaCO_3/L				
45	17,300	50	96 h	3
171	31,600–40,600	50	96 h	3
Crustaceans				
Amphipod, <i>Gammarus pseudolimnaeus</i>	67,000	50	96 h	3
Freshwater prawn, <i>Macrobrachium lamarrei</i>	1840	50	96 h	4
Cladoceran, <i>Daphnia magna</i>	435	50	24 h	5
Fish				
Climbing perch, <i>Anabas</i> sp.	75,000	50	96 h	16
Mud skipper, <i>Boleophthalmus dussumieri</i>	30,500–85,000	50	96 h	6, 17
Golden shiner, <i>Notemigonus crysoleucas</i>	55,000	50	96 h	18
Rainbow trout, <i>Oncorhynchus mykiss</i>				
Weight 0.2 g				
Water pH 7.8	12,200	50	96 h	7
Water pH 7.0	7600	50	96 h	7
Water pH 6.5	3400	50	96 h	7
Weight 25 g				
Water pH 7.8	65,500	50	96 h	7
Water pH 7.0	45,000	50	96 h	7
Water pH 6.5	20,200	50	96 h	7
Fish				
2 spp.	17,600–118,000	50	96 h	8
3 spp.				
Softwater	<18,000	50	96 h	9
Hardwater	>133,000	50	96 h	9
Salmon fingerlings, <i>Oncorhynchus</i> sp.	200	53	12 w	9
Goldfish, <i>Carassius auratus</i>	110,000	50	96 h	10
Water hardness, in mg CaCO_3/L				
20	37,500	50	96 h	3
220	>90,000	50	96 h	3
Channel catfish, <i>Ictalurus punctatus</i>				
Age 4 weeks	1500	50	30 days	19
Age 4 weeks	14,800	50	96 h	19
Bluegill, <i>Lepomis macrochirus</i>				
Water hardness, in mg CaCO_3/L				
20	118,000	50	96 h	3
44	113,000	50	96 h	3
45	110,000–170,000	50	96 h	3
120	213,000	50	96 h	3
171	130,000–135,000	50	96 h	3
360	133,000	50	96 h	3
Striped bass, <i>Morone saxatilis</i>	30,400	50	96 h	3

Table 2.4 (continued) Acute Toxicities of Hexavalent and Trivalent Chromium to Aquatic Life

Chemical Species, Ecosystem, Taxonomic Group, Organism, Modifiers, and Other Information	Concentration ($\mu\text{g/L}$)	Percent Dead	Duration of Test^a	References^b
Fathead minnow, <i>Pimephales promelas</i>				
Age 3–14 days	900 (100–1600)	50	30 days	19
Age 3–14 days	23,900	50	96 h	19
Age 1–7 days	<12,000	0	7 days	20
Age 1–7 days	12,000–24,000	some	7 days	20
Guppy, <i>Poecilia reticulata</i>				
Adult	19,200	50	240 h	21
Adult	28,000	50	125 h	21
Adult	150,000	50	7 h	21
Marine				
Molluscs, 3 spp.	14,000–105,000	50	96 h	3
Annelids				
Polychaetes				
<i>Neanthes arenaceodentata</i>	550	50	28 d	11
<i>N. arenaceodentata</i>	200	50	56 d	11
<i>Nereis virens</i>	1000	50	21 d	11
<i>Capitella capitata</i>	280	50	28 d	11
<i>Capitella capitata</i>	5000	50	96 h	11
4 spp.	2000–7500	50	96 h	3
Echinoderms				
Starfish, <i>Asterias forbesi</i>	32,000	50	96 h	3
Crustaceans				
7 spp.	2000–98,000	50	96 h	3
Copepod, <i>Tisbe holothuriae</i>	8100	50	48 h	12
Copepod, <i>Acartia clausi</i>	8830–19,270	50	48 h	13
Blue crab, <i>Callinectes sapidus</i>				
Early life stages	930	50	96 h	14
Early life stages	320	50	40 d	14
Fish				
Small-mouthed hardy head,				
<i>Atherinasoma</i>	36,000	50	96 h	8
<i>microstoma</i>	19,300	0	168 h	8
Yellow-eye mullet,				
<i>Aldrichetta</i>	24,000	50	96 h	8
<i>forsteri</i>	17,900	0	96 h	8
Atlantic silverside, <i>Menidia menidia</i>				
Larva	12,400–14,300	50	96 h	3
Juvenile	20,100	50	96 h	3
Mummichog, <i>Fundulus heteroclitus</i>	91,000	50	96 h	3
Speckled sanddab, <i>Citharichthys stigmaeus</i>	30,000–31,000	50	96 h	3
TRIVALENT CHROMIUM				
Freshwater				
Molluscs				
Snail, <i>Amnicola</i> sp.	8400	50	96 h	3
Annelids				
Worm, <i>Nais</i> sp.	9300	50	96 h	3
Arthropods				
Cladoceran, <i>Daphnia magna</i>				
Water hardness, in mg CaCO ₃ /L				
48	2000	50	96 h	3
52	16,800	50	96 h	3

Table 2.4 (continued) Acute Toxicities of Hexavalent and Trivalent Chromium to Aquatic Life

Chemical Species, Ecosystem, Taxonomic Group, Organism, Modifiers, and Other Information	Concentration ($\mu\text{g/L}$)	Percent Dead	Duration of Test ^a	References ^b
99	27,400	50	96 h	3
110	26,300	50	96 h	3
195	51,400	50	96 h	3
215	58,700	50	96 h	3
Amphipod, <i>Gammarus</i> sp.	3200	50	96 h	3
Insects, 4 spp.	2000–64,000	50	96 h	3
Fish				
Climbing perch	120,000	50	96 h	16
9 spp.	3300–71,900	50	96 h	3
3 spp.				
Soft water	<3000	50	96 h	9
Hard water	72,000	50	96 h	9
Salmon fingerlings	200	0	12 w	9
Rainbow trout				
Juveniles	4400	50	96 h	15
Eggs	495	100	30 d	15
Fathead minnow				
Water hardness, mg CaCO_3/L				
20	5070	50	96 h	3
203	7000–29,000	50	96 h	3
360	67,400	50	96 h	3
Marine				
Molluscs				
American oyster, <i>Crassostrea virginica</i>	10,300	50	96 h	3
Annelids				
Polychaete, <i>Neanthes arenaceodentata</i>	12,500	0	21 d	11
Crustaceans				
Crab, <i>Sesarma haematocheir</i> , zoea	56,000	50	96 h	3
Copepod, <i>Acartia clausi</i>	17,000	0	48 h	13
Fish				
Yellow-eye mullet	53,000	50	96 h	8
2 spp.	3300–7500	50	96 h	8

^a Abbreviations: h = hour; d = day; w = week.^b 1, Mangi et al. 1978; 2, Buikema et al. 1974; 3, USEPA 1980; 4, Marti et al. 1983; 5, Jouany et al. 1982; 6, Krishnaja and Rege 1982; 7, Van der Putte 1981b; 8, Negilski 1976; 9, Steven et al. 1976; 10, Riva et al. 1981; 11, Reish 1977; 12, Moraitou-Apostolopoulou and Verriopoulos 1982a; 13, Moraitou-Apostolopoulou and Verriopoulos 1982b; 14, Bookhout et al. 1984; 15, Stevens and Chapman 1984; 16, Venungopal and Reddy 1992b; 17, Kundu et al. 1995; 18, Hartwell et al. 1989; 19, Gendusa et al. 1993; 20, Pickering and Lazorchak 1995; 21, Khangarot and Ray 1990.

or synergistic effects, as was the case with nickel salts in acute toxicity to guppies (Khangarot and Ray 1990). More research is needed to fully elucidate chromium's mode of action in solution. The organisms most sensitive to Cr^{+6} , as judged by 96-h LC50 values, were freshwater crustaceans and rotifers, and marine crustaceans, for which LC50 values were 445 to 3100 $\mu\text{g/L}$. Longer exposures of 28 to 84 days produced LC50 values of 200 to 500 $\mu\text{g/L}$ (Table 2.4). Other investigators had confirmed that Cr^{+6} is more toxic to freshwater daphnids and teleosts in water of comparatively low alkalinity, low pH, and low total hardness (Steven et al. 1976; Muller 1980). In marine teleosts, the toxicity of Cr^{+6} increased at elevated temperatures; furthermore, chromium was additive in toxicity when present as a component in a complex mixture of cadmium, zinc, and Cr^{+6} salts, (Negilski 1976).

For trivalent chromium and freshwater biota, toxicity was significantly increased in comparatively soft waters; this pattern was especially pronounced for daphnids (Table 2.4). Among freshwater teleosts, survival was reduced at comparatively low pH (U.S. Environmental Protection

Table 2.5 Maximum Acceptable Toxicant Concentration (MATC) Values for Hexavalent and Trivalent Chromium to Aquatic Life Based on Life Cycle or Partial Life Cycle Exposures

Chemical Species, Ecosystem, Organism	MATC ($\mu\text{g/L}$, ppb)	Reference ^a
HEXAVALENT CHROMIUM		
Freshwater		
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Water hardness, mg CaCO_3/L		
34	50–110	1, 7
45	200–350	2
Fish, 7 species, embryo-larval stages in soft water	73–2167	6
Lake trout, <i>Salvelinus namaycush</i>	110–194	1, 7
Channel catfish, <i>Ictalurus punctatus</i>	150–310	1, 7
Brook trout, <i>Salvelinus fontinalis</i>	200–350	2
White sucker, <i>Catostomus commersoni</i>	290–538	1
Bluegill, <i>Lepomis macrochirus</i>	522–1122	1, 7
Fathead minnow, <i>Pimephales promelas</i>	>1000–3950	3, 7
Northern pike, <i>Esox lucius</i>	538–963	1
Walleye, <i>Stizostedion vitreum</i>	>2161	1
Saltwater		
Polychaete worm, <i>Neanthes arenaceodentata</i>	17–38	4
Mysid shrimp, <i>Mysidopsis bahia</i>	88–198	2
TRIVALENT CHROMIUM		
Freshwater		
Rainbow trout	30–157	5, 7
Cladoceran, <i>Daphnia magna</i>	47–93	2
Fathead minnow	750–1400	2

^a 1, Sauter et al. 1976; 2, USEPA 1980; 3, Pickering 1980; 4, Reish 1977; 5, Stevens and Chapman 1984; 6, Dave et al. 1987; 7, Holdway 1988.

Agency [USEPA] 1980). Also, organisms exposed previously to Cr^{+3} salts were not unusually sensitive or resistant when subjected to additional Cr^{+3} , suggesting that they were unable to acclimatize or to become sensitized to Cr^{+3} (Stevens and Chapman 1984). As judged by 96-h LC50 values, Cr^{+3} was toxic to sensitive freshwater organisms at concentrations of 2000 to 3000 $\mu\text{g/L}$, or slightly less toxic than Cr^{+6} (Table 2.4). Toxicity of Cr^{+3} , like that of Cr^{+6} increased with increasing exposure in rainbow trout (*Oncorhynchus mykiss*). However, Cr^{+3} was significantly less toxic than Cr^{+6} in freshwater to salmon fingerlings, and was dramatically less toxic than Cr^{+6} to polychaetes and crustaceans (but not to molluscs or teleosts) in saltwater (Table 2.4).

Maximum acceptable toxicant concentrations (MATC) of chromium to aquatic life were derived from life cycle or partial life cycle exposures and expressed as the highest concentration tested having no significant adverse effect on the characteristics measured — usually survival, growth, and reproduction — and the lowest concentration at which these effects were observed. For chromium and freshwater teleosts, MATC values ranged from as low as 51 to 105 $\mu\text{g/L}$ in rainbow trout to as high as 1000 to 31,950 $\mu\text{g/L}$ in fathead minnows (Table 2.5). The most sensitive saltwater organism tested was a polychaete worm with a MATC range of 17 to 38 $\mu\text{g/L}$ (Table 2.5). For Cr^{+3} the MATC range for freshwater organisms was 47 to 1400 $\mu\text{g/L}$, which was quite similar to that for Cr^{+6} for freshwater life. No MATC data were available for Cr^{+3} and marine biota.

2.5.3 Terrestrial Invertebrates

Data on toxicity of chromium to terrestrial invertebrates are sparse. Studies conducted in India showed that a concentration of 10 to 15 mg/L of Cr^{+6} in irrigation water, when applied to soils for agricultural purposes, was lethal to two species of earthworms in 58 to 60 days (Soni and Abbasi 1981; Abbasi and Soni 1983).

2.5.4 Mammals and Birds

Acute and chronic adverse effects of chromium on warm-blooded organisms are caused mainly by Cr⁺⁶ compounds. There is little conclusive evidence of toxic effects caused by Cr⁺² or Cr⁺³ compounds (Langard and Norseth 1979). Most investigators agree that chromium in biological materials is probably always in the trivalent state, that greatest exposures to Cr⁺³ in the general human population are through the diet (but no adverse effects have been reported from such exposures), and that no organic trivalent chromium complexes of toxicological importance have been described. Studies with guinea pigs (*Cavia spp.*) fed Cr⁺³ for 21 weeks at concentrations up to 50 mg/kg dietary Cr⁺³ showed no adverse effects (Preston et al. 1976). Domestic cats were apparently unaffected after exposure to aerosol levels of 80 to 115 mg Cr⁺³/m³ for 1 h daily for 4 months, or after consuming diets with high amounts of chromic (Cr⁺³) salts over a similar period (Langard and Norseth 1979). When chromium was administered by injection, trivalent salts were substantially less toxic than hexavalent salts in producing effects in embryos of golden hamsters (Gale 1978). A similar pattern was evident in mice and in embryos of chickens. The LD50s for mice were 260 mg/kg body weight for Cr⁺³, but only 5 mg/kg body weight for Cr⁺⁶ (Steven et al. 1976). In rats (*Rattus sp.*), route of exposure and compound tested were important. Rats given a single dermal dose of various hexavalent chromium compounds had LD50 values that ranged from 400 mg Cr/kg BW for sodium dichromate to 680 mg Cr/kg BW for ammonium dichromate; potassium dichromate and sodium chromate were intermediate in toxicity (Outridge and Scheuhammer 1993). When the same four hexavalent chromium compounds were administered via inhalation, LD50s after 4 h of exposure ranged between 33 and 82 mg Cr/m³; females were more sensitive than males (Outridge and Scheuhammer 1993; USPHS 1993).

Steven et al. (1976), in studies with Cr⁺⁶ in dogs, showed that 100 mg/kg in food for 3 months was fatal, that 11.2 mg/L in drinking water was not lethal over a 4-year period (although significant accumulation was observed), and that 6.0 mg/L in drinking water for 4 years had no measurable effects. In rats, 1000 mg/kg dietary Cr⁺⁶ represented the toxic threshold, but all animals survived 134 mg/L of Cr⁺⁶ in drinking water for 3 months (Steven et al. 1976). For most mammalian experimental animals, including mice (*Mus sp.*), dogs (*Canis familiaris*), rabbits (*Oryctolagus sp.*), cats (*Felis domesticus*), and guinea pigs, the minimum injected fatal dose of Cr⁺⁶ ranged from 1 to 5 mg/kg body weight, although doses of 0.2 to 0.5 mg/kg body weight produced marked kidney damage (Steven et al. 1976). Repeated sublethal injections of Cr⁺⁶ did not promote tolerance in mice, but rather decreased the minimum lethal dose, suggesting that the animals were unable to develop tolerance to repeated chromium exposures (Steven et al. 1976). Investigators have not yet been able to identify a specific hexavalent chromium compound, or group of compounds, that could account for the most pronounced biological activity (Langard and Norseth 1979). A lethal oral dose of Cr⁺⁶ for a 14-year-old boy was estimated to be 10 mg/kg body weight — much lower than that tolerated by test animals on a repeated basis over a period of several months (Steven et al. 1976). A 44-year-old man who ingested 4.1 mg Cr⁺⁶/kg body weight as chromic acid died of severe gastrointestinal hemorrhage one month after ingestion (USPHS 1993).

Domestic chickens (*Gallus sp.*) appear to be more resistant than mammals. No adverse effects were observed in chickens exposed to 100 mg/kg dietary Cr⁺⁶ in a 32-day study (Rosomer et al. 1961), although embryolethal and teratogenic effects have been observed in the range of 0.2 mg/kg (Gilani and Marano 1979) to 1.7–22.9 mg/kg (Ridgeway and Karnofsky 1952), depending on the method of administration. For chicken embryos, the LD50 values (mg/kg body weight) were 22.9 for Cr⁺³ and 1.7 for Cr⁺⁶ (Ridgeway and Karnofsky 1952).

2.6 SUBLETHAL EFFECTS

2.6.1 General

Under laboratory conditions, chromium is mutagenic, carcinogenic, and teratogenic to a wide variety of organisms, and Cr⁺⁶ has the greatest biological activity. However, information is lacking

on the biological activities of water-soluble Cr⁺³ compounds, organochromium compounds, and their ionic states. Aquatic plants and marine polychaete worms appear to be the most sensitive groups tested. In exposures to Cr⁺⁶, growth of algae was inhibited at 10.0 µg/L, and reproduction of worms at 12.5 µg/L. At higher concentrations, Cr⁺⁶ is associated with abnormal enzyme activities, altered blood chemistry, lowered resistance to pathogenic organisms, behavioral modifications, disrupted feeding, histopathology, osmoregulatory upset, alterations in population structure and species diversity indices, and inhibition of photosynthesis. Not all sublethal effects observed were permanent, but the potential for acclimatization of organisms to chromium is not well documented. The great variability among species and tissues in the accumulation or concentration of chromium is attributed partly to the route of administration, partly to the concentration of chromium and its chemical species, and partly to numerous biotic and physicochemical modifiers. High accumulations of chromium have been recorded among organisms from the lower trophic levels, but there is little evidence of biomagnification through food chains. Marine bivalve molluscs, for example, accumulated measurable concentrations at ambient water concentrations of 5.0 µg/L of Cr⁺⁶, but the significance of chromium residues in molluscs and other organisms is not well understood. Depuration of accumulated chromium among organisms differs markedly, but usually follows a complex multicompartmental excretion pattern.

2.6.2 Aquatic Organisms: Freshwater

Bacteria

The role of sewage bacteria in chromium kinetics and cycling is unresolved and promises to be a fruitful field of research. Of 362 bacterial isolates from Cr⁺⁶ liquid sanitary sewage and chemical waste sludges, only 1 — an isolate of *Arthrobacter* sp. — could tolerate 400 mg/L of Cr⁺⁶ (Coleman and Paran 1983). However, this isolate could not effectively accumulate chromium at comparatively low ambient levels of 5 mg/L of Cr⁺⁶, whereas *Agrobacter* sp., another isolate, could. Hexavalent chromium in a wide array of forms showed dose-dependent responses for mutagenic activity in the bacterium *Salmonella typhimurium* (Del Carratore et al. 1984). Moreover, among 56 metal compounds tested, Cr⁺⁶ elicited the strongest mutagenic responses in *Bacillus subtilis* (Hatherill 1981). In some tests, Cr⁺³ was genetically active, but only when present as a stable organic complex (Del Carratore et al. 1984).

Algae and Macrophytes

Growth of freshwater algae was reduced at Cr⁺⁶ concentrations of 10 µg/L for *Chlamydomonas reinhardtii*, 20 µg/L for *Chlorella pyrenoidosa*, and >45 µg/L for other species tested. Effects were most pronounced in water of low alkalinity (USEPA 1980; Wong and Trevors 1988; Outridge and Scheuhammer 1993). Frond growth of the common duckweed, *Lemna minor*, the most sensitive aquatic plant tested, was reduced at 10 µg Cr⁺⁶/L in 14 days (Mangi et al. 1978). Jouany et al. (1982) reported that a green alga, *Chlorella vulgaris*, biomagnified Cr⁺⁶ from the medium about 1000 times in 28 days at ambient concentrations of 300 µg/L; growth was inhibited at 445 µg Cr⁺⁶/L in 96 h; and adenosine triphosphate (ATP) production was reduced at 470 µg/L in 24 h. At 10 µg Cr⁺⁶/L in the medium, bioconcentration factors for the chlorophytes *Hydrodictyon reticulatum* and *Oedogonium* sp. ranged from 200 to 600 in 14 days (Mangi et al. 1978). Accumulation of chromium by living and dead plant tissue is extensive, uptake linearly approximating concentration on a logarithmic basis (Mangi et al. 1978). Trivalent chromium is far less effective than Cr⁺⁶ in producing root weight inhibition in Eurasian watermilfoil, *Myriophyllum spicatum*: 9900 µg Cr⁺³/L vs. 1900 µg Cr⁺⁶/L (USEPA 1980). A similar case is made for terrestrial plants, such as barley, wherein hexavalent chromium at 100 µg/L and trivalent chromium at 1000 µg/L produced comparable growth inhibition (Outridge and Scheuhammer 1993).

Invertebrates

Hexavalent chromium was associated with adverse effects in invertebrates of widely separated taxa:

- Reduced survival and fecundity of the cladoceran *Daphnia magna* at a concentration of 10 µg/L and exposure for 32 days (USEPA 1980)
- Growth inhibition of the protozoan *Chilomonas paramecium* at 1100 to 3000 µg/L at temperatures of 10 to 30°C during exposures of 19 to 163 h (Honig et al. 1980)
- Abnormal movement patterns of larvae of the midge *Chironomus tentans* at 100 µg/L in 48 h (Catalan 1982)
- Temporary decrease in hemolymph glucose levels in the freshwater prawn *Macrobrachium lamarrei* surviving 1840 µg/L Cr⁺⁶ for 96 h (Murti et al. 1983)

Trivalent chromium was less effective than Cr⁺⁶ in reducing fecundity of *Daphnia magna*: 44 µg Cr⁺³/L vs. 10 µg Cr⁺⁶/L (USEPA 1980). Annelid worms (*Tubifex* sp.) accumulated about 1 mg total chromium/kg whole body during exposure for 2 weeks in sediments containing 175 mg Cr⁺³/kg, suggesting that benthic invertebrates have only a limited ability to accumulate chromium from sediments or clays (Neff et al. 1978).

Fishes

Among sensitive species of freshwater teleosts, Cr⁺⁶ concentrations of 16 to 21 µg/L in the medium resulted in reduced growth of rainbow trout and chinook salmon (*Oncorhynchus tshawytscha*) fingerlings during exposure of 14 to 16 weeks, and altered plasma cortisol metabolism in rainbow trout after 7 days (USEPA 1980). Rainbow trout avoid water containing 28 µg Cr⁺⁶/L; however, avoidance thresholds increased linearly if the fish were pre-exposed to 800 µg Cr⁺⁶/L for 7 to 20 weeks (Anestis and Neufeld 1986). Locomotor activity in bluegills (*Lepomis macrochirus*) increased after 2 weeks in 50 µg Cr⁺⁶/L (USEPA 1980). The avoidance threshold for golden shiner (*Notemigonus crysoleucas*) is 73 µg Cr⁺⁶/L (Hartwell et al. 1989). Exposure of cichlids (*Tilapia sparrmanii*) to 98 µg Cr⁺⁶/L for 96 h led to clotting defects that caused internal bleeding, with effects exacerbated by increasing water pH in the range pH 4 to 9 (van Pittius et al. 1992; Wepener et al. 1992). Long-term exposure of rainbow trout for 180 days to high, but environmentally realistic, concentrations of 200 µg Cr⁺⁶/L resulted in elevated levels of chromium in kidney (3.5 mg/kg fresh weight), liver (2.0), and muscle (0.6). After 90 days in chromium-free media, chromium levels were 1.6, 1.3, and 0.5 mg/kg FW, respectively (Calamari et al. 1982). Time required to reach median asymptotic uptake ranged from 36 to 55 days for various tissues; extrapolated values for almost complete equilibrium were 237 to 365 days (Calamari et al. 1982). In seaward-migrating coho salmon (*Oncorhynchus kisutch*), salinity tolerance and serum osmolality were impaired during exposure to 230 µg Cr⁺⁶/L for 4 weeks (Sugatt 1980a). In juvenile coho salmon, disease resistance and serum agglutinin production both decreased after 2 weeks in water containing 500 µg/L (Sugatt 1980b).

At high environmental concentrations of Cr⁺⁶ (i.e., 2.0 mg/L in water) and at alkaline pH, concentrations in rainbow trout tissues were greatest in gill, liver, kidney, and digestive tract. After transfer of the fish to chromium-free media, residues tended to remain high in kidney and liver. Concentration in gill tissues tended to be greater at pH 7.8 than at pH 6.5 (Van der Putte et al. 1981a). Studies with perfused gills showed that the transfer of chromium was directly coupled with the transfer of oxygen from the external solution to the internal perfusion medium and that this transfer was significantly more rapid at pH 6.5 than at alkaline pH (Van der Putte and Part 1982). Uptake rate of Cr⁺⁶ was rapid, equilibrium usually being reached in 2 to 4 days of exposure for various tissues, except for gill, which continued to accumulate chromium with increasing exposure

at acidic pH. In rainbow trout, the excretion pattern was biphasic. The biological half-life of the short-lived component (34% of the total chromium) was 1.0 day, and that of the long-lived component was 25.6 days (Van der Putte et al. 1981a). Exposure of isolated intestine tissues of rainbow trout to chromium leads to an initial dose-dependent inhibition of alkaline phosphatase activity; this enzyme is sensitive to chromium ion, especially Cr⁺⁶ (Boge et al. 1992).

Various effects are reported in freshwater teleosts following exposure to comparatively high sublethal concentrations of hexavalent chromium. In the snakehead (*Channa punctatus*), enzyme activities were altered in a wide variety of organs and tissues after exposure for 30 days to 2.6 mg/L (Sastry and Sunita 1984). The effects became life threatening after exposure for 120 days (Sastry and Tyagi 1982; Sastry and Sunita 1982, 1983). Gill histopathology was documented in the air-breathing catfish (*Saccobranchus fossilis*) after immersion in 5.6 mg Cr⁺⁶/L for 7 days (Khangarot and Tripathi 1990, 1992). Growth rate of larvae of the fathead minnow (*Pimephales promelas*) was reduced at 6 mg/L during exposure for 7 days (Pickering and Lazorchak 1995). The rudd (*Scardinus erythrophthalmus*), exposed to Cr⁺⁶ for 24 h, did not accumulate detectable levels of chromium in tissues during exposure to 16 mg/L, but did during exposures to 20 mg/L; the kidney contained the highest residues — 10.3 mg Cr/kg fresh weight (Van Hoof and Van San 1981). Climbing perch (*Anabas scandens*) exposed for 30 days to 25 mg Cr⁺⁶/L or 25 mg Cr⁺³/L showed depletion of glycogen and glucose reserves of liver and kidney, and decreased activity of respiratory enzymes (various dehydrogenases) and ATPases; in all cases, Cr⁺⁶ produced the greater effect (Venugopal and Reddy 1992a, 1992b, 1993). In the mudskipper (*Boleophthalmus dussumieri*), chromosomal aberrations in the gill increased after injection of 1.0 mg/kg body weight or exposure to 24 mg/L in the medium for 24 h (Krishnaja and Rege 1982). Mudskippers exposed to 30 to 60 mg Cr⁺⁶/L for 72 h had a dose-duration inhibition in specific activity of brain and muscle Na⁺, K⁺-ATPase and other ATPases (Kundu et al. 1995).

Chromium is considered to be a cofactor for insulin activity and part of an organic glucose tolerance factor (Shiau and Chan 1993). In common carp (*Cyprinus carpio*) fed low-protein diets, the addition of chromium chloride salts in the diet (equivalent to 60 µg Cr⁺³/kg BW) or injected intraperitoneally (2.5 µg/kg BW) significantly decreased plasma glucose levels (Hertz et al. 1989). Trivalent chromium supplementation in the diet improved glucose utilization in carp and tilapia when fed diets for 10 weeks containing 2 mg Cr/kg ration equivalent to 5% BW daily. Chromic oxide was more effective than chromium chloride, and both were more effective than sodium chromate tetrahydrate (Shiau and Chan 1993). Chromic oxide fed in the diet for 12 weeks at 0.5% and 2% to tilapia fingerlings improved glucose utilization and nutrient digestibility; the 0.5% diet was more efficient than the 2% diet (Shiau and Liang 1995).

Chromium uptakes and effects in teleosts were modified significantly by many biological and abiotic variables, including water temperature and pH, the presence of other contaminants or compounds, and sex and tissue specificity. In rainbow trout, only males showed significant changes in liver enzyme activity during exposure to 200 µg Cr⁺⁶/L for 6 months; the effects were intensified by the presence of nickel and cadmium salts in solution (Ariollo et al. 1982). Rainbow trout are able to regulate chromium somewhat, either actively, by reduced absorption or increased excretion, or passively, by the limitation of binding sites for chromium *in vivo* (Buhler et al. 1977). Tests with goldfish (*Carassius auratus*) and high Cr⁺⁶ concentrations indicated that lethal and sublethal effects were more pronounced at comparatively high water temperatures and reduced pH; further, chromium residue levels were abnormally high in dead or moribund fish, suggesting that residue values from dead or dying fish should be interpreted with extreme caution (Riva et al. 1981). In rainbow trout, acute chromium poisoning caused morphological changes in gills, kidney, and stomach tissues at pH 7.8, but only in the gills at pH 6.5 (Van der Putte et al. 1981b). Chromium uptake in trout increased when 10 µg/L of ionic cadmium was present in solution (Calamari et al. 1982) — again demonstrating that uptake patterns are not necessarily predictable for single components in complex mixtures.

2.6.3 Aquatic Organisms: Marine

Algae and Macrophytes

Algae and higher plants accumulated chromium from seawater by factors up to 8600 (Van As et al. 1973), and from solutions containing 50 mg/L of chromium by a factor of 18 in 48 h (Sivalingam 1978). Algae also accumulated chromium from sewage sludge, showing increases in chromium burdens of 25 to 60 mg/kg dry weight (Montgomery et al. 1978). The unusually high chromium concentrations observed in some species of algae and macrophytes from Narragansett Bay, Rhode Island (Phelps et al. 1975) and from Puerto Rico (Bernhard and Zattera 1975) almost certainly came from chromium wastes discharged from electroplaters (in Narragansett Bay) and from other anthropogenic sources (in Puerto Rico). A similar situation probably exists wherever grossly elevated chromium levels are observed.

Although chromium is abundant in primary producers, there is little evidence of biomagnification through marine food chains consisting of herbivores and carnivores (Osterberg et al. 1964). Baptist and Lewis (1969) followed the transfer of assimilated and unassimilated radiochromium through an experimental food chain that included phytoplankton, brine shrimp, postlarval fish, and adult fish. When chromium was successively transferred through each of the four trophic levels, concentrations declined after each transfer. Comparisons of the results from the food chain with laboratory studies on chromium uptake from seawater suggest that the food chain, despite the successive declines, was generally the more efficient pathway for uptake of chromium by all trophic levels.

Among sensitive species of marine algae, concentrations of 10 µg/L of Cr⁺⁶ partly inhibited growth of *Olisthodiscus lutens*. All cultures, including those in which growth was inhibited, contained viable, active (>75%) cells at the end of 10 days. Inhibitory effects were reversed by chelators such as EDTA (Mahoney 1982), suggesting that naturally occurring ligands and sequestering agents in seawater may alleviate the toxicity of Cr⁺⁶, and perhaps other metals. In the giant kelp (*Macrocystis pyrifera*), photosynthesis was inhibited 20% in 5 days at 1000 µg/L of Cr⁺⁶, and 50% in 4 days at 5000 µg/L (USEPA 1980); this kelp appears to be one of the more resistant aquatic plants.

Molluscs

Edible tissues of commercially important North American molluscs contained 0.1 to 0.6 mg Cr/kg fresh weight (Hall et al. 1978). Although this concentration is in general agreement with molluscan data from other geographic areas (Eisler 1981), Shuster and Pringle (1968) reported values (mg Cr/kg fresh weight) in edible portions as high as 3.4 in oysters (*Crassostrea virginica*), 5.8 in hardshell clams (*Mercenaria mercenaria*), and 5.0 in softshell clams (*Mya arenaria*). The ability of marine molluscs to accumulate chromium far in excess of that in ambient seawater was documented by Papadopoulou (1973), who found that the chromium concentration in 5 species of bivalves from Greek waters exceeded that in seawater by 16,000 times (*Pinna nobilis*) to 260,000 times (*Astralium rogosum*). No deleterious health effects have been reported among consumers of molluscs that contained occasional high chromium residues. Anthropogenic and natural chromium gradients in sediments or the water column were reflected in the wide range of values reported for this element in field collections of clams (Phelps et al. 1975; Eisler et al. 1978) and mussels (Alexander and Young 1976; Fowler and Oregoni 1976; Lande 1977; Karbe et al. 1977).

Two factors known to modify chromium accumulations in molluscs are the weight of the organism and the salinity of the medium. Concentrations of chromium in clams were reported to decrease with increasing body weight (Eisler et al. 1978) and increasing salinity (Olson and Harrel 1973). Accumulation of chromium by oysters (*Crassostrea gigas*) was independent of sediment chromium levels and dependent on organism size — suggesting some homeostatic regulation of

this metal (Ayling 1974). In a 20-week laboratory study of chromium accumulation rates by oysters (*C. virginica*), Shuster and Pringle (1969) continuously subjected the animals to seawater solutions containing 50 or 100 µg Cr⁺⁶/L. After 5, 10, or 20 weeks in 50 µg/L, maximum whole body concentrations (mg Cr/kg fresh weight) were 2.4, 3.7, and 6.3, respectively (up from control values of <0.12); in 100 µg/L, the values were 4.4 (5 weeks), 6.4 (10 weeks), and 11.5 (20 weeks). Preston (1971) concluded that *C. virginica*, under laboratory conditions, accumulated chromium more readily by direct absorption from the medium than from ingestion of radiochromium-labeled algae (*Chlamydomonas* spp.). In natural environments, however, chromium concentration is likely to be greater in the food supply than in the water. As a consequence, food might be the primary source of chromium to oysters, even though accumulation occurs more readily by direct absorption (Preston 1971).

Clams, oysters, and mussels accumulate chromium from the medium or from contaminated sediments at comparatively low concentrations. For example, oysters subjected to 5.0 µg Cr⁺⁶/L for 12 weeks contained 3.1 mg Cr/kg dry weight in soft parts and retained 52% of the accumulated chromium after they were transferred to chromium-free seawater for 28 weeks (Zaroogian and Johnson 1983). Mussels (*Mytilus edulis*) subjected to the same dose-time regimen contained 4.8 mg/kg, but retained only 39% after 28 weeks of depuration. Both oysters and mussels contained higher residues after exposure to 10.0 µg Cr⁺⁶/L for 12 weeks — 5.6 and 9.4 mg Cr/kg dry weight in soft parts, respectively — and both contained substantial (30 to 58%) residues after 28 weeks in a chromium-free environment (Zaroogian and Johnson 1983). In studies with mussels and softshell clams (*Mya arenaria*), Capuzzo and Sasner (1977) demonstrated that chromium in New Hampshire sediments (contaminated with Cr⁺³ from tannery wastes) was bioavailable to clams by diffusion from seawater, and that both diffusion and particulate uptake were important pathways for mussels. Accumulation was observed at sediment chromium concentrations as low as 150 mg/kg. Kaolinite sediments containing up to 1200 mg Cr⁺³/kg produced the most pronounced adverse effects on filtration rates and ciliary activity of bivalve molluscs, leading the authors to conclude that chromium that has accumulated in areas affected by industrial wastes might have serious consequences to filter-feeding bivalves.

It is emphasized that Cr⁺³, probably because of its very low solubility in seawater, appears to have a much lower bioavailability to most groups of marine animals than Cr⁺⁶, which is more water soluble (Carr et al. 1982). The clam *Rangia cuneata* appears to be an exception: it accumulated up to 19 mg Cr/kg in soft parts, on a dry weight basis, during exposure for 16 days to chromium-contaminated muds, and retained most of it for an extended period; the estimated biological half-time was 11 days (Carr et al. 1982). In general, benthic invertebrates rarely accumulate chromium from contaminated sediments (82 to 188 mg Cr⁺³/kg); only a few examples have been recorded (Neff et al. 1978).

Nematodes

Representatives of this phylum have been used extensively as indicators of stressed environments. Population structure and species diversity of free-living nematodes inhabiting sediments in the New York Bight were moderately influenced by the heavy-metal content of sands. In medium-grained sands, species diversity was inversely correlated with increased concentrations of chromium and other metals. Sands containing 3.0 to 21.5 mg Cr/kg were also marked by high relative abundances of one or two nematode species; the tolerance of these species to chromium stress probably exceeded that of the normal nematode inhabitants of such sediments (Tietjen 1980).

Crustaceans

In general, chromium seldom exceeds 0.3 mg/kg fresh weight in edible crustacean tissues (Eisler 1981). The highest value (0.6 mg Cr/kg fresh weight) reported in muscle of rock crab (*Cancer*

irroratus) was from specimens collected near an ocean dump site receiving large quantities of metals. Digestive glands and gills from these crabs also contained the highest chromium residues for these tissues in crustaceans (Greig et al. 1977).

Sather (1967) observed that uptake and loss of radiochromium by the crab *Podophthalmus vigil* was independent of sex and eyestalk hormone influences. Most of the radiochromium accumulated in gills. Equilibrium was reached in gill and muscle in 2 to 3 days, but in midgut and hemolymph in 4 to 5 days. Iron interfered with chromium uptake and retention. Tennant and Forster (1969) demonstrated that chromium concentrated in setae, gills, and hepatopancreas of Dungeness crab (*Cancer magister*) and suggested that surface adsorption and physiological processes were both instrumental in chromium accumulation. Barnacles (*Balanus* sp.) incorporated Cr⁺⁶ in soft tissues up to 1000 times over ambient concentrations, reaching equilibrium in 7 days (biological half-life for some components was 120 days); however, Cr⁺³, which precipitates in seawater, was quickly removed by filtering activity, was not concentrated in soft tissues, and was rapidly excreted by way of the digestive system (van Weerelt et al. 1984).

Sediment chromium concentrations of 3200 mg/kg in the New Bedford (Massachusetts) Acushnet estuary, and 100 mg/kg in the New York Bight have been recorded (Doughtie et al. 1983). Massive cuticular lesions suggestive of shell disease characterized up to 30% of the lobsters, crabs, and shrimp collected from the New York Bight, and these lesions could also be induced in crustaceans exposed to New York Bight sediments in the laboratory. This shell disease syndrome has been induced in 41% of grass shrimp (*Palaemonetes pugio*) during exposure to 0.5 mg Cr⁺⁶/L for 28 days (Doughtie et al. 1983). It is proposed that chromium interferes with the normal functions of subcuticular epithelium, particularly cuticle formation, and subsequently causes structural weaknesses or perforations to develop in the cuticle of newly molted shrimp. Because of these chromium-induced exoskeletal deficiencies, a viaduct for pathogenic bacteria and direct chromium influx is formed that perpetuates the development of the lesion.

Of the 65,000 tons of chromium compounds used annually in exploratory oil drilling, a significant portion enters the marine environment through the discharge of used drilling muds. It has been estimated that more than 225 tons of drilling mud may be used in a single 3000-m well (Carr et al. 1982). One of the most frequently used muds in offshore drilling operations is a chrome lignosulphonate mud containing barium sulphonate, bentonite clay, and ferrochrome or chrome lignosulphonates (Carr et al. 1982). The bioavailability of chromium to grass shrimp from used chrome lignosulphonate drilling muds is most pronounced at the mud aqueous layers. At chromium concentrations of 248 µg/L in the mud aqueous fraction, grass shrimp accumulated 23.7 mg Cr/kg dry weight whole body after 7 days (Carr et al. 1982). Concentrations of drilling mud of 1% or greater in seawater were toxic to sensitive species of crustaceans (Neff et al. 1981). Uptake of 4 to 5 mg/kg was reported in grass shrimp exposed to sediments containing 188 mg Cr/kg (Neff et al. 1978). The toxicity of chromium-contaminated drilling muds to grass shrimp may sometimes be attributable to large residuals of petroleum hydrocarbons in the sediments (Conklin et al. 1983).

Annelids

Studies of uptake and excretion of Cr⁺³ by *Hermione hystrix* (Chipman 1967) showed that Cr⁺³ was not readily accumulated from seawater, owing to the formation of particles and surface adsorption phenomena. Furthermore, little accumulation was evident on contact with contaminated sediments. Hexavalent chromium in the medium was readily accumulated by *Hermione*; the process was slow and only small amounts were taken up in 19 days — i.e., 0.03 to 0.10 mg/kg fresh weight from media containing 3 to 10 µg Cr⁺⁶/L. Higher body burdens of 0.5 to 1.8 mg Cr/kg fresh body weight were reported at 100 to 500 µg Cr⁺⁶/L, but some deaths were noted at these concentrations. Chromium accumulation by *Hermione* is a passive process and directly related to Cr⁺⁶ concentration in the medium. At least two rates of biological loss are involved, one of 8 days and another of 123 days. Chipman (1967) concluded that most of the chromium accumulated by *Hermione* from

long exposure is bound in a body component having a slow turnover rate and an estimated biological half-life of about 123 days.

Uptake of Cr⁺⁶ from seawater has been reported for *Neanthes arenaceodentata*. Whole *Neanthes* contained 30.0 mg Cr/kg dry weight after exposure for 150 days in 30 µg Cr⁺⁶/L (Mearns and Young 1977) and 0.5 to 1.6 mg Cr/kg fresh weight after exposure for 440 days (Oshida et al. 1976). Both of these observations were similar to those of Chipman (1967), after adjustment for wet and dry weights. Concentrations as low as 12.5 µg Cr⁺⁶/L decreased brood size in *Neanthes* (Mearns et al. 1976; Oshida et al. 1976), although no significant body residues were evident. Uptake of Cr⁺⁶ by *Neanthes* was related to dose at low ambient chromium concentrations. Worms subjected to 2.6, 4.5, 9.8, or 16.6 µg Cr⁺⁶/L for 309 days contained 0.5, 0.7, 2.2, and 2.5 mg Cr/kg whole fresh organism, respectively (Oshida and Word 1982). There was no direct relationship between tissue concentration and brood size, suggesting that chromium in *Neanthes* attaches to proteins in the body wall, gut, and parapodial regions (Oshida and Word 1982).

Neanthes arenaceodentata is the most sensitive marine organism yet tested. In worms exposed to sublethal concentrations of Cr⁺⁶, feeding was disrupted after 14 days at 79 µg/L (USEPA 1980), reproduction ceased after 440 days (three generations) at 100 µg/L (Oshida et al. 1981), brood size was reduced after 309 to 440 days at 12.5 to 16.0 µg/L (Oshida et al. 1981; Oshida and Word 1982), and abnormalities in larval development increased after 5 months at 25 µg/L (Reish 1977). On the other hand, exposure for 293 days (two generations) in 50,400 µg Cr⁺³/L caused no adverse effects on survival, maturation time required for spawning, or brood size (Oshida et al. 1981). The polychaete *Capitella capitata* was more resistant than *Neanthes*; a decrease in brood size was noted only after exposure for 5 months to 50 and 100 µg Cr⁺⁶/L (USEPA 1980).

Echinoderms

With the exception of two sea urchin samples collected from Puerto Rico, most chromium residues reported in echinoderms have been less than 1.0 mg/kg dry weight (Eisler 1981). The exceptions — elevated levels of 24 and 43 mg/kg fresh weight of whole organism in Puerto Rican sea urchins — were not reflected in sea cucumber muscle from the same vicinity (Fukai 1965), and thus should be viewed with caution. Echinoderms from the United Kingdom and environs were comparatively low in chromium; concentrations were less than 0.46 mg Cr/kg dry weight whole organism (Riley and Segar 1970). Embryos of a sea urchin (*Anthocidaris* sp.) developed normally in solutions containing 3.2 to 4.2 mg Cr/L, but failed to develop at 8.4 to 10.0 mg Cr/L (Okubo and Okubo 1962; Kobayashi 1971). Larvae of another species of sea urchin (*Hemicentrotus* sp.) were more sensitive, showing abnormal development or dying within 24 h at concentrations of less than 1.0 mg Cr/L (Okubo and Okubo 1962). Hexavalent chromium at 6.0 mg/L was associated with abnormal development in embryos of *Anthocidaris crassispina* (Kobayashi 1977).

Fishes

Trivalent chromium is relatively innocuous to the gray mullet (*Chelon labrosus*). Mullet held for 60 days in aquaria with sediments containing 46 mg Cr⁺³/kg dry weight and fed diets containing 4.4 to 13.8 mg Cr⁺³/kg dry weight ration had normal growth, survival, macroscopic physiology, and behavior; however, when compared to controls (6.4 mg Cr/kg sediments, 0.3 to 0.9 mg/kg DW ration), liver concentrations were elevated: 34 mg/kg DW vs. 2 (Walsh et al. 1994). Trivalent chromium, as chromic oxide, in the diet has been used as an indigestible marker to measure nutrient digestibility in American lobsters and freshwater-reared Arctic char (*Salvelinus alpinus*). The addition of 1% trivalent chromium to the diet of seawater-reared Arctic char results in altered intestinal microflora and increased lipids in the feces (Ringo 1993), and suggests that Cr⁺³ use for this purpose be discontinued.

Individual tissues of most species of marine finfishes contained between 0.1 and 0.6 mg Cr/kg fresh weight (Hall et al. 1978). For still unexplained reasons, chromium concentrated in the scales of some species collected in Greek waters, values ranging up to 97.0 mg Cr/kg dry weight (Papadopoulou and Kassimati 1977). Chromium concentrations also vary significantly among different species of fish collected from the same geographic area. For example, muscle chromium concentration was 1430 times greater in a porgy (*Pachymetopan grande*) than in a goosefish (*Lophius piscatorius*) from the same collection (Van As et al. 1973).

Accumulation of chromium under controlled conditions has been documented for speckled sanddab, *Citharichthys stigmaeus* (Mearns and Young 1977) and Atlantic croaker, *Micropogon undulatus* (Baptist et al. 1970). Sanddabs held in seawater solutions containing 3 to 5 mg Cr⁺⁶/L contained up to 100 mg Cr/kg intestine (dry weight), 10 in liver, and 3 in muscle (Mearns and Young 1977). Sanddabs accumulated significant concentrations of chromium in various tissues during long-term exposure in seawater concentrations as low as 16 µg Cr⁺⁶/L (Mearns and Young 1977). Baptist et al. (1970), who studied the retention of radiochromium-51 in croakers following a single intraperitoneal injection, wrote that retention was expressed as two exponential rate functions: 70 days for the long-lived component and 20 days for the short-lived component.

2.6.4 Birds

Male domestic chickens fed diets containing up to 100 mg Cr⁺⁶/kg ration for 32 days showed no adverse effects in survival, growth, or food utilization efficiency (Rosomer et al. 1961). However, teratogenic effects were documented in chicken embryos after eggs had been injected with Cr⁺⁶. Deformities included short and twisted limbs, microphthalmia, exencephaly, everted viscera, growth stunting, and parrot beaks (Ridgeway and Karnofsky 1952; Gilani and Marano 1979). The highest incidence of teratogenic effects was observed at Cr⁺⁶ concentrations that caused some deaths, and when the administration route was through the chorioallantoic membrane as opposed to the yolk. No teratogenic effects were observed with Cr⁺³ salts (Ridgeway and Karnofsky 1952).

Young American black ducks (*Anas rubripes*) absorbed anionic chromium species more readily than cationic forms from the intestines, strongly indicating that ionic chromium state should be considered when avian dietary toxicity studies are being planned (Eastin et al. 1980). In another study with black ducks, adults were fed diets containing 0, 20, or 100 mg/kg anionic Cr⁺³ and ducklings from these pairs were fed the same diets for 7 days; tests of avoidance responses of the ducklings to a fright stimulus showed that the chromium had no significant effect on their behavior (Heinz and Haseltine 1981).

2.6.5 Mammals

Chromium is causally associated with mutations and malignancy (Leonard and Lawerys 1980; Norseth 1981; Nieboer and Shaw 1988; Yassi and Nieboer 1988; USPHS 1993; Shimada et al. 1998). Under appropriate conditions, chromium is a human and animal carcinogenic agent; its biological effects depend on chemical form, solubility, and valence. In general, nearly all Cr⁺⁶ compounds are potent mammalian mutagens and all forms of Cr⁺⁶ — both water-soluble and water-insoluble compounds — are respiratory carcinogens in humans; metallic chromium and Cr⁺³ are essentially nontoxic (Gale 1978; Nieboer and Shaw 1988; Yassi and Nieboer 1988). However, exposure to water-solubilized Cr⁺³ has caused cancers and dermatitis in workers and toxicity in rabbits (Hatherill 1981). In the chromate-producing industry, workers who developed respiratory cancer had been exposed to 30 to 1100 µg/m³ chromium in air for periods of 4 to 24 years, and workers producing chromate pigment who developed respiratory cancer had been subjected to an estimated Cr⁺⁶ exposure of 500 to 1500 µg/m³ for 6 to 9 years. Carcinogens released in the chromate manufacturing process have not yet been identified (Post and Campbell 1980). Levels as low as 10 µg/m³ of Cr⁺⁶ in air produced strong irritation in nasal membranes, even after short exposures.

In some persons whose lower respiratory tissues became chromium-sensitized, asthmatic attacks occurred at levels of Cr⁺⁶ as low as 2.5 µg/m³ (Steven et al. 1976). Cancer risks in occupational exposure have declined over the past 50 years due to improvements in the production process and industrial hygiene (USPHS 1993). There is no evidence of chromium sensitization in mammals other than humans. In the only animal study demonstrating a carcinogenic effect of an inhaled chromate, adenocarcinomas were reported in the bronchial tree of mice exposed throughout life to CaCrO₄ dust at 13 mg/m³ (4330 µg Cr⁺⁶/m³) for 35 h weekly (Langard and Norseth 1979). Trivalent chromium compounds did not produce respiratory cancers (Steven et al. 1976). Interstitial fibrosis of the lungs was found in rats exposed via inhalation to 0.1 mg/m³ of Cr⁺⁶ or Cr⁺³ for 22 h daily over 18 months (USPHS 1993). In rabbits, both Cr⁺³ and Cr⁺⁶, given 1.7 mg/kg body weight daily for 6 weeks, adversely affected blood and serum chemistry, and both produced significant morphological changes in liver (Tandon et al. 1978); similar results were observed in rats (Laj et al. 1984). Although damage effects and residue accumulations were greater in rabbits treated with Cr⁺⁶, water-soluble Cr⁺³ compounds also may have significant biological activity (Tandon et al. 1978).

Hexavalent chromium compounds may cause skin ulceration, irritative dermatitis, ulcerations in mucous membranes, and perforations of the nasal septum. That inhalation of Cr⁺⁶ compounds may cause bronchial carcinomas has been well documented in humans (Langard and Norseth 1979; Yassi and Nieboer 1988). Inhalation exposure of mice to 1.8 mg Cr⁺⁶/m³ for 12 months, 2 days weekly, resulted in emphysema and nasal septum perforation (USPHS 1993). Skin lesions or ulcers were produced in guinea pigs when solutions containing 30,000 mg Cr⁺⁶/L were applied to abraded skin or if the natural oils were removed from the skin beforehand; Cr⁺³ in concentrations as high as 100,000 mg/L had no ulcerogenic effects (Steven et al. 1976). Allergic guinea pigs developed dermatitis when exposed to solutions of either Cr⁺⁶ or Cr⁺³ at concentrations as low as 10 µg/L (Steven et al. 1976). In nonallergic animals, these effects were observed after repeated exposures to solutions containing 1000 to 3000 mg/L of Cr⁺³ or Cr⁺⁶ salts. Local sarcomas in muscle and local carcinomas of the skin have also been demonstrated in small laboratory animals exposed to Cr⁺⁶ (Langard and Norseth 1979). Kidney and liver lesions in rats were observed when the drinking water contained 134 mg Cr⁺⁶/L for 2 to 3 months (Steven et al. 1976).

Hexavalent chromium has established its mutagenic activity in a wide array of screening tests, whereas insoluble Cr⁺³ forms appear to be inactive, in analogous evaluations — perhaps because Cr⁺³ absorption is poor in the systems analyzed (Hatherill 1981). Studies with tissue cultures of ovary cells of the Chinese hamster showed that the addition of 52 µg Cr⁺⁶/L not only induced sister chromatid exchanges but also inhibited cell proliferation. There was no measurable effect at 0.52 µg Cr⁺⁶/L. Trivalent chromium at 520 µg/L did not measurably affect cell proliferation or chromatid exchanges (Uyeki and Nishio 1983). Genotoxic effects of Cr⁺⁶ are reversed by the addition of reducing agents or ascorbic acid (Hatherill 1981; Uyeki and Nishio 1983). Chromosomal rearrangements and aberrations were recorded in rabbit cells after exposure to Cr⁺⁶ (Hatherill 1981).

Chromium compounds, especially hexavalent chromium compounds, are associated with spermidal, embryocidal, teratogenic, and other adverse effects on reproduction (Nieboer and Yassi 1988). Teratogenic effects induced by intravenous administration of 5 mg Cr⁺⁶/kg body weight to pregnant Syrian golden hamsters (*Mesocricetus auratus*) included cleft palates and defects in the ossification of the skeletal system (Gale 1978; Outridge and Scheuhammer 1993). Pregnant hamsters that received an oral dose of 15 mg Cr/kg body weight, as chromic trioxide, produced pups with a 64% malformation frequency (Domingo 1994). Pregnant mice given chromium-contaminated drinking water on gestation days 1 to 19 (equivalent to 57 mg Cr/kg body weight daily) had increased fetal absorption and postimplantation loss, and males had decreased spermatogenesis after eating diets for 7 weeks that contained 3.5 to 4.6 mg Cr⁺⁶/kg ration (USPHS 1993).

Chromium is the most common skin sensitizer known to human males (Haines and Nieboer 1988). Up to 26% of all males tested and 10% of females were sensitive to potassium dichromate patch tests. The highest frequency of chromium-sensitive individuals was found in Brazil, Belgium, and North America, especially Detroit and New Orleans. Frequency of chromium dermatitis was

highest in construction workers using cement. Other occupational exposures associated with chromium sensitivity include chromium plating, tanning of leather, application of anticorrosive agents, and printing. Oral ingestion of chromium compounds can sometimes lead to skin reactions in sensitive people (Haines and Nieboer 1988). Hexavalent chromium compounds are more potent inducers and elicitors of skin sensitivity than trivalent chromium compounds, probably because Cr⁺⁶ compounds can penetrate the skin more readily than Cr⁺³ compounds (Nieboer and Jusys 1988).

Accumulations of chromium in tissues and organs depend heavily on its chemical form, route of entry, and amount administered (Yamaguchi et al. 1983). Trivalent chromium is the normal form of chromium in the mammalian diet. It is localized primarily in blood, liver, spleen, kidney, and body soft tissues, with long-term storage in liver and spleen (Nieboer and Jusys 1988). Tissue accumulations were significant in dogs exposed to drinking water concentrations of 11.2 mg Cr/L; but were nil at 6 mg/L (Steven et al. 1976). Although both Cr⁺³ and Cr⁺⁶ accumulated in brain, kidney, and myocardium of rabbits, the accumulation of Cr⁺⁶ was highest in brain and that of Cr⁺³ in kidney; for both valence states there was no correlation between dose and concentration of stored chromium, or extent of tissue damage (Hatherill 1981). Tissue residues in mice given 0.1 mg Cr⁺⁶/kg in diet and water during lifetime exposure ranged from 0.1 mg Cr/kg fresh weight in liver to 0.7 in heart; mice given 5.1 mg/kg diet for a similar period contained 0.5 to 1.8 mg Cr/kg fresh weight in tissues, the residues being highest in the heart and spleen (Schroeder et al. 1964). Trivalent chromium was poorly absorbed from the intestinal tract of rats (<1% of an oral dose), whereas absorption of Cr⁺⁶ ranged from 3 to 6% (Langard and Norseth 1979). However, both Cr⁺³ and Cr⁺⁶ traverse placental barriers in mice when administered intravenously (Steven et al. 1976; Langard and Norseth 1979). All chemical forms of chromium, except chromates, cleared rapidly from the blood of rats. At dose levels of 60 to 250 µg/kg body weight, Cr⁺⁶ tended to accumulate in the reticuloendothelial system, liver, spleen, and bone marrow; at the much lower doses of 10 and 1 µg/kg body weight, major accumulation sites were bone, marrow, spleen, testes, and epididymis (Langard and Norseth 1979). Female rats given a single intravenous injection of radiochromium-51 depurated the isotope primarily by urinary clearance, and secondarily by fecal and residual clearances over an 11-day period. Retained radiochromium-51 accumulated over time in bone, kidney, spleen, and liver (Onkelinx 1977). For multicompartmental excretion patterns recorded in rats, biological half-lives of the three components were estimated to be 0.5, 5.9, and 83.4 days; in mammals, chromium is excreted primarily in urine (Langard and Norseth 1979). At least three distinct Cr⁺⁶ excretion patterns exist in rats:

- Blood has a single component, with a biological half-life of 13.9 days
- Testes, brain, kidney, and lung have two components
- Liver has three components with half-lives of 2.4 h, 52.8 h, and 15.7 days (Yamaguchi et al. 1983).

Excretion patterns for Cr⁺³ in rats were unpredictable and difficult to calculate (Yamaguchi et al. 1983). The excretion patterns for fecal chromium among 40 grazing Angus cows given 20 g dietary Cr₂O₃ (13.6 g Cr⁺³) daily for 72 days was diurnal; excretion was lowest at 8 p.m. and highest at 9 a.m. (Hopper et al. 1978).

2.7 FIELD INVESTIGATIONS

There is a wealth of data concerning the effects of chromium on living organisms under laboratory conditions simulating those encountered in the vicinity of high chromium discharges and accumulations typical of electroplating plants, tanneries, ocean dumping sites, and municipal waste outfalls. However, little research has been conducted under actual field conditions, except in three general fields: occupational exposures of humans in the chromate industry (discussed earlier),

accidental poisoning of livestock resulting from oil field activities, and chromium accumulations in ecosystems impacted by discharges associated with cooling waters or cooling towers.

All cases of accidental chromate poisoning in cattle have resulted from the exposure of animals to chromate compounds associated with oil field activities. Chromates are used as a corrosion inhibitor between the pipe and casing and are often added to drilling fluids (in the form of chromelignosulfonate) to improve thermal stability. One recorded case involved 20 mature cows and their 8-month-old calves, grazing in a native pasture where an oil well had just been completed. One cow and calf died and another cow and calf became uncoordinated and thin, and the feces contained bloody mucus. The calf soon died. The cow aborted, but appeared to recover completely. Liver from the dead calf had 14.8 mg Cr/kg fresh weight vs. 1.8 in controls; levels of arsenic and lead were not elevated (Reagor and McDonald 1980). The cause of death was the consumption by the animals of concentrated sodium chromate found near the well site. In other cases, 2 of 80 heifers died after consuming concentrated zinc chromate, and 10 cows and one calf died after they had ingested ammonium chromate. In poisoned cows, chromium concentrations were 500 mg/kg in stomach contents, 15.8 mg/kg fresh weight in kidney vs. 3.0 mg/kg in controls, and 1.1 mg/L in blood vs. 0.02 mg/L for controls (Kerr and Edwards 1981).

Chromium is widely used as a corrosion inhibitor in cooling waters by the electric power industry. Its use in this capacity involves addition of a Cr⁺⁶ salt, typically sodium dichromate, which forms an oxide on metal surfaces. Chromates are subsequently released to surface waters in high concentrations, compared with background levels of chromium in most freshwaters. In White Oak Lake (eastern Tennessee), which received chronic inputs of chromates from cooling towers located on two tributary streams, typical Cr⁺⁶ concentrations of 3 to 10 mg/L in waste effluents produced 100 to 300 µg/L of Cr⁺⁶ in White Oak Lake vs. 5 µg/L in a control area (Elwood et al. 1980). Concentrations of chromium in muscle of bluegills and largemouth bass from White Oak Lake did not differ significantly from those in fish from a control site — suggesting that these species either effectively regulated chromium concentration or that the elevated chromium levels in White Oak Lake (where 20 to 73% of the total chromium was Cr⁺⁶) were in a form that was unavailable for absorption into tissues. Elwood et al. (1980) suggested that chromium is an element with a determinant concentration in fish, and that accumulation is independent of environmental concentration. This concept requires validation. Noteworthy is the observation that chromium concentrations were lower in muscle and body of older freshwater teleosts — an observation consistent with the findings of Eisler (1984), who noted that liver chromium decreased with increasing age in marine teleosts.

Cooling towers of uranium enrichment facilities and gaseous diffusion plants, similar to those of 1000-MW conventional steam electric stations, contain a chromate zinc-phosphate compound to inhibit corrosion and fouling within the cooling system. A small fraction of the cooling water, containing about 20 mg Cr⁺⁶/L, becomes entrained within the exit air flow and is deposited as drift on the landscape, together with other salts found in the recirculating water system, such as sodium pentachlorophenate, chromated copper arsenate, and acid copper chromate. Effects of the chromium component on biological systems have been under investigation in Kentucky and Tennessee for many years (Taylor and Parr 1978; Taylor 1980; Taylor et al. 1975, 1979, 1983). Analysis of vegetation along distance gradients from the cooling towers identified areas of significant drift deposition, accumulation, and magnitude of atmospheric transport over the landscape. At 13 m downwind from the point source, plant foliar concentrations of chromium were highest in winter at 1390 mg/kg dry weight, decreasing to 190 in spring, and to 173 in summer as the demand for cooling — and hence the operation time of the facility — decreased. Decreased accumulations on foliage probably reflected high mobility due to leaching, and the short life span of individual leaves. In contrast, chromium concentrations in plant litter at 13 m increased from 894 mg/kg dry weight during winter to 1890 mg/kg in summer and 2140 mg/kg in autumn. Accumulation of chromium in the litter was probably related to the higher surface-to-volume ratio in the litter biomass resulting from seasonal senescence of foliage. Taylor and his coworkers emphasized that no adverse biological

effects were observed in native vegetation bearing high chromium residues. Concentrations in plants and litter decreased with increasing distance from the cooling towers: concentrations in foliage at 168, 530, and 923 m downwind were 157, 10, and 1.3 mg/kg (dry weight), respectively; for litter, these values were 421, 24, and 5.8. Potted tobacco plants (*Nicotiana tabacum*) proved to be sensitive indicators of chromium contamination. Tobacco plants placed 15 m from the towers contained 30 times background levels after 1 week and up to 237 mg/kg dry weight in 5 weeks; in plants placed 200 m downwind, leaf growth was reduced 75% after 7 weeks. Beetles and crickets collected near the towers contained 9 to 37 mg Cr/kg in gut contents (vs. 0.5 to 0.8 mg/kg for controls); however, assimilation rates were not measured. Cotton rats (*Sigmodon hispidus*) trapped in a fescue field adjacent to a large mechanical draft cooling tower contained up to 10 times more chromium in hair, pelt, and bone than controls, but accumulations were negligible in viscera and other internal organs. Licking of the coat by rats appeared to be a primary route of chromium uptake — a likelihood confirmed experimentally by Langard and Nordhagen (1980). Feeding of radiochromium-51 to cotton rats demonstrated low assimilation (0.8%) and rapid initial loss of Cr⁺⁶ (99% in 1 day) — suggesting that chromium is neither essential to cotton rats nor accumulated to any great extent through ingestion of drift-contaminated vegetation or inhalation of drift-contaminated air (Taylor 1980). Biological half times of chromium assimilated by man and cotton rats were similar: 616 and 693 days, respectively. The magnitude of the half times suggests that chromium derived from a chromate has a high potential for biological interaction, but that fractional assimilation is very low — thus reducing the likelihood of toxic effects.

Chromium does not appear to biomagnify in aquatic or terrestrial food chains. In virtually all studies in both marine and freshwater environments involving birds and mammals there was no biomagnification of chromium in the food web, but rather decreasing concentrations with increasing trophic level (Outridge and Scheuhammer 1993). Similar results were reported in freshwater and marine food webs involving invertebrates and fishes, and along the terrestrial food chain of soil–plant–animal (Holdway 1988; USPHS 1993).

Biomarkers that demonstrate chromium exposure under field conditions is under active investigation. Laboratory studies with Prussian carp (*Carassius auratus gibelio*) exposed for 3 to 9 days to 25 to 100 µg Cr⁺⁶/L or 50 to 200 µg Cr⁺³/L show a dose-dependent increase in the frequency of micronuclei in erythrocytes, and this increase is considered indicative of increasing DNA damage (Al-Sabti et al. 1994). Similar increases in micronuclei were observed in Prussian carp from the River Ljubjanica near chromium-containing outfalls from leather waste products in the Republic of Slovenia (Al-Sabti et al. 1994).

2.8 RECOMMENDATIONS

As reported here, sensitive species of freshwater aquatic organisms showed reduced growth, inhibited reproduction, and increased bioaccumulation at about 10.0 µg/L and higher of Cr⁺⁶, and other adverse effects at 30.0 µg/L and higher of Cr⁺³. Among marine organisms, measurable accumulations were recorded in oysters and worms at 5.0 µg/L of Cr⁺⁶, algal growth was reduced at 10.0 µg/L, and reproduction of polychaete annelid worms was inhibited at 12.5 µg/L; in all situations, Cr⁺³ was less damaging than Cr⁺⁶. For mammals, 5.1 mg Cr⁺⁶/kg dietary levels in food and water of mice was associated with elevated tissue residues. The significance of chromium residues is unclear, but available evidence suggests that organs and tissues of fish and wildlife that contain 4.0 mg total Cr/kg dry weight and higher should be viewed as presumptive evidence of chromium contamination. Aerosol concentrations in excess of 10.0 µg Cr⁺⁶/m³ are potentially harmful to human health; in the absence of supporting data, this value is recommended for protection of sensitive species of wildlife, especially migratory waterfowl. More research is recommended on carcinogenic and mutagenic properties of chromium on fish (Holdway 1988), and on algal and bacterial physiology (Wong and Trevors 1988).

The U.S. Public Health Service (USPHS 1993) recommends that occupational exposure to hexavalent chromium compounds should not exceed 1 µg/m³ air for a 10-h workday and 40-h workweek because all hexavalent chromium compounds are potential carcinogens. Other recommendations include more research on:

1. The nature of speciation of chromium in soil and water
2. Bioavailability of chromium compounds from environmental media
3. Food chain biomagnification
4. Release data of chromium from anthropogenic sources to the biosphere
5. Reliable and more recent monitoring data of chromium in air, water, and food, with emphasis on chromium levels in tissues and body fluids of animals living near hazardous waste sites
6. Methods for determining biomarkers of exposure and effect, for determining parent compounds and degradation products in environmental media (USPHS 1993)

Proposed criteria for the protection of various environmental compartments against chromium are numerous, disparate, and often contradictory (Table 2.6). Some of this confusion may be attributable to the general lack of confidence in analyses of chromium residues conducted some years ago, and some to the continued inability to quantify chemical species and ionic states of chromium. Uncertainties about the metabolic role of organochromium compounds, water-soluble Cr⁺³ species, and their interactions with other components in complex and potentially toxic mixtures, further confound the issue. The essentiality of chromium to some, but not all, species of mammals is recognized, but comparable data for other groups of organisms are missing. Finally, the wide range in sensitivities and accumulation rates documented between different taxonomic groups, and even among closely related species, to Cr⁺³ and Cr⁺⁶ salts merits elucidation.

Table 2.6 Proposed Chromium Criteria for Protection of Human Health and Natural Resources

Category and Criterion (units in parentheses)	Chromium Concentration	Reference ^a
FRESHWATER AQUATIC LIFE PROTECTION; WATER (µg/L)		
USA	<0.29 Cr ⁺⁶ as 24 h average; not to exceed 21 Cr ⁺⁶ at any time	1
Water hardness, in mg CaCO ₃ /L		
50	<2200 Cr ⁺³ at any time	1
100	<4700 Cr ⁺³ at any time	1
200	<9900 Cr ⁺³ at any time	1
Colorado	<25 Cr ⁺⁶ ; <100 Cr ⁺³	2
Florida		
Effluent discharges	<500 Cr ⁺⁶ ; <1000 total chromium	2
Recovery waters	<50 total chromium	
Indiana		
Most waters	Not to exceed 0.1 times the 96-h LC50 of aquatic species	2
Lake Michigan	<50 total chromium	2
Canada	<10 Cr ⁺⁶	8
MARINE AQUATIC LIFE PROTECTION; WATER (µg/L)		
USA	<18 Cr ⁺⁶ as 24-h average; not to exceed 1260 Cr ⁺⁶ at any time	1
USA	Insufficient database for Cr ⁺³ at this time, but presumably less stringent than Cr ⁺⁶	1
California	<2 total chromium, 6 month median; <8 total chromium, daily maximum; <20 total chromium, instantaneous mix	2

Table 2.6 (continued) Proposed Chromium Criteria for Protection of Human Health and Natural Resources

Category and Criterion (units in parentheses)	Chromium Concentration	Reference^a
California		
Waste discharges into marine waters	<5 total chromium for 50% of measurements; <10 for 10% of measurements	3
GREAT LAKES BENTHOS; SEDIMENTS (mg/kg dry weight)		
Nonpolluted	<25	9
Moderately polluted	25–75	9
Heavily polluted	>75	9
HUMAN HEALTH		
Air ($\mu\text{g}/\text{m}^3$)		
Acceptable		
Arizona	11.0, 1-h average; 3.8, 24-h average	7
California, Maryland, Maine	0.00 at any time	7
Kansas, North Carolina	0.0000833, annual average	7
Rhode Island	0.00009, annual average	7
Montana	0.07, annual average	7
Texas	0.1, annual average	7
New York	0.167, annual average	7
Virginia	0.5–8.3, 24-h average	7
North Dakota	5.0, 8-h average	7
USA	<50 total chromium	6
Ceiling air, occupational exposure (mg/m³)		
Chromic acid and hexavalent chromium compounds	0.05–<0.1	7
Water-soluble divalent and trivalent chromium compounds	<0.5	7
Metallic chromium and insoluble salts	0.5–<1.0	7
All hexavalent chromium compounds; 10-h daily, 40-h workweek; recommended	<0.001	7
Diet		
Normal dietary intake	50–200 μg Cr ⁺³ daily, equivalent to 0.7–2.9 $\mu\text{g}/\text{kg}$ BW daily for a 70-kg adult	8
Normal dietary intake	30–100 μg total chromium daily	5
Drinking water ($\mu\text{g}/\text{L}$)		
USA	<50 Cr ⁺⁶ ; <170,000 Cr ⁺³	1, 7
USA, total chromium		
Recommended	<100	7
No adverse effects expected		
Children	<1400 for 10 days	7
Children	<240 for >10 days	7
Adults	<840 for >10 days	7
Adults	<120 for lifetime exposure	7
California	<50 total chromium	2
Colorado	<50 Cr ⁺⁶ ; <50 Cr ⁺³	2
Florida	<50 total chromium	2
Brazil	<50 total chromium	4
Former Soviet Union	<600 total chromium	4
Europe	<50 Cr ⁺⁶	7

Table 2.6 (continued) Proposed Chromium Criteria for Protection of Human Health and Natural Resources

Category and Criterion (units in parentheses)	Chromium Concentration	Reference^a
Tissue residues (µg/kg fresh weight)		
Normal		
Hair	234	7
Lung	204 (29–898)	7
Milk	0.3 (0.06–1.6)	7
Nail	520	7
Serum	0.06 (0.01–0.17)	7
Urine	0.4 (0.2–1.8)	7
Safe		
Soft tissues	<30 total chromium	2
AGRICULTURAL CROPS		
Sewage sludge (kg/ha)		
Missouri		
Maximum addition when soil cation exchange capacity (in meq/100 g) is		
<5	560	9
5–15	1120	9
>15	2250	9
New York, acceptable	336–500	9
Vermont		
Sandy loam	<140	9
Silt loam	<280	9
Clay loam	<560	9
Soils (mg/kg dry weight)		
Canada		
Cleanup indicated	>120	9
Nonagricultural use	<1000	9
Acidic soils (pH <6.5); Alberta; acceptable	<600	9
The Netherlands		
Acceptable	<100	9
Moderately contaminated	250–800	9
Requires cleanup	>800	9
USA	53 (1–1500)	9
New Jersey	<100	9
Water (µg/L)		
Irrigation, Colorado	<100 of Cr ⁺⁶ ; <100 of Cr ⁺³	2
Groundwater, Florida	<50 total chromium	2
RUMINANT MAMMALS (mg/kg fresh weight)		
Indicative of chromium intoxication		
Blood	>1.0	8
Kidney, liver	>15.0	8
Acutely toxic and perhaps fatal		
Blood	>4.0	8
Diet	>500.0	8
Liver	>30.0	8

Table 2.6 (continued) Proposed Chromium Criteria for Protection of Human Health and Natural Resources

Category and Criterion (units in parentheses)	Chromium Concentration	Reference^a
WILDLIFE (mg/kg dry weight)		
Diet		
Potential adverse effects on health and reproduction	>10 total chromium in ration	8
Tissue		
Normal, depending on species and tissue	0.1–15.0 (up to 100 times higher in chromium-contaminated environments)	8, 11
Probable exposure to chromium	>4.0	10

^a **1**, USEPA 1980; **2**, Ecological Analysts 1981; **3**, Reish 1977; **4**, Pfeiffer et al. 1980; **5**, Langard and Norseth 1979; **6**, Steven et al. 1976; **7**, U.S. Public Health Service 1993; **8**, Outridge and Scheuhammer 1993; **9**, Beyer 1990; **10**, Eisler 1986; **11**, Zilincar et al. 1992.

2.9 SUMMARY

Most authorities agree on eight points:

1. Chromium levels are elevated in soil, air, water, and biota in the vicinity of electroplating and metal-finishing industries, publicly owned municipal treatment plants, tanneries, oil drilling operations, and cooling towers
2. Hexavalent chromium (Cr^{+6}) is the most biologically active chromium chemical species, although little is known about the properties of organochromium compounds, water-soluble species, or their interactions in complex mixtures
3. Chromium chemistry is imperfectly understood, and existing analytical methodologies are inadequate for quantification of chromium species and ionic states
4. Trivalent chromium (Cr^{+3}) is an essential trace element in humans and some species of laboratory animals, but the database is incomplete for other groups of organisms
5. At high environmental concentrations, chromium is a mutagen, teratogen, and carcinogen
6. No biomagnification of chromium has been observed in food chains, and concentrations are usually highest at the lowest trophic levels
7. Toxic and sublethal properties of chromium are modified by a variety of biological and abiotic factors
8. Sensitivity to chromium varies widely, even among closely related species

As reported here, adverse effects of chromium to sensitive species have been documented at 10.0 µg/L (ppb) of Cr^{+6} and 30.0 µg/L of Cr^{+3} in freshwater and 5.0 µg/L of Cr^{+6} in saltwater and, to wildlife, 10.0 mg of Cr^{+6} per kilogram of diet (ppm). Tissue levels in excess of 4.0 mg total Cr/kg dry weight should be viewed as presumptive evidence of chromium contamination, although the significance of tissue chromium residues is unclear. Some of these findings are in sharp contrast to chromium criteria proposed by regulatory agencies.

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CHAPTER 3

Copper

3.1 INTRODUCTION

Copper (Cu) is plentiful in the environment and essential for the normal growth and metabolism of all living organisms (Schroeder et al. 1966; Carbonell and Tarazona 1994). Abnormal levels of copper intake may range from levels so low as to induce a nutritional deficiency to levels so high as to be acutely toxic (U.S. Environmental Protection Agency [USEPA] 1980). Copper is probably the first metal worked by humans some 70 to 80 centuries ago (Schroeder et al. 1966). The earliest known artifacts of hammered copper date from about 6000 BCE. After 4000 BCE, melting and casting of copper was common in the Near East. Smelting was developed about 3000 BCE and bronze around 2500 BCE. Brass, a copper alloy, was developed in Roman times. Copper derives from the Latin *cuprum*, a corruption of *cyprium* — Cyprus being the source of Egyptian and Roman copper (Schroeder et al. 1966). Copper was identified in terrestrial plants in 1817 (Gallagher 1979), in marine invertebrates in 1833 (Schroeder et al. 1966), in vertebrates in 1838 (Gallagher 1979), and in hemocyanin — the blue respiratory pigment of molluscs and crustaceans — in 1880 (Schroeder et al. 1966). But the metabolic importance of copper in plants and animals was not suspected until the 1920s when diseases due to copper deficiency began to be recognized (National Academy of Sciences [NAS] 1977; Gallagher 1979). Copper deficiency in vertebrates, for example, is associated with anemia, gastrointestinal disturbances, aortic aneurisms, bone development abnormalities, and death (Aaseth and Norseth 1986).

Copper toxicosis in terrestrial higher plants is rare but occurs on mine spoils and where copper-rich manures or fungicides are used excessively (Schroeder et al. 1966; NAS 1977; Alva et al. 1995; Arduini et al. 1995). Copper is among the most toxic of the heavy metals in freshwater and marine biota (Schroeder et al. 1966; Betzer and Yevich 1975) and often accumulates and causes irreversible harm to some species at concentrations just above levels required for growth and reproduction (Hall et al. 1988). Birds and mammals, when compared to lower forms, are relatively resistant to copper, but diets containing elevated concentrations of copper are sometimes fatal to ducklings (Wood and Worden 1973) and livestock when fed for extended periods. Domestic sheep (*Ovis aries*) are the most susceptible farm animals to chronic copper poisoning, and effects include liver damage, impaired reproduction, reduced resistance to diseases, jaundice, and death (Gopinath and Howell 1975; Higgins 1981; Bires et al. 1993).

Many reviews and annotated bibliographies are available on copper ecology and toxicology, including those by Eisler (1973, 1979, 1998), Eisler and Wapner (1975), NAS (1977), Eisler et al. (1978, 1979), Nriagu (1979a, 1979b), USEPA (1980), Aaseth and Norseth (1986), and Agency for Toxic Substances and Disease Registry [ATSDR] (1990).

3.2 SOURCES AND USES

3.2.1 General

The United States is the major world producer and consumer of copper and its compounds. Most of the copper produced is used to manufacture electrical equipment, pipe, and machinery. Releases of copper to the global biosphere — which may approach 1.8 million metric tons per year — come mostly from anthropogenic activities such as mining and smelting, industrial emissions and effluents, and municipal wastes and sewage sludge. Copper compounds are widely used as biocides to control nuisance algae and macrophytes, freshwater snails that may harbor schistosomiasis and other diseases, ectoparasites of fish and mammals, marine fouling organisms, and mildew and other diseases of terrestrial crop plants. Copper compounds are also used in agricultural fertilizers, in veterinary and medical products, in the food industry, and as a preservative of wood and other materials.

3.2.2 Sources

Global copper production during the past 60 centuries is estimated at 307 million metric tons, most of which (79%) has occurred since 1900; annual global production of copper is now estimated at 13.6 million tons (Nriagu 1979c). Copper occurs naturally in many minerals and as uncombined metal. The three most important sources of copper are chalcocite (Cu_2S), chalcopyrite (CuFeS_2), and malachite ($\text{CuCO}_3 \cdot \text{Cu}(\text{OH})_2$; ATSDR 1990).

In 1986, domestic consumption of copper in the United States was 2.14 million metric tons, and mine production was 1.14 million metric tons, mostly from mines in Arizona, New Mexico, and Michigan. The major copper deposits in the United States are of hydrothermal origin and are uniformly distributed in fractures or veins (ATSDR 1990). Copper is the major toxic component in streams impacted by active placer mines (Buhl and Hamilton 1990). About 60% of copper metal is eventually recycled; in 1986, smelting of scrap copper produced an additional 0.9 million metric tons of copper. Also in 1986, 1.1 million tons of copper were imported into the United States, mostly from Canada, Chile, Peru, and Mexico (ATSDR 1990).

The amount of copper entering the global ecosystem annually is unknown, but estimates range from 211,000 metric tons (Nriagu 1979c) to 1.8 million metric tons (NAS 1977). About 80.7% of this copper is deposited in terrestrial compartments, 15.7% in the hydrosphere, and 3.6% to the atmosphere (Nriagu 1979c). The residence time for copper in the deep ocean is 1500 years; in soils it may be retained for as long as 1000 years; in air, copper persists for about 13 days (Nriagu 1979c). Copper in the atmosphere results mainly (73%) from human activities such as copper production and combustion of fossil fuels; the remainder is from natural sources that include seasalt sprays, windblown dusts, volcanic particles, and decaying vegetation (Nriagu 1979c, 1979d).

Input of copper into aquatic ecosystems has increased sharply during the past century and includes inputs from waste discharges into saline waters, industrial discharges into freshwater, and leaching of antifouling marine paints and wood preservatives (Nriagu 1979c). Present anthropogenic inputs of copper are two to five times higher than natural loadings. The atmosphere is a primary recipient of these inputs (Nriagu 1979d). In mining and industrial areas, precipitation of atmospheric fallout is a significant source of copper to the aquatic environment (USEPA 1980). More than 99.9% of oceanic copper falls as clay and manganese oxide particles in precipitation (NAS 1977). In the lower Great Lakes, direct atmospheric inputs of copper — in metric tons per year — range from 55 to 2300 for Lake Michigan, 120 to 330 for Lake Erie, and 72 to 123 for Lake Ontario. Regional disparities in atmospheric deposition of copper are related to the intensity of industrial activity and to the regional wind systems (Nriagu 1979d).

Copper in soils may come from a variety of anthropogenic sources:

- Mining and smelting activities
- Other industrial emissions and effluents
- Traffic
- Fly ash
- Dumped waste materials
- Contaminated dusts and rainfall
- Sewage and sludge
- Pig slurry
- Composted refuse
- Agricultural fertilizers, pesticides, and fungicides (Nriagu 1979c; Thornton 1979; Ma 1984; ATSDR 1990; Roncero et al. 1992; Alva et al. 1995).

In the case of Florida citrus groves, copper-containing fertilizers applied during the early 1900s accounted for as much as 34 kg Cu/ha annually, and routine fungicidal sprays contributed another 10 kg Cu/ha annually. Surface soils (0 to 15 cm) from some mature citrus groves contained as much as 540 kg Cu/ha (Alva et al. 1995). Copper deposition rates in soils are higher in cities and near highways, railroads, power plants, and industrial activities (Nriagu 1979d), but a Kansas landfill near a freshwater stream had no significant effect on copper concentrations in water, sediments, crayfish, and sunfish (Morrissey and Edds 1994).

3.2.3 Uses

Metallic copper end uses include electrical (70%), construction (15%), machinery (6%), transportation (4%), and ordnance (2%). The top domestic markets for copper and its alloys in 1986 were, in order of importance, plumbing, building wire, telecommunications, power utilities, in-plant equipment, air conditioning, automotive electrical, automotive nonelectrical, business electronics, and industrial valves and fittings (ATSDR 1990). A small percentage of copper production is used to manufacture chemicals, mainly copper sulfate. Of the copper sulfate used domestically, 65% is used in agriculture for fungicides, algicides, nutritional supplements, insecticides, and repellents; 28% is used industrially in froth flotation production of chromated copper arsenate wood preservatives, in electroplating, and in the manufacture of azo dyes; and 7% is used in water treatment to control nuisance algae (ATSDR 1990).

Copper is widely used to control unwanted species of freshwater algae and macrophytes (Bartley 1967; NAS 1977; USEPA 1980; Rowe and Prince 1983; Havens 1994). Chelated copper products are claimed to be effective algicides in hard water. The chelation of copper by organic compounds, such as ethanolamines or ethanalamine complexes, protects copper from precipitation and complexation (Straus and Tucker 1993). Copper sulfate is approved by the U.S. Environmental Protection Agency (USEPA) as an algicide in waters used to raise fish for human consumption (Straus and Tucker 1993). In algae, copper inhibits photosynthesis, nitrogen fixation, and phosphorus uptake. It selectively eliminates cryptophytes but spares diatoms (Havens 1994). Copper sulfate at low concentrations has been used to control freshwater algae in Wisconsin since 1918 without any conclusively proven effect on diversity or abundance of nontarget species (Mackenthun and Cooley 1952). But reduced abundance of freshwater benthos was noted in Lake Monona, Wisconsin, which received 771 metric tons of copper to control algae over a 26-year period and had sediment levels as high as 1093 mg Cu/kg DW (Mackenthun and Cooley 1952). Copper sulfate used to control algal blooms in Wisconsin lakes at 1.25 mg Cu/L killed nontarget fishes, crustaceans, snails, and amphibians in 14 days or less. However, 0.25 mg Cu/L was not fatal to these species in 20 days (Hasler 1949). Concentrations as low as 0.03 mg Cu/L inhibited growth in two of four species of nuisance aquatic weeds in Lake Mendota, Wisconsin, and 0.3 mg Cu/L was fatal to all four species (Hasler 1949). Copper sulfate controls algae in cranberry bogs at 0.4 mg Cu/L, but this concentration

also kills resident fishes (Deubert and Demoranville 1970). Copper was not measurable in the surface waters of cranberry bogs within 10 days of treatment, regardless of initial copper concentration; it is probable that copper was adsorbed onto bog soils (Deubert and Demoranville 1970). In England, copper sulfate was effective at 1.0 mg Cu/L in controlling algae and most species of aquatic weeds for 1.6 km downstream of treatment for 6 months during the summer; only 0.25 mg Cu/L was necessary in autumn and winter for effective aquatic weed control (Chancellor et al. 1960). During copper treatment to control plants, aquatic snails were greatly reduced or eliminated, but fishes seemed unaffected. Sensitive aquatic weeds included *Myriophyllum spicatum*, *Elodea canadensis*, *Potamogeton* spp., and *Lemna minor*; sensitive genera of algae included *Oedogonium*, *Spirogyra*, *Enteromorpha*, and *Mougeotia* (Chancellor et al. 1960).

In California, 4.23 million kg of copper compounds are used each year in agriculture, of which almost 1.4 million kg are applied as copper sulfate pentahydrate to flooded rice fields for control of algae and tadpole shrimp (Crosby 1999). Most of the copper precipitates as copper hydroxycarbonate within the first hour, with negligible loss to the atmosphere or from runoff. The remainder in rice field water is complexed with dissolved organic matter and is biologically unavailable to algae and shrimp. However, the major part accumulates in the soil, where it presents a threat to future plant agriculture at that site, although intentional mobilization may be possible (Crosby 1999).

In Iowa lakes, copper sulfate was used to control summer blooms of various species of toxic blue-green algae. Prior to treatment, blooms of *Anabaena flos-aquae*, *Aphanizomenon flos-aquae*, and *Microcystis aeruginosa* were associated with deaths of migratory waterfowl, game birds, songbirds, game, and domestic animals (Rose 1954). Most of these species of algae were controlled within 24 h by 1.0 mg Cu/L as copper sulfate. Copper treatment had no adverse effects on bottom fauna, but populations of crustaceans (daphnids, copepods, entomostracans) were reduced. One year after treatment, no deaths of birds or mammals were recorded (Rose 1954).

Copper salts are intentionally added to drinking water supplies of some municipalities to control growth of algae; concentrations as high as 59 µg Cu/L are maintained in New York City (USEPA 1980).

Copper compounds are used routinely and widely to control freshwater snails that serve as intermediate vectors of schistosomiasis and other diseases that afflict humans (Hasler 1949; NAS 1977; Rowe and Prince 1983; Winger et al. 1984; Al-Sabri et al. 1993). These compounds include copper sulfate, copper pentachlorophenate, copper carbonate, copper-tartaric acid, Paris green (copper arsenite-acetate), copper oxide, copper chloride, copper acetyl acetone, copper dimethyl dithiocarbamate, copper ricinoleate, and copper rosinate (Cheng 1979). Also, many species of oyster enemies are controlled by copper sulfate dips. All tested species of marine gastropods, tunicates, echinoderms, and crabs that had been dipped for 5 seconds in a saturated solution of copper sulfate died if held in air for as little as a few seconds to 8 h; mussels, however, were resistant (MacKenzie 1961).

Copper sulfate is used to control protozoan fish ectoparasites including *Ichthyophthirius*, *Trichodina*, and *Costia*. The effectiveness of the treatment diminishes with increasing total alkalinity and total hardness of the water (Straus and Tucker 1993). Copper compounds now used to control protozoan parasites of cultured red drum (*Sciaenops ocellatus*) include copper sulfate, copper sulfate plus citric acid, and chelated copper compounds (forms of copper bound by sequestering agents, such as ethanolamine); chelated copper compounds are considered less toxic to fish than copper sulfate and at least as effective in controlling parasites (Peppard et al. 1991).

Copper is the active agent in many antifouling paints applied to watercraft (Aaseth and Norseth 1986; Hall et al. 1988). The growing use of copper-based paints subsequent to the prohibition in 1982 of tributyltin-based paints (Hall et al. 1988) is associated with elevated copper concentrations in Pacific oysters (*Crassostrea gigas*) farmed in the Bay of Arcachon, France (Claisse and Alzieu 1993).

Copper compounds are used in agriculture to treat mildew and other plant diseases; in the food industry as preservatives, additives, or coloring agents; in preservatives of wood, leather, and fabrics; in coin manufacture; and in water treatment (ATSDR 1990; Roncero et al. 1992). The use of copper-containing pesticides is traditional along the Mediterranean Coast, especially the use of Bordeaux mixture, a copper sulfate-based fungicide that has been widely used for more than a century to

prevent mildew on grape vines (Romeu-Moreno et al. 1994). However, at current application rates of about 0.8 mg Cu/cm², Bordeaux mixture significantly reduces the life span and breeding rate of the fruit fly (*Drosophila melanogaster*) (Marchal-Segault et al. 1991).

Copper is widely used in veterinary clinics in medical products (Roncero et al. 1992). Copper sulfate is used by veterinarians to treat cattle and sheep for helminthiasis and infectious pododermatitis (NAS 1977). Cuprol (a 1% solution of cupric oleinate) is used to control lice (Aaseth and Norseth 1986). Copper is routinely used as a growth supplement in the diets of swine (*Sus* sp.) in the United Kingdom and elsewhere; diets may contain as much as 250 mg Cu/kg ration (USEPA 1980). The intensity of pig farming within about 10 km from the coast may influence copper content in estuarine sediments. For example, intensive pig farming in coastal Brittany, France, increased soil copper concentrations by 0.6 kg/ha annually and increased coastal sediment copper concentrations to as high as 49.6 mg/kg DW (Arzul and Maguer 1990).

In human medicine, metallic copper is used in some intrauterine devices, and various copper compounds are used as emetics and to treat rheumatoid arthritis (USEPA 1980; Aaseth and Norseth 1986). Some individuals wear copper bracelets as treatment for arthritis although its therapeutic value has little support (USEPA 1980).

3.3 CHEMICAL AND BIOCHEMICAL PROPERTIES

3.3.1 General

This section demonstrates that (1) free ionic copper (Cu²⁺) is the most toxic chemical species of copper and that copper bioavailability is modified by many biological and abiotic variables; (2) copper metabolism and sensitivity to copper of poikilotherms differs from that of mammals; and (3) copper interactions with inorganic and organic chemicals are substantial and must be considered when evaluating copper hazards to natural resources.

3.3.2 Chemical Properties

Copper is a soft heavy metal, atomic number 29, a density in elemental form at 20°C of 8.92 g/cc and a melting point of 1083.4°C (USEPA 1980; Aaseth and Norseth 1986; [Table 3.1](#)). Copper has two natural isotopes: Cu-63 (69.09%) and Cu-65 (30.91%) (NAS 1977).

Table 3.1 Some Properties of Copper and Copper Sulfate

Property	Copper	Copper Sulfate
Chemical and other names	Copper	Cupric sulfate, blue vitriol, cupric sulfate, Roman vitriol, Salzburg vitriol, blue copperas, copper (II) sulfate
Chemical formula	Cu	CuSO ₄
Oxidation state	0	2+
CAS (Chemical Abstract Services) number	7440-50-8	7758-98-7
Molecular weight	63.546	159.60
Color and form	Reddish solid	Blue crystals
Melting point	1083.4°C	Decomposes slightly at >200°C
Boiling point	2567°C	Decomposes to CuO at 650°C
Density	8.92	3.603
Solubility		
Water	Insoluble	143 g/L
Organic solvents	Insoluble	Soluble in methanol, slightly soluble in ethanol

From Agency for Toxic Substances and Disease Registry (ATSDR). 1990. Toxicological Profile for Copper. U.S. Pub. Health Serv., Atlanta, Georgia, TP-90-08. 143 pp.

Copper exists in four oxidation states: Cu⁰, Cu⁺¹, Cu⁺², and Cu⁺³ (ATSDR 1990). Elemental copper (Cu⁰) is readily attacked by organic and mineral acids that contain an oxidizing agent and is slowly soluble in dilute ammonia; halogens attack elemental copper slowly at room temperature to yield the corresponding copper halide (USEPA 1980). Elemental copper is not oxidized in water (Aaseth and Norseth 1986). Cuprous copper (Cu⁺¹) exists only in water solution when complexed, usually in a tetrahedral form, with affinity for sulfur and nitrogen ligands (Schroeder et al. 1966). Cuprous copper is unstable in aerated aqueous solution over the pH range 6 to 8 and will undergo auto-oxidation-reduction into elemental copper (Cu⁰) and cupric ion (Cu⁺²) (USEPA 1980; Aaseth and Norseth 1986). The only cuprous ion (Cu⁺¹) compounds that are stable in water are extremely insoluble ones such as cuprous chloride, CuCl (ATSDR 1990). Cuprous ion-complexes may be formed in seawater by photochemical processes and persist for several hours. The cupric ion (Cu⁺²) is the one generally encountered in water. Cupric ions are coordinated with six water molecules in solution (ATSDR 1990). Cupric ion ordinarily forms planar, less stable chelates with nitrogen and oxygen ligands (Schroeder et al. 1966). In seawater and sediment interstitial waters, the free cupric ion (Cu⁺²) is the most readily available and toxic inorganic species of copper; however, the free ion concentration is sensitive to complexation and is less available to aquatic biota in the presence of natural organic chelators and high salinities (Bryan and Langston 1992). Cupric ions account for about 1% of the total dissolved copper in seawater and less than 1% in freshwater (Boyle 1979). Trivalent copper (Cu⁺³) probably does not occur naturally (Schroeder et al. 1966). It is strongly oxidizing and occurs only in a few compounds; none of these compounds is now considered industrially important or environmentally significant (ATSDR 1990).

Copper speciation in freshwater is figured in detail by Leckie and Davis (1979). In freshwater, the solubility of copper salts is decreased under reducing conditions and is further modified by water pH, temperature, and hardness; size and density of suspended materials; rates of coagulation and sedimentation of particulates; and concentration of dissolved organics. The chemical form of copper in freshwater is important in controlling geochemical and biological processes. But the lack of knowledge on the adsorption characteristics of most cupric (Cu⁺²) ion complexes contributes to uncertainties about the behavior of known copper species (Leckie and Davis 1979). Ionic copper (Cu⁺²) and some copper hydroxyl species are correlated with high toxicity to aquatic life; however, carbonato species (CuHCO₃⁺, CuCO₃, Cu(CO₃)₂⁻) are much less toxic than other copper complexes (Meador 1991). The major chemical species of copper in freshwater are Cu(CO₃)₂⁻ and CuCO₃ (Boyle 1979). Cupric ion is the dominant toxic copper species at pH less than 6; the aqueous copper carbonate complex is dominant from pH 6.0 to 9.3 (USEPA 1980). This equilibrium is altered in the presence of humic acids, fulvic acids, amino acids, cyanide, certain polypeptides, and detergents (USEPA 1980). Most cupric salts dissolve readily in freshwater to produce the aquo ion, Cu(H₂O)₆⁺² (Leckie and Davis 1979). Divalent copper chloride, nitrate, and sulfate are highly soluble in water (USEPA 1980; Table 3.1), but copper carbonate, cupric hydroxide, cupric oxide, and cupric sulfide will precipitate from solution or form colloidal suspensions when excess cupric ions are present (USEPA 1980).

In seawater, the major chemical species of copper are Cu(OH)Cl and Cu(OH)₂ and these account for about 65% of the total copper in seawater (Boyle 1979). The levels of copper hydroxide (Cu(OH)₂) increase from about 18% of the total copper at pH 7.0 to 90% at pH 8.6; copper carbonate (CuCO₃) dropped from 30% at pH 7.0 to less than 0.1% at pH 8.6 (USEPA 1980). The dominant copper species in seawater over the entire ambient pH range are copper hydroxide, copper carbonate, and cupric ion (USEPA 1980). Bioavailability and toxicity of copper in marine ecosystems is promoted by oxine and other lipid soluble synthetic organic chelators (Bryan and Langston 1992).

Copper concentrations in sediment interstitial pore waters correlate positively with concentrations of dissolved copper in the overlying water column and are now used to predict the toxicity of test sediments to freshwater amphipods (Ankley et al. 1993). Sediment-bound copper is available to deposit-feeding clams, especially from relatively uncontaminated anoxic sediments of low pH (Bryan and Langston 1992). The bioavailability of copper from marine sediments, as judged by increased copper in sediment interstitial waters, is altered by increased acid volatile sulfide (AVS)

content (Casas and Crecelius 1994). But acid volatile sulfide is not an appropriate partitioning phase for predicting copper bioavailability of freshwater sediments (Ankley et al. 1993).

3.3.3 Metabolism

Copper is part of several essential enzymes including tyrosinase (melanin production), dopamine beta-hydroxylase (catecholamine production), copper-zinc superoxide dismutase (free radical detoxification), and cytochrome oxidase and ceruloplasmin (iron conversion) (Aaseth and Norseth 1986). All terrestrial animals contain copper as a constituent of cytochrome *c* oxidase, monophenol oxidase, plasma monoamine oxidase, and copper protein complexes (Schroeder et al. 1966). Excess copper causes a variety of toxic effects, including altered permeability of cellular membranes. The primary target for free cupric ions in the cellular membranes are thiol groups that reduce cupric (Cu^{+2}) to cuprous (Cu^{+1}) upon simultaneous oxidation to disulfides in the membrane. Cuprous ions are reoxidized to Cu^{+2} in the presence of molecular oxygen; molecular oxygen is thereby converted to the toxic superoxide radical O^{-2} , which induces lipoperoxidation (Aaseth and Norseth 1986).

Aquatic Organisms — Bioavailability and toxicity of copper to aquatic organisms depends on the total concentration of copper and its speciation (Hung et al. 1990). In hard, moderately polluted waters, 43 to 88% of the copper is associated with suspended solids and not available to biota (Shaw and Brown 1974). Copper toxicity to aquatic biota is related primarily to the dissolved cupric ion (Cu^{+2}) and possibly to some hydroxyl complexes (NAS 1977; Hall et al. 1988; Hung et al. 1990). Soluble copper is largely complexed with carbonate, amino acids, or humic substances. Cupric copper — one of the most toxic forms — constitutes 0.1 to 0.2% of this soluble material (Shaw and Brown 1974). The toxicity of copper in its complexed, precipitated, or adsorbed form is less than that of the free ionic form (Hall et al. 1988; Hung et al. 1990). In aquatic invertebrates, copper causes gill damage at high concentrations, and in fishes it interferes with osmoregulation (Hodson et al. 1979). Elevated concentrations of copper interfere with oxygen transport and energy metabolism; tissue hypoxia is the cause of death and is associated with reductions in the activities of regulatory enzymes of ATP-synthesizing pathways (Hansen et al. 1992b).

In freshwater algae, movement of copper into cells occurs mainly by physical transport; the plasmalemma is the initial site of copper binding. Copper on the plasmalemma increases its permeability, as shown by the leakage of potassium and other ions from copper-treated cells and entry of copper into intracellular sites (Stokes 1979).

Marine prosobranch gastropods, like several other groups of molluscs and arthropods, normally accumulate and store copper and use it in the synthesis of hemocyanin, a blood pigment (Betzer and Yevich 1975). In gastropods, copper may elicit secretions of mucus by goblet cells; bind to hydrophilic regions of the external membranes of epithelial cells, altering their biochemical and biophysical properties; or disrupt the normal functioning of peroxidase and ferritin (Cheng 1979). Peroxidation products, such as hydroperoxides and malondialdehyde, are toxic to vital functions of membranes and cells. Bivalve molluscs challenged with ionic copper show significant increases in these products (Chelomin and Belcheva 1992). Exposure of gastropods to high sublethal concentrations of copper completely inhibits succinic dehydrogenase activity at whole-body concentrations between 4.7 and 11.9 mg Cu/kg DW soft parts, causes a measurable decrease in heart beat rate, and adversely affects surface epithelia, especially those covering the head-foot and rectal ridge, disrupting osmoregulation and producing water accumulation in tissues (Cheng 1979). The primary lethal effect of copper in gastropod molluscs is caused by disruption of the transporting surface epithelium (Cheng 1979).

In crabs, the gills are a major target organ of copper toxicity; waterborne copper decreases hemocyanin–oxygen affinity (Truchot and Boitel 1992). Exposure of shore crabs (*Carcinus maenas*) to lethal concentrations of copper is associated with reductions in activity of glycolytic enzymes but, unlike fishes, did not involve cellular energy deprivation (Hansen et al. 1992b). Copper-tolerant

strains of aquatic mayflies (*Baetis thermicus*) have evolved in Japan. Tolerance is attributed to the ability to induce a metal-binding protein that preferentially sequesters copper over cadmium and zinc (Suzuki et al. 1989).

In fishes, the gill surface's low affinity for metal allows greater entry of the metal to the intracellular compartment. Once there, more complex binding sites are present. Binding to these ligands causes one or more of the following toxic mechanisms: (1) blocking of the essential biological functional groups of biomolecules; (2) displacing the essential metal ion in molecules; or (3) modifying the active conformation of biomolecules. These mechanisms may account for the specific inhibition of ion transport from ionic (Cu^{+2}) copper exposure (Reid and McDonald 1991). Studies with radiocopper-64 and rainbow trout (*Oncorhynchus mykiss*) show that the external gill epithelial surface has a relatively low affinity for copper, allowing copper to penetrate intracellular compartments. Copper disrupts gill function of rainbow trout by impairing transepithelial ion exchange, for example, impairing or upsetting electrolyte balance by inhibiting active uptake or stimulating passive loss (Reid and McDonald 1991). Copper toxicity to rainbow trout in hard water is related to the total concentration of soluble copper (copper carbonate, $CuCO_3$; cupric ion, Cu^{+2}) in the test medium rather than to either of these two forms alone (Shaw and Brown 1974). Long-term retention of copper accumulations in fish tissues is characterized by high half-time persistence after copper administration and binding of copper to proteins in a nonexchangeable or slowly exchangeable pool (Carbonell and Tarazona 1994).

Copper detoxifying mechanisms in fishes include the induction of metallothioneins, allowing copper retention for weeks or months after absorption without producing toxic effects (Hogstrand et al. 1991; Hylland et al. 1992; Carbonell and Tarazona 1994; Marr et al. 1995). Hepatic metallothionein contents of individual fishes usually reflect the accumulation of copper in that organ (Hogstrand et al. 1991). This strongly supports the use of metallothionein as an indicator of copper stress (Hogstrand 1991).

In tench (*Tinca tinca*), hepatic alterations observed after exposure to lethal concentrations of copper (75 mg/L for 4 to 12 days) include accumulation of various pigments in Kupffer cells and hepatocytes. Death was attributed to deficient oxygen transport and consumption and to the lytic effect of copper on various cell membranes, eventually causing massive necrosis in large areas of the liver parenchyma (Roncero et al. 1992). In rapidly growing juvenile flounders (*Paralichthys* spp.), copper blocks calcium transport, possibly through interference with gill chloride cells. Copper inhibition of calcium accumulation is alleviated by removing copper from the medium (Dodoo et al. 1992).

Mammals — Copper homeostasis plays an important role in the prevention of copper toxicity. After copper requirements are met, excess copper absorbed into gastrointestinal mucosal cells is bound to metallothionein and excreted when the cell is sloughed. Copper that eludes the intestinal barrier is stored in the liver or incorporated into bile and excreted in feces. The most likely pathway for the entry of toxic amounts of copper would be long-term inhalation or entry through the skin. Both of these pathways allow copper to pass unimpeded into the blood (ATSDR 1990). The levels of copper in the mammalian body are held constant by alterations in the rate and amount of copper absorbed, its distribution, and rate and route of excretion (ATSDR 1990). Many factors interfere with copper absorption, including competition for binding sites, as with zinc; chelation, as with phytates; and interaction with ascorbic acid, which aggravates copper deficiency by decreasing copper absorption and — with excess copper — reduces the toxic effects (USEPA 1980; ATSDR 1990).

Two inherited human diseases that represent abnormal copper metabolism are Menkes' syndrome and Wilson's disease. Menkes' syndrome, with symptoms similar to those of copper deficiency, is characterized by a progressive brain disease, abnormally low copper concentrations in liver and other tissues, and diminished ability to transfer copper across the absorptive cells of the intestinal mucosa (USEPA 1980; Aaseth and Norseth 1986). Wilson's disease (hepatolenticular degeneration) is the only significant example of copper toxicity in humans. Wilson's disease is an autosomal recessive disorder that affects normal copper homeostasis and is characterized by excessive

retention of hepatic copper, decreased concentration of serum ceruloplasmin, impaired biliary copper excretion, and hypercupremia. Systemic manifestations of Wilson's disease are hepatic and renal lesions and hemolytic anemia (Schroeder et al. 1966; Goresky et al. 1968; Baker 1969; USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). Certain strains of mutant rats with reduced excretion of biliary copper spontaneously develop hepatitis because of the extremely gross deposition of copper in the liver (Sugawara et al. 1994). Most humans afflicted with Wilson's disease usually die before puberty, although some survive to age 35 (Schroeder et al. 1966). Postmortems of Wilson's patients show that livers had as much as 7.5% copper and kidney ash had up to 2.7%. There is no evidence, however, that persons with normal homeostatic mechanisms are subject to any chronic degenerative disorders resulting from modern exposures to copper (Schroeder et al. 1966). Unusually susceptible human populations to copper poisoning include those afflicted with Wilson's disease, infants and children under one year of age, those with liver damage or chronic renal disease, individuals undergoing dialysis (excess copper in the dialysate), and those with an inherited deficiency of the enzyme glucose-6-phosphate dehydrogenase (ATSDR 1990).

Ingested copper travels through the gastrointestinal (GI) tract, where some of it is absorbed into the blood and becomes associated with plasma albumin and amino acids (Sugawara et al. 1994) or is used to maintain copper levels in erythrocytes (USEPA 1980). Albumin-bound copper is eventually transported to the liver; however, minor fractions are transported into the bone marrow, the erythrocytes, or other tissues (Aaseth and Norseth 1986). Most of the circulating copper is translocated within minutes. During the next few hours, blood copper concentrations increase, and Cu becomes an integral part of the ceruloplasmin molecule (Goresky et al. 1968). Gastrointestinal absorption is normally regulated by the copper status in the body. In general, up to 50% of small doses (i.e., less than 1 µg in rats) are absorbed, whereas large doses are absorbed to a lesser extent (Aaseth and Norseth 1986). In humans, about 40% of the dietary copper is absorbed (USEPA 1980). Absorbed copper is freely exchangeable with copper loosely bound to the alpha-globulin ceruloplasmin, where it is exchanged in the cupric form (Schroeder et al. 1966). Copper is stored mainly in liver, brain, heart, kidney, and muscle; in tissues and blood cells, copper is bound to proteins, including many enzymes (Aaseth and Norseth 1986). Amino acids facilitate the entry of Cu into liver cells, and a small proportion of copper in serum is bound to amino acids (Goresky et al. 1968). About 80% of the absorbed copper is bound to metallothionein in the liver; the remainder is incorporated into compounds such as cytochrome *c* oxidase (USEPA 1980; ATSDR 1990). Copper accumulations in animals are associated with increased number and increased size of copper-containing lysosomes in hepatocytes. In liver, copper is initially bound to a metallothionein-like, low-molecular-weight protein, and later it appears in a high-molecular-weight protein, ceruloplasmin, which reenters the circulation. Ceruloplasmin transports copper to tissues and also functions as an oxidase (Aaseth and Norseth 1986). The amount of copper absorbed is usually far in excess of metabolic requirements (Sugawara et al. 1994). Of the copper retained in the body, almost all plays a particular physiological role in the function of at least 12 specific copper proteins, such as cytochrome *c* oxidase and tyrosinase. Thus, only extremely small concentrations of free copper ions are normally found in body fluids (NAS 1977).

Retention of radiocopper injected into humans is high; only 10% is excreted within 72 h in urine and feces, and 50% in four weeks (Aaseth and Norseth 1986). Most (72%) of the unabsorbed copper is excreted in the feces primarily by way of the biliary duct, the salivary glands, or the intestinal mucosa; a minor portion is excreted by way of sweat and menses (Schroeder et al. 1966; USEPA 1980; ATSDR 1990). In mammals, copper is excreted mainly via the bile in association with glutathione or unidentified high-molecular-weight molecules. However, the transport mechanisms of copper from liver cells into bile are essentially unknown (Aaseth and Norseth 1986). In rats, biliary excretion of copper is increased by increased flow of bile, increased body temperature, or administration of adrenal steroids (Sugawara et al. 1994).

Mechanisms implicated in copper poisoning include free radical production, alteration in activities of several enzymes, and interference with metallothionein synthesis. At the cellular level,

copper has several primary mechanisms of toxicity that alter protein configuration and biological activity. These include the catalysis of peroxidation reactions and subsequent generation of free radicals that damage lipids and proteins, interactions with R groups of proteins — particularly SH groups, and acting as a substituent for other metals in metalloproteins (Sanders et al. 1994). Copper, in relative excess, is a cytotoxic metal with injury related to the process of lipid peroxidation. Isolated rat hepatocytes exposed to copper solutions for as long as 90 min show a concentration- and time-related decrease in cell viability as judged by loss of intracellular potassium and aspartate aminotransferase, an increase in lipid peroxidation, and a decrease in glutathione (Stacey and Klaassen 1981). Falling disease in cattle, dogs, and chickens is associated with a cardiovascular disorder caused by reduced activity of lysal oxidase, a Cu-requiring enzyme necessary for elastic tissue formation and maintenance (USEPA 1980). Metallothionein synthesis acts as a protective mechanism against buildup of excessive amounts of the essential, but potentially toxic, copper ions, possibly before the development of other control processes. In livers of newborn lambs, rabbits, mice, and hamsters, copper concentrations are usually directly related to the metallothionein content in cytoplasmic fractions (Bakka and Webb 1981). In sheep, elevated serum glutamic oxaloacetic transaminase (SGOT) levels were linked to elevated copper concentrations in blood at least 1 to 6 weeks before obvious external signs of copper poisoning. SGOT measurements in sheep serum seem to constitute an adequate early warning of the approach of the hemolytic crisis and eventual death of the animal from chronic copper poisoning (MacPherson and Hemingway 1969).

3.3.4 Interactions

Copper interacts with numerous compounds normally found in natural waters. The amounts of the various copper compounds and complexes present in solution depend on water pH, temperature, and alkalinity and on the concentrations of bicarbonate, sulfide, and organic ligands (USEPA 1980). In animals, copper interacts with essential trace elements such as iron, zinc, molybdenum, manganese, nickel, and selenium and also with nonessential elements including silver, cadmium, mercury, and lead; interactions may be either beneficial or harmful to the organism (Kirchgessner et al. 1979). The patterns of copper accumulation, metabolism, and toxicity from these interactions frequently differ from those produced by copper alone. Acknowledgment of these interactions is essential to understanding copper toxicokinetics.

Aluminum

Mixtures of copper and aluminum were more than additive in toxicity to ova of brown trout, *Salmo trutta* (Sayer et al. 1991)

Cadmium

Exposure of algae to low sublethal concentrations of copper (0.03 µg/L) increases their sensitivity toward additional copper challenge and to cadmium (Cd) salts (Visviki and Rachlin 1994a). In freshwater clams (*Anodonta cygnea*) exposed for 46 days to a mixture of high concentrations of copper (139 µg/L) and cadmium (122 µg/L), cadmium accumulation is reduced 90% and copper accumulation reduced 50% (Holwerda 1991). Exposure of crayfish (*Cambarus bartoni*) to 12.5 µg Cd/L for 72 h results in significantly increased copper stores in the hepatopancreas; however, isopods similarly exposed had decreased copper stores in antennal glands (Mwangi and Alikhan 1993). In the presence of copper, barnacles tend to accumulate cadmium (Powell and White 1990). In fishes, copper–cadmium interactions occur in Mozambique tilapia (*Oreochromis mossambicus*) during single and combined exposures. Waterborne copper tends to increase whole-body cadmium content of tilapia at all tested copper concentrations and exposure durations (as high as 400 µg Cu/L for 96 h); however, cadmium exposure tends to lower copper concentrations in tissues of tilapia (Pelgrom et al. 1994).

In birds, copper concentrations in kidneys of the willow ptarmigan (*Lagopus lagopus*) are positively correlated with concentrations of cadmium (Wren et al. 1994).

In mammals, cadmium inhibits copper absorption across the intestinal mucosa (Aaseth and Norseth 1986). Intercorrelations of copper with cadmium and zinc in livers of polar bears (*Ursus maritimus*) are probably mediated by metallothioneins, which may contain all three metals (Braune et al. 1991). In rats, copper protects against nephrotoxicity induced by cadmium, provided that copper is administered 24 h prior to cadmium insult. Specifically, rats given 12.5 mg Cu/kg BW by way of subcutaneous injection 24 h before receiving 0.4 mg Cd/kg BW — when compared to a group receiving Cd alone — did not have excessive calcium in urine and renal cortex or excessive protein in urine. Thus, 2.8 mg Cu/kg BW protects against 0.25 mg Cd/kg BW (Liu et al. 1992).

Iron

Iron-reducing bacteria from a copper-contaminated sediment were more tolerant of copper adsorbed to hydrous ferric oxide (HFO) than were pristine-sediment bacteria (Markwiese et al. 1998). Copper-tolerant bacteria were more efficient in reducing contaminated HFO, with greater potential for copper mobilization in aquatic sediments (Markwiese et al. 1998).

Mixtures of copper and iron salts were more than additive in toxicity to ova of brown trout (Sayer et al. 1991).

In muscle of Weddell seals (*Leptonychotes weddelli*), copper is positively correlated with iron (Szefer et al. 1994). In general, concentrations of copper in all tissues of all marine vertebrates examined are positively correlated with concentrations of iron (Eisler 1984).

The primary function of the mammalian red blood cell is to maintain aerobic metabolism while the iron atom of the heme molecule is in the ferrous (Fe^{+2}) oxidation state; however, copper is necessary for this process to occur (USEPA 1980). Excess copper within the cell oxidizes the ferrous iron to the ferric (Fe^{+3}) state. This molecule, known as methemoglobin, is unable to bind oxygen or carbon dioxide and is not dissociable (Langlois and Calabrese 1992). Simultaneous exposure of sheep to mixtures of cupric acetate, sodium chlorite, and sodium nitrite produced a dose-dependent increase in methemoglobin formation (Calabrese et al. 1992; Langlois and Calabrese 1992).

The addition of iron to diets of domestic pigs increases their resistance to copper poisoning (USEPA 1980), but this is an exception. High intake of iron, in general, adversely affects copper status in ruminants, guinea pigs, and rats; the mechanisms for this phenomenon are unknown (Yu et al. 1994). Genetically anemic and normal strains of rats fed high-iron diets had reduced kidney copper concentrations in both groups. This was associated with decreased absorption and biliary excretion of copper (Yu et al. 1995).

Manganese

Copper in livers and muscles of Weddell seals was positively correlated with manganese (Szefer et al. 1994). In general, manganese and copper are positively correlated in tissues of marine vertebrates (Eisler 1984). Uptake of copper from copper-contaminated freshwater sediments by annelid worms is related to the amount of reducible manganese oxide in the sediments (Diks and Allen 1983).

Molybdenum

In terrestrial vegetation, molybdenum and sulfur interfere with copper-induced deficiencies (Gupta 1979). Copper poisoning in cattle and other ruminants is governed by dietary concentrations of molybdenum and sulfate (Lewis et al. 1967; Todd 1969; Buckley and Tait 1981; Eisler 1989). Molybdenum and sulfur in mammalian diets cause a decrease in the availability of copper because of the formation of the biologically unavailable copper–thiomolybdate complex (Aaseth and Norseth 1986). Cattle die when grazing for extended periods on pastures where the ratio of copper to molybdenum

is less than 3 to 1, or if they are fed low-copper diets containing molybdenum at 2 to 20 mg Mo/kg ration (Eisler 1989). Wilson's disease is induced in rabbits by feeding a diet high in molybdates and sulfates, suggesting that the disease is not solely the result of copper intoxication (Goresky et al. 1968).

Zinc

Copper is positively correlated with zinc in gills of two species of fishes from the Mediterranean Sea (Romeo et al. 1994). Mixtures of copper and zinc salts in marine or freshwater fishes are more-than-additive in toxicity, producing more deaths in 96 h than expected on the basis of individual components (Eisler and Gardner 1973; Birge and Black 1979; Hodson et al. 1979). Mixtures of copper and zinc are generally acknowledged to be more-than-additive in toxicity to a wide variety of aquatic organisms (Birge and Black 1979; Hodson et al. 1979; Fernandez and Jones 1990; Eisler 1993). But mixtures of copper (0 to 90 µg/L) and zinc (0 to 1200 µg/L) are only additive in action to a marine bacterium (*Photobacterium phosphoreum*), decreasing its luminescence after exposure for 30 min (Parrott and Sprague 1993). Sometimes mixtures of copper and zinc salts are less-than-additive in action, as judged by DNA, RNA, and protein contents of newly hatched fathead minnows (*Pimephales promelas*) exposed for 4 days (Parrott and Sprague 1993).

In birds, copper and zinc concentrations are positively correlated in kidneys of the willow ptarmigan (*Lagopus lagopus*; Wren et al. 1994) and in kidneys and livers of common murres (*Uria aalge*; Stewart et al. 1994).

In mammals, copper absorption across the intestinal mucosa is inhibited by concomitant high oral intake of zinc (Aaseth and Norseth 1986). In livers from Weddell seals, copper is positively correlated with zinc (Szefer et al. 1994). The addition of zinc to swine diets protects against copper toxicosis caused by eating diets containing 250 mg Cu/kg ration (USEPA 1980).

Other Inorganics

Copper interacts with lead, magnesium, silver, and other elements. Dose-dependent frequency of deformities were observed in chironomid larvae held in water containing 1 to 100 µg Cu/L for 5 generations; copper and lead mixtures — up to 500 µg Pb/L — interacted to produce more-than-additive deformity frequency (Janssens de Bisthoven et al. 1998). In mammals, supplemental copper promotes urinary excretion of lead from the body and loss of lead from tissues (Flora 1991). In shore crabs (*Carcinus maenas*), ionic copper displaces ionic magnesium in gills, leading to inhibition of phosphoryl transfer (Hansen et al. 1992b). In embryos of the Pacific oyster (*Crassostrea gigas*), silver — at 0.5 to 15.5 µg silver/L — enhances adverse effects when copper concentrations exceed 6.0 µg Cu/L (Coglianese and Martin 1981). Silver positively correlates with copper in livers of Weddell seals, but the correlation is negative in muscles (Szefer et al. 1994).

In fishes, additive or more-than-additive toxicity occurs with mixtures of salts of copper and mercury, copper-zinc-phenol, and copper-nickel-zinc (Birge and Black 1979). Accumulation of copper in gills of fathead minnows during exposure to 16 µg Cu/L is reduced by added ionic calcium, which competes with Cu for gill binding sites (Playle et al. 1992).

Organic Compounds

Sequestering agents, increasing salinity, sediments, and other variables all reduce toxicity and accumulation of copper in tested species of aquatic plants and invertebrates. Chelating agents, such as nitrilotriacetic acid, reduce the toxicity of ionic copper to six species of estuarine phytoplankton (Erickson et al. 1970). Sensitivity of freshwater zooplankton communities varies seasonally. Communities are most sensitive to copper stress (20 or 40 µg Cu/L) during exposure for 5 weeks in spring rather than in summer or autumn because, in part, of reduced dissolved organic carbon concentrations in the spring (Winner et al. 1990). Adverse effects of copper on survival of marine copepods are reduced or eliminated by the presence of clay minerals, diatoms, ascorbic acid, sewage

effluents, water extracts of humic acids, and certain soil types (Lewis et al. 1972). Chelators, such as EDTA, and more alkaline pH increase the survival and larval developmental rates of copepods challenged with copper through increased complexation of cupric ions (Sunda et al. 1990). Natural fulvic acids, which comprise 75% of dissolved humic substances, reduce the acute toxicity of copper to rotifers (Porta and Ronco 1993). A significant reduction in radiocopper-64 accumulation by clams (*Macoma balthica*) occurs at high concentrations of dissolved organic ligands. Reduction is more pronounced at 3.0% salinity than 1.0% salinity (Absil et al. 1993). The presence of sediments in assay containers reduces the toxicity of copper to freshwater gastropods (Winger et al. 1984). Copper uptake by brine shrimp (*Artemia franciscana*) increases with decreasing pH and decreasing carbonate complexation (Blust et al. 1991). Studies with a freshwater shrimp (*Paratya australiensis*) and copper salts show that uncomplexed cupric ions are the most toxic chemical species in solutions containing nitrilotriacetic acid or glycine; however, the singly charged copper-glycine⁺ complex also appears to be mildly toxic (Daly et al. 1990a). Shrimp (*Paratya* sp.) are more resistant to copper in higher alkalinity waters (Daly et al. 1990b) and under conditions of increasing dissolved organic matter (Daly et al. 1990c).

In freshwater fishes, mixtures of copper with anionic detergents or various organophosphorus insecticides cause more-than-additive toxicity (Hodson et al. 1979). In marine vertebrates, copper in tissues is positively correlated with metal-binding proteins (Eisler 1984). Accumulations of copper in gills of fathead minnows during exposure to 16 µg Cu/L is reduced by added EDTA, which reduces bioavailability of copper through complexation (Playle et al. 1992). Copper LC50 (96 h) values (i.e., concentrations of ionic copper in solution at start of the test estimated to kill 50% of the test species in 96 h, to larval fathead minnows) range from a low of 2 µg/L at low pH and low dissolved organic carbon to 182 µg/L at pH 6.9 and dissolved organic carbon of 15.6 mg/L (Welsh et al. 1993). Acidification and the removal of dissolved organic carbon increases the toxicity of copper to fathead minnows in natural waters of low alkalinity and explains 93% of the variability in field toxicity data for that species (Welsh et al. 1993).

In mammals, phenobarbital and phenytoin increase serum ceruloplasmin concentrations (Aaseth and Norseth 1986). Chronic copper poisoning in sheep is exacerbated when diets contain heliotrope plants (*Heliotropium* sp., *Echium* spp., *Senecio* sp.). Aggravated effects of the heliotrope plants include reduced survival and a twofold to threefold increase in liver and kidney copper concentrations when compared to control animals fed copper without heliotropes (Howell et al. 1991). Rats given acutely toxic doses of 2,3,7,8-tetrachlorodibenzo-para-dioxin had elevated concentrations of copper in liver and kidney because of impaired biliary excretion of copper (Elsenhans et al. 1991). Morphine increases copper concentrations in the central nervous system of rats, and dithiocarbamates inhibit biliary excretion (Aaseth and Norseth 1986). In human patients, urinary excretion of copper is increased after treatment with D-penicillamine, calcium disodium EDTA, or calcium trisodium diethylenetriamine penta acetic acid (Flora 1991).

3.4 CARCINOGENICITY, MUTAGENICITY, AND TERATOGENICITY

3.4.1 General

No definitive evidence exists demonstrating that copper or copper compounds at environmentally realistic concentrations are the causative agents in the development of carcinogenicity, mutagenicity, or teratogenicity (USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). However, under controlled conditions of grossly elevated exposures, some studies suggest that copper is a potential carcinogen in rodents (USEPA 1980; ATSDR 1990; Toussaint and Nederbragt 1993); a mutagen in rodents (Aaseth and Norseth 1986; ATSDR 1990), sheep (Bires et al. 1993), and grasshoppers (Bhunya and Behura 1986); and a teratogen in fish (Birge and Black 1979), rodents, and other small laboratory animals (Aaseth and Norseth 1986).

3.4.2 Carcinogenicity

The carcinogenic classification of copper is Group 3 or D; that is, it is not classifiable as to its carcinogenicity in humans (ATSDR 1990). No definitive evidence exists showing that copper or copper compounds cause cancer in mammals (USEPA 1980; Aaseth and Norseth 1986; ATSDR 1990). Although hypercupremia is sometimes associated with neoplasms (USEPA 1980), some copper compounds seem to have an inhibitory effect on the development and growth of malignant tumor cells (Aaseth and Norseth 1986). Copper is not associated with an elevated incidence of cancer in humans or animals exposed by way of inhalation, oral, dermal, or intramuscular injection routes. A slightly increased incidence of reticulum cell sarcoma was noted in mice 18 months after a single subcutaneous injection of copper 8-hydroxyquinoline, but this needs to be verified (ATSDR 1990).

Sensitivity of cancerous cells to copper may reflect cell DNA content. Two closely related rat hepatoma cell lines differed in sensitivity to copper toxicity by a factor of four; DNA content in each cell line decreased with increasing copper concentrations, but at different rates. Severity of toxicity was associated with increasing accumulations of copper in the cell nucleus and with decreasing DNA (Toussaint and Nederbragt 1993).

3.4.3 Mutagenicity

Grasshoppers (*Oxya velox*) injected intra-abdominally with relatively high concentrations of soluble copper showed a 1.6% frequency of chromosomal anomalies in meiotic cells of testes 24 h after injection (Bhunya and Behura 1986); however, no control data were presented. Copper-induced DNA strand breaks in rats and chromosomal aberrations and sperm abnormalities in mice suggest that copper is a potential human mutagen (ATSDR 1990). Copper salts affect chromosomes *in vitro* in the presence of hydrogen peroxide and ascorbic acid and can also increase the frequency of noncomplementary nucleotides in the synthesized DNA double helix (Aaseth and Norseth 1986). Sheep, age 1.5 years, given about 10.7 mg Cu/kg BW daily — in addition to other metals — until they died (65 to 84 days later) show a significant increase in sister chromatid exchanges in bone marrow (Bires et al. 1993). However, the specific role of copper on survival and mutagenicity is unclear and requires verification.

3.4.4 Teratogenicity

Grossly elevated concentrations of dissolved copper produce teratogenicity in fish embryos. A significant number of malformed fish larvae came from eggs treated with 500 µg Cu/L (Birge and Black 1979). In studies with laboratory animals and elevated concentrations of copper salts, copper penetrates the placental barrier into the fetus; intramuscular injection of 4 mg Cu/kg BW early in pregnancy adversely affects fetal central nervous system development (Aaseth and Norseth 1986). In humans, no definitive data are available on whether copper can cause birth defects; however, incubation of human spermatozoa with metallic copper results in loss of sperm motility (Aaseth and Norseth 1986).

3.5 CONCENTRATIONS IN FIELD COLLECTIONS

3.5.1 General

Copper concentrations in air, soil, water, sediments, and other abiotic materials are elevated as a result of human activities, especially near copper smelters and mines, urban areas, municipal and industrial wastewater outfalls, marinas containing copper-based antifouling paints, and agricultural soils receiving prolonged applications of copper-based fungicides (Table 3.2). Maximum copper

Table 3.2 Copper Concentrations in Selected Abiotic Materials

Material, Units of Concentration, and Other Variables	Concentration^a	Reference^b
AIR, µg/m³		
Near copper smelters	1–2; Max. 5.0	1, 2
Nonurban locations	0.16–0.21; Max. 1.2	3
Remote locations	Usually <0.001; sometimes 0.001–0.003; Max. 0.012	4
South Pole	0.00004	5
Urban locations	0.15–0.18; Max. 1.6	4
United States	0.01–0.67	5
U.S. cities	Usually 0.09–0.81; sometimes 0.81–2.4; infrequently >2.4	2, 6
Uncontaminated	0.001–0.2	1, 7
COAL, µg/kg dry weight (DW)	17,000	7
DRINKING WATER, µg/L		
Conducted via copper pipes	Max. 1000	1
Private houses		
White Plains, New York	540	6
Bridgeport, Connecticut	185	6
Vermont		
Private houses	75–1400	6
Hospital	17–730	6
United States	134; Max. 8350;	1, 2
	0.2	7
GLACIERS, µg/kg fresh weight (FW)		
GROUNDWATER, µg/L		
New Jersey	About 5.0	1
LAKES AND RIVERS, µg/L		
Canada	1–8	1
Contaminated vs. noncontaminated	50–100 vs. 1–7	6
Lake Ascosa, Nicaragua, 1991–92	Usually <2.0; mean 3.1; Max. 13.1	8
Ligurian Sea drainage	<0.3–1.75 (equivalent to 3.5–7.1 tons annually)	22
New Jersey	3.0	1
Sweden; near brassworks vs. reference site	9.4 vs. 1.0	21
United States	5.3 (0.83–105.0); usually <2.0–4.2	1, 5, 7
MANURE, µg/kg DW		
Cattle	5000	1
MINE TAILINGS, mg/kg DW		
Butte Lake, Canada, 1982	7100	9
MUNICIPAL WATER SUPPLIES, µg/L	8.3 (0.6–250.0)	6
OIL, µg/kg FW		
Crude	140	7
Shale	70,000	7
POND WATER, µg/L		
Massachusetts	(<10–105)	1
POULTRY LITTER, mg/kg DW	1196	10
PRECIPITATION, µg/L		
Soluble vs. total	6.0 vs. 12.3	4
ROCKS, µg/kg DW		
Crustal and sedimentary	24,000–45,000	6, 7
Sandstones	10,000–40,000	11
Shales	30,000–150,000	11
Marine black shales	20,000–300,000	11
SEAWATER, µg/L		
Central Texas coast	Max. 50.0	12
Chesapeake Bay, Maryland; 1985–86; dissolved	11.7 (ND-80.0)	13
In water flowing through copper pipes	45.0	6
Mediterranean, northwestern coast	Max. 22.4	12
North Sea	0.2–2.6	14
Oceanic		

Table 3.2 (continued) Copper Concentrations in Selected Abiotic Materials

Material, Units of Concentration, and Other Variables	Concentration^a	Reference^b
Dissolved	0.15	7
Total	0.06–6.7	5, 12, 13
Surface waters		
Atlantic Ocean	0.06–0.21	1
East Arctic Ocean	0.13	1
Taiwan, coastal		
Total	10.2	15
Particulate	2.49	15
Dissolved	7.75	15
Labile	2.19	15
Inorganic labile	2.15	15
Free labile	0.04	15
Nonlabile	5.56	15
Polar nonlabile	3.81	15
Nonpolar nonlabile	1.75	15
Taiwan, near copper recycling facility		
Total	0.8–737.0	15
Dissolved	3.5–36.5	15
Particulates	0.2–723.0	15
United Kingdom estuaries		
Contaminated	3–176	14
Noncontaminated	2–3	14
SEDIMENTS, mg/kg DW		
England and Wales, streams	7–70	17
Lake Ascosa, Nicaragua; 1991–92	(36.6–73.7)	8
Long Island Sound, New York; 1984–85	190	18
Southwest England		
Carnon River (water 1080 µg Cu/L)	1650: Max. 6500	14
Fowey (water 7–21 µg Cu/L)	50; Max. 370	14
Red River (water 17– 35 µg Cu/L)	590	14
Sweden; freshwater lakes; 1988		
3–5 km from smelter	707–2531	19
50–80 km from smelter	37–54	19
United Kingdom estuaries, contaminated vs. noncontaminated	>2000 vs. 10	14
SEDIMENT INTERSTITIAL WATERS, µg/L		
Butte Lake, Canada; 1982	Max. 14.8	9
Clean vs. copper-contaminated sediments	<10 vs. 100	14
SEWAGE SLUDGE, mg/kg DW		
Missouri	390 (45–5200)	16
Primary sludge	21 (3–77)	1
United States, 23 cities	991 (126–7729)	1
SOILS, mg/kg DW		
Global	(2–250)	1, 5
Italy	51	20
Near copper production facility	7000	1
To 100 cm depth		
Total	20	7
Organic fraction	350	7
Under oak trees	3.5	6
Under maple trees	6.0	6
United States	19 (1–70)	11, 16

^a Concentrations are shown as means, range (in parentheses), maximum (Max.), or nondetectable (ND).

^b 1, ATSDR 1990; 2, USEPA 1980; 3, Nriagu 1979a; 4, Nriagu 1979d; 5, Aaseth and Norseth 1986; 6, Schroeder et al. 1966; 7, Nriagu 1979c; 8, Cruz et al. 1994; 9, Pedersen 1983; 10, van der Watt et al. 1994; 11, NAS 1977; 12, Neff and Anderson 1977; 13, Hall et al. 1988; 14, Bryan and Langston 1992; 15, Hung et al. 1990; 16, Beyer 1990; 17, Thornton 1979; 18, Turgeon and O'Connor 1991; 19, Johnson et al. 1992; 20, Arduini et al. 1995; 21, Hogstrand et al. 1991; 22, Migon 1993.

concentrations in selected abiotic materials are 5 µg/m³ in air, 5 µg/L in groundwater, 12 µg/L in rainwater, 300 mg/kg DW in black shales, 1200 mg/kg DW in poultry litter, 6500 mg/kg DW in marine sediments, 7000 mg/kg DW in soils, and 7700 mg/kg DW in sewage sludge ([Table 3.2](#)).

Copper concentrations in field collections of plants and animals are usually elevated in areas treated with copper-containing herbicides, near smelters, and from heavily urbanized and industrialized areas (Stokes 1979; Eisler 1984; Winger et al. 1984; Read and Martin 1993; Swiergosz et al. 1993; Fishelson et al. 1994; Storm et al. 1994). The amount and distribution of copper in animal tissues varies with tissue, organism age, sex, and amount of copper in the diet (Cuill et al. 1970; NAS 1977; USEPA 1980; Fishelson et al. 1994). Additional and more detailed information on copper concentrations in field collections of plants and animals is found in Jenkins (1980) and Eisler (1979, 1981).

In terrestrial vegetation, copper is usually less than 35 mg/kg DW except near smelters, where it may approach 700 mg/kg DW, and in copper-accumulator plants that may normally contain as much as 13,700 mg/kg DW ([Table 3.3](#)). In aquatic vegetation, copper is elevated in metals-contaminated water bodies, reaching concentrations as high as 1350 mg/kg DW in eelgrass (*Zostera* spp.) from contaminated bays vs. 36 mg/kg DW in conspecifics from reference sites ([Table 3.3](#)).

Copper concentrations in terrestrial invertebrates range from 137 to 408 mg/kg DW. Soil invertebrates are not likely to accumulate copper but are important in recycling copper through terrestrial food webs. Aquatic invertebrates seldom contain as much as 95 mg Cu/kg DW, regardless of collection locale. Exceptions include whole amphipods and lobster hepatopancreas (335 to 340 mg/kg DW) from copper-contaminated sites and many species of molluscs that normally contain 1100 to 6500 mg Cu/kg DW ([Table 3.3](#)).

Maximum concentrations of copper in elasmobranchs and teleosts from all collection sites range from 7 to 15 mg/kg DW in eyeballs, intestines, muscle, scales, vertebrae, heart, and gonads and from 16 to 48 mg/kg DW in gills, kidneys, skin, and spleens. They reach 53 mg/kg DW in whole animals, 155 mg/kg DW in stomach contents, 208 mg/kg DW in feces, and 245 mg/kg DW in livers ([Table 3.3](#)).

Data on copper concentrations in field collections of amphibians and reptiles are scarce. Crocodile eggs contain as much as 60 mg Cu/kg DW; however, some toads (*Bufo* spp.) may contain as much as 2100 mg Cu/kg DW in livers without apparent adverse effects ([Table 3.3](#); Goldfischer et al. 1970).

Birds from contaminated sites may contain as much as 9 to 28 mg Cu/kg DW in eggs, muscle, and stomach contents; 43 to 53 mg/kg DW in kidneys, feces, and feathers; and 367 mg/kg DW in livers ([Table 3.3](#)).

Marine mammals usually contain less than 44 mg Cu/kg DW in all tissues except livers. Copper in livers seldom exceeds 116 mg/kg DW except in polar bears (146 mg/kg DW), and manatees, *Trichechus manatus*, (1200 mg/kg DW) from a copper-contaminated site ([Table 3.3](#)). Maximum copper concentrations in terrestrial mammals from all collection sites are usually less than 29 mg/kg DW in all tissues except kidneys (108 mg/kg DW) and livers (1078 mg/kg DW; [Table 3.3](#)).

3.5.2 Abiotic Materials

Copper concentrations in abiotic materials are comparatively elevated near copper smelters and urban areas ([Table 3.2](#)). Copper concentrations are also elevated in drinking water from copper pipes, in poultry and livestock manures, mine tailings, fossil fuels, shales ([Table 3.2](#)), sewage sludge, and in wastes from plating industries, foundries, and coking plants (ATSDR 1990). Drinking waters from certain locales contain elevated concentrations of copper added intentionally to control algal growth; drinking water may account for 10 to 20% of the daily intake of copper in humans (USEPA 1980).

Copper is found in the rocks and minerals of the earth's crust, occurring usually as sulfides and oxides, and sometimes as metallic copper (USEPA 1980). The mean concentration of copper in the upper lithosphere ranges from 70 to 100 mg/kg, ranking 14th among the trace elements in this

Table 3.3 Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
TERRESTRIAL PLANTS		
Red maple, <i>Acer rubrum</i> ; leaf; Ontario, Canada; distance from smelter		
1.6 km	37 DW	1
2.6 km	26 DW	1
10.4 km	19 DW	1
28.9 km	16 DW	1
Copper plant mint, <i>Aeolanthus biformifolius</i> ; Zaire		
Leaf	2150–2600 DW	1
Flower stem	2150–3500 DW	1
Corm	2600–13,700 DW	1
Whole	10,000–13,700 DW	1
Agricultural crops, various		
Hair grass, <i>Deschampia flexuosa</i> ; Ontario, Canada; distance from smelter	3–36 DW	2
1.7 km	726 DW	1
2.1 km	121 DW	1
7.4 km	103 DW	1
52.7 km	13 DW	1
Ferns, seven species; leaves	0.51 (0.22–0.98) FW	1
Fungi		
Seven species, whole	2.4 (1.5–3.0) FW	3
Various species		
Cap	Max. 131.7 DW	1
Spore	Max. 165.0 DW	1
Stalk	Max. 14.2 DW	1
Whole	Max. 95.9 DW	1
Grasses, various species	5 DW	2
Moss, <i>Hypnum cupressiforme</i>		
Wales; distance downwind from smelter		
Up to 3 km	All dead	1
8 km	62–68 DW	1
25 km	18–19 DW	1
Control site	11 DW	1
Sweden; near industries		
Legumes, various	Max. 265–580 DW	1
Lichens, various species	15 DW	2
Arctic		
Near copper smelter; Sudbury, Ontario	5 DW	4
(15–20) DW		4
Tomato, <i>Lycopersicon esculentum</i> ; United States		
Fruit	14 (8–34) DW	1
Leaf	(3–12) DW	1
Terrestrial plants, various species; seeds	1.1 (0.6–2.9) FW	3
Poppy, <i>Papaver orientale</i> ; pods	14.3 FW	3
Lichen, <i>Parmelia baltimorensis</i> ; Washington, D.C.; various years		
1938	17 DW	1
1958	22 DW	1
1970	32 DW	1
Norway spruce, <i>Picea abies</i>		
Connecticut		
Leaf	6.0 DW	1
Twig	15.0 DW	1
England		
Bark	5.0 DW	1
Wood	0.6 DW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Sweden		
Bark	25.0 DW	1
Needle	(4.4–8.1) DW	1
Root	(8–21) DW	1
Twig	(42–76) DW	1
Wood	2.0 DW	1
Trees, various species; leaves	1.8 (0.6–5.2) FW	3
Tundra plants; whole; Spitsbergen, Norway; 1987		
Lichens, 14 species	1.8–36.7 DW	5
Mosses, four species	3.4–33.0 DW	5
Vascular plants, five species	3.9–10.0 DW	5
Elm, <i>Ulmus americana</i> ; wood	7.9 FW	3
Corn <i>Zea mays</i>		
Grain		
East Asia	1.6 FW	1
Lower Dahomey	(1.0–2.9) DW	1
United States	8 (4–17) DW	1
From soils with Cu additions of 360 kg Cu/ha		
Grain	1.7–2.8 DW	6
Leaves	7.8–12.5 DW	6
AQUATIC PLANTS		
Algae and macrophytes; 11 species; Brazil; November 1989; whole	2.4–6.9 DW	14
Alga, <i>Ascophyllum nodosum</i>		
England; polluted bay vs. reference site	68 (46–96) DW vs. 12 (6–18) DW	1
Norway; polluted fjord vs. reference site	(45–240) DW vs. 5.5 (4–8) DW	1
Freshwater macrophytes; various species	2.5–256.0 DW	15
Water milfoil, <i>Myriophyllum</i> spp.	10.0–41.3 DW	1
Brown alga, <i>Pelvetia canaliculata</i> ; whole		
Norway	55 DW	1
Scotland	5–16 DW	1
Pondweed, <i>Potamogeton</i> spp.; whole; Pennsylvania	5.0–102.9 DW	1
Eelgrass, <i>Zostera</i> spp.		
Denmark; 1979–80; metals-contaminated site vs. reference site		
Leaves	9–13 DW vs. 5–6 DW	16
Roots	27.4 DW vs. 6–7 DW	1
Portugal and Spain; contaminated bay vs. reference site	1350 DW vs. (9–36) DW	1
PORIFERA		
Sponges; three species; whole	13–34 DW	1
COELENTERATES		
Jellyfish, <i>Cyanea capillata</i> ; whole		
New England	8.2 DW	1
Sweden	68.0 DW	1
Octacorals; Venezuela; whole; five species	0.9–3.1 DW	17
TERRESTRIAL INVERTEBRATES		
Honeybee, <i>Apis mellifera</i> ; Czechoslovakia; industrial locations vs. reference site; 1986–87		
Foraging workers	32–37 DW vs. 20–24 DW	7
Honey	1.1–1.7 DW vs. 0.6 DW	7
Pollen	6.1–8.2 DW vs. 5.4 DW	7

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Landsnail, <i>Arianta arbustorum</i> ; urban areas vs. reference site; Innsbruck, Austria; 1987; soft parts	188 (30–408) DW vs. 84 (46–104) DW	8
Bumblebee; four species of <i>Bombus</i> ; queens; whole; Sweden; April 1991	18–23 (11–38) DW	9
Pine moth, <i>Bupalus piniarius</i> ; pupae; whole; Finland, 1987; industrialized area vs. reference site	Max. 137 DW vs. 53 DW	10
Earthworm, <i>Lumbricus rubellus</i> ; Cardiff, Wales; 1984; contaminated soils (2740 mg Cu/kg DW soil) vs. reference site (26 mg Cu/kg DW soil)		
Anterior alimentary canal	85.4 DW vs. 18.2 DW	11
Posterior alimentary canal	64.4 DW vs. 21.1 DW	11
Remainder	23.2 DW vs. 10.1 DW	11
17-year cicadas, <i>Magicicada</i> spp.; Maryland; 1987; whole	(33.2–60.3) DW	12
Pine noctuid, <i>Panolis flammea</i> ; pupae; whole; Finland, 1987; industrialized area vs. reference site	Max. 89 DW vs. 20 DW	10
Cuckoo bumblebee, <i>Psithyrus bohemicus</i> ; queens; Sweden; April, 1991; whole	19 (12–29) DW	9
Spiders, whole; from old-field subjected to 11 years of nutrient enrichment (3410 g Cu/ha yearly) vs. reference site (2–3 g Cu/ha yearly)		
Garden orb weaver, <i>Argiope aurantia</i>	110 DW vs. 80 DW	13
Wolf spiders, Lycosidae	130 DW vs. 85 DW	13

AQUATIC MOLLUSCS

Antarctic scallop, <i>Adamussium colbecki</i> ; Ross Sea; 1987–88 vs. 1990		
Digestive gland	12.6 vs. 3.5 FW	18, 19
Gills	6.5 DW vs. 1.4 FW	18, 19
Gonad	4.7 DW vs. ND	18
Kidney	4.0 DW vs. ND	18
Mantle	3.5 DW vs. ND	18
Muscle	1.6 DW vs. ND	18
Freshwater mussel, <i>Amblema</i> sp.; Texas		
Digestive gland	9.5 FW	1
Foot	2.9 DW	1
Gill	6.1 DW	1
Mantle	3.6 DW	1
Blood clam, <i>Anadara granosa</i> ; soft parts; Malaysia	0.7–0.8 FW; 6.3 (4.5–8.0) DW	20, 21
Freshwater mussel, <i>Anodonta grandis</i> ; soft parts; Manitoba, Canada; 1986	45.3 (5–80) DW	22
Lake mussel, <i>Anodonta piscinalis</i> ; gills		
No glochidia	5.4 DW	23
With glochidia	8.0 DW	23
Ocean quahog, <i>Arctica islandica</i>		
Soft parts		
Block Island Sound	10.0 DW	24
Chesapeake Bay	5.4 DW	24
Georges Bank	3.5–10.3 DW	24
New York Bight	11.3 DW	24
Western Baltic Sea, 1992–93		
Adductor muscle	1.8–2.2 DW	24
Digestive gland	13.5 DW	24
Foot	3.1 DW	24
Gills	6.7 DW	24
Kidney	40.1 DW	24
Mantle	5.0 DW	24
Soft parts	14.3–15.3 DW	24

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Whelk, <i>Buccinum undatum</i> ; soft parts		
Irish Sea	180 DW	1
Scotland	78 DW	1
Channeled whelk, <i>Busycon canaliculatum</i>		
Digestive gland	(32–1135) FW	1
Muscle	(12–21) FW	1
Cephalopods; liver	150 FW	3
Scallop, <i>Chlamys operculis</i>		
Kidney	240.0 FW	1
Shell	2.1 FW	1
Soft parts	1.7 FW	1
Pacific oyster, <i>Crassostrea gigas</i>		
Shell	(1.6–2.9) DW	1
Hong Kong, 1989; various locations		
Gill	840 DW	25
Mantle	509 DW	25
Muscle	750 DW	25
Soft parts	344–422 DW; max. 1071 DW	25
Visceral mass	383 DW	25
Arcachon Bay, France, soft parts		
1979–82	48.3–63.8 DW	26
1983–87	67.7–116.2 DW	26
1988–91	101.8–135.0 DW	26
Soft parts		
England	(340–6480) DW	1
South Africa	33.0 DW	1
Tasmania	(9.4–84.4) DW	1
United States	(7.8–38.0) FW	1
Taiwan		
Soft parts; 1989; seawater had 5.0–23.6 µg Cu/L from discharges of copper recycling facility	4401 DW; green in color	27
Soft parts		
From copper-contaminated environment	2225 DW	28
As above; after 6 days in clean seawater	746 DW	28
As above; after 32 days in clean seawater	344 DW	28
American oyster, <i>Crassostrea virginica</i>		
Florida, soft parts		
From a canal lined with chromated-copper-arsenate wood vs. reference site	150–200 FW vs. 10 FW; elevated concentrations were associated with greenish color and higher frequency of histopathology of digestive gland diverticula	29
Reference site oysters transplanted into above canal		
After 3 months	130 FW	29
After 4 months	220 FW; no increase in frequency of digestive gland lesions	29
North Carolina, soft parts		
Marina sites	36.7 FW	30
Open water sites	7.1 FW	30
At 12‰ salinity	6.0 FW	31
At 33‰ salinity	2.0 FW	31
Soft parts		
Alabama	20 (4–78) FW	1
Chesapeake Bay	(5–240) FW	1
Eastern USA	91 (7–517) FW	1
Georgia	(48–261) DW	1
Gulf of Mexico states	16 (6–27) FW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Maryland (green oysters)	Max. 1120 DW	1
NW Atlantic	46 (11–110) DW	1
Rhode Island	121 (92–140) FW	1
Texas	161 DW	1
Virginia; 1972–73		
At 7.5‰ salinity	29 FW	31
At 9.5‰ salinity	16 FW	31
At 12‰ salinity	12 FW	31
At 13.5‰ salinity	3 FW	31
Zebra mussel, <i>Dreissena polymorpha</i> ; soft parts; caged for 15–60 days; water contained 0.8–1.4 µg Cu/L and particulates had 0.3–3.2 µg Cu/L	12.6–17.7 DW	32
Zebra mussel; soft parts; the Netherlands; 1994; Rhine-Meuse delta vs. reference site	1.9–2.7 FW vs. 1.1 FW	133
Freshwater mussels; two species; soft parts; St. Lawrence River; 1989–90; sediment copper ranged from 4 to 148 mg/kg DW	7.8–16.2 DW	33
Octopus, <i>Eledone cirrhosa</i> ; English Channel; October, 1987		
Branchial hearts	335 DW	34
Digestive gland	448–463 DW	34
Genital tract	60–66 DW	34
Gill	268 DW	34
Kidney	594 DW	34
Mantle	102 DW	34
Muscle	17 DW	34
Whole	122 DW	34
Mud snail, <i>Ilyanassa obsoleta</i> ; soft parts; North Carolina		
Marina sites	402.2 FW	30
Open-water sites	219.5 FW	30
Baltic clam, <i>Macoma balthica</i> ; soft parts; The Netherlands; 1990–92		
Acid-soluble fraction	4.1 (2.7–6.7) DW	35
Total copper	13.8–22.6 DW	35
Lagoon mussel, <i>Mytella strigata</i> ; soft parts; Baja California, Mexico; 1989–91	Max. 3.9 DW	36
Common mussel, <i>Mytilus edulis</i>		
Shell		
California	(<5.8–8.6) DW	1
England	9.6 DW	1
Japan	(1.2–2.8) DW	1
New Zealand	3.0 DW	1
Soft parts		
California	(5.0–11.2) DW	1
Canada, Halifax	13.7–154.3 DW	39
England	(7–11) DW	1
Long Island Sound, New York		
1983	1.0–2.3 FW	38
1986–87	15 DW	37
Norway	(3.0–130.0)	1
Portugal and Spain	(6.5–14.0) DW	1
Mussel, <i>Mytilus smaragdium</i> ; soft parts; copper-contaminated environment vs. 6 days in clean seawater	20.2 DW vs. 1.8 DW	28
Mussels; <i>Mytilus</i> spp.; soft parts; United States; 1970s vs. 1980s		
Bodega Bay, California	6.9 DW vs. 7.7 DW	40
Narragansett Bay, Rhode Island	11.0 DW vs. 14.0 DW	40
Octopus, <i>Octopus vulgaris</i> ; hepatopancreas	4880 DW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Squid, <i>Ommastrephes bartrami</i> ; liver	195 (17–696) DW	1
Clam, <i>Paphia undulata</i> ; soft parts; Malaysia; 1993	0.9–1.1 FW	20
Scallop, <i>Pecten jacobaeus</i> ; Adriatic Sea; June 1988		
Digestive gland	16.6 DW	18
Gills	6.3 DW	18
Gonad	10.3 DW	18
Kidney	17.5 DW	18
Mantle	3.3 DW	18
Muscle	1.1 DW	18
Green-lipped mussel, <i>Perna viridis</i> ; Hong Kong; soft parts; March, 1986	Max. 35.1 DW	41
Tropical rock oyster, <i>Saccostrea cucullata</i> ; soft parts		
Australia, 1983–84; near sewage discharge vs. reference site	285 DW vs. 34 DW	42
Hong Kong, March 1986	Max. 556 DW	41
Sydney rock oyster, <i>Saccostrea commercialis</i> ; soft parts; Georges River, Australia; 1970s vs. 1980s	20–46 FW vs. 14–93 FW	43
Cuttlefish, <i>Sepia officinalis</i> ; English Channel; October, 1987		
Branchial hearts	256 DW	34
Digestive gland	313–317 DW	34
Genital tract	55–56 DW	34
Gill	183 DW	34
Kidney	185 DW	34
Mantle	141 DW	34
Muscle	9 DW	34
Whole	59 DW	34
Freshwater clam, <i>Sphaerium</i> sp.; soft parts; Illinois	10.1 DW	1
Squid, <i>Symplectoteuthis ovalaniensis</i> ; liver	1720 DW	1
Freshwater mussel, <i>Unio</i> sp.; soft parts	11.9–19.3 DW	32

AQUATIC ARTHROPODS

Amphipods, various species; whole; Antarctica; 1989	31.3 (30.7–32.0) DW	44
Crayfish, <i>Astacus astacus</i> ; raw vs. cooked		
Hepatopancreas	52.0 FW vs. 31.0 FW	45
Muscle	5.7 FW vs. 11.0 FW	45
Mayfly, <i>Baetis thermicus</i> ; whole; larvae; Japan; metal-contaminated river (28.6 µg Cu/L) vs. reference site	73.5 FW vs. 4.0 FW; Cu localized in midgut epithelial cells	46
Crustaceans; 17 species; whole; Antarctic Ocean; 1985–88		
Two species	5.5–7.7 DW	47
Three species	37–42 DW	47
Six species	53–68 DW	47
Four species	81–107 DW	47
Two species	123–149 DW	47
Benthic crab, <i>Dorippe granulata</i> ; Hong Kong (contaminated harbor)		
Exoskeleton	7.7 DW	48
Gills	123.9 DW	48
Hemolymph	53.2 FW	48
Midgut gland	114.9 DW	48
Muscle	36.6 DW	48
Euphausiids; Antarctic and Atlantic Oceans; 1985–86; whole		
<i>Euphausia superba</i>	55 (30–86) DW	49
<i>Meganyctiphanes norvegica</i>	58 (40–83) DW	49

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Lobster, <i>Homarus vulgaris</i> ; England		
Blood	32 FW	1
Exoskeleton	3 FW	1
Gill	26 FW	1
Liver	335 FW	1
Muscle	4 FW	1
Ovaries	50 FW	1
Stomach fluid	10 FW	1
Testes	1 FW	1
Urine	2 FW	1
Whole	17 FW	1
Insects; immature benthic species; whole; from copper-contaminated river up to 60 km downstream from outfall (779 mg Cu/kg DW sediments) vs. reference site (18 mg Cu/kg DW sediments)		
Plecoptera	84 DW vs. 16–32 DW	50
Trichoptera	204 DW vs. 11–18 DW	50
Mayflies, four species; whole; nymphs	11–17 DW	1
Beach hopper (amphipod), <i>Orchestia gammarellus</i> ; whole; North Sea; 1989–90; reference site vs. contaminated site	Usually <70 DW vs. >145 DW (Max. 340 DW)	51
Crayfish, <i>Pacifastacus leniusculus</i> ; raw vs. cooked		
Hepatopancreas	44 FW vs. 17 FW	45
Muscle	5 FW vs. 8 FW	45
Shrimp, <i>Pandalus jordani</i> ; muscle	14.3–18.2 DW	1
Brown shrimp, <i>Penaeus aztecus</i> ; Texas		
Exoskeleton	32 DW	1
Muscle	18–29 DW	1
Whole	34 DW	1
Viscera	173 (65–260) DW	1
Oceanic amphipods, <i>Themisto</i> spp.; whole; Antarctic and Atlantic Oceans; 1985–86	28–31 (13–79) DW	49
AQUATIC ANNELIDS		
Polychaete, <i>Lycastis ouanaryensis</i> ; whole; India; 1984–85; contaminated site vs. reference site	32–95 DW vs. 4–27 DW	52
Tubificid worm, <i>Tubifex tubifex</i> ; whole; Illinois	23 (10–42) DW	1
ECHINODERMS		
Sea star (Asteroidea), <i>Pisaster brevispinus</i> ; California		
Gonad	(2–10) DW	1
Hepatic caecum	(18–38) DW	1
Stomach	(5–40) DW	1
TUNICATES		
Sea squirt, <i>Ciona intestinalis</i>		
California		
Tunic	55 DW	1
Viscera	73 DW	1
Sweden, whole	13 DW	1
ELASMOBRANCHS AND FISHES		
Rockbass, <i>Ambloplites rupestris</i> ; Ontario, Canada		
Gill	2.1 FW	1
Kidney	3.0 FW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Liver	4.9 FW	1
Muscle	1.7 FW	1
Jolthead porgy, <i>Calamus bajonado</i> ; Puerto Rico		
Eye	1.3 FW; 6.7 DW	1
Gills	1.2 FW; 3.5 DW	1
Intestine	2.4 FW; 10.0 DW	1
Muscle	0.4 FW; 1.5 DW	1
Scales	4.9 FW; 6.9 DW	1
Vertebra	8.3 FW; 14.0 DW	1
Oceanic whitetip shark, <i>Carcharhinus longimanus</i> ; Puerto Rico		
Liver	1.3 FW; 2.2 DW	1
Muscle	0.5 FW; 2.4 DW	1
Skin	8.6 FW; 21.0 DW	1
Vertebra	3.5 FW; 11.0 DW	1
White sucker, <i>Catostomus commersoni</i> ; northern Ontario; September, 1986; copper-contaminated site (water 9.7 µg Cu/L, sediments 232 mg/kg DW) vs. reference site (2.1 µg/L water, 10 mg/kg DW sediments)		
Feces	208 DW vs. 49 DW	53
Gill	15 DW vs. 6 DW	53
Kidney	26 DW vs. 14 DW	53
Liver	83 DW vs. 50 DW	53
Stomach Contents	155 DW vs. 7 DW	53
Blackfin icefish, <i>Chenocephalus aceratus</i> ; Antarctica; 1989		
Liver	4.5 FW	44
Muscle	1.5 DW	44
African sharp-tooth catfish, <i>Clarias gariepinus</i> ; South Africa; 1988–89; metals-contaminated lake (sediments 216 mg Cu/kg DW)		
Muscle, body fat, vertebra, gonads	9–15 DW	54
Intestine, spleen, liver, kidney, heart, gills	26–46 DW	54
Brain	100 DW	54
Lake whitefish, <i>Coregonus clupeaformis</i> ; liver; Lake Superior vs. Lake Michigan	2.4 FW vs. 8.5 FW	1
Bloater, <i>Coregonus hoyi</i> ; liver; Lake Superior vs. Lake Michigan	2.4 FW vs. 7.4 FW	1
Spotted seatrout, <i>Cynoscion nebulosus</i> ; whole; South Carolina; 1990–93	0.03–2.9 FW (0.0–19.0) FW	55
Adriatic anchovy, <i>Engraulis encrasicolus</i>		
Liver	3.9 FW	1
Muscle	0.7 FW	1
Whole	1.1 FW	1
Northern pike, <i>Esox lucius</i> ; Ontario		
Gill	1.9 FW	1
Kidney	2.6 FW	1
Liver	10.9 FW	1
Freshwater fishes; Lake Tanganyika, Burundi; two commercially important species (<i>Lates</i> sp., <i>Stolothrissa</i> sp.)		
Gonads	2.0 DW	56
Heart	2.9 DW	56
Intestine	3.2 DW	56
Liver	11.9 DW	56
Muscle	1.7 DW	56
Whole	3.2 DW	56

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Freshwater fishes; Tennessee; muscle	0.1–0.9 FW; Max. 2.2 FW	58
Freshwater fishes; USA, nationwide; whole; 8 species 1984	0.65 FW; Max. 23.1 FW	57
1980–81	0.65 FW; Max. 24.1 FW	57
1978–79	0.82 FW; Max. 38.7 FW	57
Mummichog, <i>Fundulus heteroclitus</i> ; whole		
Body length 40–51 mm	59 AW	132
Body length 54–121 mm	45–49 AW	132
Atlantic cod, <i>Gadus morhua</i> ; Norway		
Gill	(4–19) DW	1
Liver	(8–18) DW	1
Muscle	(1–3) DW	1
Brown bullhead, <i>Ictalurus nebulosus</i> ; Ontario, Canada		
Gill	1.8 FW	1
Kidney	2.5 FW	1
Liver	30.3 FW	1
Muscle	1.3 FW	1
Dab, <i>Limanda limanda</i> ; liver; German Bight; March 1990; males vs. females	4.3–10.4 FW vs. 5.5–16.0 FW	130
Black marlin, <i>Makaira indica</i> ; Australia		
Liver	4.6 (0.5–22.0) FW	1
Muscle	0.4 (0.3–1.2) FW	1
Blue marlin, <i>Makaira nigricans</i> ; muscle		
Japan	0.4 (0.1–0.7) FW	1
Puerto Rico	1.3 (0.4–2.6) FW; 2.7 (1.5–10.0) DW	1
Red mullet (Mullidae), <i>Mullus barbatus</i> ; gills; Coutou, France	17.6–48.1 DW	59
Hump rock cod (Nototheniidae), <i>Notothenia gibberifrons</i> ; Antarctica; 1989; muscle	0.85 DW	44
Kelp bass, <i>Paralabrax clathratus</i> ; California; Los Angeles site near effluent discharge of steam utility plant vs. Catalina Island (reference site)		
Eyeball	8.0 DW vs. 4.0 DW	1
Gonad	6.0 DW vs. 5.0 DW	1
Heart	1.5 DW vs. 12.0 DW	1
Liver	5.0 DW vs. 6.0 DW	1
Muscle	5.0 DW vs. 2.0 DW	1
Southern flounder, <i>Paralichthys lethostigma</i> ; South Carolina; 1990–93; whole	1.1–1.9 (0.0–22.2) FW	55
Yellow perch, <i>Perca flavescens</i> ; Michigan; 1993; Torch Lake (34 µg Cu/L) vs. reference site (10 µg Cu/L)		
Ovaries	5.0 DW vs. 2.1 DW	60
Testes	3.5 DW vs. 1.3 DW	60
Southern mouth brooder, <i>Pseudocrenilabrus philander</i> ; South Africa; whole fish; mine-polluted impoundment	9 (4–26) DW	61
Winter flounder, <i>Pleuronectes americanus</i>		
New York		
Muscle	(0.5–1.1) FW	1
Liver	(2.7–13.8) FW	1
Texas		
Muscle	1.0 (0.6–1.5) DW	1
Skin	1.7 (1.2–2.1) DW	1
Atlantic guitarfish, <i>Rhinobatos lentiginosus</i>		
Liver	6.6 DW	1
Muscle	2.2 DW	1
Stomach	6.2 DW	1
Red drum, <i>Sciaenops ocellatus</i> ; South Carolina; 1990–93; whole	0.4–9.2 (0.0–52.9) FW	55

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Spanish mackerel, <i>Scomberomorus maculatus</i>		
Liver	3.3 DW	1
Muscle	2.3 DW	1
Painted comber, <i>Serranus cabrilla</i> ; gills; Coutou, France	5.3–27.2 DW	59
Sharks, 10 species; British and Atlantic waters; 1984–88		
Gills	0.05–2.2 FW	62
Gonads	0.1–4.9 FW	62
Heart	0.03 FW	62
Jaws	1.7–3.3 FW	62
Kidney	0.02–4.0 FW	62
Liver	0.2–7.8 FW	62
Muscle	0.2–2.4 FW	62
Pancreas	0.7 FW	62
Skin	0.6–12.1 FW	62
Spleen	0.03–2.5 FW	62
Vertebra	0.5–5.9 FW	62
Spiny dogfish, <i>Squalus acanthias</i>		
Liver	4.5 DW	1
Muscle	2.3 DW	1
Spleen	16.0 DW	1
Bluefin tuna, <i>Thunnus thynnus</i> ; Spain		
Heart	4.2 FW; 18.1 DW	1
Intestine	1.4 FW; 5.8 DW	1
Kidney	8.6 FW; 27.8 DW	1
Liver	74.0 FW; 245.0 DW	1
Ovary	(1.4–2.3) FW; (5.4–11.0) DW	1
Spleen	1.2 FW; 4.4 DW	1
Red hake, <i>Urophycis chuss</i>		
Liver	(3.2–6.0) FW	1
Muscle	(0.5–0.7) FW	1
Swordfish, <i>Xiphias gladius</i> ; muscle	(0.3–1.4) FW	1
AMPHIBIANS AND REPTILES		
Frogs; Maryland, 1990–91; tadpoles		
Northern cricket frog, <i>Acris crepitans</i> ; whole	9.8–15.7 DW	131
Gray treefrog, <i>Hyla versicolor</i> ; whole	7.4–12.6 DW	131
Green frog, <i>Rana clamitans</i>		
Gut vs. remainder	21.5 DW vs. 6.7 DW	131
Frogs and toads; Yugoslavia; liver; near mercury mines		
European toad, <i>Bufo bufo</i>	56.2–81.4 FW	1
Toad, <i>Bombina variegata</i>	(5.0–5.6) FW	1
European frog, <i>Rana temporaria</i>	318.9 FW	1
Giant toad, <i>Bufo marinus</i> ; liver		
Australia	Max. 1640 DW	63
Dominican Republic		
Black livers	1248–2091 DW	63
Yellow livers	367–469 DW	63
American crocodile, <i>Crocodylus acutus</i> ; egg; Florida	(0.9–15.0) FW	1
BIRDS		
Western grebe, <i>Aechmophorus occidentalis</i> ; Puget Sound, Washington; 1985–86; sediments had 52 mg Cu/kg DW		
Diet (fish muscle)	0.3–0.5 FW	64
Liver	12.7–17.6 DW	64

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Mallard, <i>Anas platyrhynchos</i> ; Canada; 1975; feathers; near smelter vs. reference site	23 DW vs. 7–14 DW	65
Black duck, <i>Anas rubripes</i> ; Canada; 1975; feathers; near smelter vs. reference site	53 DW vs. 10 DW	65
Ducks, <i>Anas</i> spp.; Poland; 1988–91		
Kidney	9.9 (3.5–30.0) FW	66
Liver	58.0 (11.0–200.0) FW	66
Muscle	4.5 (2.1–10) FW	66
Lesser snow geese, <i>Anser c. caerulescens</i> ; Wrangel Island, Russia; June 1992; 2 subpopulations		
Subpopulation that overwintered in British Columbia and northern Washington, feeding mainly on vegetative plant parts		
Eggs	3.0 DW	135
Liver	47 (20–87) DW	135
Subpopulation that overwintered in Central Valley of California feeding mainly on rice seeds		
Eggs	3.0 DW	135
Liver	78 (25–627) DW	135
Geese, <i>Anser</i> spp.; Poland; 1988–91		
Liver	80 (29–160) FW	66
Muscle	4.0 (1.6–8.8) FW	66
Antarctica; February–March 1989		
Blue eyed cormorant, <i>Phalacrocorax atriceps</i> ; muscle	10 DW	67
Southern giant petrel, <i>Macronectes giganteous</i> ; muscle	7.2 DW	67
Adelie penguin, <i>Pygoscelis adeliae</i>		
Liver	11.9 (11.0–12.6) DW	67
Muscle	7.9 (6.5–8.5) DW	67
Chinstrap penguin, <i>Pygoscelis antarctica</i>		
Feces	37.6 (35.1–49) DW	67
Liver	12.6 (12–13) DW	67
Muscle	9.7 (9.5–10.1) DW	67
Gentoo penguin, <i>Pygoscelis papua</i>		
Liver	26.5 (24.0–27.6) DW	67
Muscle	8.2 (7.7–8.9) DW	67
Redhead, <i>Aythya americana</i> ; Louisiana and Texas; 1987–88; liver	7.3 (3.9–11.5) DW	68
Canvasback, <i>Aythya valisineria</i> ; Louisiana; 1987–88; liver; females	Usually 76–187 DW	69
Ruffed grouse, <i>Bonasa umbellus</i> ; liver	5.2 FW	3
Willet, <i>Catoptrophorus semipalmatus</i> ; San Diego Bay; 1994; sediment vs. stomach contents		
Naval Air Station	3 DW vs. 17 DW	136
Tijuana Slough National Wildlife Refuge	12 DW vs. 34 DW	136
Lesser kestrel, <i>Falco naumanni</i> ; nonviable eggs; Spain; 1988–91	3.1 (0.2–7.1) FW	3
Bald eagle, <i>Haliaeetus leucocephalus</i> ; eggs		
Florida	(0.7–1.2) FW; (4.8–8.0) DW	1
Maine	(0.3–0.6) FW; (2.0–5.0) DW	1
Wisconsin	(0.5–1.2) FW; (3.0–9.0) DW	1
Willow ptarmigan, <i>Lagopus lagopus</i> ; Norway; winter 1986–87; kidney; adults vs. juveniles	2.8–4.9 FW (Max. 8.0 FW) vs. 1.9–3.6 FW (Max. 5.5 FW)	71
Lesser black-backed gull, <i>Larus fuscus</i>		
Egg	1.0 FW	1
Kidney	14.0 DW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Liver	17.0 DW	1
Muscle	14.0 DW	1
Marine birds, New Zealand; 1975–83		
Albatrosses, eight species; adults vs. juveniles		
Feather	44.0 FW vs. 18.4–32.3 FW	72
Liver	5.0–8.6 FW vs. 12.2–225.3 FW	72
Gulls, <i>Larus</i> spp.; adults vs. juveniles		
Feather	13.1–20.0 FW vs. 25.3–60.5 FW	72
Liver	5.0–6.6 FW vs. 23.8–35.0 FW	72
Penguins, three species; liver; adults vs. juveniles	4.3–13.2 FW vs. 8.5–18.5 FW	72
Petrels, 19 species; adults vs. juveniles		
Feather	14–40 FW vs. 20–79 FW	72
Liver	4–45 FW vs. 8–75 FW	72
Shearwaters, three species of <i>Puffinus</i> ; liver; adults vs. juveniles	6.4–7.2 FW vs. 4.6–446.3 FW	72
Surf scoter, <i>Melanitta perspicillata</i> ; San Francisco Bay; 1985; liver; January vs. March	37.8 (29.3–47.0) DW vs. 50.1 (41.3–58.3) DW	73
Turkey, <i>Meleagris gallopavo</i> ; Poland; 1988–91		
Kidney	3.0 (2.3–5.2) FW	66
Liver	4.7 (3.1–13.0) FW	66
Muscle	0.3 (0.2–0.4) FW	66
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg		
Florida	(0.9–1.1) FW	1
South Carolina	(0.7–1.3) FW	1
Liver; Florida, Georgia; South Carolina	(4.3–9.0) FW	1
Flamingo, <i>Phoenicopterus ruber roseus</i> ; France; 1988		
Blood serum, nestlings	0.25 (0.13–0.51) FW	74
Feather, adults	Max. 7.43 DW	74
Seabirds, 19 species; pelagic; North Pacific Ocean; 1982–87		
Kidney	4.7 FW	75
Liver	5.9 FW; Max. 7.7 FW	75
Muscle	5.1 FW	75
Seabirds		
Liver; 11 species	Means 14–64 DW	137
3 species		
Bone, fat	<1.0 DW	137
Lung, pancreas, spleen, gonads, uropygial gland, skin, eyeball	1–5 DW	137
Brain, heart, stomach, intestine, muscle	7–10 DW	137
Liver, gall bladder, kidney	11–15 DW	137
Shorebirds; Chile; November 1981–March 1982; near abandoned copper mine; liver vs. stomach contents		
Sanderling, <i>Calidris alba</i>	(9.2–11.5) FW vs. no data	76
Oyster catcher, <i>Haematopus ostralegus</i>	8.0 (6.8–8.6) FW vs. (24.4–27.2) FW	76
Kelp gull, <i>Larus dominicanus</i>	(3.8–6.3) FW vs. (0.8–3.4) FW	76
Grey gull, <i>Larus modestus</i>	6.2 (4–7.4) FW vs. (30–46.7) FW	76
Franklin's gull, <i>Larus pipixcan</i>	(4.7–5.5) FW vs. no data	76
Whimbrel, <i>Numenius phaeopus</i>	(3.9–17.8) FW vs. (6.1–86.4) FW	76
Eider, <i>Somateria mollissima</i> ; Norway		
Egg	4.0 DW	1
Kidney	43.0 DW	1
Liver	367.0 DW	1
Muscle	13.0 DW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Tree swallow, <i>Tachycineta bicolor</i> ; nestlings; acidified (pH 4.8) vs. reference (pH 6.7) lakes; Ontario, Canada; 1986–89		
Kidney	12.8 DW vs. 10.4 DW	77
Liver	42.6 DW (elevated metallothionein) vs. 17.3 DW	77
Redshank, <i>Tringa totanus</i> ; liver; feeding on sandworms (<i>Nereis diversicolor</i>) containing 500–1000 mg Cu/kg DW	30 DW	78
Waterfowl; livers; 46 species		
20 species	6–50 DW	135
16 species	51–100 DW	135
7 species	101–200 DW	135
Ring-necked duck, <i>Aythya collaris</i> ; Chesapeake Bay	263 DW	135
Pochard, <i>Aythya ferina</i> ; England	603 DW	135
Eider, <i>Somateria mollissima</i> ; Spitsbergen	900 DW	135

MARINE MAMMALS

Gray whale, *Eschrichtius robustus*; stranded along North American west coast; 1988–91

Brain	2.4 FW	79
Kidney	2.4 (0.5–4.9) FW	79
Liver	9.2 (0.6–25.0) FW	79
Stomach contents	21.0 (3.0–66.0) FW	79

Pilot whale, *Globicephala melaena*; stranded on Cape Cod, Massachusetts, 1986–90

Adults		
Brain	9.1 (5.7–12.3) DW	80
Kidney	14.7 (7.4–21.0) DW	80
Liver	15.5 (9.9–20.3) DW	80
Ovary	5.5 (2.8–8.4) DW	80
Fetuses		
Brain	5.1 (4.4–6.2) DW	80
Kidney	20.0 (8.1–28.1) DW	80

Gray seal, *Halichoerus grypus*; British Isles and vicinity; 1988–89

Blubber	<0.1 FW	81
Kidney	(3.2–27.0) FW	81
Liver	(4.0–26.0) FW	81, 82
Muscle	2.5 FW	81

Leopard seal, *Hydrurga leptonyx*; Antarctic; 1989

Kidney	32.6 (22.5–43.8) DW	83
Liver	105.0 (98.0–116.0) DW	83
Muscle	4.0 (2.5–8.4) DW	83
Stomach contents	14.4 (13.3–16.4) DW	83

Pygmy sperm whale, *Kogia breviceps*; Argentina; found dead

Heart	6.9 FW	84
Kidney	7.4 FW	84
Liver	10.3 FW	84
Other tissues	<2.3 FW	84

Weddell seal, *Leptonychotes weddelli*; Antarctic; 1989

Kidney	22.8 (21.7–24.5) DW	83
Liver	57.4 (28–87) DW	83
Muscle	2.8 (2.1–3.1) DW	83

Crabeater seal, *Lobodon carcinophagus*; Antarctic 1989

Kidney	25.6 (18.9–39.5) DW	83
Liver	71.1 (42–105) DW	83
Muscle	3.3 (2.7–4.3) DW	83

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Baikal seal, <i>Phoca sibirica</i> ; Siberia; 1992; immatures vs. adults		
Kidney	7.3 FW vs. 5.1 FW	138
Liver	4.9 FW vs. 3.5 FW	138
Muscle	1.4 FW vs. 1.0 FW	138
Harbour seal, <i>Phoca vitulina</i> ; British Isles; 1988–89; liver	7–21 FW	82
Common harbour porpoise, <i>Phocoena phocoena</i>		
England; 1988–89; liver	6–160 FW	82
Greenland; 1988–89		
Kidney	5.5 (3.7–8.0) FW	85
Liver	12.0 (5–50) FW	85
Muscle	2.0 (1.1–5.4) FW	85
Skin	1.0 (0.6–1.9) FW	85
Whales; unidentified; 1989; found dead		
Blubber	0.2–1.7 FW	81
Liver	6.6–8.7 FW	81
Muscle	3.0 FW	81
La Plata river dolphin, <i>Pontoporia blainvillii</i> ; Argentina; found dead		
Kidney	14 FW	84
Liver	16 FW	84
Other tissues	<2.8 FW	84
Striped dolphin, <i>Stenella coeruleoalba</i> ; Wales; 1989; found dead		
Blubber	0.3–0.7 FW	81
Muscle	2.1 FW	81
Manatee, <i>Trichechus manatus</i> ; Florida; 1977–81; liver	175.0 (4.4–1200.0) DW	86
Dolphin, <i>Tursiops gophysurus</i> ; Argentina; found dead		
Blubber	4.0 FW	84
Kidney	29.5 FW	84
Liver	77.7 FW	84
Melon	2.7 FW	84
Muscle	6.3 FW	84
Stomach contents	1.2 FW	84
Bottlenose dolphin, <i>Tursiops truncatus</i>		
England; 1988–89; liver	4–12 FW	82
Wales; 1989		
Blubber	0.9–1.1 FW	81
Muscle	2.5 FW	81
Polar bear, <i>Ursus maritimus</i>		
Canada, Northwest Territories; 1982–84; liver	81–146 DW	87
Svalbard (Arctic Ocean region); 1978–89; adults vs. juveniles		
Kidney	8.3 FW vs. 6.2 FW	88
Liver	42 FW vs. 33 FW	88
Welsh coast and Irish Sea; adults of 17 species of marine mammals; found dead; 1989–91; liver	Usually between 3.2 and 30.0 FW	89

TERRESTRIAL MAMMALS

Impala, <i>Aepyceros melampus</i> ; Kruger National Park, South Africa; 1989		
Kidney	(3–141) FW	90
Liver	(3–444) FW	90
Moose, <i>Alces alces</i>		
Alaska		
Hair	(5.2–11.7) DW	1
Hoof	(3.2–5.3) DW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Estonia; 1980–82		
Kidney	5.1 FW	91
Liver	3.1 FW	91
Poland; 1977–87; muscle	(0.9–2.6) FW	91
Sweden; 1979–80		
Kidney	(2.2–7.4) FW	91
Liver	(3.2–96.0) FW	91
Arctic fox, <i>Alopex lagopus</i> ; Norway; 1984–86; liver	6.0 (2.4–26.0) FW	92
Wood mouse, <i>Apodemus sylvaticus</i>		
Kidney	(3.7–6.0) FW	1
Liver	(2.6–18.1) FW	1
Testes	(12.2–18.7) FW	1
Whole	(2.8–5.5) FW	1
Bison, <i>Bison bison</i> ; Canada; 1986		
Kidney	6.7 (5.5–8.0) FW	91
Liver	35 (13–52) FW	91
European bison, <i>Bison bonasus</i> ; Poland; 1987		
Kidney	4.4 FW	91
Liver	3.4 FW	91
Muscle	2.0 FW	91
Cattle, <i>Bos</i> spp.		
Poland; 1987–91		
Kidney	5.6 FW	93
Liver	29.0 FW	93
Muscle	1.2 FW	93
South Africa; 1989; found dead near copper smelter; surface soil had 103 mg Cu/kg DW (14 at reference site)		
Kidney	36 (6–83) FW; 108 DW	90
Liver	359 (161–600) FW; 1078 DW	90
Various locations; liver	38.2–156.1 DW	94
Water buffalo, <i>Bubalus</i> sp.; Kruger National Park, South Africa; 1989; liver	Usually 18–80 FW; (6–144) FW	90
Bactrian camel, <i>Camelus bactrianus</i> ; China; 1992		
Normal		
Blood	0.86 FW	95
Hair	6.4 DW	95
Camels with sway disease (severe copper deficiency)		
Nonpregnant females		
Blood	0.36 FW	95
Hair	4.3 DW	95
Pregnant camels vs. post-partum		
Blood	0.17 FW vs. 0.26 FW	95
Hair	3.0 DW vs. 3.3 DW	95
Dog, <i>Canis familiaris</i>		
Brain	3.9 FW; 19 DW	96
Kidney	6.9 FW; 26 DW	96
Liver	82 FW; 336 DW	96
Muscle	1.1 FW; 3.7 DW	96
Serum	0.7 FW	96
Whole body	2.3 FW	96
Coyote, <i>Canis latrans</i> ; kidney	5.2 FW	97
Goat, <i>Capra hircus</i> ; mother vs. newborn		
Hair	8.9 DW vs. 8.3 DW	1
Kidney	9.8 DW vs. 19.0 DW	1
Liver	11.3 DW vs. 63.3 DW	1

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Roe deer, <i>Capreolus capreolus</i> ; Poland; 1987–91		
Kidney	7.8 FW	91
Liver	28.0 FW	91
Muscle	4.5 FW	91
European red deer, <i>Cervus elaphus</i>		
The Netherlands; 1989–92		
Kidney	54–86 DW	98
Liver	14–18 DW	98
Poland; 1986–91		
Kidney	5.4 FW	91
Kidney	9.4 DW	99
Liver	12.0 FW	91
Muscle	6.3 FW	91
Muscle	19.0 DW	99
Bank vole, <i>Clethrionomys glareolus</i>		
Poland; 1990; whole, less stomach and gastrointestinal tract	5.7–9.5 DW	100
Poland; 1985; various sites		
Bone	18.2–22.7 DW	101
Fur	12.0–14.5 DW	101
Kidney	43.4–73.8 DW	101
Liver	27.6–31.2 DW	101
Remainder	12.5–28.8 DW	101
Horse, <i>Equus caballus</i> ; liver	10.3–51.5 DW	94
North American porcupine, <i>Erethizon dorsatum</i>		
Heart	8.4 FW	97
Lung	4.7 FW	97
Human, <i>Homo sapiens</i>		
Healthy adults vs. adults with Wilson's Disease		
Bone	2.9 FW vs. 31.0 FW	58
Brain	5.4 FW vs. 54.9 FW	58
Cornea	3.8 FW vs. 35.1 FW	58
Kidney	2.8 FW vs. 36.2 FW	58
Liver	7.8 FW vs. 99.2 FW	58
Normal adults		
Aorta	82–280 AW	97
Blood	1.0 FW	102
Brain	310–540 AW	97
Hair	31 DW	102
Heart	310–420 AW	97
Kidney	220–880 AW	97
Liver	480–2000 AW; 10 FW	58, 97
Lung	140–470 AW	97
Pancreas	96–310 AW	97
Serum	1.64 FW	102
Spleen	93–470 AW	97
Whole body	1.4 (1.0–1.7) FW	58, 102
Fetus (33 weeks)	22.0 FW	103
Full term (still birth)	37.9 FW	103
Newborn, whole	4.0 FW	102
Diet, adults		
Beverages	0.44 FW	97
Condiments	6.8 FW	97
Dairy products	1.8 FW	97
Most fruits	0.82 FW	97
Coconut seed	3.3 FW	97
Most grains and cereals	2.0 FW	97

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Grapenuts	15.0 FW	97
Meats	3.9 (0.95–11.0) FW	97
Beef liver	11.0 FW	97
Nuts	14.8 FW	97
Most oils and fats	4.6 FW	97
Lecithins	21.0 FW	97
Most seafoods	1.5 (0.5–3.4) FW	97
Oysters	137.1 FW	97
Most vegetables	1.2 FW	97
Peas, split, green, dry	12.3 FW	97
Woodchuck, <i>Marmota monax</i> ; liver	9.4 FW	97
Mice, <i>Mus</i> spp.		
Fat	2.4 FW	97
Kidney	3.8 FW	97
Liver	2.0 FW	97
Lung	3.9 FW	97
Deer, <i>Odocoileus</i> spp.		
Brain	0.3–2.4 FW	97
Hooves	0.6 FW	97
Kidney	5.8–8.4 FW	97
White-tailed deer, <i>Odocoileus virginianus</i> ; Texas; 1979–80; uranium mining district vs. reference site		
Antlers	16.7 (0.5–71.0) FW vs. 18.0 (0.6–94.0) FW	104
Liver	0.5–94.0 FW vs. <1.0–>70.0 FW	104
Muskrat, <i>Ondatra zibethicus</i> ; Virginia; 1986–88; contaminated site (many chemicals; 68 mg Cu/kg DW sediment) vs. reference site (26 mg Cu/kg DW sediment); kidney	12.9 DW vs. 11.1 DW	105
Rabbit, <i>Oryctolagus</i> sp.; Poland; 1990; industrialized area vs. reference site		
Heart	5.9 FW vs. 3.0 FW	106
Kidney	6.6 FW vs. 2.6 FW	106
Liver	5.8 FW vs. 3.1 FW	106
Muscle	2.4 FW vs. 1.2 FW	106
Muskox, <i>Ovibus moschatus</i> ; Canadian Arctic; 1985–90		
Kidney	11 DW	107
Liver	67 DW	107
Domestic sheep, <i>Ovis aries</i>		
Copper-poisoned vs. normal sheep		
Blood	1.74–9.1 FW vs. 0.6–1.6 FW	108
Kidney	60 FW vs. 5 FW	109
Liver	432 FW vs. 12 FW	109
Muscle	2.5 FW vs. 2.1 FW	109
Spleen	19 FW vs. 5 FW	109
England; in paddock near heavily traveled highway for 150 days vs. reference site		
Blood	0.98 FW vs. 0.97 FW	110
Wool, tip	28.6 DW vs. 12.4 DW	110
Poland; 1988–91		
Kidney	5.7 (3.1–13.0) FW	66
Liver	41 (7–98) FW	66
Muscle	0.9 (0.8–1.3) FW	66
Raccoon, <i>Procyon lotor</i> ; fat	1.2 FW	97
Caribou, <i>Rangifer tarandus</i> ; Canadian Arctic; 1985–90		
Kidney	29 DW	107
Liver	68 DW	107

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Rat, <i>Rattus</i> spp.		
Mature and aged		
Brain	6.6 FW	97
Heart	1.0 FW	97
Kidney	0.9 FW	97
Liver	0.7 FW	97
Lung	0.9 FW	97
Spleen	0.3 FW	97
Tumors		
Hepatic	2.5 FW	94
Ovarian	5.9 FW	97
Mammary	1.3 FW	97
Young, whole	0.52 FW	97
Gray squirrel, <i>Sciurus carolinensis</i> ; liver	4.8 FW	97
Shrews, <i>Sorex</i> spp; England; 3 km from lead-zinc smelter vs. 23 km		
Carcass		
Immature	21.2 DW vs. 11.9 DW	111
Mature	21.7 DW vs. 13.1 DW	111
Kidney		
Immature	19.2 DW vs. 6.5 DW	111
Mature	13.6 DW vs. 8.8 DW	111
Liver		
Immature	32.5 DW vs. 14.8 DW	111
Mature	23.3 DW vs. 22.9 DW	111
Rock squirrel, <i>Spermophilus variegatus</i>		
Bone	(4.0–7.8) DW	1
Liver	(12.1–24.1) DW	1
Wild boar, <i>Sus scrofa</i>		
Germany; 1988; near metal foundry vs. reference site; liver	20.0 (10.9–49.6) FW vs. 15.9 (5.7–26.7) FW	112
The Netherlands; 1989–92; kidney vs. liver	17–24 DW vs. 4–20 DW	
Poland, 1986–91		
Kidney	1.7 FW; 17.2–24.5 DW	91, 99
Liver	1.8 FW	91
Muscle	1.6 FW; 6.4–7.4 DW	91, 99
Swine, <i>Sus</i> sp.; Poland; 1987–91		
Kidney	8.4 (2.1–44.0) FW	113
Liver	8.5 (1.1–41.0) FW	113
Muscle	1.1 (0.1–14.0) FW	113
Red fox <i>Vulpes vulpes</i> ; liver	41.8 FW	97
INTEGRATED STUDIES		
Canada; northern Ontario; August 1988; Lake Manitouwadge (contaminated) vs. Lake Wowun (reference site)		
Sediments	93 DW vs. 3 DW	114
Water (soluble copper)	0.015 FW vs. 0.002 FW	114
Invertebrates	89 DW vs. 57 DW	114
White sucker, <i>Catostomus commersoni</i>		
Bone	4 DW vs. 3 DW	114
Digestive tract	107 DW vs. 16 DW	114
Gill	9 DW vs. 3 DW	114
Kidney	31 DW vs. 10 DW	114
Liver	98 DW vs. 46 DW	114
Muscle	5 DW vs. 3 DW	114
Ovary	13 DW vs. 8 DW	114

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Testes Canada; Sudbury, Ontario; 1970	10 DW vs. 2 DW	114
Soils; distance from smelter 0.8–1.9 km	940–2070 DW	115
7.4–13.5 km	940–1620 DW	115
49.8 km	20–30 DW	115
Red maple, <i>Acer rubrum</i> ; foliage; distance from smelter 1.6 km	37 DW	115
6.5–18 km	19–28 DW	115
Wavy hairgrass, <i>Deschampia flexuosa</i> ; distance from smelter 1.6 km	726 DW	115
7.4 km	103 DW	115
49.8 km	13 DW	115
Lowbush blueberry, <i>Vaccinium angustifolium</i> ; foliage; distance from smelter 1.6 km	75 DW	115
4.6 km	35 DW	115
6.5–31 km	14–22 DW	115
India; river near Madras; receives industrial wastes		
Sediments	760–930 DW	116
Water	0.01–0.04 FW	116
Alga, <i>Enteromorpha intestinalis</i> ; whole	12.3 FW	116
Oyster, <i>Crassostrea madrasensis</i> ; soft parts	4.2 FW	116
Crustaceans, whole	Max. 18.4 FW	116
Fishes, muscle	Max. 0.09 FW	116
Israel; Acre Valley; 1988–91		
Molluscs; soft parts		
Bivalves	9.4–13.3 DW	117
Gastropods	31.0–48.0 DW	117
African sharp-tooth catfish, <i>Clarias gariepinus</i> ; liver	Max. 92.0 DW	117
Italy; Goro Bay; 1991–92		
Sediments	42–54 DW	118
Seawater	0.0005–0.0022 FW	118
Mussel, <i>Mytilus galloprovincialis</i> ; soft parts; purged for 48 h in aerated synthetic seawater vs. not purged	6.9 DW vs. 13.1 DW	118
New Zealand; pasture soil contaminated by runoff from an adjacent timber treatment plant; 1993; copper-contaminated soils (70–1233 mg Cu/kg DW soil) vs. reference site (25 mg Cu/kg DW soil)	In less-contaminated soils, plant-feeding nematodes were predominant. With increasing copper loadings, bacterial-feeding and predatory nematodes dominated; at highest loadings, microbial biomass declined	119
New Zealand; pasture contaminated by runoff from chromated copper arsenate timber preservation facility; 1991; control surface soils contained an average of 19 mg Cu/kg DW, low contamination 109 mg/kg, medium contamination 425 mg/kg, and high contamination 835 mg/kg DW soil		
Vegetation	Herbage yield decreased with increasing copper loadings; after 35 days roots had 10.5 mg Cu/kg DW in controls, 14.6 in low group, 18.4 in medium group and 23.9 in high group	120
Earthworms, <i>Lumbricus rubellus</i> , <i>Aporrectodea rosea</i>	Earthworms absent from plats with medium and high contamination. Surface casts of <i>L. rubellus</i> had 17.5 mg/kg DW in low contamination soils vs. 7.0 in controls; for <i>A. rosea</i> . These values were 13.3 vs. 7.0	120

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Nematodes	Most abundant in low-contamination soils; proportion of predatory nematodes in population increased with increasing copper contamination	120
Soil microflora Norway; small lakes; 1991; near highway vs. reference site	Reduced with increasing contamination	120
Freshwater mussel, <i>Anodonta piscinalis</i> ; soft parts	3.5 FW vs. 3.1 FW	121
Perch, <i>Perca fluviatilis</i>		
Liver	1.6 FW vs. 1.5 FW	121
Muscle	0.16 FW vs. 0.19 FW	121
South Africa; metal-polluted wetland; 1989		
Sediments	67.4 (44.3–93.3) DW	122
Sago pondweed, <i>Potamogeton pectinatus</i> ; whole	29.0 DW	122
Red-knobbed coot, <i>Fulica cristata</i> ; feeding on <i>Potamogeton pectinatus</i>		
Egg contents	8.5 DW	122
Egg shell	5.5 DW	122
Gonads	32.6 (10.8–59.9) DW	122
Internal organs	24.5 (0.4–125.1) DW	122
Stomach contents	37.0 (11.3–90.1) DW	122
Taiwan 1995–96		
Pacific oyster, <i>Crassostrea gigas</i> ; soft parts	909 (113–2805) DW	134
Fish; 8 species; muscle	Max. 6.8 DW	134
Shrimp; 2 species; muscle	Max. 27.5 DW	134
Wales; 1989; coastal area		
Sediments	8.0 DW	123
Anemones, whole	0.6 FW	123
Soft corals, whole	1.0 FW	123
Mussels, soft parts	1.2 FW	123
Crab, hepatopancreas	58.0 FW	123
Lugworms, whole	3.9 FW	123
Tunicates, whole	2.6 FW	123
Fishes, four species; liver	1.6–4.4 FW	123
United States; Florida; 1979; national wildlife refuge; treated with copper-containing herbicides vs. nontreated areas		
Water	Max. 0.56 FW after 1 h to 0.04 FW after 24 h vs. 0.027 FW	124
Detritus	Max. 20.1 DW after 7 days vs. 12–13 DW	124
Aquatic plants	Max. 151.3 DW after 14 h vs. 9–10 DW	124
Apple snail, <i>Pomacea paludosa</i> ; soft parts		
Adults	82.3 DW after 7 days vs. 17–21 DW	124
Immatures	80.3 DW after 7 days vs. 113–22 DW	124
United States; Kansas; 1990; near landfill; upstream vs. downstream site		
Sediments	8.2–17.9 DW vs. 12.4–14.6 DW	125
Water	0.01–0.018 vs. 0.007–0.019 FW	125
Crayfish, <i>Orconectes nais</i> ; whole	60.3–61.3 DW vs. 56.2–77.7 DW	125
Orangespotted sunfish, <i>Lepomis humilis</i> ; whole	1.5–7.3 DW vs. 1.4–2.5 DW	125
United States; Maryland and Pennsylvania; 1985; at disposal facilities for dredged materials; low soil copper site (15 mg/kg DW) vs. high soil copper site (150 mg/kg DW)		
Common reed, <i>Phragmites australis</i> ; whole	2.8 DW vs. 4.7 DW	126
Ladybug, <i>Coccinella septempunctata</i> ; whole	14 DW vs. 17 DW	126
Earthworms, <i>Eisenia foetida</i> ; whole	21 DW vs. 57 DW	126
House mouse, <i>Mus musculus</i> ; whole less skin and tail	13 DW vs. 18 DW	126

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
United States; Montana; 1990; wetland contaminated by mining wastes (arsenic, cadmium, copper, lead, zinc)		
Soil	532.0 DW	127
Water	0.078 FW	127
Vegetation		
Above ground	7.2–24.2 DW	127
Below ground	75.0–274.0 DW	127
Meadow vole, <i>Microtus pennsylvanicus</i>		
Carcass	2.8 FW	127
Kidney	5.1 FW	127
Liver	4.2 FW	127
Testes	1.9 FW	127
Deer mice, <i>Peromyscus maniculatus</i>		
Carcass	3.4 FW	127
Kidney	5.7 FW	127
Liver	5.7 FW	127
Testes	1.5 FW	127
United States; Ohio; 1987; old-field community; treated with sewage sludge for 10 years beginning in 1978; treated plots vs. reference site		
Sludge	320–381 DW vs. not applicable	128
Soil	Sludge loading equivalent to 15–37 DW vs. no data	128
Plants, stems		
Japanese brome, <i>Bromus japonicum</i>	5.9 DW vs. 6.0 DW	128
Bluegrass, <i>Poa</i> spp.	7.4 DW vs. 6.3 DW	128
Raspberry, <i>Rubus</i> sp.	4.7 DW vs. 3.4 DW	128
Foxtail, <i>Setaria</i> sp.	6.3 DW vs. 2.9 DW	128
Earthworms, <i>Lumbricus rubellus</i>	17–23 DW vs. no data	128
Meadow vole, <i>Microtus pennsylvanicus</i>		
Kidney	3.3 DW vs. 3.0 DW	128
Liver	3.1 DW vs. 3.5 DW	128
United States; Pennsylvania; Palmerton zinc smelter; 1986 (6 years after smelter was closed); near smelter vs. distant sites		
Soil	190 DW vs. <30 DW	129
Litter	552 DW vs. <70 DW	129
Green frog, <i>Rana clamitans</i> ; tadpoles; whole	0.8 FW vs. 0.3 FW	129
Eastern red-backed salamander, <i>Plethodon cinereus</i> ; whole less gastrointestinal tract	2.2 FW vs. 1.7 FW	129
White-tailed deer, <i>Odocoileus virginianus</i>		
Bone	11 DW vs. 16 DW	129
Kidney	29 DW vs. 33 DW	129
Liver	122 DW vs. 149 DW	129
Eastern cottontail rabbit, <i>Sylvilagus floridanus</i>		
Bone	6.7 DW vs. 6.7 DW	129
Kidney	21.5 DW vs. 17.8 DW	129
Liver	19.2 DW vs. 14.8 DW	129
Muscle	11.9 DW vs. 9.6 DW	129

^a Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND)

^b 1, Jenkins 1980; 2, NAS 1977; 3, Schroeder et al. 1966; 4, Hutchinson 1979; 5, Jozwik 1990; 6, Reed et al. 1993; 7, Veleminsky et al. 1990; 8, Berger and Dallinger 1993; 9, Lindquist 1993; 10, Heliovaara and Vaisanen 1990; 11, Morgan and Morgan 1990; 12, Clark 1992; 13, Larsen et al. 1994; 14, Karez et al. 1994; 15, Stokes 1979; 16, Brix and Lyngby 1982; 17, Jaffe et al. 1992; 18, Mauri et al. 1990; 19, Viarengo et al. 1993; 20, Mat 1994; 21, Mat et al. 1994; 22, Pip 1990; 23, Balogh and Mastala 1994; 24, Swaileh and Adelung 1994; 25, Cheung and Wong 1992; 26, Claisse and Alzieu 1993; 27, Han and Hung 1990; 28, Han et al. 1993; 29, Weis et al. 1993a; 30, Byers 1993; 31, Huggett et al. 1975; 32, Camusso et al. 1994; 33, Metcalfe-Smith 1994; 34, Miramand

Table 3.3 (continued) Copper Concentrations (milligrams of copper per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW] in field collections of representative plants and animals)

and Bentley 1992; **35**, Bordin et al. 1994; **36**, Paez-Osuna et al. 1994; **37**, Turgeon and O'Connor 1991; **38**, Greig and Sennefelder 1985; **39**, Ward 1990; **40**, Lauenstein et al. 1990; **41**, Chu et al. 1990; **42**, Talbot et al. 1985; **43**, Brown and McPherson 1992; **44**, Szefer et al. 1993; **45**, Jorhem et al. 1994; **46**, Sumi et al. 1991; **47**, Petri and Zauke 1993; **48**, Depledge et al. 1993; **49**, Rainbow 1989; **50**, Cain et al. 1992; **51**, Moore et al. 1991; **52**, Athalye and Gokhole 1991; **53**, Munkittrick et al. 1991; **54**, Bezuidenhout et al. 1990; **55**, Mathews 1994; **56**, Sindayigaya et al. 1994; **57**, Schmitt and Brumbaugh 1990; **58**, ATSDR 1990; **59**, Romeo et al. 1994; **60**, Ellenberger et al. 1994; **61**, de Wet et al. 1994; **62**, Vas 1991; **63**, Goldfischer et al. 1970; **64**, Henny et al. 1990; **65**, Ranta et al. 1978; **66**, Falandysz et al. 1994; **67**, Szefer et al. 1993; **68**, Michot et al. 1994; **69**, Custer and Hohman 1994; **70**, Negro et al. 1993; **71**, Wren et al. 1994; **72**, Lock et al. 1992; **73**, Ohlendorf et al. 1991; **74**, Amiard-Triquet et al. 1991; **75**, Honda et al. 1990; **76**, Vermeer and Castilla 1991; **77**, St. Louis et al. 1993; **78**, Bryan and Langston 1992; **79**, Varanasi et al. 1994; **80**, Meador et al. 1993; **81**, Morris et al. 1989; **82**, Law et al. 1991; **83**, Szefer et al. 1994; **84**, Marcovecchio et al. 1990; **85**, Paludan-Muller et al. 1993; **86**, O'Shea et al. 1984; **87**, Braune et al. 1991; **88**, Norheim et al. 1992; **89**, Law et al. 1992; **90**, Gummow et al. 1991; **91**, Falandysz 1994; **92**, Prestrud et al. 1994; **93**, Falandysz 1993a; **94**, Cuill et al. 1970; **95**, Zong-Ping et al. 1994; **96**, Goresky et al. 1968; **97**, Schroeder et al. 1966; **98**, Wolkers et al. 1994; **99**, Swiergosz et al. 1993; **100**, Zakrzewska et al. 1993; **101**, Sawicka-Kapusta et al. 1990; **102**, USEPA 1980; **103**, Bakka and Webb 1981; **104**, King et al. 1984; **105**, Halbrook et al. 1993; **106**, Krelowska-Kulas et al. 1994; **107**, Gamberg and Scheumhammer 1994; **108**, MacPherson and Hemingway 1969; **109**, Todd 1969; **110**, Ward and Savage 1994; **111**, Read and Martin 1993; **112**, Launer et al. 1991; **113**, Falandysz 1993b; **114**, Miller et al. 1992; **115**, Hutchinson 1979; **116**, Govindarajan and Rao 1992; **117**, Fishelson et al. 1994; **118**, Fagioli et al. 1994; **119**, Bardgett et al. 1994; **120**, Yeates et al. 1994; **121**, Baekken 1994; **122**, van Eeden and Schoonbee 1993; **123**, Morris et al. 1989; **124**, Winger et al. 1984; **125**, Morrissey and Edds 1994; **126** Beyer et al. 1990; **127**, Pascoe et al. 1994; **128**, Levine et al. 1989; **129**, Storm et al. 1994; **130**, Hylland et al. 1992; **131**, Sparling and Lowe 1996; **132**, Eisler and LaRoche 1972; **133**, Hendricks et al. 1998; **134**, Han et al. 1998; **135**, Hui et al. 1998; **136**, Hui and Beyer 1998; **137**, Kim et al. 1998; **138**, Watanabe et al. 1998.

category (Schroeder et al. 1966). Copper in the environmental crust averages 50 mg/kg, but is higher (140 mg/kg) in ferromagnesium minerals (NAS 1977). Soil contamination by copper occurs around all known smelter locations; contamination may persist for decades, and plants and animals are often unable to survive the harsh chemical environments created (Hutchinson 1979). Italian soils have higher copper concentrations (51 mg/kg DW) than those of other European counties, probably as a result of the widespread and prolonged application of copper-based fungicides in Italian orchards and vineyards (Arduini et al. 1995).

Copper concentrations in lake sediments within a radius of 80 km from a smelter in northern Sweden are positively correlated with proximity to the smelter (Johnson et al. 1992). In some cases, lake sediments are sinks for copper, with little release to the overlying lake water. For example, copper-bearing mine tailings in Butte Lake, British Columbia, do not undergo oxidative diagenesis because of a rapid rate of accumulation and short exposure time to dissolved oxygen in bottom waters (Pedersen 1983). In Michigan, lakes with elevated concentrations of copper (34 µg/L) have low densities of fish populations (Ellenberger et al. 1994). In the Elizabeth River estuary of southern Chesapeake Bay, anthropogenic copper and other chelatable metals are present at concentrations sufficient to adversely affect growth and survival of the copepod *Acartia tonsa* (Sunda et al. 1990). In Norway, freshwater fish are present only when copper is less than 60 µg/L and some humic acids are present (Hodson et al. 1979). Successful reproduction of the spotted salamander (*Ambystoma maculatum*) occurs at low water concentrations of copper (<10 µg/L), lead, and aluminum, and high concentrations of silicon. Failed reproduction occurs at low water concentrations of silicon, and elevated concentrations of copper (>25 µg/L), lead, and aluminum (Blem and Blem 1991).

In marine ecosystems, the high copper levels measured in heavily contaminated coastal areas sometimes approach the incipient lethal concentrations for some organisms (Neff and Anderson 1977). Elevated copper concentrations in marine and estuarine environments may result from atmospheric deposition, industrial and municipal wastes, urban runoff, rivers, and shoreline erosion. Chesapeake Bay, for example, receives more than 1800 kg of copper daily from these sources (Hall et al. 1988). Copper concentrations in abiotic marine materials are generally higher near shore than

off shore. Copper is elevated in sediments of many marinas, probably from the copper antifouling bottom paints used on boats housed there (Hall et al. 1988). In New Zealand, copper concentrations in contaminated inshore sediments frequently exceed 100 mg Cu/kg DW vs. 14 mg Cu/kg DW at noncontaminated sites (Roper and Hickey 1994). The fine particle fraction of sediments collected near bulkheads made of chromated copper arsenate (CCA)-treated wood contain elevated concentrations of copper, chromium, and arsenic; metal concentrations decreased with increasing distance from the bulkhead. Sediments, for example, decreased from 11 mg Cu/kg DW in the vicinity of treated bulkheads to less than 2 mg/kg DW at more distant sites (Weis and Weis 1994).

3.5.3 Terrestrial Plants and Invertebrates

In general, copper concentrations in terrestrial vegetation seldom exceed 35 mg/kg DW, except near point sources of copper contamination and in certain copper-tolerant species (Table 3.3). The highest copper concentration recorded in nonaccumulator plants is 726 mg/kg DW in hair grass (*Deschampia flexuosa*) near a smelter (Table 3.3). Several species of terrestrial plants accumulate spectacular concentrations of copper. Mint plants (*Aeolanthus* spp., *Elsholtzia* spp.) growing in copper-rich soils contain unusually high concentrations and are used as economic indicators of copper deposits in the former Soviet Union and the People's Republic of China (Jenkins 1980). The copper plant mint (*Aeolanthus biformifolius*), for example, normally contains as much as 13,700 mg Cu/kg DW whole plant (Table 3.3). Copper-tolerant species of mosses, lichens, fungi, and higher plants occur in Greenland, Canada, the former Soviet Union, Africa, and elsewhere. In Zambia and Rhodesia, the copper-tolerant *Becium homblei* is found only in soils containing more than 1000 mg Cu/kg and is believed responsible for the discovery of copper deposits in those nations (Hutchinson 1979). Some species of copper-indicator plants in Zambia tolerate as much as 70,000 mg Cu/kg in the soil and accumulate as much as 3000 mg Cu/kg in leaves (Hutchinson 1979).

Copper is not accumulated from soils by most crop plants, suggesting a soil–plant barrier for copper (Levine et al. 1989). Thus, corn (*Zea mays*) did not accumulate copper from soils treated with 365 kg of copper per surface hectare (as copper-rich pig manure or copper sulfate) over a 13-year period. Corn yield is not affected under these conditions (Reed et al. 1993).

Copper burdens in terrestrial invertebrates are highest in organisms collected near industrial locations and urban areas or from copper-contaminated soils. The highest copper concentration recorded among terrestrial invertebrates is 408 mg Cu/kg DW soft parts in gastropods from urban areas (Table 3.3). Copper concentrations in pine moths (*Bupalus piniarius*) and pine noctuids (*Panolis flammea*) from industrialized areas range from 89 to 137 mg/kg DW, but are lower than dietary concentrations and suggest negligible accumulation (Heliovaara and Vaisanen 1990). Accumulations of as much as 60 mg Cu/kg DW in 17-year cicadas (*Magicicada* spp.) pose no apparent dietary threat to insectivorous birds (Clark 1992).

Earthworms from soils heavily contaminated with copper (2740 mg/kg DW soil) can regulate copper more efficiently than cadmium and lead. However, copper is more toxic to earthworms than lead or zinc in the soil, due, in part, to the inability of most soft tissues to synthesize copper-binding ligands when challenged with copper (Morgan and Morgan 1990).

In woodland ecosystems, copper concentrations in the litter horizon are rarely exceeded by those in soil animals — which play a key role in copper cycling (Wieser 1979). Meiofaunal feces comprise an efficient distributing system through which copper and other nutrients are cycled through the food web of woodland ecosystems. During a 12-month cycle the total copper bound in litter progresses through a cycle of chemical binding states. It may be released from a strongly chelated organic complex as the litter is attacked by the digestive juices of animals, or it may be discharged in soluble form with the feces and become complexed again by the activity of micro-organisms in these feces. When feces are ingested by coprophagous animals, such as isopods, the copper may become trapped in proteins or membrane-bound vesicles (Wieser 1979).

3.5.4 Aquatic Organisms

Copper is essential for the successful growth and development of many species of aquatic organisms, but its rate and extent of accumulation and retention are modified by numerous biological and abiotic variables. Abiotic variables known to modify copper concentrations in tissues of aquatic biota include water temperature, pH, salinity, and depth; the presence of other inorganics, organics, and chelators; the chemical species of copper; and proximity to anthropogenic point sources of copper. Biological variables affecting copper accumulations in marine organisms include the organism's age, size, and developmental stage; physiological or genetic adaptation to high copper substrates; inherent species differences; and tissue specificity, such as the thorax of barnacles, gill and osphradium of gastropods, and livers of teleosts (Eisler 1979). Among marine organisms, the highest accumulations are generally found in molluscan tissues and soft parts, especially those of cephalopods and oysters. In order of decreasing copper accumulations, molluscs are followed by crustaceans, macrophytes, annelids, tunicates, algae, echinoderms, and coelenterates. Lowest concentrations of copper were consistently found among the vertebrates — elasmobranchs, fishes, mammals — and strongly indicates a discrimination against copper among the highest marine trophic levels examined (Eisler 1979, 1981). Aquatic molluscs and arthropods that possess hemocyanin — a copper-containing respiratory pigment — have elevated tissue and plasma copper concentrations when compared to the ambient medium (Neff and Anderson 1977). Unlike many species of invertebrates, no vertebrate animal has a copper pigment as the main metallic constituent of blood (Schroeder et al. 1966). Marine organisms without hemocyanin have lower tissue concentrations of copper than those with it (Neff and Anderson 1977).

Diet is the most important route of copper accumulation in aquatic animals, and food choice influences body loadings of copper. For example, whole-body copper concentrations in aquatic insects from copper-contaminated rivers are highest in detritivores (as high as 102 mg/kg DW), followed by predators (54 mg/kg DW) and omnivores (43 mg/kg DW; Cain et al. 1992). Little or no biomagnification of copper is evident in freshwater food chains (Stokes 1979).

Copper concentrations in freshwater macrophytes near mining areas are elevated (as much as 256 mg/kg DW) compared to conspecifics collected from more remote sites (Stokes 1979). Bioconcentration factors (ratio of milligrams of copper per kilogram fresh weight organism to milligrams of copper per liter of ambient water) for copper by various species of freshwater algae range from 770 to 83,000. In general, copper accumulations in algae are higher at pH 8 than at pH 5; under conditions of low oxygen and reduced illumination; at low ambient concentrations of calcium, cobalt, zinc, magnesium, manganese, and organic chelators; and at high ambient concentrations of fluoride (Stokes 1979). Benthic communities in the vicinity of bulkheads made of chromated copper arsenate-treated wood had elevated concentrations of these elements, reduced species richness and diversity, and reduced numbers of total organisms when compared to reference sites (Weis and Weis 1994). American oysters (*Crassostrea virginica*) from a canal lined with chromated copper arsenate-treated wood had 150 mg Cu/kg FW soft parts vs. 20 mg Cu/kg FW in oysters from a more distant site (Weis and Weis 1993).

Copper concentrations in cephalopod molluscs are, in general, higher than those in bivalve molluscs. In cephalopods, 50 to 80% of the copper is localized in the digestive gland (Miramand and Bentley 1992). Copper concentrations in tissues of clams (*Macoma balthica*) in San Francisco Bay are associated with seasonal variations in tissue weight, concentrations of copper in the sediments, and anthropogenic inputs from nearby sources (Cain and Luoma 1990). In cockles (*Cerastoderma edule*), copper concentrations in tissues decrease with increasing age, decrease in summer when compared to other seasons, and increase with increasing sediment copper concentrations (Savari et al. 1991). In the cockle (*Anadara trapezium*), tissue copper concentrations are positively related to dissolved copper concentrations in the water column and independent of sediment copper concentrations (Scanes 1993). Small freshwater clams (*Anodonta grandis*) have higher copper concentrations in soft tissues than large clams because small clams take up copper

at a greater rate and excrete it more slowly than large clams (Pip 1990). A similar case is made for oysters and other bivalve molluscs (Weis et al. 1993a). Zebra mussels (*Dreissena polymorpha*) regulate body copper concentrations at water copper levels of 13 µg Cu/L and lower (Camusso et al. 1994). Proximity to point sources, such as sewage discharge plants, is associated with elevated copper burdens in common mussels, *Mytilus edulis* (Ward 1990). Copper concentrations increased in mussels (*Mytilus* spp.) analyzed in the coastal mussel watch program between the late 1970s and the late 1980s. This may be due to increased availability of copper from anthropogenic sources; however, concentrations of other metals (silver, nickel, cadmium, lead, zinc) in mussels analyzed during this period showed a decrease (Lauenstein et al. 1990).

Pacific oysters near a copper recycling facility in Taiwan have elevated concentrations of copper (as high as 4400 mg/kg DW soft parts), a characteristic green color, and low survival after exposure to waste effluents for 3 months (Hung et al. 1990). Diet is the major pathway by which greenish-colored Pacific oysters accumulate copper. Initial daily accumulation rates are as high as 214 mg Cu/kg DW soft parts (Han and Hung 1990). Elimination of 50% of the copper from green Pacific oysters with elevated copper loadings takes only 11.6 days vs. 25.1 days in reference oysters (Han et al. 1993). Elevated concentrations of copper in Pacific oysters (135 mg/kg DW soft parts) near a marina in Arcachon Bay, France, are attributed to the ban on tributyltin antifouling paints in 1982 and the subsequent growth of the use of copper-based antifouling paints (Claisse and Alzieu 1993). Copper concentrations in soft tissues of the American oyster are higher in oysters from low-salinity waters than those from more saline waters; accumulations are not related to sediment copper concentrations in the immediate environment (Huggett et al. 1975). In Maryland, copper concentrations in tissues of the American oyster are seasonally highest in July and lowest in October and higher in low-salinity waters than in high-salinity waters (Roesijadi 1994). In Australia, copper concentrations in oyster soft parts from the Georges River, New South Wales, rose from 20 mg/kg FW to 46 mg/kg FW in the 1970s to as high as 93 mg/kg FW in 1987, possibly as a result of urban and industrial discharges; this concentration exceeds the recommended limit of 70 mg Cu/kg FW in shellfish edible tissues for protection of human health in Australia (Brown and McPherson 1992).

In amphipod (*Orchestia gammarellus*) crustaceans, copper concentrations vary seasonally due to variable copper loadings, are higher in organisms from contaminated sites than reference sites, and higher in females with juveniles in the brood pouch than females without juveniles (Moore et al. 1991). The existence of copper-rich granules is common to all invertebrate phyla; these granules are usually found in the digestive gland or its evolutionary equivalent, and their formation is related to high concentrations of copper in the immediate environment (Weeks 1992). The tolerance of talitrid amphipods to high concentrations of ambient copper is attributable, in part, to the formation of intracellular granules within the cells of the ventral caeca (Weeks 1992). In the crab (*Carcinus mediterraneus*), tissue copper concentrations are lower in winter than in summer and correlate positively with total protein and hemolymph copper contents (Devescovi and Lucu 1995). Elevated copper burdens in hemolymph of crabs probably reflects the incorporation of copper atoms in the structure of hemocyanin, the major hemolymph protein (Depledge et al. 1993). Marine decapod crustaceans regulate tissue copper concentrations within the range of 25 to 35 mg/kg DW (Neff and Anderson 1977).

In *Limnodrilus* sp., an oligochaete worm, copper bioavailability from surficial freshwater sediments is associated with the amount of copper present in the manganese oxide fraction of the sediment. The redox potential and pH in the gut of *Limnodrilus* allows the dissolution of the manganese oxide coating, making copper and other metals available for uptake (Diks and Allen 1983).

Copper concentrations in freshwater fishes collected nationwide in the United States have not changed significantly since 1978 (Schmitt and Brumbaugh 1990). In 1984, samples with the highest copper concentrations were Mozambique tilapia (*Tilapia mossambica*) from Hawaii and white perch (*Morone americana*) from the Susquehanna River in Maryland. These locations have historically

yielded fish with relatively high concentrations of copper. In Hawaii, this may develop from copper-containing pesticides (Schmitt and Brumbaugh 1990). Copper concentrations in fishes are usually higher in liver than other tissues, higher in fish from copper-contaminated lakes than reference lakes, and higher in small fish than large fish of the same species (Cuill et al. 1970; Eisler 1984; ATSDR 1990; de Wet et al. 1994; Table 3.3). Residue data on copper in fish that are dead on collection are probably worthless for purposes of risk assessment owing to copper accumulation after death (Eisler and Gardner 1973). Among sharks collected in British waters, copper concentrations in all tissues are highest from inshore demersal species and lowest from offshore pelagic species, with males having higher copper concentrations in liver than females (Vas 1991).

Copper concentrations in tissues of marine vertebrates tend to decrease with increasing age of the organism (Law et al. 1992; Watanabe et al. 1998). Concentrations of copper in marine and coastal vertebrates — including elasmobranchs, teleosts, and pinniped mammals — are related to the age of the animal. Regardless of species or tissues, except brain, concentrations decrease with increasing age of the organism; brain copper concentrations in marine mammals increase with organism age (Eisler 1984). Decreases in tissue copper content are also associated with spawning migrations of salmonids when entering freshwater from the sea and with reproductive cycles of cod and other gadoids (Eisler 1984). In the copper-contaminated Miramichi River, Canada, populations of Atlantic salmon (*Salmo salar*) are reduced in numbers due to poor survival and reproduction (Sprague et al. 1965). Copper-containing mine wastes entering the Northwest Miramichi River cause many adult Atlantic salmon on their normal upstream spawning migration to return prematurely downstream; about 62% do not reascend. Downstream returns of salmon rose from 1% to 3% before pollution to 10% to 22% during 4 years of pollution. During some periods, dissolved copper and zinc concentrations exceed the lethal levels for immature salmon and the avoidance concentrations for subadults (Sprague et al. 1965; Saunders and Sprague 1967).

In polar bears, concentrations of copper in liver are 3 to 5 times higher than their seal diet (Braune et al. 1991). Copper concentrations in liver and kidney of polar bears are lower in juveniles than adults (Norheim et al. 1992), which is contrary to a reverse trend noted in most species of vertebrates. Neonatal marine mammals, for example, have higher concentrations of copper in liver than those found in the mother (Law et al. 1992). The use of copper herbicides in Florida to control aquatic plants may be hazardous to the endangered manatee. Copper concentrations in livers of these aquatic herbivores from areas of high copper herbicide use are as high as 1200 mg/kg DW. The maximum copper concentrations in livers of copper-challenged manatees are higher than any copper concentration measured in any species of free-ranging mammalian wildlife and are comparable to copper concentrations in livers of some species of domestic animals poisoned by copper (O’Shea et al. 1984).

3.5.5 Amphibians and Reptiles

Eggs of the Jefferson salamander (*Ambystoma jeffersonianum*) from a series of ponds that contain 1 to 25 µg Cu/L have — at the higher copper concentrations — a reduction in hatching success and an increase in embryonic mortality (Horne and Dunson 1995).

For reasons unknown, livers of some adult giant toads (*Bufo marinus*) normally contain grossly elevated concentrations of copper (>2000 mg/kg DW). The toads’ livers are undamaged by this level of copper, and this lack of effect is in sharp contrast to human patients with Wilson’s disease (2000 mg Cu/kg DW liver) wherein hepatocyte degeneration, necrosis, and ultimately cirrhosis result (Goldfischer et al. 1970). In toad livers, the copper is sequestered in lysosomes, which seems to protect the cell from the toxic effects of copper. In contrast, copper in liver of humans with Wilson’s disease is diffusely distributed in the cytoplasm of hepatocytes and is associated with severe and often fatal pathological changes (Goldfischer et al. 1970).

3.5.6 Birds

Season of collection and organism age affect copper concentrations in avian tissues. In livers of surf scoters (*Melanitta perspicillata*) from San Francisco Bay, copper concentrations are higher in March than in January; in livers of canvasbacks (*Aythya valisineria*) from Louisiana, concentrations are lower in November than later months; and in primary flight feathers of mallards (*Anas platyrhynchos*) and black ducks (*Anas rubripes*) from the vicinity of a smelter in Sudbury, Ontario, copper concentrations are highest in autumn (Ranta et al. 1978). Copper concentrations in tissues of coastal seabirds tend to decrease with increasing age (Eisler 1984). In New Zealand, younger marine birds have higher concentrations of copper in livers than adults (Lock et al. 1992), but juveniles and adults of common murres (*Uria aalge*) from Scotland have similar concentrations of copper in kidneys, livers, and muscle (Stewart et al. 1994).

In general, birds retain a very small portion of copper and other metals ingested (Bryan and Langston 1992). It is therefore noteworthy that livers of some canvasbacks collected in Louisiana (Custer and Hohman 1994) and livers of some mute swans (*Cygnus olor*) from England (Bryan and Langston 1992) both contain more than 2000 mg Cu/kg DW. In the case of mute swans, several thousands of milligrams of copper per kilogram dry weight occur in the blackened livers; blackening is attributed to ingestion of flakes of copper-based antifouling paints (Bryan and Langston 1992). Tree swallows (*Tachycineta bicolor*) nesting near acidified aquatic ecosystems accumulate sufficient copper from the diet to induce elevated hepatic metallothionein concentrations (St. Louis et al. 1993). Copper concentrations in stomach contents of willets (*Catoptrophorus semipalmatus*) from San Diego Bay tend to reflect sediment copper concentrations (Hui and Beyer 1998). However, there is no evidence of copper biomagnification in the sediment food chain of sediment–pond-weed–red-knobbed coot (*Fulica cristata*; van Eeden and Schoonbee 1993).

3.5.7 Mammals

Impalas (*Aepyceros melampus*) found dead in Kruger National Park, South Africa, had elevated concentrations of copper in livers (maximum 444 mg/kg FW) and kidneys (maximum 141 mg/kg FW); authors assert that copper poisoning is the most likely cause of death (Gummow et al. 1991), but this needs verification. Copper concentrations in bones, kidneys, and livers of white-tailed deer (*Odocoileus virginianus*) near a copper smelter and from distant sites are about the same. However, deer near the smelter have significantly elevated concentrations of cadmium in kidneys and livers, lead in bone, and zinc in kidneys (Storm et al. 1994).

Only a small portion (0.037%) of copper mining wastes discharged into riparian wetlands is bioavailable to resident rodents, as judged by measurements of copper in carcasses of mice and voles (Pascoe et al. 1994). Populations of brown-backed voles (*Clethrionomys rufocanus*) and other microtine rodents (*Microtus* spp., *Lemmus*) are low or absent in the vicinity of Russian copper–nickel smelters (Kataev et al. 1994). The reasons for this decline are unknown but may be due to a decrease in the abundance of important food plants (lichens, mosses, seed plants), and — as shown in preference studies — to an avoidance of plants from the contaminated area (Kataev et al. 1994). Bank voles (*Clethrionomys glareolus*) from areas of Poland subjected to various degrees of industrial contamination have copper concentrations in tissues comparable to those in animals from polluted sites in North America and the United Kingdom (Sawicka-Kapusta et al. 1990). Compared to animals from a reference site, muskrats (*Ondatra zibethicus*) from a site contaminated by copper and other chemicals have higher concentrations of copper in kidneys, smaller spleens, larger adrenals, less fat, and lower body weight (Halbrook et al. 1993).

In Poland near copper foundries, livers from cattle (*Bos* sp.) have higher copper concentrations (35 to 140 mg/kg FW) than cattle from agricultural regions (7 to 32 mg/kg FW); however, kidney copper concentrations are comparable for both regions (Falandysz 1993a). Cattle found dead in South Africa near a copper smelter have elevated levels of copper in liver (600 mg/kg FW;

1078 mg/kg DW); airborne copper from the smelter is considered the most likely cause of death (Gummow et al. 1991). Sheep held for 150 days in a paddock near a heavily-travelled highway have significantly elevated copper concentrations in wool; these differences are not as pronounced in hair from horses (*Equus caballus*) and alpacas (*Lama pacos*) held under similar conditions (Ward and Savage 1994).

Interspecies differences in copper contents are considerable. Serum from domestic dogs (*Canis familiaris*) lacks the strong copper binding site available on the serum albumin molecule of humans and rats. Accordingly, copper concentrations in livers from dogs (82 mg/kg FW; 336 mg/kg DW) are normally about 12 times higher than those of human livers and 19 times higher than those of rat livers (Goresky et al. 1968).

Human foods that are particularly rich in copper (20 to 400 mg Cu/kg) include oysters, crustaceans, beef and lamb livers, nuts, dried legumes, dried vine and stone fruits, and cocoa (USEPA 1980). In humans, copper is present in every tissue analyzed (Schroeder et al. 1966). A 70-kg human male usually contains 70 to 120 mg of copper (USEPA 1980). The brain cortex usually contains 18% of the total copper, liver 15%, muscle 33%, and the remainder in other tissues — especially the iris and choroid of the eye. Brain gray matter (cortex) has significantly more copper than white matter (cerebellum); copper tends to increase with increasing age in both cortex and cerebellum. In newborns, liver and spleen contain about 50% of the total body burden of copper (USEPA 1980). Liver copper concentrations were usually elevated in people from areas with soft water (Schroeder et al. 1966). Elevated copper concentrations in human livers are also associated with hepatic disease, tuberculosis, hypertension, pneumonia, senile dementia, rheumatic heart disease, and certain types of cancer (Schroeder et al. 1966).

3.6 COPPER DEFICIENCY EFFECTS

3.6.1 General

Adverse effects of copper deficiency can be documented in terrestrial plants and invertebrates, poultry, small laboratory animals, livestock — especially ruminants — and humans. Data are scarce or missing on copper deficiency effects in aquatic plants and animals and in avian and mammalian wildlife. Copper deficiency in sheep, the most sensitive ruminant mammal, is associated with depressed growth, bone disorders, depigmentation of hair or wool, abnormal wool growth, fetal death and resorption, depressed estrous, heart failure, cardiovascular defects, gastrointestinal disturbances, swayback, pathologic lesions, and degeneration of the motor tracts of the spinal cord (NAS 1977).

3.6.2 Terrestrial Plants and Invertebrates

Copper is an essential micronutrient of all higher plants studied, being a cofactor for the enzymes polyphenol oxidase, monophenol oxidase, laccase, and ascorbic acid oxidase (Schroeder et al. 1966). In copper-deficient soils, copper is strongly held on inorganic and organic exchange sites and in complexes with organic matter (Thornton 1979), causing reduced availability of copper to vegetation in these soils. Copper deficiency in terrestrial plants is usually associated with reduced growth, abnormally dark coloration in rootlets, and chlorotic leaves (Gupta 1979). In agricultural crops, copper deficiency occurs at <1.6 mg dissolved Cu/kg DW soil (Thornton 1979), and in sensitive plants at <2 to <5 mg total Cu/kg DW leaves (Gupta 1979). In fruit trees, copper deficiency is characterized by death of apical buds, formation of multiple buds, and yellowing (chlorosis) of the leaf margins (NAS 1977). Copper deficiency in alfalfa (*Medicago sativa*) and clover (*Trifolium* spp.) is associated with a faded green leaf color, growth inhibition, and withering (Gupta 1979). In grasses, copper deficiency is characterized by chlorosis, stunting, and necrosis, and in cereals by pale color, reduced growth, and a reduction in the number of pollen grains (Gupta 1979).

Increased yields of various crops occur when copper salts are added to fertilizers at 300 to 800 mg Cu/m³ (NAS 1977). In corn (*Zea mays*) and other vegetables, younger plants are more sensitive to copper deficiency than mature plants; in all cases, copper-deficient vegetables show chlorosis, reduced growth and reproduction, and low survival (Gupta 1979).

No evidence of copper deficiency exists in terrestrial species of invertebrates examined. However, relatively low concentrations of copper stimulated growth and reproduction. Reproduction in mites (*Platynothrus peltifer*) increases when fed diets containing 28 mg Cu/kg DW (vs. 13 mg/kg in controls) for 3 months (Denneman and van Straalen 1991). Also, juveniles of earthworms (*Eisenia andrei*) show increased growth at 18 mg Cu/kg DW soil after 12 weeks (van Gestel et al. 1991).

3.6.3 Aquatic Organisms

No documented report of fatal copper deficiency is available for any species of aquatic organism, and no correlation is evident in aquatic biota for the presumed nutritional copper requirements of a species and its sensitivity to dissolved copper (Neff and Anderson 1977). Extremely low copper concentrations (5.5 and 6.7 mg/kg DW) in whole bodies of 2 of 17 species of crustaceans from the Antarctic Ocean support the hypothesis that certain Antarctic species may show copper deficiencies or reduced metal requirements (Petri and Zauke 1993).

3.6.4 Birds and Mammals

Copper deficiency is not a major public health concern in the United States (Percival 1995). It is rarely observed in humans except in cases of severely malnourished children or those with Menkes' disease — an X-linked recessively inherited disorder. This disease is a severe congenital copper deficiency marked by slow growth, progressive cerebral degeneration, convulsions, temperature instability, bone alterations, and peculiar steel-like hair (ATSDR 1990; Yoshimura et al. 1995). Treatment of Menkes' disease is now restricted to parenteral administration of copper salts, although complete prevention of neurodegradation is difficult to obtain (Yoshimura et al. 1995). Copper deficiency is sometimes reported in humans after intestinal resection surgery (reduced absorptive surface), in people who consume high levels of zinc (zinc induces intestinal metallothionein that blocks copper transport), in infants who consume a diet based on cow milk (cow milk is a poor source of copper), and in genetic cases (Percival 1995). Moderate copper deficiency also exists in burn and trauma patients, two groups at high risk for sepsis (DiSilvestro et al. 1995).

An inherited abnormal copper metabolism has been established in certain strains of mice, rats, and dogs (Sugawara and Sugawara 1994). Feeding a copper-deficient diet to these animals may prevent acute hepatitis. In rats with abnormal copper metabolism and hereditary hepatitis, feeding a copper-deficient diet (0.5 mg Cu/kg ration for 35 days) prevents copper accumulation (94 to 139 mg Cu/kg DW liver) and dysfunction. Feeding a normal diet of 30 mg Cu/kg DW ration to these rats produces liver Cu concentrations of 375 mg/kg DW (Sugawara and Sugawara 1994). Administered copper protects copper-deficient strains of mice against neurodegradation, and protects ponies against selenium poisoning when pretreated with 20 or 40 mg Cu/kg BW (Stowe 1980).

Chickens (*Gallus domesticus*) given diets deficient in copper (less than 2.7 mg Cu/kg ration) have anemia, poor growth, low survival, and a high frequency of cardiovascular and skeletal lesions (Carlton and Henderson 1963, 1964a, 1964b). It is emphasized, however, that copper deficiency does not usually arise from eating a copper-poor diet because copper is found ubiquitously in foods (Percival 1995). Chickens, turkeys (*Meleagris gallopavo*), cattle, and pigs deficient in copper are prone to sudden death (Gallagher 1979). Sudden death in some copper-deficient species is sometimes associated with rupture of a major blood vessel or rupture of the heart (Carlton and Henderson 1964b; NAS 1977; ATSDR 1990; Saari et al. 1994). Male weanling rats given a copper-deficient diet of 0.13 mg Cu/kg ration (vs. copper-normal diet of 5.7 mg Cu/kg ration) for 7 weeks show high mortality (24%) from cardiac rupture; ruptured hearts had elevated concentrations of sodium,

potassium, and calcium, and depressed magnesium (Saari et al. 1994). Copper deficiency in weanling rats is confirmed by low activities of ceruloplasmin in serum and superoxide dismutase in liver and serum (DiSilvestro et al. 1995). Skeletal deformities and leg fractures occur in copper-deficient chickens, dogs, pigs, sheep, cattle, and children because of decreased tensile strength of bones (Carlton and Henderson 1964a; NAS 1977; Gallagher 1979). In lambs from copper-deficient ewes, locomotor disturbances of gait or posture occur because of lesions of excessive myelination of the central nervous system (Gallagher 1979).

Copper deficiency in humans and other mammals is characterized by slow growth, hair loss, anemia, weight loss, emaciation, edema, altered ratios of dietary copper to molybdenum and other metals, impaired immune response, decreased cytochrome oxidase activity, central nervous system histopathology, decreased phospholipid synthesis, fetal absorption, and eventually death (NAS 1977; Gallagher 1979; Kirchgessner et al. 1979; USEPA 1980; ATSDR 1990; Percival 1995).

In laboratory white rats, signs of copper deficiency include reductions in tissue copper concentrations; reduced activities of cytochrome oxidase, superoxide dismutase, succinoxidase, and ceruloplasmin; increased activity of 7-ethoxyresorufin O deethylase (EROD) in small intestines; anemia associated with low hematocrit and hemoglobin; increased acute inflammatory response; increased sensitivity to endotoxins; central nervous system lesions; and reduced phospholipid synthesis (Gallagher 1979; Johnson and Smith 1994; Schuschke et al. 1994; DiSilvestro et al. 1995). Copper-deficient rats also have prolonged sleeping times and significant reductions in activities of aniline hydroxylase and hexobarbital oxidase in liver (Moffitt and Murphy 1973). Earliest signs of copper deficiency in rats include low concentrations of copper in livers (1.4 to <3.0 mg/kg DW vs. 12.6 to 15.0 mg/kg DW in controls); profound reductions in activities of cytochrome oxidase and succinoxidase; and reductions in hematocrit, hemoglobin, ceruloplasmin, and phospholipid synthesis (Gallagher 1979; Johnson and Smith 1994). Severe copper deficiency in rats results in anemia characteristic of defective hemoglobin synthesis resulting from abnormal use of iron by mitochondria in heme synthesis (Johnson and Smith 1994). Copper-deficient rats are extraordinarily sensitive to endotoxins and die after receiving normally sublethal doses of various endotoxins (DiSilvestro et al. 1995). Copper deficiency-induced lesions in the central nervous system are produced experimentally in rats and guinea pigs and are a characteristic feature of Menkes' disease (Gallagher 1979).

Sway disease of Bactrian camels (*Camelus bactrianus*) — characterized by anemia, emaciation, falling, fractures, and death — is caused by copper deficiency associated with high molybdenum content in soils and forage. Deficiency effects are aggravated during reproduction (Zong-Ping et al. 1994).

Sheep fed copper-deficient diets of less than 2.5 mg Cu/kg DW ration (vs. a normal diet of 11.0 mg Cu/kg DW) produce a high frequency of swaybacked lambs. Swaybacks have lower concentrations of copper in liver than nonswaybacked lambs from copper-deficient ewes. Both groups have lower concentrations of copper in livers than normal lambs (Lewis et al. 1967; Buckley and Tait 1981).

Copper deficiency effects are reported in mink (*Mustela vison*) and domestic swine. Copper deficiency in mink, as judged by reduced survival, occurs by feeding rations containing the equivalent of 3.5 mg Cu/kg BW daily for a period of 50 weeks (ATSDR 1990). Swine, which seem to have higher copper requirements than mink, given low copper diets equivalent to 15 to 36 mg Cu/kg BW daily for 7 days have decreased hemoglobin, hematocrit, and growth rate (ATSDR 1990).

Dietary copper deficiency increases the acute inflammatory response in rats and other small laboratory animals (Schuschke et al. 1994). The release of inflammatory mediators, such as histamine and serotonin, from mast cells increases the vascular permeability of postcapillary venules and results in edema. In copper-deficient rats, release of histamine from mast cells correlates positively with frequency of the acute inflammatory response. Copper-deficient rats (0.6 mg Cu/kg DW ration for 4 weeks) have more mast cells in muscle than copper-adequate controls given diets containing 6.3 mg Cu/kg DW ration; however, histamine content of mast cells is not affected (Schuschke et al. 1994). An early clinical sign of copper deficiency is a reduction in the number of circulating neutrophils; the mechanism for copper-deficient neutropenia (leukopenia in which

the decrease in white blood cells is chiefly neutrophils) is unknown (Percival 1995). Proposed mechanisms to account for neutropenia from copper deficiency include:

1. Early destruction of bone marrow progenitor cells
2. Impaired synthesis of neutrophils from progenitor cells
3. A decrease in the rate of cellular maturation in the bone marrow
4. Impaired secretion of neutrophils from the bone marrow
5. Rapid clearance of circulating copper-deficient neutrophils (Percival 1995)

3.7 LETHAL AND SUBLETHAL EFFECTS

3.7.1 General

Copper is toxic to sensitive species of terrestrial vegetation at >40 µg/L nutrient solution (seedlings of pines, *Pinus* spp.), at >10 mg/kg DW leaves (cucumber, *Cucumis sativus*), and >60 mg extractable Cu/kg DW soil (sweet orange, *Citrus sinensis*; Table 3.4). Among sensitive species of terrestrial invertebrates, adverse effects on survival, growth, or reproduction occur at 2 µg Cu/cm² on paper discs (earthworms), >50 mg Cu/kg diet (larvae of gypsy moth, *Lymantria dispar*), and 53 to 70 mg Cu/kg DW soil (earthworms and soil nematodes; Table 3.4).

Table 3.4 Effects of Copper on Representative Terrestrial Plants and Invertebrates

Organism, Copper Concentration or Dose, and Other Variables	Effects	Reference ^a
PLANTS		
Agricultural crops from soils containing dissolved copper		
0.0–1.6 mg/kg soil	Copper deficiency in susceptible crops	1
1.7–2.4 mg/kg soil	Slight deficiency	1
2.5–4.0 mg/kg soil	Deficiency unlikely	1
>4.0 mg/kg soil	Soil well supplied with copper	1
Sweet orange, <i>Citrus sinensis</i> ; 4-year-old trees; M3 extractable soil copper >60 mg/kg DW (from treated plots containing about 120 kg Cu/ha)	Growth adversely affected; positive correlation between copper concentrations in feeder roots (4 to 450 mg Cu/kg DW) and M3 extractable soil copper	17
Cucumber, <i>Cucumis sativus</i> ; leaves		
<2 mg/kg dry weight (DW)	Deficient	2
2–10 mg/kg DW	Sufficient	2
>10 mg/kg DW	Toxic	2
Soybean, <i>Glycine max</i> ; leaves		
<4 mg/kg DW	Deficient	2
10–30 mg/kg DW	Sufficient	2
>50 mg/kg DW	Toxic	2
Pasture grasses; above-ground portions		
<5 mg/kg DW	Deficient	2
5–12 mg/kg DW	Sufficient	2
>12 mg/kg DW	Toxic	2
Seedlings of stone pine, <i>Pinus pinea</i> and maritime pine, <i>Pinus pinaster</i> ; exposed to nutrient solutions containing 0.4 (controls) 4, 40, or 200 µg Cu/L for as long as 4 weeks		
4 µg/L	Slight to no enhancement of root elongation	16
40 µg/L	Taproot elongation reduced but partial growth recovery in 7 days; cell membrane damage evident after 10 days	16
200 µg/L	Root growth completely inhibited within 3 days in both species	16

Table 3.4 (continued) Effects of Copper on Representative Terrestrial Plants and Invertebrates

Organism, Copper Concentration or Dose, and Other Variables	Effects	Reference ^a
Faba bean, <i>Vicia faba</i> ; cultured hydroponically with nutrient solutions containing 100 mg Cu/L for 24 days; shoots analyzed before (day 4) and after (day 24) 20-day infestation by the black bean aphid, <i>Aphis fabae</i> . Controls were raised in copper-free nutrient solutions	Aphid infestation caused a significant reduction in copper content of shoots from 51 mg Cu/kg DW to 17 mg/kg; copper in control was 25 mg/kg DW prior to aphid infestation and 14 mg/kg after 20-day infestation	3
INVERTEBRATES		
Earthworm, <i>Aporrectodea caliginosa</i> ; cocoons; exposed to aqueous solutions of copper chloride at 0–20 mg Cu/L for 14 days at 20°C and 100% relative humidity, and then to either desiccation or frost for 14 days	No adverse effects at 6 and 12 mg Cu/L. At 20 mg Cu/L, none survived at –3°C and 95% survived at 0°C; embryos contained up to 200 mg Cu/kg DW — comparable to concentrations found in various earthworm tissues from copper-contaminated soils	18
Soil nematode, <i>Caenorhabditis elegans</i>		
70 mg/kg DW sandy soil for 24 h	LC50	4
105 mg/L for 24 h; no soil	LC50	4
1061 mg/kg loam substrate for 24 h	LC50	4
2476 mg/L for 24 h; loam substrate	LC50	4
Soil ciliate, <i>Colpoda steini</i>		
250 µg/L for 24 h	Growth reduced 50%	5
Fruitfly, <i>Drosophila melanogaster</i>		
In culture medium containing 80 µg Cu/cm ² for 4 weeks	Survival reduced 35%; copper elevated in cytoplasm, Malpighian tubule epithelial cells, and other tissues	6
Earthworms, three species; 40–238 mg/kg soil; exposure duration unknown	No effect on growth, survival, or reproduction	7
Earthworm, <i>Eisenia andrei</i> ; juveniles; exposure for 12 weeks		
18 mg/kg DW soil	Growth stimulated	8
56 mg/kg DW soil	No effect on growth or reproduction	8
100 mg/kg DW soil	<50% effective in reducing growth; inhibited sexual development	8
Earthworm, <i>Eisenia fetida</i>		
32 mg/kg DW soil for 56 days	No effect on cocoon production	9
53.3 (32.5–186.0) mg/kg DW soil for 56 days	Cocoon production reduced 50%	9
210 mg/kg DW soil for 56 days	No deaths	9
555 (460–678) mg/kg DW soil for 56 days	50% dead	9
683 (570–812) mg/kg DW soil for 14 days	50% dead	9
Earthworm, <i>Eisenia fetida andrei</i>		
Adults held in soil containing as much as 300 mg Cu/kg DW for 3 weeks; resultant cocoons incubated in uncontaminated soil for 5 weeks to assess hatchability	No adverse effects on cocoon production or hatchability in soil containing 60–120 mg Cu/kg DW; adult growth retarded during exposure at 300 mg/kg DW	10
Earthworm, <i>Lumbricus rubellus</i>		
100–150 mg/kg DW soil	Decreased cocoon production	11
150–300 mg/kg DW soil	Decrease in litter breakdown activity	11
>300 mg/kg DW soil	Reduced growth and increased mortality	11
1000 mg/kg DW soil for 6 weeks	Lethal to 50%	11
Earthworm, <i>Lumbricus terrestris</i>		
Exposed for 5 days to filter paper disc containing 0.5, 1, 2, 4, or 8 µg Cu/cm ²	At 4 µg/cm ² and higher, mortality was >90%; 20% were dead at 2 µg/cm ² , and none were dead at lower concentrations. Whole worms contained, in mg Cu/kg DW, 5.9 in controls, 28.5 in the 0.5 group, and 73.1 in the 1.0 group. At sublethal concentrations, worms had decreased lysozyme activity in coelomic fluid and coelomocytes	12

Table 3.4 (continued) Effects of Copper on Representative Terrestrial Plants and Invertebrates

Organism, Copper Concentration or Dose, and Other Variables	Effects	Reference ^a
Gypsy moth, <i>Lymantria dispar</i> Larvae were fed diets containing 10, 50, 250, or 1250 mg Cu/kg ration from first instar to pupation; effects measured on development rate, growth, survival, and reproductive success	No adverse effects at 10 mg/kg diet. Significant adverse effects at 50 mg/kg and higher on development and reproductive success and at 250 mg/kg and higher on growth	13
Oribatid mite, <i>Platynothrus peltifer</i> Fed diets with 13 (control), 28, 64, 168, 598, or 1498 mg Cu/kg DW diet for 3 months	No deaths at any dose.	7
84 mg/kg DW soil Soil faunal communities Forest soil treated to contain 100, 200, 400, or 600 mg Cu/kg DW; nematodes and macroarthropods enumerated after 7 days	Reproduction increased at 28 mg/kg but decreased steadily with increasing dose. The no-observable-effect-concentration (NOEC) for reproduction was 168 mg/kg diet; the NOEC for growth was 598 mg/kg. Copper concentrations in whole mites increased significantly at dietary loadings >168 mg/kg NOEC on growth, survival, or reproduction	7
Termites, subterranean; Karachi, Pakistan; termite-infested area (<i>Microtermes</i> spp., <i>Heterotermes</i> spp., <i>Coptotermes</i> spp., <i>Odontotermes</i> spp.) Fir (<i>Abies pindrow</i>) wooden stakes coated with 5% copper sulfate in gelatin solution vs. uncoated stakes	Sensitive species of nematodes and mites were reduced in number at 100 mg/kg soil; total nematode and arthropod numbers declined at 200 mg/kg and higher Copper-treated stakes prevented termite attack in soil up to 4 years vs. severe termite damage within 6 months in control stakes	14 15

^a 1, Thornton 1979; 2, Gupta 1979; 3, Crawford et al. 1990; 4, Donkin and Dusenberry 1993; 5, Forge et al. 1993; 6, Marchal-Segault et al. 1991; 7, Denneman and van Straalen 1991; 8, van Gestel et al. 1991; 9, Spurgeon et al. 1994; 10, van Gestel et al. 1989; 11, Ma 1984; 12, Goven et al. 1994; 13, Gintenreiter et al. 1993; 14, Parmelee et al. 1993; 15, Roomi et al. 1990; 16, Arduini et al. 1995; 17, Alva et al. 1995; 18, Holmstrup et al. 1998.

Sensitive species of representative freshwater plants and animals die within 96 h at waterborne copper concentrations of 5.0 to 9.8 µg/L (Hodson et al. 1979; Table 3.5). The most sensitive freshwater species have LC50(96 h) values between 0.23 and 0.91 µg Cu/L and include daphnids (*Daphnia* spp.), amphipods (*Gammarus pseudolimnaeus*), snails (*Physa* spp.), and chinook salmon (*Oncorhynchus tshawytscha*; USEPA 1980; Table 3.5). In general, mortality of tested aquatic species is greatest under conditions of low water hardness (as measured by CaCO₃), starvation, elevated water temperatures, and among early developmental stages (Hodson et al. 1979; Table 3.5). Toxicity testing of copper-contaminated sediments to amphipods (*Hyalella azteca*) and daphnids (*Daphnia magna*) using techniques of enzyme inhibition and growth rate show that these variables are more sensitive in accurately predicting copper sensitivity than LC50(48 h) values (Kubitz et al. 1995) and should be considered when assessing risk of contaminated sediments to freshwater systems. The most sensitive saltwater species to copper have LC50(96 h) values from 28 to 39 µg/L and include summer flounders (*Paralichthys dentatus*), copepods (*Acartia tonsa*), and softshell clams (*Mya arenaria*; USEPA 1980; Eisler 1995; Table 3.5). Adverse sublethal effects of copper on representative species of estuarine algae, molluscs, and arthropods frequently occur at 1 to 10 µg/L (Bryan and Langston 1992; Table 3.5).

No data are available on copper toxicity to avian wildlife. Experiments with domestic poultry show that copper accumulates in livers of mallard ducklings at dietary concentrations as low as 15 mg/kg DW ration; that gizzard histopathology and a reduction in weight gain of chicks (*Gallus* sp.) occur at 250 to 350 mg Cu/kg DW ration; and that growth of turkey poult is improved at

60 mg Cu/kg DW ration and inhibited at 120 mg/kg DW ration, with signs of gizzard histopathology at 500 mg/kg DW ration (Wood and Worden 1973; Poupolis and Jensen 1976; NAS 1977; Kashani et al. 1986; [Table 3.6](#)).

Copper is lethal to mammals through a variety of routes ([Table 3.7](#)). Single oral doses of 6 to 637 mg Cu/kg BW are fatal to humans. A single oral dose of 200 mg/kg BW is usually fatal to cattle. Dietary copper is lethal when eaten for extended periods at more than 80 mg Cu/kg ration in sheep (equivalent to 5.1 to 10.7 mg Cu/kg BW daily), more than 238 mg/kg ration in pigs, and more than 4000 mg/kg ration in rats (equivalent to more than 133 mg Cu/kg BW daily; [Table 3.7](#)).

Adverse sublethal effects of copper to sensitive mammals occur in human infants at drinking water concentrations more than 3 mg Cu/L; in cattle at dietary levels greater than 20 mg Cu/kg BW by way of intraperitoneal injection and more than 4.2 mg Cu/kg BW via drinking water; in sheep given daily oral doses of 7.5 to 15.0 mg Cu/kg BW or fed diets containing more than 37.3 mg Cu/kg ration; in rats at >100 mg Cu/kg ration (equivalent to >7.9 mg Cu/kg BW daily), >400 mg Cu/L drinking water, or >2.0 to 2.5 mg Cu/kg BW daily via injection; and in pigs at more than 14.5 mg Cu/kg BW daily via diet. Elevated copper concentrations (328 mg Cu/kg DW) occur in livers of surviving cattle fed diets containing 8.2 mg Cu/kg ration; of sheep (1109 mg/kg DW liver) fed diets containing 37.3 mg Cu/kg ration; and of rats (710 mg/kg FW liver) given intraperitoneal injections of 3.75 mg Cu/kg BW daily for 18 weeks ([Table 3.7](#)).

3.7.2 Terrestrial Plants and Invertebrates

Copper is toxic to sensitive plants when plant nutrient solutions contain >40 to 200 µg Cu/L, when leaves have >10 to 12 mg Cu/kg DW, and when extractable copper in soils is >60 mg/kg DW soil ([Table 3.4](#)). Excess copper inhibits root elongation and branching and reduces the ability of the plant to explore the soil for water and nutrients (Arduini et al. 1995). Root damage occurs in pine seedlings (*Pinus* spp.) after exposure for 10 days to nutrient solutions that contain 40 µg Cu/L. A lower concentration of 4 µg Cu/L has no adverse effects on root growth and morphology, while a higher concentration of 400 µg Cu/L completely inhibits root growth within 3 days (Arduini et al. 1995).

Severely reduced crop growth was measured in soils treated with 750 kg Cu/ha annually for 13 years wherein the soil pH declined from 6.1 to 4.7 during this period (Boon et al. 1998). Laboratory studies showed that planting of copper-tolerant grass (*Agrostis capillaris*) on these soils resulted within 10 weeks in faster bacterial growth, more protozoans, and more nematodes in comparison to fallow controls. Boon et al. (1998) concluded that metal-tolerant plant species can reestablish the necessary food base to support organism growth and can reverse the loss of soil function due to high copper levels under acidic conditions.

Poultry litter is a useful agricultural by-product with high nitrogen and phosphorus content and is frequently added to agricultural soils. Poultry litter from northern Georgia containing 1196 mg Cu/kg DW and applied at a final rate of 5 to 15 mg Cu/kg soil to fields of Sudex (*Sorghum bicolor* × *S. sudanense*) did not affect copper levels of treated Sudex or produce any evidence of toxicity (van der Watt et al. 1994). However, most terrestrial vegetation in the United States, Sweden, Wales, and other locales is usually adversely affected by emissions from copper mines, brass foundries, and copper smelters (Hutchinson 1979). Damage to vegetation persists for at least 50 years after closure of a copper smelter because of copper, arsenic, and lead in the soil. Particularly sensitive to copper in the soils are white pine (*Pinus strobus*) and red maple (*Acer rubrum*). Less sensitive are Douglas fir (*Pseudotsuga menziesii*) and lodgepole pine (*Pinus contorta*; Hutchinson 1979).

Earthworms (*Eisenia fetida*) held in soils containing 53 mg Cu/kg DW show a 50% reduction in cocoon production in 56 days; 32 mg Cu/kg soil had no effect on cocoon production (Spurgeon et al. 1994). The LC50 (56 days) value for earthworms is 555 mg Cu/kg DW soil; no deaths occur at 210 mg/kg soil during this period. Copper is more toxic to *Eisenia fetida* than are salts of cadmium, zinc, or lead (Spurgeon et al. 1994). Copper adversely affects the earthworm *Lumbricus rubellus* (Ma 1984). Concentrations of 150 mg Cu/kg surface soil from an accidental spill of copper

sulfate in grasslands reduced earthworm populations by about 50%; surface soil concentrations of 260 mg Cu/kg kill almost 100% of the *Lumbricus*. Copper is most toxic to *Lumbricus* at low soil pH (4.8 to 7.1) and at low temperatures (Ma 1984). Earthworm cocoons, however, were relatively unaffected by copper at concentrations <12 mg Cu/L, and at 20°C unless stressed by desiccation or frost (Holmstrup et al. 1998). Cocoons of *Aporrectodea calignosa* were unaffected at 20 mg Cu/L except under conditions of low relative humidity (95% relative humidity vs. 97.5% or 100%), and temperatures of -3, and -6°C, but not 0°C (Holmstrup et al. 1998).

Tests show that the presence of soil reduces the toxicity of copper to the soil-dwelling nematode *Caenorhabditis elegans*; copper toxicity to nematodes increases with increasing densities of bacteria and increasing concentrations of sodium chloride or potassium chloride (Donkin and Dusenberry 1993). Terrestrial isopods efficiently assimilate and store copper as detoxified granules in the hepatopancreas; this activity is in contrast to many species of marine crustaceans that are unable to assimilate, detoxify, or otherwise regulate copper (Weeks and Rainbow 1993).

3.7.3 Aquatic Organisms

Plants

Photosynthesis and growth in sensitive species of freshwater algae are inhibited by copper concentrations of 1 to 6 µg/L (NAS 1977; [Table 3.5](#)). For sensitive species of estuarine phytoplankton, copper is lethal at 50 µg/L and most toxic under conditions of decreasing salinity, pH, and concentrations of chelators (Erickson et al. 1970). Sensitivity to copper varies widely among species of estuarine algae (Erickson et al. 1970; [Table 3.5](#)). Some species, for example, grow normally at concentrations as high as 10 mg Cu/L during exposure for 9 days (Piccinni and Coppelotti 1982). In mesocosm studies, 50 µg Cu/L caused a reduction of about 80% in total zooplankton and total algal biovolumes; the algal assemblage that persisted was dominated by diatoms (Havens 1994). Copper-resistant strains of *Euglena gracilis* challenged with high sublethal concentrations of copper for 5 days had an altered cysteine metabolism (Coppelotti 1989).

Some species of aquatic plants absorb or adsorb dissolved copper at extremely high rates ([Table 3.5](#)). Bioconcentration factors for copper and freshwater alga (*Chlorella* sp.) range from 203 to 2000 after exposure for 14 to 30 h (USEPA 1980). Seagrass (*Heterozostera tasmanica*) in seawater containing 42 µg Cu/L for several weeks contain 2700 mg Cu/kg DW; seagrasses in media containing 0.3 µg Cu/L contain 2.5 mg Cu/kg DW; and intermediate values are reported for 10 µg Cu/L (306 to 564 mg/kg DW) and 20 µg/L (1280 mg/kg DW; Ahsanullah and Williams 1991). Some freshwater aquatic macrophytes accumulate as much as 54,500 mg Cu/kg DW, as was the case for *Lemna* sp. during exposure to 1000 µg Cu/L; a lower dose regimen of 35 µg Cu/L results in 256 mg Cu/kg DW *Lemna* (Stokes 1979).

Table 3.5 Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
PLANTS		
Algae; mixed culture; 5 µg/L	Photosynthesis reduced	1
Aquatic weeds, fresh water 170 µg/L for 99 days, continuous exposure	Eliminated or controlled most submerged species; adverse effects first noted at day 34. Weeds contained 360 to 4280 mg Cu/kg dry weight (DW)	2
250–1000 µg/L for 99 days, continuous exposure	Unsuccessful in controlling emergent aquatic weeds; successful in eliminating filamentous algae and most submerged species	2

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Marine alga, <i>Chlamydomonas bulloso</i> ; 49.9 µg/L for 96 h	Growth reduced 50%	3
Green alga (fresh water), <i>Chlamydomonas reinhardtii</i>		
18 µg/L for 24 h	Reduction in number of cells bearing flagella	4
21 µg/L for 7 days	Growth normal	5
32 µg/L for 7 days	Growth reduced 50%	5
60 µg/L for 10 min	Flagella shed; flagellar refabrication inhibited for 24 h	4
79 µg/L for 72 h	Growth inhibited 50%	5
Freshwater alga, <i>Chlorella</i> spp.		
1.0 µg/L	Growth reduced	1
6.3 µg/L	Photosynthesis inhibited	1
Marine alga, <i>Dunaliella salina</i>		
0.031 µg/L for 8 months	Minor adverse effects on lipid metabolism	6
380 µg/L for 96 h	Growth reduced 50%; negligible effects on cellular ultrastructure	3, 6
Marine alga, <i>Dunaliella tertiolecta</i>		
8000 µg/L for 48 h	Growth normal	7
12,000–16,000 µg/L for 48 h	Adverse effects on photosynthesis, cell division rates, and pigment metabolism	7
Euglena, <i>Euglena gracilis</i> ; 10,000 µg/L for 5 days	Adverse sublethal effects, including altered free cysteine metabolism	8
	Complete inhibition of growth	1
Freshwater diatom, <i>Nitzschia palea</i> ; 5 µg/L Alga, <i>Ochromonas danica</i>		
10,000 µg/L for as long as 9 days	Growth normal	11
Aquatic moss, <i>Rhynchostegium riparioides</i> ; 4.5 (controls), 9, 21, or 50 µg/L for 27 days followed by 14 days in clean media	Copper accumulation plateaued after 18 days. Maximum concentrations reached, in mg/kg DW, were 900 (9 µg/L group) 2000 (20 µg/L group) and 3500 (50 µg/L group). At end of depuration mosses had lost about 50% of accumulated copper	12
Freshwater alga, <i>Scenedesmus acutiformis</i> ; 100 µg/L for 20 min at pH 4.8, 5.8, or 6.8	Copper concentrations, in mg/kg DW, increased from 400 (pH 4.8) to 750 (pH 5.8) to 4000 (pH 6.8)	10
Freshwater alga, <i>Scenedesmus subspicatus</i>		
56 µg/L for 72 h	Growth normal	5
120 µg/L for 72 h	Growth reduced 50%	5
Marine alga, <i>Scrippsiella faeroense</i> ; 5 µg/L for 5 days	Growth inhibited 50%	1
Marine alga, <i>Thalassiosira pseudonana</i> ; 5 µg/L for 72 h	Growth inhibited 50%	1
PROTISTS		
Freshwater protozoan ciliate, <i>Tetrahymena pyriformis</i>		
3818 µg/L for 96 h	Growth normal	5
8000 µg/L for 48 h	Growth inhibited 50%	5
Marine protozoan, <i>Euplotes vannus</i> ; exposure for 6 days		
100 µg Cu/L	Growth stimulated	170
200 µg Cu/L	Tolerated; growth normal	170
400 µg/L	Accumulations of 239 mg Cu/kg DW; depressed growth; morphological cell alterations	170

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
CNIDARIANS		
Sea anemone, <i>Anemonia viridis</i> ; 50 or 200 µg/L for 5 days	Immediate tentacle retraction; copious production of mucus; progressive visible bleaching and loss of zooxanthellae	13
Hydroid, <i>Campanularia flexuosa</i>		
1.4 µg/L for 11 days	Enzyme disruption	1
10–13 µg/L for 11 days	Growth rate reduced	1
Ctenophore, <i>Pleurobrachia pileus</i> ; 33 µg/L for 24 h	Fatal to 50%	1
PLATYHELMINTHES		
Trematode, <i>Posthodiplostomum minimum</i>		
Cercariae		
26 µg Cu/L	LC50 in 12 h	173
32 µg Cu/L	LC50 in 9 h	173
<i>Posthodiplostomum</i> -infected snail (<i>Physa gyrina</i>) intermediate host		
38.0 µg Cu/L	LC50 in 7 days	173
44.6 µg Cu/L	64% dead in 96 h	173
89.2 µg Cu/L	87% dead in 96 h	173
ROTIFERS		
Freshwater rotifer, <i>Brachionus calyciflorus</i>		
2.5–5.0 µg/L	MATC ^b	14
14 µg/L for 5 h	Swimming behavior impaired 50%	14
25 µg/L for 5 h	All immobilized	14
26 µg/L for 24 h	Fatal to 50%	14, 15
34 µg/L for 5 h	Feeding rate reduced 50%	15
43 µg/L for 24 h	Feeding rate reduced 50%	16
80 µg/L for 24 h	No deaths when molar ratio of fulvic acid to copper was 1:1	17
NEMATODES		
Free-living nematode, <i>Caenorhabditis elegans</i>		
260 µg/L for 96 h	LC50	18
22,000 µg/L for 24 h	LC50	18
MOLLUSCS		
Freshwater unionid mussel, <i>Anodonta cygnea</i>		
2.1 (95% confidence interval [CI] of 0.01–7.2) µg/L for 72 h	Reduction by 50% in valve closure of glochidia; ability to infect fish reduced	19
5.3 µg/L for 48 h	Valve closure rate reduced 50%	19
Freshwater mussel, <i>Anodonta grandis</i>		
17 µg/L for 24 h	Valve closure normal	20
33 µg/L for 24 h	Valve closure rate reduced 50%	20
44 µg/L for 24 h	Fatal to 50%	20
Bay scallop, <i>Argopecten irradians</i>		
5.0 µg/L for 119 days	All dead	1
5.8 µg/L for 42 days	Growth rate reduced 50%	1
Freshwater snail, <i>Biomphalaria glabrata</i> ; 60 µg/L for 60 h	Lethal; epithelial cell histopathology	21
Freshwater snail, <i>Bulinus globosus</i> ; 707 µg/L for 24 h	LC50	22

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Channeled whelk, <i>Busycon canaliculatum</i> 100 µg/L for 54 days	Copper concentrations, in mg/kg FW, were 43 (vs. 35 in controls) in gills and 25 (vs. 16) in osphradium	23
500 µg/L for 16 days	All dead	23
Snail, <i>Campeloma decisum</i> >30 µg/L for 24 h	Motility inhibited	24
1700 µg/L for 96 h	LC50	24
Asiatic clam, <i>Corbicula fluminea</i> 5.5 µg/L for 30 days	Growth normal; soft tissues contained 80 mg Cu/kg DW (vs. 40–60 in controls)	25
8.4–26.7 µg/L for 30 days	Some deaths; growth reduction in juveniles and adults; soft parts had 205–278 mg Cu/kg DW	25
19.2 µg/L for 30 days	LC50	25
Pacific oyster, <i>Crassostrea gigas</i> Adults		
10 µg/L for 14 days	LC20	27
100 µg/L	No deaths in 96 h; 30% dead in 14 days	27
560 µg/L for 96 h	LC50	27
Embryos, exposed for 48 h 5 µg/L	94–98% normal development vs. 97–99% in controls	28
6.5 µg/L	8–25% abnormal (retarded shell size, reduced growth, erratic swimming behavior)	28
10 µg/L	26–79% abnormal	28
18 µg/L	No embryos developed normally	28
American oyster, <i>Crassostrea virginica</i> ; adults with soft parts containing 837 mg/kg DW were held in flowing seawater of 1–2 µg Cu/L for 56 weeks	No significant depuration; soft parts contained 746–1526 mg/kg DW during exposure	26
Clam, <i>Donax incarnatus</i> 4.0 µg/L for 4 h		
26.1 µg/L for 96 h	Increased oxygen consumption and increased ammonia excretion	29
Zebra mussel, <i>Dreissena polymorpha</i> 4.5, 9, 21, or 50 µg/L for 27 days followed by 14 days in clean media	LC50	29
13 µg/L for 9 weeks	No deaths. Filtration rate reduced in 50 µg/L group during exposure but not afterwards. Maximum concentrations, in mg/kg DW soft parts, were about 30 (9 µg/L), 70 (21 µg/L), and 100 (50 µg/L); about 18% of the accumulated copper was lost during depuration	12
>28 µg/L for 48 h	No effect on survival or filtration rate	30
41–43 µg/L for 48 h to as long as 9 weeks	Copper accumulation	31
90 µg/L for 9 weeks	Filtration rate reduced 50%	30, 31
Black abalone, <i>Haliotis cracherodii</i> ; 50 µg/L for 96 h	28% dead; 78% reduction in filtration rate	30
Red abalone, <i>Haliotis rufescens</i> ; 86 µg/L for 96 h	LC50	1
Freshwater mussel, <i>Lamellidens marginalis</i> 250 µg/L for 96 h	LC50	1
250, 500, 750, or 1000 µg/L for 30 days	Moribund; complete dissolution of crystalline style in 9.8 h: style reforms in 2.5 h on transfer to uncontaminated media and this may be useful as indicator of copper stress	32
5000 µg/L for 96 h	No deaths. Initial dose-dependent increase in respiratory rate and decrease in growth rate; similar to controls by day 30	33
	LC50	32, 33

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Baltic clam, <i>Macoma balthica</i> ; 40 µg/L for 48 h	Copper in soft parts was 23.5 mg/kg DW vs. 20.0 in controls	34
Clam, <i>Macoma liliana</i> ; juveniles held in sediments containing <1 (controls), 5, 10, 15, 25, 30, 50, 70, or 140 mg/kg DW. Effects on avoidance in 96 h, burial rate in 90 min, and survival in 10 days were measured	Maximal avoidance was in sediments containing 25 mg/kg and higher (interstitial water had 113 µg Cu/L). Ability to bury in sediments was inhibited in sediments containing 15 mg/kg and higher (pore water of 120 µg/L). Reduced survival at 30 mg/kg DW sediment and higher	35
Quahog clam, <i>Mercenaria mercenaria</i> 25 µg/L for 77 days 640–6400 µg/L	53% dead Dose-dependent increase in cytotoxicity by isolated brown cells	1 36
Scallop, <i>Mizuhopecten yessoensis</i> ; 25 µg/L for 21 days	Hepatopancreas had 513 mg/kg DW (vs. <50 in controls); accumulations accompanied by a significant increase in hydroperoxide and malondialdehyde contents in microsomal membranes and alterations in lipid peroxidation rates	37
Softshell clam, <i>Mya arenaria</i> 35 µg/L for 168 h 39 µg/L for 96 h 86 µg/L for 504 h 3000 µg/L for 336 h	LC50 at 22°C LC50 LC50 at 17.5°C No deaths at 4°C	38, 160 1 38, 160 38, 160
Common mussel, <i>Mytilus edulis</i> 0, 1, 3.2, 10, 32, or 100 µg/L for 7 days; mantle tissue analyzed for heat shock protein 60	Adverse effects on growth in the 32 and 100 µg/L groups; dose-dependent protein increase at 3.2 µg/L and higher	39
Mussels age 2.5 months continuously exposed to 0, 1, 5, or 10 µg/L for 21 months. Growth, histopathology, and residues in soft parts measured after 12, 18, and 21 months	Growth adversely affected in the 10 µg/L group; histopathology evident in the 5 and 10 µg/L groups. After 21 months, concentrations in soft parts, in mg/kg FW, were 5.5 in controls and the 1.0 µg/L group, 19.2 in the 5 µg/L group, and 62 in the highest exposure group	40
1, 3.2, 10, 32, or 100 µg/L for 7 days	No effect on protein activity in gill and mantle at 32 µg/L and lower; increased accumulations at 100 µg/L. At 32 µg/L and higher growth was reduced. At 100 µg/L survival decreased and copper concentrations increased from 24 to 89 mg/kg DW in gill and from 14 to 54 mg/kg DW in mantle	41
2 µg/L for 30 days 5–6 µg/L for 10 days 50 µg/L for 6 days, then transferred to clean seawater	Spawning frequency reduced 50% Growth reduced 50% Lysosomal destabilization in all age groups; ability to recover declined with increasing age	42 42 43
430 µg/L for 120 h	Cardiac activity reduced 50% within 4 h and reduction persisted for 120 h	44
Dipped for 5 sec in CuSO ₄ solutions containing 5, 10, 25, or 50 grams/L and stored in air for 6, 24, or 48 h	Fatal at 5 to 10 g/L if kept out of water for 24 h; fatal at 10–20 g/L if stored only a few hours. Oysters (<i>C. virginica</i>) survived this treatment	45
Mussel, <i>Mytilus galloprovincialis</i> 15 µg/L for 5 days	Stimulates the synthesis of thionein-like copper-binding proteins in gill, mantle, and digestive gland	46

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
40 µg/L for 6 days	Gills contained 22.3 mg Cu/kg FW (vs. 2.4 in controls); digestive gland had 6.8 mg/kg FW (3.0). Exposed mussels show stimulated lipid peroxidation rates in tissues	47
80 µg/L for 2 h	Induces the synthesis of copper-binding proteins similar to that of metallothioneins in gills and mantle	46
Common limpet, <i>Patella vulgata</i> ; 10 µg/L for 6 h Brown mussel, <i>Perna indica</i>	Pedal mucus production reduced 40%	48
2–6 µg/L for 4 h 21.8 µg/L for 96 h	Increased oxygen consumption LC50	29 29
Green mussel, <i>Perna viridis</i>	Reduction in filtration rate, growth, and oxygen to nitrogen ratio; histopathology of digestive cells and tissues. Residues, in mg/kg FW, were 38.2 in digestive gland vs. 2.6 in controls and 24.7 in total soft parts vs. 1.3 in controls	49
25 µg/L for 2 weeks	LC50	49
86 µg/L for 96 h		
Snail, <i>Physa integra</i>	No adverse effects on growth, survival, or feeding	24
15 µg/L for 6 weeks		
39 µg/L for 96 h	LC50	1, 24
Apple snail, <i>Pomacea paludosa</i> ; 24–57 µg/L for 96 h	LC50	50
Cuttlefish, <i>Sepia officinalis</i> ; eggs; 4 (control), 50, 100, or 200 µg/L for 8 weeks	Dose-dependent decrease in hatching time and survival; no external malformations	51
Freshwater snail, <i>Thiara tuberculata</i>		
450 µg/L for 20 days	Progressive decline over time in oxygen consumption	52
2180 µg/L for 72 h	LC50; survivors had decreased oxygen consumption	52
Giant clam, <i>Tridacna derasa</i> ; embryos age 1 h; exposed at 27°C		
0.1 µg/L for 72 h	LC50	53
1.0 µg/L for 72 h	LC65	53
10.0 µg/L for 72 h	LC91	53
Clam, <i>Villorita cyprinoides</i>		
450 µg/L for 120 h	No deaths	54
1000, 3000, or 5000 µg/L for 120 h	No deaths. Hemolymph protein levels reduced at 1000 and 3000 µg/L, but not in 5000 µg/L	54, 161
Freshwater mussel, <i>Villosa iris</i>		
24 µg/L for 24 h	Valve closure normal	55
27–29 µg/L for 24 h	50% reduction in valve closure	55
83 µg/L for 24 h	LC50	55
CRUSTACEANS AND ARACHNOIDS		
Copepod, <i>Acartia clausi</i> ; 52 µg/L for 96 h	LC50	1
Copepod, <i>Acartia tonsa</i> ; 31 µg/L for 96 h	LC50	1
Amphipod, <i>Allorchestes compressa</i>		
3.7 µg/L for 4 weeks	Extrapolated concentration causing detectable decreases in survival and biomass	9
10 µg/L for 4 weeks	Lowest concentration tested causing adverse effects on growth and survival; bioconcentration factor (BCF) of 51,500	9
500 µg/L for 96 h	LC50	9

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Cladoceran, <i>Bosmina longirostris</i>		
1.4 µg/L for 48 h; starved	50% immobilized	56
3.7 µg/L for 48 h; fed	50% immobilized	56
16 µg/L for 15 days	Growth rate reduced	158
18 µg/L for 15 days	Survival reduced	158
Lesser blue crab, <i>Callinectes similis</i>		
50 µg/L for 118 days	No effect on survival or molting during exposure	57
250 µg/L; juveniles	LC50 (30 days); LC100 (68 days)	57
500 µg/L	50% of megalops dead in 3.7 days; 50% of juveniles dead in 7.7 days; all juveniles dead in 49 days	57
Crayfish, <i>Cambarus bartoni</i> ; copper-tolerant strain exposed to 19 (controls), 125, 250, or 500 µg/L for 4 weeks; concentrations in controls (mg/kg DW) vs. all experimental groups (mg/kg DW)		
Exoskeleton	54 DW vs. 78–116 DW	58
Gills	368 DW vs. 571–1167 DW	58
Hepatopancreas	1778 DW vs. 1494–2346 DW	58
Muscle	88 DW vs. 99–129 DW	58
Viscera	92 DW vs. 158–276 DW	58
Shore crab, <i>Carcinus maenas</i>		
500 µg/L for 5–18 days	Gill histopathology; some recovery after exposure	59
500 µg/L for 28 days		
Controls (fed) vs. exposed (fed); values in mg/kg DW		
Carapace	5 DW vs. 51 DW	60
Midgut gland	26 DW vs. 474 DW	60
Controls (starved) vs. exposed (starved); values in mg/kg DW		
Carapace	4 DW vs. 72 DW	60
Midgut gland	298 DW vs. 583 DW	60
2000 µg/L for 5 days	Some deaths; severe gill cellular hyperplasia	59
Daphnid, <i>Ceriodaphnia dubia</i>		
9.5 µg/L for 48 h	LC50 at pH 6.0–6.5	61
28 µg/L for 48 h	LC50 at pH 7.0–7.5	61
200 µg/L for 48 h	LC50 at pH 8.0–8.5	61
Chironomid, <i>Chironomus riparius</i> ; larvae; 5 generations exposed from egg to fourth instar at medium concentrations of 0, 1, 10, or 100 µg Cu/L	Mandible and mentum deformities were positively associated with increasing concentration and generation	169
Cladoceran, <i>Chydorus sphaericus</i>		
3.3 µg/L for 48 h; starved	50% immobilized	56
7.6 µg/L for 48 h; fed	50% immobilized	56
Amphipod, <i>Corophium volutator</i> ; exposed to <0.1, 50, or 100 µg/L for 14 days in seawater under conditions of normoxia, moderate hypoxia (29% oxygen saturation), and hypoxia (19% oxygen saturation)	Exposure to increasing levels of copper resulted in a significant increase in total body copper concentrations (from 76 to 174 mg/kg DW), and a lowering of egg production; mortality was higher at low oxygen saturations and high copper concentrations (max. 35% dead at 100 µg/L and 19% saturation)	62
Brown shrimp, <i>Crangon crangon</i> ; 330 µg/L for 96 h	LC50	1
Daphnids, <i>Daphnia ambigua</i> , <i>D. parvula</i> , <i>D. pulex</i> ; 49 µg/L for lifetime exposure	Reduced productivity	1
Daphnid, <i>Daphnia carinata</i> ; 28 µg/L for 96 h	LC50	63
Daphnid, <i>Daphnia magna</i>		

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
5.9 µg/L for 21 days	Growth reduced 10%; bioconcentration factor (BCF) of 4900; maximum whole-body concentration of 43 mg/kg DW	64
10 µg/L for 96 h	LC50 at 45 mg CaCO ₃ /L	1
10 µg/L, life cycle	Inhibited reproduction	1
11.4–16.3 µg/L	MATC ^b at 51 mg CaCO ₃ /L	1
16.1 µg/L for 21 days	Growth reduced 50%	64
20–43 µg/L	MATC ^b at 104 mg CaCO ₃ /L	1
26–59 µg/L for 48 h; fed	LC50; no weight loss among survivors	65
28–58 µg/L for 48 h; starved	LC50; survivors had significant weight loss	65
59 µg/L for 26 h	Feeding rate reduced 50%	16
69 (37–110) µg/L for 21 days	LC50	64
200 µg/L for 96 h	LC50 at 226 mg CaCO ₃ /L	1
Daphnid, <i>Daphnia pulex</i>		
0.003–0.3 µg/L for 21 days	Increased reproduction	66
3 µg/L for 21 days	Impaired reproduction	66
5 µg/L for 70 days	Decreased survival beginning at day 58; no effect on reproduction	67
20–37 µg/L for 48 h	LC50	66, 67, 68
20 µg/L for 6 h daily for 70 days	Decreased survival and brood size	67
30 µg/L for 15 days	No significant effect on growth or survival	158
Daphnid, <i>Daphnia pulicaria</i>		
7.2–11.4 µg/L for 96 h	LC50 at 44–48 mg CaCO ₃ /L	1
17.8–27.3 µg/L for 96 h	LC50 at 95–245 mg CaCO ₃ /L	1
Amphipod, <i>Gammarus pseudolimnaeus</i>		
<4.6 µg/L for 15 weeks (two generations)	No adverse effects	24
4.6–8 µg/L	MATC ^b at 45 mg CaCO ₃ /L	1
6.2–12.9 µg/L for 5 weeks	Decreased survival	24
20 µg/L for 96 h	LC50	24
Amphipod, <i>Gammarus pulex</i>		
Immersed in solutions containing 2.6 (controls), 11, 14.6, 18.2 or 23.1 µg/L for 100 days	Population density doubled in the controls and the 11 µg/L group. Rate of increase was adversely affected at 14.6 and 18.2 µg/L; the high-dose group lost population. Low-dose groups were composed mainly of juveniles; at 14.6 µg/L and higher, the number of juveniles decreased; and at 18.2 µg/L and higher, number of adults decreased	69
33 µg/L for 240 h	LC50	69
Mysid shrimp, <i>Holmesimysis costata</i> ; 17 µg/L for 96 h	LC50	70
American lobster, <i>Homarus americanus</i>		
48 µg/L for 96 h	Larval LC50	1
100 µg/L for 96 h	Adult LC50	1
Amphipod, <i>Hyalella azteca</i>		
1.3 (control), 5.6, 10, 18, 32, 56, or 100 µg/L for 10 weeks beginning at age 1-week	Survival reduced at 32 µg/L and higher; no significant copper accumulations over controls in all groups	71
1.3 (control), 5.6, 10, 18, 32, 56, 100, or 180 µg/L for 4 weeks; adults	Copper residues, in mg/kg DW, were 98 in controls; 122–150 for the 5.6–32 µg/L groups, and >196 for the high dose groups	71
17 µg/L for 96 h	LC50 at pH 6.0–6.5, adults	61
31 (28–35) µg/L for 10 days	LC50, juveniles	73
34 µg/L for 96 h	LC50; age 6–8 days	72
52 µg/L for 96 h	LC50; age 20–24 days	72
87 µg/L for 96 h	LC50 at pH 8.0–8.5	61

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Horseshoe crab, <i>Limulus polyphemus</i>		
Embryos		
2 mg Cu/L	LC50 (72 h), Sandy Hook Bay, New Jersey	171
171 mg Cu/L	LC50(72 h), Delaware Bay, Delaware	171
Larvae, Sandy Hook		
100 mg Cu/L	Normal survival and molting	171
637 mg Cu/L	LC50 (72h)	171
Freshwater prawn, <i>Macrobrachium rosenbergii</i> ; 12 µg/L for 96 h	LC50	74
Freshwater prawn, <i>Macrobrachium rude</i> ; 18–65 µg/L for 96 h	LC50–LC84	63, 75
Macroinvertebrate communities; 11.3 µg/L for 10 days	Abundance was reduced by 75% in laboratory studies vs. 44% in field experimental streams; number of taxa was reduced 56% in the laboratory vs. 10% in field streams	76
Peneid Shrimp, <i>Metapenaeus ensis</i>		
160 µg/L for 48 h	LC50 for larvae	77
250 µg/L for 2 h	Feeding inhibited >50%	77
4760 µg/L for 48 h	LC50 for postlarvae	77
Cladoceran, <i>Moina irrasa</i>		
1.4 µg/L for 24 h	LC50 at pH 5.0, 30°C	78
2.8 µg/L for 24 h	LC50 at pH 6.5, 30°C	78
3.3 µg/L for 96 h	LC50 at pH 5.0, 20°C	78
5.5 µg/L for 48 h	LC50 at pH 5.0, 25°C	78
6.5 µg/L for 96 h	LC50 at pH 6.5, 20°C	78
7.5 µg/L for 96 h	LC50 at pH 8.0, 20°C	78
11.8 µg/L for 48 h	LC50 at pH 8, 25°C	78
19.7 µg/L for 24 h	LC50 at pH 8, 20°C	78
Mysid shrimp, <i>Mysidopsis bahia</i> ; 38–77 µg/L	MATC ^b	1
Norway lobster, <i>Nephrops norvegicus</i>		
10 µg/L for 30 days; 4.9 cm in length	Copper concentrations were elevated in most tissues, especially ovary (to 393 from 115 mg/kg DW), but not hepatopancreas or external eggs	79
100 µg/L for 14 days	LC100	79
Crab, <i>Paragrapuspus quadridentatus</i>		
110–250 µg/L for 96 h	LC16–LC84 for larvae	80
170 µg/L for 96 h	LC50 for larvae	80
Freshwater shrimp, <i>Paratya australiensis</i>		
15 µg/L, continuous exposure	Mean molt period of 23 days (range 20–27 days) vs. 25 days (18–36 days) for controls	81
40 µg/L for 96 h	LC50	81
Amphipod <i>Parhallella natalensis</i> ; 72 µg/L for 48 h	LC50	82
Crayfish, <i>Procambarus clarkii</i>		
120 µg/L for 20 days	LC50 for larvae	83
1300 µg/L for 20 days	LC50 for adults; increased copper concentrations at >480 µg/L in gills but not other tissues	83
3700 µg/L for 20 days	LC50 for embryos	83
Copepod, <i>Pseudodiaptomus coronatus</i> ; 138 µg/L for 96 h	LC50	1
Barnacle, <i>Semibalanus balanoides</i> ; 20–90 µg/L for 100 days	Dose-dependent increase in copper loadings in bodies and egg masses	84
Copepod, <i>Tigriopus japonicus</i> ; 487 µg/L for 96 h	LC50	1
Copepod, <i>Tisbe furcata</i> ; 37–57 µg/L	MATC ^b	85

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
AQUATIC INSECTS		
Midge, <i>Chironomus ninevah</i> ; 0, 20, 100, 150, or 200 µg/L for 21 days (eggs through fourth stage larvae)	Statistically significant, dose-dependent decrease in gene activity of salivary gland chromosomes at 20 µg/L and higher	86
Midge, <i>Chironomus</i> sp.; 30 µg/L for 96 h	LC50 at 50 mg CaCO ₃ /L	1
Midge, <i>Tanytarsus dissimilis</i> ; 16.3 µg/L for 10 days	LC50	1
Various species; 25 µg/L for 10 days in outdoor experimental streams	Mayflies were the most sensitive group with 67–100% reduction in numbers; chironomids had 80% reduction, and caddisflies were reduced by 16–30%	87
ANNELIDS		
Lugworm, <i>Arenicola marina</i> ; held on copper-contaminated sediments		
182–204 mg Cu/kg DW sediment	Inhibitory effects on digestive processes	172
1113 mg Cu/kg DW sediment	Lethal in 48 h	172
Ragworm, <i>Hediste diversicolor</i>		
5, 10, or 20 µg/L at four salinities and three temperatures; 1-day-old larvae	20 µg/L caused high mortality at all thermosaline regimens tested; some adverse effects noted at lower concentrations	88
247–513 µg/L for 96 h; no sediments in assay containers	LC50s at various thermosaline regimens	89
3200–4100 µg/L for 96 h; sediments present in assay containers	LC50s at various thermosaline regimens	89
Oligochaete, <i>Lumbriculus variegatus</i>		
130 µg/L for 96 h	LC50 at pH 6.0–6.5	61
500 µg/L for 96 h	LC50 at pH 8.0–8.5	61
Marine worm, <i>Nereis diversicolor</i> ; 500 µg/L at three salinities and three temperatures	Mortality was greatest at 5‰ salinity (50% dead in 44 h vs. 66–82 h at higher salinities), and at 20°C (50% dead in 32 h vs. 88–106 h at lower temperatures)	90
ECHINODERMS		
Echinoid, <i>Echinometra mathaei</i> ; 20 µg/L for 4 days	Skeletal development of larvae suppressed	1
Sea urchin, <i>Paracentrotus lividus</i> ; 10–20 µg/L for 4 days	Pluteal growth retarded	1
Sea urchin, <i>Strongylocentrotus nudus</i> ; adults held in seawater containing 25 µg Cu/L for 30 days; resultant embryos reared in uncontaminated seawater for 30 days	Food consumption of adults decreased after day 16; accelerated development of pluteal stages; all developmental stages had increased activities of acid phosphatase	91
FISH		
Topsmelt, <i>Atherinops affinis</i>		
53 µg/L for 15 min; sperm	No effect on fertilization in 48 h	92
100 µg/L for 7 days; larvae, age 5–20 days	No effect	93
109 µg/L for 15 min; sperm	Egg fertilization reduced 50% in 48 h	92
123 µg/L for 96 h; larvae	No deaths	92
137 µg/L for 7 days; larvae, age 7–20 days	LC50	93
146 µg/L for 48 h; embryos	50% abnormal development	92
180 µg/L for 7 days; larvae, age 1–3 days	No deaths	93
238 µg/L for 96 h; larvae	LC50	92
365 µg/L for 7 days; larvae, age 0–5 days	LC50	93

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Zebrafish, <i>Brachydanio rerio</i>		
0.05 µg/L for 16 days; eggs and larvae	Delayed hatch	94
0.25 µg/L for 16 days; eggs and larvae	No deaths	94
1.0 µg/L for 16 days; eggs	<50% hatched	94
1.0 µg/L; adults	No avoidance but inhibition of attraction response to L-alanine	95
50–150 µg/L for 7 days; adults	No adverse effects on survival or behavior; dose-dependent decrease in kidney leukocyte numbers and phagocytic response	96
Goldfish, <i>Carassius auratus</i>		
36 µg/L for 96 h	LC50 at 20 mg CaCO ₃ /L	1
300 µg/L for 96 h	LC50 at 52 mg CaCO ₃ /L	1
368 µg/L for 96 h	LC50 at 272 mg CaCO ₃ /L	97
White sucker, <i>Catostomus commersoni</i> ; 12.9–33.8 µg/L	MATC ^b at 45 mg CaCO ₃ /L	1
Murrel, <i>Channa punctatus</i> ; 50 or 100 µg/L for 7 days	Liver pathology	98
Catfish, <i>Clarias</i> sp.		
27, 55, or 110 µg/L for 8 weeks; whole fish analyzed for total copper at end of exposure	Copper concentrations, in mg/kg DW, were 15.7 for the low-dose group, 21.8 for the 55 µg/L group, and 31.2 for the high-dose group vs. 6.9 DW in controls	99
425 µg/L for 96 h	LC50; nonresistant strain	99
4301 µg/L for 96 h	LC50; copper-resistant strain	100
African sharp-tooth catfish, <i>Clarias gariepinus</i> ; Olifants River (water of 32–55 µg Cu/L), South Africa		
767–991 µg/L for 96 h	10–20% dead	101
1240–1380 µg/L for 96 h; adults and juveniles	LC50 at 21–28°C	101
Pacific herring, <i>Clupea harengus pallasi</i> ; 33 µg/L for 6 days; embryos	LC50	1
Common carp, <i>Cyprinus carpio</i> ; 100 µg/L for 43 days	Skin histopathology	102
Northern pike, <i>Esox lucius</i> ; 34.9–104.4 µg/L	MATC ^b at 45 mg CaCO ₃ /L	1
Freshwater fishes; eight species; embryos and larvae; 31.7–43.5 µg/L for 30–60 days	Reduced survival	103
Mummichog, <i>Fundulus heteroclitus</i>		
1000 µg/L for 96 h	Renal and lateral line canal lesions	104
1700–8000 µg/L for 96 h	LC30–LC50	104, 105
Indian catfish, <i>Heteropneustes fossilis</i>		
250 µg/L; 5 h daily for 30 days	Time-dependent increase in adverse effects on blood chemistry, liver metabolism, and respiration	106
5000 µg/L for 48–96 h	After 48 h, decreased hematocrit, erythrocyte number, and hemoglobin; after 96 h, increased liver glycogen	107, 108
10,500–25,500 µg/L for 72–96 h	LC50	107, 108
Brown bullhead, <i>Ictalurus nebulosus</i>		
4, 8, 16, 32, 64, or 104 µg/L for as long as 600 days; blood chemistry analyzed periodically	Some deaths at 104 µg/L; no deaths at lower doses; no adverse biochemical effects at 16 µg/L and lower	109
4 to 512 µg/L for as long as 20 months	Increases in liver and gill copper concentrations in survivors at 275 µg/L and higher; equilibrium reached within 30 days. Copper levels in blood were the same as in controls	110
170 to 190 µg/L for 96 h; juveniles	LC50	110

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Channel catfish, <i>Ictalurus punctatus</i> ; fingerlings Exposed for 96 h at 16 mg CaCO ₃ /L 51–65 µg/L 54–55 µg/L	LC50; chelated copper LC50; nonchelated copper	111 111
Exposed for 96 h at 239 mg CaCO ₃ /L 925–1041 µg/L 1603–1878 µg/L	LC50; nonchelated copper LC50; chelated copper	111 111
Spot, <i>Lepostomus xanthurus</i> ; 280 (240–330) µg/L for 96 h; adults	LC50	112
Green sunfish, <i>Lepomis cyanellus</i> ; 937 (686–1281) µg/L for 96 h	LC50	97
Bluegill, <i>Lepomis macrochirus</i> 21–40 µg/L 31 µg/L 40–162 µg/L for 90 days; larvae 40–162 µg/L for 24 months; adults	MATC ^b at 45 mg CaCO ₃ /L Consumed 27% fewer prey than controls Reduced survival At 162 µg/L, survival was reduced, growth retarded, and spawning inhibited. Maximum copper concentrations, in mg/kg FW, in treated fish (vs. controls) were 13 in gills (3), 480 in liver (7), and 44 in kidneys (22)	1, 114 113 114 114
236–892 µg/L for 96 h; adults 261 µg/L for 7 days, then subjected to a drop in dissolved oxygen over 60 min from 7.8 to 1.3 mg/L and then allowed to recover in copper-free aerated water	LC50 No deaths during copper exposure. During hypoxia; 2 of 77 died; survivors had hyperglycemia, lower plasma sodium, lower liver ATP, and higher plasma potassium than did nonexposed controls. Authors concluded that previous copper exposure causes some hypoxia responses to be accentuated in an additive manner	97, 115, 173 115
1100 µg/L for 96 h; larvae 4300 µg/L for 48 h	LC50 LC50	114 116
Atlantic silverside, <i>Menidia menidia</i> ; 136 µg/L for 96 h; larvae	LC50	1
Tidewater silverside, <i>Menidia peninsulae</i> ; 140 (110–180) µg/L for 96 h; larvae	LC50	112
Striped bass, <i>Morone saxatilis</i> 50–100 µg/L for 96 h; larvae 150 µg/L for 96 h; fingerlings 2680 µg/L for 96 h; fingerlings; 5‰ salinity 7880–8080 µg/L for 96 h; fingerlings; 10–15‰ salinity	LC50 at 68 mg CaCO ₃ /L LC50 at 68 mg CaCO ₃ /L LC50 LC50	1 1 117 117
Cutthroat trout, <i>Oncorhynchus clarkii</i> 37 µg/L for 96 h 232 µg/L for 96 h	LC50 at 18 mg CaCO ₃ /L LC50 at 204 mg CaCO ₃ /L	1 1
Coho salmon, <i>Oncorhynchus kisutch</i> 0, 15, 60, or 90 µg/L for 170 h; yearlings	No deaths; distress noted at 60 and 90 µg/L. Dose-dependent elevation in serum cortisol. When challenged with seawater, copper-exposed salmon had lowered survival and dose-dependent depression in serum chloride levels	118
5–30 µg/L for as long as 172 days; yearlings	Altered downstream migration patterns, lowered gill ATPase activity, and reduced survival. When subjected to >20 µg/L, appetite was depressed for several weeks to months	119
15.1–31.9 µg/L for 96 h; juveniles	LC50	120

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
18.2 µg/L for 31 days then challenged with seawater	Reduced survival during adaptation to seawater	121
24.6 µg/L for 31 days; fingerlings	Reduced survival; survivors unable to adapt to seawater	121
26 µg/L for 96 h; alevins	LC50 at 25 mg CaCO ₃ /L	1
46 µg/L for 96 h; adults	LC50 at 20 mg CaCO ₃ /L	1
60 µg/L for 96 h; smolts	LC50 at 95 mg CaCO ₃ /L	1
60–74 µg/L for 96 h; yearlings	LC50 at 95 mg CaCO ₃ /L	1, 119
70 or 140 µg/L for 14 weeks; fingerlings	Loss of appetite and reduced growth. Copper concentrations, in mg/kg DW, at end of study for the controls, the 70 µg/L group, and the 140 µg/L group were 2.9, 5.6, and 9.8 in gills, and 5.7, 6.1, and 7.5 in kidneys	122
70 or 140 µg/L for 14 weeks; liver cytosol samples from fingerlings	Copper concentrations in the low-molecular-weight fractions of the 70 µg/L group were higher than controls after 6 weeks and increased rapidly; those of the 140 µg/L group increased in the first 2–4 weeks then leveled off. Increasing levels of metallothioneins were detected in low-molecular-weight fractions of copper-exposed salmon. In the high-molecular-weight fractions, copper concentrations in both groups increased after 8–10 weeks	123
140 or 210 µg/L for 78 h; yearlings	Median survival times were 60 h for the low-dose group and 48 h for the high-dose group; survivors had elevated serum cortisol. Livers were normal but kidney and gill histopathology was evident in both groups	118
220–280 µg/L for 168 h; fingerlings	LC50	122
310 µg/L for 168 h; prior exposure to 70 µg/L for 16 weeks; fingerlings	LC50	122
550 µg/L for 168 h; prior exposure to 140 µg/L for 16 weeks; fingerlings	LC50	122
Rainbow trout, <i>Oncorhynchus mykiss</i>		
0.1 µg/L for 1 h	Avoidance by fry	1
Yearlings exposed to 6.4, 16, or 26.9 µg Cu/L for up to 21 days	Adverse effects on survival during first 48 h and decrease in respiratory burst activity at all concentrations tested. At high dose, percentage of monocytes increased and lymphocyte percent decreased	168
7.0 µg/L for 200 h; smolts	LC10	1
8.0 µg/L for 2 h	Depressed olfactory bulbar electrical responses to the standard stimulant L-serine	124
9.0 µg/L for 200 h; swimup stage	LC10	1
11.4–31.7 µg/L	MATC ^b at 45 mg CaCO ₃ /L	1
13.8 µg/L for 96 h; juveniles	LC50	120
19.0 µg/L for 200 h; alevins	LC10	1
20–30 µg/L for 96 h	LC50 at 30–32 mg CaCO ₃ /L	1
21.5 µg/L for 30 days; juveniles	No adverse effects; no altered susceptibility to <i>Aeromonas hydrophila</i> infections	125
22 µg/L for 37 to 41 weeks; two groups: age 14 days postfertilization and posthatch. Controls were held in water containing 4 µg/L	Survival of embryo group reduced 30%. Alterations in cell architecture in both treated groups were noted as early as week 8 posthatch. Both groups had	126, 127

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
36 µg/L for 96 h; alevins	irreversible histopathology of the olfactory organ after 7 months; no histopathology in controls. After 8 months, controls preferred their own rearing water but both copper-exposed groups showed no preference; some recovery 2 to 10 weeks after removal from copper	120
50 µg/L for 24 h; adults	LC50 No deaths; some degeneration of sensory receptors	128
50 µg/L for 21 days; juveniles	Rapid and sustained elevation of plasma cortisol levels; altered plasma cholesterol and sodium levels	129
55 µg/L for 28 days; juveniles	Initial inhibition of sodium uptake and whole body sodium content that were normal by day 28. Abnormal liver enzyme activity. Liver copper increased from 23 mg/kg FW at start to 113 mg/kg FW at day 28	164, 165
70 µg/L	Avoidance by juveniles	166
70–514 µg/L for 96 h	LC50 at 194–370 mg CaCO ₃ /L	1
75 µg/L for 24 h	LC50; survivors had complete degeneration of olfactory receptors	128
90 (50–150) µg/L; embryo through posthatch	LC50 at 28 days	162
130–140 µg/L for 24 h	LC50 at pH 6.5–pH 7.5	130
308 µg/L for 24 h in freshwater vs. 400 µg/L for 24 h in 35‰ seawater	All dead in freshwater vs. no deaths in seawater and no major changes in plasma Na ⁺ , Cl ⁻ , K ⁺ , or Ca ²⁺	131
500 or 1000 µg/L for 2 or 24 h; fingerlings	Gill histopathology in low-dose, low-exposure group; damage more severe with increasing dose and exposure	131
500 µg/L for 9 days; weight 400 g; under conditions of normal and low dissolved oxygen	No signs of respiratory dysfunction; no difference in copper uptake due to dissolved oxygen levels	133
1200 µg/L for 6 h	LC50	130
4560 µg/L	Juveniles attracted	166
Fed diet containing 13 or 684 mg/kg ration for 42 days and simultaneously exposed to waterborne-copper concentrations of 5, 32, 55, or 106 µg/L (low-copper diet) or 13, 38, 62, or 127 µg/L (high-copper diet)	No adverse effects on growth, survival, or food conversion efficiency. Elevated dietary copper increased copper concentrations in liver, kidney, gill, and digesta; increasing waterborne-copper concentrations produced increasing copper concentrations in liver and kidney. For fish in the high-copper diet, the diet provided 99% of the liver copper in the 38 µg/L group, 85% in the 62 µg/L group, and 73% in the 127 µg/L group	134
Fed diets containing 25.8 mg/kg DW ration (vs. 15.8 mg/kg DW in controls) for 28 days; equivalent to 69.2 mg/kg fish (130 g) daily	Fish readily ate copper-contaminated food. Elevated copper levels in gill, liver, and muscle. Some food regurgitation on days 20–28	135
Juveniles fed diet containing 200 mg/kg DW for 32 days followed by normal (15.8 mg/kg DW) diet for 12 days	No deaths. After 32 days whole fish contained 1.5 mg/kg FW vs. 1.2 at start; copper concentrations were elevated in gill, gut, blood, skin, and mucus, but not in muscle, liver, or kidney. Copper concentrations in gill and kidney tissues were elevated 12 days after exposure, but other tissues were normal	136

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Single intravenous injection of 80 µg/kg BW; juveniles, 100–300 g in body weight	Half-time persistence in plasma was 7.2 min for the short-lived component and 3.2 h for the long-lived component. Plasma copper concentration fell from 1.1 mg/L shortly after administration to about 200 µg/L after 7.5 h	137
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
10–38 µg/L for 96 h	LC50 in soft water	1
19 µg/L for 200 h; swimup stage	LC50	1
20 µg/L for 200 h; alevins	LC50	1
26 µg/L for 200 h; smolts	LC50	1
30 µg/L for 200 h; parr	LC50	1
54–60 µg/L for 96 h; fry	LC50	138
78–145 µg/L for 24 h; fry	LC50	138
85–130 µg/L for 96 h	LC50 in hardwater	1
Green snakehead, <i>Ophiocephalus punctatus</i> ; weight 15–18 g		
5000–7500 µg/L for 24 h	Sublethal. Disrupted kidney and liver alkaline phosphatase and acid phosphatase activity	139
70,000 µg/L for 48 h	LC50	139
Nile tilapia, <i>Oreochromis niloticus</i>		
50, 100, or 200 µg/L for 8 weeks	At end of exposure, whole fish contained 34.7 and 36.1 mg/kg DW in the two lowest-dose groups and 81.0 mg/kg DW in the high-dose group (vs. 17.4 mg/kg DW in controls)	140
964 µg/L for 96 h	LC50	140
Summer flounder, <i>Paralichthys dentatus</i> ; embryos; 28 µg/L for 96 h	LC50	1
Flounder, <i>Paralichthys</i> spp.; juveniles		
6.4 µg/L for 14 days	Interference with calcium metabolism	157
448 µg/L for 14 days	LC50	157
Fathead minnow, <i>Pimephales promelas</i>		
2 µg/L for 96 h; larvae	LC50 at pH 5.6 and dissolved organic carbon (DOC) of 0.2 mg/L	141
10.6–18.4 µg/L	MATC ^b at 30 mg CaCO ₃ /L	142
14.5–33.0 µg/L	MATC ^b at 200 mg CaCO ₃ /L	142
15 µg/L for 96 h	LC50 at pH 6.6.5	143
23 µg/L for 96 h	LC50 at 20 mg CaCO ₃ /L	1
44 µg/L for 96 h	LC50 at pH 7.0–7.5	143
75–84 µg/L for 96 h	LC50 in soft water; continuous flow and static assays	142
182 µg/L for 96 h	LC50 at pH 6.9 and dissolved organic carbon of 15.6 mg/L	141
>200 µg/L for 96 h	LC50 at pH 8.0–8.5	143
210 µg/L for 96 h	LC50 at 100 mg CaCO ₃ /L	163
390 µg/L for 96 h	LC50 at 250 mg Ca/CO ₃ /L	163
430–470 µg/L for 96 h	LC50 in hard water; continuous flow and static assays	142
European flounder, <i>Platichthys flesus</i>		
Seawater-adapted; exposure for 42 days; experimentals (170 µg/L) vs. controls (3 µg/L; values in mg/kg DW tissue		
Gill	7.7 vs. 2.7	167
Kidney	13.1 vs. 4.1	167
Liver	640.2 vs. 15.6	167
Muscle	7.7 vs. 2.7	167

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Freshwater-adapted; exposure for 37 days; experimentals (15 µg/L) vs. controls (5 µg/L); values in mg/kg DW tissue		
Gill	16.2 vs. 6.5	167
Kidney	28.7 vs. 14.3	167
Liver	295.6 vs. 157.8	167
Muscle	4.9 vs. 1.8	167
Guppy, <i>Poecilia reticulata</i>		
36 µg/L for 96 h	LC50 at 20 mg CaCO ₃ /L	1
112–138 µg/L for 96 h	LC50 at 67–82 mg CaCO ₃ /L	1
Winter flounder, <i>Pleuronectes americanus</i>		
129 µg/L for 96 h; embryos	LC50	1
180 µg/L for 29.1 days; adults	Gill histopathology	144
560–3200 µg/L for 29.2 days; adults	Copper-induced histopathology of kidney, liver, and gill; reduced food intake	144
Mangrove rivulus, <i>Rivulus marmoratus</i> ; 1400 µg/L for 96 h	LC50	145
Air-breathing catfish, <i>Saccobranchus fossilis</i> ; 56, 100, or 320 µg/L for 28 days	Dose-dependent decrease in red and white blood cell numbers, hemoglobin, and hematocrit; histopathology in gill, skin, spleen, and kidney	146
Atlantic salmon, <i>Salmo salar</i>		
2.4 µg/L	Avoidance threshold in laboratory	147
12.8–621.0 µg/L	Dose-dependent inhibition of olfactory response; toxic effect mainly on transduction mechanisms of the olfactory receptor cells	148
16.9–20.6 µg/L	Avoidance threshold in field	147
32–125 µg/L for 96 h	LC50 at 8–20 mg CaCO ₃ /L	1, 147
Brown trout, <i>Salmo trutta</i>		
22.0–43.2 µg/L	MATC ^b at 45 mg CaCO ₃ /L	1
103–148 (91–165) µg/L	LC50 at 48 h, juveniles	159
Brook trout, <i>Salvelinus fontinalis</i>		
2.7 (control), 4.5, 6.1, or 9.4 µg/L for two generations	No adverse effects on growth, survival, or reproduction; no elevated copper concentrations in gill, liver, kidney, muscle, or eggs	152
3.4, 5.7, 9.5, 17.4, or 32.5 µg/L for 337 days	No significant changes in blood chemistry except for measurable decrease in plasma glutamic oxalacetic transaminase activity at 17.4 and 32.5 µg/L	149
6–15 µg/L for 2–24 h; yearlings	Increased cough frequency, increased locomotor activity, and decreased feeding response	150
9.5–17.4 µg/L	MATC ^b at 45 mg CaCO ₃ /L and pH 7.5	151
23, 39, or 68 µg/L for 6 or 21 days	At 39 and 68 µg/L, adverse effects on blood chemistry; decreases in plasma chloride and osmolarity	149
100 µg/L for 96 h; age 14 months	LC50	151
Lake trout, <i>Salvelinus namaycush</i> ; 22.0–42.3 µg/L	MATC ^b at 45 mg CaCO ₃ /L	92
Red drum, <i>Sciaenops ocellatus</i>		
250 µg/L for 96 h; juveniles	No deaths	153
520 µg/L for 96 h; juveniles	LC50 at 25°C and 8‰ salinity	153
Pearl dace, <i>Semotilus marginata</i> ; 1000–279,000 µg/L for as long as 7 h then transferred to clean water for 48 h	Decreasing survival and coordination with increasing concentration or duration of exposure after exposure to 1000 µg/L for 6 h, 9000 µg/L for 1 h, 74,000 µg/L for 0.33 h, or 279,000 µg/L for 0.25 h	154
Walleye, <i>Stizostedion vitreum</i> ; 13–21 µg/L	MATC ^b at 35 mg CaCO ₃ /L	1

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

Taxonomic Group, Organism, Copper Concentration, and Other Variables	Effects	Reference ^a
Florida pompano, <i>Trachinotus carolinus</i> ; 360–510 µg/L for 96 h	LC50	1
Arctic grayling, <i>Thymallus arcticus</i>		
2.65 µg/L for 96 h; swimup fry	LC50	120
9.6 µg/L for 96 h; fry	LC50	120
23–131 µg/L for 96 h; alevins	LC50	120
AMPHIBIANS		
Marbled salamander, <i>Ambystoma opacum</i> ; 50 µg/L for 96 h; embryos	97% survival 4 days posthatch	155
American toad, <i>Bufo americanus</i> ; tadpoles		
10 µg/L	Avoidance	166
930 µg/L	Attraction	166
Fowler's toad, <i>Bufo fowleri</i> ; 2696 µg/L for 7 days; embryos	LC50	155
Two-lined salamander, <i>Eurycea bislineata</i> ; 1120 µg/L for 48 h; juveniles	LC50	156
Narrow-mouthed toad, <i>Gastrophryne carolinensis</i>		
10 µg/L for 4 days; embryos	34% dead 4 days after hatching	155
40 (30–50) µg/L; embryos through posthatch	LC50 (7 days)	162
50 µg/L for 72 h; embryos	LC50	155
Southern gray treefrog, <i>Hyla chrysoscelis</i>		
10 µg/L for 96h; embryos	39% dead 4 days after hatching	155
40 µg/L for 7 days; embryos	LC50	155
60 µg/L for 72 h; embryos	LC50	155
Northern leopard frog, <i>Rana pipiens</i>		
10 µg/L for 96h; embryos	34% dead 4 days after hatching	155
50 µg/L for 8 days; embryos	LC50	155

^a 1, USEPA 1980; 2, Bartley 1967; 3, Visviki and Rachlin 1994a; 4, Winner and Owen 1991; 5, Schafer et al. 1994; 6, Visviki and Rachlen 1994b; 7, Abalde et al. 1995; 8, Coppellotti 1989; 9, Ahsanullah and Williams 1991; 10, Stokes 1979; 11, Piccinni and Copellotti 1982; 12, Mersch et al. 1993; 13, Harland and Ngarno 1990; 14, Janssen et al. 1994; 15, Ferrando et al. 1993; 16, Ferrando and Andreu 1993; 17, Porta and Ronco 1993; 18, Williams and Dusenberry 1990; 19, Huebner and Pynnonen 1992; 20, Jacobson et al. 1993; 21, Cheng 1979; 22, Ebele et al. 1990; 23, Betzer and Yevich 1975; 24, Arthur and Leonard 1970; 25, Belanger et al. 1990; 26, Zarroogian 1979; 27, Okazaki 1976; 28, Coglianese and Martin 1981; 29, Mathew and Menon 1993; 30, Kraak et al. 1992; 31, Kraak et al. 1994; 32, Hameed and Raj 1989; 33, Raj and Hameed 1991; 34, Bordin et al. 1994; 35, Roper and Hickey 1994; 36, Zarroogian et al. 1992; 37, Chelomin and Belcheva 1992; 38, Eisler 1977; 39, Sanders et al. 1991; 40, Calabrese et al. 1984; 41, Sanders et al. 1994; 42, Stromgren and Nielsen 1991; 43, Hole et al. 1993; 44, Gainey and Kenyon 1990; 45, MacKenzie 1961; 46, Viarengo et al. 1981; 47, Viarengo et al. 1990; 48, Davies 1992; 49, Krishnakumar et al. 1990; 50, Winger et al. 1984; 51, Paulij et al. 1990; 52, Mule and Lomte 1994; 53, Soria-Dengg and Ochavillo 1990; 54, Suresh and Mohandas 1993; 55, Jacobson et al. 1993; 56, Koivisto et al. 1992; 57, Neff and Anderson 1977; 58, Zia and Alikhan 1989; 59, Nonnotte et al. 1993; 60, Scott-Fordsmand and Depledge 1993; 61, Schubauer-Berigan et al. 1993; 62, Ericksson and Weeks 1994; 63, Mukhopadhyay et al. 1994; 64, Enserink et al. 1991; 65, Lazorchak and Waller 1993; 66, Roux et al. 1993; 67, Ingersoll and Winner 1982; 68, Dobbs et al. 1994; 69, Maund et al. 1992; 70, Martin et al. 1989; 71, Borgmann et al. 1993; 72, Collyard et al. 1994; 73, West et al. 1993; 74, Natarajan et al. 1992; 75, Vijayaraman and Geraldine 1992; 76, Clements et al. 1990; 77, Wong et al. 1993; 78, Zou and Bu 1994; 79, Canli and Furness 1993; 80, Ahsanullah and Arnott 1978; 81, Daly et al. 1992; 82, Bhat and Vamsee 1993; 83, Rice and Harrison 1983; 84, Powell and White 1990; 85, Bechmann 1994; 86, Aziz et al. 1991; 87, Clements et al. 1992; 88, Ozoh and Jones 1990; 89, Ozoh 1992a; 90, Fernandez and Jones 1990; 91, Durkina and Evtushenko 1991; 92, Anderson et al. 1991; 93, McNulty et al. 1994; 94, Dave and Xiu 1991; 95, Steele et al. 1990; 96, Rougier et al. 1994; 97, Johnson and Finley 1980; 98, Khangarot 1992; 99, Daramola and Oladimeji 1989; 100, Ebele et al. 1990; 101, van der Merwe et al. 1993; 102, Iger et al. 1994; 103, McKim et al. 1978; 104, Eisler and Gardner 1973; 105, Lin and Dunson 1993; 106, Singh and Reddy 1990; 107, Banerjee and Homechaudhuri 1990; 108, Srivastava 1982; 109, Christensen et al. 1972; 110, Brungs et al. 1973; 111, Straus and Tucker 1993; 112, Mayer 1987; 113, Sandheinrich and Atchison 1989; 114, Benoit 1975; 115, Heath 1991; 116, Dobbs et al. 1994; 117, Reardon and Harrell 1990; 118, Schreck and Lorz 1978; 119, Lorz and McPherson 1977; 120, Buhl and Hamilton 1990; 121, Stevens 1977; 122, Buckley et al. 1982; 123, McCarter et al. 1982; 124, Hara et al. 1977; 125, Snarski 1992; 126, Saucier et al. 1991a; 127, Saucier et al. 1991b; 128, Klima and Applehans

Table 3.5 (continued) Effects of Copper on Representative Aquatic Plants and Animals

1990; **129**, Munoz et al. 1991; **130**, Shaw and Brown 1974; **131**, Wilson and Taylor 1993; **132**, Kirk and Lewis 1993; **133**, Pilgaard et al. 1994; **134**, Miller et al. 1993; **135**, Handy 1993; **136**, Handy 1992; **137**, Carbonell and Tarazona 1994; **138**, Hamilton and Buhl 1990; **139**, Srivastava and Pandey 1982; **140**, Daramola and Oladimeji 1989; **141**, Welsh et al. 1993; **142**, Mount and Stephan 1969; **143**, Schubauer-Berigan et al. 1993; **144**, Baker 1969; **145**, Lin and Dunson 1993; **146**, Khangarot and Tripathi 1991; **147**, Sprague et al. 1965; **148**, Winberg et al. 1992; **149**, McKim et al. 1970; **150**, Drummond et al. 1973; **151**, McKim and Benoit 1971; **152**, McKim and Benoit 1974; **153**, Peppard et al. 1991; **154**, Tsai 1979; **155**, Birge and Black 1979; **156**, Dobbs et al. 1994; **157**, Dodoo et al. 1992; **158**, Koivisto and Ketola 1995; **159**, Marr et al. 1995; **160**, Eisler 1995; **161**, Suresh et al. 1993; **162**, Birge 1978; **163**, Benson and Birge 1985; **164**, Lauren and McDonald 1987a; **165**, Lauren and McDonald 1987b; **166**, Birge et al. 1993; **167**, Stagg and Shuttleworth 1982; **168**, Dethloff and Bailey 1998; **169**, Janssens de Bisthoven et al. 1998; **170**, Coppelotti 1998; **171**, Botton et al. 1998; **172**, Chen and Mayer 1998; **173**, Soucek and Noblet 1998.

^b MATC = Maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Cnidarians

Sea anemones (*Anemonia viridis*) in seawater solutions containing 50 or 200 µg Cu/L regulate copper by expelling zooxanthellae, which are shown to accumulate copper (Harland and Nganro 1990).

Molluscs

Initial effects of copper on mussels (*Mytilus* spp.) include valve closure, a reduction in filtration rates, and cardiac inhibition; these responses all serve to slow the uptake of copper through a reduction in mussel contact with the ambient environment and a reduction in blood flow within the organism (Gaine and Kenyon 1990). Copper impairs the structure and function of cellular membranes in mussels by stimulating the peroxidation of membrane lipids. End products of lipid peroxidation contribute to the formation of lipofuscins (Viarengo et al. 1990). Copper-induced lysosomal lipofuscin accumulations, together with metallothioneins, control copper residues at the cellular levels and are responsible for the short half-time persistence (6 to 8 days) of copper in the digestive gland of mussels (Vairengo et al. 1990). Concentrations of heat shock protein (hsp60) in mantle tissues of mussels exposed to copper increased in a dose-dependent manner; hsp60 may have potential as a biomarker of copper insult (Sanders et al. 1991). Copper-stressed common mussels (*Mytilus edulis*) die more quickly under conditions of anoxia, high temperatures, and low salinities (Weber et al. 1992). Concentrations of copper that cause a decrease in yields of normal larvae in populations of *Mytilus edulis* from unpolluted or mildly contaminated sites did not affect embryonic development of mussels from polluted sites. Cross breeding of mussels from these sites suggests that copper tolerance in mussels is mostly maternally determined (Hoare et al. 1995a). Embryos of common mussels are more sensitive to copper than veliger larvae or postlarval spat stages (Hoare et al. 1995b). A copper-induced decrease in glochidial viability is a possible explanation for the disappearance of freshwater unionid mussels from acid- and metals-contaminated waters (Huebner and Pynnonen 1992). Hole et al. (1993) state that mussels of all ages are equally susceptible to copper and that their capacity to recover declines with increasing age; however, this phenomenon needs verification.

Bioconcentration factors for marine bivalves (ratio of milligrams of copper per kilogram fresh weight soft parts to milligrams of copper per liter of medium) vary from 85 to 28,200. Bioconcentration factors for copper are highest for American oysters after exposure for 140 days (20,700 to 28,200), and lowest for bay scallops (*Argopecten irradians*) after exposure for 112 days (3310) and for softshell clams after exposure for 35 days (3300; USEPA 1980). Copper is more toxic to embryos of the tropical giant clam (*Tridacna derasa*) than to embryos of bivalves from temperate regions (Soria-Dengg and Ochavillo 1990), possibly because many tropical species of shellfish live

near their upper lethal thermal limits and are unable to withstand additional environmental stressors. Juveniles of Asiatic clams (*Corbicula fluminea*) are more sensitive than adults to ionic copper (Belanger et al. 1990).

On exposure to lethal concentrations of copper the channeled whelk (*Busycon canaliculatum*), a marine gastropod, accumulates the metal in gill and osphradium. These tissues show progressive histopathology including swelling of the gill filaments, amoebocytic infiltration of the connective tissue, and necrosis and sloughing of the mucosa (Betzer and Yevich 1975). Copper-resistant strains of freshwater gastropods are found in media containing elevated concentrations of 35 µg Cu/L (Ebele et al. 1990), suggesting physiological or genetic adaptation. Fine suspensions of copper and kaolinite mixtures are more toxic to freshwater gastropods than copper alone. Toxicity is greater at pH 8 than at pH 7 (Al-Sabri et al. 1993). The authors conclude that copper is strongly adsorbed by kaolinite in alkaline media and that the acidic pH of the snail gut enhances release of ionic copper. In freshwater gastropods, ionic copper causes hypersynthesis of lysosomal enzymes and acid and alkaline phosphatases; immature gastropods are more sensitive than adults (Winger et al. 1984).

Arthropods

Life-cycle exposures of four species of *Daphnia* to graded concentrations of copper show reductions in survival at more than 40 µg/L and reductions in growth and reproduction at 40 to 60 µg/L; heavier and larger species are the most resistant to copper (Winner and Farrell 1976; Table 3.5). Starvation increases the sensitivity of most species of freshwater cladocerans to copper (Koivisto et al. 1992); however, there is no difference in LC50(48 h) values between fed and starved *Daphnia magna* (Lazorachak and Waller 1993). Bioavailability and toxicity of copper to *D. magna* and other tested arthropods are usually higher under conditions of increasing acidification, ionic copper, alkalinity, and temperature, or of decreasing dissolved organic carbon (Meador 1991; Taylor et al. 1994; Zou and Bu 1994). Mixtures of copper and other metals produce additive or more-than-additive effects in *D. magna* than would be expected on the basis of individual components (Enserink et al. 1991). The concept that chronic exposures to pulses of the LC50 concentrations of copper or cadmium causes no damage to freshwater organisms — provided that the average daily concentration never exceeds the no-observable-effect concentration — was tested in daphnids. The concept was true for cadmium but not copper, and the use of pulsed exposures for establishing water-quality criteria to protect aquatic life needs to be reexamined (Ingersoll and Winner 1982).

Copper uptake by aquatic arthropods occurs usually by way of the gut after eating or from the gills and other permeable surfaces in contact with the ambient medium (Weeks and Rainbow 1993). Copper accumulations by crustaceans are greatest at elevated (summer) temperatures and during molting (Powell and White 1990). A relatively high bioconcentration factor of 2000 is documented for copper and freshwater stoneflies (*Pteronarcys californica*; USEPA 1980), but the reasons for this phenomenon are unknown. The high tolerance to copper and other metals of mayfly larvae (*Baetis thermcius*), and high copper accumulations, is attributed, in part, to the selective induction of metal binding proteins in the gut (Sumi et al. 1991). Marine amphipods readily accumulate dissolved copper from seawater in a dose-dependent manner (Weeks and Rainbow 1991). But some species of talitrid amphipods are unable to meet their copper requirements from seawater alone and depend on dietary sources of copper (Weeks and Rainbow 1993). Mesocosm studies with freshwater zooplankton assemblages show that increasing copper concentrations in the range 0 to 50 µg/L cause a reduction in total zooplankton and changes in diversity. Within 4 days, copepods became dominant at the expense of cladocerans (Havens 1994).

Soldier crabs (*Mictyris longicarpus*) accumulate copper mostly from sediments rather than the water column (Weimin et al. 1994). The fine particles of sediment trapped as food contain bioavailable fractions of copper and other metals, and these significantly correlate with metal concentrations in the body of the crab. However, copper accumulations from sediments by soldier crabs

occurs only at an artificially high concentration (1900 mg Cu/kg DW sediment), which also had toxic effects. Soldier crabs seem unable to regulate copper within their body (Weimin et al. 1994).

In shore crabs, several days of exposure to sublethal concentrations of waterborne copper cause extensive damage to gill epithelium; at lethal concentrations, tissue hypoxia is probably the major effect of copper (Nonnotte et al. 1993). Starved shore crabs show a reduction in carapace copper concentrations and heavier midgut glands; starvation in combination with copper exposure (500 µg/L) results in an increase in copper in the carapace and a decrease in carapace calcium (Scott-Fordsmand and Depledge 1993). Shore crabs in seawater with high (10 mg/L) levels of waterborne copper show reductions in hemolymph sodium, gill sodium-potassium-ATPase activity, activities of various midgut gland enzymes (hexokinase, phosphofructokinase, pyruvate kinase), and hemolymph electrolytes (Hansen et al. 1992a, 1992b).

In the rusty crayfish (*Orconectes rusticus*), toxicity of copper at high concentrations is due to the coagulatory action on cellular proteins and to interference with respiratory processes; at low concentrations, copper causes degenerative changes in certain tissues and interferes with glutathione equilibrium (Hubschman 1967). Larvae of the red crayfish (*Procambarus clarkii*) exposed to copper as embryos are less sensitive than those exposed after hatching, suggesting acclimatization (Rice and Harrison 1983).

Annelids

Aquatic oligochaetes (*Lumbriculus variegatus*) do not accumulate significant amounts of copper when compared to controls after exposure for 30 days in sediments containing as much as 90.1 mg Cu/kg DW or in water containing as much as 2.3 µg Cu/L (Ankley et al. 1994). Adult lugworms (*Arenicola marina*) living in sediments containing 182 to 204 mg Cu/kg DW sediment had inhibited digestive processes; authors concluded that the digestive systems of lugworms, and perhaps other deposit feeders, are vulnerable to copper-contaminated sediments (Chen and Mayer 1998). Larvae of the sandworm (*Nereis diversicolor*) are more resistant to copper with increasing organism age and with increasing temperature and salinity of the medium (Ozoh and Jones 1990). In adult sandworms, whole-body loadings of copper usually increase with increasing temperature in the range of 12 to 22°C and with decreasing salinity in the range 0.7 to 3.1% (Ozoh 1992b). However, copper–temperature–salinity interactions are significant and complex in this species (Ozoh 1994).

Fishes

Adverse sublethal effects of copper on behavior, growth, migration, and metabolism occur in representative species of fishes at nominal water concentrations between 4 and 10 µg/L. In sensitive species of teleosts, copper adversely affects reproduction and survival from 10 to 20 µg Cu/L (Hodson et al. 1979; [Table 3.5](#)). Copper exerts a wide range of physiological effects in fishes, including increased metallothionein synthesis in hepatocytes, altered blood chemistry, and histopathology of gills and skin (Iger et al. 1994). At environmentally realistic concentrations, free copper:

- Adversely affects resistance of fishes to bacterial diseases
- Disrupts migration (that is, fishes avoid Cu-contaminated spawning grounds)
- Alters locomotion through hyperactivity
- Impairs respiration
- Disrupts osmoregulation through inhibition of gill Na⁺-K⁺-activated ATPase
- Is associated with tissue structure and pathology of kidneys, liver, gills, and other hematopoietic tissues
- Impacts mechanoreceptors of lateral line canals
- Impairs functions of olfactory organs and brain
- Is associated with changes in blood chemistry, enzyme activities, and corticosteroid metabolism (Hodson et al. 1979).

Copper-induced cellular changes or lesions occur in kidneys, lateral line, and livers of several species of marine fishes (Gardner and LaRoche 1973).

Copper-induced mortality in teleosts is reduced in waters with high concentrations of organic sequestering agents and in genetically resistant species (Hodson et al. 1979). At pH values less than 4.9 (that is, at pH values associated with increased aluminum solubility and toxicity), copper may contribute to the demise of acid-sensitive fishes (Hickie et al. 1993). Copper affects plasma Na^+ and gill phospholipid activity; these effects are modified by water temperature and hardness (Hansen et al. 1993). In red drum, copper toxicity is higher at comparatively elevated temperatures and reduced salinities (Peppard et al. 1991). Copper is acutely toxic to freshwater teleosts in soft water at concentrations between 10 and 20 $\mu\text{g/L}$ (NAS 1977). In rainbow trout, copper toxicity is markedly lower at high salinities (Wilson and Taylor 1993). Comparatively elevated temperatures and copper loadings in the medium cause locomotor disorientation of tested species (Kleerekoper 1973). Copper may affect reproductive success of fish through disruption of hatch coordination with food availability or through adverse effects on larval fishes (Ellenberger et al. 1994). Chronic exposure of representative species of teleosts to low concentrations (5 to 40 $\mu\text{g/L}$) of copper in water containing low concentrations of organic materials adversely affects survival, growth, and spawning; this range is 66 to 120 $\mu\text{g Cu/L}$ when test waters contain enriched loadings of organic materials (Hodson et al. 1979).

Larval and early juvenile stages of eight species of freshwater fishes are more sensitive to copper than embryos (McKim et al. 1978) or adults (Hodson et al. 1979). But larvae of topsmelt (*Atherinops affinis*) are increasingly sensitive to copper with increasing age. Topsmelt sensitivity is associated with increasing respiratory surface area and increasing cutaneous and branchial uptake of copper (McNulty et al. 1994).

Sublethal exposure of fishes to copper suppresses resistance to viral and bacterial pathogens (Rougier et al. 1994) and, in the case of the air-breathing catfish (*Saccobranchus fossilis*), affects humoral and cell-mediated immunity, the skin, and respiratory surfaces (Khangarot and Tripathi 1991). Rainbow trout exposed to 50 $\mu\text{g Cu/L}$ for 24 h — a sublethal concentration — show degeneration of olfactory receptors that may cause difficulties in olfactory-mediated behaviors such as migration (Klima and Applehans 1990). The primary site of sublethal copper toxicity in rainbow trout is the ion transport system of the gills (Hansen et al. 1993). In European sea bass (*Dicentrarchus labrax*), copper compromises the defense system of red blood cells against active forms of oxygen, leading to increased membrane lipid peroxidation (Roche and Boge 1993).

Dietary copper is more important than waterborne copper in reducing the survival and growth of rainbow trout larvae (Woodward et al. 1994). Simultaneous exposure of rainbow trout to dietary and waterborne copper results in significant copper assimilation. Diet is the main source of tissue copper; however, the contribution of waterborne Cu to tissue burdens increases as water concentrations rise (Miller et al. 1993).

Rate and extent of copper accumulations in fish tissues are extremely variable between species and are further modified by abiotic and biological variables. Copper accumulations in fish gills increase with increasing concentrations of free copper in solution, increasing dissolved organic carbon (DOC), and decreasing pH and alkalinity (Playle et al. 1993a, 1993b). Starved Mozambique tilapia accumulated significantly more copper from the medium in 96 h than did tilapia fed a diet containing 5.9 mg Cu/kg DW ration (Pelgrom et al. 1994). The bioconcentration factor for whole larvae of the fathead minnow was 290 after exposure for 30 h, but only 0.1 in muscle of bluegills after 660 h (USEPA 1980). Prior exposure of brown bullheads (*Ictalurus nebulosus*) to sublethal copper concentrations for 20 days before exposure to lethal copper concentrations produces higher copper concentrations in tissues of dead bullheads than in those not previously exposed; however, the use of tissue residues is not an acceptable autopsy procedure for copper (Brungs et al. 1973). Rising copper concentrations in blood plasma of catfish (*Heteropneustes fossilis*) seem to reflect copper stress, although the catfish appear outwardly normal. Plasma copper concentrations of catfish

increase from 290 µg Cu/L in controls at start to 380 µg Cu/L in survivors at 72 h (50% dead); a plasma copper concentration of 1060 µg Cu/L at 6 h is associated with 50% mortality (Banerjee and Homechaudhuri 1990). In rainbow trout, copper is rapidly eliminated from plasma; the half-time persistence is 7 min for the short-lived component and 196 min for the long-lived component (Carbonell and Tarazona 1994).

Attraction to waters containing low (11 to 17 µg/L) concentrations of copper occurs in several species of freshwater teleosts, including goldfish (*Carassius auratus*) and green sunfish (*Lepomis cyanellus*). However, other species, including white suckers (*Catostomus commersonii*), avoid these waters (Kleerekoper 1973). In avoidance/attraction tests, juvenile rainbow trout avoided waters containing 70 µg Cu/L but were significantly attracted to water containing 4560 µg Cu/L. A similar pattern was observed in tadpoles of the American toad, *Bufo americanus* (Birge et al. 1993). Copper concentrations in the range of 18 to 28 µg/L interfere with bluegill growth and prey choice (Sandheinrich and Atchison 1989). Copper interferes with the ability of fish to respond positively to L-alanine, an important constituent of prey odors; concentrations as low as 1 µg Cu/L inhibit this attraction response in some species (Steele et al. 1990).

Increased tolerance to copper was observed in fathead minnows after prolonged exposure to sublethal concentrations, but tolerance was not sustained on removal to clean water. Copper tolerance in fathead minnows is attributed to increased production of metallothioneins (Benson and Birge 1985). Copper tolerance in rainbow trout seems dependent on changes in sodium transport and permeability (Lauren and McDonald 1987a).

Integrated Studies

Bioconcentration and biomagnification of copper occurs in the food chain of diatom (*Skeletonema costatum*) to clam (*Donax cuneatus*) to prawn (*Penaeus indicus*). All species accumulate copper from the medium, and clams and shrimp from the diet. Maximum concentrations after exposure to 200 µg Cu/L and diets for 10 days, in mg Cu/kg FW, are 2.8 in whole diatoms, 13.6 in clam soft parts, and 33.9 in whole shrimp (Rao and Govindarajan 1992). In the marine food chain of phytoplankton to clam (*Tellina tenuis*) to juvenile plaice (*Pleuronectes platessa*), copper accumulates in a concentration-dependent manner in viscera of plaice. All organisms held in 10, 30, or 100 µg Cu/L solutions for 100 days had reduced growth. Copper concentrations, in mg Cu/kg DW at day 100, in soft parts of clams *T. tenuis* were 270 in the 10 µg/L group, 470 in the 30 µg/L group, and 1100 in the 100 µg/L group vs. less than 50 in the controls. For plaice viscera, these values were 30 in controls, 71 in the 10 µg/L group, 147 in the 30 µg/L group, and 467 mg/kg DW in the 100 µg/L group (Saward et al. 1975). Accumulations in Pacific oysters held in copper-loaded sediments are similar to those of oysters contaminated through ingestion of diatoms (*Haslea ostrearia*). However, accumulations are highest in Pacific oysters when exposed through the medium (Ettajani et al. 1992). In that study, a concentration of 30 µg Cu/L medium for 21 days resulted in copper concentrations of 137 mg/kg DW in diatoms and 1320 mg/kg DW in oyster soft parts. Oysters fed contaminated diatoms in the study had 419 mg Cu/kg DW soft parts. Oysters held in sediments containing 108 mg Cu/kg DW — a level reached after exposure for 21 days to 300 µg Cu/L — had 401 mg Cu/kg DW (Ettajani et al. 1992). Copper-induced changes in population density and community metabolism occur in an aquatic mesocosm of algae, protozoans, rotifers, oligochaetes, and bacteria; death of rotifers, algae, and oligochaetes occur at concentrations as low as 700 µg Cu/L. Adverse effects occur at 300 to 700 µg Cu/L but are negated by increasing concentrations of dissolved organic matter (Sugiura et al. 1982).

Transfer of copper from wood treated with chromated copper arsenate (CCA) occurs in estuarine algae (*Ulva*, *Enteromorpha*), American oysters, mud snails (*Nassarius obsoletus*), and fiddler crabs (*Uca* spp.; Weis and Weis 1992). Algae, barnacles, and mussels from CCA-treated lumber show elevated concentrations of copper when compared to reference sites. The epibiotic estuarine community that

forms on CCA-treated wood has lower species richness, diversity, and biomass when compared to untreated lumber (Weis et al. 1993b). Copper is trophically transferred from CCA-exposed American oysters to predatory gastropods (*Thais* sp.), resulting in reduced gastropod feeding and growth (Weis and Weis 1993).

3.7.4 Birds

No data are available on the toxicity of copper to avian wildlife. All studies with birds and copper use domestic chickens, ducks, or turkeys (Table 3.6). Copper, however, may indirectly affect avian wildlife by curtailing certain prey species. Winger et al. (1984), for example, show that apple snails (*Pomacea paludosa*) are not only extremely susceptible to copper (LC₅₀ of 24 to 57 µg/L in 96 h; immatures most sensitive), but are the primary food of the snail kite (*Rostrhamus sociabilis*), an endangered species. The decline of the apple snail in southern Florida coincided with the use of copper-diquat to control hydrilla aquatic weeds (*Hydrilla verticillata*), with serious implications for the snail kite (Winger et al. 1984).

In the domestic chicken, adverse effects of copper occur in chicks fed diets containing 350 mg Cu/kg ration for 25 days (reduced weight gain) and in adults given a dietary equivalent of more than 28 mg Cu/kg BW (Table 3.6). Chicks fed diets of 500 mg Cu/kg ration show damage to the gizzard lining; damage effects are attributed to the shedding of gizzard glandular cells into the keratin-like koilin layer, disrupting koilin production (Bremner 1979). Copper-induced gizzard histopathology in growing chicks is not reversed by zinc or Vitamins B₁₂ or E (Poupoulis and Jensen 1976). Supplementing chick diets with copper did not prove markedly advantageous (Poupoulis and Jensen 1976), provided that normal rations had about 4 mg Cu/kg and adequate iron (Carlton and Henderson 1964b). Unlike mammals, chicks fed copper-supplemented diets do not have elevated copper concentrations in liver or signs of liver damage (Bremner 1979). Broiler hens housed on slats made of lumber pressure-treated with chromated copper arsenate show severe foot-pad dermatitis and excessive mortality after 17 weeks. However, arsenic and cresylic acid — not copper — may be the responsible agents (Sander et al. 1994).

Ducklings (*Anas* spp.), unlike chicks, accumulate copper in livers when fed diets supplemented with high loadings of copper (Wood and Worden 1973). Domesticated mallards show a dose-time dependent increase in copper liver concentrations, with a maximum concentration of 254 mg Cu/kg DW liver (Table 3.6). Mallards seem to prefer drinking water containing 100 mg Cu/L over distilled water (Table 3.6); however, these birds were molting and this may have influenced their response because trace mineral requirements rise during molting (Rowe and Prince 1983).

In turkeys, natural diets with as much as 800 mg Cu/kg ration have no adverse effects on growth or survival. But purified diets are toxic to turkeys in three weeks, and purified diets that contain as little as 50 mg Cu/kg ration produce adverse effects (Waibel et al. 1964). Turkeys fed purified diets with supplemented copper show a dose-dependent increase in mortality and decrease in growth; these effects are attributed to a copper-accelerated dietary deterioration (Supplee 1964). Turkey growth and survival are acceptable when fed purified diets supplemented with as much as 800 mg Cu/kg ration provided that effective levels of added antioxidant (0.02% ethoxyquin) and stabilized sources of Vitamins A and D are present (Supplee 1964).

3.7.5 Mammals

Wilson's disease is the only naturally occurring neuropathological condition in humans and other mammals in which copper poisoning is implicated. People with Wilson's disease have severe pathological changes in the brain, especially in the basal ganglia, and in the liver. Pathology is associated with excess copper in tissues (Doherty et al. 1969). Copper concentrations in tissues from children who die from Wilson's disease are as much as 2217 mg/kg DW in liver and 1245 mg/kg DW in kidney (Table 3.7). Long-term exposure of humans to copper dust irritates the nose, eyes,

Table 3.6 Effects of Copper on Selected Birds

Organism, Copper Dose, and Other Variables	Effects	Reference ^a
MALLARD, <i>Anas platyrhynchos</i>		
Fed diets containing 15 or 135 mg/kg ration for 18 days; ducklings	Livers from low-dose group had 30 mg/kg dry weight (DW) at day 4 and 107 mg/kg at day 18; values for the high-dose group were 45 mg/kg at day 4, 74 mg/kg at day 7, and 254 mg/kg DW at day 18	1
For 15 days adults were given a choice of distilled water or water with 30, 60, or 100 mg/L	Ducks consumed significantly more water treated at 100 mg/L than distilled water; no preference was evident at lower doses	2
DUCKS, <i>Anas</i> spp.		
Ducklings fed diets containing 15 or 50 mg/kg ration for 51 days	Livers from control ducklings had 9.3 mg/kg DW. Livers from both treated groups had about 17 mg/kg DW at day 9, 37 mg/kg at day 30, and 47 mg/kg DW at day 51	1
Ducklings fed diet containing 200 mg/kg DW ration for 58 days	Copper concentrations in livers increased from 23 mg/kg DW at day 23 to 141 at day 44; at day 58 it had declined to 80 mg/kg DW	1
DOMESTIC CHICKEN, <i>Gallus</i> spp.		
Chicks age 1-day fed copper-deficient diet of 0.7 mg/kg ration or copper-adequate diet of 8.0 mg/kg ration for 46 weeks	Chicks fed copper-deficient diet had >50% mortality and high frequency of cardiovascular and skeletal lesions. Chicks on copper-adequate diet had negligible mortality, no histopathology, and normal growth 95% dead of copper deficiency	3, 4
Chicks fed diet containing 1.5 mg/kg ration for 60 days	Normal growth but high frequency of vascular rupture	5
Chicks fed diet containing 2.7 mg/kg ration for 60 days	Good survival and growth	5
Chicks fed diet containing 8.7 mg/kg feed for 60 days	Reduced weight gain in the 350 mg/kg group; other groups same as controls	6
Day-old chicks fed diets containing 10 (control), 100, 200, or 350 mg/kg ration for 25 days	Livers from controls had 5.9 mg/kg DW; treated groups were similar to controls, with copper concentrations in livers between 4.3 and 8.5 mg/kg DW	1
Chicks fed diets containing 15 or 50 mg/kg ration for 51 days	After 2 to 6 weeks, chickens were weak, anorectic, and lethargic; 35% were anemic	6
Adults were fed diets equivalent to 28 mg/kg body weight (BW) daily for the first week, 42 mg/kg BW daily for week 2, and 100 mg/kg BW daily until anemia, toxicosis, or death occurred	Maximum copper concentration in liver was 17.2 mg/kg DW at day 20; by day 58 it had dropped to 7.2 mg/kg DW	1
Chicks fed diet containing 200 mg/kg DW for 58 days	No gizzard erosion in controls; chicks fed the 250 mg/kg diet grew better than other treated groups but some had gizzard erosion. Chicks fed the 500 and 1000 mg/kg diets had decreased growth, decreased feed efficiency, and a high frequency of gizzard erosion. Severity of gizzard erosion was significantly reduced in the 500 mg/kg group (but not the 1000 mg/kg group) by adding 0.35% cholic acid	7
Chicks fed diets supplemented with 250, 500, or 1000 mg/kg ration for 4 weeks	Controls and the 250 mg/kg group had lower concentrations of copper in liver than those fed diets containing 500 mg/kg and higher. Copper concentration in the 2000 mg/kg group increased from 3 mg/kg DW at day 3 to 1790 mg/kg at day 48 (vs. 11.3 mg/kg DW in controls)	8
Laying hens fed diets supplemented with 250, 500, 1000, or 2000 mg/kg ration for 48 days		

Table 3.6 (continued) Effects of Copper on Selected Birds

Organism, Copper Dose, and Other Variables	Effects	Reference ^a
TURKEY, <i>Meleagris gallopavo</i>		
Day-old pourets fed diets containing 0, 60, 120, or 240 mg/kg ration and adequate levels of methionine for 24 weeks	Diets containing 60 mg/kg improved body weight at age 8 weeks; the 120 and 240 mg/kg diets inhibited growth for the first 8 weeks but not during the next 16 weeks	9
Week-old pourets fed a purified corn starch, isolated soy protein diet supplemented with 50 to 800 mg/kg ration for 3 weeks	Dose-dependent increase in mortality and decrease in growth	10
Week-old pourets fed corn-soybean meal supplemented with 100 to 800 mg/kg ration	No adverse effects on survival; growth reduced only at 800 mg/kg diet	10
Day-old pourets fed diet containing 500 mg/kg ration for 24 weeks	Reduced growth and increased gizzard histopathology	9

^a 1, Wood and Worden 1973; 2, Rowe and Prince 1983; 3, Carlton and Henderson 1963; 4, Carlton and Henderson 1964a; 5, Carlton and Henderson 1964b; 6, National Academy of Sciences 1977; 7, Poupoulis and Jensen 1976; 8, Stevenson and Jackson 1978; 9, Kashani et al. 1986; 10, Supplee 1964.

and mouth and causes headaches, dizziness, nausea, and diarrhea (USEPA 1980; ATSDR 1990). Drinking water that contains higher than normal concentrations of copper may cause vomiting, diarrhea, stomach cramps, nausea, and greenish or bluish stools and saliva. Intentionally high intakes of copper may result in liver and kidney damage, and sometimes death, especially in children. The seriousness of the effects of copper is expected to increase with increasing dose and duration of exposure (USEPA 1980; ATSDR 1990). Human tissues directly exposed to copper or copper salts will suffer adverse effects because of copper absorption. This is the case for copper bracelets on sweaty skin, for certain intrauterine devices, and for copper dental fillings (USEPA 1980). In monkeys, copper used as dental fillings in deciduous teeth caused more severe pulp damage than did other materials studied (USEPA 1980).

Mammals and birds are 100 to 1000 times more resistant to copper than other animals (Schroeder et al. 1966). But excessive dietary intakes of copper by 20- to 50-fold over normal levels may have serious effects in mammals. Depending on the species, growth and food intake may be reduced, anemia may develop, and liver, kidney, brain, and muscle may degenerate, often resulting in death (Bremner 1979; ATSDR 1990). Copper poisoning in mammals may result from consumption of plants treated with copper-containing pesticides, from the veterinary use of copper sulfate to control helminthiasis and infectious pododermatitis in cattle and sheep, and from the ingestion of contaminated soils and vegetation near copper mining and refining operations (NAS 1977). Emissions from copper mines and smelters are often associated with deaths of horses, cows, and sheep; pasture lands, in some cases, are fit for grazing only after heavy rains (Hutchinson 1979).

Ruminant mammals are significantly more sensitive to copper than nonruminant mammals and poultry (Schroeder et al. 1966; NAS 1977). Signs of copper poisoning in ruminants include vomiting, excessive salivation, abdominal pain, diarrhea with greenish-tinted feces, pathology of internal organs, elevated copper concentrations in livers, altered enzyme activities in liver and serum, and collapse and death within 24 to 48 h (NAS 1977). Young calves may develop copper toxicosis at relatively low copper intakes, especially when receiving milk-based diets. Goats, however, seem resistant to copper toxicosis (Bremner 1979). Among ruminants, domestic sheep are particularly susceptible to copper insult from grazing on pastures treated with copper-containing fungicides and molluscicides or from inadvertently consuming diets specially formulated for pigs that contain large amounts of copper as a swine growth stimulant (Todd 1969; Bremner 1979).

Chronic copper poisoning in domestic sheep is first characterized by a period of passive accumulation of copper in the tissues. This period varies from a few weeks to more than a year. During this time the animal appears outwardly normal although the liver may contain more than 1000 mg Cu/kg DW and plasma activities of aspartate transaminase, sorbitol dehydrogenase, lactic

dehydrogenase, and arginase increase, indicating that liver damage has occurred. During the last few weeks of the passive phase, and prior to the so-called toxic phase, liver histopathology of parenchymal cells and copper-containing Kupffer cells occurs. The toxic phase, which is an acute illness and referred to as the hemolytic crisis, usually results in death 2 to 4 days later. During this phase sheep refuse to eat but have an excessive thirst. The eyes are usually sunken. The venous blood is chocolate colored. The liver is jaundiced. The kidneys are completely gorged with hemoglobin breakdown products and the medulla and cortex are black. The spleen is enlarged, with the parenchyma a deep brown to black color. The onset of these signs in sheep is associated with liberation of copper from the liver and a massive increase in blood copper concentrations. The increased blood copper concentrations lead to an increase in blood methemoglobin and a sudden fall in the erythrocyte glutathione level immediately followed by massive hemolysis and kidney damage, leading to uremia and death. At the time of crisis, elevated serum creatine phosphokinase activity suggests that muscle cell membranes are affected, and elevated serum glutamic oxaloacetate transaminase (SGOT) and lactic dehydrogenase activities indicate progressive liver necrosis (Doherty et al. 1969; Todd 1969; Thompson and Todd 1974; Bremner 1979). It is emphasized that (1) blood copper status and liver function in sheep experimentally poisoned with copper sulfate are linked to elevated SGOT activities 1 to 6 weeks in advance of obvious external signs (MacPherson and Hemingway 1969); (2) copper chloride is 2 to 4 times more toxic than copper sulfate to sheep (NAS 1977); and (3) the use of copper-enriched feeding stuffs increases the risk of chronic copper poisoning in sheep fed purified rations (Froslie et al. 1983). Also, sheep that accumulate higher than normal amounts of copper in the liver (i.e., 1900 mg Cu/kg DW) are more severely affected by lupinosis (acute liver atrophy due to poisoning by ingestion of plants of *Lupinus* spp.) than sheep with normal (40 mg/kg DW) concentrations of copper in the liver (Gardiner 1967).

Copper toxicosis in lambs of domestic sheep occurs at dietary concentrations between 8 and 60 mg Cu/kg ration. The wide range of dietary concentrations is a function of copper availability. Availability, in turn, is influenced by dietary composition, genetic influence, age, breed, sex, physiological state, and interactions with other dietary constituents including iron, zinc, and molybdenum (Bremner 1979). Chronic copper poisoning in lambs occurs at dietary levels as low as 27 mg Cu/kg DW ration (Buckley and Tait 1981). During the passive phase, lambs — like adults — have normal plasma copper concentrations and seem outwardly unaffected. Unlike adults, copper accumulates in livers of lambs during a shorter period (several weeks to months vs. months to years). Signs of hemolytic crisis and death within a few days are similar for both adults and lambs. Elevated plasma aspartate aminotransferase (AAT) activity in lambs — up to 10 times higher than controls — occurs 4 to 8 weeks before the hemolytic crisis (Buckley and Tait 1981) and strongly indicates a need for more research on the usefulness of AAT and other enzymes as early indicators of copper stress. A recommended treatment for lambs diagnosed with chronic copper poisoning is 20 mL of a mixture containing 100 mg of ammonium molybdate and 1 g of sodium sulfate administered orally 5 days weekly (Doherty et al. 1969).

In domestic pigs, copper toxicosis results from eating diets containing 250 mg Cu/kg ration and is characterized by anemia, jaundice, elevated levels of Cu in serum and liver, and elevated serum AAT activity (USEPA 1980). Shortly before death, copper-poisoned pigs had white noses, poor balance, stomach histopathology, orange cirrhotic livers, anorexia, and anemia (Higgins 1981).

In rodents, copper administered by single intraperitoneal or subcutaneous injection is lethal at 3 to 7 mg Cu/kg BW ([Table 3.7](#)). Mice died when their drinking water contained 640 mg Cu/L ([Table 3.7](#)). In rats, copper accumulation in kidneys and lungs is similar regardless of route of administration (Romeu-Moreno et al. 1994). Concentrations of copper in serum of rats (*Rattus* sp.) reflect dietary copper; concentrations in liver and kidney are directly related to serum Cu and ceruloplasmin (Petering et al. 1977). As serum Cu concentrations rise in rats, levels fall for serum cholesterol, triglycerides, and phospholipids (Petering et al. 1977).

Table 3.7 Effects of Copper on Selected Mammals

Organism, Copper Dose, and Other Variables	Effects	Reference ^a
CATTLE, <i>Bos</i> spp.		
Fed diet containing 8.2 mg/kg ration for 333 days	Copper concentration in liver increased from 111 to 328 mg/kg dry weight (DW)	1
Fed diets containing 20 to 125 mg/kg ration for extended period	Intoxication	2
Single dose; 200 mg/kg body weight (BW)	Lethal	2
PONY, <i>Equus</i> sp.		
Ponies given a single oral dose of 20 or 40 mg/kg BW were challenged 24 h later with oral doses of 2, 4, 6, or 8 mg selenium/kg BW	All ponies given 20 or 40 mg/kg BW were unaffected by selenium, regardless of dosage; without copper pretreatment, signs of severe Se toxicosis — including lethargy, colic, and death — developed in ponies given 6 or 8 mg Se/kg BW	3
Fed diet containing 800 mg/kg ration for 6 months	No adverse effects	4
HUMANS, <i>Homo sapiens</i>		
3 mg/L drinking water for 9 months	Liver damage in infants	5
30 mg/L drinking water; single exposure; total intake unknown	Vomiting, diarrhea, stomach cramps	5
6 to 637 mg/kg BW; single exposure (attempted suicides)	13 of 53 patients died; death attributed to shock and hepatic or renal complications	5
Children who died from Wilson's disease vs. normal children		
Brain	2090 mg/kg ash weight (AW), equivalent to 31 mg/kg fresh weight (FW) or 129 mg/kg DW vs. 290 mg/kg AW	6
Heart	6800 mg/kg AW, equivalent to 75 mg/kg FW or 298 mg/kg DW vs. 340 mg/kg AW	6
Kidney	27,160 mg/kg AW, equivalent to 299 mg/kg FW or 1245 mg/kg DW vs. 250 mg/kg AW	6
Liver	74,570 mg/kg AW, equivalent to 820 mg/kg FW or 2217 mg/kg DW vs. 1300 mg/kg AW	6
Pancreas	1200 mg/kg AW vs. 160 mg/kg AW	6
Spleen	1930 mg/kg AW vs. 100 mg/kg AW	6
MICE, <i>Mus</i> spp.		
Strain genetically deficient in copper (Menkes disease) given subcutaneous injections of 50 µg copper chloride (CuCl_2) on postnatal days 7 and 10. Before therapy, liver copper concentration was 3.1 mg/kg FW (vs. 30.1 mg/kg FW in normal mice)	Seven months postinjection there was some reduction in neurodegeneration; copper was distributed normally in liver; in intestine, copper accumulated in histiocytes	7
120 µg/m ³ air for 1–2 weeks	Alveoli thickening	5
<3.3 mg/kg BW; single intraperitoneal (ip) injection	No effect on oxygen consumption or body temperature	8
3.3–8.0 mg/kg BW; single ip injection	Dose-dependent reduction in oxygen consumption and body temperature	8
4.02 mg/kg BW; single ip injection	50% dead	8
Drinking water equivalent of 4.2 mg/kg BW daily for 850 days	Decreased growth and survival	5
Drinking water equivalent of 42.5 mg/kg BW daily as copper glutamate; lifetime exposure	Maximal lifespan reduced from 986 days to 874 days	5
640 mg/L drinking water for 850 days	Decreased survival	5

Table 3.7 (continued) Effects of Copper on Selected Mammals

Organism, Copper Dose, and Other Variables	Effects	Reference ^a
MINK, <i>Mustela vison</i>		
Dietary equivalent of 3.5 mg/kg BW daily for 50 weeks	Decreased survival (deficiency)	5
Dietary equivalent of 13.5 mg/kg BW daily for 50 weeks	Some deaths; no adverse effect on reproduction of survivors	5
RABBIT, <i>Oryctolagus</i> sp.		
600 µg/m ³ air for 4 to 6 weeks	No adverse systemic or immunological effects	5
DOMESTIC SHEEP, <i>Ovis aries</i>		
Ewes were fed a copper-deficient diet of 1.3 to 2.5 mg/kg DW ration. At mating, livers contained 20 to 106 mg/kg DW; after lambing, livers contained 3 to 12.3 mg/kg DW	22 of 54 (41%) lambs from ewes fed a copper-deficient diet developed swayback; these lambs had liver concentrations of 5.9 (1.5–11.0) mg/kg DW vs. 6.9 (2.5–14) mg/kg DW in non-swaybacked lambs	11
Ewes from vicinity of copper production plant receiving daily dietary intake of 465 mg/ewe (10.7 mg/kg BW daily) vs. control ewes with average daily dietary intake of 29 mg Cu/ewe (0.67 mg Cu/kg BW daily)	All ewes near copper facility were dead by day 89 vs. none dead in controls. At day 35, ewes near copper production plant had 11.8 mg/kg DW in wool vs. <7 mg/kg DW in controls	9
Merino sheep, 6 to 9 months old; given 5.1 mg/kg BW 5 times weekly for 28 weeks through the mouth as copper sulfate. Heliotrope and nonheliotrope diets	Some deaths. Yellow discoloration of sclera of eye; passing of red-colored urine. Copper concentrations, in mg/kg DW, from sheep fed nonheliotrope diets were 1394 in liver (824 in controls) and 132 in kidney (20 in controls). Sheep on heliotrope diet had 2783 mg/kg DW in liver and 321 mg Cu/kg DW in kidney	10
Oral administration of 7.5 mg/kg BW daily for 83 days, as copper sulfate	Severe morphological changes in liver, kidney, and brain; tissue damage continued after cessation of copper and was sufficiently severe to lead to repeated hemolytic crises. Maximum copper concentrations at day 83 were 3289 mg/kg DW in liver (138 in controls), and 683 in kidney (15 in controls)	12
Lambs fed diets containing 9.1 (control) or 37.3 mg/kg ration for 11 weeks	Normal growth and survival. At slaughter, liver copper concentrations, in mg/kg DW, were 372 in controls and 1109 in the treated group; plasma aspartate aminotransferase was elevated in the high-dose group	13
Lambs fed diets containing 11 (control), 18, or 25 mg/kg ration for 10 weeks	Survival and growth normal in all groups. Liver concentrations, in mg/kg DW, were 239 (11 mg/kg group), 454 (18 mg/kg group), and 721 (25 mg/kg group)	13
Rams, age 4.5 to 5.5 years; daily intake of 15 mg/kg BW for 50 days	Increased concentrations of copper in ejaculates (16 mg/kg DW vs. 2 in controls) and liver (1435 mg/kg DW vs. 63). Sperm motility in test rams was significantly decreased, abnormalities were increased, and testes copper was elevated (96–101 mg/kg DW vs. 60–69 in controls)	14
Equivalent of 20 mg/kg BW daily for 9 weeks Lambs fed diet containing 80 mg/kg DW ration for 6 weeks	Hemolysis Postmortem examination of 17 lambs that died suddenly showed brain histopathology, particularly in white matter of midbrain, pons, and cerebellum. Severe liver cirrhosis and necrosis of kidney tubules. Liver copper elevated at 3225 to 4325 mg/kg DW	15 16

Table 3.7 (continued) Effects of Copper on Selected Mammals

Organism, Copper Dose, and Other Variables	Effects	Reference ^a
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Dietary route		
Male weanlings fed copper-deficient (0.13 mg/kg ration) or copper-adequate (5.7 mg/kg ration) diets for 49 days	24% of the copper-deficient rats died of cardiac rupture; ruptured hearts had lower magnesium and higher sodium, phosphorus, and calcium. Copper-adequate rats had 21.7 mg/kg DW liver vs. 2.2 in copper-deficient rats in which hearts had ruptured	17
Low copper diet of 1 mg/kg DW ration vs. 5 mg/kg diet for 12 weeks	Dose-dependent increase in copper concentrations in kidney, liver, and plasma. Low Cu status increases retention of cadmium in liver	18
100 mg/kg diet for 20 weeks	Increased blood pressure	5
250 mg/kg diet for 3 months	No deaths	5
500 mg/kg diet for 3 months	Kidney damage	5
1000 mg/kg diet for 3 months	Stomach and liver damage	5
2000 mg/kg diet for 1 to 3 weeks	Liver and kidney damage	5
4000 mg/kg diet (133 mg/kg BW daily) for 1 week	Increased mortality	5
6000 mg/kg diet (300 mg/kg BW daily) for 2 weeks	Weanlings died from extensive centrilobular necrosis	5
Equivalent to 7.9 mg/kg BW daily for 90 days	Increased serum glutamic oxaloacetic transaminase enzyme activity	5
Equivalent to 10 mg/kg BW daily for 20 weeks	Increased blood pressure; increased hemoglobin	5
Equivalent to 40 mg/kg BW daily for 30 days	Anemia, increased liver enzyme activity, increased cholesterol and urea	5
Equivalent to 130 mg/kg BW daily for 18 weeks	Decreased body growth; decreased testes weight	5
Equivalent to 144 mg/kg BW daily for 4 weeks	Decrease in rate of body weight gain	5
Drinking water route		
0.25, 2, or 16 mg/L for 109 to 119 days	Serum copper rose from 44 µg/L (controls) to 106 µg/L (0.25 mg/L group) to 848 (2 mg/L) to 943 µg/L (16 mg/L group); dose-dependent decrease in serum cholesterol, triglycerides, and phospholipids	19
50 or 150 mg/L for 15 to 30 days	No adverse effect on liver microsomal activity	20
398 to 450 mg/L for 15 to 30 days	Reduction in liver aniline hydroxylase activity; liver histopathology	5, 20
Inhalation route		
Copper sulfate spray containing 330 g/L for daily exposures of 1 h for as long as 10 days	Concentrations of copper in liver, in mg/kg FW, were 32 after 6 hr, 84 after 5 days, and 285 after 10 days	27
Injection route		
0.26 mg/rat daily as copper sulfate for 60 days; subcutaneous (sc) injection	Treated rats had 1000 mg/kg FW liver (vs. 4.7 in controls); lowered hemoglobin, hematocrit, and red cell counts; mean survival time of 67 days; hepatic and renal histopathology	15
0.625, 1.25, 2.5, or 3.75 mg/kg BW daily for 18 weeks; intraperitoneal injection	Dose-time-dependent increase in copper concentrations in liver, spleen, and lung; little accumulation in muscle and skin. Reduced growth at 2.5 and 3.75 mg/kg BW daily; reduced survival at 3.75 mg/kg BW. Maximum copper concentrations recorded, in mg/kg FW (vs. saline controls,) were 710 in liver (<5), 212 in kidney (<10), 7 in lung (<1.5), 27 in spleen (<2.0) 6 in bone (<2.0) and 2.2 in testes (<1.6)	21
Adult males given 2 mg/kg BW daily as copper acetate for 14 days; intra-peritoneal injection	Increased serum ceruloplasmin and white blood cell number	22

Table 3.7 (continued) Effects of Copper on Selected Mammals

Organism, Copper Dose, and Other Variables	Effects	Reference ^a
Other routes Isolated cells from adrenal and testes held in media containing 0.065, 0.65, or 6.5 mg/kg for 2 h	No effect at lowest doses. High dose caused decreased survival of cells from both organs and reduced testosterone production	23
RODENTS, various species		
3–7 mg/kg BW; single ip or sc injection	50% dead	15
COMMON SHREW, <i>Sorex araneus</i>		
Newly weaned shrews fed diets equivalent to 2.13 mg copper/shrew daily for 12 weeks; uncontaminated diets contained 25.1 mg/kg DW ration	No effect on growth, survival, or tissue copper burdens; kidney and liver copper concentrations increased in response to cadmium dosing	24, 25
DOMESTIC PIG, <i>Sus</i> spp.		
Dietary equivalent of 14.6 mg/kg BW daily for 54 days	Decreased hemoglobin and hematocrit; decreased growth rate	5
Dietary equivalent of 36 mg/kg BW daily for 7 weeks	Decreased hemoglobin, altered serum enzyme activity	5
Fed diets containing <150 mg/kg ration for 9 months	No copper accumulations over controls in liver (16–48 mg/kg DW) or kidney (20–49 mg/kg DW); growth promoting effects	26
Fed diets supplemented with 238–250 mg/kg ration, as copper sulfate, from age 3 weeks for 9 months	High mortality, usually between age 14 and 20 weeks. Dead pigs had 1300 mg/kg DW in liver and 95 mg/kg in liver; survivors had as much as 2100 mg/kg DW liver, 670 mg/kg DW kidney, and 3.3 mg/L serum	26
Fed diets containing 700 mg/kg ration for several months	High mortality; survivors had anemia, gastric ulcers, liver pathology, and 100–170 mg/kg FW in liver	15

^a 1, Miltmore et al. 1978; 2, Gummow et al. 1991; 3, Stowe 1980; 4, Bremner 1979; 5, ATSDR 1990; 6, Schroeder et al. 1966; 7, Yoshimura et al. 1995; 8, Gordon et al. 1990; 9, Bires and Vrzgula 1990; 10, Howell et al. 1991; 11, Lewis et al. 1967; 12, Gopinath and Howell 1975; 13, Buckley and Tait 1981; 14, Gamcik et al. 1990; 15, Aaseth and Norseth 1986; 16, Doherty et al. 1969; 17, Saari et al. 1994; 18, Panemangelore 1993; 19, Petering et al. 1977; 20, Moffitt and Murphy 1973; 21, Lal and Sourkes 1971; 22, Jehan and Motlag 1994; 23, Ng and Liu 1990; 24, Dodds-Smith et al. 1992a; 25, Dodds-Smith et al. 1992b; 26, Higgins 1981; 27, Romeu-Moreno et al. 1994.

3.8 PROPOSED CRITERIA AND RECOMMENDATIONS

Proposed copper criteria for the protection of agricultural crops, aquatic life, terrestrial invertebrates, poultry, laboratory white rats, livestock, and human health are summarized in Table 3.8.

Copper is essential to normal plant growth, and copper deficiency is known in various agricultural crops, such as vegetables and grains (Gupta 1979). Crops seem to be protected against copper deficiency when growing soils contain >10 mg Cu/kg DW and leaves >6 mg Cu/kg DW (Table 3.8). With some exceptions, agricultural crops are protected against copper toxicosis when irrigation waters contain <1.0 mg Cu/L and soils <170 mg Cu/kg DW (Table 3.8), but adverse effects occur on root development of seedling pines at irrigation water concentrations as low as 200 µg Cu/L (Arduini et al. 1995) and on growth of citrus trees when extractable copper in the soil exceeds 60 mg/kg DW (Alva et al. 1995). States allow application of sewage sludge to agricultural soils if total copper in the sludge does not exceed 1000 mg/kg DW (100 mg/kg DW in Florida), or if the application rate for sludge does not exceed 280 kg sewage sludge per surface acre (50 kg/ha in Wisconsin; Table 3.8). The practice by some localities of applying raw sewage sludge to crop soils

on the basis of kg sludge/surface acre ratio should be discouraged unless the sludge is periodically analyzed for copper and other contaminants.

Proposed criteria to protect most species of freshwater aquatic life from copper toxicity or deficiency include maximum water concentrations over a 24-h period of 12 µg Cu/L in soft water and 43 µg/L in hard water, sediment concentrations <480 mg Cu/kg DW, and, in rainbow trout, a zinc/copper ratio in gill or opercle >1.5 (Table 3.8). However, the proposed maximum water concentration range of 12 to 43 µg Cu/L exceeds the 5 to 10 µg/L range that is lethal or teratogenic to sensitive species of fishes and amphibians (Birge and Black 1979) and overlaps the 18 to 28 µg/L range that inhibits growth and ability to discriminate prey for other species (Sandheinrich and Atchison 1989). Some scientists state that laboratory studies tend to overestimate the adverse effects of copper on freshwater abundance and diversity and suggest more research on field mesocosms receiving water directly from the system under investigation (Clements et al. 1990). In marine ecosystems, copper concentrations should not exceed 23 µg Cu/L at any time, and sediments should contain less than 200 mg Cu/kg DW (Table 3.8). But adverse sublethal effects of copper to representative species of estuarine algae, molluscs, and arthropods frequently occur at less than 10 µg Cu/L (Bryan and Langston 1992). Also, extrapolation of laboratory data on copper and marine benthos to actual field conditions is difficult because of changing environmental conditions, such as thermosaline regimes and the nature of the sediment substrate (Ozoh 1992c).

Among sensitive species of terrestrial invertebrates, earthworms show disrupted enzyme activities at whole-body concentrations as low as 28.5 mg Cu/kg DW (Table 3.8). Soil copper concentrations between 53 and 100 mg/kg DW kill soil nematodes and soil faunal communities (Parmelee et al. 1993; Donkin and Dusenberry 1993) and cause a reduction in cocoon production of earthworms (Ma 1984; Spurgeon et al. 1994). Diets that contain between 50 and 63 mg Cu/kg ration inhibit development and reproduction in gypsy moths and oribatid mites (Denneman and van Straalen 1991; Gintenreiter et al. 1993). The wood louse (*Porcellio scaber*), an isopod, is proposed as a bioindicator of copper contamination in terrestrial ecosystems because whole-body concentrations seem to reflect copper loadings in the isopod's immediate environment (Hopkin et al. 1993; Table 3.8). More research is recommended on isopods and other sentinel organisms.

Quantitative data are missing on copper effects on avian and mammalian wildlife, and this represents a high-priority research need. Some data are available for copper and poultry and livestock, but extrapolation of these results to wildlife species is contraindicated in view of the wide range in sensitivities to copper between species. Domestic chickens show good growth and survival when their diets contain adequate iron and more than 4 and less than 200 mg Cu/kg ration (Carlton and Henderson 1964b). In sheep — and some other mammals — prior knowledge of copper stress would allow adequate time for treatment (i.e., prophylactic dosing with ammonium molybdate plus sodium sulfate or intravenous injection of chelating agents) to prevent sudden death during copper-induced hemolytic crisis (MacPherson and Hemingway 1969). In sheep, for example, elevated SGOT activity is an early indicator of copper poisoning and is measurable 1 to 6 weeks before the hemolytic crisis stage (MacPherson and Hemingway 1969). Providing prophylactic licks containing zinc sulfate and sulfur to African cattle, buffaloes, and impalas seems to be successful in protecting against the lethal effects of excess airborne copper in the grazing area (Gummow et al. 1991).

The proposed domestic drinking water criterion of <1.0 mg Cu/L for the protection of human health is not based on copper toxicosis but on the unpleasant taste which develops with higher levels of copper in drinking water (USEPA 1980). Increased copper levels (>1.3 mg Cu/L) in household water supplies caused by corrosion of copper plumbing materials may adversely affect infants and young children among residents of newly constructed or renovated homes (Knobeloch et al. 1994). Human groups at greatest risk to copper toxicosis now include young children subjected to unusually high concentrations of copper in soft or treated water held in copper pipes or vessels, medical patients with Wilson's disease, medical patients treated with copper-contaminated fluids in dialysis or parenteral administration, people with a glucose-6-phosphate dehydrogenase (G-6-PD)

deficiency (about 13% of the Afro-American male population has a G-6-PD deficiency) who drink water containing >1.0 mg Cu/L, and occupationally exposed workers (USEPA 1980).

Other copper research areas that seem to merit additional effort include:

1. Establishment of specific biomarkers for copper toxicity (ATSDR 1990)
2. Development of a national system to verify incidents of deficiency and excess of copper and interrelated trace elements in species of concern (NAS 1977)
3. Clarification of copper interactions with molybdenum, sulfate, iron, and zinc in plant and animal metabolisms (NAS 1977; Eisler 1989, 1993)
4. The role of copper in carcinogenesis, mutagenesis, and teratogenesis (NAS 1977; ATSDR 1990) because preliminary evidence suggests that exposures to grossly elevated concentrations of copper produces teratogenicity in fish (Birge and Black 1979) and mammals (Aaseth and Norseth 1986), carcinogenicity in rodents (USEPA 1980; ATSDR 1990; Toussaint and Nederbragt 1993), and mutagenicity in rodents (ATSDR 1990), sheep (Bires et al. 1993), and grasshoppers (Bhunya and Behura 1986)
5. Mechanisms by which copper deficiency results in neutropenia, with emphasis on the process of cellular differentiation and the viability of neutrophils in blood and marrow (Percival 1995)
6. Copper status effects on resistance to endotoxin-induced injuries because burn and trauma patients show moderate copper deficiency and high risk to sepsis, and copper deficient rats are sensitive to endotoxins causing sepsis (DiSilvestro et al. 1995)
7. The role of aquatic organisms in copper cycling in aquatic ecosystems (Stokes 1979)
8. Mechanisms of copper tolerance or acclimatization to high doses of copper (ATSDR 1990)
9. The relation between copper toxicosis, copper absorption rates, and copper retention (Stokes 1979; ATSDR 1990)
10. Effects on reproduction, neurotoxicity, and immune response (ATSDR 1990)
11. Biochemistry and physiology of copper proteins (NAS 1977)
12. Measurement of flux rates of ionic copper from metallic copper (ATSDR 1990)
13. Determination of safe levels of copper in livestock and poultry feeds (NAS 1977), and in diets of avian and mammalian wildlife

Table 3.8 Proposed Copper Criteria for the Protection of Natural Resources and Human Health

Resource, Criteria, and Other Variables	Effective Copper Concentration	Reference ^a
AGRICULTURAL CROPS		
Irrigation water	<1.0 mg/L	1
Leaves		
Severe deficiency	<4 mg/kg dry weight (DW)	2
Deficient	<5 mg/kg DW	1, 3
Mild to moderate deficiency	4 to 5 mg/kg DW	1, 3
Deficiency rare	>6 mg/kg DW	2
Sewage sludge		
Europe, acidic soils	50 to 140 kg/ha	4
United States		
All agricultural lands	<1000 mg/kg DW	5
Florida	<100 mg/kg DW	4
Illinois	<280 kg/ha	4
Maryland, Massachusetts	140 to 280 kg/ha ^b	4
Minnesota, Missouri	140 to 560 kg/ha ^c	4
New York		
Agricultural soils	<125 kg/ha	4
Forests	<280 kg/ha	4
Wisconsin, acidic soils	50 to 140 kg/ha	4
Soils		
Deficient	<10 mg/kg DW	6
Safe	<280 kg/ha ^d	7
M-3 extractable soil copper	<60 mg/kg DW	8

Table 3.8 (continued) Proposed Copper Criteria for the Protection of Natural Resources and Human Health

Resource, Criteria, and Other Variables	Effective Copper Concentration	Reference^a
Canada		
Agricultural lands	<100 mg/kg DW	4
Acidic soils, Alberta	<200 mg/kg DW	4
Industrial and other lands	<300 mg/kg DW	4
Former Soviet Union, maximum allowable concentration	3 mg/kg DW when extracted with ammonium acetate buffer	4
The Netherlands		
Normal	50 mg/kg DW	4
Moderately contaminated	100 mg/kg DW	4
Requires remediation	>500 mg/kg DW	4
United States, New Jersey	<170 mg/kg DW	4
AQUATIC LIFE, FRESHWATER		
Sediments		
Great Lakes		
Nonpolluted	<25 mg/kg DW	4
Moderately polluted	25 to 50 mg/kg DW	4
Heavily polluted	>50 mg/kg DW	4
Reduced abundance of benthos	480 to 1093 mg/kg DW	9
Toxic to benthos	>9000 mg/kg DW	9
Tissue concentrations; rainbow trout, <i>Oncorhynchus mykiss</i> ; ratio of zinc to copper in gill or opercle		
Normal	Ratio >1.5	10
Probably copper-poisoned	Ratio 0.5 to 1.5	10
Acute copper poisoning	Ratio <0.5	10
Water		
Safe. No adverse effects on rainbow trout exposed from fertilization through 4 days after hatching		
In soft or medium water	2 to 5 µg/L	11
In hard water	5 to 8 µg/L	11
Death or teratogenicity in eggs of sensitive species of fishes and amphibians	5 to 10 µg/L	11
United States		
Safe; total recoverable copper; 24 h average	<5.6 µg/L	12
Maximum allowable concentration at 50 mg CaCO ₃ /L	12 µg/L	12
Maximum allowable concentration at 100 mg CaCO ₃ /L	22 µg/L	12
Maximum allowable concentration at 200 mg CaCO ₃ /L	43 µg/L	12
Inhibits fish growth and ability of fish to discriminate prey	18 to 28 µg/L	13
Chesapeake Bay; proposed for protection of 90% of species tested		
Acute exposures		
All species	<6.3 µg/L ^f	35
Benthos	<6.9 µg/L	35
Fishes	<10.8 µg/L	35
Chronic exposures		
All species	<3.8 µg/L ^f	35
Fishes	<3.9 µg/L	35
The Netherlands; total recoverable copper; maximum allowable concentration	<50 µg/L	14
AQUATIC LIFE, MARINE		
Seawater		
Safe. Total recoverable copper, 24 h average	<4.0 µg/L; not to exceed 23 µg/L at any time	12
Safe. Maximum concentration	<5.0 µg/L	15

Table 3.8 (continued) Proposed Copper Criteria for the Protection of Natural Resources and Human Health

Resource, Criteria, and Other Variables	Effective Copper Concentration	Reference^a
Chesapeake Bay; recommended for protection of 90% of species tested		
Acute exposures		
All species	<6.3 µg/L ^f	35
Benthos	<4.1 µg/L	35
Fishes	<16.1 µg/L	35
Chronic exposures		
All species	<6.4 µg/L ^f	35
Sediments		
Avoidance by clams	>5 mg/kg DW	16
Clam burrowing ability inhibited (water concentrations of 113 to 120 µg Cu/L)	>15 mg/kg DW	16
Not polluted	<40 mg/kg DW	15
Moderately polluted	40 to 60 mg/kg DW	15
Very polluted	>60 mg/kg DW	15
Reduced species diversity; sensitive species absent	>200 mg/kg DW	17
Toxic to juvenile bivalve molluscs	>2000 mg/kg DW	17
TERRESTRIAL INVERTEBRATES		
Earthworms, whole; disrupted lysozyme activity in coelomic fluid and coelomocytes	>28.5 mg/kg DW	18
Isopod, <i>Porcellio scaber</i> ; whole		
Deficiency	Unknown	19
Uncontaminated	<250 mg/kg DW	19
Low contamination	250 to 400 mg/kg DW	19
Medium contamination	400 to 600 mg/kg DW	19
High contamination	600 to 1000 mg/kg DW	19
Very high contamination	>1000 mg/kg DW	19
POULTRY, DIETS		
Deficient	<8.7 mg/kg DW ration; some deaths at 0.7 to 1.5 mg/kg DW ration; high frequency of vascular rupture at 2.7 mg/kg DW ration	3, 20, 33
Safe	<200 mg/kg DW feed	17
Recommended for growing chickens	>4 mg/kg DW diet plus adequate iron	20
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Minimal	3 to 6 mg/kg FW diet; 0.15–0.3 mg/kg body weight (BW) daily	5
Adequate	10 mg/kg DW diet	21
LIVESTOCK		
All species except sheep; diet		
Deficient	<5 mg/kg DW	2
Minimal	>5 to <15 mg/kg DW	1
Adequate	20 to 30 mg/kg DW	2
Cattle, <i>Bos</i> sp.; liver, copper-poisoned	>150 mg/kg fresh weight (FW); >450 mg/kg DW	22
Sheep, <i>Ovis aries</i>		
Toxic	20 to 30 mg/kg DW diet	2
Pig, <i>Sus</i> sp.		
Diet		
Safe	3 to 5 mg/kg DW	5
United Kingdom, maximum	200 mg/kg DW ^e	23

Table 3.8 (continued) Proposed Copper Criteria for the Protection of Natural Resources and Human Health

Resource, Criteria, and Other Variables	Effective Copper Concentration	Reference^a
Tissue concentrations		
Fatal anemia with jaundice and stomach ulcerations; kidney vs. liver	95 to 800 mg/kg DW vs. 1300 to 2600 mg/kg DW	23
HUMAN HEALTH		
Air		
Montana	<0.26 µg/m³ for 8 h; <1.57 µg/m³ for 24 h	5
Massachusetts	<0.54 µg/m³ for 24 h	5
Connecticut, North Dakota	<2 µg/m³ for 8 h	5
Florida	<4 µg/m³ for 8 h	5
Nevada	<5 µg/m³ for 8 h	5
Virginia	<16 µg/m³ for 24 h	5
New York	<20 µg/m³ for 1 year	5
United States; workplace; 8 h daily		
Fumes	<0.1 to <0.2 mg/m³	5
Dusts and mists	<1.0 mg/m³	5
Total	<1.0 mg/m³	12
Daily intake, all sources		
Deficiency in children	<0.1 µg/kg BW	12
Infants, normal	14 to 80 µg/kg BW; 0.5 to 1.0 mg	12, 24, 25
Children, normal	40 to 100 µg/kg BW; 1 to 2 mg	12, 24, 25
Teenagers and adults, normal	28 to 40 µg/kg BW; 2 to 4 mg	5, 12, 24, 25
Adults, safe and adequate	2 to 3 mg	5
Adults, maximum	40 µg/kg BW daily equivalent to 2.8 mg daily for 70 kg adult	34
Adults, toxic	15 mg in single dose	12
Diet		
Australia		
Seafood	<30 mg/kg FW	30
Shellfish; soft parts	<70 mg/kg FW; <266 mg/kg DW	27, 28
Fish muscle	<15 mg/kg FW	31
Malaysia; bivalve molluscs; soft parts	<30 mg/kg FW	29
Spain, total diet	<20 mg/kg DW	32
Drinking water		
United States, safe	<1.0 mg/L (exceeded by about 1% of all samples)	12
Kansas, Rhode Island	<1.0 mg/L	5
Minnesota	<1.3 mg/L	5
Proposed, United States	<1.3 mg/L	5
Satisfactory smell and taste	<1.0 to 1.3 mg/L	5, 12
Associated with diarrhea, abdominal cramps, and nausea	>1.3 mg/L	26
Health advisory for children and adults	Not to exceed 1.3 mg/L for more than 1 day	5
Adverse taste	>1.5 mg/L	12
Fish and shellfish collection locales; marine	<4 µg/L	27
Tissues; human		
Blood; deficient vs. adequate	<0.8 mg/L vs. 1.03 mg/L	12
Serum; normal vs. toxic	1.64 mg/L vs. 2.86 mg/L	12

^a 1, NAS 1977; 2, Gupta 1979; 3, Carlton and Henderson 1963; 4, Beyer 1990; 5, ATSDR 1990; 6, King et al. 1984; 7, Reed et al. 1993; 8, Alva et al. 1995; 9, Mackenthun and Cooley 1952; 10, Carbonell and Tarazona 1993; 11, Birge and Black 1979; 12, USEPA 1980; 13, Sandheinrich and Atchison 1989; 14, Enserink et al. 1991; 15, Fagioli et al. 1994; 16, Roper and Hickey 1994; 17, Bryan and Langston 1992; 18, Goven et al. 1994; 19, Hopkin et al. 1993; 20, Carlton and Henderson 1964b; 21, Dodds-Smith et al. 1992a; 22, Gummow et al. 1991; 23, Higgins 1981; 24, Aaseth and Norseth 1986; 25, Schroeder et al. 1966; 26, Knobeloch et al. 1994; 27, Talbot et al. 1985; 28, Brown and McPherson 1992; 29, Mat 1994; 30, Greig and Sennefelder 1985; 31, Mathews 1994; 32, Daramola and Oladimeji 1989; 33, Carlton and Henderson 1964a; 34, Han et al. 1998; 35, Hall et al. 1998.

Table 3.8 (continued) Proposed Copper Criteria for the Protection of Natural Resources and Human Health

- ^b Soil cation exchange capacity less than 5 meq/100 g for 140 kg/ha and more than 5 meq/100 g for 280 kg/ha.
- ^c Soil cation exchange capacity ranges from less than 5 to more than 15 meq/100 g.
- ^d Higher levels of 365 kg Cu/ha had no effect on corn yield or copper content in corn.
- ^e Diet should also contain 150 mg Zn/kg and 200 mg Fe/kg to further reduce the chances of copper toxicity to pigs.
- ^f Concentrations >50 µg Cu/L are routinely measured in the Chesapeake and Delaware Canal and infrequently in other portions of Chesapeake Bay.

3.9 SUMMARY

Copper discharges to the global biosphere are due primarily to human activities, especially mining, smelting, and refining copper and the treatment and recycling of municipal and industrial wastes. Some copper compounds, especially copper sulfate, also contribute to environmental copper burdens because they are widely and intensively used in confined geographic areas to control nuisance species of aquatic plants and invertebrates, diseases of terrestrial crop plants, and ectoparasites of fish and livestock.

Copper concentrations in field collections of abiotic materials and living organisms are usually elevated in the vicinity of human activities and intensive copper use. Maximum copper concentrations recorded in selected abiotic materials are 5 µg/m³ in air, 5 µg/L in groundwater, 12 µg/L in rainwater, 1200 mg/kg DW in poultry litter, 7000 mg/kg DW in soils, and 7700 mg/kg DW in sewage sludge. In terrestrial vegetation, copper is usually less than 35 mg/kg DW except near smelters, where it may approach 700 mg/kg DW and in certain copper-accumulator plants that may normally contain as much as 13,700 mg/kg DW. Aquatic vegetation from copper-contaminated sites contain as much as 1350 mg Cu/kg DW vs. 36 mg/kg DW in conspecifics from reference sites. Terrestrial invertebrates from industrialized areas may contain from 137 to 408 mg Cu/kg DW whole organism. Aquatic invertebrates seldom contain as much as 95 mg Cu/kg DW, regardless of collection locale. Exceptions include whole amphipods and lobster hepatopancreas (335 to 340 mg/kg DW) from copper-contaminated sites and many species of molluscs that normally contain 1100 to 6500 mg Cu/kg DW. Data are scarce on copper concentrations in field populations of amphibians and reptiles: crocodile eggs may contain as much as 60 mg Cu/kg DW and livers of some toads may contain as much as 2100 mg Cu/kg DW without apparent adverse effects. Maximum copper concentrations in tissues of fishes, elasmobranchs, birds, and marine mammals from all collection sites are low when compared to more primitive organisms and never exceed 53 mg Cu/kg DW, except liver (146 to 367 mg/kg DW); an exception is liver from endangered manatees (1200 mg/kg DW) collected at a site treated with a copper-containing herbicide. Maximum copper concentrations in all tissues of terrestrial mammals, regardless of collection locale, are low and seldom exceed 29 mg/kg DW, except kidneys (108 mg/kg DW) and livers (1078 mg/kg DW) from animals near a copper refinery.

Copper deficiency is not a major public health concern in the United States, although skeletal deformities and leg fractures may occur in some copper-deficient children. Copper deficiency effects occur, however, in various species of terrestrial plants (reduced growth, necrosis, reduction in number of pollen grains, death), chickens (poor growth, high frequency of cardiovascular and skeletal lesions, low survival), turkeys (sudden death), rats (defective hemoglobin synthesis, lesions of the central nervous system, low survival, altered blood and liver enzyme activities), guinea pigs (lesions of the central nervous system), dogs (leg fractures), sheep and other ruminant mammals (sudden death, skeletal deformities), pigs (poor growth, decreased hemoglobin and erythrocytes, skeletal deformities), mink (reduced survival), and camels (anemia, emaciation, falling, fractures, death).

Data are scarce or missing on copper deficiency effects in aquatic flora and fauna and in avian and terrestrial mammalian wildlife; additional studies of copper deficiency in these groups are merited. In sensitive terrestrial agricultural crops, copper deficiency occurs at less than 1.6 mg

dissolved Cu/kg DW soil and less than 5 mg total Cu/kg DW leaves. For domestic chickens, copper deficiency occurs when diets containing less than 2.7 mg Cu/kg ration are fed. Male weanling rats show deficiency effects when fed diets containing 0.13 mg Cu/kg ration vs. a copper-normal diet of 5.7 mg Cu/kg ration; earliest signs of copper deficiency in rats include low concentrations of copper in livers (less than 3.0 mg/kg DW vs. 12.6 to 15.0 mg/kg DW in controls), reductions in activities of cytochrome oxidase and succinoxidase, and prolonged sleeping times. Ewes of Bactrian camels fed copper-deficient diets of less than 2.5 mg Cu/kg DW ration (vs. normal diet of about 11.0 mg Cu/kg DW) produce a high frequency of swaybacked lambs. Copper deficiency in mink is produced at daily intake rates equivalent to 3.5 mg Cu/kg BW for 50 weeks. Swine require high intakes of copper to avoid deficiency; daily intakes of less than 36 mg Cu/kg BW are associated with reductions in growth rate, hemoglobin, and hematocrit.

Copper and its compounds are not carcinogenic, mutagenic, or teratogenic at environmentally realistic concentrations, but under controlled conditions of grossly elevated exposures some studies suggest that copper is a potential carcinogen in rodents; mutagen in rodents, sheep, and grasshoppers; and teratogen in fish and small laboratory animals. More research is needed in this area.

Bioavailability and toxicity of copper to aquatic organisms depends on the total concentration of copper and its speciation. Both availability and toxicity are significantly reduced by increased loadings of suspended solids and natural organic chelators and increased water hardness. Toxicity to aquatic life is related primarily to the dissolved cupric ion (Cu^{+2}) and possibly to some hydroxyl complexes. Cupric copper (Cu^{+2}) is the most readily available and toxic inorganic species of copper in fresh water, seawater, and sediment interstitial waters. Cupric ion accounts for about 1% of the total dissolved copper in seawater and less than 1% in fresh water. In fresh water, cupric copper and some copper hydroxyl species are correlated with high toxicity to aquatic life, although carbonato species are much less toxic than other copper complexes. More research seems needed on the adsorption characteristics of most cupric ion complexes. In solution, copper interacts with numerous inorganic and organic compounds resulting in altered bioavailability and toxicity. Acknowledgment of these interactions is essential to the understanding of copper toxicokinetics. In aquatic invertebrates, copper disrupts gill epithelium at high concentrations, and in fishes it interferes with osmoregulation; death is caused by tissue hypoxia associated with disrupted ATP synthesis. Copper detoxifying mechanisms in fishes include the induction of metallothioneins, allowing copper retention for weeks or months after absorption without toxicity. In higher vertebrates, excess copper is cytotoxic and alters protein configuration and lipid peroxidation rates. Mechanisms implicated in copper poisoning of mammals include free radical production, alteration in activities of several enzymes, and inhibited metallothionein synthesis. In mammals, copper is normally excreted via the bile in association with glutathione or unidentified high-molecular-weight proteins.

Excess copper is toxic to representative species of plants and animals. Significant adverse effects in terrestrial plants occur at concentrations as low as 40 μg Cu/L of nutrient solution, more than 10 mg Cu/kg DW in leaves, and greater than 60 mg extractable Cu/kg DW of soil. Sensitive species of terrestrial invertebrates show a reduction in growth, survival or reproduction at more than 50 mg Cu/kg diet or 53 to 70 mg Cu/kg DW of soil. Many species of freshwater plants and animals die within 96 h at waterborne copper concentrations of 5.0 to 9.8 μg Cu/L, and sensitive species of freshwater molluscs, crustaceans, and fishes die at 0.23 to 0.91 μg Cu/L within 96 h. The most sensitive tested species of marine molluscs, crustaceans, and fishes have an LC50 (96 h) range from 28 to 39 μg Cu/L; significant sublethal effects to representative species of estuarine algae, molluscs, and arthropods frequently occur at 1 to 10 μg Cu/L. Mammals and birds are at least 100 times more resistant to copper than other organisms, but ruminant mammals are significantly more sensitive to copper than nonruminant animals and poultry. Excessive dietary intakes of copper by 20- to 50-fold over normal levels may, however, have serious adverse effects on birds and mammals. No data are available on copper toxicity to avian wildlife. Studies with poultry demonstrate that copper accumulates in livers at dietary concentrations as low as 15 mg Cu/kg DW ration, inhibits growth at 120 mg Cu/kg DW ration, and causes gizzard histopathology at 250 mg Cu/kg DW ration.

Copper is lethal to representative species of mammals through a variety of routes: single oral doses of 6 to 637 mg Cu/kg BW in humans and 200 mg/kg BW in cattle or diets with more than 80 mg Cu/kg ration (about 5.1 to 10.7 mg Cu/kg BW daily) fed to sheep or more than 238 mg/kg ration (more than 133 mg/kg BW daily) fed to rats. Adverse sublethal effects of copper to sensitive mammals occur:

- In human infants at drinking water concentrations greater than 3 mg/L
- In cattle at more than 4.2 mg/kg BW by way of drinking water or more than 20 mg/kg BW via diet
- In sheep given daily oral doses of 7.5 to 15.0 mg/kg BW or fed diets containing more than 37.3 mg/kg ration
- In rats given more than 7.9 mg/kg BW daily by way of diet (equivalent to more than 100 mg Cu/kg DW ration)
- In pigs at more than 14.5 mg/kg BW daily via diet.

Numerous and disparate copper criteria are proposed for protecting the health of agricultural crops, aquatic life, terrestrial invertebrates, poultry, laboratory white rats, and humans ([Table 3.8](#)); however, no copper criteria are now available for protection of avian and mammalian wildlife, and this needs to be rectified. Several of the proposed criteria do not adequately protect sensitive species of plants and animals and need to be reexamined. Other research areas that merit additional effort include biomarkers of early copper stress; copper interactions with interrelated trace elements in cases of deficiency and excess; copper status effects on disease resistance, cancer, mutagenicity, and birth defects; mechanisms of copper tolerance or acclimatization; and chemical speciation of copper, including measurement of flux rates of ionic copper from metallic copper.

3.10 LITERATURE CITED

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CHAPTER 4

Lead

4.1 INTRODUCTION

Lead (Pb) has been known for centuries to be a cumulative metabolic poison; however, acute exposure is lessening. Of greater concern is the possibility that continuous exposure to low concentrations of the metal as a consequence of widespread environmental contamination may result in adverse health effects (Nriagu 1978b). Environmental pollution from lead is now so high that body burdens in the general human population are closer than the burdens of any other toxic chemical to those that produce clinical poisoning (Hejtmancik et al. 1982). Further, lead is a mutagen and teratogen when absorbed in excessive amounts, has carcinogenic or cocarcinogenic properties, impairs reproduction and liver and thyroid functions, and interferes with resistance to infectious diseases (U.S. Environmental Protection Agency [USEPA] 1979). In the United States, about 9% of the children aged 1 to 5 years have blood lead levels $>100 \mu\text{g/L}$, high enough to produce adverse health effects (Ronis et al. 1998c). Among non-Hispanic black children in this age group, about 21% had blood lead levels $>100 \mu\text{g/L}$ and 4.2% had $>200 \mu\text{g/L}$. In some undeveloped Asiatic and eastern European countries blood lead concentrations $>1000 \mu\text{g/L}$ occur in children living near lead smelters (Ronis et al. 1998c).

Ecological and toxicological aspects of lead and its compounds in the environment have been extensively reviewed (Wetmore 1919; Bellrose 1959; Aronson 1971; Barth et al. 1973; National Research Council of Canada [NRCC] 1973; Holl and Hampp 1975; Boggess 1977; Rolfe and Reinbold 1977; Forbes and Sanderson 1978; Nriagu 1978a, 1978b; USEPA 1979, 1980, 1985; Levander 1979; Tsuchiya 1979; Branica and Konrad 1980; Jenkins 1980; National Academy of Sciences [NAS] 1980; Eisler 1981, 1988; Harrison and Laxen 1981; Demayo et al. 1982; Mudge 1983; De Michele 1984; Feierabend and Myers 1984; Walsh and Tilson 1984; Lumeij 1984; Feierabend and Russell 1986; U.S. Fish and Wildlife Service [USFWS] 1986a; Kania and Nash 1986; Lansdown and Yule 1986; McDonald 1986; Sanderson and Bellrose 1986; Pain 1987; Albert and Badillo 1991; U.S. Public Health Service [USPHS] 1993; Blus 1994). There is agreement by all authorities on five points. First, lead is ubiquitous and is a characteristic trace constituent in rocks, soils, water, plants, animals, and air. Second, more than 4 million metric tons of lead are produced worldwide each year, mostly for the manufacture of storage batteries, gasoline additives, pigments, alloys, and ammunition. The widespread broadcasting of lead through anthropogenic activities, especially during the past 40 years, has resulted in an increase in lead residues throughout the environment — an increase that has dislocated the equilibrium of the biogeochemical cycle of lead. Third, lead is neither essential nor beneficial to living organisms; all existing data show that its metabolic effects are adverse. Fourth, lead is toxic in most of its chemical forms and can be incorporated into the body by inhalation, ingestion, dermal absorption, and placental transfer to the fetus. Fifth, lead is an accumulative metabolic poison that affects behavior, as well as the

hematopoietic, vascular, nervous, renal, and reproductive systems. In humans, lead causes stillbirths, miscarriages, inhibited development of fetuses, decreased male fertility, and abnormal sperm. Severe damage to the central nervous system from exposure to large amounts of lead may result in stupor, convulsions, coma, and death. Children who survive lead poisoning are often permanently retarded or have permanent neurological handicaps. At subclinical injury levels, lead causes slight, but irreversible, damage to brain development in growing children.

Natural resources are also affected by environmental lead contamination, and some wildlife species numbers may be reduced as a result. For example, waterfowl deaths resulting from the ingestion of spent lead shot pellets from shotgun shells were discovered more than 100 years ago in Italy and in the United States; since then, lead poisoning of waterfowl has occurred in 20 countries (Pain et al. 1995). In North America alone, approximately 3000 tons of lead shot are expended annually into lakes, marshes, and estuaries by several million waterfowl hunters (USFWS 1986, 1987). Spent pellets are eaten by waterfowl and other birds, because they mistake them for seeds or for pieces of grit. These pellets may be retained in the gizzard for weeks, where they are reduced chemically and mechanically, form soluble toxic salts, and cause characteristic signs of lead intoxication — especially lethargy and emaciation (Street 1983). At least 2% of all North American waterfowl — or about 2 million ducks and geese (Lumeij 1985) — die each year as a direct result of ingesting lead shot (Bellrose 1951). These deaths contribute to the decline of some species, such as the canvasback, *Aythya valisineria* (Dieter 1979), pintail, *Anas acuta* (White and Stendell 1977), northern pintail, *Anas acuta* (Mateo et al. 1997b), black duck, *Anas rubripes* (Pain and Rattner 1988), common pochard, *Aythya ferina* (Mateo et al. 1997b), spectacled eiders, *Somateria fischeri* (Flint et al. 1997), graylag goose, *Anser anser* (Mateo et al. 1998), and mute swan, *Cygnus olor* (O'Halloran et al. 1988; Blus 1994). Up to seven times more waterfowl died from lead toxicosis as a result of ingesting spent pellets than from wounding by hunters (Zwank et al. 1985). In addition, lead-poisoned waterfowl show delayed mortality from lead-induced starvation, are readily captured by predators, are susceptible to disease, and reproduce poorly (Dieter 1979). Susceptibility is markedly influenced by species, by the number and size of shot ingested, and by the types of foods eaten (White and Stendell 1977). Swans are among the more vulnerable waterfowl. In England, lead poisoning through the ingestion of discarded lead fishing sinkers was the major cause of death in the mute swan (Birkhead 1983). For all species of swans in England, about half died as a direct result of lead poisoning (Demayo et al. 1982). In Washington State, 30% of the endangered trumpeter swans (*Cygnus buccinator*) found dead had died of lead poisoning from ingestion of lead shot (Kendall and Driver 1982; Blus 1994; Lagerquist et al. 1994). Fatal lead poisoning of swans through ingestion of shotgun pellets, fishing sinkers, and lead-contaminated sediments is reported in several geographic locations (Koh and Harper 1988; Sears 1988; Spray and Milne 1988; Blus et al. 1989, 1991; Degernes 1991; Lesher 1991; Beyer et al. 1998a). Lead toxicosis from ingested fishing sinkers was the most common cause of death in adult breeding loons (*Gavia immer*) in New England, and may be an important factor limiting loon populations (Pokras and Chafel 1992).

Lead poisoning mortality has occurred in over 30 species of birds other than waterfowl (Pain et al. 1997). Lead toxicosis caused by ingestion of spent shot and other lead objects was reported for the whooping crane, *Grus americana* (Snyder et al. 1992), sandhill crane, *Grus canadensis* (Windingstad et al. 1984), mourning dove, *Zenaidura macroura* (Locke and Bagley 1967), and wild turkey, *Meleagris gallopavo* (Stone and Butkas 1978). Secondary poisoning has been documented in at least six species of raptors that ate food containing lead shot (especially hunter-wounded animals): golden eagle, *Aquila chrysaetos* (Bezzel and Funfstuck 1995), Andean condor, *Vultur gryphus* (Locke et al. 1969), bald eagle, *Haliaeetus leucocephalus* (Pattee and Hennes 1983), honey buzzard, *Pernis apivorus* (Lumeij et al. 1985); king vulture, *Sarcorhampus papa* (Decker et al. 1979), and California condor *Gymnogyps californianus* (Janssen et al. 1986).

The availability of lead-based paints, discarded oil filters, used crankcase oil, lead storage batteries, or pastures contaminated by industrial lead operations make lead one of the most common

causes of accidental poisoning in domestic animals (Demayo et al. 1982). Cattle and horses in the vicinity of a lead smelter in California developed signs of lead poisoning, and many died between 1880, when the smelter opened, and 1971, when the smelter closed (Burrows 1981). Of the mules used in the early mining of lead, all died during their first year of service (Burrows 1981). Lead toxicosis has been reported in buffalos and cattle in India after they ate green fodder near a factory that recycled lead from old batteries (Kwatra et al. 1986). Total milk yield declined sharply, and stillbirths and abortions increased significantly in cattle that ingested lead-contaminated hay; the field from which the hay had been cut had a history as a site for clay pigeon shoots and contained an estimated 3.6 tons of lead shot pellets (Frape and Pringle 1984). In sheep grazing in areas near lead mines, the frequency of abortions was high, and the learning behavior of the lambs was impaired (Demayo et al. 1982). Many species of zoo animals, including monkeys, fruit-eating bats, and parrots, have been fatally poisoned from ingestion of flaking lead-based paint on the walls and bars of their cages (NRC 1973). Ingestion of lead-based paint chips was one cause of epizootic mortality of fledgling Laysan albatross, *Diomedea immutabilis*, at Midway Atoll in 1983 (Sileo and Fefer 1987). At present, there is no known dietary requirement for lead in domestic animals, nor has it been shown unequivocally that lead plays any beneficial role (NRCC 1973). On the contrary, lead demonstrably and adversely affects weight, survival, behavior, litter size, and skeletal development (Tsuchiya 1979), and induces teratogenic and carcinogenic responses in some species of experimental animals (NRCC 1973; USEPA 1980).

Lead is not essential for plants, and excessive amounts can cause growth inhibition, as well as reduced photosynthesis, mitosis, and water absorption (Demayo et al. 1982). The decline of some European spruce forests has been attributed to excessive concentrations of lead in the atmosphere (Backhaus and Backhaus 1986). Lead is toxic to all phyla of aquatic biota, though effects are modified significantly by various biological and abiotic variables (Wong et al. 1978). Wastes from lead mining activities have severely reduced or eliminated populations of fish and aquatic invertebrates, either directly through lethal toxicity or indirectly through toxicity to prey species (Demayo et al. 1982). Health advisories warning anglers against eating lead-contaminated fish have been posted in Missouri (Schmitt and Finger 1987). The significant increases in lead concentration shown by marine corals between 1954 and 1980 were representative of the increases noted in other biota as a direct result of increased global lead availability during that period (Dodge and Gilbert 1984).

4.2 SOURCES AND USES

Lead is a comparatively rare metal, with an average abundance in the earth's crust of 16 mg/kg (EPA 1980); it is also a major constituent of more than 200 identified minerals, of which only three are sufficiently abundant to form mineral deposits (USEPA 1980): galena (PbS), angleside ($PbSO_4$), and cerusite ($PbCO_3$). Galena, the primary form of lead in the natural state, is often associated with sphalerite (ZnS), pyrite (FeS_2), chalcopyrite ($CuFeS_2$), and other sulfur salts (May and McKinney 1981). Most (88%) of the domestic primary lead production originates from stratabound deposits in southeastern Missouri, another 8% from Idaho's Coeur d'Alene district, and the rest from deposits in Colorado and Utah. Primary lead is smelted and refined at plants in Texas, Montana, Nebraska, Missouri, and Idaho. Scrap or secondary lead accounted for about half the domestic consumption in 1978; by 1980, more lead was produced from secondary sources than from domestic ores (May and McKinney 1981). In 1989, nine mines in southeastern Missouri produced 89% of the total domestic output of lead ores and concentrates; other mines in Idaho, Alaska, and Montana contributed 10.4% of the domestic output; the remainder was a by-product from the mining of other commodities in Arizona, California, Colorado, Idaho, Illinois, Nevada, New Mexico, Tennessee, and Utah (USPHS 1993).

About 4 million tons of lead are refined annually worldwide (Table 4.1). Domestic lead consumption is 1.3 million tons annually, of which about half is used in storage battery manufacture

Table 4.1 World Lead Production, Consumption, and Principal End Uses

Production Consumption, and Use	Metric Tons, in thousands
Production, 1978	
Mined lead	3625
Refined lead	4202
Consumption	
1977	2995
1980	3801
Principal End Uses of Refined Lead	
1977	
Storage batteries	1478
Pigments and chemicals	369
Tetraalkyllead	292
Cable covering	216
Pipe and sheeting	160
Other	480
1980	
Storage batteries	1330
Tetraethyllead	380
Cable covering	380
Solder	380
Litharge	190
Building construction	190
Caulking	190
Other	760

Modified from Harrison, R.M. and D.P.H. Laxen. 1981. *Lead Pollution. Causes and Control.* Chapman and Hall, NY. 168 pp.; Demayo, A., M.C. Taylor, K.W. Taylor, and P.V. Hodson. 1982. Toxic effects of lead and lead compounds on human health, aquatic life, wildlife plants, and livestock. *CRC Crit. Rev. Environ. Control* 12:257-305.

and, until recently, about 20% in the manufacture of gasoline antiknock additives such as tetramethyllead (TML) and tetraethyllead (TEL) (Table 4.2). Domestic use in 1990 was 1.28 million tons, most of which was used in the manufacture of lead-acid storage batteries (80%), as well as ammunition and metal alloys (12.4%), and the rest in ceramics, ballast, oxides, and gasoline additives (USPHS 1993). New uses of lead that seem environmentally innocuous include protection shielding against radiation exposure in computers, televisions, and certain medical instruments; in lead alloy solders; in super conductors; to manufacture certain ceramics and precision glass products; and in energy generation (USPHS 1993). Lead enters the atmosphere mainly through smelter emissions, primarily as PbSO₄ and PbO-PbSO₄, and through vehicle emissions, which include unburned lead, TEL, TML, and various lead halides, sulfates, phosphates, and oxides (Harrison and Laxen 1981). The primary method of lead disposal is recycling, estimated at 50,000 tons annually in the United States (USPHS 1993). Domestically, 70 to 75% of the consumed lead is considered to be recyclable, mostly from lead-acid storage batteries. Municipal and hazardous waste landfills receive about 25,000 tons of lead wastes annually, usually from ammunition and ordnance (USPHS 1993).

Lead and its compounds have been known to humans for about 7000 years, and lead poisoning has occurred for at least 2500 years (Barth et al. 1973). In Egypt, between 5000 and 7000 BCE, lead was used for glazing pottery, solder, ornaments, net sinkers, anchors, caulking, coins, weights, aqueducts, piping, and cooking utensils (Nriagu 1978a). The biocidal properties of lead were familiar to the ancient Egyptians, and they sometimes used lead salts for homicidal purposes (De Michele 1984). Lead encephalopathy (inflammation of the brain) has been recognized since 400 BCE among workers in the lead trades; initial symptoms are dullness, irritability, ataxia, headaches, memory loss, and restlessness. These symptoms often progressed to delirium, mania, coma, convulsions, and sometimes death. The same general effects were described in young children and infants, among which mortality was sometimes 40% (USEPA 1980). Extensive use of lead by

Table 4.2 Use Patterns for Lead in Selected Countries

Use	Thousands of Metric Tons (percent)		
	USA	Europe ^a	Japan
Storage batteries	613 (47)	392 (34)	93 (40)
Cable sheathing	14 (1)	145 (13)	16 (7)
Pigments and chemicals	303 (23)	294 (26)	62 (27)
Alloys	75 (6)	50 (4)	15 (7)
Ammunition	66 (5)	^b (—)	^b (—)
Other	226 (18)	267 (23)	44 (19)
Total	1297	1148	230

^aFrance, West Germany, Italy, UK^bNot reported.

From U.S. Environmental Protection Agency (USEPA). 1979. The health and environmental impacts of lead and an assessment of a need for limitations. *U.S. Environ. Protection Agency Rep.* 560/2-79-001. 494 pp.

the Romans, circa 500, in pipes for water transport, in cosmetics, and as a wine sweetener (Harrison and Laxen 1981), is estimated to have increased environmental lead levels to about five times the existing background levels (Eisenreich et al. 1986). The decline of the Roman Empire may have been hastened by endemic lead poisoning — a theory supported by residue data showing high lead concentrations in bones and remains of Roman aristocrats (Nriagu 1978a) — perhaps through ingestion of excessive amounts of wine laced with lead (De Michele 1984). After the fall of the Romans, the use of lead declined sharply. In the 14th century, gunpowder was introduced into Europe and was the impetus for the development of a weapon that fired a malleable metal pellet: a lead shot (USEPA 1979). Otherwise, the metal's resistance to corrosion led to its use as lead sheets applied as roofing for cathedrals and as protective encasement of underground pillars.

In 1721, the first lead mine was established in the New World by English settlers at Falling Creek, Virginia, primarily to supply bullets and shot (USEPA 1979). By 1750, European and British lead smelting operations were flourishing (Nriagu 1978a). In 1763, lead deposits in southeastern Missouri were permanently opened (USEPA 1979). The 18th century's Industrial Revolution produced an estimated tenfold increase in existing lead background levels (Eisenreich et al. 1986). In the late 1700s, symptoms of acute lead poisoning recorded among industrial workers were called "Mill Reek" or "Devonshire Colic" (NRCC 1973). Lead poisoning in Mexico was documented in 1878 among users of lead salts for glazing ceramics, a practice that persists today (Albert and Badillo 1991). Lead poisoning was frequently recorded among U.S. lead miners in 1870 through 1900, especially in Utah, Colorado, and New Mexico. By 1880, the United States had surpassed Germany and Spain in the mining and refining of lead, and has continued as the leader in the output of refined lead (USEPA 1979). Air pollution from combustion of leaded gasoline containing TEL rose in the 1920s (NRCC 1973). In the mid-1940s, atmospheric lead concentrations increased sharply due to massive increases in lead emissions from automobiles. Since then, increased lead emissions to the atmosphere have matched trends in gasoline lead content and consumption (Eisenreich et al. 1986; Smith et al. 1987). In 1957, the United States was overtaken by Australia and the U.S.S.R. in domestic mine production of lead; however, in 1967, the opening of the "New Lead Belt" in Missouri revived mining in the United States, and subsequently lead was produced at the annual rate of 450,000 to 550,000 metric tons (USEPA 1979). In 1975, the United States was again the leading lead producer from mine sources, accounting for 16% of the world total; at that time, about 70% of the world lead production came from the U.S., the U.S.S.R., Australia, Canada, Peru, Mexico, China, Yugoslavia, and Bulgaria (Tsuchiya 1979.). In 1986, world mine production of lead was 2,352,000 tons, of which U.S. mine production was 353,000 tons, or 15% of the world total, and production in Missouri was 308,000 tons, or 87% of the U.S. total (personal communication, R. L. Amistadi, Doe Run Company, St. Louis, Missouri). In 1987, the leading lead producers of

the world produced 2,110,000 metric tons: the U.S.S.R. produced 24% of the total, Australia 23%, Canada 20%, the U.S. 15%, Mexico 9%, and Peru 9% (Albert and Badillo 1991).

Human exposure to lead sources is highly variable. In Mexico, for example, lead exposure is comparatively elevated in workers who manufacture or use lead-glazed pottery, urban populations exposed to high air lead concentrations due to the continued use of lead fuel additives, workers in industries that manufacture ballast and pigments, consumers who routinely eat canned foods such as hot peppers (2.4 mg Pb/kg) and fruit products (2.1 mg Pb/kg), and for the general population living in the vicinity of smelters, refineries, and other industries that emit lead (Albert and Badillo 1991). In the United States, consumption of leaded gasoline in automobiles was completely phased out in 1980; however, leaded gasoline is still available at airport pumps for propelled aircraft and this, as well as leaky underground fuel storage tanks, comprise potential sources of human exposure (Mulroy and Ou 1998).

4.3 CHEMICAL PROPERTIES

Elemental lead is a bluish-gray, soft metal of atomic weight 207.19 and atomic number 82; it melts at 327.5°C, boils at 1749°C, and has a density of 11.34 g/cm³ at 25°C. Metallic lead is sparingly soluble in hard, basic waters to 30 µg/L, and up to 500 µg/L in soft, acidic waters. Lead has four stable isotopes: Pb-204 (1.5%), Pb-206 (23.6%), Pb-207 (22.6%), and Pb-208 (52.3%). Of its 24 radioactive isotopes, two (Pb-210, Tb 1/2 of 22 years; Pb-212, Tb 1/2 of 10 hours) have been used in tracer experiments. Lead occurs in four valence states: elemental (Pb⁰), monovalent (Pb⁺), divalent (Pb⁺²), and tetravalent (Pb⁺⁴); all forms are environmentally important, except possibly Pb⁺. In nature, lead occurs mainly as Pb⁺²; it is oxidized to Pb⁺⁴ only under strong oxidizing conditions, and few simple compounds of Pb⁺⁴ other than PbO₂ are stable. Some lead salts are comparatively soluble in water (lead acetate, 443 g/L; lead nitrate, 565 g/L; lead chloride, 9.9 g/L), whereas others are only sparingly soluble (lead sulfate, 42.5 mg/L; lead oxide, 17 mg/L; lead sulfide, 0.86 mg/L); solubility is greatest at elevated temperatures in the range 0 to 40°C. Of the organoleads, tetraethyllead (TEL) and tetramethyllead (TML) are the most stable and the most important because of their widespread use as antiknock fuel additives. Both are clear, colorless, volatile liquids, highly soluble in many organic solvents; however, solubility in water is only 0.18 mg/L for TEL, and 18.0 mg/L for TML. Boiling points are 199°C for TEL and 110°C for TML. Both undergo photochemical degradation in the atmosphere to elemental lead and free organic radicals, although the fate of automotive organoleads has yet to be fully evaluated. Additional information on the general chemistry of lead and its compounds was reviewed by NRCC (1973), Boggess (1977), Nriagu (1978a), USEPA (1979, 1980), Tsuchiya (1979), Harrison and Laxen (1981), and Demayo et al. (1982).

Lead chemistry is complex. In water, for example, lead is most soluble and bioavailable under conditions of low pH, low organic content, low concentrations of suspended sediments, and low concentrations of the salts of calcium, iron, manganese, zinc, and cadmium. Accordingly, solubility of lead is low in water, except in areas of local point source discharges (Harrison and Laxen 1981; Scoullos 1986). Lead and its compounds tend to concentrate in the water surface microlayer (i.e., the upper 0.3 mm), especially when surface organic materials are present in thin films (Demayo et al. 1982). Organolead compounds are generally of anthropogenic origin and are found mostly in the aquatic environment as contaminants. However, some organolead complexes form naturally, and their rate of formation may be affected by man-made organoleads (Nriagu 1978a). In surface waters, lead exists in three forms: dissolved labile (e.g., Pb⁺², PbOH⁺, PbCO₃), dissolved bound (e.g., colloids or strong complexes), or as a particulate (Benes et al. 1985). The labile forms represent a significant part of the Pb input from washout of atmospheric deposits, whereas particulate and bound forms were common in urban runoff and ore-mining effluents (Benes et al. 1985). The solubility of lead compounds in water is pH dependent, and ranges from about 10 g Pb/L at pH 5.5, to less than 1 µg Pb/L at pH 9.0 (USEPA 1980); little detectable lead remains in solution at pH >8.0.

(Prause et al. 1985). At pH 6.5 and water alkalinity of 25 mg CaCO₃/L, elemental Pb⁺² is soluble to 330 µg/L; however, Pb⁺² under the same conditions is soluble to 1000 µg/L (Demayo et al. 1982). In acidic waters, the common forms of dissolved lead are salts of PbSO₄ and PbCl₄, ionic lead, cationic forms of lead hydroxide, and (to a lesser extent) the ordinary hydroxide Pb(OH)₂. In alkaline waters, common species include the anionic forms of lead carbonate and hydroxide, and the hydroxide species present in acidic waters (NRCC 1973). Unfortunately, the little direct information available about the speciation of lead in natural aqueous solutions has seriously limited our understanding of lead transport and removal mechanisms (Nriagu 1978a).

Most lead entering natural waters is precipitated to the sediment bed as carbonates or hydroxides (May and McKinney 1981). Lead is readily precipitated by many common anions; desorption and replacement by other cations is extremely slow (Boggess 1977). In some acidic lakes, the deposition of particulate lead correlated strongly with the deposition of aluminum and carbon, especially during periods of increasing pH (White and Driscoll 1985). Precipitation of sparingly soluble lead compounds is not a primary factor controlling the concentration of dissolved lead in stream waters. Migration and speciation of lead was strongly affected by water flow rate, with increasing flow rate resulting in increased concentrations of particulate and labile lead and a decrease in bound forms. At low stream flow, lead was rapidly removed from the water column by sedimentation (Benes et al. 1985).

In the sediments, lead is mobilized and released when the pH decreases suddenly or ionic composition changes (Demayo et al. 1982). However, there was no significant release of lead from dredge spoils suspended in estuarine waters of different salinities for 4 weeks (Prause et al. 1985). Some Pb⁺² in sediments may be transformed to tetraalkyllead compounds, including TML, through chemical and microbial processes. There is also the possibility of methylation of ionic lead *in vivo* by fish and other aquatic biota, but the mechanisms are unclear (May and McKinney 1981). Methylation of lead in sediments was positively related to increasing temperatures, reduced pH, and microbial activity, but seemed to be independent of lead concentration (Demayo et al. 1982). In general, the concentration of tetraalkylleads in sediments is low, representing less than 10% of total lead (Chau et al. 1980).

Degradation of tetraethyllead in soils not contaminated with gasoline is complete in 14 days (Mulroy and Ou 1998). In subsoils contaminated with lead gasoline, however, 4 to 17% of the applied TEL was still present after 77 days. The retardation of TEL degradation in leaded gasoline-contaminated soils is attributed to the presence of gasoline hydrocarbons. As long as gasoline hydrocarbons remain in the soil, TEL may also remain, most likely in the gasoline hydrocarbon phase (Mulroy and Ou 1998).

4.4 MODE OF ACTION

Lead modifies the function and structure of kidney, bone, the central nervous system, and the hematopoietic system and produces adverse biochemical, histopathological, neuropsychological, fetotoxic, teratogenic, and reproductive effects (Boggess 1977; Nriagu 1978b; De Michele 1984; Eisler 1988; Hsu et al. 1998). The mechanism underlying lead-induced growth suppression is thought to involve disruption of pituitary growth hormone during puberty (Ronis et al. 1998a). Inorganic lead absorbed into the mammalian body enters the bloodstream initially and attaches to the red blood cell. There is a further rapid distribution of the lead between blood extracellular fluid and other storage sites that is so rapid that only about half the freshly absorbed lead remains in the blood after a few minutes. The storage sites for lead are uncertain, although they are probably in soft tissues as well as bone; the half-time residence life (T_b 1/2) of inorganic lead is estimated to be 20 days in blood, 28 days in whole body, and 600 to 3000 days in bone (Harrison and Laxen 1981). Lead levels in bone exert an influence on plasma lead levels. There is concern that previously accumulated lead stores in bone may constitute an internal source of exposure, particularly during

periods of increased bone mineral loss, such as pregnancy or lactation (Hernandez-Avila 1998). Inorganic lead in the environment can be biologically methylated to produce alkyllead compounds (Walsh and Tilson 1984). Bile is an important route of excretion; ingested lead probably proceeds sequentially from gut, to blood, to bone and soft tissue, and by way of the bile to small intestine and fecal excretion (De Michele 1984).

Tetraalkyllead mode of action differs from that of inorganic lead. Although initial entry is still by way of the bloodstream, the lead is evenly distributed between blood plasma and the red blood cells. Tetraalkylleads are lost rapidly from the bloodstream, although some reappear in 5 to 10 hours associated exclusively with the red blood cells, probably as trialkyllead, though a fraction may be converted to inorganic lead. The organoleads concentrate in liver, and it is there that tetraalkyllead is probably converted to trialkyllead. Otherwise, the lead is widely dispersed throughout the body with $T_{1/2}$ values of 200 to 350 days (Harrison and Laxen 1981). Tetraethyllead, by virtue of its high solubility in lipids, is rapidly accumulated in non-bony tissues, particularly the brain, where the onset of signs of poisoning is rapid (Nriagu 1978b). Short-term repeated exposures of rats (*Rattus* spp.) to TEL results in a neurotoxic syndrome consisting of altered reactivity to noxious stimulation through disruption of forebrain-area function (Hong et al. 1983). In marine systems, unstable TEL is rapidly accumulated by marine organisms, probably through controlled diffusion processes. Once assimilated, this compound can be dealkylated into an ionized chemical species and react at the molecular level within the cells (Gnassia-Barelli and Romeo 1993). Several fish species metabolize tetraalkylleads to trialkyllead compounds by way of their mixed function oxidase system (Wong et al. 1981). The trialkyllead derivatives are considered responsible for the toxicity of the parent compound (Walsh and Tilson 1984). Trialkylleads and dialkylleads rapidly traverse biological membranes in bird eggs and accumulate in the yolk and developing embryo (Forsyth et al. 1985). At present, the organolead mode of action is poorly understood, but organolead compounds are known to inhibit amino acid transport, uncouple oxidative phosphorylation, and inhibit cerebral glucose metabolism (Hong et al. 1983).

Biochemically, lead exerts deleterious effects on hematopoiesis through derangement of hemoglobin synthesis, resulting in a shortened life span of circulating erythrocytes, often resulting in anemia. Two essential enzymes in heme formation that are extremely sensitive to lead are delta aminolevulinic acid dehydratase (ALAD), which catalyzes the dehydration of delta amino levulinic acid (ALA) to form porphobilinogen (PBG), and ferrochelatase (= heme synthetase), which catalyzes the insertion of Fe^{+2} into protoporphyrin IX (PP). This second reaction requires the presence of glutathione and ascorbic acid. Some of the intermediates in heme follow sequentially: ALA, PBG, uroporphyrinogen III, coproporphyrinogen III, protoporphyrinogen IX, and PP. It is now well established that ALAD and ferrochelatase are the most sensitive biochemical indicators of lead exposure, the net result being lowered ALAD activity and elevated PP activity (Barth et al. 1973; Nriagu 1978b; USEPA 1979, 1980; Tsuchiya 1979; Harrison and Laxen 1981; Hoffman et al. 1981; De Michele 1984; Schmitt et al. 1984, 1993; Lumeij 1985; Scheuhammer 1989; USPHS 1993). An increase in glutathione content observed in lead-exposed fish may be due to an increase in glutathione synthesis rather than to a decrease in use of the tripeptide or to its sequestration by lead (Thomas and Juedes 1992).

Inhibition of blood ALAD activity after exposure to lead has been documented in many species of freshwater and marine teleosts (Hodson 1976; Hodson et al. 1977, 1980; Johansson-Sjöbeck and Larsson 1979; Krajnovic-Ozretic and Ozretic 1980; Demayo et al. 1982; Schmitt et al. 1984, 1993; Haux et al. 1986), in the freshwater cladoceran, *Daphnia magna* (Berglind et al. 1985), in ducks, quail, doves, swallows, raptors, and songbirds (Finley et al. 1976.; Dieter and Finley 1978; Dieter 1979; Hoffman et al. 1981; Franson and Custer 1982; Kendall et al. 1982; Kendall and Scanlon 1982; Eastin et al. 1983; Franson et al. 1983; Hoffman et al. 1985a, 1985b; Beyer et al. 1988; Scheuhammer 1989), and in humans, sheep, mice, rats, rabbits, and calves (Barth et al. 1973; Boggess 1977; Nriagu 1978b; Tsuchiya 1979; Heitmancik et al. 1982; Hayashi 1983; Peter and Strunc 1983; Schlick et al. 1983; Gietzen and Wooley 1984; Zmudzki et al. 1984). Lead-induced ALAD inhibition has been recorded not only in blood, but also in brain, spleen, liver, kidney, and

bone marrow (Johansson-Sjöbeck and Larsson 1979; Hoffman et al. 1981, 1985a, 1985b; Schlick et al. 1983; Friend 1985). Time for ALAD recovery to normal levels is dose dependent, organ specific, and usually directly correlated with blood lead concentrations (Finley et al. 1976; Hodson et al. 1977; Dieter 1979; Hayashi 1983; Friend 1985). ALAD activity levels in lead-stressed teleosts were normal 3 to 11.7 weeks postadministration (Hodson et al. 1977; Johansson-Sjöbeck and Larsson 1979; Krajnovic-Ozretic and Ozretic 1980; Demayo et al. 1982); this range was 2 to 14 weeks in birds (Dieter and Finley 1978; Kendall et al. 1982; Kendall and Scanlon 1982; Friend 1985), and 3 to 12 weeks in mammals (Barth et al. 1973; Schlick et al. 1983). The physiological significance of depressed blood ALAD activity levels, except perhaps as an early indicator of lead exposure, is debatable. Aside from a few instances of moderate anemia in workers at lead smelters, other abnormalities noted were not regarded as serious (Barth et al. 1973 Lead-induced depression in ALAD activity in mallard (*Anas platyrhynchos*) ducklings and ring-necked pheasant (*Phasianus colchicus*) chicks was not associated with signs of overt toxicity (Eastin et al. 1983); a similar case is made for lead-stressed domestic chickens (*Gallus* sp.) showing 98% reduction in ALAD activity (Franson and Custer 1982), and for American kestrel (*Falco sparverius*) showing an 80% reduction (Franson et al. 1983). Birds may be more sensitive than mammals to lead-induced depressions in blood ALAD activity (Dieter et al. 1976). In ducks, for example, inhibition of ALAD would be more harmful than a comparable depression in mammals, for three reasons (Dieter et al. 1976). First, metabolic activity is greater in nucleated duck erythrocytes than in human erythrocytes. Second, ducks require porphyrin synthesis not only for hemoglobin production (as in humans), but also for production of respiratory heme-containing enzymes. Finally, the half-life of erythrocytes is shorter in ducks than in humans: 40 days vs. 120 days.

Elevated blood protoporphyrin IX activity resulting from lead inhibition of heme synthetase has been documented for humans and small mammals (Peter and Strunc 1983) and for many species of birds (Anders et al. 1982; Carlson and Nielsen 1985; Friend 1985; Franson et al. 1986; Beyer et al. 1988); recovery to normal levels occurs in a lead-free environment in 2 to 7 weeks. Franson et al. (1986) endorsed the blood protoporphyrin IX technique instead of ALAD as a means of measuring lead stress because of its comparative simplicity and lower cost.

Other chemical changes that have been observed as a result of lead exposure include:

- Increased serum creatinine and serum alanine aminotransferase in birds, suggestive of kidney and liver alterations (Hoffman et al. 1981)
- Changes in potassium, chloride, glucose metabolism (Haux and Larsson 1982) and calcium binding proteins (Behra 1993) in rainbow trout, *Oncorhynchus mykiss*
- A decrease in brain acetylcholinesterase activity in rats (Gietzen and Wooley 1984).

In kidney, lead tends to accumulate in the proximal convoluted tubule cells of the renal cortex, producing morphological changes such as interstitial fibrosis, edema, and acid-fast intranuclear inclusion bodies, as well as biochemical changes (Locke et al. 1966; Boggess 1977; Nriagu 1978b; USEPA 1980; De Michele 1984). Renal intranuclear inclusion bodies occurred in 83% of mallards experimentally poisoned by dietary lead acetate or lead shot (Beyer et al. 1988); similar results have been reported in other species of birds (Clemens et al. 1975; Anders et al. 1982) and in primates, cattle, and bats (Zook et al. 1972; Osweiler and Van Gelder 1978; Colle et al. 1980; Tachon et al. 1983).

In the cladoceran *Daphnia magna*, about 90% of the total body lead burden is adsorbed to the exoskeleton (Berglind et al. 1985). In animals with a vertebral column, total amounts of lead tend to increase with age. By far the most lead is bound to the skeleton, especially in areas of active bone formation (Barth et al. 1973; Tsuchiya 1979; USEPA 1980; Hejtmancik et al. 1982; Mykkonen et al. 1982; Peter and Strunc 1983; De Michele 1984; Eisler 1984; Berglind et al. 1985; Marcus 1985). The retention of lead stored in bone pools poses a number of difficulties for the usual multicompartmental loss-rate models. Some lead in bones of high medullary content, such as the

femur and sternum, have relatively long retention times, i.e., Tb 1/2 of >20 years in humans, whereas lead stored in bones of low medullary content have Tb 1/2 values of 20 to 200 days, similar to the values for lead in soft tissues and blood (Tsuchiya 1979; Marcus 1985). In birds, medullary bone undergoes sequences of bone formation and destruction associated with the storage and liberation of calcium during eggshell formation, indicating that sex and physiological condition primarily influence lead kinetics in avian bone (Finley and Dieter 1978). Marcus (1985) endorsed the use of diffusion models based on the exchange of lead between blood in canaliculi and the crystalline bone of the osteon to account for retention and bioavailability. More research is needed on the role of bone in lead kinetics.

Lead damages nerve cells and ganglia, and alters cell structure and enzyme function. Axonal degenerative changes, especially in neuronal cell bodies, were recorded in lead-poisoned freshwater snails (*Viviparous ater*), leading to altered protein synthesis (Fantin et al. 1985). Mallards dosed orally with lead shot developed demyelinating lesions in vagal, branchial, and sciatic nerves, and showed vascular damage in the cerebellum; lesions were similar to those in lead-intoxicated guinea pigs (*Cavia* sp.), rats, and guinea hens, *Gallus* sp. (Hunter and Wobeser 1980). Crop stasis in birds, which is characterized by paralysis of the alimentary tract, impaction of food in the gizzard and proventriculus, and regurgitation of crop fluid, has been produced by lead shot or lead acetate solutions. Lead induces crop dysfunction by acting either directly on the smooth muscle or on associated nerve plexuses of crop tissue, depending on the route of administration (Clemens et al. 1975; Boyer et al. 1985; Boyer and Di Stefano 1985). Mammals, including humans, undergo similar alimentary distress following intakes of lead (Boyer et al. 1985).

Effects of lead on the nervous system are both structural and functional, involving the cerebellum, spinal cord, and motor and sensory nerves; the result may be deterioration of intellectual, sensory, neuromuscular, and psychological functions (Nriagu 1978b). The pathogenesis of lead-induced injury to the nervous system is poorly understood, but may be mediated through vascular damage, the direct action of lead on neurons, or alterations in porphyrin metabolism (Hunter and Wobeser 1980). Retarded brain growth in prenatal guinea pigs has been recorded at subclinical levels of lead (i.e., at concentrations producing no elevation in blood lead and no change in body weight), and this effect is potentiated at temperatures of 42°C (Edwards and Beatson 1984). Lead may cause a transient disturbance in the blood-brain barrier during early postnatal growth of rats. This effect is associated with the presence of hemorrhagic lesions, suggesting focal damage to the vessels as an important event in the pathogenesis of lead encephalopathy to suckling rats (Sundstrom et al. 1985). Brain histopathology has been recorded in lead-poisoned chickens (Narbaitz et al. 1985) and cattle (Osweiler and Van Gelder 1978). Brain lead concentrations are usually among the lowest in body organs, but the brain is one of the main sites of action. During chronic lead poisoning, distribution of lead in the brain is positively related to both dose and duration of exposure; preferential accumulation is in the hippocampus area. Significant amounts of lead persisted in rat brain tissue up to 4 weeks after the withdrawal of lead treatment (Collins et al. 1982). The role of organolead compounds in hippocampal function is largely unknown (Czech and Hoium 1984).

Absorption and retention of lead from the gastrointestinal tract, the major pathway of intake, varies widely because of the age, sex, and diet of the organism. Diet is the major modifier of lead absorption and of toxic effects in many species of domestic and laboratory animals, waterfowl, and aquatic organisms. In fact, the lack of certain major minerals in the diet often affected toxicity and storage of lead in tissue more than did doubling the dosages of lead in the diet (Levander 1979). Dietary deficiencies in calcium, zinc, iron, Vitamin E, copper, thiamin, phosphorus, magnesium, fat, protein, minerals, and ascorbic acid increased lead absorption and its toxic effects (Longcore et al. 1974b; Forbes and Sanderson 1978; Levander 1979; Sleet and Soares 1979; Colle et al. 1980; USEPA 1980; Hodson et al. 1980; De Michele 1984; Stone and Fox 1984; Zmudzki et al. 1983, 1984; Carlson and Nielsen 1985; Gilmartin et al. 1985). Toxic effects of lead-stressed fauna also were exacerbated when animals were fed diets containing excess cadmium, lactose, ethylenediaminetetraacetic acid,

zinc, fat, protein, sodium citrate, ascorbate, amino acids, Vitamin D, copper, mercury, fiber content, and nitrilotriacetic acid (Clemens et al. 1975; Forbes and Sanderson 1978; Nriagu 1978b; Levander 1979; USEPA 1980; Krajnovic-Ozretic and Ozretic 1980; Burrows and Borchard 1982; Hamir et al. 1982; Zmudzki et al. 1983, 1984; De Michele 1984; Carlson and Nielson 1985). Protection against various toxic effects of ingested lead was provided by measured dietary supplements of calcium, iron, zinc, ascorbic acid, Vitamin E, and thiamin (Krajnovic-Ozretic and Ozretic 1980; Gilmartin et al. 1985; Ghazaly 1991). Many other conditions affect lead absorption, including size of lead particle (USEPA 1980; Hamir et al. 1982), type of lead compound ingested (USEPA 1980), presence of other compounds that act synergistically (Barth et al. 1973) or antagonistically (Luoma and Bryan 1978), and dosage (Finley and Dieter 1978). For example, smaller lead particles, <180 µm in diameter, were absorbed from the intestinal tract up to seven times more rapidly than larger particles of 180 to 250 µm (USEPA 1980). However, when large pieces of lead are ingested, such as lead shot, they may lodge in the gastrointestinal tract, dissolve slowly, and cause lead poisoning (Nriagu 1978b). Also, lead phthalates were absorbed more rapidly than carbonates, acetates, sulfides, and naphthanates, in that order (USEPA 1980). It is evident that all of these variables, as well as diet, need to be considered in risk assessment of lead.

4.5 CONCENTRATIONS IN FIELD COLLECTIONS

4.5.1 General

Lead concentrations were usually highest in ecosystems nearest lead mining, smelting, and refining activities; lead storage battery recycling plants; areas of high vehicular traffic; urban and industrialized areas; sewage and spoil disposal areas; dredging sites; and areas of heavy hunting pressure. In general, lead does not biomagnify in food chains. Older organisms usually contain the greatest body burdens, and lead accumulations are greatest in bony tissues. It seems that resources that are now at high risk (i.e., increased mortality, reduced growth, or impaired reproduction) from lead include the following:

- Migratory waterfowl that congregate at heavily-hunted areas
- Raptors that eat hunter-wounded game
- Domestic livestock near smelters, refineries, and recycling plants
- Wildlife that forage extensively near heavily traveled roads
- Aquatic life in proximity to mining activities, lead arsenate pesticides, metal finishing industries, lead alkyl production, and lead aerosol fallout
- Crops and invertebrates growing or living in lead-contaminated soils.

Data on background concentrations in nonbiological and living resources are cited extensively in Bernhard and Zattera (1975), Nriagu (1978a, 1978b), Wong et al. (1978), Branica and Konrad (1980), Jenkins (1980), Eisler (1981, 1988), Harrison and Laxen (1981), and Demayo et al. (1982).

4.5.2 Nonbiological Samples

Average lead concentrations in nonbiological materials worldwide were much higher in sediments (47,000 µg/kg), soils (16,000), and sediment interstitial waters (36) than in atmospheric and other hydrospheric compartments ([Table 4.3](#)). Most of the lead discharged into surface waters is rapidly incorporated into suspended and bottom sediments, and most will ultimately be found in marine sediments (Harrison and Laxen 1981). Sediments now constitute the largest global reservoir of lead; sediment interstitial waters and soils constitute secondary reservoirs ([Table 4.3](#)).

Table 4.3 Amounts of Lead in Global Reservoirs

Reservoir	Concentration ($\mu\text{g/kg}$)	Total Lead in Pool (millions of metric tons)
Atmosphere	0.0035	0.018
Lithosphere		
Soils	16,000	4800
Sediments	47,000	48,000,000
Hydrosphere		
Oceans	0.02	27.4
Sediment interstitial waters	36	12,000
Lakes and rivers	2	0.061
Glaciers	0.003	0.061
Groundwater	20	0.082
Biosphere		
Land biota		
Living	100	0.083
Dead	3000	2.1
Marine biota		
Living	500	0.0008
Dead	2500	2.5
Freshwater biota		
All	2500	0.825

Modified from Nriagu, J.O. (ed.). 1978a. *The Biogeochemistry of Lead in the Environment. Part A. Ecological Cycles*. Elsevier/North Holland Biomedical Press, Amsterdam. 422 pp.

Lead concentrations were elevated in certain nonbiological materials as a result of nonhunting human activities and natural processes (Table 4.4). In sediments, lead concentrations ranged from 3 mg/kg in carbonate marls off the Florida coast to more than 11,000 mg/kg at Sorfjord, Norway, the site of massive discharges of lead-containing industrial and domestic wastes (Nriagu 1978a). Lead contaminates sediments from sources as diverse as steelworks, shipyards, crude oil refineries, cement and ceramic factories, lead storage battery recycling plants, and heavy traffic (Scoullos 1986). Mining activities are also important. High concentrations of lead were measured in sediments (up to 2200 mg/kg) and detritus (up to 7000 mg/kg) of the Big River in southeastern Missouri (Czarneski 1985). The Big River drains what was once the largest lead-mining district in the world; commercial mining was extensive between the early 1700s and 1972. During this period more than 200 metric tons of tailings accumulated within the Big River watershed as a result of seepage from tailings ponds, from erosion of tailings piles on the banks, and through accidental discharges (Niethammer et al. 1985).

In soils, lead concentrates in organic-rich surface horizons (NRCC 1973). In one instance, only 17 mg of soluble Pb/kg was found in soils 3 days after the addition of 2784 mg of lead (as lead nitrate)/kg (NRCC 1973). The estimated residence time of lead in soils is about 20 years; complete turnover in topsoil is expected every few decades (Nriagu 1978a). In forest litter, however, the mean residence time of lead is lengthy; estimates range from 220 years (Turner et al. 1985) to more than 500 years (Friedland and Johnson 1985).

Lead may leach from loamy soils of clay target shooting sites, where soils contain about 50,000 mg Pb/kg (about 40% Pb as particulate Pb shot in the most contaminated areas); leachates at 100 mm depth contained up to 3.4 mg Pb/L vs. little or no lead in leachates collected from soil containing background concentrations of lead (Rooney and McLaren 1999).

Lead deposited on roadways is removed in drainage water, and later accumulated in roadside soils (Harrison et al. 1985). Amounts of lead in roadside soils increase as a direct result of the combustion of gasoline containing organolead additives. In general, the amounts of lead were greatest along roads with the highest density of vehicular traffic, and amounts decreased rapidly with increasing distance from the roadway (Harrison and Dyer 1974; Boggess 1977; Chmiel and Harrison 1981; Way and Schroder 1982; Table 4.4). Elevated levels of lead in soils were also

recorded from the vicinity of storage battery reclamation plants, smelting activities, and mining and milling operations (Boggess 1977; Burrows 1981; Kisselberth et al. 1984). Fly ash from coal burned in homes or privately hauled from power plants, which contains 100 to 450 mg Pb/kg and is frequently used to reclaim land for the growth of forage and pasture crops and as an alkaline amendment in the reclamation of strip mined areas (Nriagu 1978a), is considered another source of soil lead. Two additional sources of lead in soils are municipal sewage sludge and lead-arsenate pesticides (Nriagu 1978a). Sewage sludge, which contains up to 100 mg Pb/kg and is applied as a fertilizer and soil conditioner at the rate of 50 million tons annually, may increase topsoil levels by as much as 25 mg Pb/kg. Lead arsenate, a pesticide used to reduce bird hazards near airport runways by controlling earthworm abundance, and also to control pests in fruit orchards, represents another local source of lead contamination to soils.

Table 4.4 Lead Concentrations in Selected Nonbiological Materials

Material (units)	Concentration ^a	Reference ^b
AIR (µg/m³)		
Nonurban areas	0.1	1
Urban areas	(0.3–2.5)	2
Metropolitan areas	(2–10)	1
Rural roads	6	2
Heavy traffic	40	2
Near industrial sources	May exceed 1000	1
RAIN (µg/L)		
Minnesota		
1979		
Rural	6	3
Urban	29	3
1983		
Rural	2	3
Urban	4	3
ATMOSPHERIC DEPOSITION (g/ha)		
New Jersey Pine Barrens		
1971–79	350	4
1980–82	140	4
ICE (µg/L)		
Greenland		
800 BCE	0.001	2
1750	0.01	2
1940	0.07	2
1973	>0.2	2
SOILS (µg/kg dry weight)		
Near lead smelter		
Missouri	128	5
British Columbia	>1000	5
Distance from highway		
2 m	500	6
20 m	312	6
40 m	112	6
60 m	46	6
Near metal smelter	(1200–2700)	7
Control site	(99–490)	7
Near factory	(210–485)	8
Reference site (1000 m distant)	(10–30)	8

Table 4.4 (continued) Lead Concentrations in Selected Nonbiological Materials

Material (units)	Concentration^a	Reference^b
Worldwide	10 (2–200)	9
USA	20 (10–700)	9
FOREST LITTER (g/ha)		
Vermont	20,000	10
New Jersey	7600	4
WATER (µg/L)		
Egypt, Nile River Industrialized area	9.5	11
Sweden Polluted lake Shallow water	3.3 (1.5–4.5)	12
Deep water	(8–41)	12
Reference lake	0.1	12
Greece, seawater Industrialized area	(2–5.5)	13
USA Maine Pre-snowmobile	4.1	14
Ice-out	135	14
Nationwide Rivers	5 (0.6–120)	9
Streams	23	9
England Coastal sea water	Max. 2.3	9
Offshore	(0.02–0.03)	9
SOLIDS ENTERING SURFACE WATERS (mg/kg dry weight)		
Street dust Urban	(1000–4000)	15
Rural	440	15
Highway runoff Suspended sediments	(3100–5800)	15
Settleable solids	16,000	15
Sewage sludge	(100–1400)	15
Suspended sediments in mineralized areas	(1000–8000)	15
SEDIMENTS (µg/kg dry weight)		
Egypt, Nile River Industrialized area	Max. 1800	11
Greece Near major industries	(500–600)	13
Several km distant	40	13
Preindustrial levels	10	13
Norway Sorfjord	Max. 11,000	16
Sweden Polluted lake	(2000–2500)	12
Reference lake	110	12
USA Chesapeake Bay, 1979–81	(1–134)	17
Upper Mississippi River	13 (0.4–86)	18
Southeastern Missouri, Big River, 1979–1981 Sediments	(1400–2200)	19
Organic detritus	(800–7000)	19
Florida	3	16

Table 4.4 (continued) Lead Concentrations in Selected Nonbiological Materials

Material (units)	Concentration ^a	Reference ^b
Oceanic		
Near shore	20	9
Deep sea	45	9
Clay	9	9
Carbonate	80	9
INTEGRATED STUDY (µg/kg)		
Tennessee stream		
Water	(0.01–0.019)	9
Dissolved solids	(30–84)	9
Coarse particles	(124–653)	9
Colloidal particles	(62–2820)	9

^a Concentrations are shown as mean, minimum and maximum (in parentheses), and maximum (Max.).

^b 1, USEPA 1980; 2, NRCC 1973; 3, Eisenreich et al. 1986; 4, Turner et al. 1985; 5, Burrows 1981; 6, Krishnayya and Bedi 1986; 7, Beyer et al. 1985; 8, Edwards and Clay 1977; 9, Demayo et al. 1982; 10, Friedland and Johnson 1985; 11, Fayed and Abd-El-Shafy 1985; 12, Haux et al. 1986; 13, Scoullos 1986; 14, Adams 1975; 15, Harrison and Laxen 1981; 16, Nriagu 1978a; 17, Di Giulio and Scanlon 1985; 18, Wiener et al. 1984; 19, Czarneski 1985.

Lead reaches the aquatic environment through industrial and municipal discharges, in atmospheric deposition, from weathering processes in areas of natural lead mineralization, and in highway runoff (USEPA 1980; Harrison and Laxen 1981; Birdsall et al. 1986). Industrial lead input to aquatic environments is estimated at 10 times that introduced by natural weathering processes (Scoullos 1986); sewage and aerosols are major sources (Harrison and Laxen 1981). Snowmobile exhausts are considered a major source of lead in some locations; concentrations up to 135 µg Pb/L have been recorded in surface waters at the time of ice breakup (Adams 1975). On the other hand, lead content in water (and sediments) of a fly ash settling pond at a coal-fired power plant did not increase as a result of plant operations (White et al. 1986). Isotopic lead ratios ($^{207}\text{Pb}/^{206}\text{Pb}$) and Pb/Ca atomic ratios can demonstrate anthropogenic perturbations of the lead cycle in present-day food webs. As judged by these ratios, lead in teeth of contemporary California sea otters (*Enhydra lutis*) from Alaska have increased by two- to 15-fold over their preindustrial counterparts that died about 2000 years ago. Lead in preindustrial otters derived from natural deposits, while lead in contemporary animals was primarily from Asia and western Canada and was dominated by lead aerosols or industrial waste lead deposits (Smith et al. 1990, 1992).

Anthropogenic activities leading to increased air lead levels include primary and secondary lead smelting, the burning of gasoline containing lead antiknock agents, coal combustion, storage battery manufacture, and pigment production (NRCC 1973). It is generally agreed that combustion of leaded gasoline is the primary source of atmospheric lead. Atmospheric lead is usually attached to aerosols <0.2 µm in diameter, is efficiently scavenged by precipitation, has a short atmospheric residence time that is usually measured in days but may range up to 14 weeks depending on meteorological conditions, and may be transported long distances (i.e., hundreds or thousands of kilometers) from emitting sources (NRCC 1973; Harrison and Laxen 1981; Harrison et al. 1985; Eisenreich et al. 1986). Along roadways, more than 90% of lead emissions are dispersed by the atmosphere away from the immediate vicinity of the road; air lead levels stabilize at low levels about 30 m from the road as a result of rapid settling of particles >5 µm in diameter, and from the downwind traverse of particles entrained in the turbulent atmosphere (Boggess 1977; Harrison et al. 1985). Since 1970, the lead content in gasoline has decreased; profiles of lead in dated sediment cores and lead in atmospheric aerosols suggest that the environment is responding to the decreasing

use of leaded gasoline, and that atmospheric lead concentrations and fluxes will continue to decrease substantially if the use of lead in gasoline is further decreased (Eisenreich et al. 1986). Atmospheric deposition of lead to the Great lakes in 1983 was conservatively estimated at 891 tons, with an upper limit of 1252 tons; these values are considerably lower than those from the early 1970s and may be due, in part, to the decrease in the lead content of gasoline (Gatz et al. 1989).

4.5.3 Fungi, Mosses, Lichens

Concentrations of lead were highest in specimens collected near metal smelters, lead mines, industrial areas, and urban locations ([Table 4.5](#)). Lead concentrations were 9 to 13 times greater in a lichen (*Parmelia baltimorensis*) collected in Washington, D.C., in 1970 than in the same lichen collected 34 years earlier (Jenkins 1980).

4.5.4 Terrestrial Plants

Elevated lead contents were recorded in various species of plants from the vicinity of metal smelters, roadsides, soils heavily contaminated with lead, natural ore deposits, and lead recycling factories ([Table 4.5](#)). Bioavailability of lead in soils to plants is limited but is enhanced by reduced soil pH, reduced content of organic matter and inorganic colloids, reduced iron oxide and phosphorus content, and increased amounts of lead in soils (NRCC 1973; Boggess 1977). Lead, when available, becomes associated with plants by way of active transport through roots and by absorption of lead that adheres to foliage (Boggess 1977). Lead concentrations were always higher in the older parts of plants than in shoots or flowers (Bunzl and Kracke 1984; [Table 4.5](#)).

Damage to plants with elevated lead contents is usually negligible but varies widely among species. Atmospheric lead may have contributed to the decline of European spruce forests. The mean lead content of needles and litter was significantly higher where tree decline was most pronounced than in areas where forests were unaffected (Backhaus and Backhaus 1986). Lead can have deleterious effects on plant growth processes at reported lead levels in urban areas and may similarly affect plants in rural areas in the future (Rolle and Reinbold 1977). A reduction in yield of corn or soybeans is expected in low-binding capacity soils with lead levels greater than 200 mg/kg (Rolle and Reinbold 1977). Hay grown near roadsides may be toxic to horses and cattle (Rolle and Reinbold 1977). In extreme cases, reforestation has been initiated in areas where forage is so heavily contaminated with lead that it has become necessary to slaughter domestic livestock because the amounts of lead in their livers and kidneys is unacceptably high (Edwards and Clay 1977). Typical area reforestation includes removal of contaminated forage by cutting, bailing, and burying native grasses; burning stubble and litter; and adding agricultural lime at the rate of 2244 kg/ha (2000 pounds/acre) to all soils within 1525 m (5000 feet) of sites where lead levels exceed 175 mg/kg (Edwards and Clay 1977).

4.5.5 Terrestrial Invertebrates

In earthworms, lead levels were highest in those closest to highways and in areas with high volumes of traffic (Goldsmith and Scanlon 1977; [Table 4.5](#)). Various species of insects and soil invertebrates from roadsides, from areas receiving sewage sludge, and from metal smelter environs also contain high amounts of lead ([Table 4.5](#)). Amounts of lead in whole body were higher in earthworms, millipedes, and woodlice collected from soil and plant litter near highways than away from highways; soil and litter seem to be major reservoirs of lead in roadside communities (Beyer and Moore 1980). In contrast, lead concentrations in the eastern tent caterpillar (*Malacosoma americanum*) were lower than those reported for roadside soil and litter invertebrates, and were about 76% of that in leaves of its host, the black cherry *Prunus serotina* (Beyer and Moore 1980).

The use of terrestrial invertebrates as sentinel organisms has been suggested for monitoring lead. The spider *Araneus umbricatus*, for example, contained lead body burdens that correlated with that in a lichen (*Lecanora conizaeoides*) that is used to monitor atmospheric lead (Clausen 1984). Similarly, the woodlouse (*Porcellio scaber*) seems to reflect lead concentrations in adjacent soil or leaf litter (Hopkin et al. 1986).

4.5.6 Aquatic Biota

Nationwide, there has been a significant decline in lead concentrations of whole freshwater fish from 1976/77 to 1984, continuing a decrease that became evident in 1978/79 (Schmitt and Brombaugh 1990). Nationwide monitoring of freshwater fishes conducted periodically by the U.S. Fish and Wildlife Service (National Biocontaminant Monitoring Program) showed that whole-body lead burdens were highest for Atlantic coast streams, the Great Lakes drainage, the Mississippi River system, the Columbia River system, and in certain Hawaiian streams (May and McKinney 1981).

- Major sources of lead in Atlantic coast streams included wastes from metal-finishing industries, brass manufacturing, lead alkyl production, primary and secondary lead smelting, coal combustion, and manufacture of lead oxide.
- For the Great Lakes, especially for the Lake St. Clair collection site, industrial sources and urban lead aerosol fallout from the Detroit area were major sources.
- In the Mississippi River system, naturally occurring deposits of lead ores and effluents from zinc producers and industrial dischargers were prevalent.
- The Columbia River system was characterized by lead inputs from natural geologic deposits, industrial effluents, and the mining and smelting of lead.
- Hawaiian streams received most of their lead from urban runoff, vehicle sources, and agricultural and residential use of lead arsenate (May and McKinney 1981).

Fish collected from 1979 to 1981 in the Big River, Missouri, near a ruptured tailings pond dam where lead concentrations in tailings approached 4000 mg/kg, contained greatly elevated whole-body lead burdens of 9 to 18 mg/kg fresh weight (Schmitt et al. 1984). Increased blood lead concentrations in longear sunfish (*Lepomis megalotis*) from this area were associated with decreased blood ALAD activity and altered mechanical and biochemical properties of bone (Dwyer et al. 1988). By comparison, the highest lead concentration recorded to date in the National Biocontaminant Monitoring Program is 6.7 mg/kg fresh weight in whole Mozambique tilapia (*Tilapia mosambica*) from Honolulu in 1979 (Lowe et al. 1985). Catostomids from contaminated portions of the Big River contained elevated blood lead levels, depressed blood ALAD activity levels, and lead concentrations in edible tissues exceeding 0.3 mg/kg fresh weight — a level considered hazardous to human health (Schmitt et al. 1984). The Missouri Department of Health later issued an advisory against eating catostomids caught in a 65-km section of the Big River (Czarneski 1985). Whitefish, *Coregonus* spp., from lead-contaminated Swedish lakes, showed depressed blood ALAD and blood chemistry derangement when compared to fish from a reference lake, suggesting that lead affects natural populations of fish in a manner similar to that observed in laboratory studies (Haux et al. 1986).

In general, freshwater algae, invertebrates, and fish had comparatively elevated lead concentrations when collected near industrialized areas, ponds with high numbers of lead shot, urban areas, lead mines, tailings ponds (Table 4.5), areas of historic mining activities (Schmitt et al. 1993), and near highways (Baekken 1994). For marine biota, lead residues were generally highest where lead concentrations were high in the water: near bridges, near industrial disposal areas, near sewage and disposal areas, near dredging sites, and at mining sites (Table 4.5). Lead concentrations in soft parts of American oysters (*Crassostrea virginica*) were higher in smaller oysters than in larger ones, much lower than the lead burden of the surrounding sediments, and strongly correlated with the

iron content of the geochemical environment (Jiann and Presley 1997). However, soft parts of larger bivalve molluscs from Greenland had higher lead burdens than did smaller bivalves (Dietz et al. 1996). Lead concentrations in tissues of Arctic char (*Salvelinus alpinus*) from Austria were positively correlated with increasing water temperature, increasing age, and decreasing water alkalinity. Enhanced lead accumulation during the summer was a consequence of increasing metabolic rate (Kock et al. 1995a, 1995b). The ability of parasitic acanthocephalans to accumulate high concentrations of lead may prove to be a useful indicator of lead contamination in the aquatic environment; however, the underlying mechanism of accumulation requires additional research (Sures et al. 1994).

Among aquatic biota, lead concentrations were usually highest in algae and benthic organisms, and lowest in upper trophic level predators. No significant biomagnification of lead occurs in aquatic food chains (Bogges 1977; Rolfe and Reinbold 1977; Branica and Konrad 1980; Demayo et al. 1982; Flegal 1985; Henny et al. 1991; Dietz et al. 1996; [Table 4.5](#)). Lead concentrations in cartilaginous and bony fishes (and also birds and mammals) were usually highest in areas of high human and vehicular density, and near lead mines and ore concentration plants. Lead concentrations in aquatic (and terrestrial) vertebrates tend to increase with increasing age of the organism, and to localize in hard tissues such as bone and teeth (Eisler 1981, 1984). In stream sediments, lead was highest in urban streams and lowest in the rural streams, reflecting lead inputs from storm runoff; species diversity was greater in the rural streams, due partly to lowered contaminant loadings, including lead (Rolfe and Reinbold 1977).

The significance of organolead residues in aquatic life is unknown and merits additional research. In Ontario, Canada, about 16% of all fish sampled contained tetraalkyllead compounds, although none were recorded in water, vegetation, or sediments from the collection sites (Chau et al. 1980). Tetramethyllead reportedly was produced from biological and chemical methylation of several inorganic and organic lead compounds in the aquatic environment, and has been detected at low concentrations in marine mussels, lobsters, and bony fishes (Wong et al. 1981).

4.5.7 Amphibians and Reptiles

Tadpoles of bullfrogs (*Rana catesbeiana*) and green frogs (*R. clamitans*) from drainages along highways with different daily average traffic volumes (4272 to 108,800 vehicles per day) contained elevated amounts of lead (up to 270 mg/kg dry weight), which were positively correlated with lead in sediments and with average daily traffic volume. Lead in tadpoles living near highways may contribute to the lead levels reported in wildlife that eat tadpoles. Diets with amounts of lead similar to those in tadpoles collected near heavily traveled highways have caused adverse physiological and reproductive effects in some species of birds and mammals (Birdsall et al. 1986). Elevated lead concentrations were also recorded in various species of amphibians and reptiles collected near lead smelters and mines ([Table 4.5](#)).

4.5.8 Birds

In general, lead concentrations were highest in birds from urban locations (perhaps reflecting greater exposure to automotive and industrial contamination) and in birds near lead mining and smelting facilities. Lead residues are also greatest in older birds (especially in bone, because of accumulation over time), in sexually mature females, and in waterfowl that have ingested lead shot pellets and other lead objects ([Table 4.5](#)). In eastern Canada, elevated lead concentrations in wing bones of ducks are attributed to waterfowl hunting, nonferrous metal mining and smelting, and urban and industrial development. Ingestion of spent lead shot pellets from waterfowl hunting is the primary source of elevated lead exposure for wild ducks in eastern Canada; however, proximity to metal mining sites, especially silver, gold, copper, and zinc mines was also important (Scheuhammer and Dickson 1996).

Continued deposition of lead shot by hunters into wetlands habitats exposes birds to lead. Lead shot is a substantial localized source of contamination, especially in prime waterfowl habitat (Bellrose 1951, 1959; NRCC 1973; White and Stendell 1977; Stendell et al. 1979; Wobeser 1981; Clausen et al. 1982; Longcore et al. 1982; Mudge 1983; Driver and Kendall 1984; Hall and Fisher 1985; Castrale 1989; Pain 1991; Best et al. 1992; Harper and Hindmarsh 1990; Kingsford et al. 1994; Wheeler 1995; Mateo et al. 1998). It is estimated that several million hunters deposit more than 6000 metric tons of lead shot annually into lakes, marshes, and estuaries. This represents about 6440 pellets per bird bagged. Shot densities as great as 330,000 to 860,000 pellets/ha (up to 2,124,000/acre) have been estimated in some locations (Wobeser 1981; Whitehead and Tschirner 1991; Best et al. 1992), and more than 2.6 million shot/ha were estimated for the Ebro Delta, Spain in 1992/93 (Mateo et al. 1997b), although concentrations of 34,000 to 140,000/ha are more common (Longcore et al. 1982; Driver and Kendall 1984). For example, lead shot in bottom sediments from Merrymeeting Bay, Maine, a prime waterfowl staging area, averaged 99,932 shot/ha (274,000/acre), and ranged from 59,541 to 140,324/ha; shot were significantly more numerous in silt than in sand sediments. In general, shot sink more rapidly in soft than in firm substrates, and there is only slight carryover of shot from one season to the next in areas with silt or peat bottoms (Wobeser 1981). In agricultural soils, normal tillage practices may reduce lead shot availability by as much as 73% (Castrale 1989). In some locations, however, lead exposure and lead poisoning in waterfowl will continue to occur despite the conversion to steel shot for waterfowl hunting (Rocke et al. 1997).

Waterfowl and other birds ingest spent shot during feeding and retain them as grit in the gizzard; the pellets are eroded and soluble lead is absorbed from the digestive tract. In many species, the ingestion of a single pellet is often fatal. Most deaths, however, go unnoticed and unrecorded. Species such as the mallard and pintail that feed in shallow water by sifting through bottom mud are more likely to encounter shot than are species that feed on submerged vegetation or at the surface (Wobeser 1981). Several techniques are used to determine the presence of ingested shot in gizzards of birds; these include fluoroscopy of intact gizzards, X-ray of gizzard contents (the most reliable), and microscopic visual examination (Pain and Eon 1993). Shot ingestion in waterfowl is higher where shot densities in sediments are high and grit is absent (Pain 1990), and higher during spring than in autumn for diving ducks (Havera et al. 1992). Incidence of ingested shot in five species of waterfowl harvested in Yucatan, Mexico, in 1986 to 1988 was 10.3% (Thompson et al. 1989). Ingested lead shot frequency was 8.1% in American black ducks (*Anas rubripes*) sampled in Maine during the hunting seasons of 1976 through 1980 (Longcore et al. 1982). Gizzards of black ducks from Prince Edward Island, Canada, examined between 1988 and 1991 had a 7.1% frequency of ingested shot (Daury et al. 1994), and those from Wallace Bay, Nova Scotia, in 1987 had a 13% frequency of ingested shot (Schwab and Daury 1989). In Dartmouth, Nova Scotia, in 1988, 96% of overwintering black ducks had elevated blood lead concentrations (>0.1 mg Pb/L), and 76% had detrimental concentrations in excess of 0.2 mg/L (Daury et al. 1993). In dry seasons, species that probe for food deep in the sediment are especially susceptible (Hall and Fisher 1985; Harper and Hindmarsh 1990). In England, ingested pellets occurred in 3.2% of the total waterfowl in 16 species examined. Incidences of shot were relatively high (7.1% to 11.8%) in four species (Mudge 1983): greylag goose (*Anser anser*), gadwall (*Anas strepera*), pochard (*Aythya ferina*), and tufted duck (*Aythya fuligula*). A very high incidence (>22 to 100%) of shot ingestion was recorded in the gizzards of various species of hunter-shot waterfowl in Japan (Ochiai et al. 1993a), the Netherlands, Greece, France, Spain, and Italy (Lumeij and Scholten 1989; Pain and Handrinos 1990; Mateo et al. 1998). At least 8000 mallards in Britain die each winter of lead toxicosis from ingestion of spent shot (Mudge 1983). It is estimated that about 2.4 million ducks die worldwide of lead shot poisoning each year, and this estimate does not include population losses resulting from the sublethal effects of lead (Wobeser 1981). Among larger species of waterfowl, outbreaks of lead poisoning have been documented in Canada geese (*Branta canadensis*), whistling swans (*Cygnus columbianus*), trumpeter swans, and mute swans (Eskildsen and Grandjean 1984). Lead-poisoned waterfowl tend to seek seclusion and often die in areas of heavy cover. These

carcasses are rapidly removed by predators and scavengers (Wheeler 1995) and may result in secondary lead poisoning, especially among raptors such as the bald eagle (Feierabend and Myers 1984; Reichel et al. 1984). Of 293 bald eagles found dead nationwide between 1978 and 1981, 17 (5.8%) probably died of lead poisoning after ingesting hunter-killed or hunter-crippled waterfowl containing lead pellets (Reichel et al. 1984). Unlike the emaciated state of birds with chronic lead poisoning, bald eagles acutely poisoned by lead may be in good body condition if high concentrations of lead are rapidly absorbed (Langelier et al. 1991; Gill and Langelier 1994).

Raptors are susceptible to lead poisoning wherever lead shot is used for hunting. As raptor populations are often small and reproduction rates low, their populations are particularly vulnerable to adult mortality (Pain and Amiard-Triquet 1993). Lead exposure, especially poisoning, was a major factor affecting the California condor population during 1982–86. The probable source of lead was bullet fragments in carrion on which condors were feeding (Wiemeyer et al. 1988). Of 162 golden eagles (*Aquila chrysaetos*) sampled in California in 1985/86, 5.6% had elevated blood lead concentrations (>0.6 mg Pb/kg), and 2.5% had >1.0 mg Pb/kg blood. Lead was probably ingested from feeding on deer carcasses and offal from hunter-killed deer (Pattee et al. 1990).

Elevated tissue lead concentrations in field collections of birds were associated with a variety of adverse effects. Lead concentrations in livers of the Canada goose (*Branta canadensis*) and goldeneye (*Bucephala clangula*) found dead near mining and smelting activities in northern Idaho ranged from 8 to 38 mg Pb/kg FW; these levels exceeded the lower lethal limit of 5 mg Pb/kg FW liver in experimental birds (Blus et al. 1995). At the Ebro Delta in Spain in 1991/92, as many as 27% of the mallards had tissue lead concentrations sufficiently elevated to qualify as clinically lead-poisoned: >1.5 mg Pb/kg FW liver, >3 mg Pb/kg FW kidney (Guitart et al. 1994). In Poland, livers of dead and sick nestlings of sparrows (*Passer spp.*) had >2 mg Pb/kg DW, and healthy birds <2 mg Pb/kg DW (Pinowski et al. 1993). Toxic lead concentrations (up to 70 mg/kg FW liver) in chicks of the Laysan albatross (*Diomedea immutabilis*) in Hawaii were associated with proximity to buildings and the presence of lead paint chips in the proventriculus (Work and Smith 1996). Elevated blood lead concentrations were associated with ingested shot in gizzards of diving ducks (Havera et al. 1992), black ducks (Daury et al. 1993), and Canada geese (De Stefano et al. 1991, 1992, 1995), and with reduced blood ALAD activity in mallards (Tirelli et al. 1996). Blood lead concentrations in Canada geese from the eastern prairie population in 1986 to 1988 were below levels of recent lead exposure in areas where lead shot had never been used. In areas where lead shot was still in use, as many as 10% of the geese had blood lead levels >0.18 mg/L. The use of steel shot is substantially reducing the effect of lead poisoning in this population and other populations of geese and ducks (De Stefano et al. 1991, 1995).

Lead poisoning through the ingestion of anglers' lead weights was the major cause of death in the mute swan (*Cygnus olor*) in England. Between 1983 and 1985, lead poisoning was most common in areas where the largest number of lead weights were found and accounted for at least 76% — and perhaps up to 94% — of the local swan deaths (Sears 1988, 1989). In Ireland, about 60% of all mute swans found dead from 1984 to 1986 died from lead poisoning; lead sources included spent gunshot from clay pigeon shooting sites in northern Ireland and lost or discarded anglers' weights elsewhere (O'Halloran et al. 1988). Ingestion of lead artifacts (shotgun pellets, fishing sinkers) accounted for about 20% of the known mortality of trumpeter swans (*Cygnus buccinator*) in Idaho, Wyoming, and Montana, where the population has been declining for several decades. In Washington, the incidence of lead-induced mortality was higher and accounted for nearly 50% of the known mortalities (Blus et al. 1989). In Minnesota, lead poisoning of trumpeter swans from ingestion of shot was responsible for 23% of the documented deaths in 1987, and 54% in 1988/89. The increased mortality was attributed to drought conditions that lowered water levels and allowed swans to reach previously inaccessible lake bottoms containing spent lead shot (Degernes 1991). The treatment protocol for lead-poisoned trumpeter swans (blood Pb >0.4 mg/L) included supportive therapy (rehydration fluids, force feeding, injection of vitamins, iron salts, and 5-fluorocystine),

chelation therapy (calcium EDTA), and lead removal from the gizzard using gastric lavage; treatment was successful in about 53% of the cases (Degernes et al. 1990).

Ingestion of spent shot was associated with mortality of black swans (*Cygnus atratus*) in South Australia (Koh and Harper 1988), and up to 47% of all whooper swans (*Cygnus cygnus*) in Scotland in 1980 to 1986 (Spray and Milne 1988). Sediment ingestion by swans and other waterfowl is sometimes the main route of exposure to lead (Beyer et al. 1997). Sediment — not shot or diet — was the primary source of lead ingested by tundra swans (*Cygnus columbianus*) from the Coeur d'Alene River Basin in Idaho, as judged by fecal analysis. Sediment ingestion by tundra swans is associated with ingestion of wild rice (Beyer et al. 1998a). Dead tundra swans found near a lead mining complex in Idaho were attributed to ingestion of sediments that contained up to 8700 mg Pb/kg and plants that contained up to 400 mg Pb/kg (Blus et al. 1991). Chelation therapy using sodium calcium edetate was successful in treating the clinical signs of lead poisoning (i.e., those with blood Pb concentrations >0.4 mg/L) in mute swans in 49% of the cases (Sears et al. 1989). Subcutaneous injections of 0.25 mL/kg BW of a 25% w/v solution of sodium calcium edetate were given 1 to 3 times daily for at least 7 days. About 22% of treated swans survived for at least 2 years. However, results indicate that lead-poisoned swans, despite treatment, have a 59% reduction in survival when compared with untreated swans living in flocks (Sears et al. 1989).

Lead concentrations in feathers reflected population increases or declines of common terns (*Sterna hirundo*) from Long Island, New York. Lead in feathers of adult common terns decreased significantly from 5.6 mg/kg DW in 1978 to 1.0 mg/kg DW in 1985, were stable until 1988, and then increased (to 3.0 mg/kg DW) through 1992 (Burger et al. 1994). Lead declines in feathers coincided with environmental decreases in lead from the phasing out of leaded gasoline in vehicles. Source of the increased lead from 1989 to 1994 is unclear, but may result from increased dredging in the New York area in the early 1990s or from increased amounts of lead paint removed from bridges during repainting operations in the late 1980s and early 1990s (Burger et al. 1994). There was a positive correlation between lead concentrations in maternal feathers of common terns and their eggs (Burger and Gochfeld 1991). Lead concentrations in feathers of pigeons (*Columba livia*) from the Czech Republic were unaffected by season of collection, sex, area of collection, or diet; however, concentrations were lowest in nestlings and increased with increasing age (Janiga et al. 1990).

The relation between embedded shot and lead toxicosis is unclear. The incidence of embedded shot in various species of waterfowl ranged from 11% to 43% in adults, and 2% to 11% in immatures (Perry and Artmann 1979; Perry and Geissler 1980). Many birds that were struck by shotgun pellets but survived may have died prematurely or been eaten by predators. In one study, the bodies of 23% of adult Atlantic brant (*Branta bernicla hrota*) that died from starvation in New Jersey in 1977 contained embedded lead shot (Kirby et al. 1983). The effects on survival and fecundity of receiving and carrying relatively high frequencies of embedded shot might be significant, and during years of low adult numbers might have substantial population consequences (Kirby et al. 1983).

Lead in seeds and invertebrates within rights-of-way of major highways probably is not a hazard to adult ground-foraging songbirds, as judged from experiments with the European starling (*Sturnus vulgaris*). However, the effects of lead on survival of fledglings are unknown, although lead causes reductions in blood hemoglobin, hematocrit, ALAD activity, and brain weight (Grue et al. 1986). In another study, lead concentrations in feather, carcass, and stomach contents of adult and nestling barn swallows (*Hirundo rustica*) were greater near a major U.S. highway than in a rural area; however, the number of eggs and nestlings, the body weight of nestlings at 17 days of age, and body weights of adults were similar in the two colonies, suggesting that contamination of roadsides with lead from automobile emissions is not a major hazard to birds that feed on flying invertebrates (Grue et al. 1984).

Signs of lead poisoning, i.e., depressed blood ALAD activity or elevated blood lead levels, were reported for birds near a metal smelter (Beyer et al. 1985; Henny et al. 1991), in 17% of canvasbacks (*Aythya valisineria*) from Chesapeake Bay in 1974 (Dieter et al. 1976), and in three species of

waders from the Dutch Wadden Sea living in an urban postnuptial molting area (Goede and de Voogt 1985). In some species and locales, such as mallards from California national wildlife refuges, males had significantly higher blood lead concentrations than did females (Mauser et al. 1990). Reduced body mass of 10% was documented in overwintering canvasbacks that had lead shot in their gizzards when compared to birds with no lead shot in gizzards (Hohman et al. 1990). The decline in submerged aquatic vegetation in Chesapeake Bay and the later shift in diet of some waterfowl species of Chesapeake Bay from the vegetation (lead content 2.2 to 18.9 mg/kg dry weight) to the softshell clam *Mya arenaria* (1.3 to 7.6 mg Pb/kg dry weight), or to other bivalve molluscs (0.8 to 20.4 mg Pb/kg dry weight), probably did not increase dietary lead burdens in these species (Di Giulio and Scanlon 1985).

The significance of trace amounts of organolead residues in birds is unknown. Trialkyllead seems to concentrate in avian kidney, but contributes less than 5% of the total amount of lead in kidneys (Johnson et al. 1982).

4.5.9 Mammals

The highest body burdens of lead reported in mammals were near urban areas of dense vehicular traffic, near metal mines and smelters, adjacent to petrochemical refinery industries, or near plants that reclaimed storage batteries. Concentrations were higher in older organisms, especially in bone and hematopoietic tissues (Table 4.5; Goldsmith and Scanlon 1977; Way and Schroder 1982; Blus and Henny 1990; Hariono et al. 1993; Thies and Gregory 1994; Medvedev 1995). A similar pattern of lead occurrence and distribution was evident for human populations (Barth et al. 1973; Heinze et al. 1998). In Italy, tissue lead concentrations in mice correlated positively with vehicular traffic densities. Mice from the highest traffic flow areas also had genetic damage as judged by an increased frequency of micronucleated erythrocytes and abnormal sperm cells (Ieradi et al. 1996).

Diet provides the major pathway for lead exposure, and amounts in bone are indicative of estimated lead exposure and metabolism (Chmiel and Harrison 1981; Ma et al. 1991). Amounts of whole-body lead and feeding habits of roadside rodents were correlated: body burdens were highest in insectivores such as shrews, intermediate in herbivores, and lowest in granivores (Boggess 1977; Getz et al. 1977c). Food chain biomagnification of lead, although uncommon in terrestrial communities, may be important for carnivorous marine mammals, such as the California sea lion (*Zalophus californianus*); accumulations were highest in hard tissues, such as bone and teeth, and lowest in soft tissues, such as fat and muscle (Braham 1973). A similar pattern was observed in the harbor seal, *Phoca vitulina* (Roberts et al. 1976).

The most sensitive index of lead intoxication in populations of deer mice was the formation of acid-fast-staining intranuclear inclusion bodies within proximal convoluted tubule cells of kidney; secondary indicators included decreased body weight, renal edema, reticulocytosis, increased urinary ALA excretion, and decreased hematocrit (Mierau and Favara 1975). Mierau and Favara (1975) concluded that lead pollution from automobile exhausts has had little impact on deer mice, and that severe lead poisoning is unlikely at traffic densities below 200,000 vehicles per day. Others, however, believe that lead emissions from automotive exhausts may pose unnecessary risks to various species of bats, rodents, and mule deer (*Odocoileus hemionus*). Estimated doses of lead ingested by the little brown bat (*Myotis lucifugus*) and highway populations of shrews and voles equaled or exceeded dosages that have caused death or reproductive impairment in domestic animals; further, mean lead concentrations in bats and shrews near highways exceed those reported for small rodents with lead-induced renal abnormalities collected from abandoned lead-mining sites (Clark 1979). Mule deer from the Rocky Mountain National Park, Colorado, that graze on (heavily contaminated) roadside forage must consume 1.4% of their daily intake from roadsides before harmful amounts of lead (3 mg Pb/day) are obtained (Harrison and Dyer 1984); however, this value needs to be verified.

Cows (*Bos bovis*) adjacent to a lead battery reclamation plant showed signs of lead toxicosis, including muscle tremors, blindness, dribbling urine, and drooling. Mice trapped within 400 m of the plant had acid-fast-staining intranuclear inclusions in renal tubular epithelial cells — a useful diagnostic indicator of lead poisoning. A faulty air pollution control system at the plant caused deposition of particulate lead on the cornfield used for cattle forage and was the probable source of the lead toxicosis in the animals (Kisseberth et al. 1984). Industrial airborne lead pollution is responsible for contamination of cattle and horses (*Equus caballus*) within 1000 m of the source, resulting in elevated blood lead levels in both species, stillbirths and abortions in cattle, and some deaths in horses (Edwards and Clay 1977).

Proximity to the smokestacks of metal smelters is positively associated with increased levels of lead in the hair (manes) of horses and in tissues of small mammals, and is consistent with the results of soil and vegetation analyses (USEPA 1972). Lead concentrations were comparatively high in the hair of older or chronically impaired horses (USEPA 1972). However, tissues of white-tailed deer (*Odocoileus virginianus*) collected near a zinc smelter did not contain elevated levels of lead (Sileo and Beyer 1985). Among small mammals near a metal smelter, blood ALAD activity was reduced in the white-footed mouse but normal in others, e.g., the short-tailed shrew (Beyer et al. 1985). The interaction effects of lead components in smelter emissions with other components, such as zinc, cadmium, and arsenic, are unresolved (USEPA 1972) and warrant additional research.

Table 4.5 Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
FUNGI, MOSSES, AND LICHENS		
Fungi, 4 species		
Near metal smelter	4 DW	1
Control site	2 DW	1
Moss, <i>Brachythecium rivulare</i>		
Near lead mines	(1330–8206) DW	2
Moss, <i>Hypnum cupressiforme</i>		
Sweden, museum specimens; year of collection		
1860	(18–27) DW	3
1880	(20–37) DW	3
1900	(40–70) DW	3
1920	(22–90) DW	3
1940	(15–70) DW	3
1960	(65–75) DW	3
1968	(70–90) DW	3
Vicinity urban industry	Max. 11,611 DW	4
Mushrooms		
Spain; 1994–95; fruiting body; 13 species; maximum values		
4 species	< 1 DW	195
7 species	1–3 DW	195
1 species	3.5 DW	195
1 species	10.4 DW	195
Worldwide; 95 species		
Hymenophore	1.1 (0.2–6.9) DW	195
Rest of fruiting body	1.0 (0.1–10.4) DW	195
Lichen, <i>Parmelia baltimorensis</i>		
Washington, D.C.		
1938	106 DW	5
1958	270 DW	5
1970	(950–1371) DW	5
Connecticut, 1971	198 DW	5

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
ALGAE AND MACROPHYTES		
Acorns and berries, 4 species		
Near metal smelter	4 DW	1
Control site	3 DW	1
Aquatic macrophytes, whole		
Nile River, Egypt		
Industrialized area	Max. 22 DW	6
Aquatic plants, 7 species		
From lead shot seeded area		
Roots	19 DW	7
Shoots	3 DW	7
Control area		
Roots	5 DW	7
Shoots	1 DW	7
Swiss chard, <i>Beta vulgaris cicla</i> ; leaf		
15 m from highway	220 DW	5
20 m from highway	154 DW	5
Control area	<3 DW	5
Alga, <i>Blidingia minima</i> ; whole, Raritan Bay, NJ		
Water Pb content		
0.002 mg/L	12 DW	8
0.01 mg/L	172 DW	8
Brome grass, <i>Bromus</i> spp.		
Grown in soil with 680 mg Pb/kg	34 DW	5
Control	7 DW	5
Weed, <i>Cassia</i> sp., India		
Distance from highway (meters)		
2	(208–303) DW	9
20	(90–97) DW	9
40	(55–68) DW	9
60	(20–22) DW	9
Green alga, <i>Cladophora</i> sp.		
Missouri, tailings pond	11,300 DW	5
1.6–4.0 km downstream	(200–4600) DW	5
6.1–9.6 km downstream	(100–2600) DW	5
Alga, <i>Enteromorpha linza</i> ; whole, Raritan Bay, NJ		
Water Pb content		
0.002 mg/L	18 DW	8
0.01 mg/L	68 DW	8
Red fescue grass, <i>Festuca rubra</i>		
Leaf, Wales, UK; distance downwind from smelter		
1.5 km	814 DW	4
8 km	30 DW	4
25 km	14 DW	4
>25 km	(5–12) DW	4
Foliage, 8 species		
Near metal smelter	21 DW	1
Control site	10 DW	1
Alga, <i>Fucus distichus</i> ; distance from lead deposit		
1 km	1 DW	10
2 km	0.6 DW	10
Alga, <i>Fucus vesiculosus</i> ; whole, Raritan Bay, NJ;		
water Pb content		
0.002 mg/L	8 DW	8
0.01 mg/L	38 DW	8

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Lettuce, <i>Lactuca sativa</i>		
Lead-contaminated areas	71 FW	11
Uncontaminated areas	0.5 FW	11
Mule deer forage, CO, roadside		
1978	59 DW	12
1979	42 DW	12
Rice, <i>Oryza sativa</i>		
Grown 10 m from highway		
Grain	0.2 DW	13
Straw	5.8 DW	13
Grown 230 m from highway		
Grain	0.2 DW	13
Straw	2.1 DW	13
Spruce, <i>Picea abies</i> , Germany, 1984		
Declining spruce forest		
Litter	416 DW	14
Needles	13 DW	14
Nondeclining stand		
Litter	213 DW	14
Needles	2 DW	14
Shortleaf pine, <i>Pinus echinata</i> ; Missouri, leaf; distance from smelter, km		
0.8	3546 (420–11,750) DW	15
0.8–1.6	497 (101–1475) DW	15
1.6–2.4	274 (52–1050) DW	15
2.4–3.2	142 (62–412) DW	15
3.2	123 (22–661) DW	15
Pondweed, <i>Potamogeton</i> sp.		
Missouri, tailings pond	11,300 DW	5
1.6 km downstream	3500 DW	5
8.1 km downstream	100 DW	5
Black cherry, <i>Prunus serotina</i> ; leaves, 1978		
Near roadway	(9–14) DW	16
>30 m distant	(2–6) DW	16
Potato, <i>Solanum tuberosum</i>		
Lead-contaminated areas	13 FW	11
Uncontaminated areas	1 FW	11
Submerged aquatic vegetation, 1979–81, Chesapeake Bay, 5 species	7.4 (0.5–30) DW	17
Alga, <i>Ulva</i> sp.; whole, Raritan Bay, NJ; water Pb content		
0.002 mg/L	20 DW	8
0.01 mg/L	76 DW	8
Blueberry, <i>Vaccinium pallidum</i>		
Leaf, Missouri; distance from smelter		
1.6–3.2 km	495 (141–874) DW	5
3.2–4.8 km	203 DW	5
4.8–6.5 km	76 DW	5
6.5–8.1 km	68 DW	5
8.1–9.7 km	64 DW	5
9.7–11.3 km	41 (29–101) DW	5
Vegetation		
Vermont forest		
Root bark	33 DW	18
Twigs	28 DW	18
Bark	23 DW	18

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Root wood	10 DW	18
Foliage	3 DW	18
Wood	3 DW	18
New Jersey Pine Barrens		
Roots	18 DW	19
Bark	15 DW	19
Foliage	4 DW	19
Wood	0.5 DW	19
Near roadway, UK 1979		
Grass	63 DW	20
Grass seeds	99 DW	20
Hawthorn, <i>Crataegus</i> spp.		
Leaves	146 DW	20
Fruit	4 DW	20
Control site, UK 1979		
Grass	2 DW	20
Grass seeds	4 DW	20
Hawthorn		
Leaves	4 DW	20
Fruit	2 DW	20
Grass		
Near factory	(830–1840) DW	21
1000 m distant		
Growing	(120–1200) DW	21
Dead and litter	(370–1570) DW	21
1700 m distant		
Growing	(240–420) DW	21
Dead and litter	(170–1970) DW	21
Near lead smelter, forage		
Missouri	979 FW	22
British Columbia	(100–200) FW	22
Kansas, vegetation		
Near highway	11 DW	23
Distant site	3 DW	23

INVERTEBRATES

Limpet, <i>Acmaea digitalis</i> ; California		
Near bridges		
Soft parts	931 DW	24
Shell	108 DW	24
Lead-free area		
Soft parts	8 DW	24
Shell	9 DW	24
Bee, <i>Apis</i> sp.		
Honey		
Lead-contaminated area	(1–8) FW	11
Uncontaminated area	<0.5 FW	11
Sea urchin, <i>Arbacia lixula</i>		
Soft parts, Italy		
Unpolluted	21 DW	25
Polluted	58 DW	25
Beetles, <i>Coleoptera</i> , UK 1979		
Near roadway	32 DW	20
Control site	1 DW	20

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Bivalve molluscs, 3 species, soft parts, Chesapeake Bay, 1979–81	5 (0.6–27) DW	17
Crawfish, <i>Cambarus</i> sp., whole, Missouri		
At tailings pond	500 DW	26
1 km downstream	400 DW	26
25 km downstream	2 DW	26
Dung beetles, whole		
Near roadway	13 DW	23
Distant site	6 DW	23
Earthworms, whole		
Blacksburg, VA, 1974		
From high traffic density area (21,000 vehicles/day)		
6 m from highway	51 DW	27
18 m distant	32 DW	27
From low traffic density area (1100 vehicles/day)		
18 m distant	12 DW	27
Near highway	(38–331) DW	16
American oyster, <i>Crassostrea virginica</i> ; Galveston Bay, Texas; 1992–93; soft parts		
Summer	1–1.5 DW	89
Winter and spring	0.3–0.5 DW	89
Zebra mussel, <i>Dreissena polymorpha</i> ; soft parts; Netherlands; 1994; Rhine-Meuse Delta vs. reference site	0.32–0.47 FW vs. 0.09 FW	196
Earthworm, <i>Eisenia rosea</i> ; whole, Illinois		
Control areas	32 DW	5
From areas receiving sludge at 1600 kg Pb/hectare	624 DW; Max. 981 DW	5
Earthworm, <i>Eisenoides carolinensis</i> , whole, uncontaminated area	2100 DW	28
Insects, various species		
Distance from highway		
0–7 meters		
Sucking	16 DW	29
Chewing	27 DW	29
Predatory	31 DW	29
13–20 meters		
Sucking	9 DW	29
Chewing	10 DW	29
Predatory	20 DW	29
>20 meters		
Sucking	5 DW	29
Chewing	5 DW	29
Predatory	6 DW	29
Kansas, 1978		
Near roadway	50 DW	30
Control site	15 DW	30
Lepidopteran larvae, UK, 1979		
Near roadway	118 DW	20
Control site	<1 DW	20
Earthworm, <i>Lumbricus terrestris</i> , whole, Maryland		
Distance from highway, meters		
3.0	269 DW	31
6.1	113 DW	31
12.2	80 DW	31
24.4	43 DW	31
48.8	52 DW	31

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Eastern tent caterpillar, <i>Malacosoma americanum</i> ; whole, 1978		
Near roadway	7 DW	16
>10 m distant	<5.3 DW	16
Millipedes, Diplopoda		
UK 1979		
Near roadway	162 DW	20
Control site	34 DW	20
USA		
Near highway	(43–82) DW	16
Coral, <i>Montastrea annularis</i>		
Virgin Islands, 1980, skeleton		
Polluted reef (sewage, dredging)	0.4 FW	32
Pristine reef	0.09 FW	32
Blue mussel, <i>Mytilus edulis</i> , soft parts		
Germany	(2–6) DW	5
New Zealand	12 (<3–25) DW	5
Norway	(2–3100) DW	5
England	9 DW; (0.5–3) FW	5
Australia	(0.7–10) FW	5
Spain	(2–15) DW	5
Greenland	(2–21) FW	5
Beetle, <i>Nicrophorus tomentosus</i> , whole		
Near metal smelter	3 DW	1
Control site	2 DW	1
Grass shrimp, <i>Palaemonetes pugio</i> , whole, Virginia		
Natural marsh	0.2 DW	33
Spoil disposal area	11 DW	33
Shrimp, <i>Pandalus montagui</i> , soft parts		
Sewage dump area	31 DW	34
Control area	24 DW	34
Sea urchin, <i>Paracentrotus lividus</i> , soft parts, Italy		
Unpolluted	20 DW	25
Polluted	42 DW	25
Caterpillar, <i>Poretherria dispar</i> , whole		
Near metal smelter	9 DW	1
Control site	3 DW	1
Blackfly, <i>Simulium</i> sp., larva		
Missouri		
Tailings pond	14,233 DW	26
Illinois	24 DW	29
Slugs, Gastropoda, UK, 1979		
Near roadway	141 DW	20
Control site	27 DW	20
Spiders, Aranea, UK, 1979		
Near roadway	560 DW	20
Control site	<1 DW	20
Tubificid worms		
Rural streams	16 DW	35
Urban streams	367 DW	35
Woodlice, Isopoda		
UK, 1979		
Near roadway	152 DW	20
Control site	19 DW	20
USA		
Near highway	(380–682) DW	16

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
FISH		
Spotted wolffish, <i>Anarhichas minor</i> , near lead mine, Greenland		
Liver	Max. 1.8 FW	36
Muscle	Max. 0.12 FW	36
European eel, <i>Anguilla anguilla</i> ; Weser River, Germany; 1991		
Bile	0.03 FW	90
Intestine	0.09 FW	90
Liver	0.18 (0.12–0.28) FW	90
Adult parasites, whole		
Acanthocephalan, <i>Paratenuisentis</i> sp.	3.7 (2.1–5.6) FW	90
Nematode, <i>Anguillicola</i> sp.	0.02 FW	90
Coastal marine fishes, USA		
Liver		
5 species	(<0.1–0.2) FW	37
20 species	(0.2–0.4) FW	37
33 species	(0.4–0.6) FW	37
13 species	(0.6–0.8) FW	37
6 species	(0.8–1) FW	37
5 species	(1–3) FW	37
Muscle		
5 species	(0.1–0.3) FW	37
92 species	(0.3–0.5) FW	37
51 species	(0.5–0.7) FW	37
7 species	(0.7–1) FW	37
4 species	(1–3) FW	37
Whitefish, <i>Coregonus</i> spp., Sweden, liver		
Polluted lake	(6–7) DW	38
Reference lake	<1 DW	38
Fish		
Upper Mississippi River (Minnesota-Iowa), 1979		
Common carp, <i>Cyprinus carpio</i>		
Whole	3 (1–12) DW	39
Liver	9 (2–32) DW	39
Bluegill, <i>Lepomis macrochirus</i>		
Whole	0.4 (0.2–1.1) DW	39
Fish		
England; 1985–87; Rivers Brett and Chelmer		
European eel, <i>Anguilla anguilla</i>		
Liver	0.6 (0.04–3.8) FW	91
Muscle	0.06 FW; Max. 0.8 FW	91
Roach, <i>Rutilus rutilus</i>		
Liver	Max. 0.6 FW	91
Muscle	0.06 (0.01–0.8) FW	91
Five additional species		
Liver	Max. 0.3 FW	92
Muscle	0.05 FW; Max. 0.36 FW	92
Nigeria; Lagos lagoon; 9 species; smoke-dried		
Heads	10.4 DW	93
Muscle	6.7 DW	93
Skin	12.2 DW	93
Whole	9.0 DW	93

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Missouri, 9 species		
Blood	0.13–1.7 FW	94
Carcass	0.03–1.3 FW	94
Fish, freshwater, whole		
Nationwide, USA		
1971	Max. 1.4 FW	40
1972	0.4 (Max. 5.2) FW	40
1973	Max. 1.4 FW	40
1976–77	0.3 FW	41
1978–79	0.2 (0.1–6.7) FW	42
1980–81		
Mean	0.17 FW	42, 96
Max.	1.9 FW	42, 96
85th percentile	0.25 FW	42, 96
1984–85		
Mean	0.11 FW	96
Max.	4.9 FW	96
85th percentile	0.22 FW	96
Russia, Lake Baikal; 1992		
Sculpins, whole		
<i>Comephorus</i> spp.	0.6–3.3 (0.6–8.5) FW	95
<i>Cottocomorphorus</i> spp.	Max. 0.6 FW	95
<i>Paracottus</i> sp.	Max. 0.2 FW	95
Southeastern Missouri, Big River		
Upstream from mine site		
Catostomids	0.4–0.8 FW	42
Longear sunfish, <i>Lepomis megalotis</i>	18 FW	42
Black redhorse, <i>Moxostoma duquesnei</i>	15 FW	42
Smallmouth bass, <i>Micropterus dolomieu</i>	9 FW	42
Bluegill, whole		
Missouri, mine tailings pond,		
At pond	128 DW	26
1 km downstream	23 DW	26
65 km downstream	5 DW	26
Longear sunfish; Missouri; summer 1980; stream contaminated with mine tailings vs. reference site		
Bone	0.3 FW vs. 0.02 FW	87
Blood	0.9 FW vs. 0.03 FW	87
Perch, <i>Perca fluviatilis</i> ; Norway; 1991; lake near highway vs. reference lake		
Liver	0.8 FW vs. 0.3 FW	97
Muscle	0.08 FW vs. no data	97
Plaice, <i>Platichthys flesus</i> , whole		
Polluted area, UK		
Age 2+	20 DW	43
Age 3+	24 DW	43
Age 4+	26 DW	43
Age 5+	28 DW	43
Uncontaminated area, UK		
Age 2+	14 DW	43
Age 3+	16 DW	43
Age 4+	18 DW	43
Age 5+	19 DW	43
Arctic char, <i>Salvelinus alpinus</i> ; Austria; acidic lake with 0.5 µg Pb/L; kidney	19.0 DW	98

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
AMPHIBIANS AND REPTILES		
Amphibians, whole		
Near metal smelter	No species found	1
Control site, 5 species	12 DW	1
Snapping turtle, <i>Chelydra serpentina</i> ; Big River, Missouri (contaminated with lead mine tailings of 1000–3000 mg Pb/kg tailings) vs. reference site		
Blood	2.5 FW vs. 0.3 FW	99
Bone	115 FW vs. 1 FW	99
Brain	0.3 FW vs. 0.2 FW	99
Carapace	33 FW vs. 1 FW	99
Liver	0.5 FW vs. 0.2 FW	99
Muscle	0.2 FW vs. 0.1 FW	99
Bullfrog, <i>Rana catesbeiana</i> ; tadpoles; South Carolina; 1997		
With digestive tract		
Body	5.4 DW; 1.1 FW	197
Tail	0.3 DW; 0.05 FW	197
Whole	3.9 DW; 0.8 FW	197
Without digestive tract		
Body without gut	0.8 DW	197
Tail	0.3 DW	197
Digestive tract	28.5 DW	197
Whole	3.2 DW	197
Frog, <i>Rana</i> sp., tadpole, whole		
Missouri, tailings pond	4139 DW	26
Distance downstream from tailings pond		
1 km	552 DW	26
25 km	37 DW	26
Reptiles; Punjab, India; urban vs. rural areas; species unidentified		
Cobra scales (shed skins)	201 DW vs. 5 DW	100
Wall-lizard scales	151 DW vs. 7 DW	100
Southeastern Missouri, 1981–82, Big River		
Bullfrog, <i>Rana catesbeiana</i> , carcass		
Upstream from mine site	1 (Max. 6) FW	45
Downstream	33 (Max. 300) FW	45
Northern water snake, <i>Nerodia sipedon</i> , carcass		
Upstream	0.2 (Max. 0.6) FW	45
Downstream	7 (Max. 14) FW	45
Common box turtle, <i>Terrapene carolina</i> (age 15 years)		
Near lead smelter, Missouri		
Humerus	51 FW	46
Femur	64 FW	46
Liver	21 FW	46
Kidney	24 FW	46
Blood	6 FW	46
Skin	0.4 FW	46
Near Morgantown WV, Control site (age 17 years)		
Humerus	4 FW	46
Femur	4 FW	46
Liver	1 FW	46
Kidney	2 FW	46

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Blood	0.1 FW	46
Skin	0.1 FW	46
South African clawed frog, <i>Xenopus laevis</i>		
Fed worms from lead-contaminated soils		
Bone	24 FW	47
Skin	3 FW	47
Muscle	1 FW	47
Kidney	15 FW	47
Liver	7 FW	47
Fed uncontaminated worms		
Bone	5 FW	47
Skin	0.8 FW	47
Muscle	0.6 FW	47
Kidney	3 FW	47
Liver	1 FW	47
BIRDS		
Sharp-shinned hawk, <i>Accipiter striatus</i> ; eastern United States; 1991–93; liver	0.07 (0.03–0.14) FW	101
Wood duck, <i>Aix sponsa</i> ; Northern Idaho; lead-contaminated area vs. reference site; maximum values		
Blood	8.0 FW vs. 0.6 FW	86
Diet	610.0 FW vs. 0.6 FW	86
Liver	14.0 FW vs. <0.06 FW	86
Intestinal digesta	32.0 DW vs. 8.4 DW	102
Mallard, <i>Anas platyrhynchos</i>		
Virginia; 1986; lead poisoned from ingested skeet shot; liver Ebro Delta, Spain; 1991–92; from lead shot areas containing 60,000–544,750 shot pellets/ha	21 FW	103
Bone	42 (8–211) FW	104
Brain	1 (0.1–117) FW	104
Kidney	1 (<0.05–30) FW	104
Liver	0.8 (0.06–22) FW	104
Pancreas	3 (1–14) FW	104
Spleen	1 (0.1–2) FW	104
California; August 1987; National Wildlife Refuges; blood		
69% (background)	<0.2 FW	105
12% (elevated)	0.2–0.5 FW	105
19% (toxic)	>0.5 FW	105
France; 1987–90; 12.8% contained ingested lead shot; blood		
22% of birds containing shot	>0.4 FW	191
Italy; Autumn 1990; blood	0.46 (0.1–1.2) FW	106
American black duck, <i>Anas rubripes</i> ; wintering in Tennessee; 1986–88; blood		
All birds		
88%	<0.2 FW	107
12%	>0.2 FW	107
Adults, 14.4%	>0.2 FW	107
Juveniles, 8.2%	>0.2 FW	107
White-fronted geese, <i>Anser albifrons</i> ; Japan; died from ingestion of spent lead shot; liver	6.9–67.7 FW	190

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Golden eagle, <i>Aquila chrysaetos</i>		
California; Kern and Ventura counties; 1985–86; blood; males vs. females		
Adults	0.08 FW (Max. 0.19 FW) vs. 0.40 FW (Max 5.5 FW)	108
Subadults	0.28 FW (Max. 4.1 FW) vs. 0.19 (Max. 1.3 FW)	108
All birds	0.26 FW vs. 0.25 FW	108
Idaho; 1977–86; found dead or moribund; liver	8.9 (0.2–26.0) FW	146
Idaho; 1989–94; blood		
58% (background)	<0.2 FW	109
42% (elevated)	>0.2 FW	109
28% (toxic)	>0.6 FW	109
Canvasback, <i>Aythya valisineria</i>		
Blood		
Chesapeake Bay, 1974		
Normal	(0.059–0.064) FW	48
Abnormal (17%)	0.263 FW	48
Louisiana, 1991–94		
Abnormal (60%)	>0.2 FW	194
Wingbone		
La Crosse, Wisconsin		
1976		
Males	18 (6–56) DW	49
Females	5 (1–20) DW	49
Immatures		
Males	0.8 (0.1–4) DW	49
Females	1 (0–21) DW	49
1977		
Males	11 (9–12) DW	49
Females	8 (1–48) DW	49
Immatures		
Males	0.8 (<0.1–7) DW	49
Females	<0.5 DW	49
Keokuk, Iowa		
1976		
Males	6 (4–10) DW	49
Females	5 (1–20) DW	49
Immatures		
Males	0.5 (0.1–2) DW	49
Females	1 (0.1–22) DW	49
1977		
Males	2 (0.2–19) DW	49
Females	4 (1–19) DW	49
Birds		
Alaska; eiders; 1992–94; found dead or moribund		
Spectacled eider, <i>Somateria fischeri</i>		
Blood	8.5 FW	135
Liver	26–38 FW	135
Common eider, <i>Somateria mollissima</i> ; liver	52 FW	135
Australia; New South Wales; 1992; 6 locations; 716 ducks representing 7 species; liver		
709 of 716 ducks	0.06–0.35 (<0.01–2.8) FW	110
3 of 716	>2 FW	110
4 of 716	>6 FW, Max. 16 FW	110

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Australia; Victoria; 1992; hunter-killed waterfowl; 3 species of ducks		
Bone	22–39 (0.1–168) DW	136
Liver	8–25 (0.05–94) FW	136
California, 1980–81		
Turkey vulture, <i>Cathartes aura</i> ; breeding adults vs. nonbreeding adults		
Feathers	0.5–1.9 DW vs. 0.7–6.4 DW	115
Kidney	0.2–1.9 FW vs. 0.2–5.6 FW	115
Liver	0.1–0.8 FW vs. 0.4–1.7 FW	115
Common raven, <i>Corvus corax</i>		
Bone	0.6–9.1 DW	115
Feather	1.5–5.6 DW	115
Kidney	0.1–1.1 FW	115
Liver	0.7–1.5 FW	115
California condor, <i>Gymnogyps californianus</i>		
Feather	1.9–14.0 DW	115
Potential food items		
Mule deer, <i>Odocoileus hemionus</i> , flesh	0.06–17.5 FW	115
Cattle, <i>Bos</i> sp.		
Muscle	0.8 FW	115
Placenta	0.7 (0.2–1.8) FW	115
Sheep, <i>Ovis</i> sp., flesh	0.04 FW	115
England; 1981–92; 16 species of raptors; liver; max. values		
6 species	2–6 DW	137
6 species	7–15 DW	137
4 species	>15 DW	137
Florida		
Wading birds; 9 species; nestlings; found dead; 1987–91; liver		
All locations	0.3 (0.1–6.3) FW	112
Everglades vs. mangrove areas	0.5 FW vs. 0.2 FW	112
Waterbirds; 8 species; 1991–93		
Eggs	<0.01–0.15 FW	113
Liver	Usually <0.2 FW; Max. 2.4 FW	113
France; raptors; liver		
Diurnal, 11 species	0.1–0.7 DW; Max. 2.6 DW	138
Nocturnal, 5 species	0.1–0.4 DW; Max. 5.2 DW	138
Lead-contaminated	7.6–711.0 DW	138
France; waterbirds; 9 species; Rhone River delta; 1988–89		
Bone	0.4–9.2 (0.1–206.0) DW	139
Feather	1.6–5.9 (0.3–39.0) DW	139
Liver	0.2–3.1 DW; Max. 51.0 DW	139
Idaho; 1987; near mining and smelting activities		
Mallard, <i>Anas platyrhynchos</i>		
Blood	Max. 10.2 FW	140
Liver	Max. 2.8 FW	140
American robin, <i>Turdus migratorius</i> ; nestlings		
Blood	Max. 0.87 FW	140
Liver	Max. 5.6 FW	140
Waterfowl, found dead, liver		
Illinois; Mississippi River; spring 1985–86; diving ducks; blood		
Canvasback, <i>Aythya valisineria</i>	0.31 FW	141

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Lesser scaup, <i>Aythya affinis</i>	0.22 FW	141
Ring-necked duck, <i>Aythya collaris</i>	0.55 FW	141
Netherlands; found dead; 1991		
Grey heron, <i>Ardea cinerea</i>		
Bone	1.0 DW; Max. 1.4 DW	143
Kidney	1.0 (0.2–2.6) DW	143
Liver	1.4 (0.4–2.1) DW	143
Buzzard, <i>Buteo buteo</i>		
Bone	1.6 (0.4–22.5) DW	143
Kidney	0.9 (0.2–3.7) DW	143
Liver	0.7 (0.1–10.9) DW	143
Common eider, <i>Somateria mollissima</i>		
Bone	3.0 (1.1–8.1) DW	143
Kidney	0.7 (0.3–2.6) DW	143
Liver	0.7 (<0.1–4.9) DW	143
Poland		
House sparrow, <i>Passer domesticus</i> ; nestlings; liver		
Healthy	2.9 DW	145
Sick	3.7 DW	145
Dead	5.3 DW	145
Tree sparrow, <i>Passer montanus</i> ; nestlings; liver		
Healthy	2.5 DW	145
Sick	3.4 DW	145
Dead	4.8 DW	145
Seabirds		
Mid-Pacific Ocean; 1990; 5 species; adults; feather	1.4–2.7 DW	142
New York Bight; 1989; 5 species		
Eggs	0.3–6.7 DW	144
Feather, fledglings	0.8–4.1 DW	144
Southwestern Russia; 24 species; 1993–95; bone		
7 species	0.04–0.92 DW	114
12 species	2.2–9.4 DW	114
3 species	13.0–13.7 DW	114
2 species	25.7–30.0 DW	114
Galveston Bay, Texas, 1980–81, 3 species, liver	(0.1–0.5) FW	50
Probers with lead shot in gizzards		
Bone	11 FW	51
Feather	4 FW	51
Liver	0.3 FW	51
Probers without lead shot in gizzards		
Bone	6 FW	51
Feather	5 FW	51
Liver	<0.1 FW	51
Non-probers		
Bone	6 FW	51
Feather	2 FW	51
Liver	<0.1 FW	51
Ruffed grouse, <i>Bonasa umbellus</i>		
Virginia, rural areas		
Liver	2.3 DW	52
Bone	2.8 (0.4–9) DW	52
Canada goose, <i>Branta canadensis</i> ; Manitoba; 1986–88; blood	0.18 FW	111
Knot, <i>Calidris canutus</i> ; feather		
Juvenile	2 DW	53
Adult	7 DW	53

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Lesser snow goose, <i>Chen caerulescens</i> <i>caerulescens</i> ; California; 1982–83; lead-poisoned		
Kidney	100 (41–254) DW	116
Liver	117 (61–205) DW	116
Houbara bustard, <i>Chlamydotis undulata maqueenii</i> ; captive flock; United Arab Emirate; died from ingestion of lead-based paint (6600 mg Pb/kg DW paint)		
Brain	Max. 4.3 FW	117
Kidney	Max. 47.0 FW	117
Muscle	Max. 1.1 FW	117
Fecal samples with paint particles	398.0 FW	117
Marsh harrier, <i>Circus aeruginosus</i> ; France		
Blood; 1990–92		
Captive birds	0.05–0.11 FW	119
Wild birds		
31% (elevated)	>0.3 FW	119
14% (poisoned)	>0.6 FW	119
Blood; 1994–95		
Subadults	0.01 FW	118
Adults		
Hunting season	0.35–0.8 FW	118
Other times	<0.3 FW	118
Rock dove, <i>Columba livia</i>		
Slovakia; bone; found dead or captured		
Body weight >350 g	24.8 DW	198
Body weight <350 g	35.8 DW	198
Females	27.7 DW	198
Males	18.1 DW	198
Rural locations	29.7 DW	198
Urban locations	50.8 DW	198
United Kingdom		
Urban area		
Kidney		
Female	204 DW; (9–30) FW	54
Male	122 DW	54
Bone		
Female	338 DW	54
Male	126 DW	54
Rural area		
Kidney		
Female	6 DW; (1.2–1.9) FW	54
Male	8 DW	54
Bone		
Female	16 DW	54
Male	19 DW	54
Tokyo, Japan		
Femur		
Urban areas	(16–31) FW	55
Suburban areas	(2–3) FW	55
Kidney		
Urban areas	(2–3) FW	55
Suburban areas	<1 FW	55
Feather		
Juveniles	11.5 DW	120
Adults	15.6 DW	120

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Nestlings, various ages		
<15 days	7.8 DW	120
16–20 days	9.3 DW	120
21–25 days	14.5 DW	120
Trumpeter swan, <i>Cygnus buccinator</i>		
Western USA; 1976–87		
Blood	Max. 0.71 FW	121
Liver	Max. 37.0 FW	121
Wisconsin; 1989; died of lead poisoning; 6 lead shot found in gizzard; blood	2.4 FW	122
Tundra swan, <i>Cygnus columbianus</i>		
Coeur d'Alene River Basin, Idaho vs. reference site; feces	800 DW (90th percentile was 2700 DW) vs. 2.1 DW	123
Northern Idaho near mining and smelting complex; 1987–89; dead or moribund vs. apparently healthy birds from reference site		
Liver	6.4–40.0 FW vs. Max. 1.0 FW	124
Blood	1.3–9.6 FW vs. 0.5–2.3 FW	124
Mute swan, <i>Cygnus olor</i>		
Chesapeake Bay, MD; sediments had 5–10 mg Pb/kg DW; 1995		
Suspected of having ingested lead shot or sinkers		
Intestinal digesta	36.0 DW	126
Liver	7.6 DW	126
No evidence of lead intoxication		
Intestinal digesta	1.6 (<1.5–6.4) DW	126
Liver	1.5 (<1.0–6.3 DW)	126
Denmark, 1982		
Blood		
Adults	0.25 (0.13–0.54) FW	56
Juveniles	0.11 (0.07–0.39) FW	56
England; 1982–85; blood		
From unfished gravel pits (16% with blood Pb >0.4 mg/L)	0.21 (0.001–1.28) FW	128
From fished gravel pits (59% with blood Pb >0.4 mg/L)	0.79 (0.004–9.62) FW	128
Ireland; found dead from lead poisoning		
Gizzard	13 (6–85) FW	127
Heart	14 (6–730) FW	127
Kidney	113 (40–350) FW	127
Liver	315 (93–450) FW	127
Muscle	19 (8–273) FW	127
Pancreas	67 (20–155) FW	127
Scotland; 1980–96; died of lead poisoning		
Blood	0.52 FW	125
Kidney	662.0 DW	125
Whooper swan, <i>Cygnus cygnus</i> ; Scotland; 1980–86; died from lead poisoning		
Blood	0.48 FW	125
Kidney	223.0 DW	125
Peregrine falcon, <i>Falco peregrinus</i>		
Baltimore, Maryland, Age 7+		
Liver	0.8 FW	57
Kidney	1.4 FW	57

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Prey organism		
Rock dove		
Urban		
Blood	1 (0.3–17) FW	57
Liver	3 FW	57
Kidney	9 FW	57
Whole	5 FW	57
Rural		
Blood	<0.1 FW	57
Liver	0.4 FW	57
Kidney	0.5 FW	57
Whole	0.3 FW	57
Laysan albatross, <i>Diomedea immutabilis</i> ; chicks; Hawaii; 1994		
Blood	74% had >0.2 FW; Max. 26.7 FW	129
Liver	74% had >2.0 FW; Max. 70.5 FW	129
Common loon, <i>Gavia immer</i>		
Liver, lead-poisoned	(21–39) FW	58
Liver		
Healthy birds	<2.0 FW	130
Lead sinkers in gizzard	11.5 (5–18) FW	130
No lead in gizzard	0.06 FW; Max. 0.11 FW	130
Whooping crane, <i>Grus americana</i> ; yearling; 1984; died of lead poisoning		
Blood	5.7 FW	131
Kidney	10.4 FW	131
Liver	24.0 FW	131
Mississippi sandhill crane, <i>Grus canadensis pulla</i> ; Mississippi; 1992; found dead after ingesting metallic object; liver	70.0 FW	132
California condor, <i>Gymnogyps californianus</i> ; 1980–86		
Subadults, lead-poisoned; found dead		
Blood	1.8 FW	133
Feathers	9.9 DW	133
Kidney	47.0 FW	133
Liver	6–35 FW	133
Subadults; live; non-lead-poisoned		
Feather	1.8 FW	133
Kidney	0.4 FW	133
Liver	<1.0 FW	133
Live condors; blood		
1982	ND–5.5 FW	133
1983	0.06 FW	133
1984	0.07–1.2 FW	133
1985	ND–1.8 FW	133
1986	0.06–4.2 FW	133
Griffon vulture, <i>Gyps fulvus</i> ; Spain; 1994; died of lead poisoning 36 h after admittance to rehabilitation center; liver	52.0 DW; 12.6 FW	134
Bald eagle, <i>Haliaeetus leucocephalus</i>		
British Columbia; 1988–91; found dead or moribund		
Blood	>0.8 FW	148
Bone	7.3 DW	148
Kidney	12.0–25.0 FW; 34.0 DW	147–149
Liver	5–50 FW	147, 149

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Nationwide, 1978–81, found dead, suspected lead poisoning		
Liver	28 (11–61) FW	59
Liver		
Control	0.6 FW	60
Lead-poisoned	21 FW	61
Idaho; 1977–86; found dead or moribund; liver	25.7 (0.2–51.0) FW	146
Barn swallow, <i>Hirundo rustica</i>		
Near Baltimore-Washington Parkway, 1979		
Feather		
Male	67 (55–82) DW	62
Female	54 (43–68) DW	62
Nestling	2 (2–3) DW	62
Carcass		
Male	5 (4–6) DW	62
Female	9 (6–12) DW	62
Nestling	2 (1–2) DW	62
Stomach contents		
Male	5 DW	62
Female	7 DW	62
Nestling	3 DW	62
Reference colony, 1979		
Feather		
Male	24 (21–28) DW	62
Female	19 (16–22) DW	62
Nestling	2 (2–3) DW	62
Carcass		
Male	4 (3–5) DW	62
Female	5 (3–7) DW	62
Nestling	1 DW	62
Stomach contents		
Male	0.2 DW	62
Female	2 DW	62
Nestling	2 DW	62
Herring gull, <i>Larus argentatus</i>		
Eggs; Long Island, NY		
1989	2.5 DW	151
1991–93	0.5–0.9 DW	151
1994	0.4 DW	151
Feathers; fledglings; 1990		
New York	1.7–2.5 DW	150
NY-NJ harbor	1.8–3.5 DW	150
New Jersey	1.0–1.5 DW	150
Virginia	1.6 DW	150
Franklin's gull, <i>Larus pipixcan</i> ; Minnesota; 1994		
Eggs	1.3 DW	152
Diet (earthworms)	0.26 DW	152
Feathers		
Females	3.2 DW	152
Males	2.8 DW	152
House sparrow, <i>Passer domesticus</i> , Illinois		
Urban areas		
Feather	158 DW	63
Intestine	26 DW	63
Liver	12 DW	63
Lung	7 DW	63

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Kidney	34 DW	63
Femur	130 DW	63
Muscle	2 DW	63
Rural areas		
Feather	27 DW	63
Intestine	2 DW	63
Liver	0.6 DW	63
Lung	0.9 DW	63
Kidney	3 DW	63
Femur	17 DW	63
Muscle	0.9 DW	63
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg		
South Carolina 1971–72	0.03 (0.01–0.11) FW	64
Florida, 1969–70	0.03 (0.01–0.05) FW	64
Liver		
Found dead		
1972		
Georgia	0.1 FW	64
Florida	0.1 FW	64
1973		
South Carolina	0.3 FW	64
Florida	0.2 FW	64
Shot, 1970		
Florida	0.1 FW	64
South Carolina	0.1 FW	64
Ring-necked pheasant, <i>Phasianus colchicus</i> ; Poland; 1986; 3 locations		
Bone	1.1–1.5 DW	153
Crop contents	1.2–7.3 DW	153
Feather	3.4–9.4 DW	153
Kidney	8.8–42.3 DW	153
Liver	4.6–8.4 DW	153
Muscle	0.5–2.1 DW	153
Greater flamingo, <i>Phoenicopterus ruber</i> ; Spain; liver 1991; gizzards with 18–37 ingested shot pellets; found dead	37–112 FW	155
1992–94; lead-poisoned	192 (<2.5–992.2) DW	192
Caribbean flamingo, <i>Phoenicopterus ruber ruber</i> ; Yucatan, Mexico; 1989; died of lead poisoning; liver	313 DW	154, 193
Sora rail, <i>Porzana carolina</i>		
Maryland		
Lead shot in gizzard		
Liver	(0.1–17) FW	65
Bone	(1–127) DW	65
No lead shot in gizzard		
Liver	(<0.01–0.08) FW	65
Bone	(<0.4–42) DW	65
Songbirds, carcass		
Near metal smelter, 10 species	56 (9–240) DW	1
Control site, 9 species	15 (6–25) DW	1
Southeastern Missouri, 1981–82, Big River		
Green backed heron, <i>Butorides striatus</i>		
Liver		
Upstream from mine site	0.1 (Max. 0.3) FW	45
Downstream	0.5 (Max. 1.5) FW	45

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Northern rough-winged swallow, <i>Stelgidopteryx serripennis</i>		
Carcass		
Upstream of mine site	0.5 (Max. 5) FW	45
Downstream	1 (Max. 15) FW	45
Common tern, <i>Sterna hirundo</i>		
Egg contents	0.09 FW	156
Feathers		
Males	1.3 DW	156
Females	1.6 DW	156
European starling, <i>Sturnus vulgaris</i>		
Nesting near highway, Maryland		
Carcass	(4–10) DW	66
Feathers	(7–52) DW	66
Stomach contents	(84–94) DW	66
Control site		
Carcass	(1–3) DW	66
Feathers	(3–14) DW	66
Stomach contents	(6–7) DW	66
Nationwide, whole less beaks, skins, wings, and feet		
1971	1.3 (0.1–6.6) FW	67
Chicago, Ill.	5.0 FW	67
Indiana, urban	3.4 FW	67
Quincy, MA	6.6 FW	67
Jamestown, NY	5.1 FW	67
1973	0.9 (<0.1–3.2) FW	68
Urban	1.1 (<0.1–3.2) FW	68
Rural	0.7 (<0.1–2.4) FW	68
Robin, <i>Turdus migratorius</i> ; Illinois		
Urban areas vs. rural areas		
Feather	79 DW vs. 25 DW	63
Intestine	24 DW vs. 3 DW	63
Liver	10 DW vs. 2 DW	63
Lung	10 DW vs. 2 DW	63
Kidney	25 DW vs. 7 DW	63
Femur	133 DW vs. 41 DW	63
Muscle	1 DW vs. 1. DW	63
Blackbird, <i>Turdus merula</i> ; first primary feathers; Germany; 1984–86; metals-contaminated site		
Age of bird (days) and feather treatment		
(4) unwashed	8.5 DW	157
(26) washed	16.9 DW	157
(150) washed	24.8 DW	157
(400) washed	60.5 DW	157
(400) unwashed	450.0 DW	157
Waterfowl, nationwide, 7 species, wingbones, 1972–73	(<0.5–361.0) DW	69
Mallard, <i>Anas platyrhynchos</i>		
Adult	12 DW	69
Immature	10 DW	69
Pacific flyaway	6 DW	69
Alaska	8 DW	69
Washington	24 DW	69

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Oregon		
Columbia River	45 DW	69
Other	15 DW	69
California		
Merced	15 DW	69
Sacramento	38 DW	69
Other	25 DW	69
Northern pintail, <i>Anas acuta</i>		
Adult	7 DW	69
Immature	6 DW	69
Mottled duck, <i>Anas fulvigula</i>		
Adult	48 DW	69
Immature	40 DW	69
Canvasback		
Adult	17 DW	69
Immature	8 DW	69
Redhead, <i>Aythya americana</i>		
Adult	26 DW	69
Immature	24 DW	69
Lesser scaup, <i>Aythya affinis</i>		
Adult	3 DW	69
Immature	2 DW	69
Black duck, <i>Anas rubripes</i>		
Adult	8 DW	69
Mourning dove, <i>Zenaida macroura</i> ; New Mexico; 1985–87; liver		
August	3.3 FW	158
October	0.5 FW	158
December	0.0 FW	158

MAMMALS

Field mouse, *Apodemus sylvaticus*

Near abandoned lead mine

Whole body	(9–14) DW	70
Kidney	(39–46) DW	70
Liver	(12–13) DW	70
Bone	(189–352) DW	70
Brain	(6–13) DW	70
Muscle	(7–10) DW	70

Control area

Whole body	1 DW	70
Kidney	(9–13) DW	70
Liver	(5–8) DW	70
Bone	(11–21) DW	70
Brain	(3–4) DW	70
Muscle	(5–6) DW	70

Short-tailed shrew, *Blarina brevicauda*

Carcass

Near metal smelter	109 DW	1
Control site	18 DW	1

From area of high traffic levels
(>12,000 vehicles/day)

Total body	18 DW	71
Gut	24 DW	71
Spleen	4 DW	71
Liver	5 DW	71

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Lung	17 DW	71
Kidney	12 DW	71
Femur	67 DW	71
Muscle	10 DW	71
From area of low traffic levels (<400 vehicles/day)		
Total body	6 DW	71
Gut	3 DW	71
Spleen	2 DW	71
Liver	1 DW	71
Lung	8 DW	71
Kidney	4 DW	71
Femur	12 DW	71
Muscle	5 DW	71
Cow, <i>Bos bovis</i>		
Missouri, hair		
Near lead smelter		
Fall	94 DW	72
Winter	87 DW	72
Spring	96 DW	72
Summer	66 DW	72
Control area		
Fall	2 DW	72
Winter	4 DW	72
Spring	2 DW	72
Summer	1 DW	72
Dung		
Near roadway	10 DW	23
Distant site	8 DW	23
Dog, <i>Canis familiaris</i>		
Blood		
Healthy	(0.01–0.05) FW	73
Lead-poisoned	(0.06–0.15) FW	73
Red deer, <i>Cervus elaphus</i> ; Austria; 1909–1990; antlers	0.9–2.3 DW	159
Bank vole, <i>Clethrionomys glareolus</i>		
Whole body		
Near abandoned lead mine	(16–21) DW	70
Control area	(2–3) DW	70
Big brown bat, <i>Eptesicus fuscus</i>		
Whole, minus GI tract and large embryos		
Males	47 (20–90) FW	74
Females	32 (20–56) FW	74
Guano	61 DW	74
Stomach contents	4 DW	74
Horse, <i>Equus caballus</i>		
Near smelter, British Columbia		
Liver	18 FW	22
Kidney	16 FW	22
Bone	88 FW	22
Near lead smelter (some deaths), California		
Liver	(15–222) FW	75
Kidney	(14–80) FW	75
Blood	(0.4–0.5) FW	75
Control areas		
Blood	(0.1–0.3) FW	5

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Common chipmunk, <i>Eutamias townsendii</i>		
Hair		
Roadside location	235 DW	76
Control area	6 DW	76
Germany; 1983–86		
Roe deer, <i>Capreolus capreolus</i>		
Kidney	0.2–0.9 FW	160
Liver	0.2–0.7 FW	160
European hare, <i>Lepus europaeus</i>		
Kidney	0.4–1.8 FW	160
Liver	1.0–4.7 FW	160
Gorilla, <i>Gorilla gorilla gorilla</i> ; 35-year-old male at death in a Mexican zoo had various bacterial and protozoan infections and lead poisoning of unknown origin		
Blood serum	<0.2 FW	189
Kidney	0.9 FW	189
Liver	28.5 FW	189
Human, <i>Homo sapiens</i>		
Diet		
Dairy products	0.003–0.08 FW	161
Meat, fish, poultry	0.002–0.16 FW	161
Grains and cereals	0.002–0.14 FW	161
Vegetables	0.005–0.65 FW	161
Fruits and fruit juices	0.005–0.22 FW	161
Oils, fats, shortenings	0.002–0.03 FW	161
Sugar and adjuncts	0.006–0.07 FW	161
Beverages	Max. 0.000041 FW	161
Diet; children age 2–3 years; daily intake in mg Pb per kg ration		
From lead-contaminated homes	0.0374 FW	199
Reference sites	0.0014–0.0082 FW	199
Daily average intake in mg Pb/day; 1984 vs. 1990		
Infants age 6–11 months	0.016 vs. 0.004	161
Age 2 years	0.023 vs. 0.004	161
Age 14–16 years	0.029–0.041 vs. 0.006–0.008	161
Age 25–30 years	As above	161
Age 60–65 years	0.030–0.038 vs. 0.002–0.008	161
School children; Indonesia; blood		
Central District	0.083 FW with 27% >0.1 FW	162
Southern District	0.069 FW	162
Tissue residues, normal adults		
Plasma	0.00054 FW	163
Whole blood	0.119 FW	163
Patella	23.3 DW	163
Tibia	11.7 DW	163
Marine mammals		
Australia; 16 species; most found stranded		
Blubber	Usually <0.3 FW; (<0.05–3.4) FW	164
Bone	0–62 FW; Usually <4.0 FW	164
Kidney	Max. 0.77 FW; Max. 2.0 DW	164
Liver	<0.01–1.0 FW	164
Muscle	<0.05–0.25 FW	164
Canadian Arctic; 1982–94; maximum values recorded		
Beluga, <i>Delphinapterus leucas</i>		
Kidney	0.038 FW	165

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Liver	0.057 FW	165
Muscle	0.44 FW	165
Skin	0.29 FW	165
Narwhal, <i>Monodon monoceros</i>		
Kidney	0.08 FW	165
Liver	0.08 FW	165
Muscle	0.04 FW	165
Skin	0.007 FW	165
Ringed seal, <i>Phoca hispida</i>		
Liver	0.79 FW	165
Muscle	0.09 FW	165
Prairie vole, <i>Microtus ochrogaster</i> ; Illinois, whole body		
Near heavy traffic	8 DW	77
Control area	3 DW	77
House mouse, <i>Mus domesticus</i> ; Rome, Italy; feral; from areas of low traffic flow (10 vehicles/h) vs. high traffic flow (5000 vehicles/h)		
Bone	87 DW vs. 398 DW	166
Kidney	14 DW vs. 62 DW	166
Liver	8 DW vs. 30 DW	166
Polecat, <i>Mustela putorius furo</i> ; Switzerland and France; 1983–85; kidney	0.4 (ND-5.8) FW	167
Mink, <i>Mustela vison</i> ; Idaho; lead-contaminated site vs. reference site		
Liver		
1981–82	4.1 (0.4–22.0) FW vs. 0.3 (ND-3.2) FW	168
1986–87	3.2 (0.2–34.0) FW vs. no data	168
Stomach contents		
1981–82	3.8 FW vs. 1.6 (0.3–3.6 FW)	168
1986–87	3.7 (0.2–51.0) FW vs. no data	168
Little brown bat, <i>Myotis lucifugus</i>		
Whole	17 (11–29) FW	74
Guano	65 DW	74
Stomach contents	26 FW	74
Bats, <i>Myotis</i> spp., Florida 1981–83		
Guano	(3–6) DW	78
The Netherlands; 1988–93		
Red deer, <i>Cervus elaphus</i> ; age < 6 months vs. age 8 years		
Kidney	1.8 DW vs. 0.5 DW	169
Liver	0.9 DW vs. 0.8 DW	169
Rib	2.5 DW vs. 3.7 DW	169
Diet, all ages	0.97 DW	169
Wild boar, <i>Sus scrofa</i> ; age <6 months vs. age 1.5–8 years		
Kidney	1.3 DW vs. 1.1 DW	169
Liver	1.4 DW vs. 0.9 DW	169
Rib	4.8 DW vs. 9.7 DW	169
Diet, all ages	5.3 DW	169
White-tailed deer, <i>Odocoileus virginianus</i>		
Near zinc smelter, Pennsylvania		
Feces	16 (6–37) DW	79
Bone	9 (4–17) DW	79
Teeth	6 (3–11) DW	79
Kidney	2 (1–3) DW	79
Liver	<2 DW	79

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Control area, 100 km from smelter		
Feces	8 (4–16) DW	79
Bone	6 (3–11) DW	79
Teeth	2 (1–4) DW	79
Kidney	0.8 (0.5–1) DW	79
Liver	<0.4 DW	79
Muskrat, <i>Ondatra zibethicus</i>		
Liver		
Upstream from mine site	0.2 (Max. 0.3) FW	45
Downstream	0.7 (Max. 1.6) FW	45
Sheep, <i>Ovis aries</i>		
Muscle	<0.2 FW	80
Liver	<1.5 FW	80
Kidney	<1.1 FW	80
Sheep forage		
Grass		
Green	<12 FW	80
Old	<33 FW	80
Other	<24 FW	80
White-footed mouse, <i>Peromyscus leucopus</i>		
Carcass		
Near metal smelter	17 DW	1
Control site	7 DW	1
Deer mice, <i>Peromyscus maniculatus</i>		
From high density traffic area		
Bone	52 DW	81
Kidney	9 DW	81
Liver	3 DW	81
Brain	1 DW	81
Feces	154 DW	81
From low density traffic area		
Bone	5 DW	81
Kidney	3 DW	81
Liver	1 DW	81
Brain	0.1 DW	81
Feces	7 DW	81
Roadside locations		
Brain	(0.6–0.8) DW	5
Liver	(0.9–3) DW	5
Kidney	(2–8) DW	5
Bone	(14–52) DW	5
Hair	235 DW	5
Control areas		
Brain	0.1 DW	5
Liver	1 DW	5
Kidney	3 DW	5
Bone	5 DW	5
Hair	6 DW	5
Illinois, 1982		
Distance from lead battery reclamation plant		
100 m		
Liver	4 FW	82
Kidney	13 FW	82
Bone	79 FW	82
1000 m		
Liver	1 FW	82

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Kidney	3 FW	82
Bone	2 FW	82
Whole, 1978–79		
Near Cu-Zn mine		
Juveniles	4 FW	83
Adults	5 FW	83
Control site		
Juveniles	0.5 FW	83
Adults	0.7 FW	83
Raccoon, <i>Procyon lotor</i>		
Alabama; 1992–93; males vs. females		
Kidney	4.7 FW vs. 5.2 FW	171
Liver	5.1 FW vs. 1.5 FW	171
Connecticut, lead-intoxicated		
Liver, kidney	>35 FW	84
Eastern USA; summer 1992; blood		
New Jersey	0.044 FW; Max. 0.17 FW	172
Pennsylvania	0.026 FW	172
Laboratory-confined	0.025 FW	172
All raccoons	0.038 FW	172
Fruit bats, <i>Pteropus</i> sp.; Brisbane, Australia; found dead or traumatized; urban vs. non-urban areas		
Brain	2 DW vs. 0.8 DW	170
Fur	21 DW vs. 1 DW	170
Heart	1 DW vs. 1 DW	170
Humerus	108 DW vs. 13 DW	170
Kidney	98 DW vs. 1 DW	170
Liver	37 DW vs. 2 DW	170
Lung	3 DW vs. 0.6 DW	170
Muscle	2 DW vs. 0.4 DW	170
Rib	178 DW vs. 22 DW	170
Skull	204 DW vs. 11 DW	170
Spleen	6 DW vs. 1 DW	170
Teeth	167 DW vs. 12 DW	170
Reindeer, <i>Rangifer tarandus fennica</i> ; northwest Russia; 1986–90		
Antlers	22 (5–65) DW	177
Bone	42 (3–146) DW	177
Teeth	30 (3–85) DW	177
Commensal rat, <i>Rattus norvegicus</i>		
Houston, Texas, 1978–79		
Urban		
Bone	125 FW	85
Kidney	9 FW	85
Stomach contents	31 FW	85
Feces	72 FW	85
Rural		
Bone	8 FW	85
Kidney	3 FW	85
Stomach contents	3 FW	85
Feces	8 FW	85
Rodents		
Rodents; 3 species; San Francisco Bay, CA; 1989; pickleweed habitat; kidney		
House mouse, <i>Mus musculus</i>	0.8–9.8 DW	173
Deer mouse, <i>Peromyscus maniculatus</i>	0.6–1.9 DW	173
California vole, <i>Microtus californianus</i>	0.7–6.2 DW	173

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
England; juveniles and adults; contaminated grasslands site established on fluospar tailings vs. reference site		
Wood mouse, <i>Apodemus sylvaticus</i>		
Bone	72 DW vs. 65 DW	174
Gut contents	145 DW vs. 17 DW	174
Kidney	23 DW vs. 10 DW	174
Liver	13 DW vs. 7 DW	174
Whole	21 DW vs. 13 DW	174
Short-tailed field vole, <i>Microtus agrestis</i>		
Bone	121 DW vs. 28 DW	174
Gut contents	208 DW vs. 19 DW	174
Kidney	22 DW vs. 6 DW	174
Liver	11 Dw vs. 5 DW	174
Whole	42 DW vs. 9 DW	174
Common shrew, <i>Sorex araneus</i>		
Bone	641 DW vs. 41 DW	174
Gut contents	427 DW vs. 73 DW	174
Kidney	81 DW vs. 18 DW	174
Liver	23 DW vs. 5 DW	174
Whole	100 DW vs. 11 DW	174
Metals-contaminated site vs. reference site; maximum values		
Common shrew (mean intake of 19–53 mg Pb/kg BW daily)		
Kidney	323 DW vs. 178 DW	175
Liver	9.2 DW vs. 8.7 DW	175
Short-tailed field vole (mean intake of 2–10 mg Pb/kg BW daily)		
Kidney	14 DW vs. 8 DW	175
Liver	4 DW vs. 3 DW	175
Roadside rodents; 1976; whole, minus GI tract and large embryos		
Short-tailed shrew, <i>Blarina brevicauda</i>		
Near highway	26 (6–130) FW	74
Distant site	2 FW	74
Meadow vole, <i>Microtus pennsylvanicus</i>		
Near highway	2 (0.2–5) FW	74
Distant site	<1.4 FW	74
White-footed mouse, <i>Peromyscus leucopus</i>		
Near highway	5 (0.4–41) FW	74
Distant site	1 (0.3–13) FW	74
Common shrew, <i>Sorex araneus</i> , UK, 1979		
Near roadway		
Liver	17 DW	20
Kidney	46 DW	20
Bone	193 DW	20
Pelt	10 DW	20
Control site		
Liver	<1 DW	20
Kidney	9 DW	20
Bone	41 DW	20
Pelt	3 DW	20
Rodents; near Coeur d'Alene River, Idaho; 1987; whole; adult vs. juvenile		
Deer mouse, <i>Peromyscus maniculatus</i>	34 FW vs. 43 FW	88
Voles, <i>Microtus</i> spp.	28 FW vs. 20 FW	88

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Russia; Lake Ladoga, 1990–93		
Bearded seal, <i>Erignathus barbatus</i>		
Hair	1.4 (0.6–2.1) DW	176
Ringed seal, <i>Phoca hispida ladogensis</i>		
Hair	6.3 (0.3–40) DW	176
Kidney	0.6 FW; Max. 1.3 FW	176
Liver	0.7 FW; Max. 2.4 FW	176
Muscle	0.6 (0.2–15) FW	176
Slovenia; 1985–88; game (deer and boar); near lead mine and smeltery vs. reference site		
Heart	0.3 (0.05–8) FW vs. 0.7 (<0.05–16) FW	178
Kidney	1.3 FW; Max. 8.6 FW vs. 1.6 FW; Max. 31.1 FW	178
Liver	1.0 FW; Max. 7.9 FW vs. 0.4 FW; Max. 3.3 FW	178
Mexican free-tailed bat, <i>Tadarida brasiliensis</i> ; 1991; liver; females vs. males		
Carlsbad Cavern, NM		
May	1.9 FW vs. 3.5 FW	179
August	4.4 FW; Max. 13.7 FW vs. 3.7 FW; Max. 16.0 FW	179
Vickery Cave, OK		
May	2.2 FW; Max. 7.0 FW vs. 5.4 FW; Max. 49.4 FW	179
August	5.1 FW vs. 5.3 FW	179
Bottlenose dolphin, <i>Tursiops truncatus</i>		
South Carolina; found stranded; liver	<0.1 FW	180
Captive animal died after ingesting lead-containing air gun pellets vs. control		
Kidney cortex	4.2 FW vs. <0.15 FW	181
Liver	3.6 FW vs. <0.7 FW	181

INTEGRATED STUDIES

Great Lakes, Lake Ontario		
Plankton	4 DW	11
Zooplankton	(1–5) DW	11
Fish	(0.1–0.13) FW	11
Idaho; Coeur d'Alene River; 1986–87		
Sediments		
Vicinity of smelter	>2000 DW	182
Reference site	<300 DW	182
Osprey, <i>Pandion haliaetus</i> ; nesting near smelter vs. reference site; blood		
Adults	0.2 (ND–0.82) FW vs. 0.04 (ND–0.16) FW	182
Nestlings	0.09 (ND–0.42) FW vs. 0.02 FW	182
Fish, 6 species; smelter site vs. reference site		
Muscle	Max. 0.49 FW vs. Max. 0.11 FW	182
Whole	3.1–21.6 FW vs. <0.05–0.17 FW	182
Greenland; 1978–93		
Molluscs, 5 species; soft parts	0.07–0.9 FW	183
Crustaceans, 6 species		
Exoskeleton	0.08–0.18 FW	183
Muscle	0.01–0.05 FW	183
Fish, 4 species, all tissues	Max. 0.15 FW	183
Seabirds, 4 species		
Kidney	Max. 0.08 FW	183

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
Liver	Max. 0.05 FW	183
Muscle	<0.02 FW	183
Ringed seal, <i>Phoca hispida</i> ; all tissues	ND–0.06 FW	183
Marine food chain, Central Pacific		
Seawater	0.006 FW	44
Phytoplankton	0.05 FW	44
Zooplankton	0.04 FW	44
Carnivores, muscle		
Intermediate (anchovy)	0.02 FW	44
Top (tuna)	0.0003 FW	44
Mexico		
Mexico City		
Soil	Max. 890 DW	184
Vegetation		
Unwashed	Max. 564 DW	184
Washed	Max. 20 DW	184
Playon de Mexiquillo; 1992–93		
Sand	23 DW; Max. 66 DW	185
Seawater	0.35 DW	185
Leatherback turtle, <i>Dermochelys coriacea</i> ; egg shells after hatching	11.6 DW; Max. 17.8 DW	185
New Jersey; trap and skeet range in operation for at least 30 years; shot zone vs. reference site		
Soil	75,000 DW vs. 0.07 DW	186
Short-tailed shrew, <i>Blarina brevicauda</i>		
Femur	437 DW vs. 12 DW	186
Kidney	1506 DW vs. 2 DW	186
Liver	34 DW vs. 0.5 DW	186
White-footed mouse, <i>Peromyscus leucopus</i>		
Femur	245 DW vs. 4 DW	186
Kidney	35 DW vs. 2 DW	186
Liver	5 DW vs. 1 DW	186
Green frog, <i>Rana clamitans</i> ; adults		
Femur	1728 DW vs. 2 DW	186
Kidney	96 DW vs. 1 DW	186
Oklahoma pond		
Water	0.013 FW	11
Sediments		
Surface	529 DW	11
12 cm depth	206 DW	11
Plankton	281 DW	11
Benthos	37 DW	11
Mosquitofish, <i>Gambusia</i> sp.	11 DW	11
Pennsylvania: Palmerton zinc smelter (closed in 1980); 1987		
Litter	Max. 3460 DW	187
Soil	Max. 4160 DW	187
Green frog; tadpoles; whole less GI tract	Max. 5 FW	187
Red-backed salamander, <i>Plethodon cinereus</i> ; whole less GI tract	Max. 12.3 FW	187
White-footed mouse, bone	Max. 78 DW	187
Cottontail rabbit, <i>Sylvilagus floridanus</i>		
Bone	Max. 147 DW	187
Kidney	Max. 15.2 DW	187
Liver	Max. 15.1 DW	187

Table 4.5 (continued) Lead Concentrations in Field Collections of Representative Species of Plants and Animals (Values shown are in mg Pb/kg [ppm] fresh weight [FW] or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a	Reference ^b
White-tailed deer, <i>Odocoileus virginianus</i>		
Bone	19.6 DW	187
Kidney	5.5 DW	187
Liver	3.7 DW	187
Spain; Tarragona coast; 23 economically-important marine species; edible portions; 4 locations		
Molluscs	Max. 2.4 FW	188
Crustaceans	Max. 1.6 FW	188
Fishes	Max. 1.1 FW	188

^a Concentrations are listed as mean, (minimum-maximum), and maximum (Max.).

^b 1, Beyer et al. 1985; 2, McLean and Jones 1975; 3, Ruhling and Tyler 1968; 4, Goodman and Roberts 1971; 5, Jenkins 1980; 6, Fayed and Abd-El-Shafy 1985; 7, Behan et al. 1979; 8, Seeliger and Edwards 1977; 9, Krishnayya and Bedi 1986; 10, Bohn 1979; 11, Demayo et al. 1982; 12, Harrison and Dyer 1984; 13, Ter Haar 1970; 14, Backhaus and Backhaus 1986; 15, Bolter et al. 1973; 16, Beyer and Moore 1980; 17, Di Giulio and Scanlon 1985; 18, Friedland and Johnson 1985; 19, Turner et al. 1985; 20, Chmiel and Harrison 1981; 21, Edwards and Clay 1977; 22, Burrows 1981; 23, Robel et al. 1981; 24, Graham 1972; 25, Sheppard and Bellamy 1974; 26, Gale et al. 1976; 27, Goldsmith and Scanlon 1977; 28, Beyer and Cromartie 1987; 29, Anderson 1977; 30, Udevitz et al. 1980; 31, Gish and Christensen 1973; 32, Dodge and Gilbert 1984; 33, Drifmeyer and Odum 1975; 34, Mackay et al. 1972; 35, Boggess 1977; 36, Bollingberg and Johansen 1979; 37, Hall et al. 1978; 38, Haux et al. 1986; 39, Wiener et al. 1984; 40, Walsh et al. 1977; 41, May and McKinney 1981; 42, Lowe et al. 1984; 43, Hardisty et al. 1974; 44, Flegal 1985; 45, Niethammer et al. 1985; 46, Beresford et al. 1981; 47, Ireland 1977; 48, Dieter et al. 1976; 49, Fleming 1981; 50, King and Cromartie 1986; 51, Hall and Fisher 1985; 52, Kendall et al. 1984; 53, Goede and de Voogt 1985; 54, Johnson et al. 1982; 55, Ohi et al. 1974; 56, Eskildsen and Grandjean 1984; 57, De Ment et al. 1986; 58, Locke et al. 1982; 59, Reichel et al. 1984; 60, Bagley and Locke 1967; 61, Mulhern et al. 1970; 62, Grue et al. 1984; 63, Getz et al. 1977a; 64, Blus et al. 1977; 65, Stendell et al. 1980; 66, Grue et al. 1986; 67, Martin and Nickerson 1973; 68, White et al. 1977; 69, Stendell et al. 1979; 70, Roberts et al. 1978; 71, Getz et al. 1977c; 72, Dorn et al. 1974; 73, NRCC 1973; 74, Clark 1979; 75, Knight and Burau 1973; 76, Raymond and Forbes 1975; 77, Getz et al. 1977b; 78, Clark et al. 1986; 79, Sileo and Beyer 1985; 80, Bunzl and Kracke 1984; 81, Mierau and Favara 1975; 82, Kisseberth et al. 1984; 83, Smith and Rongstad 1982; 84, Ditors and Nielsen 1978; 85, Way and Schroder 1982; 86, Blus et al. 1993; 87, Dwyer et al. 1988; 88, Henny et al. 1994; 89, Jiann and Presley 1997; 90, Sures et al. 1994; 91, Barak and Mason 1990a; 92, Barak and Mason 1990b; 93, Okeye 1994; 94, Schmitt et al. 1993; 95, Watanabe et al. 1996; 96, Schmitt and Brumbaugh 1990; 97, Baekken 1994; 98, Kock et al. 1995a; 99, Overmann and Krajicek 1995; 100, Kaur 1988; 101, Wood et al. 1996; 102, Beyer et al. 1997; 103, Schwab and Padgett 1988; 104, Guitart et al. 1994; 105, Mauser et al. 1990; 106, Tirelli et al. 1996; 107, Samuel et al. 1992; 108, Pattee et al. 1990; 109, Craig and Craig 1995; 110, Kingsford et al. 1994; 111, DeStefano et al. 1991; 112, Spalding et al. 1997; 113, Rodgers 1997; 114, Lebedeva 1997; 115, Wiemeyer et al. 1986; 116, Gordus 1993; 117, Bailey et al. 1995; 118, Pain et al. 1997; 119, Pain et al. 1993a; 120, Janiga et al. 1990; 121, Blus et al. 1989; 122, Abel and Grossman 1992; 123, Beyer et al. 1998a; 124, Blus et al. 1991; 125, Spray and Milne 1988; 126, Beyer et al. 1998b; 127, O'Halloran et al. 1989; 128, Sears 1988; 129, Work and Smith 1996; 130, Pokras and Chafel 1992; 131, Snyder et al. 1992; 132, Franson and Hereford 1994; 133, Wiemeyer et al. 1988; 134, Mateo et al. 1997c; 135, Franson et al. 1995; 136, Norman et al. 1993; 137, Pain et al. 1995; 138, Pain and Amiard-Triquet 1993; 139, Pain et al. 1992; 140, Blus et al. 1995; 141, Havera et al. 1992; 142, Burger et al. 1992; 143, Hontelez et al. 1992; 144, Burger and Gochfeld 1993; 145, Pinowski et al. 1993; 146, Craig et al. 1990; 147, Langelier et al. 1991; 148, Elliott et al. 1992; 149, Gill and Langelier 1994; 150, Burger 1997; 151, Burger and Gochfeld 1995b; 152, Burger and Gochfeld 1996; 153, Swiergosz 1991; 154, Schmitz et al. 1990; 155, Ramo et al. 1992; 156, Burger and Gochfeld 1991; 157, Weyers and Gluck 1988; 158, Best et al. 1992; 159, Tataruch 1995; 160, Lutz and Veckermann 1991; 161, USPHS 1993; 162, Heinze et al. 1998; 163, Hernandez-Avila et al. 1998; 164, Kemper et al. 1994; 165, Wagemann et al. 1996; 166, Ieradi et al. 1996; 167, Mason and Weber 1990; 168, Blus and Henny 1990; 169, Kuiters 1996; 170, Hariono et al. 1993; 171, Khan et al. 1995; 172, Hamir et al. 1994; 173, Clark et al. 1992; 174, Cooke et al. 1990a; 175, Ma et al. 1991; 176, Medvedev et al. 1997; 177, Medvedev 1995; 178, Doganoc and Gacnik 1995; 179, Thies and Gregory 1994; 180, Beck et al. 1997; 181, Shlosberg et al. 1997; 182, Henny et al. 1991; 183, Dietz et al. 1996; 184, Albert and Badillo 1991; 185, Vazquez et al. 1997; 186, Stansley and Roscoe 1996; 187, Storm et al. 1994; 188, Schuhmacher et al. 1990; 189, Sill et al. 1996; 190, Ochiai et al. 1993b; 191, Mauvais and Pinault 1993; 192, Mateo et al. 1997a; 193, Aguirre-Alvarez 1989; 194, Franson et al. 1996; 195, Garcia et al. 1998; 196, Hendriks et al. 1998; 197, Burger and Snodgrass 1998; 198, Janiga and Zemberyova 1998; 199, Melnyket et al. 1999.

4.6 LETHAL AND SUBLETHAL EFFECTS

4.6.1 General

Lead adversely affects survival, growth, reproduction, development, and metabolism of most species under controlled conditions, but its effects are substantially modified by numerous physical, chemical, and biological variables. In general, organolead compounds are more toxic than inorganic lead compounds; food chain biomagnification of lead is negligible; and the younger, immature organisms are most susceptible. Uptake of lead by terrestrial plants is limited by the low bioavailability of lead from soils; adverse effects seem to occur only at total concentrations of several hundred mg Pb/kg soil.

In aquatic environments, waterborne lead was the most toxic form. Adverse effects were noted on daphnid reproduction at 1.0 µg Pb⁺²/L, on rainbow trout survival at 3.5 µg tetraethyllead/L, and on growth of marine algae at 5.1 µg Pb⁺²/L. High bioconcentration factors were recorded for filter-feeding bivalve molluscs and freshwater algae at 5.0 µg Pb⁺²/L.

Ingestion of spent lead shot by migratory waterfowl and other birds is a significant cause of mortality in these species, as well as in raptors that eat the waterfowl killed or wounded by hunters. Forms of lead other than shot are unlikely to cause clinical signs of lead poisoning in birds, except for certain alkyllead compounds that bioconcentrate in aquatic food items. Among sensitive species of birds, survival was reduced at doses of 75 to 150 mg Pb⁺²/kg BW or 28 mg alkyllead/kg BW; reproduction was impaired at dietary levels of 50 mg Pb⁺²/kg; and signs of poisoning were evident at doses as low as 2.8 mg alkyllead/kg BW.

The veterinary medical literature on lead toxicosis is abundant for domestic livestock and small laboratory animals but notably lacking for feral mammals. Among sensitive species of mammals, survival was reduced at acute oral doses as low as 5 mg/kg BW in the rat, at chronic oral doses of 0.3 mg/kg BW in the dog, and at dietary levels of 1.7 mg Pb/kg BW in the horse. Sublethal effects were documented in monkeys given doses as low as 0.1 mg Pb/kg BW daily (impaired learning 2 years postadministration) or fed diets containing 0.5 mg Pb/kg (abnormal social behavior). Reduction in ALAD activity was recorded in blood of rabbits given 0.005 mg Pb/kg BW, and in mice given 0.05 mg Pb/kg BW. Tissue residues increased in mice given 0.03 mg Pb/kg BW, and in sheep given 0.05 mg Pb/kg BW.

4.6.2 Terrestrial Plants and Invertebrates

Fruits and vegetables acquire lead by surface deposition from rainfall, dust, and soil, and by biological uptake through the root system (USEPA 1980). Foliar absorption of lead and transport to the root could account for a significant portion of the lead in root tissues; however, this transport process varies widely among species. Dollard (1986) showed that this pathway accounted for 35% of the root lead content in the radish (*Raphanus sativus*), but for <3% in carrots (*Daucus carota*) and beans (*Phaseolus vulgaris*). Corn (*Zea mays*) contained 30 mg Pb/kg dry weight when grown in soils containing lead concentrations of 924 mg/kg, but only 17 mg/kg when grown in soils containing 786 mg Pb/kg. Sadiq (1985) concluded that contamination of soils with up to 800 mg Pb/kg probably does not elevate concentrations of lead in corn plants. Within any plant species, however, there are lead-resistant and lead-sensitive breeds; some genetically fixed resistant species grow in soils containing up to 10,000 mg Pb/kg (Holl and Hampp 1975).

Plants readily accumulate lead from soils of low pH or low organic content; however, uptake is significantly reduced after the application of lime or phosphate, which converts lead to hydroxides, carbonates, or phosphates of relatively low solubility (Demayo et al. 1982). Lead persists for lengthy periods in forest litter; the estimated Tb 1/2 is 220 years (Turner et al. 1985). High levels of lead persisted for at least 6 years in litter, soil, amphibians, and mammals after zinc smelting was discontinued in Palmerton, Pennsylvania (Storm et al. 1994). Lead seems to be tightly bound by

most soils, and substantial amounts must accumulate before it affects the growth of higher plants (Boggess 1977). Although lead is preferentially bound in soils by organics and oxides, interaction kinetics of lead with other metals are complex and largely unknown (Bjerre and Schierup 1985). For example, uptake of lead from soils by oat seeds (*Avina sativa*) was inhibited by cadmium salts and reduced in loamy or organic soils; further, lead in soils interfered with manganese uptake and also increased the availability of cadmium and other heavy metals (Bjerre and Schierup 1985).

Lead inhibits plant growth, reduces photosynthesis, and reduces mitosis and water absorption (Demayo et al. 1982). Inhibition of photosynthesis is attributed to the blocking of protein sulfhydryl groups and to changes in phosphate levels in living cells (Holl and Hampp 1975). For two species of roadside weeds (*Cassia* spp.), pollen germination was reduced by 90% and seed germination by 87% at lead levels of about 500 mg/kg dry weight in soil and about 300 mg/kg dry weight in foliage (Krishnayya and Bedi 1986). Normal germination rates were recorded at lead levels of 46 mg/kg in soil and 22 mg/kg dry weight in foliage; however, some adverse effects were evident at lead levels of 12 to 312 mg/kg in soil, and 55 to 97 mg/kg dry weight in foliage (Krishnayya and Bedi 1986). Tetraethyllead from automobile exhaust fumes is known to react in the light to produce the highly phytotoxic triethyllead cation (Backhaus and Backhaus 1986), which can freely permeate the plasma membranes of plant cells (Stournaras et al. 1984). Growth of cultures of soybean (*Glycine max*) cells exposed to 207 µg Pb/L (as triethyllead salts) was inhibited before the cells died (Stournaras et al. 1984). There is no evidence for biomagnification of lead in the food chain of vegetation, to cattle, to dung, to the dung beetle (Robel et al. 1981), nor is there convincing evidence that any terrestrial vegetation is important in food chain biomagnification of lead (USEPA 1980). Concentrations of lead in soil litter ranged from 3200 mg/kg in locations near a zinc smelter in Palmerton, Pennsylvania, to 150 mg/kg at sites 105 km distant; relative concentrations of cadmium, zinc, and copper were similar (Beyer et al. 1984). In woodlice (*Porcellio scaber*) fed litter from these locales for 8 weeks, survival decreased as metal content in the litter increased, but the major cause of death was zinc poisoning and not lead poisoning (Beyer et al. 1984). Woodlouse (*Oniscus asellus*) hepatopancreas that were collected 3 km downwind of a metal smelter contained large amounts of zinc, copper, cadmium and lead. Centipedes (*Lithobius variegatus*) that ate woodlice hepatopancreas did not assimilate lead even though the food contained concentrations that were many times greater than normally encountered (Hopkin and Martin 1984). However, survival and reproduction were reduced in woodlice (*P. scaber*) fed soil litter treated with 12,800 mg Pb/kg, as lead oxide, for 64 weeks, or two generations (Beyer and Anderson 1985). This amount of lead is similar to the amounts reportedly associated with reductions in natural populations of decomposers, such as fungi, earthworms, and arthropods. The poisoning of decomposers may disrupt nutrient cycling, reduce the number of invertebrates available to other wildlife for food, and contribute to food chain contamination (Beyer and Anderson 1985). The effects of lead on soil microbial populations is unknown (Boggess 1977).

Herbivorous land snails (*Helix* spp.) are important in lead cycling through contaminated ecosystems (Dallinger and Wieser 1984; Beeby 1985). *Helix pomatia* fed lettuce enriched with lead (about 1000 mg Pb/kg dry weight lettuce) for 32 days contained 1301 mg Pb/kg dry weight in the mid-gut gland (vs. 52 in controls), and much lower amounts (<30 mg/kg) in other tissues. After the snail had fed on uncontaminated lettuce for 50 days, lead remained elevated at 1203 mg/kg in the mid-gut gland, which contained more than 90% of the total body burden (Dallinger and Wieser 1984).

4.6.3 Aquatic Biota

In general, the responses of aquatic species to lead insult differed markedly (Table 4.6). Among sensitive species, however, several trends were evident:

1. Dissolved waterborne lead was the most toxic form
2. Organic lead compounds were more toxic than inorganic forms

3. Adverse effects on daphnid reproduction were evident at 1.0 µg Pb⁺²/L
4. High bioconcentrations were measured in oysters at 1.0 µg Pb⁺²/L and in freshwater algae at 5.0 µg Pb⁺²/L
5. Tetramethyllead was acutely toxic to rainbow trout at 3.5 µg/L
6. Growth inhibition of a marine alga was reported at 5.1 µg Pb⁺²/L
7. For all species, effects were most pronounced at elevated water temperatures and reduced pH, in comparatively soft waters, in younger life stages, and after long exposures ([Table 4.6](#))

Lead is toxic to all phyla of aquatic biota, but its toxic action is modified by species and physiological state, and by physical and chemical variables. Wong et al. (1978) stated that only soluble waterborne lead is toxic to aquatic biota, and that free cationic forms are more toxic than complexed forms. The biocidal properties of soluble lead are also modified significantly by water hardness: as hardness increases, lead becomes less bioavailable because of precipitation increases (NRCC 1973). In salmonids, for example, the toxicity and fate of lead are influenced by the calcium status of the organism, and this relationship may account for the reduced effects of lead in hard or estuarine waters. In coho salmon (*Oncorhynchus kisutch*), an increase in waterborne or dietary calcium reduced uptake and retention of lead in skin and skeleton (Varanasi and Gmur 1978).

Organolead compounds are, in general, more toxic than inorganic lead compounds to aquatic organisms. Ethyl derivatives were more toxic than methyl derivatives, and toxicity increased with increasing degree of alkylation, tetraalkylead being the most toxic (Chau et al. 1980; Babich and Borenfreund 1990). Tetraethyllead was about 10 times more effective than tetramethyllead in reducing oxygen consumption by coastal marine bacteria, and was 1.5 to 4 times more toxic than tetramethyllead to marine teleosts (Marchetti 1978). Tetramethyllead chloride was 20 times as toxic as Pb(NO₃)₂ to freshwater algae, and twice as toxic as trimethyllead acetate (Wong et al. 1978). In seawater, the release of tetraalkylead compounds is more likely than accumulation to result in acutely toxic effects; however, alkyllead compounds degrade rapidly to trialkyllead chlorides, which are only 0.1 to 0.01 as toxic as TEL compounds (Haddock and Taylor 1980). Alkyllead compounds are accumulated more readily by freshwater teleosts than are inorganic lead compounds. The BCF values for tetramethyllead and rainbow trout, for example, ranged from 124 in lipids after exposure for 1 day, to 934 after 7 days (Demayo et al. 1982). Depuration of tetramethyllead is rapid. The estimated Tb 1/2 values range from 30 hours for intestinal lipids to 45 hours for skin and cephalic fat deposits (Wong et al. 1981). Some microorganisms in lake sediments transform certain inorganic and organic lead compounds into the more toxic tetramethyllead, but the pathways are not well understood (Wong et al. 1978).

Lethal solutions of lead (as well as of many other heavy metals) cause increased mucus formation in fishes. The excess coagulates over the entire body and is particularly prominent over the gills, interfering with respiratory function and resulting in death by anoxia (Aronson 1971; NRCC 1973). Increasing waterborne concentrations of lead over 10 µg/L are expected to provide increasingly severe long-term effects on fish and fisheries (Demayo et al. 1982; Ruby et al. 1993). Fish that are continuously exposed to toxic concentrations of waterborne lead show various signs of lead poisoning: spinal curvature, usually as lordosis; anemia; darkening of the dorsal tail region, producing a black-tail effect due to selective destruction of chromatophores but not of melanophores; degeneration of the caudal fin; destruction of spinal neurons; ALAD inhibition in erythrocytes, spleen, liver, and renal tissues; reduced ability to swim against a current; destruction of the respiratory epithelium; basophilic stippling of erythrocytes; elevated lead concentrations in blood, bone, gill, liver, and kidney; muscular atrophy; paralysis; renal pathology; growth inhibition; retardation of sexual maturity; altered blood and lipid chemistry; testicular and ovarian histopathology; and death (Aronson 1971; NRCC 1973; Adams 1975; Davies et al. 1976; Holcombe et al. 1976; Hodson et al. 1977, 1980, 1982; Johansson-Sjöbeck and Larsson 1979; Reichert et al. 1979; Ozoh 1980; Demayo et al. 1982; Kumar and Pant 1984; Rai and Qayyum 1984; Hodson and Spry 1985; Haux et al. 1986; Thomas and Huedes 1992; Tulasi et al. 1992; Ruby et al. 1993; Conner

and Fowler 1994). The prevalence of signs is closely correlated with duration of exposure to lead and to its uptake (Hodson et al. 1982). Toxic effects of lead uptake in fishes are increased under conditions favoring their rapid growth. Hodson et al. (1982) have shown that the rate of intoxication by lead (as judged by uptake rates into tissues and incidence and prevalence of black tail) did not increase with fish size, but rather with growth rate.

Rooted aquatic plants, such as wild rice (*Zizania aquatica*), can accumulate up to 67 mg Pb/kg dry weight when cultured in tanks contaminated with high concentrations of powdered lead (equivalent to 7400 kg Pb/ha); however, this level is not considered hazardous to waterfowl feeding on wild rice (Behan et al. 1979). Lead content in plants collected from heavily hunted areas near refuges did not differ from those collected in the protected areas (Behan et al. 1979), which suggests that lead bioavailability to rooted aquatics is substantially lower from shot than from powdered lead.

In another study with rooted macrophytes, *Navicula* sp. and *Elodea canadensis* rapidly accumulated lead from solutions containing 1.0 mg Pb⁺²/L, i.e., 70 mg Pb/kg dry weight per minute; the process was overwhelmingly passive (Everard and Denny 1985). Depuration was rapid; 90% of the lead sorbed during the first hour by shoots of *Elodea* was released within 14 days after transfer to clean water, though 10% seemed to be irreversibly bound (Everard and Denny 1985).

Certain emergent aquatic plants, especially hydrilla (*Hydrilla verticillata*) and duckweed (*Lemna obscura*), removed 97 to 98% of all soluble lead from solution in the vicinity of a lead battery site in Tampa, Florida, suggesting that phytoremediation may be feasible as the basis of a lead removal technology (Gallardo et al. 1999).

High accumulations of lead from ambient seawater by marine plants is well documented; concentration factors vary from 13,000 to 82,000 for algae from Raritan Bay, New Jersey (Seeliger and Edwards 1977), and from 1200 to 26,000 for algae from Sorfjorden, Norway (Melhuus et al. 1978). Studies on the kinetics of lead uptake and retention in two species of marine algae (*Phaeodactylum tricornutum*, *Platymonas subcordiformes*) showed that both species accumulated lead from the medium at ambient concentrations of 20 µg/L and higher (Schulz-Baldes and Lewin 1976). In the first phase, usually completed within minutes after addition of lead, cells of *Phaeodactylum* became saturated when the lead reached a remarkable 11,640 mg/kg dry weight. In the second phase, the lead content of *Platymonas* continued to rise slowly, but that of *Phaeodactylum* declined after 2 or 3 days. In both species the content of bound lead increased with increasing exposure time, suggesting that during prolonged exposure lead is initially adsorbed to the cell surface, then translocated into the cell wall, the plasma membrane, and eventually the cytoplasm (Schulz-Baldes and Lewin 1976).

Sediments are not only sinks for lead but may also act as a source of lead to aquatic biota after contamination from the original source has subsided (Knowlton et al. 1983). The uptake of lead from artificially contaminated pond sediments was recorded in roots and foliage of submersed aquatic macrophytes (*Potamogeton foliosus*, *Najas guadalupensis*) and in the exoskeleton of crayfish (*Orconectes nais*). Accumulation of lead in crayfish primarily was through adsorption; most was lost through molting, though some internal uptake and elimination occurred without molting (Knowlton et al. 1983). Crustacean molts represent 15% of the lead body burden and are probably more significant than fecal pellets in lead cycling processes (Fowler 1977). Uptake of lead from sediments containing 7 mg Pb/kg DW is reported for the stone loach (*Noenacheilus barbatulus*) (Douben and Koeman 1989), but this needs verification.

Median BCF values in aquatic biota exposed to various concentrations of Pb⁺² for 14 to 140 days varied from about 42 in fish to 2570 in mussels; intermediate values were 536 for oysters, 500 for insects, 725 for algae, and 1700 for snails (USEPA 1985). There are several notable exceptions to this array: significantly higher values have been reported in crustacean hepatopancreas (Heyraud and Cherry 1979), in various species of freshwater invertebrates (Spehar et al. 1978), in fish bone (Demayo et al. 1982) and liver (Haux and Larsson 1982), and in whole oysters (Zaroogian et al. 1979). In oysters, for example, BCF values varied from 3450 to 6600 after exposure to solutions

containing 1.0 to 3.3 µg Pb⁺²/L for 140 days, but oysters and their progeny were apparently unaffected at whole-body burdens (less shell) up to 11.4 mg Pb/kg dry weight (Zaroogian et al. 1979). Many species of aquatic biota contain lead in amounts >1000 mg/kg fresh weight (>10,000 mg/kg dry weight), including some marine seaweeds, freshwater macrophytes and algae, annelids, crustaceans, echinoderms, molluscs, and teleosts (Wong et al. 1978). Presumably, the lead was sorbed passively, and little, if any, was incorporated biologically. Variations in lead concentrations in aquatic biota probably reflect the ability of individual species to adsorb waterborne lead, and may be a direct function of the ratio of surface to body weight (Demayo et al. 1982). The residence time of lead in aquatic biota seems to be related to the route of administration: Tb 1/2 values were 9 days by waterborne routes and 40 days by diet (Vighi 1981).

Although lead is concentrated by biota from water, there is no convincing evidence that it is transferred through food chains (Wong et al. 1978; USEPA 1979; Branica and Konrad 1980; Settle and Patterson 1980). Lead concentrations tended to decrease markedly with increasing trophic level in both detritus-based and grazing aquatic food chains (Wong et al. 1978). In the marine food chain of seawater (<0.08 µg Pb/L), to a brown alga (*Egregia laevigata*), to the red abalone (*Haliotis rufescens*), lead concentrations in the alga and abalone were both <0.04 mg Pb/kg fresh weight after 6 months, indicating negligible biomagnification (Stewart and Schulz-Baldes 1976). When seawater contained 1000 µg Pb/L, young abalones that fed on *Egregia* for 6 months contained up to 21 mg Pb/kg fresh weight, but neither growth nor activity was affected; lead selectively accumulated in the digestive gland (38 mg/kg) and was lowest in muscle (<1 mg/kg) — the part normally consumed by humans (Stewart and Schulz-Baldes 1976). In the freshwater food chain of an alga (*Selenastrum capricornutum*), to a daphnid (*Daphnia magna*), to the guppy (*Poecilia reticulata*), lead accumulation progressively decreased from the alga to the guppy. Thus, in organisms held for 28 days in solutions containing 5 µg Pb/L, lead content was 460 mg/kg dry weight in the alga, 23 mg/kg in the grazing daphnids, and 4 to 16 mg/kg in the guppies that fed on the daphnids (Vighi 1981). Concentrations of lead in the freshwater snail, *Lymnaea peregra*, collected near an abandoned lead mine were positively correlated with the lead content in its diet. The digestive glands contained up to 5600 mg/kg dry weight (Everard and Denny 1984). The gut contents of eels (*Anguilla anguilla*) grazing on contaminated snails contained up to 4350 mg Pb/kg, but the lead was rapidly released; feces from both snails and eels return the lead to the ecosystem as particulates and detritus (Everard and Denny 1984).

As discussed earlier, lead clearly inhibits the formation of heme at several points, adversely affects blood chemistry, and accumulates in hematopoietic organs of aquatic organisms. In addition, it:

- Interferes with chlorophyll formation in plants by inhibiting the conversion of coproporphyrinogen to protoporphyrinogen by competing with iron
- Inhibits allantoise formation in annelids
- Inhibits alpha-glycerophosphate dehydrogenase activity in trout
- Increases glutamic oxalacetate transaminase activity in *Daphnia*
- Affects neural and hormonal systems that control activity and metabolic rates in fish
- Interacts with polar sites of glycoproteins in epidermal mucus of fish
- May inhibit Vitamin C and tryptophan metabolism (Wong et al. 1978).

Fish may be more resistant to lead than mammals. For example, isolated liver hepatocytes of channel catfish were about 40 times more resistant to lead than rat liver hepatocytes as judged by ALAD inhibition (Conner and Fowler 1994).

Some populations of freshwater isopods are tolerant to lead. Inasmuch as nontolerant isopods from an unpolluted site can be made tolerant by exposure to low levels, it is suggested that naturally occurring tolerance may be achieved by acclimatization (Fraser 1980). Research is needed on lead transformation mechanisms, on toxic forms of lead and interaction effects with other compounds, and on effects of lead-contaminated sediments on benthos (Wong et al. 1978).

Table 4.6 Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
FRESHWATER		
Algae and macrophytes		
Alga, <i>Selenastrum capricornutum</i>		
5 µg/L for 28 days	BCF of 92,000	1
50 µg/L for 28 days	BCF of 26,000	1
Alga, <i>Chlamydomonas reinhardtii</i>		
207 µg/L for 3 h	BCF of 26; some inhibition of photosynthesis	2
1000 µg/L for 3 h	BCF of 20; 50% inhibition of photosynthesis	2
4140 µg/L for 24 h	Lethal	2
Alga, <i>Microcystis aeruginosa</i>		
450 µg/L for 8 days	Immobilization	3
Invertebrates		
Chironomid, <i>Chironomus riparius</i> ; 5 generations exposed from egg to fourth instar to 0, 5, 50, or 500 µg Pb/L		
Daphnid, <i>Daphnia magna</i>		
1 µg/L for 19 days	Reproductive impairment, 10%	4
10 µg/L for 19 days	Reproductive impairment, 50%	4
30 µg/L for 21 days	Reproductive impairment, 16%	3, 5
Water hardness (mg CaCO ₃ /L)		
52, 9–16.7 µg/L, lifetime exposure	MATC	3
102, 78–181 µg/L, lifetime exposure	MATC	3
151, 85–193 µg/L, lifetime exposure	MATC	3
54, 612 µg/L for 96 h	LC50	3
110, 952 µg/L for 96 h	LC50	3
152, 1.91 mg/L for 96 h	LC50	3
45, 300 µg/L for 21 days	LC50	6, 7
45, 450 µg/L for 48 h	50% immobilized	3, 7
Snail, <i>Lymnaea palustris</i>		
12–54 µg/L, lifetime exposure	MATC	3
Snail, <i>Lymnaea palustris</i>		
3.8 µg/L, lifetime exposure	No deaths	8
19 µg/L, lifetime exposure	Significant mortality	8
36 µg/L, lifetime exposure	50% reduction in biomass	8
48 µg/L, lifetime exposure	100% reduction in biomass	8
54 µg/L lifetime exposure	Hatching success reduced; survivors dead by age 80 days	8
Protozoan, <i>Entosiphon sulcatum</i>		
20 µg/L for 72 h	Immobilization	3
Amphipod, <i>Gammarus pseudolimnaeus</i>		
28.4 µg/L for 60 days	LC50	5
124.0 µg/L for 96 h	LC50	9
Aquatic invertebrates		
32 µg/L for 28 days	BCF 1000–9000	5
Protozoan, <i>Uronema</i> sp.		
70 µg/L for 20 h	Immobilization	3
Midge, <i>Tanytarsus dissimilis</i>		
258 µg/L for 10 days	LC50	3
Isopod, <i>Asellus meridianus</i>		
Nontolerant strain		
280 µg/L for 48 h	LC50	5
From lead-contaminated river		
3500 µg/L for 48 h	LC50	5

Table 4.6 (continued) Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
Daphnid, <i>Daphnia hyalina</i> 600 µg/L for 48 h	LC50	6
Snail, <i>Viviparus ater</i> 1.0 mg/L for 7 days 117.0 mg/L for 96 h	Neuronal cytolysis LC50	10 10
Chironomid, <i>Chironomus tentans</i> ; larvae 2.7 mg/L for 48 h	LC50	31
Aquatic insects, 5 species 3.5–64.0 mg/L for 7–14 days	LC50	5
Isopod, <i>Asellus aquaticus</i> Nontolerant strain Pretreated for 5 days to 100 mg Pb/L then exposed to 794.0 mg/L for 48 h	LC50	11
No pretreatment 330.0 mg/L for 48 h	LC50	11
Fishes		
Bluegill, <i>Lepomis macrochirus</i> Isolated fin cells; various organolead compounds; exposed for 24 h 0.9 µg/L 2.3 µg/L 6.2 µg/L 62.0 µg/L	LC50 for triethyllead LC50 for trimethyllead LC50 for dimethyllead LC50 for diethyllead	43 43 43 43
Water hardness 41 mg CaCO ₃ , 70–120 µg Pb/L for lifetime exposure	MATC	16
Rainbow trout, <i>Oncorhynchus mykiss</i> Tetramethyl lead Weight 1 gram, 3.5 µg/L for 72 h Weight 1 gram, 3.5 µg/L for 7 days Weight 1 gram, 3.5 µg/L for 14 days Weight 20 grams, 24 µg/L for 8–14 days	LC50 BCF of 726 for whole trout LC50 Some deaths at day 8; BCF of 17,300 for intestinal lipids at day 10 and 12,540 at day 14	12 12 12 12
Pb ⁺² 10 µg/L for 30 days 10 µg/L for 12 days; sexually-maturing males exposed during spermatogenesis 13 µg/L for 4 weeks 13 µg/L for 32 weeks 14 µg/L for 14 days 75 µg/L for 30 days 300 µg/L for 30 days plus 7 weeks post exposure	ALAD depression, 21% Decreased number of spermatocytes; increase in spermatogonial cysts Erythrocyte ALAD inhibition Anemia; reduced blood ALAD activity Reduced stamina ALAD depression, 74% ALAD depression, 86%; anemia; basophilic stippling of erythrocytes	13 32 6 3 3 13 13
Eyed eggs 10.0 mg total Pb/L for 56 h 20.0 total Pb/L for 20 h	LC50 LC50	14 14
Water hardness (mg CaCO ₃ /L) 28		
4.0–7.6 µg total Pb/L, lifetime exposure beginning with pre-hatch fry 4.1–7.6 µg dissolved Pb/L, lifetime exposure 7.2 µg total Pb/L for 19 months 7.2–14.6 µg total Pb/L, lifetime exposure	MATC MATC No harmful effects MATC	5 15 6 15

Table 4.6 (continued) Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
7.6–14.6 µg total Pb/L, lifetime exposure beginning with post-hatch fry	MATC	5
14.6 µg total Pb/L for 19 months	Vertebral deformities; caudal fin erosion	6
1.2 mg dissolved Pb/L for 96 h	LC50	5
35		
71–146 µg total Pb/L, lifetime exposure	MATC	3
353		
18–32 µg dissolved Pb/L, lifetime exposure	MATC	15
18.2 µg total Pb/L for 19 months	No adverse effects	6
31 µg total Pb/L for 19 months	Vertebral deformities; caudal fin erosion	6
120–360 µg dissolved Pb/L, lifetime exposure	MATC	15
1.0 mg Pb/L for 6–16 days	None dead in 6 days; 50% dead in 11 days; all dead in 16 days; no osmoregulatory effect, even at lethal exposure	33
1.4 mg dissolved Pb/L for 96 h	LC50	15
506.5 mg total Pb/L for 96 h	LC50	15
Brown trout, <i>Salmo trutta</i>		
Yolk-sac fry exposed to 2.5, 5.2, or 10.4 µg Pb/L for 30 days at pH 4.5 in soft or hard water	All dead at 2 high dose levels and >90% dead at 2.5 µg/L in soft water; no deaths in any hard water group	45
Yolk-sac fry exposed to 10 µg Pb/L	Adverse effects on growth and development in groups hatched and maintained in soft, acid water	46
Zebrafish, <i>Brachydanio rerio</i>		
Embryos exposed for 16 days		
<20 µg/L	Normal hatch	41
<30 µg/L	Survival normal	41
480 µg/L	Lethal	41
Eggs exposed to 50 µg total Pb/L for 24 h	Pigmentation patterns of fry irreversibly altered	17
Eggs exposed to 72 µg total Pb/L for 24 h	Hatching inhibited	17
Common carp, <i>Cyprinus carpio</i> ; recently-fertilized eggs exposed to 25–186 µg/L at pH 7.5 or 5.6	At pH 7.5, lead increased heart rate and decreased body movements. At pH 5.6 there was a dose-dependent reduction in survival and increase in spinal cord deformities	42
Lake trout, <i>Salvelinus namaycush</i>		
Water hardness 33 mg CaCO ₃ /L, 48–83 µg total Pb/L, lifetime exposure	MATC	16
Brook trout, <i>Salvelinus fontinalis</i>		
Water hardness 44 mg CaCO ₃ /L		
39–84 µg dissolved Pb/L for 3 generations	MATC	5, 18
58–119 µg total Pb/L for 3 generations	MATC	3, 5, 18
119 µg total Pb/L for 3 generations	First generation: BCF of 571 for liver and 1806 for kidney. Second generation: BCF of 420 for liver, 1504 for kidney; severe spinal deformities in 34%. Third generation: spinal deformities in 21%, reduction in body weight	18
134 µg total Pb/L for 21 days	Growth reduction	6
235 µg Pb/L for 2 generation deformities	All with spinal	18
3.4 mg dissolved Pb/L for 96 h	LC50	18
4.1 mg total Pb/L for 96 h	LC50	18
Channel catfish, <i>Ictalurus punctatus</i>		
Water hardness 36 mg CaCO ₃ , 75–136 µg Pb/L, lifetime exposure	MATC	16
White sucker, <i>Catostomus commersoni</i>		
Water hardness 34 mg CaCO ₃ , 119–253 µg Pb/L, lifetime exposure	MATC	5

Table 4.6 (continued) Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
Rosy barb, <i>Barbus conchonius</i> 126 µg/L for 8 weeks 378 µg/L for 96 h	No deaths; altered blood chemistry LC50	40 40
Cyprinid, <i>Puntius conchonius</i> 127 µg Pb/L for 4 months 379 µg Pb/L for 96 h	Gonadal pathology LC50	19 19
Goldfish, <i>Carassius auratus</i> 200 µg Pb/L for 4–5 days	ALAD inhibition	6
Northern pike, <i>Esox lucius</i> Water hardness 34 mg CaCO ₃ /L, 253–483 µg Pb/L for lifetime exposure	MATC	5
Air-breathing catfish, <i>Clarias lazera</i> 270 µg/L for 240 h 1.72 mg/L for 96 h	Whole body content of 6.8 mg Pb/kg FW LC50	31 31
Threespine stickleback, <i>Gasterosteus aculeatus</i> 300 µg Pb/L for 96 h	LC100	6
European eel, <i>Anguilla anguilla</i> Juveniles held in 300 µg/L for 30 days	Increase in number of white blood cell lymphocytes and blood plasma lactate levels; most blood chemistry variables were normal	39
Mozambique tilapia, <i>Oreochromis niloticus</i> 330 µg/L for 240 h 2.15 mg/L for 96 h 18, 24, or 33 mg Pb L as lead acetate for up to 21 days	Whole body concentration of 14.9 mg Pb/kg FW LC5 Dose-dependent decrease in plasma glucose and cholesterol	31 31 34
Smallmouth bass, <i>Micropterus dolomieu</i> Water hardness 152 mg CaCO ₃ /L Fingerlings exposed to 405 µg Pb/L for 90 days Swim-up fry exposed to 2.8 mg Pb/L for 96 h Fingerlings held in 29.0 mg Pb/L for 96 h Eggs and sac-fry held in >15.9 mg Pb/L for 96 h	No effect on growth behavior, blood chemistry LC50 LC50 LC50	20 20 20 20
Fathead minnow, <i>Pimephales promelas</i> Juveniles exposed for 4 weeks to 0.0, 0.5, or 1.0 mg Pb/L as lead acetate 1.0 mg/L for 28 days Water hardness (mg CaCO ₃ /L) 20; 6.5 mg Pb/L for 96 h 360; 460.0 mg Pb/L for 96 h	Brain serotonin and norepinephrine levels higher and feeding success inhibited in lead-exposed groups Altered brain neurotransmitter rhythms LC50 LC50	35 36 7 7
Climbing perch, <i>Anabas testudineus</i> 1.25–20 mg Pb/L for 30 days 5 mg/L for 30 days 60 mg/L for 96 h	Dose-dependent (up to 5 mg/L) accumulations in blood and ovary, decrease in gonadosomatic index and number of ova No deaths. Reduction in liver and ovary total lipids, phospholipids, and cholesterol; increases in free fatty acid levels and lipase activity LC50	37, 38 38 37
Amphibians		
Toad, <i>Bufo arenarum</i> Newly-fertilized eggs held in 120 µg/L–32 mg Pb/L as lead nitrate for 72 h 120 µg/L 250 µg/L	Normal development 25% arrested development	49 49

Table 4.6 (continued) Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
470–950 µg/L	LC50 (48 h); high frequency of malformations in survivors	49
2–4 mg/L 8–32 mg/L	Survivors had arrested development LC100 (48 h)	49 49
Larvae exposed for 120 h to lead or lead and zinc mixtures		
8 mg Pb/L	LC60	50
8 mg Pb/L + 4 mg Zn/L	LC65	50
8 mg Pb/L + 8 mg Zn/L	LC15	50
8 mg Pb/L + 16 mg Zn/L	LC5	50
American toad, <i>Bufo americanus</i> ; tadpoles held in lead-enriched waters (0, 500, 750, or 1000 µg Pb/L) for 144 h then given choice of lead-containing solutions (0, 500, 750, or 1000 µg/L) in fluvorium	No deaths. Toads did not prefer or avoid lead-containing solutions	48
Jefferson salamander, <i>Ambystoma jeffersonianum</i> ; embryos (4-days postfertilization) exposed for 21 days to 130–800 µg Pb/L at pH 4.5 and 5.5	At low pH, lead aids development and protects against arrested growth in a dose-dependent manner; normal hatch and development at pH 5.5 and 800 µg Pb/L	47
Green frog, <i>Rana clamitans</i> ; tadpoles Exposed to 500–1000 µg Pb/L as lead nitrate for 144 h then tested in preference/avoidance apparatus	No significant preference or avoidance of lead by controls or lead-exposed tadpoles and no effects on locomotor activity	52
Exposed to 750 µg/L as lead nitrate for 120–144 h	Sublethal exposure to lead adversely affected learning and memory as judged by increased response times and fewer avoidances in associating illumination with shock	53
750–1000 µg/L	Altered feeding behavior and erratic locomotor activity	48
Bullfrog, <i>Rana catesbeiana</i> ; tadpoles exposed to 500–1000 µg Pb/L as lead nitrate for 144 h	No effect on preference or avoidance responses to plumes of lead-contaminated water or on spontaneous locomotor activity. Lead-exposed tadpoles had significantly greater variability in activity than did controls	51
Reptiles		
Slider turtle, <i>Trachemys scripta</i> Hatchlings, aged 6 months, given single intramuscular injection of 50 or 100 mg Pb/kg BW as lead acetate	No significant effect on growth, survival, or behavior	55
Hatchlings, age 3 weeks, given single intramuscular injection of 250, 1000, or 2500 mg Pb/kg BW and observed for 6 months	Dose-dependent decrease in survival; dose-dependent impaired behavior (righting response) in survivors; normal growth in survivors after 4 months. At 120 days, all dead in high dose group, 75% dead in medium dose group; 17% dead in low dose group, and 8% dead in controls	55
MARINE		
Algae and macrophytes		
Diatom, <i>Skeletonema costatum</i>		
0.05 µg Pb/L for 12 days	No effect on growth	21
5.1 µg Pb/L for 12 days	50% growth inhibition	3
10.0 µg Pb/L for 12 days	100% growth inhibition	21
Alga, <i>Phaeodactylum tricornutum</i> Pb ⁺²		
20 µg Pb/L for <1 h	BCF 582,000	22
>5.0 mg Pb/L for 96 h	LC50	23

Table 4.6 (continued) Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
Tetramethyl Pb 1.3 mg Pb/L for 96 h	LC50	23
Trimethyl Pb 800 µg Pb/L for 96 h	LC50	23
Triethyl Pb 100 µg Pb/L for 96 h	LC50	23
Tetraethyl Pb 100 µg Pb/L for 96 h	LC50	23
Phytoplankton, mixed populations 21 µg Pb/L for 4 days	Reduced biomass	3
Alga, <i>Dunaliella tertiolecta</i>		
Tetraethyl Pb 150 µg/L for 96 h	Growth inhibition	3
Tetramethyl Pb 1.65 mg/L for 96 h	Growth inhibition	3
Invertebrates		
American oyster, <i>Crassostrea virginica</i> , soft parts		
1.0 µg/L for 140 days	BCF of 6600	24
3.3 µg/L for 140 days	BCF of 3454	24
Common mussel, <i>Mytilus edulis</i>		
Pb ⁺²		
10 µg/L for 63 days	BCF of 12,580 for kidney and 1580 for soft parts	25
476 µg/L for 96 h	LC50, larvae	3
500 µg/L for 150 days	BCF of 25,670 for soft parts	26
>500 mg/L for 96 h	LC50, adults	23
Triethyl lead		
1.1 mg/L for 96 h	LC50; BCF 10	23
Trimethyl lead		
500 µg/L for 96 h	LC50; BCF 23	23
Tetramethyl lead		
270 µg/L for 96 h	LC50; BCF 170	23
Tetraethyl lead		
100 µg/L for 96 h	LC50; BCF 120	23
Softshell clam, <i>Mya arenaria</i> ; soft parts		
14 µg/L for 42 days	BCF of 158 at 0–10°C	27
14 µg/L for 14 days	BCF of 351 at 16–22°C	27
70 µg/L for 42 days	BCF of 180 at 0–10°C	27
70 µg/L for 7 days	BCF of 237 at 16–22°C	27
Mysid, <i>Mysidopsis bahia</i>		
17–37 µg/L for lifetime	MATC	3
Sandworm, <i>Neanthes arenaceodentata</i>		
20 µg/L for 23 days	Inhibited reproduction at 1.5% salinity	28
3.1 mg/L for 28 days	Inhibited reproduction at 2.0% salinity	28
7.7 mg/L for 96 h	LC50 at 20°C	28
10.7 mg/L for 96 h	LC50 at 15°C	28
Shrimp, <i>Crangon crangon</i>		
Pb ⁺²		
375 mg/L for 96 h	LC50	23
Trimethyl lead		
8.8 mg/L for 96 h	LC50; BCF 1	23
Triethyl lead		
5.8 mg/L for 96 h	LC50; BCF 2	23
Tetramethyl lead		
110 µg/L for 96 h	LC50; BCF 20	23

Table 4.6 (continued) Lethal and Sublethal Effects of Lead^a to Selected Species of Aquatic Organisms

Ecosystem, Taxonomic Group, Species, Dose, and Other Variables	Effect ^b	Reference ^c
Tetraethyl lead 20 µg/L for 96 h	LC50; BCF 650	23
American lobster, <i>Homarus americanus</i> 50 µg/L for 30 days	Reduced ALAD activity; biochemical alterations in antennal gland; BCF 2760 for antennal gland, and 58 for gill	3, 29
Protozoan, <i>Cristigera</i> sp. 150 µg/L for 12 h	Reduced growth	3
Amphipod, <i>Ampelisca abdita</i> 547 µg/L for 96 h	LC50	3
Dungeness crab, <i>Cancer magister</i> 575 µg/L for 96 h	LC50	37
Sea urchin, <i>Anthocidaris crassispina</i> (embryos) 1.1 mg/L for 48 h	Development normal	30
2.2 mg/L for 48 h	Development inhibited	30
Fish		
Plaice, <i>Pleuronectes platessa</i>		
Tetramethyl lead 50 µg/L for 96 h	LC50; BCF 60	23
Tetraethyl lead 230 µg/L for 96 h	LC50; BCF 130	23
Triethyl lead 1.7 mg/L for 96 h	LC50; BCF 2	23
Trimethyl lead 24.6 mg/L for 96 h	LC50; BCF 1	23
Diethyl lead 75.0 mg/L for 96 h	LC50	23
Pb ⁺² 180.0 mg/L for 96 h	LC50	23
Dimethyl lead 300.0 mg/L for 96 h	LC50	23
Mummichog, <i>Fundulus heteroclitus</i> 315 µg/L for 96 h	LC50	3
Atlantic croaker, <i>Micropogonias undulatus</i> ; juveniles; oral ingestion of lead chloride equivalent to 12 mg Pb/kg BW daily for up to 6 weeks	Significant increases in the glutathione contents of liver and intestine during first week that plateaued; significant increases in brain and kidney glutathione after 6 weeks. Maximum residues, in mg Pb/kg FW, were 50 in intestine, 20 in kidney, 2 in liver, and <1 in brain	44

^a As total lead, unless indicated otherwise.^b BCF = bioconcentration factor; MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolic upset during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.^c 1, Vighi 1981; 2, Irmer et al. 1986; 3, EPA 1985; 4, Berglind et al. 1985; 5, Demayo et al. 1982; 6, Wong et al. 1978; 7, NRCC 1973; 8, Borgmann et al. 1978; 9, Spehar et al. 1978; 10, Fantin et al. 1985; 11, Fraser 1980; 12, Wong et al. 1981; 13, Johansson-Sjöbeck and Larsson 1979; 14, Rombaugh 1985; 15, Davies et al. 1976; 16, EPA 1980; 17, Ozoh 1980; 18, Holcombe et al. 1976; 19, Kumar and Pant 1984; 20, Coughlan et al. 1986; 21, Rivkin 1979; 22, Schulz-Baldes and Lewin 1976; 23, Maddock and Taylor 1980; 24, Zarogian et al. 1979; 25, Schulz-Baldes 1974; 26, Schulz-Baldes 1972; 27, Eisler 1977; 28, Reish and Gerlinger 1984; 29, Gould and Grieg 1983; 30, Kobayashi 1971; 31, Oladimeji and Offem 1989; 32, Ruby et al. 1993; 33, Sola et al. 1994; 34, Ruparelia et al. 1989; 35, Weber et al. 1991; 36, Spieler et al. 1995; 37, Tulasi et al. 1989; 38, Tulasi et al. 1992; 39, Santos and Hall 1990; 40, Gill et al. 1991; 41, Dave and Xiu 1991; 42, Stouthart et al. 1994; 43, Babich and Borenfreund 1990; 44, Thomas and Juedes 1992; 45, Sayer et al. 1989; 46, Sayer et al. 1991; 47, Horne and Dunsen 1995; 48, Steele et al. 1991; 49, Perez-Coll et al. 1988; 50, Herkovits and Perez-Coll 1991; 51, Steele et al. 1989; 52, Taylor et al. 1990; 53, Strickler-Shaw and Taylor 1990; 54, Janssens de Bisthoven et al. 1998; 55, Burger et al. 1998.

4.6.4 Amphibians and Reptiles

Lead poisoning in adult leopard frogs (*Rana pipiens*) is indicated by a series of signs: sloughing of integument; sluggishness; decreased muscle tone; decreases in red blood cells, white blood cells, neutrophils, and monocytes; erosion of the gastric mucosa; and (before death) excitement, salivation, and muscular twitching. The 30-day LC50 value for adult *R. pipiens* was 105 mg Pb/L, but some deaths and elevated liver residues were noted at water concentrations as low as 25 mg/L (Kaplan et al. 1967). Toad (*Bufo arenarum*) eggs are comparatively sensitive to ionic lead, with LC50 (48 h) values of 0.47 to 0.9 mg/L, and a high incidence of malformations in survivors (Perez-Coll et al. 1988). Zinc seems to confer a degree of protection against lead toxicosis in toad eggs (Herkovits and Perez-Coll 1991). In soft water (99 mg CaCO₃/L), some marbled salamanders (*Ambystoma opacum*) exposed to 1.4 mg Pb/L died in 8 days (USEPA 1985). At about 1.0 mg/L, lead blocked synaptic transmission by competitive inhibition of calcium in the bullfrog, *Rana catesbeiana* (Kober and Cooper 1976). At 0.5 mg Pb/L, tadpoles of *Rana utricularia* required additional time to metamorphose; and at 1.5 mg Pb/L, thyroid histopathology was recorded and the delay in metamorphosis was more pronounced (Yeung 1978). Tadpoles of the bullfrog and the green frog (*Rana clamitans*) do not avoid lead concentrations shown to produce behavioral deficiencies, i.e., >0.5 mg Pb/L (Steele et al. 1991). Lead interferes with the normal development of newly fertilized eggs of a toad (*Bufo arenarum*) at concentrations of 250 µg Pb/L and higher (Perez-Coll et al. 1988).

No data were available on toxic or sublethal effects of lead to reptiles under controlled conditions.

4.6.5 Birds

Lead poisoning resulting from the ingestion of lead shotgun pellets has been recognized as a cause of waterfowl deaths since the late 1800s (Wetmore 1919; Bellrose 1959). More than a million ducks — especially mallards — and geese die annually from lead shot poisoning (Clemens et al. 1975; Lumeij et al. 1989; Roscoe et al. 1989; Sanderson 1989; Whitehead and Tschartner 1991; Murase et al. 1993). The principal cause is the ingestion of spent shot by migrating birds feeding in heavily hunted areas. The pellets are retrieved from the marshy bottoms of shallow and deep water by waterfowl in search of food and grit. Shot retained in the gizzard is solubilized by a combination of the powerful muscular grinding action and the low pH (2.0 to 3.5) of gizzard contents. The released lead is available for absorption, producing weakened birds whose reproductive abilities are reduced and that may starve or fall prey to predators (Clemens et al. 1975). There does not appear to be a no-effect level for lead in waterfowl, and the activities of certain enzymes are inhibited at blood lead concentrations of <50 µg/L (Pain 1996). Ionic lead was 10 to 100 times more effective in reducing avian blood ALAD activity than were ionic copper, cadmium, and inorganic or methyl mercury (Scheuhammer 1987a). Absorbed lead causes a variety of effects leading to death, including damage to the nervous system, muscular paralysis, inhibition of heme synthesis, immunotoxic effects, and damage to kidneys and liver (Mudge 1983; Eisler 1988; Rocke and Samuel 1991). Lead poisoning in waterfowl is a debilitating disease in which death follows exposure in an average of 2 to 3 weeks (Friend 1985). During this time, affected birds lose mobility, tend to avoid other birds, and become increasingly susceptible to predation and other causes of mortality. Accordingly, acute large-scale die-offs of lead-poisoned waterfowl are uncommon (Friend 1985).

The relationship between incidence of lead shot in waterfowl gizzards and biological effects varies widely and is probably a function of shot availability caused by differences in shooting intensity, size of pellets, availability of grit, firmness of soil and sediments, and depth of surface water (Street 1983). Also, lead accumulations and the frequency of avian lead toxicosis following

ingestion of lead shot are modified by the age and sex of the bird, geographic location, habitat, and time of year (Finley and Dieter 1978; Mudge 1983; Srebocan and Rattner 1988). There is a growing body of evidence linking waterfowl poisoning with ingestion of lead-contaminated sediments, especially in certain areas of Idaho impacted by mining wastes (Chupp and Dalke 1965; Blus et al. 1991; Beyer et al. 1998a; Heinz et al. 1999). In the common bobwhite (*Colinus virginianus*), tissue lead accumulation can occur from ingestion of lead-contaminated sediments, although there were no signs of overt lead toxicity (Connor et al. 1994).

The effect of diet on vulnerability to lead makes interpretation of published information on experimental lead poisoning in waterfowl extremely difficult (Chasko et al. 1984). For example, many mallards on a diet of corn die within 10 to 14 days after ingesting a single lead shot, whereas similar birds on a balanced commercial duck ration appear outwardly normal after ingesting as many as 32 pellets of the same size (Wobeser 1981). Also, multiple nutritional deficiencies may have additional effects in potentiating the toxicity of lead in mallards (Carlson and Nielsen 1985). Under conditions of reduced dietary calcium availability, such as can occur in acid-impacted environments, birds risk increased uptake of lead (and other metals) and may accumulate toxic concentrations more rapidly (Scheuhammer 1996). Enhanced accumulation of lead was accompanied by an increased synthesis of metallothioneins and a greater inhibition of ALAD activity (Scheuhammer 1996).

Birds of prey may ingest lead in the form of shot from dead or crippled game animals, or as biologically incorporated lead from lead-poisoned waterfowl, small roadside mammals, and invertebrates (Stendell 1980; Pattee 1984; Franson 1996). Lead poisoning in carnivorous birds has been reported in various species of eagles, condors, hawks, harriers, owls, vultures, and falcons, and most — if not all — cases seem to result from ingestion of lead shot in food items (Custer et al. 1984; Wiemeyer et al. 1988; Nelson et al. 1989; Craig et al. 1990; Pain and Amiard-Triquet 1993; Pain et al. 1993a, 1993b, 1995). Some raptors ingest many shot in a short time. For example, the stomach of a bald eagle suspected of dying from lead poisoning contained 75 shot (Jacobson et al. 1977). Results of experimental lead shot poisoning of bald eagles ([Table 4.7](#)) confirmed results of nationwide monitoring showing that 5.4% of all dead eagles found in 1974/1975 died of lead poisoning, as evidenced by liver lead levels of 23 to 38 mg/kg fresh weight (Pattee et al. 1981). Ingestion of food containing biologically incorporated lead, while contributing to the lead burden of carnivorous birds, is unlikely in itself to cause clinical lead poisoning (Custer et al. 1984). A similar case is made for lead residues in soil and biota following field applications of lead arsenate (Stendell et al. 1989), for powdered lead (Franson et al. 1983), and forms of lead other than shot ([Table 4.7](#)). The strong indication is that the form in which lead is ingested is crucial.

Signs of lead poisoning in birds have been extensively documented (Bellrose 1951, 1959; Jordan and Bellrose 1951; Clemens et al. 1975; Forbes and Sanderson 1978; Hunter and Wobeser 1980; Pattee et al. 1981; Wobeser 1981; Franson and Custer 1982; Johnson et al. 1982; Eastin et al. 1983; Kendall and Scanlon 1983; Street 1983; Di Giulio and Scanlon 1984; Fimreite 1984; Gjerstad and Hanssen 1984; Hudson et al. 1984; Anderson and Havera 1985; Burger and Gochfeld 1985; Carlson and Nielsen 1985; Friend 1985; Hoffman et al. 1985a; Lumeij 1985; Beyer et al. 1988, 1998c; Scheuhammer and Wilson 1990; Lawler et al. 1991; Murase et al. 1993; Ochiai et al. 1993b; Franson 1996; Pain 1996). Outwardly, lead-poisoned birds show the following signs:

- Loss of appetite
- Lethargy
- Weakness
- Emaciation
- Tremors
- Drooped wings
- Green liquid feces
- Impaired locomotion, balance, and depth perception

Internally, lead-poisoned birds show:

- Microscopic lesions of the proventricular epithelium, pectoral muscles, brain, proximal tubular epithelium of the kidney, and bone medullary osteocytes
- An enlarged bile-filled gall bladder
- Anemia
- Elevated protoporphyrin IX levels in blood
- Decreased ALAD activity levels in blood, brain, and liver
- Reduced brain weight
- Abnormal skeletal development
- Cephalic edema
- Esophageal impaction

Postmortem examination of lead-poisoned birds may show:

- Edematous lungs
- Serous fluid in the pleural cavity
- Bile regurgitation
- Abnormal gizzard lining
- An unusually pale, emaciated, and dehydrated carcass
- Elevated lead levels in liver (>2 mg/kg fresh weight, >10 mg/kg dry weight), kidney (>6 mg/kg dry weight), and blood (> 0.2 mg/L)

Beyer et al. (1998c) aver that the most reliable indicators of lead poisoning in waterfowl include impactions of the upper alimentary tract, submandibular edema, myocardial necrosis, biliary discoloration of the liver, and hepatic lead concentrations of at least 38 mg/kg DW or 10 mg/kg FW.

Toxic and sublethal effects of lead and its compounds on birds held under controlled conditions vary widely with species, with age and sex, and with form and dose of administered lead (Table 4.7). Several generalizations are possible: decreased blood ALAD and increased protoporphyrin IX activity levels are useful early indicators of lead exposure; lead shot and certain organolead compounds are the most toxic forms of lead; nestlings are more sensitive than older stages; and tissue lead concentrations and pathology both increase in birds given multiple doses over extended periods (Scheuhammer 1987a, 1987b; Table 4.7). Blood lead concentrations of lead-poisoned waterfowl may be reduced with initiation of disodium calcium ethylenediamine tetraacetate therapy; however, ALAD levels remained depressed (Murase et al. 1993).

Trialkyllead salts are 10 to 100 times more toxic to birds than are inorganic lead salts; they tend to accumulate in lipophilic soft tissues in the yolk and developing embryo, and have high potential as neurotoxicants (Forsyth et al. 1985). Accordingly, more research is needed on alkyllead toxicokinetics. Some alkyllead compounds have been implicated in bird kills. In autumn 1979, about 2400 birds of many species were found dead or disabled on the Mersey estuary, England, an important waterfowl and marsh bird wintering area; smaller kills were observed in 1980 and 1981 (Bull et al. 1983). Affected birds contained elevated lead concentrations in liver (>7.5 mg/kg fresh weight), mostly as organolead. Bull et al. (1983) suggested that trialkyllead compounds were discharged from a petrochemical factory producing alkylleads into the estuary, where they were accumulated (up to 1.0 mg/kg fresh weight) by clams (*Macoma balthica*) and other invertebrates on which the birds could feed. Birds dosed experimentally with trialkyllead compounds died with the same behavioral and internal signs found in Mersey casualties; tissue levels of trialkyllead were similar in the two groups (Osborn et al. 1983). Sublethal effects that might influence survival in the wild were found in both sublethally dosed and apparently healthy wild birds when tissue levels of trialkyllead compounds were matched in the two groups. It was concluded that trialkyllead compounds were the main cause of the observed mortalities and that many apparently healthy birds were still at risk (Osborn et al. 1983).

Nestlings of altricial species (those confined to the nest for some time after hatch) may be considerably more sensitive to lead exposure than adults, and also more sensitive than hatchlings of many precocial species (Hoffman et al. 1985a). Hatchlings of precocial species, including chickens, Japanese quail (*Coturnix coturnix*), mallards, and pheasants, are relatively tolerant to moderate lead exposure, i.e., there was no effect on growth at dietary levels of 500 mg Pb/kg, or survival at 2000 mg Pb/kg (Hoffman et al. 1985a, 1985b).

Some species of domestic birds are comparatively resistant to lead toxicosis. For example, blood lead levels of 3.2 to 3.8 mg/L in lead-stressed cockerels (*Gallus* sp.) were much higher than residues considered diagnostic for lead poisoning in most domestic mammals (except swine, which tolerated up to 143 mg Pb/L blood) (Franson and Custer 1982). Captive wild ducks dosed with No. 4 lead shot in summer or winter were more sensitive than their domesticated counterparts, as judged by lower survival, and increased weight loss following lead shot administration and may be related to increased stress and unnatural diet (Rattner et al. 1989). Fatal lead poisoning (50% mortality) is documented for a captive colony of Gentoo penguins (*Pygoscelis papua*) in a zoo in Omaha, Nebraska. The source of lead was ankle weights worn by divers who cleaned the pool; the weights contained 1- to 2-mm lead pellets that were expelled through faulty seams and ingested by the penguins (Brown et al. 1996).

Table 4.7 Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference ^a
<i>Northern pintail, Anas acuta</i>		
Single oral dose of 2 No. 5 pellets	No difference from control group in band recovery rate from hunter kills	1
<i>Mallard, Anas platyrhynchos</i>		
Single oral dose of 1 No. 4 shot	Some deaths. Residues (mg/kg fresh weight) >3 in brain, >10 in clotted heart blood, >6 in kidney, and up to 20 in liver	2
Single oral dose of 1 No. 4 shot (0.2 g)	Blood lead concentrations, in mg/L, increased from <0.1 at start to 0.1 after 24 h, 3.2 at 7 days, to 6.8 at 14 days. There were some deaths at day 21 and survivors had 0.6 mg Pb/kg blood FW. All dosed birds had immunosuppressive effects, as seen by lowered hemagglutination titers to sheep red blood cells	42
Intubated with 1 or 2 No. 4 commercial lead pellets; blood taken at 4, 8, and 24 h after death	In dead birds, blood lead declined from 6.0 mg Pb/kg FW 4 h after death, to 5.5 at 8 h, to 3.4 at 24 h; survivors had 10.5–13.9 mg Pb/kg FW during this interval	41
Single oral dose 1 No. 6 shot	Mortality 9% in 20 days	3
1 No. 4 shot	Mortality 19% in 20 days	3
2 No. 6 shot	Mortality 23% in 20 days	3
4 No. 6 shot	Mortality 36% in 20 days	3
6 No. 6 shot	Mortality 50% in 20 days	3
8 No. 6 shot	Mortality 100% in 20 days	3
Single oral dose of 1 No. 4 shot (205 mg), equal to 151 mg/kg body weight (BW)	Some deaths; blood ALAD activity depressed 30% after 3 months, 15% after 4 months	4
Single oral dose of 1 No. 4 lead shot (200 mg)	Residues (mg/kg dry weight femur) 488 in laying hen, 114 in nonlaying hen, and 9 in drake	5
Single oral dose of 1 shot (200 mg)	After 30 days, residues (mg/kg fresh weight) 1.0 in blood, 2.5 in liver, and 0.5 in brain. Decrease in ALAD activity in blood and cerebellum	6
Single oral dose of shot	Dosed birds recaptured in significantly greater numbers than controls	7

Table 4.7 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference^a
Single oral dose of tetraethyllead	LD50 of 107 mg/kg BW. Signs of intoxication included excessive drinking, regurgitation, hypoactivity, muscular incoordination, fluffed feathers, eyelid drooping, tremors, and loss of appetite. Regurgitation within 7 min, other signs as soon as 20 min, and death usually between 1 and 4 days posttreatment. Remission took up to 8 days	34
Fed diets containing 25 mg Pb/kg, as lead nitrate, for 12 weeks	No deaths; no pathology; no significant accumulations of lead in liver, kidney, or bone; no changes in hemoglobin or hematocrit; decrease in blood ALAD activity, and increase in blood lead levels — both returned to normal diet within 3 weeks on lead-free diet	8
Females fed diets for 12 weeks containing 80 mg Pb/kg ration (as lead acetate) alone or in combination with 8 mg Hg/kg (as methylmercury chloride), or 80 mg Cd/kg ration (as cadmium chloride), or a mixture of Pb, Hg, and Cd	Renal corpuscles of ducks fed Pb, Hg, or Cd alone or in two-way combinations had minor ultrastructural changes when compared to controls. The diet containing all three metals caused marked ultrastructural changes in kidney	40
Fed diets containing 100 mg Pb ⁺² /kg	Elevated levels in bone (9.6 mg/kg fresh weight vs. 0.7 in controls) and egg (1.3 vs. 0.9 in controls)	9
Fed diets containing metallic lead for 42 days 100 mg/kg diet	Elevated lead levels (mg/kg dry weight) in kidney (23), liver (7), and bone (5)	10
10 mg/kg diet	Residues (mg/kg dry weight) of 4 in kidney (vs. <0.5 in controls), 0.7 in liver (vs. <0.5 in controls), and 0.8 in bone (vs. 0.9 in controls)	10
Adult males, age 16 weeks, fed pelleted commercial duck diet for 10 weeks; diet formulated to contain 24% lead-contaminated sediment (3400 mg Pb/kg DW sediment = 816 mg Pb/kg DW total diet)	1 of 10 died vs. none in controls; survivors had atrophied breast muscles, green staining of feathers around the vent, viscous bile; green staining of the gizzard lining, and renal intranuclear inclusion bodies. Blood had 6.1 mg Pb/kg FW, liver had 2.8 mg Pb/kg FW, and feces had 1660 mg Pb/kg DW	61
Adult males, age 7 months, fed ground corn diet for 15 weeks; diet contained 24% lead-contaminated sediment (4000 mg Pb/kg DW sediment = 960 mg Pb/kg total diet)	80% dead (4 of 5); livers had 38 mg Pb/kg DW	61
As above, except mallards were fed a nutritionally balanced commercial duck diet containing 24% lead-contaminated sediments (4000 mg Pb/kg DW sediment)	No deaths; livers had 13 mg Pb/kg DW	61
Held in 1.6 ha enclosures on hunted or nonhunted wetlands; California; 1986–89; lead shot pellet density in enclosures were 15,750, 173,200, or >2 million/ha	Blood lead concentrations increased, and survival reduced with increasing shot density	39
Ducks, Anas spp.		
Single oral dose of 2 shot (254 mg) or 5 shot (635 mg)	Weight loss, emaciation, elevated lead concentrations in bone, some deaths. American black duck, <i>Anas rubripes</i> , more sensitive than mallards	11
Birds		
Dietary route, 11 species, diagnosed as lead poisoned	All had inclusions in proximal convoluted tubules of kidney; liver lead residues ranged from 3.1 to 15 mg/kg fresh weight	12

Table 4.7 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference^a
Lethal dietary administration of lead acetate, 6 species	Before death, birds were emaciated and showed increases in blood protoporphyrin and decreases in ALAD; renal intranuclear inclusion bodies were present in 83% of all birds that died from lead poisoning. Median lead concentrations (mg/kg fresh weight) ranged in the liver from 20 in male red-winged blackbirds (<i>Agelaius phoeniceus</i>) to 111 in female northern bobwhites (<i>Colinus virginianus</i>), and in the kidney from 22 mg/kg in the blackbird to 190 in the bobwhite	13
<i>Canada goose, Branta canadensis</i>		
Oral dose of 4 to 5 No. 4 shot	Lethal	43
<i>Red-tailed hawk, Buteo jamaicensis</i>		
Exposed daily via oral gavage to sublethal concentrations of 0.82 mg Pb/kg BW (given as 1.5 mg lead acetate /kg BW daily) for up to 11 weeks	Alterations in the heme biosynthetic pathway noted after 7 days. Erythrocyte ALAD activity was depressed and did not recover until 5 weeks after termination of lead treatments	45
Fed 0.82 or 1.64 mg Pb/kg BW daily as lead acetate for 3 weeks	No effect on gastric contractions or egestion of pellets of undigested materials	44
Fed 6.56 mg Pb/kg BW daily for 3 weeks as lead acetate	No effect on frequency or timing of pellet egestion	44
<i>Common bobwhite, Colinus virginianus</i>		
Fed diet for 21 days in which sediments (4.5 g Pb/kg DW) from a lake in northern Idaho contaminated with mining wastes was added to ground poultry ration at 8% dry matter intake, equivalent to about 550 mg Pb/kg DW ration	No effect on food intake or growth. Blood and tissue lead levels elevated, but no overt signs of lead toxicity. Lead concentrations (controls vs. dosed birds) were 0.6 vs. 1.3 mg/kg FW in blood, <0.1 vs. 7 mg/kg DW in liver, and <0.1 vs. 30 mg/kg DW in kidney	46
<i>Rock dove, Columba livia</i>		
Intragastric administration of 6.25 mg Pb (as lead acetate)/kg BW, daily for 64 weeks	Anemia, elevation in erythrocyte porphyrin, kidney pathology; residues (mg/kg fresh weight) of 603 in kidney, 501 in bone, 8 in liver, 2 in brain, 4.4 in blood, 0.8 in sciatic nerve, and 0.1 in crop	14
Intubation of 6.25 mg Pb (as lead acetate)/kg BW, chronic exposure	Interfered with four-step learning sequence; elevated blood lead levels remained for 5 weeks after lead exposure	15
<i>Japanese quail, Coturnix japonica</i>		
Single oral dose of tetraethyllead	LD50 of 24.6 mg/kg BW	38
Fed diets containing different forms of lead for 5 days		
5000 mg metallic Pb/kg	No effect on survival or food consumption	16
5000 mg Pb (as lead nitrate)/kg	No overt signs of toxicity	16
5000 mg Pb (as lead subacetate C ₄ H ₁₀ O ₈ Pb ₃)/kg	No overt signs of toxicity	16
2761 mg Pb(as lead arsenate)/kg	LD50	16
<i>Prairie falcon, Falco mexicanus</i>		
Fed shotgun-killed pheasants and ducks	Death, preceded by vomiting, ataxia, blindness, and convulsions. Lead shot recovered from stomach; residues (mg/kg dry weight) of 57 in liver and 78 in kidney	17

Table 4.7 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference^a
American kestrel, <i>Falco sparverius</i>		
Fed mallard homogenate containing 16 to 87 (biologically incorporated) mg Pb/kg fresh weight (FW) for 60 days	Residues of 0.4 mg/kg fresh weight in liver and 7.6 mg/kg dry weight in bone	18
Oral administration of 1 No. 9 shot daily for 60 days	Residues (mg/kg FW) of 0.4 in liver and 28.7 in bone	18
Fed control diet with 0.4 mg Pb ⁺² /kg FW	Residues of 0.1 mg/kg fresh weight in liver and 4.2 mg/ kg dry weight in bone	18
Fed pine voles (<i>Microtus pinetorum</i>) containing 38 mg Pb/kg whole-body FW (from apple orchards treated with lead arsenate) for 60 days vs. controls fed uncontaminated laboratory mice (<i>Mus musculus</i>)	At end of study kestrels had 1 mg Pb/kg FW liver vs. 0.06 in controls, and 0.7 mg/kg FW bone vs. 0.27 in controls	47
Fed diets containing 50 mg metallic Pb powder/kg for at least 5 months	Blood ALAD reduced 80%; liver residues of 1.3 to 2.4 mg/kg dry weight; no effects on blood chemistry	19
As above, except diet contained 10 mg/kg	No measurable effects	19
Fed diets containing metallic Pb powder for 6 months		
50 mg Pb/kg diet	No adverse effects on survival, egg laying, fertility, or eggshell thickness. Elevated residues (mg/kg dry weight) in humerus (13), tibia (62), and liver (2)	20
10 mg Pb/kg diet	Elevated lead in bone (4 to 9 mg/kg dry weight vs. <0.8 in controls) and in liver (3 vs. <0.5 in controls)	20
Nestlings dosed orally with metallic lead powder daily for 10 days		
625 mg/kg BW	Mortality (40% in 6 days); reduced growth; reduced kidney and liver weight; abnormal skeletal development; ALAD depression in all tissues examined; elevated burdens (mg/kg fresh weight) in kidney (15), liver (6), and brain (3)	21
125 mg/kg BW	Reduced growth, reduced brain weight, abnormal skeletal development, ALAD depressions in hematopoietic tissues, elevated burdens (mg/kg fresh weight) in kidney (7), and liver (4)	21
25 mg/kg BW	ALAD depression in all tissues examined; burdens (mg/kg fresh weight) elevated in kidney (3) and in liver 1.4)	21
Fed 60 days with cockerels (<i>Gallus</i> sp.) containing up to 448 mg (biologically incorporated) Pb/kg dry weight	No effect on survival, growth, hemoglobin, hematocrit, and erythrocyte number. Elevated burdens in kidney, liver, femur, brain, and blood	22
Chicken, <i>Gallus</i> sp.		
Fed diets containing 1.85 g Pb/kg, as lead acetate, for 4 weeks	No deaths or severe clinical hematological effects; growth rate suppressed 47%, blood lead residues 3.2 to 8.3 mg/L	23
Bald eagle, <i>Haliaeetus leucocephalus</i>		
Oral administration of 10 No. 4 shot (2000 mg)		
Eagles dying 10 to 133 days posttreatment	Residue levels (mg/kg dry weight) 0.9 in muscle, 1.4 in brain, 6 in kidney, 10 in tibia, 10.3 in humerus, 10.4 in femur, and 16.6 in liver. Loss in body weight 16% to 23% at death	24

Table 4.7 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference^a
Eagle sacrificed at day 133 posttreatment (bird went blind)	Residue levels (mg/kg dry weight) <0.1 in muscle, 2.1 in brain, 3.2 in kidney, 3.4 in liver, and 12.2 to 13.8 in bone	24
Controls	Residue levels (mg/kg dry weight) <0.1 muscle, 0.1 in brain, 0.4 in liver, 0.5 in kidney, and 4.5 to 6.6 in bone	24
<i>Willow ptarmigan, Lagopus lagopus</i>		
Single oral dose		
1 No. 6 shot (100 mg)	Weight loss of 12% in 15 days; residues of 3.3 mg/kg fresh weight in liver, 56 mg/kg dry weight in tibia	25, 26
3 No. 6 shot (300 mg)	Some deaths between days 8 and 15 posttreatment, reduced food intake, weight loss, lethargy, diarrhea; residues of 7.3 mg/kg fresh weight liver, 139 DW tibia	25, 26
6 No. 6 shot (600 mg)	If shot retained in gizzard, death resulted; residues (mg/kg) 72 fresh weight in liver, 154 dry weight in tibia	25, 26
Controls	Residues (mg/kg) 0.1 fresh weight in liver, 5 dry weight in tibia	25, 26
<i>Raptors, 4 spp.</i>		
Fed rock doves (<i>Columba livia</i>) and brown hares (<i>Lepus europaeus</i>) with lead shot for 3 weeks to 6 months	Death preceded by weight loss, convulsions, and inability to fly. Residues (mg/kg dry weight) at death ranged from 57 to 175 in liver, and 34 to 221 in kidney	27
<i>Herring gull, Larus argentatus</i>		
Chicks aged 2 days given intraperitoneal (ip) injection of 0.1 or 0.2 mg Pb/kg BW as lead nitrate and killed after 45 days	Dose-dependent increases in all tissues measured. Largest changes were in bone with controls at 0.8 mg/kg DW, the 0.1 mg/kg at 54 and the high-dose group at 131 mg/kg DW; for liver, these values were 0.05, 7, and 22, respectively; for blood, 0.01, 0.07, and 0.2; for kidney, 0.1, 7, and 41; for brain, 0.01, 0.3, and 1.6; and for muscle 0.01, 0.07, and 0.17 mg/kg DW, respectively	48
Chicks age 1 day given single ip injection of 100 or 200 mg Pb/kg BW as lead nitrate	Dose-dependent decrease in growth rate for at least 40 days postinjection; wing and tarsus bone development inhibited at end of 46-day study	50
Chicks age 1 day given single ip injection of 100 mg Pb/kg BW as lead nitrate at ages 1, 2, 4 or 6 days	Chicks were most sensitive at age 6 days than earlier stages judged by behavioral effects including balance and thermoregulation	51
Chicks, age 2 days, given a single ip injection of 0, 100, or 200 mg Pb/kg BW as lead nitrate and observed for 45 days	Control birds performed better than lead-injected gulls in begging behavior, balance and righting response, depth perception and thermoregulation behavior	49
<i>Zebra finch, Poephila guttata</i>		
Given drinking water with 10 mg Pb/L for 51 days; diets were either low in calcium (0.3% Ca) or adequate in calcium (3% Ca)	Birds given low calcium diets accumulated up to 4 times more lead in tissues than finches on high calcium diets. Lead concentrations in mg/kg DW for low Ca vs. high Ca diets were 2.4 vs. 0.6 in liver, 4.9 vs. 1.5 in kidney, and 48 vs. 8 in bone	52

Table 4.7 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference^a
Common tern, <i>Sterna hirundo</i>		
Single injection of 200 mg Pb ⁺²	Adverse effects on behavior (locomotion, balance, righting response, feeding tasks, behavioral thermoregulation); most apparent within 5 days postinjection	28
Chicks injected ip with 200–1200 mg Pb/kg BW as lead nitrate		
All birds	Dose-dependent changes in locomotion, survival, and righting response	53
100 mg/kg BW	Adverse effects	53
200 mg/kg BW	After 21 days, reduced growth rate, impaired motor coordination of head and neck, and reduced ability to manipulate fish prey	54
1000 mg/kg BW	LD50 at day 17 postinjection	53
1200 mg/kg BW	LD100 at day 17 postinjection	53
Ringed turtle-dove, <i>Streptopelia risoria</i>		
Single ip injection of 2.5 mg Pb/kg BW	No effect on hepatic ALAD activity; renal ALAD decreased with increasing lead deposition in kidney	55
Single oral dose of 2 pellets (220 mg)	Blood lead (mg/L) 4.69 at 24 h, and 0.14 at 14 days (vs. control values of 0.004 to 0.012 mg/L); blood ALAD depressed from 24 h through 14 days	29
Single oral dose of 4 shot (440 mg)	Mortality 71% at 6°C in 7 days; nil at 21°C in 9 days — but some with seizures and kidney histopathology. No spermatozoa in seminiferous tubules. Lead residues elevated in bone, liver, and brain in both groups, but more elevated in cold-stressed group	30, 31
Single oral dose of 4 shot (440 mg)	Testicular damage in adults held at 6°C or 21°C; mortality higher in cold-stressed group	32
Single oral dose of 4 shot (488 mg)	Some deaths. Intranuclear inclusion bodies in cells of kidney proximal convoluted tubules	12
Single oral dose of 75 mg Pb/kg BW, as lead acetate	Some deaths; kidney damage	12
Intubation with 75 mg Pb (as lead acetate)/kg BW daily for 7 days	Residues, (mg/kg dry weight) 457 in kidney, 29 in liver, and 12.4 in brain; seizures; depressed blood ALAD activity; blood lead concentration 311 µg/L	33
Controls	Concentrations (mg/kg DW) 8.2 in kidney, 3.0 in brain, 1.2 in liver; blood lead concentration 18 µg/L	33
Drinking water with 100 µg Pb ⁺² /L for 2 weeks before pairing, and throughout a breeding cycle	Reduction in testes weight and spermatozoa number. No effect on egg production or fertility. Bone lead levels higher than controls especially in females. Significantly higher lead concentrations in bone, liver, and feather in progeny of lead-treated parents than in controls	34
European starling, <i>Sturnus vulgaris</i>		
Oral administration (capsule) of triethylPb chloride at 2000 µg daily (28 mg/kg BW) for 11 days or until death	Mortality 100% by day 6. Dying birds showed decreased respiration, squatting, fluffed feathers, and abnormal head posture. Mean residues (mg/kg fresh weight) were 6.0 in bone, 7.3 in brain, 19.9 in kidney, 20.0 in muscle, and 40.2 in liver	35
As above, but dose was 200 µg daily (2.8 mg/kg BW)	No deaths, reduced food consumption. All tissue residues <2.0 mg/kg fresh weight (vs. <0.1 in controls)	35

Table 4.7 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Birds

Species, Route of Administration, Dose, and Other Variables	Effects	Reference ^a
Oral administration of trimethylPb chloride capsule of 2000 µg daily (28 mg/kg BW) for 11 days or death	All dead by day 6. Signs included impaired balance, tremors, fluffed feathers, uncoordinated feeding movements, weight loss, inability to fly. Residues (mg/kg FW) averaged 4.3 in bone, 11.0 in muscle, 16.7 in brain, 30.2 in kidney, and 82.4 in liver	35
As above, but dose was 200 µg daily (2.8 mg/kg BW)	No deaths, survivors hyperactive. Average tissue residues (mg/kg fresh weight) 0.4 in bone, 3.1 in muscle, 3.5 in brain, 3.7 in liver, and 5.4 in kidney	35
Starlings from pristine area in Poland were exposed in cages for 8 days near a zinc smelter	Tissue lead concentrations were 3 to 12 times higher after 8 days; stomach content lead levels increased from 2 mg/kg DW to 532, and feces increased from 0.4 to 154 mg Pb/kg DW	56
Mourning dove, Zenaida macroura		
Single oral dose of 0, 1, 2, or 4 No. 8 shot and observed for 28 days	Dose-dependent weight loss, but survivors regained weight with passing of shot. Blood ALAD levels in all dosed groups declined 95–99% within 24 h and remained depressed; mortality was not dose-related	57
As above	Blood lead concentrations rose from 0.06 mg Pb/L prior to dosing to more than 6 mg Pb/L 5 to 9 days after dosing	58
Single oral dose 1 No. 8 shot (72 mg)	Mortality 24% in 4 weeks; normal courtship and reproductive activities, but egg hatching significantly reduced; lead residues elevated in kidney, liver, and bone	36
1 No. 8 shot and held at 5 or 22°C and fed commercial pelleted ration or mixed seed	Tissue lead residues were higher in Pb-dosed birds. Doves on the pelleted diet retained shot longer and eroded more lead than did doves on the mixed seed diet. Temperature had no measurable effect on lead residues	59
Force-fed 1 No. 8 shot vs. force-fed millet seed. All doves were fitted with a radiotransmitter, released, and movements recorded for 21 days	Survival was about 60% for controls and 40% for lead-treated group, but this was not statistically significant	60
2 No. 8 shot (144 mg)	Mortality 60% in 4 weeks	36
4 No. 8 shot (288 mg)	Mortality 52% in 4 weeks	36
Single oral dose of 4 No. 8 shot	Residues (mg/kg dry weight) 345 to 639 in kidney and 58 to 215 in liver (vs. <12 in controls)	37
4 days posttreatment	Residues (mg/kg dry weight) 1279 to 1901 in kidney and 179 to 267 in liver	37
8 days posttreatment		

^a 1, Deuel 1985; 2, Longcore et al. 1974a; 3, Longcore et al. 1974b; 4, Dieter and Finley 1978; 5, Finley and Dieter 1978; 6, Dieter and Finley 1979; 7, Bellrose 1951; 8, Finley et al. 1976; 9, Haegele et al. 1974; 10, Di Giulio and Scanlon 1984; 11, Chasko et al. 1984; 12, Kendall and Scanlon 1985; 13, Beyer et al. 1988; 14, Anders et al. 1982; 15, Dietz et al. 1979; 16, Hill and Camardese 1986; 17, Redig et al. 1980; 18, Stendell 1980; 19, Franson et al. 1983; 20, Pattee 1984; 21, Hoffman et al. 1984a,b; 22, Custer et al. 1984; 23, Franson and Custer 1982; 24, Pattee et al. 1981; 25, Gjerstad and Hanssen 1984; 26, Fimreite 1984; 27, Macdonald et al. 1983; 28, Burger and Gochfeld 1985; 29, Kendall et al. 1982; 30, Kendall and Scanlon 1981; 31, Kendall and Scanlon 1984; 32, Veit et al. 1983; 33, Kendall and Scanlon 1982; 34, Kendall and Scanlon 1981; 35, Osborn et al. 1983; 36, Buerger et al. 1986; 37, Kendall and Scanlon 1983; 38, Hudson et al. 1984; 39, Rocke et al. 1997; 40, Rao et al. 1989; 41, Havera et al. 1989; 42, Trust et al. 1990; 43, Wheeler 1995; 44, Lawler et al. 1991; 45, Redig et al. 1991; 46, Connor et al. 1994; 47, Stendell et al. 1989; 48, Burger and Gochfeld 1990; 49, Burger 1990; 50, Burger and Gochfeld 1988b; 51, Burger and Gochfeld 1995; 52, Scheuhammer 1996; 53, Burger and Gochfeld 1988a; 54, Gochfeld and Burger 1988; 55, Scheuhammer and Wilson 1990; 56, Dmowski 1995; 57, Ho and Oster 1994; 58, Castrale and Oster 1993; 59, Marn et al. 1988; 60, Carrington and Mirarchi 1989; 61, Heinz et al. 1999.

4.6.6 Mammals

Three stages of recognizable lead poisoning, or plumbism, have been reported in humans (NRCC 1973): (1) mild or severe dysfunction of the alimentary tract as shown by loss of appetite, constipation, abdominal cramps, headaches, general weakness, and fatigue; (2) atrophy of forearm extensor muscles, or paralysis of these muscles and more striking atrophy; and (3) lead encephalopathy, which occurs frequently in lead-poisoned infants and young children, but only rarely in industrial workers. In general, people with hepatitis, anemia, and nervous disorders were more susceptible to lead poisoning (Barth et al. 1973). The transfer of lead across the human placenta and its potential threat to the fetus have been recognized for more than 100 years; women occupationally exposed to lead show a comparatively high abortion rate (Tachon et al. 1983). Sensitivity of the brain to the toxic effects of lead is considerably greater in the fetus than in the infant or young child (USEPA 1980). Lead is not considered carcinogenic to humans (Tsuchiya 1979), but reports of chromosomal aberrations in human blood lymphocytes (Barth et al. 1973) suggest that lead is a probable mutagen.

Signs of plumbism in domestic and laboratory animals, which are similar to those in humans, have been well documented (Barth et al. 1973; NRCC 1973; Mierau and Favara 1975; Davies et al. 1976; Roberts et al. 1976; Forbes and Sanderson 1978; Nriagu 1978b; Osweiler and Van Gelder 1978; Tsuchiya 1979; Ward and Brooks 1979; USEPA 1980; Mahaffey et al. 1980; Hamir 1981; Harrison and Laxen 1981; Burrows and Borchard 1982; Demayo et al. 1982; Hamir et al. 1982; Mykkanen et al. 1982; Tachon et al. 1983; Gietzen and Wooley 1984; Berglind et al. 1985; Ma 1996; [Table 4.8](#)). There is general agreement on several details: significant differences occur between species in response to lead insult; effects of lead are more pronounced with organolead than inorganic lead compounds; younger developmental stages are the most sensitive; and the effects are exacerbated by elevated temperatures, and by diets deficient in minerals, fats, and proteins. Tetramethyllead, for example, is about seven times more toxic than tetraethyllead to animals, and both compounds showed toxic effects earlier than did inorganic lead compounds. In severe cases, death is usually preceded by impairment of normal functions of the central nervous system, the gastrointestinal tract, and the muscular and hematopoietic systems. Signs include vomiting, lassitude, loss of appetite, uncoordinated body movements, convulsions, stupor, and coma. In nonfatal cases, signs may include depression, anorexia, colic, disturbed sleep patterns, diarrhea, anemia, visual impairment, blindness, susceptibility to bacterial infections, excessive salivation, eye blinking, renal malfunction, peripheral nerve diseases affecting the motor nerves of the extremities, reduced growth, reduced life span, abnormal social behavior, and learning impairment. Lead crosses the placenta and is passed in milk, producing early intoxication of the fetus during pregnancy and the newborn during lactation. High lead doses in mammals induce abortion, reduce or terminate pregnancy, or can result in stillbirths or an increase in skeletal malformations. These signs, together with lead levels in blood and tissues and histopathological examination, are used to diagnose lead poisoning. The best overall predictors of the risk of clinical lead effects in mammals are the blood lead concentrations and the erythrocyte protoporphyrin values, because they correlate with most toxicity endpoints of either neurological, renal, hematopoietic, or musculoskeletal nature (Ma 1996).

Lead adversely affected the survival of sensitive mammals tested at different concentrations ([Table 4.8](#)): 5 to 108 mg Pb/kg BW in rats (acute oral), 0.32 mg Pb/kg BW daily in dogs (chronic oral), and 1.7 mg Pb/kg diet in horses (chronic dietary). Adverse sublethal effects ([Table 4.8](#)) were noted in monkeys given 0.1 mg Pb/kg BW daily (impaired learning 2 years postadministration) or fed diets containing 0.5 mg Pb/kg (abnormal social behavior); in rabbits given 0.005 mg Pb/kg BW (reduced blood ALAD activity) or 0.03 mg Pb/kg BW (elevated blood lead levels); in mice at 0.05 mg Pb/kg BW (reduced ALAD activity); or in sheep at 0.05 mg Pb/kg BW (tissue accumulations).

Although lead is undeniably toxic at high levels of exposure, the implications of lower levels of exposure are poorly defined (Nriagu 1978b). Behavioral effects such as hyperactivity, distractibility, and decreased learning ability, as well as certain peripheral neuropathies, have been ascribed to subclinical lead exposure (Hejtmancik et al. 1982). Impaired learning ability of lead-stressed animals showing no obvious signs of lead intoxication has been documented for rats (Cory-Slechta

et al. 1981, 1983, 1985; Angell and Weiss 1982; Nation et al. 1982; Geist et al. 1985; Massaro et al. 1986), sheep (Nriagu 1978b; USEPA 1980), and primates (Rice 1985), although variability was great in all studies. Some learning deficits may be reversible and may not persist beyond a period of rehabilitation (Geist et al. 1985), and some may be induced only at relatively high exposure levels (Hastings et al. 1984). Abnormal social behavior (usually aggression) has been reported in baboons and monkeys (Hopkins 1970; Nriagu 1978b), although mice showed inhibited development of isolation-induced aggression (Ogilvie and Martin 1982). Altered parent-child relationships were suggested when suckling rats were used as surrogates. In that study, pregnant rats fed diets containing powdered lead nursed for longer periods than normal, and their offspring were slower to explore their environment (Barrett and Livesey 1983). Lead-exposed pups, with blood lead levels as low as 200 µg/L (considered elevated but within the “normal” range) at weaning, showed an altered dam-pup interaction that resulted in the dam spending longer periods in the nest than usual. Retarded development of lead-treated pups may account for the longer bouts of nesting by lead-stressed dams, and the delay in age at which pups explore and learn. Barrett and Livesey (1983) concluded that maternal behavior was related to delays in pup development, and that the functional isolation of pups from their environment may be the antecedent to altered behavior later in maturity. No data are currently available on effects of lead-induced altered parent-offspring relationships, impaired learning ability, or abnormal social behavior for any population of free-ranging wildlife.

Ingestion of lead-containing paint from bars or walls is a significant cause of death among captive wild animals (including many species of apes, monkeys, bears, ferrets, pinnipeds, foxes, panthers, bats, raccoons, and armadillos) and is probably underreported (Hopkins 1970; Zook et al. 1972; Fowler 1975; Forbes and Sanderson 1978; Sill et al. 1996). A similar situation exists for domestic animals — including dogs, cats, goats, horses, swine, cattle, and sheep (Dollahite et al. 1978; Forbes and Sanderson 1978; Osweiler and Van Gelder 1978; Hamir 1981). Passage of laws regulating the amount of lead in paint has decreased the frequency of lead poisoning, but many animals are still at risk from this source. Lead also occurs in used motor oils, gasoline, batteries, shot, putty, golf balls, linoleum, and printers’ ink — all of which are considered sources of lead poisoning to domestic animals (Dollahite et al. 1978).

Although the use of lead arsenate as an insecticide in orchards is diminishing, residues of lead still remain in the upper soil surface and will continue to be bioavailable almost indefinitely (Gilmartin et al. 1985).

Naturally occurring radiolead-210, which has a half-life of 22 years, is a significant contributor to the natural radiation dose in man. Comparatively high levels have been reported in certain grasses and lichens, and their consumers, such as reindeer, caribou, and ptarmigan, as well as in lanternfishes (Nriagu 1978b). The implications of this finding to wildlife health are unknown.

Treatment of lead-poisoned animals usually involves the removal of ingested lead objects and treatment with antibiotics. For example, a captive bottlenose dolphin (*Tursiops truncatus*) that had 40 lead-containing air pellets in its second stomach, as determined by radiography, was treated with 250 mg penicillamine/kg BW given orally 3 times daily for 5 days after the pellets had been removed from the stomach using an endoscope (Shlosberg et al. 1997). Anemia in chimpanzees (*Pan troglodytes*) is sometimes associated with lead toxicity (Young et al. 1994). In one case, a 19-year-old female chimpanzee with a history of excessive menstrual bleeding had a blood serum level of 1.03 mg Pb/L. The animal was successfully treated using oral chelation therapy: 2,3-dimercaptosuccinic acid at 10 mg/kg BW *per os* for 5 days, then 10 mg/kg BW for 2 weeks (Young et al. 1994).

Table 4.8 Lethal and Sublethal Effects of Lead to Selected Species of Mammals

Species, Dose, and Other Variables	Effects	Ref. ^a
Wood mouse, <i>Apodemus sylvaticus</i>		
Laboratory colony given drinking water containing 200 mg Pb/L as lead nitrate for 30 days; experimental vs. controls Femur	116.0 FW vs. 4.3 FW	33

Table 4.8 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Mammals

Species, Dose, and Other Variables	Effects	Ref.^a
Kidney	13.9 FW vs. 3.5 FW	33
Liver	6.3 FW vs. 4.6 FW	33
Cattle, cows, <i>Bos spp.</i>		
Tissue lead (mg/kg FW) 0.81 in blood, 26.4 in liver, 50.3 in kidney, and 400 in rumen contents	Clinical Pb toxicosis observed	1
Calves given 2.7 mg Pb/kg body weight (BW), as lead acetate, for 20 days; milk diet	Death	2
Calves given 3.0 to 3.5 mg Pb/kg BW daily for 3 months; grain and hay diet	No effect	2
Calves given 5 mg Pb/kg BW, as Pb acetate, for 7 days; grain and hay diet	Appeared normal	3
Calves given 5 mg Pb/kg BW, as Pb acetate, for 7 days; milk diet	Signs of lead poisoning; some deaths	3, 4
Calves given 5 mg Pb/kg BW daily for 10 to 20 days	Blindness, 16% mortality	4
Calves given forage with 5 to 6 mg Pb/kg	Fatal in 2 months	1
Calves given 5 to 6 mg Pb/kg BW daily for 3 years	Chronic toxicity	2
Adults given 6 mg Pb/kg BW daily for 3 years	No deaths	5
Calves given 6 to 7 mg Pb/kg BW daily for 2 months	Fatal	2
Fed 6 to 7 mg Pb (as Pb acetate)/kg BW daily	Intoxication within 8 weeks; most dead at day 105	6
Consumed vegetation (17 to 20 mg Pb/kg fresh weight) near Pb battery recycling plant	Some deaths, mostly younger animals; neurological signs. Lead levels, in mg/kg fresh weight, were 13.8 to 35.8 in blood, 6.9 to 96.5 in feces, 97 in liver, and 138 in kidney. Histopathology of liver and kidney	7
Calves given 20 mg Pb/kg BW daily	Fatal in 8 to 22 days	2
Accidentally exposed for 10 days to toxic levels of Pb, as lead shot, through corn silage. Silage storage area received shot from a nearby trap shooting range. Silage contained 32 mg Pb/kg	1.5% dead (2/70), 27% with signs of poisoning (kidney pathology, hemorrhaging). Tissue lead concentrations of 16 mg/kg FW in liver, >32 in kidney, and up to 0.8 in blood	6
Calves, single oral dose of 220–400 mg Pb/kg BW, as lead acetate	LD50	2
Total dose of 50 to 100 grams	Toxic	6
Dog, <i>Canis familiaris</i>		
Fed 0.32 mg Pb/kg BW daily	Chronic toxic level	4
Fed 3 mg Pb/kg BW daily, as lead carbonate	Anorexia and convulsions at 180 days	8
Fed low calcium/phosphorus diet containing 100 mg Pb/kg, equivalent to about 3.5 mg Pb/kg BW	At 12 weeks, anemia, weight loss, and renal necrosis. Tissue lead levels (mg/kg fresh weight) 1.2 in brain, 1.7 in blood, 15.7 in spleen, 23.4 in liver, 32.2 in kidney, and 735 in bone	9
Total dose of 10–25 grams	Toxic	6
Goat, <i>Capra sp.</i>		
Total dose of 20–25 grams	Toxic	6
Guinea pig, <i>Cavia cobaya</i>		
Single intraperitoneal injection of 25 mg/kg BW, as lead acetate	Reduced brain weight of newborn pigs. Effects synergized when dams were exposed to elevated (42°C) temperatures for 24 h: 88% with microencephaly vs. 5% in group given 25 mg/kg without hyperthermia	10
Bank vole, <i>Clethrionomys glareolus</i>		
Females given diets containing 2, 60, 380, or 780 mg Pb/kg ration after giving birth to litters. Lead residues in whole young voles were determined for up to age 20 days	At day 20, whole body residues, in mg Pb/kg DW, were 13 in controls, 32 in the 60 mg/kg group 124 in the 380 mg/kg group, and 293 in the 780 mg/kg group. Growth rate was reduced in the 380 and 780 mg/kg groups and survival reduced in the 780 mg/kg group	34

Table 4.8 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Mammals

Species, Dose, and Other Variables	Effects	Ref.^a
Horse, <i>Equus caballus</i>		
Tissue lead levels, in mg/kg fresh weight, of 0.39 in blood, 18 in liver, and 16 in kidney	Signs of clinical lead toxicosis observed	1
Ate forage containing 1.7 mg Pb/kg	Fatal in several months	1
Consumed 2.4 mg Pb/kg BW daily	Lethal	4
Fed 6.25 mg Pb/kg BW daily for 105 days, as lead acetate	No deaths; blood lead levels of 350–380 µg/L at day 105	6
Fed hay collected near Idaho smelter containing 423 mg Pb/kg, equivalent to about 4 mg Pb/kg BW daily	All dead in 84–100 days. Total ingested ranged from 136–154 grams	11
Fed 9.8 mg Pb/kg BW daily for 105 days, as lead acetate	No deaths; blood lead levels of 530–650 µg/L at day 105	6
Fed noncontaminated hay plus 10 mg Pg/kg BW daily, as lead acetate	All dead in 113 to 304 days. Total ingested ranged from 190–544 grams	11
Total dose of 500 to 700 grams	Toxic	6
Cat, <i>Felis domesticus</i>		
Fed pine voles (<i>Pitymys pinetorum</i>) from orchard sprayed with lead arsenate. Concentrations (mg Pb/kg dry weight) were 60.3 in whole voles, 5.7 in cat diet containing voles, and 3.2 in control cat diet	After 86 days, tissue residues elevated in cat kidney (1.3 mg Pb/kg dry weight vs. 0.2 for controls), liver (0.5 vs. 0.1), and bone (5.0 vs. 0.9)	12
Rabbit, <i>Lepus sp.</i>		
Given 0.9, 0.03, 0.06, 0.15, 0.3, or 3 mg Pb/kg BW for 6 days	Blood levels (µg Pb/L) increased from 170 (control) to 910 (0.03), 530 (0.06), 1430 (0.15), 1930 (0.3), and 5160 (3.0)	13
Exposed to 2.46 µg Pb/m ³ air for life >5 µg Pg/kg BW daily	No effect Reduced blood ALAD activity	13 13
Mouse, <i>Mus sp.</i>		
0.05 to 0.1 mg Pb/kg BW daily	Irreversible inhibition of ALAD activity in bone marrow and red blood cells	14
Tissue concentrations of 0.78 mg/kg femur bone marrow, 3.7 mg/L blood, 15.8 mg/kg brain, or 43 mg/kg liver	Inhibition of ALAD activity 50% within 10 min	14
1.5 mg Pb/kg BW daily, as tetraethyllead chloride	Reduction in success of implanted ova	8
2.2 mg/kg BW or 3 mg/kg BW daily, as tetraethyllead	Frequency of pregnancy reduced when dose given 3 to 5 days after mating	8
Pregnant females given single intrauterine injection of 20 mg Pb/kg BW on day 8 of gestation	Smaller litters, increased fetal deaths	15
800 mg Pb/L, as lead acetate, in drinking water for 11 weeks	Decrease in litter size, decreased survival of pups, and decreased birth weight	16
1000 mg Pb/L in drinking water for 9 months	No effect on survival or fertility	4
Sheep, <i>Ovis aries</i>		
Lambs fed 50 µg Pb/kg daily (about 3 mg)	Tissue accumulations	5
Lambs exposed to low levels (350 µg Pb/L blood) <i>in utero</i>	Impaired visual discrimination and learning behavior	17
1.0 mg Pb/kg BW daily, as lead acetate, for 3 months	Of 10 ewes, 3 aborted, 6 delivered normally, and 1 died; placental transfer of lead established	5
Pregnant ewes given 3 mg Pb/kg BW daily	No effect	4
4.2 mg Pb/kg BW in diet for 4 weeks before gestation, and throughout gestation and lactation	Lambs showed impaired learning	18
Fed 5 mg Pb/kg BW first 45 days of pregnancy	Bore normal full-term lambs	9
Given 5 mg Pb/kg BW daily for one year	No adverse effects	5
Pregnant ewes given 5.7 mg Pb/kg BW daily	Fatal	4

Table 4.8 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Mammals

Species, Dose, and Other Variables	Effects	Ref.^a
Nonpregnant ewes given 6 mg Pb/kg BW daily 8 mg Pb/kg BW daily for 220 days	Toxic threshold Mortality	4 5
Fed 9 mg Pb/kg BW throughout pregnancy	Aborted and died	9
Fed diet containing 138 mg/kg DW for 124 days	Elevated residues in bone (22 mg/kg vs. 2.6 in controls) and kidney (8.3 vs. 1.0)	4
Lambs fed diets containing 400 mg Pb/kg, but deficient in calcium and sulfate	Dead within 5 weeks	4
Lambs fed diets containing 400 mg Pb/kg, diet adequate in minerals	Some weight loss in 10 months, but normal otherwise	4
Single oral dose of 600 mg Pb/kg BW	Fatal	9
Total dose of 20–25 grams	Toxic	6
Primates, various species		
Cynomolgus monkey, <i>Macaca iris</i>		
Intramuscular injection of 1.0 mg Pb/kg BW daily during pregnancy or lactation	Fetus exposed to lead via placenta or maternal milk	19
1.5 mg Pb/L in drinking water as lead acetate, for 9 months (equivalent to 0.5 mg Pb/kg BW daily), or 6 mg/L (2 mg/kg BW), or 15 mg/L (5 mg/kg BW)	Increasing blood lead levels from 3rd month, according to dose; kidney pathology. Effects more severe in those on low calcium diets	20
Intramuscular injection of 5 mg Pb ⁺² /kg BW daily during pregnancy or lactation	Abortions and death in pregnant monkeys; cerebral pathology in newborns	19
Cynomolgus monkey, <i>Macaca fascicularis</i>		
Dosed orally from birth to age 200 days with 100 µg lead (as Pb acetate)/kg BW, 5 times weekly, milk substitute diet	Blood level of 254 µg Pb/L; declined to 131 µg/L over next 100–150 days. At age 3 years, impaired ability to perform motor discrimination reversal tasks	21
As above, except dose is 50 µg Pb/kg BW	Blood lead 154 µg/L (vs. 35 µg/L in controls), declining to 109 µg/L at day 150 postadministration. At age 3 years, group showed impaired color discrimination. No overt signs of toxicity, normal blood chemistry (except lead), normal growth and development skills	21
Rhesus monkey, <i>Macaca mulatta</i>		
Infants given 0.5 mg Pg/kg diet for 4 weeks	Hyperactivity, insomnia, abnormal social behavior	18
Adults given 20 mg Pb/L in drinking water for 4 weeks	No effect	18
Baboon, <i>Papio anubis</i>		
Intratracheal injection of Pb carbonate at doses of 50–135 mg Pb/kg BW for 29 to 362 days	73% dead (11/15) with total dose of 1250–7800 mg lead. Before death, some animals lost weight, became increasingly aggressive, had hepatic centrilobular necrosis, were uncoordinated and weak, and had convulsions; the blood had up to 62 mg Pb/L	22
Single injection of 105 mg Pb/kg BW	Blood lead concentrations rose from 117 µg/L at start to 3100 µg/L at day 4 postinjection; blood lead remained >1000 µg/L for at least 24 days	22
Laboratory white rat, <i>Rattus spp.</i>		
Exposed to 10 µg Pb/m ³ air for one year	Elevated tissue residues in blood, soft tissues, and bone	13
Exposed to 21.5 µg Pb/m ³ air for one year	Blood lead increased, but stabilized after 4 months; lead levels remained elevated in bone, kidney, and liver after 6 months	13
1.5 mg Pb/L in drinking water for several days	Disturbed sleep patterns	18
Weanling females given 0.0, 0.5, 5, 25, 50, or 250 mg lead (as Pb acetate)/L drinking water for 6 to 7 weeks, then mated and exposed continuously through gestation and lactation	At 25 mg/L and higher, growth retardation and delayed vaginal opening observed; some maternal deaths occurred and were associated with blood lead concentrations	23

Table 4.8 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Mammals

Species, Dose, and Other Variables	Effects	Ref.^a
Single intravenous injection (mg Pb/kg BW in parentheses)	>200 µg/L. Some pup malformations and deaths in all groups. The 5 mg/L group had elevated blood lead levels	
Tetramethyllead (80)	LD50	24
Tetraethyllead (10)	LD50	24
Trimethyllead (20 to 25)	LD50	24
Triethyllead (8)	LD50	24
Single oral dose (mg Pb/kg BW)		
Tetramethyllead (108)	LD50	24
Tetraethyllead (12)	LD50	24
Single intraperitoneal injection (mg Pb/kg BW)		
Tetramethyllead (70–100)	LD50	24
Tetraethyllead (10)	LD50	24
Trimethyllead (17)	LD50	24
Triethyllead (5)	LD50	24
5 mg Pb/L drinking water, lifetime exposure	Lowered survival and reduced longevity	4
Single intraperitoneal injection of 7 mg Pb/kg BW, as tetraethyllead	Depressed food intake, hyperactivity	25
Mature males given weekly intraperitoneal injections of 20 or 50 mg Pb/kg BW as lead acetate for 6 weeks vs. 20 or 50 mg sodium acetate/kg BW as controls	Dose-dependent increases in blood and sperm lead concentrations. Serum testosterone levels reduced in lead-exposed rats, possibly from generation of reactive oxygen species, and resulting in premature acrosome reaction and reduced sperm oocyte-penetrating capability	39
Male weanlings exposed to age 50 days to drinking water with 25 mg Pb/L, as lead acetate	At day 86: behavioral deficits; blood concentrations of 150–200 µg Pb/L; brain lead levels (µg/kg) 70 in treated group vs. 28 in controls	26
25 mg Pb/kg diet for 3 weeks	Increased locomotor activity	18
21-day-old rats exposed to 50, 100, or 500 mg Pb/L drinking water, as Pb acetate, for 335 days	Impaired behavior during first 4 months at 50 mg/L, but not thereafter. At 100 mg Pb/L and higher, behavior was impaired for at least 100 days postadministration. Brain and blood lead levels reflected exposure concentration and duration	27
Neonatal rats given 50 mg Pb/kg BW intragastrically as lead acetate, on days 6–18 postpartum	Impaired transfer of maze learning acquired during food deprivation	28
100 mg/kg BW daily, as lead nitrate	Some deaths of progeny in 3 weeks	8
Lead acetate in drinking water at 100 and 300 mg Pb/L from age 21 to 55 days	Impaired motor skills	29
Lead acetate in drinking water of pregnant females at 150 to 500 mg Pb/L from gestational day 5 until pups were weaned. Pups continued to be exposed to lead acetate in drinking water until killed between age 21 and 85 days	Dose-response decrease in birth weight and length in all lead-exposed litters. Pups had dose-dependent delay in sexual maturity (male prostate weight, female vaginal opening). Decrease in neonatal sex steroid levels and suppression of plasma testosterone levels in males and estradiol in females during puberty	36,37
200 mg/kg BW daily	50% of progeny dead in 3 weeks	8
500 mg Pb/L, as lead acetate, in drinking water ad libitum from (a) gestational day 5 through birth, (b) during pregnancy and lactation, (c) during lactation only, (d) from birth through adulthood, or (e) from gestational day 5 through adulthood	Significant adverse effects included: delayed vaginal opening and disrupted estrus cycling in female pups from groups (d) and (e); decreased birth weights in groups (a) and (b); lowered testosterone levels in male pups from (e); decreased body weight in all lead-treated groups up to weaning; reduced growth rates in group (c); males had reduced growth rates in groups (b), (d), and (e)	38

Table 4.8 (continued) Lethal and Sublethal Effects of Lead to Selected Species of Mammals

Species, Dose, and Other Variables	Effects	Ref.^a
4000 mg Pb/L in drinking water for 130 days	Serum testosterone levels depressed, Leydig cell lesions; no effect at lower concentration tested (2000 mg/L)	30
Nursing rats given diets containing zero, 2000, 4000, or 10,000 mg Pb/kg as metallic lead powder	Lead-treated rats showed dose-related response to noise stimuli. Blood levels (µg/L) in pups were 40 for controls, 250 for the 2000 mg/kg group, 360 for the 4000 mg/kg group, and 550 for the 10,000 mg/kg group	31
Cotton rat, <i>Sigmodon hispidus</i>		
Exposed to 0, 10, 100, or 1000 mg Pb/L in drinking water, as lead acetate, for 7 or 13 weeks	Altered immune function in high-dose group; spleen mass reduced in the 100 mg/kg group. All treated groups had altered blood chemistry, adverse effects on reproductive organs, and histopathology. In general, effects were more pronounced at higher doses and longer exposures	35
Swine, <i>Sus sp.</i>		
Oral doses of 64 mg Pb/kg BW, as lead acetate, 6 times weekly for 13 weeks	No deaths, reduced blood ALAD activity, blood lead concentration (a remarkable) 143 mg/L	32
As above, except doses administered intraperitoneally	All died	32
Total dose of 10–25 grams	Toxic	6

^a 1, Osweiler and Van Gelder 1983; 2, Zmudzki et al. 1983; 3, Zmudzki et al. 1984; 4, Demayo et al. 1982; 5, NRCC 1973; 6, Dollahite et al. 1978; 7, Kwatra et al. 1986; 8, Clark 1979; 9, Forbes and Sanderson 1978; 10, Edwards and Beatson 1984; 11, Burrows and Borchard 1982; 12, Gilmartin et al. 1985; 13, Barth et al. 1973; 14, Schlick et al. 1983; 15, Wide 1985; 16, Sharma and Kanwar 1985; 17, USEPA 1980; 18, Nriagu 1978b; 19, Tachon et al. 1983; 20, Colle et al. 1980; 21, Rice 1985; 22, Hopkins 1970; 23, Kimmel et al. 1980; 24, Branica and Konrad 1980; 25, Czech and Hoiium 1984; 26, Cory-Slechta et al. 1985; 27, Cory-Slechta et al. 1983; 28, Massaro et al. 1986; 29, Cory-Slechta et al. 1981; 30, Zirkin et al. 1985; 31, Barrett and Livesey 1985; 32, Lassen and Buck 1979; 33, Cooke et al. 1990b; 34, Zakrsewska 1988; 35, McMurry et al. 1995; 36, Ronis et al. 1998c; 37, Ronis et al. 1998a; 38, Ronis et al. 1998b; 39, Hsu et al. 1998.

4.7 RECOMMENDATIONS

Proposed lead criteria for the protection of natural resources and human health are numerous and disparate (Table 4.9). Some of the criteria do not provide adequate protection. Criteria for aquatic life protection, for example, range from 1.3 to 7.7 µg total waterborne Pb/L (Table 4.9; USEPA 1985); however, within this range, high accumulations and adverse effects on growth and reproduction were recorded among sensitive species. Moreover, certain organolead compounds were lethal to some species of aquatic biota within this range, but no criteria have been formulated yet for this highly toxic group of chemicals. Nor have any criteria been proposed for lead in tissues of aquatic biota connoting elevated or hazardous levels to the organism. It is noteworthy that health effects to man through ingestion of lead-contaminated seafood (and probably other fishery products) are considered negligible (Friberg 1988). Total lead concentrations observed in highly polluted areas in the 1970s were usually about one-tenth those showing effects on marine organisms (Branica and Konrad 1980).

Organolead compounds are more toxic than ionic forms. Since methylation of ionic lead *in vivo* or in stored tissues is possible, and since some liver enzyme systems are capable of converting tetraethyllead to the more toxic triethyllead species, it would appear that the recommended Canadian

permissible concentration limit of 10 mg Pb/kg fresh weight in fishery products should be reevaluated downward (Sirota and Uthe 1977). Downward evaluation has also been recommended for the standard of 2 mg/kg in the U.K., where new guidelines have been recommended for total lead and for tetraalkylead compounds in fishery products (Wong et al. 1981). Increasing use of organolead compounds as wood preservatives, as biocides, and as catalysts in the manufacture of plastics, polyurethanes, and polyvinyl chlorides (Walsh and Tilson 1984) may adversely affect survival, sensory responsiveness, and behavioral reactivity in aquatic organisms (Chau et al. 1980; Maddock and Taylor 1980; Wong et al. 1981; Demayo et al. 1982) and avian wildlife (Bull et al. 1983; Osborn et al. 1983; Forsyth et al. 1985). It seems that additional research is needed on organolead toxicokinetics, with special reference to fishery and wildlife resources.

The evidence implicating ingestion of spent lead shot as a major cause of mortality in waterfowl and other birds is overwhelming. Moreover, forms of inorganic lead — besides lead shot or other ingestible-sized lead objects — are rarely known to produce subclinical signs of lead toxicosis in avian populations. Accordingly, in the advent of the lead shot phaseout in 1986, steel shot nontoxic zones were established for the protection of bald eagles and waterfowl in 44 states. Possession of shotshells containing lead shot by hunters of waterfowl in a steel shot zone became a violation of federal regulations (USFWS 1986, 1986a, 1987). By 1991/1992, all uses of lead shot for hunting waterfowl and coots were eliminated nationwide, including in Alaska. The conversion to a nontoxic shot zone was deferred in some cases until — but not beyond — the 1991/1992 hunting season in states that demonstrated, through monitoring, compliance with the following criteria: minimum of 100 birds sampled; less than 5% of birds examined having one or more lead shot in the gizzard; and less than 5% of the birds collected having >2 mg Pb/kg fresh weight in liver, or with >0.2 mg Pb/L in blood, or with blood protoporphyrin concentrations >0.4 mg/L. In addition, the occurrence of three or more individual specimens confirmed as lead-poisoned during the monitoring year disqualified the area for deferral (USFWS 1986, 1986a, 1987). States may elect to forego monitoring and convert to nontoxic shot zones on a countywide or statewide scheduled or accelerated basis (USFWS 1986, 1987). Steel shot is the only shot currently approved by the U.S. Fish and Wildlife Service as nontoxic (Sanderson et al. 1992). Alternatives to steel shot are under investigation and include bismuth/tin, tungsten/tin, and tungsten/polymer shot (Sanderson et al. 1992; Scheuhammer and Dickson 1996). Despite the ban on lead shot in the state of Washington since 1986, mortality of swans from lead poisoning continues to occur as a result of ingestion of previously deposited lead pellets. More aggressive enforcement of steel shot regulations in Washington may help reduce or eliminate the illegal use of lead shot. This, and continued settling of lead shot deeper into bottom sediments should eventually result in reduced lead poisoning mortality of swans from ingestion of lead shot (Lagerquist et al. 1994).

In addition to the United States, the use of lead shot is now banned — sometimes voluntarily, sometimes by legislation — locally or nationally in hunting waterfowl in Australia, Canada, Italy, Mexico, Denmark, Finland, the Netherlands, Norway, Sweden, Switzerland, Germany, Japan, and the United Kingdom (Lumeij et al. 1989; Lumeij and Scholten 1989; Langelier 1991; Thomas and Owen 1995; Tirelli et al. 1996; Mateo et al. 1997; Pain et al. 1997). In 1995, the British Department of the Environment recommended that lead-free shot be used when shooting over or within 300 m of a wetland if there is a possibility that the shot would be deposited in it (Thomas and Owen 1995). Beginning in 1997, all migratory game bird hunting in Canada required the use of nontoxic shot (Scheuhammer and Dickson 1996). Legislation has been introduced — and signed by 54 countries — to protect African–Eurasian migratory birds by phasing out the use of lead shot for hunting in wetlands by the year 2000 (Pain et al. 1997). To fully protect raptors, upland game birds, and waterfowl, many researchers now recommend a global ban on the use of lead shot in hunting (Langelier 1991; Pain et al. 1993a; Pain and Amiard-Triquet 1993; Thomas and Owen 1995; Mateo et al. 1997) and in trap and skeet shooting (Roscoe et al. 1989). Continued monitoring of lead residues for waterfowl, in addition to gizzard examination for shot, should also include blood and soft tissues as indicators of short-term exposure, and bone as an indicator of longer

exposure; monitoring is recommended until lead shot is no longer widespread in the wetland environment (Havera et al. 1992).

In Louisiana, deep tillage is a management option for reducing the availability of lead shot to foraging waterfowl. Agricultural deep tillage with a vegetable plow can result in the redistribution of artificially seeded lead shot from the top 10 cm of soil to lower strata. In control sites, 92% of the shot was recovered above 10 cm vs. tillage wherein 97% of the shot was recovered below 10 cm and 75% below 20 cm (Peters and Afton 1993). In wetlands areas lacking naturally available grit and with high shot densities in soils and sediments, the provision of grit 2 to 3 mm in diameter is recommended for the reduction of lead ingestion by waterbirds (Pain 1990). Increasing water depth of wetlands during the hunting season to inhibit foraging by waterfowl in lead shot affected areas is proposed by Whitehead and Tscherner (1991). In Spain, it is recommended that hunter-killed large animals that are currently abandoned in the field should be removed or buried, thus removing the main source of metallic lead for raptors and scavengers (Mateo et al. 1997b).

Lead poisoning of swans in England is due mainly to ingestion of discarded lead weights used in angling. The use of lead weights for this purpose has been sharply curtailed through legislation since 1987, and there has been a substantial reduction in lead poisoning in the swans of the Thames River (Sears 1988, 1989; Thomas and Owen 1995). To protect swans, loons, and other large waterfowl in the United States, replacement of lead fishing weights with nontoxic substitutes is recommended.

The level of human exposure in lead-using industries has been reduced considerably in recent years; associated with this observation is the reduction in lead content of gasolines, the removal of lead-based paints for interior household use, and the reduction in lead content of outside paints (Table 4.9; Boggess 1977; Heinze et al. 1998). These actions will undoubtedly prove beneficial in reducing the elevated lead concentrations now observed in communities of flora and fauna along heavily traveled roads, and in providing additional protection to captive zoo animals and others held in enclosures with lead-painted bars and walls. The decreased use of leaded gasoline has resulted in a significant decline in lead concentrations in streams (Smith et al. 1987) and in whole-body burdens of lead in starlings collected nationwide, among which the decline was most pronounced in birds from urban areas (White et al. 1977). Continued nationwide monitoring of lead in fish and wildlife is necessary to determine if this is a continuing downward trend, and also to identify areas of high or potential lead contamination.

Data for lead effects on mammalian wildlife are scarce. Shore (1995) indicates that lead residues in soils could successfully predict lead concentrations in kidneys and livers of wood mice and field voles; however, this could not be demonstrated for shrews. In view of the large interspecies differences in lead responses reported for domestic livestock and laboratory populations of small animals (Table 4.9), more research is needed to determine if lead criteria for these groups are applicable to sensitive species of mammalian wildlife.

One of the more insidious effects documented for lead in warm-blooded organisms is neurobehavioral deficits (including learning impairments) at dose levels producing no overt signs of toxicity, i.e., apparently normal growth and developmental skills, and sometimes, nonelevated blood lead levels (USEPA 1980, 1985; Rice 1985). Behavioral deficits have been reported for young rats when blood lead levels exceeded 0.1 mg/L, in children with blood lead concentrations of 0.4 to 0.5 mg/L (USEPA 1980; Rice 1985), and in birds when lead was administered early in development (Burger and Gochfeld 1985). Behavioral impairment was recorded in 3-year-old monkeys that received 50 or 100 µg Pb/kg BW from birth to age 200 days. Blood lead levels immediately after exposure and at time of testing were 0.15 to 0.25 mg/L (age 200 days), and 0.11 to 0.13 mg/L (age 3 years). This is the first report of behavioral impairment in a primate species at blood lead concentrations that are considered to be well within the bounds of safety for children (Rice 1985). This subject appears to constitute a high-priority research need for wildlife species of concern.

Table 4.9 Proposed Lead Criteria for the Protection of Natural Resources and Human Health

Resource, (units), and Other Variables	Criterion	Reference ^a
CROPS		
Irrigation water (mg/L)		
USA		
Neutral and alkaline soils	<10	1
Acidic soils	<5	1
Chronic use	<5	2, 35
Short-term use	<20	2
Canada		
Continuous use	<5	1
Intermittent use	<10	1
Australia	<5	1
AQUATIC LIFE		
Freshwater (µg total Pb/L)		
USA		
Water hardness, in mg CaCO ₃ /L		
50	1.3 ^b , 34 ^c	3
100	3.2 ^b , 82 ^c	3, 35
200	7.7 ^b , 200 ^c	3
Great Lakes		
Superior	<100	4
Huron	<200	4
Others	<250	4
England	<100	38
The Netherlands		
Maximum in surface waters	<10	34
Adverse effects on fish embryo survival and development	>25 at acidic pH	34
Seawater (µg total Pb/L)		
USA	5.6 ^b , 140 ^c	3, 35
California		
6 month median	<2	35
Daily maximum	<8	35
Instantaneous maximum	<20	35
Water (µg/L)		
Tetraalkyllead	<1	5
Trialkyllead	<100	5
Sewage effluent limits (µg/L)		
California	<4000	4
Industrial discharge limits to surface waters (µg/L)		
Illinois	<100	4
USA	<500	4
Canada	<2000	4
Switzerland	<5000	4
BIRDS		
Birds		
Diet (mg/kg DW ration)	<5	32, 33
Blood, normal (mg/L)	<0.15	33
Mallard, <i>Anas platyrhynchos</i>; liver (mg/kg DW)		
No adverse effects	<5	60
Adverse effects on body condition and body weight	>5	60

Table 4.9 (continued) Proposed Lead Criteria for the Protection of Natural Resources and Human Health

Resource, (units), and Other Variables	Criterion	Reference ^a
<i>Canvasback, Aythya valisineria</i>		
Elevated		
Wingbones, immatures (mg/kg dry weight = DW)	>20	6
Blood (mg/L)	>0.2	7
<i>Lesser snow geese, Chen caerulescens caerulescens</i>		
Adverse effects on heart weight and fat (mg/kg DW)		
Kidney	>30	46
Liver	>30	46
<i>Trumpeter swan, Cygnus buccinator; blood (mg/kg fresh weight = FW)</i>		
No clinical signs	<0.5	37
Subclinical signs: mild depression, weight loss, anemia, and green diarrhea. Good chance of recovery with treatment	0.5–0.99	37
More pronounced clinical signs: as above plus weakness and neurological abnormalities. Fair to good chance of recovery with treatment	1.0–1.99	37
Progressively worse clinical signs; poor to fair chance of recovery with treatment	2.0–3.99	37
Similar to above; prognosis very poor with treatment	>4.0	37
<i>Mute swan, Cygnus olor</i>		
Diagnostic of lead poisoning (mg/kg FW)		
Blood	>3	53
Kidney	>31	53
Liver	>12	53
<i>American kestrel, Falco sparverius</i>		
Nestlings (mg/kg FW)		
Elevated		
Liver	>2	8
Kidney	>6	8
Poisoned		
Liver	>5	8
Kidney	>15	8
<i>Bald eagle, Haliaeetus leucocephalus</i>		
Uncontaminated (mg/kg FW)		
Liver	<2	44
Elevated (mg/kg DW)		
Kidney	>6	9
Kidney	>2–<20	36
Liver	>10	9
Sublethally poisoned (mg/kg FW)		
Blood	>0.2	43
Liver	2–10	44
Adverse effects (mg/kg FW)		
Liver	>8	44
Poisoned (mg/kg FW)		
Blood	>0.6–>0.8	36, 43, 44
Kidney	>5	45
Liver	>10	45

Table 4.9 (continued) Proposed Lead Criteria for the Protection of Natural Resources and Human Health

Resource, (units), and Other Variables	Criterion	Reference ^a
Poisoned (mg/kg DW)		
Kidney	>20	36
<i>Herring gull, Larus argentatus; feather (mg/kg DW)</i>		
Adverse effects in fledglings (delayed parental recognition; impaired thermoregulation, locomotion, and depth perception; lower chick survival)	>4	41
Raptors		
Subclinical effects (mg/kg FW)		
Blood	>0.2	30
Liver, kidney	>2	30
Toxic (mg/kg FW)		
Blood	>1	30
Liver, kidney	>3	30
Lethal (mg/kg FW)		
Blood, liver, kidney	>5	30
Waterfowl		
Safe (mg/kg FW)		
Blood	<0.1-<0.2	29, 49, 51
Liver	<2-<2.3	29, 48, 51
Elevated (mg/kg FW)		
Liver	>2	10, 29, 39
Blood	>0.2->0.5	10, 29, 38, 48
Elevated (mg/kg DW)		
Bone	>10->20	39, 40
Liver	>6	40
Poisoned (mg/kg FW)		
Liver		
Total lead	>2->8	10, 42, 51
Trimethyllead	>0.5	11
Blood	>0.2->0.6	12, 42, 43, 49, 51
Bone	>20	42
Poisoned (mg/kg DW)		
Kidney	>30	46
Liver	10->30	46, 52
Lethal (mg/kg FW)		
Blood	>1	29
Liver	>6.4->15	29, 48
Lethal (mg/kg DW)		
Liver	>10.1	52
Gizzards containing ingested lead shot (percent frequency)		
Further study indicated	>5	50
Lead shot ban in area	>10	50
MAMMALS		
Cattle, Bos spp.		
Poisoned (mg/kg FW)		
Blood	>1	13
Liver	>20	13
Kidney	>40	13
Feces	>35	13

Table 4.9 (continued) Proposed Lead Criteria for the Protection of Natural Resources and Human Health

Resource, (units), and Other Variables	Criterion	Reference ^a
Domestic livestock		
Drinking water (µg/L)		
USA	<100	1, 35
Australia	<250	1
Canada		
Horse	<500	1
Others	<1000	1
Forage (mg/kg FW)		
Horse	<80	14
Cattle	<200	14
Tissue residues		
Unstressed (mg/kg FW)		
Blood	<0.2	15
Liver	<1.1	15
Kidney	<1.2	15
Mammals, various species		
Adverse effects expected		
Daily lead intake (mg/kg body weight)	>20	55
Kidney (mg/kg DW)	>25	54, 55
Liver (mg/kg FW)	>20	58
Liver (mg/kg DW)	>10	54
Mouse, <i>Mus sp.</i>		
Elevated (mg/kg body weight daily)		
Total intake	>0.05	16
Mule deer, <i>Odocoileus hemionus</i>		
Excessive (mg/day)		
Total intake	>3	17
Raccoon, <i>Procyon lotor</i>		
Elevated (mg/kg FW)		
Liver	>10	18
Wildlife		
Blood (mg/kg FW)		
Normal	0.02–0.08	31
Safe	<0.2	31
Poisoned	>0.35, usually >0.6	31
Liver (mg/kg DW)		
Elevated	>10	31
Poisoned	>30	31
Kidney (mg/kg DW)		
Elevated	>25	31
Poisoned	>90	31
HUMAN HEALTH		
Air (µg Pb/m³)		
Safe		
USA	<1.5 (3-month arithmetic mean)	20
Connecticut	<3 ^f	35

Table 4.9 (continued) Proposed Lead Criteria for the Protection of Natural Resources and Human Health

Resource, (units), and Other Variables	Criterion	Reference ^a
Kansas	<0.357 for 1 year	35
Massachusetts		
Annual	<0.07	35
24-h	<0.14	35
Philadelphia, PA		
Annual	<1.5	35
24-h	<2.5	35
Occupational, USA		
Current	<50 ^f	20, 27
Goal	<30 ^f	35
Lead chromate	<50	35
Lead arsenate	<150	35
Metallic lead	<100	35
Proposed, worldwide	<2	28
Hazardous	>2220	26
Blood (μg Pb/L)		
Acceptable (ALAD inhibition, protoporphyrin elevation)	100–300	4, 19, 25, 26
Level of concern		
USA		
Children	>100	35
Adults	>400	35
International	>200	35
Anemia, neurobehavioral effects, some poisoning in children	>400	4, 19, 25, 26
Evidence of exposure	>500	35
Central nervous system deficits, peripheral neuropathy, intellectual deficits	500 to 700	4, 19, 25, 26
Brain structure alterations, encephalopathy	>800	4, 19, 25, 26
Life-threatening	>1000	4, 19, 25, 26
Target	150, maximum 300	4, 19, 25, 26
Drinking water (μg/L)		
USA		
1975	<500	4
1977	<250	4
1980–93	<50	19, 20, 35
Most states	<20	35
Goal	<15	35
South Africa	<500	4
Canada, Australia	<50	1
USSR, Japan	<100	2
India	10–<100	2
International	<50	35, 61
World Health Organization	<100	2
Intake, all sources (mg)		
Daily		
Unacceptable	>2.3	25
Average		
Adult	<0.3	19
Child	<0.21	19
Weekly		
Adults	<3	35
Adult, 70 kg; tolerable	1.75	59
Children	<3	35

Table 4.9 (continued) Proposed Lead Criteria for the Protection of Natural Resources and Human Health

Resource, (units), and Other Variables	Criterion	Reference ^a
Food (mg/kg FW)		
Citrus	<1	20
Dried fish		
England	(<5 DW)	35
World Health Organization	(<8 DW)	35
Raw fruits and vegetables	<7	20
Fishery products		
Canada	<10	21
Denmark		
Fish	<0.3	57
Bivalve molluscs and crustaceans, muscle	<1.0	57
USA	<0.3	22
UK		
Fish	<2 (<14 DW)	5
Shellfish	<5 (<35 DW)	5
Meat, except liver and kidney	<0.3	23, 57
Kidney	Max. 1.0	57
Liver	<0.8–1.0	23, 57
Total diet	<0.3	24, 56
Gasoline (mg/L)		
USA		
Recent	473–658 ^d	27
Proposed	131 ^e	27
UK		
1972	840	4
1978	450	4
1981	400	28
Proposed	150	28
Germany	150	4
Groundwater (µg/L)		
Wisconsin		
Preventive action limit	5	35
Enforcement standard	50	35
House paints		
Product (mg/L)	<600	27
Application (mg/m ³)	<1	35
Urinary lead levels (µg/L)		
Normal	<80	25
Acceptable	80–120	25
Excessive	120–220	25
Dangerous	>200	25

^a 1, Demayo et al. 1982; 2, Abbasi and Soni 1986; 3, USEPA 1985; 4, Harrison and Laxen 1981; 5, Maddock and Taylor 1980; 6, Fleming 1981; 7, Dieter et al. 1976; 8, Hoffman et al. 1985a; 9, Pattee et al. 1981; 10, Friend 1985; 11, Osborn et al. 1983; 12, Birkhead 1983; 13, Kwatra et al. 1986; 14, Edwards and Clay 1977; 15, Osweiler and Van Gelder 1978; 16, Schlick et al. 1983; 17, Harrison and Dyer 1984; 18, Dinters and Nielsen 1978; 19, USEPA 1980; 20, NAS 1980; 21, Sirota and Utche 1977; 22, Schmitt et al. 1984; 23, Bunzl and Kracke 1984; 24, Czarneski 1985; 25, Nriagu 1978b; 26, Barth et al. 1973; 27, USEPA 1979; 28, Barrett and Howells 1984; 29, Pain 1996; 30, Franson 1996; 31, Ma 1996; 32, Scheuhammer 1987a; 33, Scheuhammer 1987b; 34, Stouthart et al. 1994; 35, USPHS 1993; 36, Elliott et al. 1992; 37, Degernes 1991; 38, Sears 1988; 39, Norman et al. 1993; 40, Pain et al. 1992; 41, Burger 1997;

Table 4.9 (continued) Proposed Lead Criteria for the Protection of Natural Resources and Human Health

42, Havera et al. 1992b; **43**, Henny et al. 1991; **44**, Craig et al. 1990; **45**, Langelier 1991; **46**, Gordus 1993; **47**, Okoye 1994; **48**, Blus et al. 1991; **49**, Mauvais and Pinault 1993; **50**, Daury et al. 1994; **51**, Pokras and Chafel 1992; **52**, Aguirre-Alvarez 1989; **53**, O'Halloran et al. 1988; **54**, Hariono et al. 1993; **55**, Ma et al. 1991; **56**, Overmann and Krajicek 1995; **57**, Dietz et al. 1996; **58**, Sill et al. 1996; **59**, Garcia et al. 1998; **60**, Mateo et al. 1998; **61**, Rooney and McLaren 1999.

b Four-day average, not to be exceeded more than once every 3 years.

c One-hour average, not to be exceeded more than once every 3 years.

d Equals 1.8 to 2.5 g/gallon.

e Equals 0.5 g/gallon.

f Average 8-hour period.

g Blood lead levels, usually expressed as µg/deciliter, have been converted to µg/L, for uniformity, in the present work.

4.8 SUMMARY

Lead (Pb) and its compounds have been known to man for about 7000 years, and lead poisoning has been recognized for at least 2500 years. All credible evidence indicates that lead is neither essential nor beneficial to living organisms, and that all measured effects are adverse — including those on survival, growth, reproduction, development, behavior, learning, and metabolism. Various living resources are at increased risk from lead:

- Migratory waterfowl that frequent hunted areas and ingest shot
- Avian predators that eat game wounded by hunters
- Domestic livestock near smelters, refineries, and lead battery recycling plants
- Captive zoo animals and domestic livestock held in enclosures coated with lead-based paints
- Wildlife that forage extensively near heavily traveled roads
- Aquatic life in proximity to mining activities, areas where lead arsenate pesticides are used, metal finishing industries, organolead industries, and areas of lead aerosol fallout
- Crops and invertebrates growing or living in lead-contaminated soils

Adverse effects on aquatic biota reported at waterborne lead concentrations of 1.0 to 5.1 µg/L included reduced survival, impaired reproduction, reduced growth, and high bioconcentration from the medium. Among sensitive species of birds, survival was reduced at doses of 50 to 75 mg Pb⁺²/kg body weight (BW) or 28 mg organolead/kg BW; reproduction was impaired at dietary levels of 50 mg Pb/kg; and signs of poisoning were evident at doses as low as 2.8 mg organolead/kg BW. In general, forms of lead other than shot (or ingestible lead objects), or routes of administration other than ingestion, are unlikely to cause clinical signs of lead poisoning in birds. A notable exception to this generalization is the recent evidence linking waterfowl poisoning with ingestion of lead-contaminated sediments. Data for toxic and sublethal effects of lead on mammalian wildlife are missing. For sensitive species of domestic and laboratory animals, survival was reduced at acute oral lead doses of 5 mg/kg BW (rat), at chronic oral doses of 5 mg/kg BW (dog), and at dietary levels of 1.7 mg/kg BW (horse). Sublethal effects were documented in monkeys exposed to doses as low as 0.1 mg Pb/kg BW daily (impaired learning at 2 years postadministration) or fed diets containing 0.5 mg Pb/kg (abnormal social behavior). Signs of lead exposure were recorded in rabbits given 0.005 mg Pb/kg BW and in mice given 0.05 mg Pb/kg BW. Tissue lead levels were elevated in mice given doses of 0.03 mg Pb/kg BW, and in sheep given 0.05 mg Pb/kg BW. In general, organolead compounds were more toxic than inorganic lead compounds; food chain biomagnification of lead was negligible; and younger organisms were most susceptible. More research seems merited on organolead toxicokinetics (including effects on behavior and learning) and on mammalian wildlife sensitivity to lead and its compounds.

Legislation limiting the content of lead in paints, reducing the lead content in gasoline, and eliminating the use of lead shot nationwide (lead shot phaseout program/schedule started in 1986 and was fully implemented by 1991) in waterfowl hunting areas has substantially reduced environmental burdens of lead and may directly benefit sensitive fishery and wildlife resources. Continued nationwide monitoring of lead in living resources is necessary in order to correlate reduced emission sources with reduced tissue lead concentrations.

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CHAPTER 5

Mercury

5.1 INTRODUCTION

The element mercury (Hg) and its compounds have no known normal metabolic function. Their presence in the cells of living organisms represents contamination from natural and anthropogenic sources. All such contamination must be regarded as undesirable and potentially hazardous (National Academy of Sciences [NAS] 1978). The most important ore of mercury, cinnabar (mercuric sulfide), has been mined continuously since 415 BCE (Clarkson and Marsh 1982). In the period before the industrial revolution, mercury was used extensively in gold extraction and in the manufacture of felt hats and mirrors; in the 1800s, it was used in the chloralkali industry, in the manufacture of electrical instruments, and as a medical antiseptic; and since 1900, it has been used in pharmaceuticals, in agricultural fungicides, in the pulp and paper industry as a slimicide, and in the production of plastics (Clarkson and Marsh 1982). World use of mercury is estimated at 10,000 to 15,000 metric tons annually (Boudou and Ribeyre 1983), of which the United States accounts for about 18% (Clarkson and Marsh 1982).

Long-range atmospheric transport of mercury since 1940 has resulted in elevated mercury loadings in remote Canadian lakes up to 1400 km from the closest industrial centers (Lucotte et al. 1995). Since 1985, annual mercury accumulation rates in flooded Florida Everglades soils averaged 53 µg/m², which is about 4.9 times greater than rates observed around the turn of the century. The increase is attributed to increased global and regional deposition and is similar to increases reported for lakes in Sweden and the northern United States (Rood et al. 1995). In 1967, the Swedish medical board banned the sale of fish that contained high concentrations of organomercury salts, originating from about 40 lakes and rivers (Das et al. 1982). More than 10,000 Swedish lakes are closed to fishing because of excessive mercury loadings (Lindqvist et al. 1991). In 1970, after the discovery of high levels of mercury in fish from Lake St. Clair, Canada, restrictions on fishing and the sale of fish were imposed in many areas of the United States and Canada (Das et al. 1982). Since 1970, a total of 26 of the 48 states in the conterminous United States have reported mercury pollution in their waters as a direct result of human activities. These states have banned sport or commercial fishing in mercury-contaminated waters, or have issued health warnings about the consequences of eating mercury-contaminated fish or seafood from selected water courses, or have placed restrictions on fish consumption from certain streams, lakes, or rivers polluted with mercury (NAS 1978; Becker and Bigham 1995). In 1989, the state of Florida, for example, due to excessive mercury in edible tissues of various species, issued, an advisory prohibiting consumption of predatory fishes, such as largemouth bass (*Micropterus salmoides*), bowfin (*Amia calva*), and gar (*Lepisosteus* spp.) in southern Florida, and the entire Everglades watershed has been closed to hunting of alligators (Kannan et al. 1998). In general, the number of mercury-contaminated fish

and wildlife habitats has progressively increased — almost all as a direct result of anthropogenic activities (Boudou and Ribeyre 1983).

Poisoning of game birds and other wildlife in Sweden, apparently by seeds treated with organomercurials, was noticed in 1960 (Das et al. 1982). Massive kills of the grey heron (*Ardea cinerea*) in the Netherlands during 1976 were attributed to a combination of low temperatures, undernourishment, and high body burdens of mercury (Van der Molen et al. 1982). Mercury contamination has resulted in the closure of pheasant and partridge hunting areas in Alberta, Canada (Mullins et al. 1977). Mercury contamination is the most serious environmental threat to fishery and wildlife resources in the southeastern United States, with fish consumption advisories issued in the 10 states comprising this region (Facemire et al. 1995). Declining numbers of wading birds in southern Florida are attributed to mercury contamination of their food supply (Sundolf et al. 1994). In March 1989, the Florida Department of Health and Rehabilitative Services issued a health advisory recommending limited consumption of largemouth bass (*Micropterus salmoides*) and other species caught from the Everglades region of south Florida due to elevated methylmercury concentrations (2 to 3 mg/kg FW) in fish muscle (Fleming et al. 1995). The entire Everglades watershed was closed to the hunting of alligators due to excessive mercury in edible tissues of alligators (Roelke et al. 1991; Sundolf et al. 1994).

The first cases of fatal mercury poisoning in humans were reported for two men in a European chemical laboratory in 1865 (Das et al. 1982). The first documented human poisoning from an agricultural exposure to methylmercury occurred in 1940 (Das et al. 1982). As summarized by Elhassani (1983), exposure of humans to mercury compounds may result from dermal application (e.g., 1600 infants in Argentina showed symptoms of Hg poisoning after a laundry treated their diapers with a mercury disinfectant), from diet (i.e., ingestion of mercury-contaminated fish, pork, seafoods, or grains), and from contact by respiratory routes (e.g., occupational exposure of mercury fungicide applicators in Nicaragua). Sporadic incidences of human poisonings have occurred in the United States, the former Soviet Union, and Canada; and major epidemics have been reported in Japan, Pakistan, Guatemala, Ghana, Yugoslavia, and Iraq (Clarkson and Marsh 1982; Das et al. 1982; Elhassani 1983; Greener and Kochen 1983). In 1972, for example, there were 6530 hospital admissions within 18 months (459 hospital deaths) among Iraqi farmers who ate bread made from seed wheat treated with a methylmercury fungicide. A water-soluble red dye was washed off the wheat, with the assumption that the mercury would be equally soluble. Before the wheat was consumed by humans, it was fed (without apparent effect) to chickens and other livestock for only a few days; it was not realized that a lengthy latency period was involved (Das et al. 1982; Elhassani 1983). There is no effective antidote to the effects of methylmercury on the central nervous system (Elhassani 1983).

Most authorities on mercury ecotoxicology agree on six points:

- Mercury and its compounds have no known biological function, and its presence in living organisms is undesirable and potentially hazardous
- Forms of mercury with relatively low toxicity can be transformed into forms with very high toxicity through biological and other processes
- Methylmercury can be bioconcentrated in organisms and biomagnified through food chains, returning mercury directly to man and other upper trophic level consumers in concentrated form
- Mercury is a mutagen, teratogen, and carcinogen, and causes embryocidal, cytochemical, and histopathological effects
- High body burdens of mercury normally encountered in some species of fish and wildlife from remote locations emphasize the complexity of natural mercury cycles and human impacts on these cycles
- Anthropogenic use of mercury should be curtailed, because the difference between tolerable natural background levels of mercury and harmful effects in the environment is exceptionally small

These, and other aspects of mercury and its compounds in the environment as a result of anthropogenic or natural processes, have been the subject of many reviews, including those by Montague and Montague (1971), D'Itri (1972), Friberg and Vostal (1972), Jernelov et al. (1972, 1975), Keckes and Miettinen (1972), Buhler (1973), Holden (1973), D'Itri and D'Itri (1977), Eisler (1978, 1981, 1987), National Academy of Sciences [NAS] (1978), Birge et al. (1979), Magos and Webb (1979), Nriagu (1979), U.S. Environmental Protection Agency [USEPA] (1980, 1985), Jenkins (1980), Clarkson and Marsh (1982), Das et al. (1982), Boudou and Ribeyre (1983), Elhassani (1983), Clarkson et al. (1984), Robinson and Touvinen (1984), Wren (1986), Scheuhammer (1987), Lindqvist (1991), Lindqvist et al. (1991), Zillioux et al. (1993), U.S. Public Health Service [USPHS] (1994), Hamasaki et al. (1995), Porcella et al. (1995), Heinz (1996), Thompson (1996), Wiener and Spry (1996), and Wolfe et al. (1998).

5.2 SOURCES OF ENVIRONMENTAL MERCURY

The atmosphere plays an important role in the mobilization of mercury with 25 to 30% of the total atmospheric mercury burden of anthropogenic origin (NAS 1978). The global anthropogenic atmospheric emission of mercury is estimated at 900 to 6200 tons annually, of which the United States contributed 300 metric tons in 1990 with 31% from combustion of fossil fuels by power plants (Chu and Porcella 1995). Atmospheric deposition is generally acknowledged as the major source of mercury for watersheds. In northern Minnesota watersheds, for example, atmospheric deposition was the primary source of mercury, and geologic and point source contributions were not significant. Transport from soils and organic materials may also be important, but the mercury from these sources probably originates from precipitation and direct atmospheric sorption by watershed components (Swain and Helwig 1989; Sorensen et al. 1990). In Sweden, increased mercury concentrations in lakes are attributed to increased atmospheric emissions and deposition of mercury, and to acid rain (Hakanson et al. 1990). Airborne particulates may contribute to the high mercury levels found in some marine dolphins and whales (Rawson et al. 1995). A total of 60 to 80 metric tons of mercury is deposited from the atmosphere into the Arctic each year, the main sources of which are Eurasia and North America from combustion of fossil fuels to produce electricity and heat (Pacyna and Keeler 1995). However, elevated mercury concentrations in fish muscle (0.5 to 2.5 mg/kg FW) from remote Arctic lakes over extended periods (1975 to 1993) are sometimes due to natural sources of mercury (Stephens 1995). Atmospheric deposition of mercury into the Great Lakes from sources as much as 2500 km distant are documented at annual deposition rates of 15 µg Hg/m² (Glass et al. 1991). In south Florida, 80 to 90% of the annual mercury deposition occurs during the summer wet season (Guentzel et al. 1995). Dry deposition processes are important for the flux of inorganic mercury and methylmercury to Swedish forested ecosystems; for methylmercury, the most important deposition route is from the air to a relatively stable form in litter (Munthe et al. 1995).

In the Florida Everglades, 61% of the mercury is due to atmospheric deposition from anthropogenic sources, especially municipal solid waste combustion facilities (15%), medical waste incinerators (14%), paint manufacturing and application (11%), electric utility industries (11%) and private residences (2%) through combustion of fossil fuels, and electrical apparatus including fluorescent, metal halide, and mercury vapor lights (6%). All other anthropogenic sources combined — including sugarcane processing, the dental industry, open burning, and sewage sludge disposal — account for about 3% of the total mercury emitted to the environment. Virtually all of the mercury in the Florida Everglades from natural sources (39%) is attributed to release from the soil through natural processes, including microbial transformations of inorganic and organic mercury to methylmercury (Sundolf et al. 1994).

As a direct result of human activities, mercury levels in river sediments have increased fourfold since precultural times, and twofold to fivefold in sediment cores from lakes and estuaries (Das et al. 1982). Analysis of sediment cores of North American mid-continental lakes show that mercury deposition rates have increased by a factor of 3.7 since 1850 at a rate of about 2% annually (Rolphus and Fitzgerald 1995). During the past 100 years, more than 500,000 metric tons of mercury entered the atmosphere, hydrosphere, and surface soils, with eventual deposition in subsurface soils and sediments (Das et al. 1982). Several activities that contribute significantly to the global input of mercury include the combustion of fossil fuels; mining and reprocessing of gold, copper, and lead; operation of chloralkali plants; runoff from abandoned cinnabar mines; wastes from nuclear reactors, pharmaceutical plants, and military ordnance facilities; incineration of municipal solid wastes and medical wastes; and disposal of batteries and fluorescent lamps (NAS 1978; Das et al. 1982; Gonzalez 1991; Lodenius 1991; Facemire et al. 1995; Gustafsson 1995). In one case, more than 5.5 million kg of metallic mercury was released into the Carson River Drainage Basin in Nevada during historic mining operations (now closed) in which mercury was used to amalgamate gold and silver ore (Gustin et al. 1995). Mercury concentrations in sample tailings were as high as 1570 mg/kg. The air directly over the site contained 1.0 to 7.1 ng Hg/m³, and was as high as 240 ng/m³ in October 1993. The estimated range of mercury flux to the atmosphere from the site was 37 to 500 ng/m² hourly (Gustin et al. 1995).

Mercury contamination of more than 500,000 miners, adjacent Indian populations, and numerous populations of fish and wildlife is one consequence of the gold rush that took place in the early 1980s in the Amazon region of Brazil. Metallic mercury was used to agglutinate the fine gold particles through amalgamation. During this process, large amounts of mercury were lost to the river and soil; additional mercury was lost as vapor to the atmosphere during combustion of the amalgamated gold to release the gold (Barbossa et al. 1995). Elemental mercury used in seals of three trickling filters in municipal wastewater treatment plants — each seal contained several hundred kg of mercury — leaked repeatedly, discharging 157 grams of mercury and 0.4 grams of methylmercury daily; the use of mercury seals for this purpose should be discontinued (Gilmour and Bloom 1995). Also discontinued in 1967 by Finland was the use of phenyl mercury compounds as slimicides in the pulp industry (Lodenius 1991).

Major producers of mercury include the former Soviet Union, Spain, Yugoslavia, and Italy (USPHS 1994). In the United States, mercury consumption rose from 1305 metric tons in 1959 to 2359 tons in 1969 ([Table 5.1](#)). The major use of mercury has been as a cathode in the electrolytic

Table 5.1 Industrial and Other Uses of Mercury in the United States in 1959 and in 1969 (All values are in metric tons)

Use	1959		1969	
	Tons	Percent	Tons	Percent
Chloralkali process	201	15.5	716	30.4
Electrical apparatus	308	23.6	644	27.3
Antifouling and mildew paints	121	9.3	336	14.2
Control devices	213	16.3	241	10.2
Dental preparations	63	4.8	105	4.5
Catalysts	33	2.5	102	4.3
Agriculture	110	8.4	93	3.9
Laboratory	38	2.9	71	3.0
Pharmaceuticals	59	4.5	25	1.1
Pulp and paper mill	150	11.5	19	0.8
Metal amalgamation	9	0.7	7	0.3
Total	1305		2359	

Modified from Montague, K. and P. Montague. 1971. *Mercury*. Sierra Club, NY. 158 pp.

preparation of chlorine and caustic alkali (Nriagu 1979). In 1968 this use accounted for about 33% of the total U.S. demand for mercury (USEPA 1980). In regard to mercury consumption in the United States, electrical apparatus accounted for about 27%; industrial and control instruments, such as switches, thermometers, and barometers, and general laboratory appliances, 14%; antifouling and mildew-proofing paints, 12%; mercury formulations to control fungal diseases of seeds, bulbs, and vegetables, 5%; and dental amalgams, pulp and paper manufacturers, pharmaceuticals, metallurgy and mining, and catalysts, 9% (USEPA 1980). Mercury, however, is no longer registered for use in antifouling paints, nor for the control of fungal diseases of bulbs (USEPA 1980). Accurate data on recent mercury consumption in the United States were difficult to obtain. In 1987, the United States imported 636 metric tons; this fell to 329 tons in 1988, and 131 tons in 1989 (USPHS 1994). Domestic production of mercury produced as a by-product was 207 metric tons in 1990, 180 tons in 1991, and 160 tons in 1992; during this same period we imported 15 tons in 1990, 56 tons in 1991, and 100 tons in 1992 (USPHS 1994).

Mercury from natural sources enters the biosphere directly as a gas, in lava (from terrestrial and oceanic volcanic activity), in solution, or in particulate form. Cinnabar (HgS), for example, is a common mineral in hot spring deposits and a major natural source of mercury (Das et al. 1982). The global cycle of mercury involves degassing of the element from the earth's crust and evaporation from natural bodies of water, atmospheric transport (mainly in the form of mercury vapor), and deposition of mercury back onto land and water. Oceanic effluxes of mercury are tied to equatorial upwelling and phytoplankton activity and may significantly affect the global cycling of this metal. If volatilization of mercury is proportional to primary production in the world's oceans, oceanic phytoplankton activity represents about 36% of the yearly mercury flow to the atmosphere, or about 2400 tons per year (Kim and Fitzgerald 1986). Mercury finds its way into sediments, particularly oceanic sediments, where the retention time can be lengthy (Table 5.2), and where it may continue to contaminate aquatic organisms (Lindsay and Dimmick 1983). Estimates of the quantities of mercury entering the atmosphere from degassing of the surface of the planet vary widely, but a commonly quoted figure is 30,000 tons annually (Clarkson et al. 1984). In aquatic ecosystems, removal of the source of anthropogenic mercury results in a slow decrease in the mercury content of sediments and biota (NAS 1978). The rate of loss depends, in part, on the initial degree of contamination, the chemical form of mercury, physical and chemical conditions of the system, and the hydraulic turnover time (NAS 1978).

Terrestrial plants function as conduits for the transport of elemental mercury from the geosphere to the atmosphere (Leonard et al. 1998a). Estimated mercury emissions from plants in the Carson River Drainage Basin of Nevada over the growing season (0.5 mg Hg/m^2) add to the soil mercury

Table 5.2 Amount of Mercury in Some Global Reservoirs and Residence Time

Reservoir	Hg Content (metric tons)	Residence Time
Atmosphere	850	6 to 90 days
Soils	21,000,000	1000 years
Freshwater	200	—
Freshwater biota (living)	4	—
Ocean water	4,150,000,000	2000 years
Oceanic biota (living)	3	—
Ocean sediments	330,000,000,000	>1 million years

Data from National Academy of Sciences (NAS). 1978. *An Assessment of Mercury in the Environment*. Natl. Acad. Sci., Washington, D.C. 185 pp. Clarkson, T.W., R. Hamada, and L. Amin-Zaki. 1984. Mercury. Pages 285-309 in J.O. Nriagu (ed.). *Changing Metal Cycles and Human Health*. Springer-Verlag, Berlin.

emissions (8.5 mg Hg/m²) for a total landscape emission in that area of 9 mg Hg/m². In one species (tall whitetop, *Lepidium latifolium*), as much as 70% of the mercury taken up by the roots during the growing season was emitted to the atmosphere (Leonard et al. 1998a). Factors known to increase the flux of elemental mercury from terrestrial plants growing in soils with high (34 to 54 mg Hg/kg soil DW) levels of mercury include increasing air temperature in the range 20 to 40°C, increasing irradiance, increasing soil mercury concentrations, and increasing leaf area (Leonard et al. 1998b).

5.3 CHEMICAL AND BIOCHEMICAL PROPERTIES

Mercury, a silver-white metal that is liquid at room temperature and is highly volatile, can exist in three oxidation states: elemental mercury (Hg⁰), mercurous ion (Hg₂²⁺), and mercuric ion (Hg²⁺). It can be part of both inorganic and organic compounds (USEPA 1980; Clarkson et al. 1984; Table 5.3). All mercury compounds interfere with thiol metabolism, causing inhibition or inactivation of proteins containing thiol ligands and ultimately leading to mitotic disturbances (Das et al. 1982; Elhassani 1983). The mercuric species is the most toxic inorganic chemical form, but all three forms of inorganic mercury may have a common molecular mechanism of damage in which Hg²⁺ is the toxic species (Clarkson and Marsh 1982; Figure 5.1).

Chemical speciation is probably the most important variable influencing ecotoxicology of mercury, but mercury speciation is difficult, especially in natural environments (Boudou and Ribeyre 1983). Mercury compounds in an aqueous solution are chemically complex. Depending on pH, alkalinity, redox, and other variables, a wide variety of chemical species can be formed, each having different electrical charges and solubilities. For example, HgCl₂ in solution can speciate into Hg(OH)₂, Hg²⁺, HgCl⁺, Hg(OH)⁻, HgCl₃⁻, and HgCl₄²⁻; anionic forms predominate in saline environments (Boudou and Ribeyre 1983). In the aquatic environment, under naturally occurring conditions of pH and temperature, mercury may also become methylated by biological or chemical processes, or both (Beijer and Jernelov 1979; USEPA 1980; Ramamoorthy and Blumhagen 1984; Zillioux et al. 1993; Figure 5.1), although abiological methylation is limited (Callister and Winfrey 1986). Methylmercury is the most hazardous mercury species due to its high stability, its lipid solubility, and its possession of ionic properties that lead to a high ability to penetrate membranes in living organisms (Beijer and Jernelov 1979; Hamasaki et al. 1995). In general, essentially all mercury in freshwater fish tissues is in the form of methylmercury; however, methylmercury accounts for less than 1% of the total mercury pool in a lake (Regnell 1990).

Table 5.3 Some Properties of Mercury and Its Compounds^a

Property	Elemental Mercury	Mercurous Chloride	Mercuric Chloride	Methylmercury Chloride
Empirical formula	Hg	Hg ₂ Cl ₂	HgCl ₂	CH ₃ HgCl
Molecular weight	200.59	472.09	271.52	251.09 ^c
Chlorine, %	0	15.02	26.12	14.12 ^c
Mercury, %	100	84.98	73.88	79.89 ^c
Melting point, °C	-38.87	sublimes at 400–500	277	170 ^c
Density	13.534	7.15	5.4	4.063 ^c
Solubility, mg/L (ppm)				
In water	0.056	2.0	74,070	1016 ^d
In benzene	2.387 ^b	insol.	5000	6535 ^e

^a All data from *Merck Index* (1976), except where indicated.

^b Spencer and Voigt (1968).

^c Weast and Astle (1982).

^d Eisler (unpubl.), 72 h equilibrium value.

^e Eisler (unpubl.), 24 h equilibrium value.

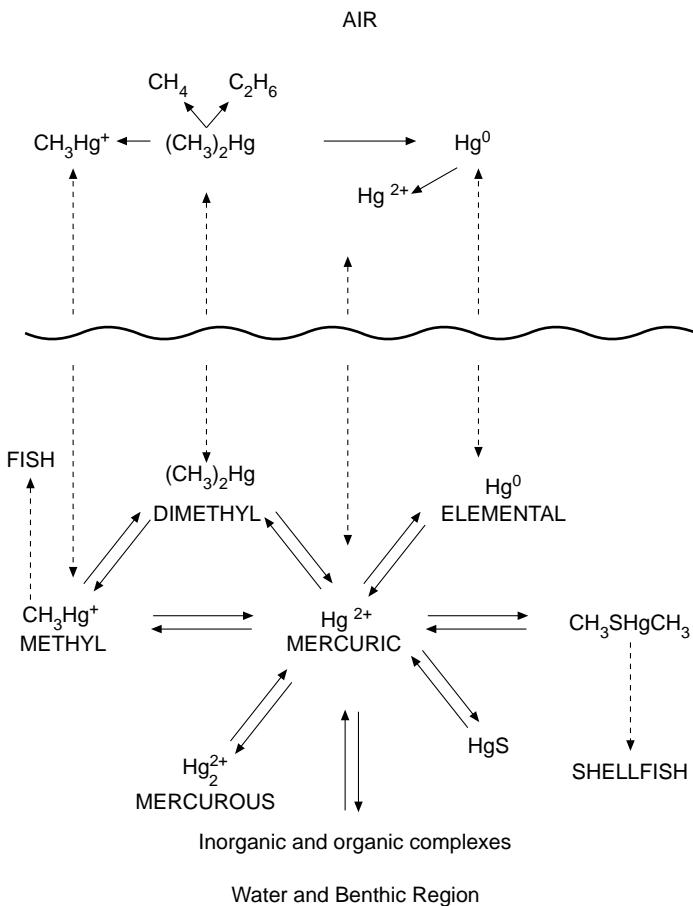


Figure 5.1 Major transformations of mercury in the environment. (Modified from Beijer, K. and A. Jernelov. 1979. Methylolation of mercury in natural waters. Pages 201-210 in J. O. Nriagu (ed.). *The Biogeochemistry of Mercury in the Environment*. Elsevier/North-Holland Biomedical Press, NY).

All mercury discharged into rivers, bays, or estuaries as elemental (metallic) mercury, inorganic divalent mercury, phenylmercury, or alkoxyalkyl mercury can be converted into methylmercury compounds by natural processes (Jernelov 1969). The mercury methylation in ecosystems depends on mercury loadings, microbial activity, nutrient content, pH and redox condition, suspended sediment load, sedimentation rates, and other variables (NAS 1978; Compeau and Bartha 1984; Berman and Bartha 1986; Callister and Winfrey 1986; Jackson 1986). Net methylmercury production was about 10 times higher in reduced sediments than in oxidized sediments (Regnell 1990). The finding that certain microorganisms are able to convert inorganic and organic forms of mercury into the highly toxic methylmercury or dimethylmercury has made it clear that any form of mercury is highly hazardous to the environment (USEPA 1980, 1985). The synthesis of methylmercury by bacteria from inorganic mercury compounds present in the water or in the sediments is the major source of this molecule in aquatic environments (Boudou and Ribeyre 1983). This process can occur under both aerobic and anaerobic conditions (Beijer and Jernelov 1979; Clarkson et al. 1984), but seems to favor anaerobic conditions (Olson and Cooper 1976; Callister and Winfrey 1986). Transformation of inorganic mercury to an organic form by bacteria alters its biochemical reactivity and hence its fate (Windom and Kendall 1979; [Figure 5.1](#)). Methylmercury is decomposed by bacteria in two phases. First, hydrolytic enzymes cleave the C-Hg bond, releasing the methyl group.

Second, a reductase enzyme converts the ionic mercury to the elemental form, which is then free to diffuse from the aquatic environment into the vapor phase. These demethylating microbes appear to be widespread in the environment; they have been isolated from water, sediments, and soils and from the gastrointestinal tract of mammals, including humans (Clarkson et.al. 1984). Some strains of microorganisms contain mercuric reductase, which transforms inorganic mercury to elemental mercury, and organomercurial lyase, which degrades organomercurials to elemental mercury (Baldi et al. 1991).

Humic substances can reduce inorganic divalent mercury (Hg^{2+}) to elemental mercury (Hg^0). In aquatic environments, Hg^0 was highest under anoxic conditions, in the absence of chloride, and at pH 4.5 (Allard and Arsenie 1991). Under these conditions, about 25% of 400 μg Hg^{2+}/L was reduced to Hg^0 in 50 h. Production of Hg^0 was reduced in the presence of europium ions and by methylated carboxyl groups in the humic substances (Allard and Arsenie 1991). Mercury is efficiently transferred through wetlands and forests in a more reactive form relative to other land-use patterns, resulting in an increased uptake by organisms inhabiting these rivers or downstream impoundments and drainage lakes (Hurley et al. 1995). The behavior and accumulation of mercury in forest soils of Guyana, South America, is related to the penetration of humic substances and the progressive adsorption onto iron oxy-hydroxides in the mineral horizons; flooding of these soils may lead to a release of 20% of the mercury initially present (Roulet and Lucotte 1995).

Methylmercury is produced by methylation of inorganic mercury present in both freshwater and saltwater sediments, and it accumulates in aquatic food chains in which the top-level predators usually contain the highest concentrations (Clarkson and Marsh 1982). The percent of total mercury accounted for by methylmercury generally increases with higher trophic levels, confirming that methylmercury is more efficiently transferred to higher trophic levels than inorganic mercury compounds (Becker and Bigham 1995). Organomercury compounds other than methylmercury decompose rapidly in the environment and behave much like inorganic mercury compounds (Beijer and Jernelov 1979). In organisms near the top of the food chain, such as carnivorous fishes, almost all mercury accumulated is in the methylated form, primarily as a result of the consumption of prey containing methylmercury; methylation also occurs at the organism level by way of mucus, intestinal bacteria, and enzymatic processes, but these pathways are not as important as diet (Huckabee et al. 1979; Boudou and Ribeyre 1983). In tissues of marine flounders, inorganic mercury compounds are strongly bound to metallothioneins and high-molecular-weight ligands; however, methylmercury has a low affinity for metallothioneins and is strongly lipophilic (Bargigiani et al. 1989).

The biological cycle of mercury is delicately balanced, and small changes in input rates, geophysical conditions, and the chemical form of mercury may result in increased methylation rates in sensitive systems (NAS 1978). For example, the acidification of natural bodies of freshwater is statistically associated with elevated concentrations of methylmercury in the edible tissues of predatory fishes (Clarkson et al. 1984). Acidification has a stronger effect on the supply of methylmercury to the ecosystem than on specific rates of uptake by the biota (Bloom et al. 1991). In chemically sensitive waterways, such as poorly buffered lakes, the combined effects of acid precipitation and increased emissions of mercury to the atmosphere (with subsequent deposition) pose a serious threat to the biota if optimal biomethylation conditions are met (NAS 1978). In remote lakes of the Adirondack mountain region in upstate New York, fish contain elevated mercury concentrations in muscle; mercury loadings in fish were directly associated with decreasing water column pH and increasing concentrations of dissolved organic carbon (DOC), although high DOC concentrations may complex methylmercury, diminishing its bioavailability (Driscoll et al. 1995). At high concentrations of monomeric aluminum, the complexation of methylmercury with DOC decreases, enhancing the bioavailability of methylmercury (Driscoll et al. 1995).

Mercury binds strongly with sulphydryl groups and has many potential target sites during embryogenesis. Phenylmercury and methylmercury compounds are among the strongest known inhibitors of cell division (Birge et al. 1979). In mammalian hepatocytes, the L-alanine carrier

contains a sulphydryl group that is essential for its activity and is inhibited by mercurials (Sellinger et al. 1991). In the little skate (*Raja erinacea*), HgCl_2 inhibits Na^+ -dependent alanine uptake and Na^+/K^+ -ATPase activity, and increases K^+ permeability. Inhibition of Na^+ -dependent alanine in skate hepatocytes by HgCl_2 is attributed to three different concentration-dependent mechanisms: (1) direct interaction with the transporters; (2) dissipation of the Na^+ gradient; and (3) loss of membrane integrity (Sellinger et al. 1991). Organomercury compounds, especially methylmercury, cross placental barriers and can enter mammals by way of the respiratory tract, gastrointestinal tract, skin, or mucus membranes (Elhassani 1983). When compared with inorganic mercury compounds, organomercurials are more completely absorbed, are more soluble in organic solvents and lipids, pass more readily through biological membranes, and are slower to be excreted (Clarkson and Marsh 1982; Elhassani 1983; Greener and Kochen 1983). Biological membranes, including those at the blood-brain interface and placenta, tend to discriminate against ionic and inorganic mercury but allow relatively easy passage of methylmercury and dissolved mercury vapor (Greener and Kochen 1983). As judged by membrane model studies, it appears that electrically neutral mercurials are responsible for most of the diffusion transport of mercury, although this movement is modified significantly by pH and mercury speciation. It seems, however, that the liposolubility of methylmercury is not the entire reason for its toxicity and does not play a major role in its transport. This hypothesis needs to be examined further in studies with living membranes (Boudou et al. 1983).

Mercury point sources and rates of particle scavenging are key factors in atmospheric transport rates to sites of methylation and subsequent entry into the marine food chain (Rolphus and Fitzgerald 1995). Airborne soot particles transport mercury into the marine environment either as nuclei for raindrop formation or by direct deposition on water (Rawson et al. 1995). In early 1990, both dimethylmercury and monomethylmercury were found in the subthermocline waters of the equatorial Pacific Ocean; the formation of these alkylmercury species in the low oxygen zone suggests that Hg^{2+} is the most likely substrate (Mason and Fitzgerald 1991; Figure 5.1).

Mercury-antagonistic and mercury-protectant drugs and compounds now include 2,3-dimercaptopropanol, polythiol resins, selenium salts, thiamin, Vitamin E, metallothionein-like proteins, and sulphydryl agents (Magos and Webb 1979; Elhassani 1983; Siegel et al. 1991; USPHS 1994; Caurent et al. 1996). Thiols ($\text{R}-\text{SH}$), which compete with mercury for protein binding sites, are the most important antagonists of inorganic mercury salts and have been used extensively in attempts to counteract mercury poisoning in humans (Das et al. 1982). Thiamin was the most effective of the Group VIB derivatives (which includes sulfur, selenium, and tellurium) in protecting against organomercury poisoning in higher animals (Siegel et al. 1991). The protective action of selenium (Se) against adverse or lethal effects induced by inorganic or organic mercury salts is documented for algae, aquatic invertebrates, fish, birds, and mammals (Magos and Webb 1979; Heisinger 1979; Chang et al. 1981; Lawrence and Holoka 1981; Das et al. 1982; Gotsis 1982; Eisler 1985; Satoh et al. 1985; Goede and Wolterbeek 1994; Paulsson and Lundbergh 1989; USPHS 1994; Caurent et al. 1996; Kim et al. 1996). For example, selenium, as sodium selenite, that was introduced into a nonacidified mercury-contaminated lake in Sweden to concentrations of 3 to 5 $\mu\text{g Se/L}$ (from 0.4 $\mu\text{g Se/L}$) and sustained at this level for 3 years resulted in declines of 50 to 85% in mercury concentrations in fish muscle (Paulsson and Lundbergh 1989). The mercury-protective effect of selenium is attributed to competition by selenium for mercury-binding sites associated with toxicity, formation of a Hg-Se complex that diverts mercury from sensitive targets, and prevention of oxidative damage by increasing the amount of selenium available to the selenium-dependent enzyme glutathione peroxidase (USPHS 1994). In seabirds, an equivalent molar ratio of 1:1 between total mercury and selenium was found in livers of individual seabirds which contained more than 100 mg Hg/kg DW ; this relation was unclear in other individuals which had relatively low mercury levels (Kim et al. 1996). The selenium-protective mechanism in birds is explained by a strong binding between mercury and selenium, possibly by the formation of a selenocysteamine methylmercury complex ($\text{CH}_3\text{HgSeCH}_2\text{CH}_2\text{NH}_3^+$), mercury binding to selenocysteine residues ($\text{CH}_3\text{HgSeCH}_2\text{CH}(\text{NH}_3)(\text{COO})\text{H}_2\text{O}$), the formation of

insoluble mercuric selenide (HgSe), or binding of mercury to SeH residues of selenoproteins, notably metallothioneins with thiols replaced by SeH (Goede and Wolterbeek 1994). However, high selenium concentrations in tissues of marine wading birds do not have their origin in elevated levels of mercury. The Se:Hg ratio in marine wading birds from the Wadden Sea is 32:1 and greatly exceeds the 1:1 ratio found when selenium is accumulated to detoxify mercury (Goede and Wolterbeek 1994). In marine mammals and humans, selenium and mercury concentrations are closely related, almost linearly in a 1:1 molar ratio (Eisler 1985). The molar ratio between mercury and selenium in marine mammals suggests that the major mechanism of detoxification is through the formation of a complex Hg-Se which leads to mercury demethylation (Caurent et al. 1996). The site of this process is the liver, in which mercury appeared mainly as inorganic, whereas in the muscle the percent of organic to total mercury was much higher. Detoxification is limited in lactating female whales, and sometimes in all the individuals of one school (Caurent et al. 1996). Selenium does not, however, protect against mercury-induced birth defects, such as cleft palate in mice (USPHS 1994). It is clear that more research is needed on mercury protectants.

Techniques for analysis of different mercury species in biological samples and abiotic materials include atomic absorption, cold vapor atomic fluorescence spectrometry, gas–liquid chromatography with electron capture detection, and inductively coupled plasma mass spectrometry (Lansens et al. 1991; Schintu et al. 1992; Porcella et al. 1995). Methylmercury concentrations in marine biological tissues are detected at concentrations as low as 10 $\mu\text{g Hg/kg}$ tissue using graphite furnace sample preparation techniques and atomic absorption spectrometry (Schintu et al. 1992).

5.4 MERCURY IN MINAMATA, JAPAN

One of the earliest and most extensively documented cases of mercury poisoning occurred in the 1950s at Minamata Bay in southwestern Kyushu, Japan (Fujiki 1963, 1980; Irukayama 1967; Matida and Kumada 1969; Kojima and Fujita 1973; NAS 1978; Elhassani 1983; Nishimura and Kumagai 1983; Doi et al. 1984; Davies 1991). The source of the mercury was waste discharged from an acetaldehyde plant that used inorganic mercury as a catalyst. Between 1932 and 1968, Minamata Bay received at least 260 tons of mercury and perhaps as much as 600 tons. A severe neurological disorder was recognized in late 1953 and had reached epidemic proportions by 1956. The mortality rate for acutely affected patients in 1957 was 32.8%. Infants born between 1955 and 1958 and diagnosed with mercury poisoning had a mental retardation rate of 29.1%, excluding congenital cases. By the end of 1960, 111 cases of poisoning were reported, and by August 1965, 41 of the 111 had died. By 1982, there were 1800 verified human victims of mercury poisoning in a total regional population of 200,000. Symptoms evidenced by human victims included sensory impairment, constriction of visual fields, hearing loss, ataxia, and speech disturbances. Congenital cases were accompanied by disturbance of physical and mental development; about 6% of babies born in Minamata had cerebral palsy (vs. 0.5% elsewhere).

In 1987, afflicted humans displayed symptoms of peripheral neuropathy (70.1%), ataxia (22.9%), constriction of the visual field (17.4%), tremor of the digits (10.2%), and dysarthria (9.2%); another 12.1% had no symptoms (Davies 1991). Nearly all patients complained of fatigue, numbness of parts of the body, and muscle cramps. Over 20,000 people are now thought to have been affected; symptoms were mainly neurological and resulted in death, chronic disability, and congenital abnormalities. As of June 1989, 1757 patients were officially diagnosed with Minamata disease, of which 765 had died and their families awarded compensation. Another 7621 people were disapproved for compensation. Another group of 918 (94 dead) were under investigation. A group of 2347 (320 dead) were awaiting official examination, and a final group of 1876 patients received health costs compensation only (Davies 1991). It is alleged that a large proportion of the population residing near Minamata Bay, especially the older population, is still incapacitated to varying degrees by the disease and that the more chronic effects are still becoming apparent (Davies 1991).

Minamata disease resulted from the discharge of methylmercury from chemical factories into Minamata Bay. Once diluted and diffused in the water, it was concentrated to a high level in fish and filter-feeding shellfish by several routes, including bioconcentration and food chain biomagnification. When these fish and shellfish were consumed by humans, methylmercury gradually accumulated to exceed a threshold value, causing intoxication. Spontaneously poisoned cats, dogs, rats, waterfowl, and pigs behaved erratically and died; flying crows and grebes suddenly fell into the sea and drowned; and large numbers of dead fish were seen floating on the sea surface (Doi et al. 1984). In laboratory studies, cats and rats fed shellfish from the bay developed the same signs as those seen in animals affected spontaneously. Abnormal mercury content — i.e., more than 30 mg/kg fresh weight — was measured in fish, shellfish, and muds from the bay, and in organs of necropsied humans and cats that had succumbed to the disease. Total mercury concentrations in tissues of fish from Minamata Bay with signs of methylmercury poisoning were about 15 mg/kg FW in liver and 8 to 24 mg/kg FW in muscle (Wiener and Spry 1996). Mercury contamination of fish and sediments was still evident in 1981, although discharges from the acetaldehyde plant ceased in 1971 (Doi et al. 1984). Plans are under way to reopen Minamata Bay for fishing in the future; however, as of June 1989 certain species of fish were still likely to have concentrations of mercury unsafe for human consumption (Davies 1991).

There is a strong relationship between the food of birds from Minamata and the mercury content in feathers; the content is highest in fish-eating seabirds and lowest in herbivorous waterfowl (Doi et al. 1984; [Table 5.4](#)). This same relationship held in birds collected from China and Korea,

Table 5.4 Mercury Concentrations in Selected Biological and Nonbiological Materials Collected From Minamata Bay, Japan and Environs (Concentrations are in mg Hg/kg [ppm] fresh weight [FW], or dry weight [DW].)

Sample, Year of Collection, and Other Variables	Concentration (mg/kg)	Reference ^a
PHYTOPLANKTON		
1974	Max. 0.32 DW	1
INVERTEBRATES		
1961		
Coelenterates	9.6 DW	2
Tunicates	35–56 DW	2
Molluscs		
Pacific scallop, <i>Chlamys ferrei nipponensis</i>		
Soft parts	48 DW	2
Pacific oyster, <i>Crassostrea gigas</i>		
Soft parts	10 DW; 5.6 FW	2
Clam, <i>Hormomya mutabilis</i>		
Foot	18–48 DW	3
Ganglion	181 DW	3
Other tissues	20–73 DW	3
Crustacean		
Crab, <i>Neptunus pelagicus</i>		
Muscle	39 DW	3
Filter-feeding molluscs		
Soft parts		
1962	Max. 43 DW	4
1963	Max. 40 DW	4
1965	Max. 35 DW	4
1967	Max. 60 DW	4
1969	Max. 16 DW	4

Table 5.4 (continued) Mercury Concentrations in Selected Biological and Nonbiological Materials Collected From Minamata Bay, Japan and Environs (Concentrations are in mg Hg/kg [ppm] fresh weight [FW], or dry weight [DW].)

Sample, Year of Collection, and Other Variables	Concentration (mg/kg)	Reference ^a
1971	Max. 16 DW	4
1972	Max. 4 DW	4
Zooplankton		
1974	Max. 1.1 DW	1
FISH		
1961		
Largescale blackfish, <i>Girella punctata</i>		
Viscera	18–27 DW	2
Muscle	12–20 DW	2
Scarbreast tuskfish, <i>Choerodon azurio</i>		
Muscle	309.1 DW	3
Liver	85.0 DW	3
Heart	36.4 DW	3
Gill	13.3 DW	3
Digestive gland	1.3 DW	3
Black porgy, <i>Sparus macrocephalus</i>		
Muscle	16.5 DW	3
Liver	32.2 DW	3
Heart	18.3 DW	3
Gill	9.1 DW	3
Digestive gland	4.0 DW	3
Muscle		
1961	23.0 DW	4
1963	3.5 DW	4
1965	11.5 DW	4
1969	Max. 50.0 DW	9
1966–72	<0.6 DW	4
1974	Max. 0.6 FW	1
BIRDS		
1955–80; feather		
Fish-eating seabirds	7.1 DW	5
Omnivorous waterfowl	5.5 DW	5
Predators	3.6 DW	5
Omnivorous terrestrial birds	1.5 DW	5
Herbivorous waterfowl	0.9 DW	5
1965–66, found dead		
Feather	4.6–13.4 FW	6
MAMMALS		
Cat, <i>Felis domesticus</i>, 1961		
Hair		
Naturally poisoned	40–52 DW	7
Experimentally poisoned	22–70 DW	7

Table 5.4 (continued) Mercury Concentrations in Selected Biological and Nonbiological Materials Collected From Minamata Bay, Japan and Environs (Concentrations are in mg Hg/kg [ppm] fresh weight [FW], or dry weight [DW].)

Sample, Year of Collection, and Other Variables	Concentration (mg/kg)	Reference ^a
Humans, <i>Homo sapiens</i>, dying of Minamata disease, 1957–89, autopsy results		
Brain	0.1–21.3 FW	9
Kidney	3.1–106.0 FW	9
Liver	2.1–70.5 FW	9
SEAWATER		
1961		
Total	0.0016–0.0036 FW	8
1974		
Filtered	0.0001 FW	1
Suspended particulates	0.000075 FW	1
MUD		
1963	28–713 DW	4
1969	19–908 DW	4
1970	8–253 DW	4
1971	14–586 DW	4
SEDIMENTS		
1973	>15–600 DW	1

^a 1, Nishimura and Kumagai 1983; 2, Matida and Kumada 1969; 3, Fujiki 1963; 4, Fujiki 1980; 5, Doi et al. 1984; 6, Kojima and Fujita 1973; 7, Jenkins 1980; 8, USEPA 1980; 9, Davies 1991.

although concentrations were significantly lower (Doi et al. 1984). There are close correlations between mercury contents of zooplankton and suspended particulate matter, and of sediments and fish muscle, suggesting a pathway from sediment to fish by way of suspended matter and zooplankton. The conversion from inorganic mercury to methylmercury is believed to have occurred primarily in zooplankton (Nishimura and Kumagai 1983).

Tokuyama Bay, Japan, received 6.6 metric tons of mercury wastes between 1952 and 1975 in wastewater from two chloralkali plants, although sediment analysis suggests that as much as 380 tons of mercury were released (Nakanishi et al. 1989). Unlike Minamata Bay, however, there were no human sicknesses reported, and the hair of residents contained 0 to 5 mg Hg/kg FW vs. 15 to 100 mg Hg/kg FW in Minamata residents. In 1970, a maximum concentration of 3.3 mg total Hg/kg FW was reported in tissues of *Squilla*, a crustacean. In 1973, a health safety limit was set of 0.4 mg total Hg/kg FW in edible fish and shellfish tissues with a maximum of 0.3 mg methylmercury/kg FW permitted; at least five species of fish had more than 0.4 mg total Hg/kg FW, and fishing was prohibited. Contaminated sediments (>15 mg total Hg/kg) were removed by dredging and reclamation between 1974 and 1977. By 1979, the mercury content of all fish, except one species, was less than 0.4 mg total Hg/kg FW; fishing was prohibited. By 1983, all fish and shellfish contained less than 0.4 mg Hg/kg FW and fishing was allowed (Nakanishi et al. 1989).

In aquatic environments where point sources of industrial contamination have been identified, the elimination of mercury discharges has usually improved environmental quality. Such improvement has been reported for Minamata Bay (Table 5.4); for sediments in Saguenay Fjord, Quebec,

when chloralkali wastes were limited; for fish residues in Canada's Lake St. Clair after two chloralkali plants were closed; and in various sections of Europe and North America when industrial discharges were eliminated (Barber et al. 1984).

5.5 CONCENTRATIONS IN FIELD COLLECTIONS

5.5.1 General

Mercury burdens in sediments and other nonbiological materials are estimated to have increased up to five times prehuman levels, primarily as a result of anthropogenic activities (NAS 1978). The residence time of mercury is comparatively short (about 11 days) in the atmosphere, but is much longer (at least 1000 years) in oceanic waters, soils, and sediments (Clarkson 1984). An elevated concentration of mercury (i.e., >1.0 mg/kg FW), usually as methylmercury, in any biological sample is often associated with proximity to human use of mercury. The elimination of mercury point-source discharges has usually been successful in improving environmental quality. However, elevated levels of mercury in biota may persist in contaminated areas long after the source of pollution has been discontinued (Rada et al. 1986). For example, mercury remains elevated in resident biota of Lahontan Reservoir, Nevada, which received about 7500 tons of mercury as a result of gold and silver mining operations from 1865 to 1895 (Cooper 1983). It is noteworthy that some groups of organisms with consistently elevated mercury residues may have acquired these concentrations as a result of natural processes, rather than from anthropogenic activities. These groups include older specimens of long-lived predatory fishes, marine mammals (especially pinnipeds), and organisms living near natural mercury-ore-cinnabar deposits.

5.5.2 Nonbiological

Mercury burdens have increased two to five times precultural levels in freshwater and estuarine sediments and freshwater lakes and rivers, but estimated increases in oceanic waters and terrestrial soils have been negligible (NAS 1978). Significant mercury enrichment in sediments of Newark Bay, New Jersey, may represent a hazard to aquatic life (Gillis et al. 1993). Total mercury concentrations in uncontaminated natural waters (presumably unfiltered) now range from about 0.001 to 0.050 µg/L ([Table 5.5](#)). In sediments that were anthropogenically contaminated with mercury, concentrations were significantly elevated (usually >20.0 mg/kg) when compared with uncontaminated sediments (usually <1.0 mg/kg). The residence time of mercury in nonbiological materials is variable and depends on a number of physicochemical conditions. Estimated half-time residence values for mercury are 11 days in the atmosphere, 1000 years in terrestrial soils, 2100 to 3200 years in ocean waters, and >250 million years in oceanic sediments (NAS 1978, as quoted in Boudou and Ribeyre 1983); the estimate was 1 month to 5 years for water from the contaminated Saguenay River in Quebec (Smith and Loring 1981). Methylmercury accounts for a comparatively small fraction of the total mercury found in sediments, surface waters, and sediment interstitial waters of Poplar Creek, Tennessee, which was initially contaminated with mercury in the 1950s and 1960s. Mercury measurements in Poplar Creek in 1993/94 showed that methylmercury accounted for 0.01% of the total mercury in sediments, 0.1% in surface waters, and 0.3% in sediment interstitial waters (Campbell et al. 1998). In Florida, methylmercury in sediments from uncontaminated southern estuaries in 1995 accounted for 0.77% of the total mercury and was not correlated with total mercury or organic content of sediments (Kannan et al. 1998).

Much of the mercury that enters freshwater lakes is deposited in bottom sediments (Rada et al. 1993). Sedimentary pools of mercury in these lakes greatly exceed the inventories of mercury in

Table 5.5 Mercury Concentrations in Selected Abiotic Materials

Material (units)	Concentration	Reference ^a
AIR (ng/m³)		
Japan		
Remote areas	<5–20	12
Urban areas	85–100	12
Siberia, 1992–93		
Summer		
Gaseous	0.7–2.3	14
Particulate	0.005–0.02	14
Winter		
Gaseous	1.2–6.1	14
Particulate	0.02–0.09	14
COAL (mg/kg DW)		
Bituminous	0.07	10
Lignite	0.12	10
Sub-bituminous	0.03	10
SEDIMENTS (mg/kg DW)		
Contaminated areas		
Near chloralkali plant		
Quebec, Canada	12	3
Norway	250 (90–350)	4
Thailand	8.4–58.0	5
Near gold mining operations		
South Dakota	0.1–4.1	6
Australia	120	7
Near Hg-fungicide plant		
Denmark	22	8
Near acetaldehyde plant		
Minamata Bay, Japan	28–713	4
Near pulp and paper mill		
Finland	746	9
Tennessee; Oak Ridge; 1993–94; mercury-contaminated in mid-1950s to early 1960s; methylmercury vs. total mercury	Max. 0.012 DW vs. 0.63–140.0 DW	15
Uncontaminated areas		
Lakes	0.1–0.3	12
Marine	0.05–0.08	12
Rivers	<0.05	12
North Central USA	0.02–0.06 (Max. 0.11)	6
South Dakota	0.02–0.1	6
Thailand	0.03	5
Finland	0.02	5
Various lakes	Usually <10.0, frequently <1.0	4
Wisconsin		
Deep precolonial strata	0.04–0.07	13
Top 15 cm	0.09–0.24	13

Table 5.5 (continued) Mercury Concentrations in Selected Abiotic Materials

Material (units)	Concentration	Reference ^a
SNOW (ng/L)		
Siberia, 1992–93		
Total mercury	8–60	14
Methylmercury	0.1–0.25	14
SUSPENDED PARTICULATE MATTER, mg/kg DW		
Germany, Elbe River, 1988, mercury-contaminated by chlor-alkali plants		
Total mercury	30; Max. 150	11
Methylmercury	2.7	
Reference site, total mercury	0.4	11
WATER (ng/L)		
Coastal seawater	<20	2
Estuarine seawater	<50	2
Glacial waters	10	2
Ground waters	50	2
Lake water		
Siberia, Lake Baikal, summer 1992–93		
Total mercury	0.14–0.77	14
Methylmercury	Max. 0.038	14
Sweden		
Total mercury	1.4–15.1	12
Methylmercury	0.04–0.8	12
United States		
Total mercury	0.4–10.7	12
Methylmercury	0.03–0.64	12
Open ocean		
Open ocean	5.3 (3.1–7.5)	1
Open ocean	<10	2
Rainwater		
Siberia, 1992–93		
Total mercury	3–20	14
Methylmercury	0.1–0.25	14
Sweden		
Total mercury	7.5–89.7	12
Methylmercury	0.04–0.6	12
Rivers and lakes		
River water	10 (Max. 50)	2
Canada, Ottawa River		
Total mercury	4.6–9.8	12
Methylmercury	1.6–2.8	12
Japan		
Total mercury	19.3–25.9	12
Methylmercury	5.8–7.0	12
Siberia, 1992–93		
Total mercury	Max. 2.0	14
Methylmercury	Max. 0.16	14
USA, Connecticut River		
Total mercury	45	12
Methylmercury	21	12
Rainwater		
Open ocean	1.0	2
Coastal ocean	10.0	2
Continents	Often >50	2

Table 5.5 (continued) Mercury Concentrations in Selected Abiotic Materials

Material (units)	Concentration	Reference ^a
Seawater		
Japan		
Total mercury	3.2–12.5	12
Methylmercury	0.2–1.0	12
United States, NY		
Total mercury	47–78	12
Methylmercury	25–33	12
Sediment interstitial water		
Total mercury	100–600	2, 15
Methylmercury	2	15

^a 1, Nishimura et al. 1983; 2, Fitzgerald 1979; 3, Smith and Loring 1981; 4, Skei 1978; 5, Suckcharoen and Lodenius 1980; 6, Martin and Hartman 1984; 7, Bycroft et al. 1982; 8, Kiorboe et al. 1983; 9, Paasivirta et al. 1983; 10, Chu and Porcella 1995; 11, Wilken and Hintelmann 1991; 12, Hamasaki et al. 1995; 13, Rada et al. 1989; 14, Meuleman et al. 1995; 15, Campbell et al. 1998.

water, seston, and fish, and the release of mercury from the sediments would significantly increase bioavailability and uptake. The dry weight mercury concentrations of sediments seem to underrepresent the significance of the shallow water sediments as a reservoir of potentially available mercury when compared to the mass per volume of wet sediment, which more accurately portrayed the depth distribution of mercury in Wisconsin seepage lakes (Rada et al. 1993). The increase in the mercury content of recent lake sediments in Wisconsin is attributed to increased atmospheric deposition of mercury, suggesting that the high mercury burdens measured in gamefish in certain Wisconsin lakes originated from atmospheric sources (Rada et al. 1989). Levels of mercury in sediments may be reflected by an increased mercury content in epibenthic marine fauna. For example, mercury concentrations in sediments near the Hyperion sewer outfall in Los Angeles, which ranged up to 820 µg/kg and decreased with increasing distance from the outfall, were reflected in the mercury content of crabs, scallops, and whelks. Concentrations of mercury were highest in organisms collected nearest the discharge, and lowest in those collected tens of kilometers away (Klein and Goldberg 1970).

Uptake from the soil is probably a significant route for the entrance of mercury into vegetation in terrestrial ecosystems. In Italy, elevated mercury concentrations in soils near extensive cinnabar deposits and mining activities were reflected in elevated mercury concentrations in plants grown on those soils (Ferrara et al. 1991). Mercury concentrations in tissues of different species of vascular plants growing on flood plain soils at Waynesboro, Virginia, were directly related to soil mercury concentrations that ranged between <0.2 and 31 mg Hg/kg DW soil (Cocking et al. 1995). In a study conducted in Fulton County, Illinois, it was shown that repeated applications of sewage sludge to land will significantly increase the concentration of mercury in surface soils (Granato et al. 1995). However, 80 to 100% of the mercury remained in the top 15 cm and was not bioavailable to terrestrial vegetation. The authors concluded that models developed by the EPA overpredict the uptake rates of mercury from sludge-amended soils into grains and animal forage, and need to be modified (Granato et al. 1995).

Creation of reservoirs by enlargement of riverine lakes and flooding of adjacent lands has led to a marked rise in rates of methylmercury production by microorganisms in sediments. This process has resulted mainly from increased microbial activity via increased use of organic materials under conditions of reduced oxygen (Jackson 1988). Increased net methylation in flooded humus and peat soils, especially in anoxic conditions, was determined experimentally and judged to be the main reason for increased methylmercury concentrations in reservoirs (Porvari and Verta 1995). Enlargement of northern Manitoba lakes to form hydroelectric reservoirs caused a rise in the mercury content of native fishes owing to stimulation of mercury methylating bacteria by submerged

terrestrial organic matter (Jackson 1991). Increased organic substrates beyond a critical amount mitigated this effect via promotion of mercury demethylation and production of mercury-binding agents such as sulfides. Variability in mercury concentrations between fish species was high and was due to differences in habitat preference, metabolic rate, age, growth rate, size, biomass, diet, and excretory pathways (Jackson 1991). Elevated mercury levels in fish flesh found after impoundment of a reservoir are predicted to decline as the reservoir ages (Anderson et al. 1995). In Labrador, Canada, omnivorous species of fishes reached background levels in 16 to 20 years; however, mercury in piscivorous species remained elevated 21 years after impoundment (Anderson et al. 1995).

High concentrations of methylmercury in subthermocline low-oxygen seawater were significantly and positively correlated with median daytime depth (<200 m to >300 m) of eight species of pelagic fishes; mean total mercury concentrations in whole fishes ranged between 57 and 377 µg/kg DW. The enhanced mercury accumulations in the marine mesopelagic compartment is attributable to diet and ultimately to water chemistry that controls mercury speciation and uptake at the base of the food chain (Monteiro et al. 1996).

5.5.3 Biological

Information on mercury residues in field collections of living organisms is especially abundant ([Table 5.6](#)). Elevated concentrations of mercury occur in aquatic biota from areas receiving high atmospheric depositions of mercury, or when mercury concentrations in the diet or water are elevated (Sorensen et al. 1990; Wiener et al. 1990a; Fjeld and Rognerud 1993). Mercury levels are comparatively elevated in fish-eating fishes, birds, and mammals (Langlois et al. 1995). In general, mercury concentrations in biota were usually less than 1.0 mg/kg FW tissue in organisms collected from locations not directly affected by man's use of the element. However, they exceed 1.0 mg/kg, and are sometimes markedly higher, in animals and vegetation from the vicinity of chloralkali plants; agricultural users of mercury; smelters; mining operations; pulp and paper mills; factories producing mercury-containing paints, fertilizers, and insecticides; sewer outfalls; sludge disposal areas; and other anthropogenic point sources of mercury (Schmitt and Brumbaugh 1990; [Table 5.6](#)). In some Minnesota lakes, mercury concentrations in fish are high enough to be potentially hazardous when ingested by mink, otters, loons, and raptors (Swain and Helwig 1989).

Certain species of macrophytes strongly influence mercury cycling. For example, *Spartina alterniflora* — a dominant salt marsh plant in Georgia estuaries — accounted for almost half the total mercury budget in that ecosystem (Windom et al. 1976). Mangrove vegetation plays a similarly important role in mercury cycling in the Florida Everglades (Tripp and Harriss 1976). These findings suggest that more research is needed on the role of higher plants in the mercury cycle.

Mercury was detectable in the tissues of almost all freshwater fishes examined, with the majority of the mercury (>80–99%) present as methylmercury (Huckabee et al. 1979; Chvojka 1988; Grieb et al. 1990; Southworth et al. 1995). Methylmercury is absorbed more efficiently than inorganic mercury from water, and probably from food, and is retained longer regardless of the uptake pathway (Huckabee et al. 1979; Hill et al. 1996). Three important factors modifying mercury uptake in aquatic organisms are the age of the organism, water pH, and the dissolved organic carbon content. In fish, for example, mercury tends to accumulate in muscle tissues of numerous species of freshwater and marine fishes and to increase with increasing age, weight, or length of the fish (Eisler 1984; Braune 1987b; Phillips et al. 1987; Chvojka 1988; Nicoletto and Hendricks 1988; Cope et al. 1990; Grieb et al. 1990; Sorensen et al. 1990; Wiener et al. 1990a; Leah et al. 1991, 1992; Rask and Metsala 1991; Lange et al. 1993, 1994; Staveland et al. 1993; Mathieson and McLusky 1995; Joiris et al. 1997; Munn and Short 1997; Stafford and Haines 1997). Mercury concentrations in muscle of freshwater teleosts were significantly higher in acidic lakes than in neutral or alkaline lakes (Allard and Stokes 1989; McMurtry et al. 1989; Cope et al. 1990; Grieb et al. 1990; Wiener et al. 1990a, 1990b; Rask and Metsala 1991; Haines et al. 1992; Lange et al. 1993). Highest levels of mercury in fish muscle were from lakes with a pH near 5.0; liming acidic lakes resulted in as much as an

80% decrease in muscle mercury content after 10 years (Andersson et al. 1995). And mercury concentrations in fish muscle were positively correlated with dissolved organic carbon concentration (McMurtry et al. 1989; Sorensen et al. 1990; Wren et al. 1991; Fjeld and Rognerud 1993).

In addition to age, water pH, and dissolved organic carbon, other variables known to modify mercury accumulation rates in aquatic organisms include water temperature, sediment mercury concentrations, lake size, season, diet, chemical speciation of mercury, and sex. Elevated water temperatures were associated with elevated accumulations of mercury. Rates of mercury methylation were positively dependent on water temperature, and mercury demethylation rates were inversely related to water temperature (Bodaly et al. 1993). Elevated mercury concentrations in fish muscle were positively correlated with sediment mercury concentrations (Munn and Short 1997): a similar case is made for benthic marine invertebrates (Becker and Bigham 1995). Mercury concentrations were inversely related to lake size in planktivorous, omnivorous, and piscivorous fishes from remote lakes in northwestern Ontario; lakes ranged in size from 89 to 35,000 surface ha and were far from anthropogenic influences (Bodaly et al. 1993). Mercury levels in muscle of marine flatfishes were higher in the spring than in the autumn (Staveland et al. 1993). In the yellow perch, *Perca flavescens*, seasonal variations in uptake rate of methylmercury and in the proportion of uptake from aqueous and food sources is attributed to seasonal variations in water temperature, body size, diet, and prey availability. Methylmercury uptake was primarily from aqueous sources during the spring and fall and was dominated by food sources in the summer (Post et al. 1996). Food chain transfer of mercury from benthic invertebrates to fishes depended primarily on the consumption rate of benthivorous fishes, and secondarily on the total invertebrate mercury pools (Wong et al. 1997). In the absence of pelagic forage fish, mercury concentrations in muscle of lake trout are likely to be depressed (Futter 1994). Trophic transfer of methylmercury is much more efficient than that of Hg^{2+} (Hill et al. 1996). Sometimes, fish pellets fed to laboratory fish may contain elevated (0.09 mg Hg/kg DW) concentrations of mercury, resulting in elevated blood mercury levels (0.06 mg Hg/L) after 10 weeks, as was the case for the Sacramento blackfish, *Orthodon microlepidotus* (Choi and Cech 1998). Sexually mature female centrarchids had significantly higher concentrations of mercury in muscle tissue than did sexually mature males (Nicoletto and Hendricks 1988), although this has not been reported for other aquatic species. Mercury concentrations in fish muscle were higher in fish from humic lakes (Rask and Metsala 1991), from lakes of low mineralization (Allard and Stokes 1989), and from lakes with low concentrations of dissolved iron (Wren et al. 1991), calcium, alkalinity, chlorophyll *a*, magnesium, phosphorus, and nitrogen (Lange et al. 1993). It is noteworthy that low atmospheric depositions of selenium did not affect mercury concentrations in muscle of brown trout (Fjeld and Rognerud 1993); that mercury and selenium in muscle of marine fishes were not correlated (Chvojka 1988; Chvojka et al. 1990); and that mercury and selenium concentrations in blood of tunas were independent of each other (Kai et al. 1988).

Reservoir construction has often been inferred to be a cause of elevated mercury concentrations in fish. Reservoir conditions facilitating the bioavailability of mercury include upstream flooding and leaching of terrestrial sediments, relatively high pH and conductivity of the water, high bacterial counts in the water, complete thermal mixing, low clay content, and low concentrations of sulfur and iron and magnesium oxides in bottom sediments (Lodenius 1983; Lodenius et al. 1983; Phillips et al. 1987; Allen-Gil et al. 1995). It is hypothesized that increases in mercury levels observed in fish were due to bacterial methylation of naturally occurring mercury in the flooded soils (Bodaly et al. 1984). Methylation and transfer of methylmercury from flooded soils to suspended particulate matter and zooplankton is rapid and involves the bioaccumulation of methylmercury by phytoplankton and the ingestion of suspended soil-derived organic particles by zooplankton (Plourde et al. 1997). Suspended particulate matter and zooplankton are disproportionate contributors to methylmercury contamination of aquatic food chains in Quebec reservoirs (Plourde et al. 1997). In general, mercury levels are higher in fish from younger oligotrophic reservoirs, and lower in fish from older eutrophic reservoirs. In both situations, tissue mercury levels usually decline as the reservoirs age

(Abernathy and Cumbie 1977). Mercury concentrations greater than 0.5 mg/kg (but less than 1.0 mg/kg) FW have been reported in trout from several wilderness lakes in northern Maine (Akielaszak and Haines 1981) and from the Adirondacks region of New York (Sloan and Schofield 1983); these values are considerably higher than might be expected for fish inhabiting remote lakes. These elevated concentrations were usually associated with lakes of low pH, low calcium, low dissolved organic carbon concentrations, and low water hardness and alkalinity.

Nationwide monitoring of whole fish during the period 1969 to 1981 demonstrated that the highest mercury concentrations (0.33 to 1.7 mg/kg FW) were in northern squawfish (*Ptychocheilus oregonensis*) from the Columbia River basin in the Pacific Northwest (Henderson and Shanks 1973; Lowe et al. 1985). Elevated mercury concentrations in this piscivorous species were attributed primarily to the presence of major cinnabar deposits and with Hg use associated with mineral mining in the Columbia River basin. Northern squawfish may have a natural tendency to accumulate high concentrations of mercury in their flesh — as is well known for older specimens of long-lived predatory fishes such as tunas, billfishes, bluefish (*Pomatomus saltatrix*), striped bass (*Morone saxatilis*), northern pike (*Esox lucius*), and many species of sharks — but mercury uptake kinetics in squawfish requires further research (Lowe et al. 1985). Of 159 species of finfish and sharks from the coastal waters of Alaska, Hawaii, and the conterminous United States, mercury concentrations in muscle were usually less than 0.3 mg/kg fresh weight (Hall et al. 1978). Mean mercury concentrations in excess of 0.5 mg/kg FW muscle were recorded in 31 species, including 10 species of sharks and 4 species of billfishes; however, these 31 species accounted for less than 0.65% of the catch intended for human consumption (Hall et al. 1978).

In birds, it is generally acknowledged that mercury concentrations in tissues and feathers are highest in species that eat fish and other birds. Mercury contamination of prey in the diet of nestling wood storks (*Mycteria americana*), an endangered species, may represent a potential concern to the recovery of this species in the southeastern United States (Garibaldi et al. 1998). Increased concentrations of total mercury in livers of diving ducks were associated with lower weights of whole body, liver, and heart, and decreased activities of enzymes related to glutathione metabolism and antioxidant activity (Hoffman et al. 1998). In seabirds, mercury concentrations were highest in tissues and feathers of species that ate fish and benthic invertebrates and lowest in birds that ate mainly pelagic invertebrates (Braune 1987a; Lock et al. 1992; Kim et al. 1996). In seabirds, the relation between tissues and total mercury concentrations is frequently 7:3:1 between feather, liver, and muscle; however, there is much variability and these ratios should be treated with caution. Factors known to affect these ratios include the chemical form of mercury present in liver, the sampling date relative to the stage of the molt sequence, and the types of feathers used for analysis (Thompson et al. 1990). Mercury concentrations in feathers of wading birds collected in Florida between 1987 and 1990 were highest in older birds that consumed large fishes (Beyer et al. 1997). Also, wading birds whose prey base consisted of larger fish had four times more mercury in their livers than did species which consumed smaller fish or crustaceans (Sundlof et al. 1994). Wading birds with minimal to moderate amounts of body fat had two to three times more mercury in liver than did birds with relatively abundant body fat reserves (Sundlof et al. 1994). Essentially all of the mercury in body feathers of all seabirds studied was organic mercury; however, more than 90% of the mercury in liver is inorganic (Thompson and Furness 1989). Mercury residues are usually highest in kidney and liver, but total mercury contents are significantly modified by food preference and availability, and by migratory patterns (NAS 1978; Delbekke et al. 1984). Also, there is an inverse relationship between total mercury and percent methylmercury in tissues of various avian species (Norheim et al. 1982; Karlog and Clausen 1983) — a pattern that seems to hold for all vertebrate organisms for which data are available. Diet and migration are the most important mercury modifiers in birds. For example, the higher levels of mercury in juvenile than in adult wood ducks (*Aix sponsa*) from Tennessee were related to dietary patterns: juveniles preferred insects, whereas adults preferred pondweed tubers; mercury residues were higher in the insects than in the pondweeds (Lindsay and Dimmick 1983). Concentrations of mercury in livers of Antarctic birds reflected mercury body

burdens accumulated during migration, while the birds were overwintering near industrialized areas. Concentrations were highest in species that ate higher trophic levels of prey and were especially pronounced for skuas, *Catharacta* spp.; however, significant inherent interspecies differences were evident (Norheim et al. 1982; Norheim and Kjos-Hanssen 1984).

Bird feathers have been used for some time as indicators of mercury loadings in terrestrial and marine environments. The keratin in bird feathers is not easily degradable, and mercury is probably firmly associated with the disulfide bonds of keratin. Consequently, it has been possible to compare mercury contents of feathers recently sampled with those from museum birds, thereby establishing a time series (Applequist et al. 1984; Thompson et al. 1992; Monteiro and Furness 1995; Odsjö et al. 1997). There is considerable variability in mercury content of seabird feathers. Concentrations in adults were higher than those in chicks and independent of adult age or sex (Thompson et al. 1991), and were lower in spring breeders than in autumn breeders (Monteiro et al. 1995). After the completion of molting, new feathers contained up to 93% of the mercury body burden in gulls (Braune and Gaskin 1987). The most probable source of elevated mercury residues in feathers of the Finnish sparrowhawk (*Accipiter nisus*) was from consumption of avian granivores that had become contaminated as a result of eating seeds treated with organomercury compounds; in 1981, 5.6 tons of methoxyethylmercury compounds were used in Finnish agriculture to protect seeds against fungi (Solonen and Lodenius 1984). Concentrations of mercury in feathers of herring gulls (*Larus argentatus*) from the German North Sea coast were higher in adults than in juveniles and two times higher after 1940 than in earlier years (Thompson et al. 1993). A maximum of 12 mg/kg FW in feathers during the 1940s was recorded, presumed to be due to high discharges of mercury during the Second World War. Concentrations dropped in the 1950s, increased in the 1970s to 10 mg Hg/kg FW, before falling again in the late 1980s. This pattern correlates well with known discharges of mercury into the Elbe and Rhine (Thompson et al. 1993). Captive Swedish eagle-owls (*Bubo bubo*), with low mercury content in feathers (<1.0 mg/kg DW), that were introduced into coastal areas quickly reflected the high (6.5 mg/kg) mercury levels in feathers of wild eagle-owls from that region. Captive birds released into inland territories, where mercury levels were near background, did not accumulate Hg in feathers (Broo and Odsjöe 1981). Mercury levels in feathers of nestling Swedish gyrfalcons (*Falco rusticolus*) showed a better correlation with mercury levels in actual food items than with levels based on adult feathers. Mercury concentrations in feathers were higher in nestlings fed partly with aquatic bird species containing more than 0.07 mg Hg/kg in pectoral muscle than in nestlings fed willow grouse (*Lagopus lagopus*) and ptarmigan (*Lagopus mutus*), both of which contained less than 0.01 mg Hg/kg in pectoral muscle (Lindberg 1984). In some instances there was a substantial time lag, up to 10 years, between the introduction of a pesticide, such as alkylmercury, its subsequent banning, and measurable declines of mercury in feathers of several species of Swedish raptors; this was the case for various species of *Falco*, *Haliaeetus*, *Bubo*, *Buteo*, and *Accipiter* (Wallin 1984). Accordingly, a reduction in mercury content in feathers of free-living birds may be sufficient to establish an improved situation.

Molting is a major excretory pathway for mercury (Honda et al. 1986). Down and feathers were effective excretion routes of mercury in contaminated gull and tern chicks (Becker et al. 1994). Some seabirds demethylate methylmercury in the liver and other tissues, and store mercury as an immobilizable inorganic form in the liver; species with a high degree of demethylation capacity and slow molting pattern had low mercury burdens in feathers (Kim et al. 1996). Egg laying is an important route in reducing the female's mercury burden, especially the first egg because egg mercury levels decline with laying sequence in gulls and terns (Becker 1992; Lewis et al. 1993). In gulls and terns, 90% of the mercury in eggs is in the form of methylmercury (Becker et al. 1993). In kittiwakes (*Rissa tridactyla*), mercury concentrations in feathers and tissues of nestlings decreased with increasing age, suggesting that egg contamination was more important in chicks than consumption of mercury-contaminated food items (Wenzel et al. 1996). Eggs of the common loon (*Gavia immer*) from Wisconsin in 1993 to 1996 had 0.9 mg Hg/kg FW, which is within the range associated with reproductive failure in sensitive avian species (Meyer et al. 1998).

Significant downward trends in mercury liver burdens of raptors in England between 1960 and 1990 (Newton et al. 1993) is a useful indicator of the prohibitions placed on mercury discharges in that region. The full significance of mercury residues in birds, however, is not fully understood. For example, all eggs of the bald eagle (*Haliaeetus leucocephalus*) collected nationwide contained detectable levels of mercury, but the mean was 0.15 mg Hg/kg (fresh weight basis) in eggs from unsuccessful nests vs. 0.11 in eggs from successful nests (Wiemeyer et al. 1984). Many other contaminants — especially organochlorine compounds — were in eagle eggs, and several were present at levels that potentially interfere with eagle reproduction (Wiemeyer et al. 1984). It is not now possible to implicate mercury as a major cause of unsuccessful eagle reproduction. In the Great Lakes, mercury has no apparent effect on reproduction or nesting success of bald eagles (Bowerman et al. 1994). Livers of 30 to 80% of some species of wading birds — such as the great blue heron, *Ardea herodias* — contained mercury concentrations greater than 30 mg Hg/kg FW; these herons appeared normal although concentrations >30 mg Hg/kg FW liver are typically associated with overt neurological signs and reproductive impairment in ducks and pheasants (Sundlof et al. 1994). If reproductive disorders are expected when concentrations in feathers of adult birds approach 9 mg total Hg/kg DW (Beyer et al. 1997), then mercury in southern Florida may be sufficiently high to reduce productivity of wading bird populations (Beyer et al. 1997), but this needs to be verified.

Many factors are known to modify mercury concentrations in tissues of the common loon (*Gavia immer*). Total mercury concentrations were higher in tissues of emaciated loons when compared with apparently healthy birds, and sometimes exceeded 100 mg Hg/kg DW in tissues of loons that were in poor condition (Scheuhammer et al. 1998b). There was a strong positive correlation between total mercury and selenium concentrations in livers and kidneys. As total mercury concentrations increased in liver and kidney of loons, the fraction that was methylmercury decreased. Livers and kidneys with the highest total mercury concentrations had only 5 to 7% of the total as methylmercury. Concentrations of methylmercury were always less than 10 mg/kg DW, regardless of total mercury concentration in liver or kidney. In contrast, methylmercury contributed 80 to 100% of the total mercury in breast muscle, which ranged between 0.7 and 35.0 mg/kg DW (Scheuhammer et al. 1998b). In general, males had higher mercury concentrations in blood and feathers than did their female mates (Scheuhammer et al. 1998a). The possible transfer of mercury to eggs by females during egg laying may account for the sexual discrepancy, in part. Adult loons had higher blood mercury concentrations (up to 13 times higher) than their chicks. Adult and chick blood mercury concentrations were correlated with mercury concentrations in their fish diet (Scheuhammer et al. 1998a). Blood mercury concentrations of loon chicks near Wisconsin lakes increased with decreasing lake pH (Meyer et al. 1998). Blood and feather mercury concentrations from the same individuals were correlated, especially in loons with the highest blood mercury levels (Evers et al. 1998). Common loons had aberrant nesting behavior and low reproductive success when mercury concentrations in prey (small fish and crayfish) exceeded 0.3 mg Hg/kg FW, levels known to occur in fish from many lakes in central Ontario; up to 30% of Ontario lakes exceeded the mercury threshold for loon reproductive impairment (Scheuhammer and Blancher 1994; Scheuhammer et al. 1998a). Populations of the common loon are also declining in the northeastern United States, and this may be due to mercury, in part, as evidenced by the high concentrations in their feathers (9.7 to 20.2 mg Hg/kg DW) — twice that of other species (Burger et al. 1994).

Human intake of total mercury from the diet normally ranges between 7 and 16 µg daily (Schumacher et al. 1994; Richardson et al. 1995). Fish consumption accounts for much of this exposure in the form of methylmercury; 27% of the intake, and 40% of the absorbed dose. Intake of inorganic mercury arises primarily from foods other than fish, and is estimated at 1.8 µg daily with 0.18 µg absorbed daily (Richardson et al. 1995). In certain areas of India, blood mercury concentrations of people who ate fish were three to four times higher than non-fish eaters (Srinivasen and Mahajan 1989). In some countries, mercury in dental amalgams accounts for 2.8 µg daily, equivalent to as much as 36% of the total mercury intake and 42% of the absorbed dose (USPHS

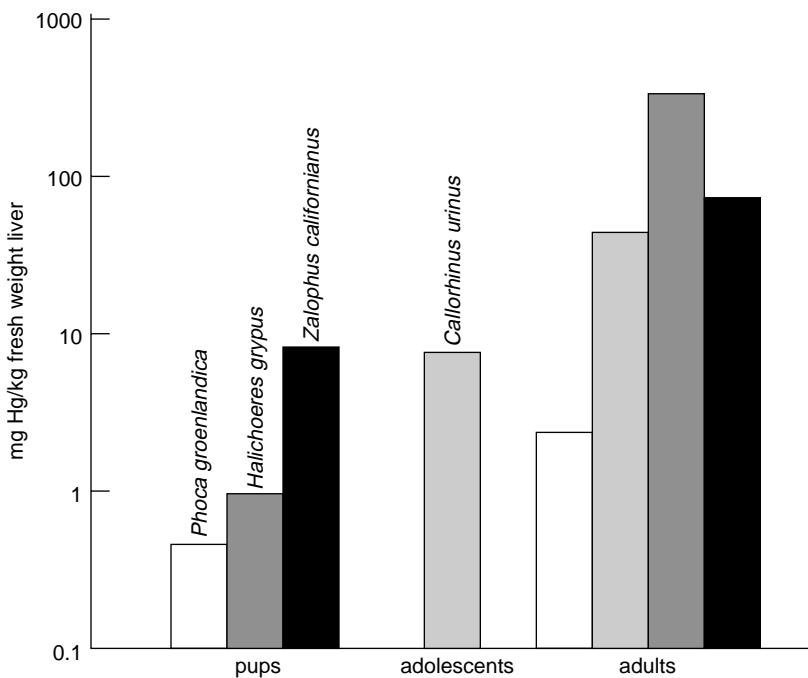


Figure 5.2 Mercury concentrations in livers of four species of pinniped mammals. (From Eisler, R. 1984. Trace metal changes associated with age of marine vertebrates. *Biol. Trace Elem. Res.* 6:165-180. With permission.)

1994; Richardson et al. 1995). Some Canadian aboriginal peoples had grossly elevated blood mercury concentrations of >100 to 660 µg Hg/L, although there was no definitive diagnosis of methylmercury poisoning (Wheatley and Paradis 1995).

Among nonhuman mammals, marine pinnipeds usually contained the highest reported concentrations of mercury in tissues (Table 5.6). The relatively high concentrations appeared to be a result of natural processes rather than anthropogenic activities, however, and probably did not represent a significant risk to pinniped health. Mercury in pinniped muscle was mostly methylmercury in both mothers and pups; pups acquired most of their mercury during gestation (Wagemann et al. 1988). In general, mercury concentrations increased significantly with increasing age of the organism, as shown in the livers of harbor seal (*Phoca groenlandica*), grey seal (*Halichoerus grypus*), California sea lion (*Zalophus californianus*), and northern fur seal (*Callorhinus ursinus*; Figure 5.2) and in various tissues of the Baikal seal (*Phoca sibirica*; Watanabe et al. 1998). The mechanisms to account for this phenomenon in pinnipeds are similar to those reported by Itano et al. (1984a, 1984b, 1984c) for the striped dolphin (*Stenella coeruleoalba*). They showed that tissue concentrations of mercury in striped dolphins increased with increasing age of the animal, reaching a plateau in 20 to 25 years; were highest in liver, although muscle accounted for about 90% of the total body mercury burden; were present in the methylated form in fetal and suckling stages, but the proportion of methylmercury decreased over time with no absolute increase after age 10 years; were excreted slowly by all developmental stages, and slowest in older dolphins (resulting in higher accumulations); and correlated strongly with selenium concentrations in all age groups. It is probable that inorganic mercury and selenium were complexed in a 1:1 molar ratio, in a form biologically unavailable to marine mammals (and probably other mammals), thereby significantly decreasing the risk of mercury toxicosis to individuals with grossly elevated mercury body burdens (Eisler 1984, 1985). The Hg/Se ratio was close to 1.0 in adults of four species of Norwegian seals provided

that tissue mercury concentrations were greater than 15 mg/kg FW (Skaare et al. 1994). Total mercury in livers of pinniped mothers (but not pups) correlated positively with selenium (Wagemann et al. 1988). Large colonies of pinnipeds and, to a lesser extent, marine birds along the western coast of the United States may make mercury available to mussels (*Mytilus californianus*) through fecal elimination of large amounts of mercury, resulting in abnormally high mercury levels in mussels from several west coast sites (Flegal et al. 1981).

Mercury concentrations in mammals are modified by age, sex, sexual condition, diet, season of collection, and other variables. Increasing concentrations of total and organic mercury in muscle and liver were observed with increasing age of fin whales (*Balaenoptera physalus*; Sanpera et al. 1993) and striped dolphins (Andre et al. 1991a), and in livers of white-tailed deer (*Odocoileus virginianus*; Khan and Forester 1995), otters (Mason and Madsen 1992), and the endangered Florida panther (*Felis concolor coryi*; Roelke et al. 1991). However, in harbor porpoises (*Phocoena phocoena*), total mercury — but not methylmercury — increased in tissues with increasing age (Joiris et al. 1991). Pregnant or lactating sperm whales (*Physeter macrocephalus*) had significantly higher mercury concentrations in muscle than nonbreeding females (Cannella and Kitchener 1992). In river otters (*Lutra canadensis*), mercury concentrations in liver and kidney were higher in males than in females (Ropek and Neely 1993). No sexual differences in liver mercury concentrations were evident in white-tailed deer (Khan and Forester 1995) or Danish otters (*Lutra lutra*; Mason and Madsen 1992). Polar bears (*Ursus maritimus*) probably obtain mercury from eating ringed seals (*Phoca hispida*), their main food (Lentfer and Galster 1987). Polar bear cubs had lower concentrations of mercury in hair than did yearlings or adults, and the low concentrations in adult hair in summer is attributed to molting (Born et al. 1991). Florida panthers found dead contained as much as 110 mg total Hg/kg FW liver, a level found lethal to feral cats in Minamata, Japan. Panthers feed primarily on raccoons, which contain as much as 3 mg Hg/kg FW (Roelke et al. 1991), but it is not known if this is the source of the elevated liver mercury in panthers.

Among furbearers in the Wisconsin River drainage system, mercury burdens were higher in fish-eating than in herbivorous species — i.e., river otter > mink (*Mustela vison*) > raccoon (*Procyon lotor*) > red fox (*Vulpes fulva*) > muskrat (*Ondatra zibethicus*) > beaver (*Castor canadensis*) (Sheffy and St. Amant 1982). In general, fur contained the highest mercury levels, followed by liver, kidney, muscle, and brain, in that order (Table 5.6; Sheffy and St. Amant 1982). Mercury levels in piscivorous furbearers collected from the Wisconsin River basin paralleled mercury levels in fish, crayfish, and bottom sediments from that system; levels in all compartments were highest about 30 km downstream from an area that supported 16 pulp and paper mills and a chloralkali plant (Sheffy and St. Amant 1982). Mercury concentrations in tissues of minks and otters trapped from various locations in Ontario between 1983 and 1985 varied as much as sixfold (Table 5.6); mercury levels in fish and crayfish from the study areas followed a similar pattern (Wren et al. 1986). Mink and river otter accumulated about ten times more mercury than did predatory fishes from the same drainage areas, suggesting that these furbearers can serve as sensitive indicators of mercury, even at very low levels of contamination (Kucera 1983). The shorttail shrew, *Blarina brevicauda*, from certain mercury-contaminated sites in Tennessee have extremely high concentrations in kidney (38.8 mg Hg/kg FW) and may be ingesting nephrotoxic levels of mercury through the diet (8.8 mg Hg/kg FW ration; Talmage and Walton 1993).

In the serow (*Capricornis crispus*), a free-ranging bovine ruminant, about 40% of the total mercury body burden was in the fleece at 0.37 mg Hg/kg FW fleece (Honda et al. 1987). Domestic sheep (*Ovis* sp.) allowed to graze for 23 months on grass contaminated with mercury (up to 6.5 mg/kg dry weight) from the atmospheric emissions of a nearby chloralkali site retained about 0.1% of the total mercury taken in by ingestion and inhalation, although residues in flesh were negligible (Edwards and Pumphrey 1982). It was concluded that contamination of grass as a result of atmospheric discharges of inorganic mercury from chloralkali sites causes no hazard, either directly to grazing animals or indirectly to humans who might ultimately consume their flesh.

Table 5.6 Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
FUNGI, LICHENS, MOSSES, PLANTS		
Mandarin orange, <i>Citrus tachibana</i> ; Japan Sprayed with Hg		
Fruit skin	0.03–0.24 FW	1
Fruit pulp	0.01–0.4 FW	1
Unsprayed		
Skin and pulp	0.01–0.05 FW	1
Fungi, <i>Cortinarius</i> spp.		
Near smelter	9.5–35.0 DW	1
Moss, <i>Dicranum scoparium</i> , whole		
Tennessee		
Exposed to fly ash	1.1 DW	1
Remote areas	0.1 DW	1
Great Smoky Mountains	0.07 DW	1
Hawaii	0.16 DW	1
Iceland	0.03 DW	1
Water hyacinth, <i>Eichhornia crassipes</i> ; from sewage lagoon in Bay St. Louis, Mississippi		
Leaves	70.0 DW	2
Lichen, <i>Hypogymnia physodes</i> , whole; Finland, 1982–83; distance, in km, from chloralkali plant		
0–1	18.0 FW	3
1–5	2.0 FW	3
5–20	0.4 FW	3
20–100	0.3 FW	3
>100	0.3 FW	3
Labrador tea, <i>Ledum</i> sp.; Alaska, over cinnabar deposit		
Stem	1.0–3.5 DW	1
Alfalfa, <i>Medicago sativa</i>		
From soil containing 0.4 mg Hg/kg		
Root	90.0 FW	1
Leaf	0.13–0.4 FW	1
From soil with <0.4 mg Hg/kg		
Leaf	0.16 FW	1
Tobacco, <i>Nicotiana tabacum</i>		
Leaf		
Treated with Hg (Japan)	1.0–1.6 FW	1
Untreated (USA)	<0.2 FW	1
Rice, <i>Oryza sativa</i> , grain		
Sprayed with Hg	0.1–0.7 FW	1
Unsprayed	0.02–0.1 FW	1
Marine flowering plant, <i>Posidonia oceanica</i>		
Near sewer outfall, Marseilles, France		
Rhizomes	2.5 DW	4
Leaves	51.5 DW	4
Roots	0.6 DW	4
Cherry, <i>Prunus avium</i>		
Europe (Slovenia), bark		
Uncontaminated areas	0.06 FW	1
High Hg in soil	6.0 FW	1
Factory area	59.0 FW	1
Mosses, <i>Sphagnum</i> spp., whole		
Finland, 1982–83		
Distance (km) from chloralkali plant		
0–1	3.8 (1.5–16.0) FW	3
1–5	0.8 (0.2–2.6) FW	3

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
5–20	0.09 (0.04–0.2) FW	3
20–100	0.05 (0.0–0.8) FW	3
>100	0.02 FW	3
AQUATIC INVERTEBRATES, FRESHWATER		
Annelids, 2 families		
From Hg-contaminated areas	0.3–0.6 FW	5
From uncontaminated areas	0.03–0.05 FW	5
Arthropods		
Sow bug, <i>Asellus</i> sp.		
Sweden, whole		
20 km below paper mill	1.9 FW	1
1–15 km above paper mill	0.06 FW	1
Crustaceans, 2 families		
From mercury contaminated areas	1.9–10.0 FW	5
From uncontaminated areas	0.06–0.56 FW	5
Insects, 8 families		
From mercury contaminated areas	0.5–5.0 FW	5
From uncontaminated areas	0.05–0.21 FW	5
Mayfly, <i>Hexagenia</i> sp., whole nymphs vs. sediments upper Mississippi River, 1989	Max. 0.13 DW vs. Max. 0.16 DW	54
Stonefly, <i>Isoperla</i> sp.		
Whole, Sweden		
17 km below paper mill	2.4 FW	1
15 km above paper mill	0.07 FW	1
Crayfish, <i>Orconectes virilis</i>		
Ontario, whole		
Central location	0.09–0.49 FW	1
From chloralkali plant location	1.4–7.4 FW	1
Crayfish, <i>Pacifastacus</i> sp.		
Lahontan Reservoir, Nevada, 1981, abdomen	5.7 FW	6
Crayfish, 5 species, Ontario, Canada, muscle	0.02–0.61 FW	53
Molluscs		
From mercury contaminated areas	0.02–2.1 FW	5
From uncontaminated areas	0.05 FW	5
AQUATIC INVERTEBRATES, MARINE		
Annelids		
Whole, 3 spp.		
Georgia, USA, estuaries		
Mercury-contaminated estuary		
Total Hg	0.7–4.5 DW	7
Methyl Hg	Max. 0.8 DW	7
Control estuary		
Total Hg	0.1–0.6 DW	7
Methyl Hg	Max. 0.13 DW	7
Arthropods		
Crustaceans, whole, 2 spp.		
Georgia, USA, estuaries		
Hg-contaminated estuary		
Total Hg	0.4–1.8 DW	7
Methyl Hg	Max. 1.0 DW	7
Control estuary		
Total Hg	0.1–0.4 DW	7
Methyl Hg	Max. 0.05 DW	7

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
American lobster, <i>Homarus americanus</i>		
Muscle		
Chesapeake Bay	0.03–0.06 FW	1
NW Atlantic	0.25–1.6 DW	1
Nova Scotia	0.15–1.5 FW	1
Spiny lobster, <i>Nephrops norvegicus</i>		
Tyrrhenian Sea, 1981		
Muscle	2.9 FW	8
Shrimp		
Edible portions		
Total Hg	0.77 FW	9
Methyl Hg	0.4 FW	9
Echinoderms		
Sea stars, 3 spp., 1981		
Venezuela, polluted area		
Gonads	3.8–8.7 DW; 0.9–1.6 FW	10
Molluscs		
From vicinity chloralkali plant, Israel, 1980–82, soft parts		
Gastropod, <i>Arcularia gibbosula</i>	18.2–38.7 DW	11
Bivalve, <i>Donax venustus</i>	Max. 6.4 DW	11
Bivalves, soft parts		
From Hg-polluted area, Denmark		
Deposit feeders	1.4–4.4 FW	12
Suspension feeders	0.9–1.9 FW	12
Edible portions		
Total Hg	0.04–0.22 FW	9
Methyl Hg	Max. 0.09 FW	9
Soft parts, 2 spp.		
Georgia, USA, estuaries		
Hg-contaminated estuary	0.5–1.2 DW	7
Control estuary	0.1–0.2 DW	7
Mussel, <i>Mytilus californianus</i>		
Soft parts		
Nationwide	<0.4 DW	13
California	0.6–2.5 DW	13
Mussel, <i>Mytilus edulis</i>		
Soft parts		
Belgium	1.0 DW	1
Spain	1.5 DW	1
New Brunswick	0.1 FW	1
Netherlands	0.1–0.3 FW	1
Great Britain	0.02–0.7 FW	1
New Zealand	0.02–0.48 FW	1
Norway	0.2–0.65 DW	1
Softshell clam, <i>Mya arenaria</i>		
Soft parts		
Chesapeake Bay, MD	0.01–0.05 FW	1
Nova Scotia	0.03–0.13 FW	1
New Brunswick		
3 km below pulp mill	0.9 FW	1
3 km below chloralkali plant	3.6 FW	1
TERRESTRIAL INVERTEBRATES		
Whole, Illinois		
Fed on Hg-treated tomato plants	0.3–11.5 FW	1
Control	0.08–0.81 FW	1

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Lacewing, <i>Chrysopa carnea</i>		
Whole, Illinois		
Fed on Hg-treated tomato plants	0.6–31.4 FW	1
Control	0.0–1.1 FW	1
FISHES		
Rock bass, <i>Ambloplites rupestris</i>		
Muscle		
Ontario	0.6–4.6 FW	1
Michigan	0.4 FW	1
Western Ontario	1.1–10.9 FW	1
Lake St. Clair	0.5–2.0 FW	1
Virginia, mercury-contaminated site vs. reference site, 1986–87		
Liver	2.9 FW vs. 0.1 FW	56
Muscle	1.4 FW vs. 0.17 FW	56
Blue hake, <i>Antimora rostrata</i>		
NW Atlantic, 2500 m depth, muscle		
1880	0.51 FW	14
1970	0.34 FW	14
Freshwater drum, <i>Aplodinotus grunniens</i>		
Whole		
Age 0	0.05 FW	15
Age I	0.13 FW	15
Age II	0.18 FW	15
California, San Joaquin River, whole body, 1986		
Common carp, <i>Cyprinus carpio</i>	0.1–0.5 DW, Max. 0.8 DW	80
Mosquitofish, <i>Gambusia affinis</i>	Max. 0.5 DW	80
Bluegill, <i>Lepomis macrochirus</i>	0.1–0.3 DW, Max. 0.41 DW	80
Largemouth bass, <i>Micropterus salmoides</i>	0.35–0.85 DW, Max. 1.9 DW	80
Canada, Waubigoon River system, Ontario, mercury-contaminated between 1962 and 1969, samples collected 1979–81		
Northern pike, <i>Esox lucius</i> , whole		
Age 0+	0.04–1.0 FW	81
Age 1+	0.09–1.2 FW	81
Yellow perch, <i>Perca flavescens</i> , yearlings, whole	0.01–0.6 FW	81
Snapper, <i>Chrysophrys auratus</i> , muscle, Sydney, Australia vs. Nowra, Australia, 1976		
Total mercury	0.32 (0.08–1.7) FW vs. 0.11 (0.01–0.78) FW	57
Methyl mercury	0.3 (0.25–0.32) FW vs. 0.1 (0.06–0.11) FW	57
Blacktail, <i>Diplodus sargus</i> ; muscle		
Mercury-polluted area	0.3–1.7 FW	11
Unpolluted area	0.04–0.64 FW	11
Haifa Bay, Israel, vs. reference site, 1990	0.6 FW vs. 0.15 FW	59
England, marine fishes, near River Tyne, 1992		
Muscle, 5 species	0.03–0.14 (0.006–0.43) FW	82
Stomach contents, 3 species	0.01–0.04 FW, Max. 0.11 FW	82
Northern pike, <i>Esox lucius</i> ; muscle		
Sweden	0.2–9.8 FW	1
Quebec	0.3–0.8 FW	1
Norway	0.1 FW	1
Saskatchewan	0.7–10.6 FW	1
Canada (normal)	0.1 FW	1
Canada (polluted)	0.5–0.7 FW	1

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Lake St. Clair	2.0–3.0 FW	1
NW Ontario mining area	5.6 FW, Max. 16 FW	1, 52
Wisconsin	0.9–1.4 FW	1
Manitoba, man-made reservoir		
Preimpoundment (1971–73)	0.25–0.35 FW	16
Postimpoundment (1979–82)	0.67–0.95 FW	16
Finland, southern 1960s vs. 1982–84	5–6 FW vs. 0.15–1.4 FW	60
Finland, northern		
Preindustrial levels	0.18–0.33 FW	61
Lake contaminated with phenylmercury until 1967		
1971–74 (sediments 2.1 mg Hg/kg DW)	1.5 FW	61
1990 (sediments 0.4 DW)	0.8 FW	61
Fish		
Muscle, 15 species (7 freshwater plus 8 marine)		
Total mercury	0.01–2.8 FW, (methylmercury content of 86–100%)	79
Dimethylmercury	<0.001 FW	79
Muscle		
Freshwater		
Total Hg	0.27–1.7 FW	9
Methyl Hg	Max. 1.4 FW	9
Marine		
Total Hg	0.11–5.7 FW	9
Methyl Hg	Max. 4.5 FW	9
Blackfish, <i>Gadopsis marmoratus</i>		
Muscle		
From Hg-contaminated sediments	Max. 0.64 FW	22
From uncontaminated sediments	Max. 0.06 FW	22
Three-spined stickleback,	0.01–0.11 FW, Max. 0.49 FW	62
Gasterosteus aculeatus, Gulf of Gdansk, whole, 1988–89		
Lahontan Reservoir, Nevada, 1981		
Muscle, 5 spp.	Max. 2.3–3.9 FW	6
Liver, 5 spp.	Max. 2.4–8.3 FW	6
Heart, 4 spp.	Max. 1.1–2.1 FW	6
Georgia, lower coastal plain, 1976–77, liver vs. muscle		
Carnivores	3.0 FW vs. 1.7 FW	83
Insectivores	1.1 FW vs. 1.1 FW	83
Omnivores	1.0 FW vs. 0.9 FW	83
Great lakes, Lake Ontario, whole fish		
Slimy sculpin, <i>Cottus cognatus</i>		
1977	0.068 FW	83
1984	0.038 FW	83
1988	0.032 FW	83
Rainbow smelt, <i>Osmerus mordax</i>		
1977	0.067 FW	84
1984	0.059 FW	84
1988	0.037 FW	84
Greenland, Barents Sea, summer 1991–92, muscle, demersal fishes		
Atlantic cod, <i>Gadus morhua</i>	(0.07–0.19) DW	85
Long rough dab, <i>Hippoglossoides platessoides</i>	0.13–0.9 (0.06–1.8) DW	85
Halibut, <i>Hippoglossus hippoglossus</i>	(0.24–1.1) DW	85
Starry ray, <i>Raja radiata</i>	(0.2–0.4) DW	85
Plaice, <i>Pleuronectes platessa</i>	0.3 (0.2–0.5) DW	85
Greenland halibut, <i>Reinhardtius hippoglossoides</i>	0.25–1.2 DW, Max. 2.5 DW	85

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Channel catfish, <i>Ictalurus punctatus</i>		
Muscle		
Lake Erie	0.3–1.8 FW	1
Lake St. Clair	0.5–2.0 FW	1
Ohio	0.1–0.4 FW	1
Illinois	0.03–0.2 FW	1
Oregon	0.02–1.5 FW	1
Georgia	0.1–1.9 FW	1
Texas	0.2–2.5 FW	1
Pumpkinseed, <i>Lepomis gibbosus</i> ; 16 lakes, Ontario, Canada, 1981		
Muscle	0.09–0.54 FW	23
Louisiana, Atchafalaya River, 1981, whole, 8 spp.	0.06–0.79 FW	17
Maine, 120 lakes, 10 species of gamefish, muscle, 1993–94	0.3–0.9 (0.07–1.2) FW	86
Black marlin, <i>Makaira indica</i>		
Muscle		
Pacific Ocean	0.6–4.3	9
NE Australia	0.5–16.5 FW	9
Blue marlin, <i>Makaira nigricans</i>		
Muscle		
Hawaii	0.4–14.0 FW	9
Total mercury	0.4–0.9 FW	9
Methylmercury	Max. 0.16 FW	9
Largemouth bass, <i>Micropterus salmoides</i>		
Muscle		
Texas	0.1 FW	1
Utah	0.3–7.3 FW	1
California	0.1–0.6 FW	1
Oregon	0.2–1.8 FW	1
Washington	0.1–0.3 FW	1
Georgia	0.1–5.4 FW	1
Michigan	0.2–0.9 FW	1
Illinois	0.03–1.2 FW	1
Arizona	0.3 FW	1
Florida, 1989–92	0.04–2.04 FW	63, 78
Whole, Florida, 1989–92		
Length 20 mm	0.05 FW	78
Length 320 mm	0.32 FW	78
Striped bass, <i>Morone saxatilis</i>		
Nevada, Lahontan Reservoir		
1981		
Single specimen, 16 years old		
Muscle	9.5 FW	6
Heart	5.6 FW	6
Liver	23.7 FW	6
Muscle		
Body weight		
<3.2 kg	<0.5 FW	24
3.2–5.7 kg	0.5 FW	24
>5.7 kg	>0.5 FW	24
Nationwide, USA, whole		
1969–70	0.26 (0.05–1.7) FW	18
Pacific Coast and Alaska	0.25 (0.05–1.7) FW	18
Southwest	0.08 (<0.05–0.14) FW	18
North Central	0.20 (<0.05–0.05) FW	18
Northeast	0.23 (<0.05–0.08) FW	18
Southeast	0.23 (<0.05–1.0) FW	18

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
1972	0.15 FW	18
1976–77	0.11 FW, Max. 0.85 FW	19, 90
1978–79	0.11 (0.01–1.1) FW	19
1980–81	0.11 (0.01–0.77) FW	19
1984–85	0.10 FW, Max. 0.37 FW, 85th percentile 0.17 FW	90
North Dakota and Minnesota, Red River of the North, 1994		
Common carp		
Liver	0.11 FW	87
Muscle	0.31 FW	87
Whole	0.18 FW	87
Channel catfish		
Liver	0.16 FW	87
Muscle	0.18 FW	87
Whole	0.11 FW	87
Yellow perch, <i>Perca flavescens</i>		
Whole		
Age 0	0.07 FW	15
Age I	0.13 FW	15
Age II	0.22 FW	15
Perch, <i>Perca fluviatilis</i> , Russia, June 1989, muscle, 350 km north of Moscow, 6 lakes, acidic vs. alkaline lakes	0.5–1.1 FW vs. 0.1–0.2 FW	64
Flounder, <i>Platichthys flesus</i> , muscle, Irish sea		
Northern areas	0.03–0.13 (0.008–0.39) DW	65
Central areas	0.16–0.48 (0.06–1.2) DW	65
Southern areas	0.16–0.40 (0.04–2.0) DW	65
Plaice, <i>Pleuronectes platessa</i> , muscle, Liverpool Bay, UK, sludge disposal ground		
Early 1970s (2.7 tons of mercury yearly)	0.5 FW	66
1991 (0.16 tons of mercury annually)	0.2 FW	66
Round whitefish, <i>Prosopium cylindraceum</i>		
Saginaw Bay, Michigan, 1977–78, fillets		
Methyl Hg	Max. 0.05 FW	25
Total Hg	Max. 0.1 FW	25
Trout, <i>Salmo</i> spp.		
Missouri		
Liver and muscle		
1946–50	3.0 FW	26
1973	0.1–0.3 FW	26
Brook trout, <i>Salvelinus fontinalis</i> , Adirondack lakes (15), New York, whole	<1.0 FW	27
Lake trout, <i>Salvelinus namaycush</i>		
Muscle		
British Columbia	1.1–10.5 FW	1
Ontario	0.3–1.3 FW	1
Quebec	0.3–1.2 FW	1
New York, Cayuga Lake, 1991, age in years		
1	0.19 DW	67
3	0.40 DW	67
5	0.58 DW	67
10	0.70 DW	67
12	0.75 DW	67
Whole, Lake Ontario, age 4 years		
1977	0.24 FW	76
1984	0.15 FW	76
1988	0.12 FW	76

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Scotland, 1982–87, sludge disposal sites vs. reference sites, muscle		
Cod	0.04–0.2 FW vs. 0.05–0.07 FW	88
Flounder, <i>Platichthys flesus</i>	0.09–0.55 FW vs. 0.1–0.13 FW	88
Plaice	0.06–0.2 FW vs. 0.03–0.1 FW	88
Whiting, <i>Merlangius merlangius</i>	0.03–0.1 FW vs. 0.06–0.08 FW	88
Scotland, Firth of Clyde, 5 species, muscle, 1991–92, Lesser-spotted dogfish, <i>Scyliorhinus caniculus</i> , muscle, Irish Sea, August 1985	0.01–0.07 (0.01–0.25) FW	89
North and NW areas	0.15–2.1 FW	68
Northeast sites	0.3–2.2 FW	68
Southeast sites	0.2–5.6 FW	68
Southwest sites	0.1–2.8 FW	68
Yellowtail kingfish, <i>Seriola grandis</i> , 1977–78, 10 km offshore from Sydney, Australia, muscle	0.15 FW, Max. 1.1 FW	69
Sharks, Australia, 1980		
Muscle, 7 spp.		
<i>Carcharhinus</i> spp.	Max. 4.3 FW	28
<i>Sphyraena</i> spp.	Max. 4.9 FW	28
Sharks, Florida, 1988–92, muscle, methylmercury, 9 species		
All species	0.88 (0.06–2.9) FW	77
4 of 9 species	1.0–2.25 FW	77
Sharks >200 cm total length	33% exceeded 1.0 FW (FDA action level)	77
Statewide survey, 1991, retail markets	1.5 FW	77
Walleye, <i>Stizostedion vitreum vitreum</i>		
Manitoba, man-made reservoir		
Muscle		
Preimpoundment (1971–77)	0.2–0.3 FW	16
Postimpoundment (1978–92)	0.6–0.8 FW	16
Washington State, Columbia River, 1994		
Muscle	0.11–0.44 FW	73
Sediments	0.05–2.8 DW	73
Wisconsin, 1980–82, muscle, low pH lakes vs. high pH lakes		
Age 4 years	0.6 FW vs. 0.2 FW	71
Age 5 years	0.8 FW vs. 0.25 FW	71
Age 7 years	1.25 (0.8–1.7) FW vs. 0.4 (0.3–0.5) FW	71
Wisconsin, 1980–89, skin-on fillets, low buffering capacity lakes vs. high buffering capacity lakes		
Total fish length		
25–35 cm	0.3 FW vs. 0.2 FW	72
40–45 cm	0.6 FW vs. 0.3 FW	72
50–55 cm	1.1 FW vs. 0.5 FW	72
>65 cm	1.5 cm vs. 0.5 FW	72
Wisconsin, 1990–91, 34 northern lakes, muscle	0.3–1.0 FW, about 50% exceeded the fish consumption advisory of 0.5 mg Hg/kg FW muscle set by the Wisconsin Department of Natural Resources	70
Thailand, various species, muscle		
Near chloralkali plant		
No waste water system, 1975–76	0.32–3.6 FW	20
With waste water system, 1978	0.1–1.4 FW	20
Control location	0.01–0.3 FW	20

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Tunas, 1981, 5 spp., muscle	1.0–6.3 FW	29
Tunas, Indian Ocean, 1985–86, blood, total mercury vs. methylmercury		
Yellowfin, <i>Thunnus albacares</i>	0.08 (0.003–0.27) FW vs. 0.01 (0.00–0.03 FW	74
Big-eye tuna, <i>Thunnus obesus</i>	0.8 (0.5–1.3) FW vs. 0.5 (0.2–0.7) FW	74
Various species		
Muscle		
From unpolluted areas	0.04–0.15 FW	21
From moderately Hg-polluted areas	>1.0 FW	21
From highly polluted areas	10.0–24.0 FW	21
Swordfish, <i>Xiphias gladius</i>		
Muscle		
NW Atlantic	2.0 FW; 8.1 DW	1
Peru	1.1–1.8 FW	1
Pacific	0.5–1.7 FW	1
W. Atlantic	0.05–4.9 FW	1
Gibraltar Strait	1.0–2.0 FW	1
Azores, November 1987, males vs. females		
<125 cm length	0.4 FW vs. 0.25 FW	75
>125 cm length	1.9 FW, Max. 4.9 FW vs. 1.1 FW	75
AMPHIBIANS AND REPTILES		
Alligator, <i>Alligator mississippiensis</i> , from mercury-contaminated areas; total mercury, 1994–95, Florida Everglades vs. Savannah River SC		
Blood	No data vs. 2.2 FW	55
Dermal scutes	5.8 DW vs. 4.6 DW	55
Kidney	36.4 DW vs. No data	55
Liver	41.1 DW vs. 17.7 DW	55
Muscle	5.6 DW vs. 4.1 DW	55
European toad, <i>Bufo bufo</i>		
Yugoslavia		
Control area		
Liver	1.5 FW	1
Kidney	1.2 FW	1
Lung	0.2 FW	1
Muscle	0.2 FW	1
Egg	0.06 FW	1
Polluted mercury mining area		
Liver	21.8–25.5 FW	1, 30
Kidney	22.8–24.0 FW	1, 30
Lung	1.7 FW	1, 30
Muscle	2.3–2.9 FW	1, 30
Egg	2.3 FW	1, 30
Loggerhead sea turtle, <i>Caretta caretta</i>		
Egg	0.01 FW	31
Crocodile, <i>Crocodylus acutus</i>		
Egg	0.7 FW	31
Bullfrog, <i>Rana catesbeiana</i>		
Lake St. Clair		
Carcass	0.1 FW	1
Liver	0.3 FW	1

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
South Carolina; 1997; tadpoles		
With digestive tract		
Body	0.24 DW; 0.05 FW	174
Tail	0.05 DW; 0.01 FW	174
Whole	0.18 DW; 0.04 FW	174
Without digestive tract		
Body without gut	0.1 DW	174
Tail	0.09 DW	174
Digestive tract	0.89 DW	174
Whole	0.14 DW	174
Leopard frog, <i>Rana pipiens</i>		
Lake St. Clair		
Carcass	0.1–0.2 FW	1
Liver	0.5–1.1 FW	1
Florida		
Liver	0.1 FW	1
Frog, <i>Rana temporaria</i>		
Yugoslavia, 1975		
From Hg-mining area		
Liver	21.0 FW	30
Kidney	16.2 FW	30
Muscle	3.4 FW	30
Egg	1.3 FW	30
From control area		
All tissues	<0.08 FW	30

BIRDS

Goshawk, <i>Accipiter gentilis</i>		
Sweden		
Feather		
1860–1946	2.2 FW	1
1947–65	29.0 FW	1
1967–69	3.1–5.1 FW	1
Finnish sparrowhawk, <i>Accipiter nisus</i>		
Feather		
Finland		
1899–1960	4.1 (2.1–7.7) DW	32
1961–70	11.1 (2.3–42.0) DW	32
1971–82	7.4 (1.0–29.0) DW	32
Germany		
1972–73	4.9 (0.4–20.3) DW	32
Norway		
1976	2.0–20.0 DW	32
Sharp-shinned hawk, <i>Accipiter striatus</i>		
Eastern USA; liver; 1991 vs. 1993	0.98 (0.06–2.2) FW vs. 0.12 FW	91
Western grebe, <i>Aechmophorus occidentalis</i> ; California		
Lake Berryessa		
1982, found dead		
Kidney	20.2 FW	92
1983, normal appearing		
Kidney	2.5 (1.1–9.0) FW	92
Liver	5.2 (2.7–11.8) FW	92
1986, found dead		
Kidney	3.7 (2.1–6.5) FW	92
Liver	7.9 (2.7–23.3) FW	92

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Clear Lake, site of abandoned mercury mine		
1984, liver	6.1 (3.7–9.8) FW	92
1992		
Brain	0.3 FW	175
Muscle	1.1 FW	175
Kidney	2.1 FW	175
Liver	2.7 FW	175
Wood duck, <i>Aix sponsa</i>		
Tennessee, 1972–73		
Juveniles		
Liver	0.4 (0.1–1.1) FW	33
Muscle	0.1 (0.05–0.4) FW	33
Fat	0.1 (0.01–0.4)	33
Adults		
Liver	0.2 (0.1–0.3) FW	33
Muscle	0.08 (0.06–0.11) FW	33
Fat	0.06 (0.01–0.11) FW	33
Blue-winged teal, <i>Anas discors</i>		
Muscle		
Lake St. Clair	0.1–2.3 FW	1
Ontario	3.8–10.4 FW	1
Wisconsin	0.0–0.5 FW	1
Illinois	0.05 FW	1
Antarctic, February–March 1989		
Adelie penguin, <i>Pygoscelis adeliae</i> ; muscle vs. liver	Max. 0.7 DW vs. Max. 2.0 DW	93
Chinstrap penguin, <i>Pygoscelis antarctica</i> ; feces	1.6 DW	93
Gentoo penguin, <i>Pygoscelis papua</i> , liver	34.7 DW	93
Golden eagle, <i>Aquila chrysaetos</i>		
Scotland, 1981–86, unhatched eggs		
Eastern district	ND	94
Western coastal district	0.39 (0.1–0.1.4) DW	94
Western inland district		
25 of 27 eggs	ND	94
2 of 27 eggs	0.21 DW, 0.56 DW	94
Great blue heron, <i>Ardea herodius</i>		
Liver		
Lake St. Clair	97.0 (14.6–175.0) FW	1
New Brunswick	4.5 FW	1
Lake Erie	0.7–4.3 FW	1
Wisconsin	0.5 (0.2–1.1) FW	1
Clear Lake, California; 1993; distance from abandoned mercury mine; 8 km vs. 23 km		
Blood	1.3 FW vs. 1.2 FW	176
Diet	0.9 FW vs. 0.5 FW	176
Feathers	2.2 FW vs. 3.1 FW	176
Kidney	1.1 FW vs. 1.1 FW	176
Liver	1.4 FW vs. 1.3 FW	176
Great white heron, <i>Ardea herodias occidentalis</i> ; Florida, 1987–89; radiotagged and recovered soon after death; liver		
Dead from known acute causes	1.8 (0.6–4.0) FW	95
Dead from chronic multiple causes	9.8 (2.9–59.4) FW	95
Dead birds with signs of kidney disease and gout	>25 FW	95
Birds		
Antarctic		
Liver		
1977–79		
4 spp.	0.5–1.3 FW	34
3 spp.	2.7–2.9 FW	34

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
1980		
5 spp.	0.5–2.1 FW	35
Belgium, 1970–81		
Liver, 30 spp.		
Aquatic birds	0.11–35.0 FW	36
Terrestrial birds	ND–14.0 FW	36
Hawaiian, 1980		
Egg, 3 spp.	0.12–0.36 FW	37
North America		
Feather		
From areas with mercury-treated seed dressing		
Seed-eating songbirds	1.6 DW	21
Upland game birds	1.9 DW	21
From untreated areas		
Seed-eating songbirds	0.03 DW	21
Upland game birds	0.35 DW	21
Northwestern Ontario, Canada, from a heavily mercury-contaminated freshwater system		
Liver		
Scavengers	57 (13.8–121) FW	38
Fish eaters	39 (1.7–91) FW	38
Omnivores	26 (9.5–53) FW	38
Invertebrate feeders	12 (3.2–28) FW	38
Vegetarians	6 (1.9–28) FW	38
Diving ducks	Max. 175	21
Muscle		
Diving ducks	Max. 23.0 FW	21
Mallard, <i>Anas platyrhynchos</i>	Max. 6.1 FW	21
Eagle-owl, <i>Bubo bubo</i> , Sweden; 1963–76; feather		
Inland populations	3.2 DW	39
Coastal populations	6.5 DW	39
1829–1933	0.3–3.6 FW	1
1964–65	12.8–41.0 FW	1
Cattle egret, <i>Bubulcus ibis</i> ; eggs; Egypt, 1986; declining colony between 1977 and 1984	0.48 (0.28–0.84) DW	96
California, Clear Lake (mercury-contaminated site); feathers		
Western grebe, <i>Aechmophorus occidentalis</i> , adults	9.8 DW	177
Great blue heron, <i>Ardea herodias</i> ; adults	6.1 DW	177
Turkey vulture, <i>Cathartes aura</i> ; adults	1.3 DW	177
Osprey, <i>Pandion haliaetus</i>		
Adults	20.0 DW	177
Juveniles	5.3 DW	177
Juveniles from reference sites	2.3 DW	177
Great skua, <i>Catharacta skua</i>		
Total mercury, adults vs. chicks, feather	7.0 (1.0–32.4) FW vs. 1.3 (0.7–2.4) FW	97
Total mercury vs. inorganic mercury, adults		
Kidney	9.7 DW vs. 5.0 DW	97
Liver	11.6 DW vs. 6.2 DW	97
Muscle	2.3 DW vs. 2.3 DW	97
Diving ducks; California; 1989; livers; Tomales Bay vs. Suisin Bay		
Greater scaup, <i>Aythya marila</i>	19 (5–66) DW vs. 6 (3–11) DW	173
Surf scoter, <i>Melanitta perspicillata</i>	19 (3–35) DW vs. 10 (5–21) DW	173
Ruddy duck, <i>Oxyura jamaicensis</i>	6 (4–9) DW vs. 4 (2–7) DW	173

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
England, 1963–90, liver		
Grey heron, <i>Ardea cinerea</i>		
1963–70	44 (20–96) FW	98
1971–75	19 (8–49) FW	98
1976–80	18 (7–46) FW	98
1981–85	10 (2–39) FW	98
1986–90	12 (4–34) FW	98
Sparrowhawk, <i>Accipiter nisus</i>		
1963–70	4.6 (2.6–8.3) FW	98
1971–75	5.6 FW	98
1976–80	3.5 FW	98
1981–85	2.3 FW	98
1986–90	1.0 (0.2–6.3) FW	98
Kestrel, <i>Falco tinnunculus</i>		
1963–70	5.8 FW	98
1976–80	1.3 FW	98
1986–90	0.2 FW	98
Common loon, <i>Gavia immer</i>		
Canada, central Ontario; 24 lakes; July–August 1992		
Breeding adults		
Blood	2.1 (0.9–4.3) FW	179
Feathers	13.3 (7.6–21.0) FW	179
Chicks		
Blood	0.14 (0.04–0.6) FW	179
Feathers	2.3 (1.4–3.4) FW	179
Eastern Canada, tissues from freezer archives		
Kidney	15.0 DW	180
Liver	19.0 DW	180
Muscle	2.9 DW	180
New England; 1990–94; found dead; liver		
Females		
Total Hg	46 (10–100) FW	181
MethylHg	3.9 (2.6–5.4) FW	181
Males		
Total Hg	56 (11–187) FW	181
MethylHg	4.3 (2.8–9.1) FW	181
Chicks		
Total Hg	1.4 FW	181
MethylHg	0.3 FW	181
Northeastern USA, found dead, breast feathers		
Adults	20.2 DW	99
Immatures	9.7 DW	99
Females	12.4 DW	99
Males	7.7 DW	99
USA and Canada; 1991–96; summers		
Adults		
Blood, whole		
Males	1.9 (0.4–7.8) FW	178
Females	1.5 (0.1–6.7) FW	178
Feathers		
Males	12.7 (4.1–36.7) FW	178
Females	9.4 (2.8–21.1) FW	178
Juveniles, age 3–6 weeks		
Blood	0.16 (0.03–0.78) FW	178
Feathers	3.8 (0.6–13.6) FW	178

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Wisconsin, summer 1991		
Lakes <pH 6.3		
Clotted blood	5 DW	100
Feathers	12 DW	100
Lakes with pH >7.0		
Clotted blood	2 DW	100
Feathers	9 DW	100
Wisconsin		
Adults; 1992–93		
Blood		
Lowest quartile	0.6–0.9 FW	182
Highest quartile	1.9–4.2 FW	182
Feathers		
Lowest quartile	3.0–9.6 FW	182
Highest quartile	13.0–21.0 FW	182
Eggs; 1993–96	0.9 FW	182
Peregrine, <i>Falco peregrinus</i>		
Feather		
1834–1849	2.5 DW	21
1941–65	>40.0 DW	21
Swedish gyrfalcon, <i>Falco rusticolus</i> ; nestlings, feather		
Percent aquatic birds in diet		
None	0.035 FW	40
4.8% biomass	0.66 FW	40
10.6% biomass	1.22 FW	40
Florida; wading birds; 1987–90		
Nestlings, feathers		
Roseate spoonbill, <i>Ajaia ajaja</i>	2.0 (0.4–5.7) DW	51
Great blue heron, <i>Ardea herodias</i>	3.5 (1.8–7.7) DW	51
Great egret, <i>Casmerodius albus</i>	7.1 (1.6–15.0) DW	51
Great white heron, <i>Ardea herodias occidentalis</i> ; feathers vs. liver		
Nestlings	4.7 (1.0–9.1) DW vs. (3.9–9.1) DW	51
Juveniles	6.7 (2.7–15.0) DW vs. (6.2–8.1) DW	51
Adults	8.2 (4.1–14.0) DW vs. 6.2 DW	51
Germany		
North Sea Coast, feathers, pre-1940 vs. post-1941		
Herring gull, <i>Larus argentatus</i>		
Adults	4.6 (1.0–7.8) FW vs. 7.9 (2.1–21.2) FW	102
Juveniles	2.0 FW vs. 4.3 FW	102
Common tern, <i>Sterna hirundo</i>		
Adults	1.0 (0.2–2.3) FW vs. 3.5 (0.4–13.9) FW	102
Juveniles	2.0 (0.4–4.9) FW vs. 4.8 (1.5–18.4) FW	102
1991		
Herring gull, adults		
Eggs	Max. 2.8 FW	101
Down	Max. 58.0 FW	101
Liver	Max. 4.0 FW	101
Black-headed gull, <i>Larus ridibundus</i> , chick body feathers		
Common tern		
Eggs	Max. 4.0 FW	101
Down	Max. 20.0 FW	101
Chick body feathers	Max. 16.0 FW	101

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Bald eagle, <i>Haliaeetus leucocephalus</i>		
Egg		
Canada, BC, 1990–92	0.08–0.29 (0.07–0.40) FW	105
Maine (highest concentrations Nationwide)		
1974	0.35–0.58 FW	41
1975	0.22–0.63 FW	41
1976	0.22–0.66 FW	41
1977	0.28–0.90 FW	41
1978	0.30 FW	41
1979	0.84–1.2 FW	41
1974–79 vs. 1980–84	0.39 FW vs. 0.41 FW	104
Maryland, 1973–79 vs. 1980–84	0.04 FW vs. 0.06 FW	104
Virginia, 1976–79 vs. 1981–84	0.07 FW vs. 0.08 FW	104
Wisconsin, 1976–83	0.13–0.14 FW	104
Florida, 1991–93		
Adults, feathers	9 (0.1–35) FW	103
Nestlings		
Blood	0.2 (0.02–0.6) FW	103
Feather	3.2 (0.8–14.3) FW	103
Found dead, liver		
Adults	3.2 FW, Max. 12.2 FW	103
Subadults	2.6 (0.4–5.4) FW	103
Nestlings	0.4 (0.1–1.0) FW	103
Great Lakes region, 1985–89, feathers		
Adult primaries	21 (3.6–48.0) DW	106
Adult secondaries	23 (5.3–66.0) DW	106
Adult retrices	19 (5–46) DW	106
Adult body	21 (0.2–48.0) DW	106
Nestlings, all feathers	9 (1.5–27.0) DW	106
Kenya, Lake Nakura, 1970 vs. 1990		
Pelican, <i>Pelecanus onocrotalus</i>		
Kidney	0.03 FW vs. 0.03 FW	107
Liver	0.02 FW vs. 0.06 FW	107
Lesser flamingo, <i>Phoenicopterus minor</i>		
Kidney	0.10 FW vs. 0.04 FW	107
Liver	0.37 FW vs. 0.26 FW	107
Herring gull, <i>Larus argentatus</i>		
Denmark, 1975–76		
Liver	0.6 (0.08–2.3) FW	42
Germany, Wadden Sea		
Egg	1.4 DW	108
Ovary	1.9 DW	108
Males vs. females		
Feather	6.4 DW vs. 4.9 DW	108
Liver	4.7 DW vs. 4.4 DW	108
Muscle	2.6 DW vs. 2.0 DW	108
Great Lakes, eggs		
1973–76	0.22–0.72 FW	109
1981–83	0.17–0.73 FW	109
1985	0.14–0.36 FW	109
1992	0.14–0.20 FW	109
Ontario		
Egg	1.5–15.8 FW	1
Albumen	16.1–22.7 FW	1
Yolk	3.4–3.5 FW	1

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
California gull, <i>Larus californicus</i>		
Lahontan Reservoir, Nevada, 1981		
Muscle	0.4 FW	6
Liver	1.0 FW	6
Egg	0.1–0.2 FW	6
Bonaparte's gull, <i>Larus philadelphia</i> , New Brunswick, Canada; autumn 1978–84		
Feather parts		
Quill	2.3 DW	110
Rachis	3.3 DW	110
Vane	3.5 DW	110
Feather groups		
Secondaries	1.9 DW	110
Wing coverts	2.3 DW	110
Primaries	2.5 DW	110
Retrices	2.8 DW	110
All feathers		
Juveniles	2.0 DW	110
Second-year	2.5 DW	110
Adults	4.1 DW	110
Adults, females vs. males	4.8 DW vs. 3.5 DW	110
Franklin's gull, <i>Larus pipixcan</i> ; Minnesota, 1994		
Feathers, males vs. females	0.84 DW vs. 0.77 DW	111
Eggs	0.14 DW	111
Diet (earthworms)	0.018 DW	111
Common merganser, <i>Mergus merganser</i> ; eastern Canada; tissues from freezer archives		
Kidney	11.0 DW	180
Liver	15.0 DW	180
Muscle	3.0 DW	180
Black-eared kite, <i>Milvus migrans lineatus</i> ; Japan; premoult (April) vs. postmoult		
Bone	0.08 DW vs. 0.07 DW	112
Brain	1.2 DW vs. 0.6 DW	112
Feathers	2.3 DW vs. 2.1 DW	112
Heart	0.4 DW vs. 0.3 DW	112
Kidney	4.7 DW vs. 1.9 DW	112
Liver	2.4 DW vs. 0.9 DW	112
Lung	2.5 DW vs. 0.8 DW	112
Muscle		
Pectoral	1.1 DW vs. 0.4 DW	112
Femoral	0.5 DW vs. 0.1 DW	112
Skin	0.2 DW vs. 0.07 DW	112
Whole body	0.92 DW vs. 0.69 DW	112
Minnesota, 1981; eggs of dead hens found on clutch		
Common goldeneye, <i>Bucephala clangula</i>	0.1 (0.02–0.4) FW	113
Hooded merganser, <i>Lophodytes cucullatus</i>	0.5 (0.1–2.4) FW	113
Wood stork, <i>Mycteria americana</i> ; nestlings; Georgia; April–June 1995; diet		
Atlantic coast colonies		
All prey items	0.4–0.7 DW; 0.1–0.2 FW	184
Freshwater only	1.1 DW; 0.3 FW	184
Inland colonies		
All prey items	0.7–1.0 DW; 0.18–0.28 FW	184

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Osprey, <i>Pandion haliaetus</i>		
Canada; northern Quebec; 1989–91; built up areas vs. natural environments; adults		
Blood, chick	1.9 FW vs. 0.4 FW	185
Brain	1.0 FW vs. 0.2 FW	185
Egg	0.22 FW vs. 0.18 FW	185
Feathers	58.1 DW vs. 16.5 DW	185
Feathers, chick	37.3 DW vs. 7.0 DW	185
Kidney	5.3 FW vs. 0.9 FW	185
Liver	3.6 FW vs. 0.7 FW	185
Muscle	1.8 FW vs. 0.4 FW	185
Stomach contents	0.8 FW vs. 0.3 FW	185
Sweden		
Feather		
1840–1940	3.5–5.0 FW	1
1940–66	>17.0 FW	1
USA, egg		
Idaho, 1973	0.06 FW	115
Florida Everglades, 1973	0.1 (0.04–0.2) FW	115
Maryland		
1973	0.05 FW	114
1986	0.1 (0.07–0.2) FW	114
Massachusetts, 1986–87	0.06 FW	114
New Jersey, 1978	(0.05–0.25) FW	115
Virginia, 1987	0.1 (0.05–0.2) FW	114
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg		
South Carolina	0.3–0.5 FW	1
Florida	0.4 FW	1
California	0.4 FW	1
Liver	0.75 DW	43
Kidney	0.68 DW	43
Feather	0.97 DW	43
Cormorant, <i>Phalacrocorax carbo</i> ; England; 1992–93; eggs that failed to hatch; rapidly-expanding colony	2.6 (1.4–7.7) DW	116
Ring-necked pheasant, <i>Phasianus colchicus</i>		
Muscle		
Denmark	0.01 FW	1
Idaho	0.0–15.0 FW	1
Indiana	0.06 FW	1
Oregon	<0.5 FW	1
Wyoming	0.2–0.6 FW	1
Colorado	0.04–0.6 FW	1
Utah	0.2 (0.01–2.1) FW	1
California	1.6–4.7 FW	1
Wisconsin	0.01–0.08 FW	1
Illinois	0.02–0.03 FW	1
White-faced ibis, <i>Plegadis chihi</i> ; egg; Carson Lake, Nevada		
1985	Means: 0.22–0.77 DW; 30% had >1.0 DW	117
1986	Means: 0.4–1.1 DW; 55% had >1.0 DW	117

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Great crested grebe, <i>Podiceps cristata</i>		
Sweden, feather		
1865–1940	<10.0 FW	1
1940–66	>14.0 FW	1
Kittiwake, <i>Rissa tridactyla</i> ; Helgoland Island, North Sea; 1992–94; nestlings found dead		
Brain		
Age 1 day	2.0 DW	118
Age 21–40 days	0.44 DW	118
Feathers		
Age 1 day	4.6 DW	118
Age 6–10 days	4.0 DW	118
Age 21–40 days	2.3 DW	118
Liver vs. Kidney		
Age 1 day	2.8 DW vs. 2.0 DW	118
Age 6–10 days	1.8 DW vs. 1.4 DW	118
Age 21–40 days	1.1 DW vs. 0.9 DW	118
Seabirds		
North and northeast Atlantic; from pre-1930s museum skins vs. post-1980; feathers		
Great skua, <i>Catharacta skua</i>	3.7 FW vs. 5.6 FW	171
Atlantic puffin, <i>Fratercula arctica</i>	1.8 FW vs. 4.0 FW	171
Northern fulmar, <i>Fulmaris glacialis</i>	4.0–4.4 FW vs. 1.4–2.9 FW	171
Manx shearwater, <i>Puffinus puffinus</i>	1.3–1.5 FW vs. 3.3–4.2 FW	171
Atlantic gannet, <i>Sula bassana</i>	6.0 FW vs. 7.2 FW	171
Canada, New Brunswick, 9 species, 1978–84		
Brain	0.04–0.36 FW	124
Kidney	0.24–5.3 FW	124
Liver	0.22–7.1 FW	124
Muscle	0.05–0.61 FW	124
Down; chicks; Germany, 1991		
Common tern, <i>Sterna hirundo</i>	5.9 (2.7–10.2) FW	126
Black-headed gull	1.0 (0.1–3.6) FW	126
Herring gull	1.4 (0.4–2.9) FW	126
Eggs, 10 species; Barents Sea, 1993	0.06–0.34 FW	120
Eggs, 15 species; Antarctic and environs; 1978–83	0.02–1.8 FW, Max. 2.7 FW	121
Feathers, 7 species; adults; Azores; 1990–92		
Petrels	12.5–22.1 DW, Max. 35.9 DW	122
Shearwaters	2.1–6.0 DW, Max. 12.4 DW	122
Terns	2.0–2.3 DW, Max. 4.0 DW	122
Feathers, 10 species	1.5–30.7 FW	125
Liver, 9 species	4.9–306.0 DW	119
Liver, 64 species; New Zealand		
Albatrosses, 8 species	17–295 DW	123
Shearwaters, 3 species	0.8–1.3 DW	123
Petrels, 19 species	0.2–140 DW	123
Penguins, 4 species	0.5–2.4 DW	123
Various, 30 species	Max. 6.7 DW	123
Tree swallow, <i>Tachycineta bicolor</i> , eggs, St. Lawrence River Basin, 1991	0.04–0.08 FW	127
Texas, eggs		
Laguna Madre, 1993–94		
Great blue heron, <i>Ardea herodias</i>	0.1 (0.02–0.2) FW	129
Snowy egret, <i>Egretta thula</i>	0.1 (0.05–0.2) FW	129
Tricolored heron, <i>Egretta tricolor</i>	0.1 (0.03–0.2) FW	129
Caspian tern, <i>Sterna caspia</i>	0.6 (0.4–0.8) FW	129

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Black skimmer, <i>Rynchops niger</i> ; Lavaca Bay vs. Laguna Vista	0.5 (0.2–0.8) FW vs. 0.19 (0.05–0.31) FW; nest success lower at Lavaca colony	128
Forster's tern, <i>Sterna forsteri</i> ; Lavaca Bay vs. San Antonio Bay	0.40 FW vs. 0.22 FW; nesting success similar	128
Mourning dove, <i>Zenaidura macroura</i>		
Liver		
Eastern United States	0.07–0.67 FW	1
MAMMALS		
Antarctica; February–March; 1989; marine mammals		
Leopard seal, <i>Hydrurga leptonyx</i>		
Kidney	Max. 6.1 DW	137
Liver	Max. 18.1 DW	137
Muscle	Max. 3.2 DW	137
Stomach contents	Max. 1.2 DW	137
Weddell seal, <i>Leptonychotes weddellii</i>		
Kidney	Max. 15.9 DW	137
Liver	Max. 48.8 DW	137
Muscle	Max. 3.6 DW	137
Crabeater seal, <i>Lobodon carcinophagus</i>		
Kidney	Max. 12.5 DW	137
Liver	Max. 16.3 DW	137
Muscle	Max. 6.2 DW	137
Australian fur seal, <i>Arctocephalus pusillus</i>		
Muscle	0.9 (0.1–1.9) FW	44
Liver	62 (1–170) FW	44
Kidney	0.6 (0.1–1.7) FW	44
Spleen	1.3 (0.0–3.8) FW	44
Brain	0.7 (0.0–2.5) FW	44
Hair	9.6 (1.1–19.8) DW	44
Woodmouse, <i>Apodemus sylvaticus</i>		
Great Britain		
In field with Hg-treated wheat seed		
Liver	Max. 7.1 FW	1
Kidney	Max. 11.7 FW	1
In chloralkali area		
Liver	Max. 0.5 FW	1
Kidney	Max. 1.3 FW	1
Control area		
Liver	Max. 0.07 FW	1
Kidney	Max. 0.3 FW	1
Fin whale, <i>Balaenoptera physalus</i> ; Spain and Iceland; 1983–86; total vs. organic mercury; maximum concentrations		
Kidney	3.3 FW vs. 0.4 FW	130
Liver	5.4 FW vs. 1.4 FW	130
Muscle	1.2 FW vs. 0.9 FW	130
Roe deer, <i>Capreolus capreolus</i> ; males, Poland; 1977–78		
From Hg-contaminated habitat		
Muscle	0.047 FW	45
Liver	0.036 FW	45
Kidney	0.053 FW	45
From uncontaminated area		
Muscle	0.013 FW	45
Liver	0.015 FW	45

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Kidney	0.027 FW	45
Serow (feral bovine ruminant), <i>Capricornis crispus</i> ; Japan; 1981–83		
All tissues	Always <0.02 FW	131
Fleece		
Fawns	0.37 FW	131
Yearlings	0.38 FW	131
Adults, up to age 10 years	0.35 FW	131
Adults, age 10–17.5 years	0.44 FW	131
Beaver, <i>Castor canadensis</i>		
Wisconsin, 1972–75		
All tissues	<0.09 FW	46
Red deer, <i>Cervus elaphus</i> ; East Slovakia; muscle	0.1 (0.03–0.4) FW	132
Florida panther, <i>Felis concolor coryi</i>		
Found dead, 1989		
Blood	21.0 FW	133
Hair	130.0 FW	133
Liver	110.0 FW	133
1978–91		
Liver		
Southeast FL vs. Southwest FL; young panthers	25.8 FW vs. 0.3 FW	133
Southwest FL; older vs. younger panthers	14.6 FW vs. 0.3 FW	133
Whole blood, females		
1.46 kittens per female per year	0.0–0.25 FW	133
0.167 kittens per female per year	>0.5 FW	133
Domestic cat, <i>Felis domesticus</i>		
Ate fish from below chloralkali plant, NW Ontario		
Brain	6.9–16.4 FW	1
Pancreas	4.3–4.9 FW	1
Kidney	0.8–13.4 FW	1
Liver	14.2–67.1 FW	1
Fur	121.0–392.0 FW	1
Humans, <i>Homo sapiens</i>		
Canada; aboriginal peoples; 1970–92; methylmercury		
Blood; 514 communities; 38,571 individuals		
23%	>0.02 FW	136
1.6%	>0.1 FW	136
0.2%	>0.2 FW	136
Maternal	Max. 0.086 FW	136
Umbilical cord blood; 2405 samples		
21.8%	>0.02 FW	136
Maximum	0.224 FW	136
Hair; Faroe Islands; number of fish meals per week		
None	0.8 DW; Max. 2.0 DW	134
1	1.6 DW; Max. 3.7 DW	134
2	2.5 DW; Max. 4.7 DW	134
4	5.2 DW; Max. 8.0 DW	134
Whole blood		
Normal	0.001–0.008 FW	134
High fish consumers	0.2 FW	134
Urine		
Normal	0.002–0.005 FW	134
Women using skin-lightening creams containing 5–10% mercuric ammonium chloride		
During use	0.109 FW	134
Discontinued use	0.006 FW	134

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Diet; Canada; adults		
Total intake, in µg daily	7.7 (= 0.11 µg/kg BW daily in 70-kg individual)	135
Absorbed dose, in µg daily	5.3 (= 0.076 µg/kg BW daily in 70-kg individual)	135
River otter, <i>Lutra canadensis</i>		
Michigan; 1987–89		
Kidney	1.5 (<0.3–6.2) DW	141
Liver	2.2 (<0.3–7.0) DW	141
Canada; Ontario; 1983–85; trapped; English River vs. Sudbury		
Brain	3.2 FW vs. 0.2 FW	138
Kidney	3.5 FW vs. 0.6 FW	138
Liver	3.5 FW vs. 0.9 FW	138
Muscle	1.1 FW vs. 0.3 FW	138
New York state; 1982–84; liver	1.3–2.2 FW	139
Winnipeg River, Manitoba, Canada, 1979–81		
Males		
Liver	Max. 8.9 FW	47
Kidney	Max. 6.5 FW	47
Brain	Max. 3.1 FW	47
Females		
Liver	Max. 3.9 FW	47
Kidney	Max. 1.8 FW	47
Brain	Max. 0.6 FW	47
Georgia; 1976–77; lower coastal plain vs. Piedmont		
Hair	24.2 FW vs. 15.2 FW	140
Liver	7.5 FW vs. no data	140
Muscle	4.4 FW vs. 1.5 FW	140
Wisconsin, 1972–75		
Brain	0.7 FW	46
Muscle	1.4 FW	46
Liver	3.3 (Max. 24) FW	46
Kidney	8.5 (Max. 21) FW	46
Fur		
Industrial area	9.5 (Max. 63) FW	46
Nonindustrial area	3.8 FW	46
Otter, <i>Lutra lutra</i> ; Denmark; 1980–90; liver		
Adults	4 (0.9–12) FW	142
Juveniles	0.3 (0.03–2) FW	142
Subadults	1.6 (0.2–6) FW	142
Bobcat, <i>Lynx rufus</i>		
Hair		
Georgia USA		
Upper coastal plain	13.1 DW	1
Lower coastal plain	0.9 DW	1
Mink, <i>Mustela vison</i>		
Canada; Ontario; 1983–85; English River vs. Sudbury		
Brain	0.5 FW vs. 0.4 FW	138
Kidney	2.1 FW vs. 0.6 FW	138
Liver	2.0 FW vs. 0.4 FW	138
Muscle	0.8 FW vs. 0.4 FW	138
New York; 1982–84; 8 locations; liver	0.9–3 (0.6–6) FW	139
Wisconsin, 1972–75		
Brain	0.5 FW	46
Muscle	1.3 FW	46

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Liver	2.1 (Max. 17) FW	46
Kidney	2.3 (Max. 12) FW	46
Fur		
Industrial area	10.5 (Max. 41) FW	46
Nonindustrial area	3.0 FW	46
Winnipeg River, Manitoba, Canada, 1979–81		
Males		
Liver	Max. 9.9 FW	47
Kidney	Max. 6.4 FW	47
Brain	Max. 2.4 FW	47
Females		
Liver	Max. 10.7 FW	47
Kidney	Max. 8.1 FW	47
Brain	Max. 2.1 FW	47
Tennessee; Oak Ridge vs. reference site; hair; adults	104.0 DW vs. Max. 14.7 DW	152
Norway; winter 1989–90; Arctic coast; maximum values		
Grey seal, <i>Halichoerus grypus</i>		
Brain	2.0 FW	143
Kidney	16.0 FW	143
Liver	48.3 FW	143
Harp seal, <i>Phoca groenlandica</i>		
Brain	0.1 FW	143
Kidney	0.4 FW	143
Liver	1.1 FW	143
Ringed seal, <i>Phoca hispida</i>		
Brain	0.4 FW	143
Kidney	0.5 FW	143
Liver	0.7 FW	143
Harbor seal, <i>Phoca vitulina</i>		
Brain	2.0 FW	143
Kidney	8.7 FW	143
Liver	16.0 FW	143
White-tailed deer, <i>Odocoileus virginianus</i> ; Alabama; 1992–93		
Kidney	0.5 (0.3–0.7) FW	144
Liver	0.1 (0.05–0.1) FW	144
Musk rat, <i>Ondatra zibethicus</i>		
Wisconsin, 1972–75		
All tissues	<0.06 FW	46
Tennessee; Oak Ridge vs. reference sites; hair		
Adults	4 (0.08–23) DW vs. 0.1–0.2 (0.03–0.6) DW	152
Juveniles	1.6 DW vs. Max. 0.2 DW	152
Sheep, <i>Ovis aries</i>		
Grazing for 23 months on Hg-contaminated field		
Diet (grass)		
Winter	6.5 DW	48
Summer	1.9 DW	48
Lung	Max. 4.0 FW	48
Kidney	Max. 3.1 FW	48
Liver	Max. 2.4 FW	48
Brain	Max. 1.1 FW	48
Flesh	<1.0 FW	48
Harp seal, <i>Phoca groenlandica</i> ; Gulf of St. Lawrence; 1984		
Mother		
Kidney	0.8 FW; 3.5 DW	145
Liver	10.4 FW; 34.7 DW	145

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Milk	0.0065 (0.0026–0.010) FW	145
Muscle	0.38 FW; 1.3 DW	145
Pup, <3 weeks-old		
Kidney	0.29 FW; 1.2 DW	145
Liver	0.32 FW; 1.1 DW	145
Muscle	0.14 FW; 0.51 DW	145
Baikal seal, <i>Phoca sibirica</i> ; Lake Baikal; Russia; 1992		
All seals		
Kidney	1.8 (0.6–3.6) FW	146
Liver	2.3 (0.2–9.1) FW	146
Muscle	0.2 (0.1–0.7) FW	146
Male, 19.5 years old		
Brain, intestine, fat, bone, skin	0.01–0.1 FW	146
Liver, pancreas, spleen, lung, stomach, heart, muscle, whole	0.11–1.0 FW	146
Hair	4.3 FW	146
Female, 13.5 years old		
Liver	1.2 FW	146
Kidney	1.7 FW	146
Hair	3.0 FW	146
Other tissues	<1.0 FW	146
Juveniles vs. Adults		
Hair	2.1 FW vs. 2.5 FW	186
Kidney	1.0 FW vs. 2.1 FW	186
Liver	0.7 FW vs. 2.8 FW	186
Muscle	0.1 FW vs. 0.3 FW	186
Harbor seal, <i>Phoca vitulina richardii</i>		
Liver		
California	269 (81–700) FW	1
Oregon	0.3–68 FW	1
Washington	1.3–60 FW	1
Pribilof Islands	0.6–9 FW	1
Harbor porpoise, <i>Phocoena phocoena</i> ; North Sea; 1987–90; maximum values; juveniles vs. adults		
Kidney	6 DW vs. 23 DW	147
Liver	6 DW vs. 504 DW	147
Muscle	3 DW vs. 24 DW	147
Sperm whale; <i>Physeter macrocephalus</i> ; southern Australia; 1976; muscle		
Breeding vs. non-breeding females	10 (8–12) DW vs. 6 (0.8–10) DW	148
All females	7 (0.8–12) DW	148
Males	6 (0.9–12) DW	148
Raccoon, <i>Procyon lotor</i>		
Alabama; 1992–93		
Kidney	0.24 FW	149
Liver	0.41 FW	149
Clear Lake, California; 1993; distance from abandoned mercury mine; 8 km vs. 23 km		
Blood	0.4 FW vs. 0.2 FW	176
Fur	22.0 FW vs. 4.0 FW	176
Liver	3.3 FW vs. 7.0 FW	176
Wisconsin, 1972–75		
Brain	<0.02 FW	46
Muscle	0.08 FW	46
Kidney	1.4 FW	46
Liver	2.0 FW	46

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Fur	3.8 FW	46
Gray squirrel, <i>Sciurus carolinensis</i> ; hair; Florida; 1974		
Rural areas	0.43 FW	1
Urban		
Age 0–1	1.0 (0.1–7) FW	1
Age >2	3 (0.3–9) FW	1
Dolphin, <i>Stenella attenuata</i> ; eastern tropical Pacific Ocean; 1977–85		
Blood	0.4 FW	150
Brain	2.0 FW	150
Blubber	7.6 FW	150
Kidney	5.6 FW	150
Liver	62.3 FW; Max. 217.5 FW	150
Muscle	2.2 FW	150
Pancreas	6.6 FW	150
Striped dolphin, <i>Stenella coeruleoalba</i>		
Adults, Japan, 1977–80		
Muscle		
Total Hg	15.2 FW	49
Methyl Hg	5.3 FW	49
Liver		
Total Hg	205.0 FW	49
Methyl Hg	7.0 FW	49
Kidney		
Total Hg	14.7 FW	49
Methyl Hg	3.2 FW	49
Whole body		
Age 1 year		
Total Hg	0.8 FW	50
Methyl Hg	0.4 FW	50
Age 3 years		
Total Hg	1.8 FW	50
Methyl Hg	1.0 FW	50
Age 4 years		
Total Hg	3.0 FW	50
Methyl Hg	1.5 FW	50
Age 14 years		
Total Hg	4.5 FW	50
Methyl Hg	2.6 FW	50
Age 20 years		
Total Hg	10.7 FW	50
Methyl Hg	3.5 FW	50
Found stranded on French Atlantic coast vs. Mediterranean coasts; 1972–80		
Intestine	Max. 23.6 FW	151
Kidney	7 FW vs. 30 FW; Max. 179 FW	150, 151
Liver	52 FW vs. 346 FW; Max. 1544 FW	150, 151
Melon fat	0.5 FW vs. 2 FW	150
Muscle	4 FW vs. 28 FW; Max. 81 FW	150, 151
Stomach	Max. 32 FW	151
Wild boar, <i>Sus scrofa scrofa</i> ; East Slovakia; muscle	0.02 (0.0–0.1) FW	132
Red fox, <i>Vulpes vulpes</i>		
Georgia, USA, fur		
Upper coastal plain	2.3 DW	1
Lower coastal plain	0.5 DW	1

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Wisconsin, 1972–75		
Fur	0.6 FW	46
Other tissues	<0.14 FW	46
Brown bear, <i>Ursus arctos</i> ; Slovak Republic; 1988–90		
Fat	Max. 0.06 FW	153
Kidney	0.2 FW; Max. 0.9 FW	153
Liver	0.04 FW; Max. 0.8 FW	153
Muscle	0.004 FW; Max. 0.04 FW	153
Polar bear, <i>Ursus maritimus</i>		
Alaska; 1972; total mercury; young vs. adults		
Northern area		
Liver	22.4 FW vs. 38.1 FW	154
Muscle	0.15 FW vs. 0.19 FW	154
Western area		
Liver	3.9 FW vs. 4.8 FW	154
Muscle	0.04 FW vs. 0.04 FW	154
Greenland; adults; hair		
NW Greenland; 1978–89	8 (5–14) DW	155
Eastern Greenland; 1984–89	4.6 (2.5–8.8) DW	155
Svalbard; 1980; recently-molted	2.0 (1.0–4.6) DW	155
California sea lion, <i>Zalophus californianus</i>		
Liver		
Mother	73–1026 DW	1
Pup	0.9–16 DW	1
Kidney		
Mother	4–43 DW	1
Pup	0.6–6.7 DW	1
INTEGRATED STUDIES		
Adriatic Sea; mercury-contaminated area vs. reference site; various seafood products of commerce; edible portions		
Total mercury	0.33 FW, Max. 1.9 FW vs. 0.15 FW, Max. 0.5 FW	156
Methylmercury	0.16 FW, Max. 0.8 FW vs. 0.13 FW, Max. 0.5 FW	156
Antarctica; Terra Nova Bay; 1989–91		
Sediments	0.012 DW	172
Phytoplankton	0.04 DW	172
Invertebrates	0.07–0.39 (0.02–1.2) DW	172
Fish, 4 species		
Muscle	0.3–0.8 (0.01–1.8) DW	172
Liver	0.2–0.5 (0.1–0.8) DW	172
Kidney	0.3–1.0 (0.1–2.6) DW	172
Gills	0.06–0.4 (0.01–1.0) DW	172
Gonads	0.2–0.3 (0.01–0.4) DW	172
Birds		
Petrel, <i>Pagodroma nivea</i>		
Eggs	0.6 DW	172
Feathers	0.5 DW	172
Skua, <i>Catharacta maccormicki</i>		
Eggs	1.6 DW	172
Feathers	2.9 DW	172
Guano	0.2 DW	172
Chick plumage	1.9 DW	172

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Adelie penguin, <i>Pygoscelis adeliae</i>		
Egg	0.3 DW	172
Feathers	0.8 DW	172
Guano	0.2 DW	172
Chick plumage	0.4 DW	172
Stomach contents	0.08 DW	172
Muscle	0.6 DW	172
Liver	1.6 DW	172
Kidney	1.2 DW	172
Brain	0.4 DW	172
Testis	0.4 DW	172
Weddell seal, <i>Leptonychotes weddelli</i> , adult		
Muscle	1.8 DW	172
Liver	44.0 DW	172
Spleen	24.0 DW	172
Pancreas	1.5 DW	172
Brazil; Madeira River; gold mining area; maximum values		
Sediments	157.0 DW	157
Fish muscle	2.7 FW	157
Human hair	26.7 DW	157
Air ($\mu\text{g}/\text{m}^3$)	292	157
Brazil; gold mining site; 1992		
Sediments	Max. 0.04 DW	158
Soil	Max. 0.04 DW	158
Fish muscle		
Spotted catfish, <i>Pseudoplatystoma coruscans</i>	0.3 FW, Max. 1 FW	158
Black river piranha, <i>Pygocentrus nattereri</i>	0.3 (0.1–0.5) FW	158
Bird feather		
Black vulture, <i>Coragyps atratus</i>	6.2 FW	158
Crested caracara, <i>Polyborus plancus</i>	6.8 FW	158
Brazil; Amazon gold mining region		
Water	Max. 0.008 FW	159
Fish muscle	0.04–0.61 FW (87–100% organic mercury)	159
Humans (reference site)		
Blood	Max. 0.065 FW (Max. 0.010 FW)	159
Hair	Max. 32.0 FW (Max. <2 FW)	159
Urine	Max 0.156 FW (Max. 0.007 FW)	159
Cattle and pigs		
Blood	0.012–0.015 FW	159
Hair	0.1–1.3 FW	159
Canada; northern Quebec; 1989–90; total mercury		
Sediment	Max. 0.18 DW	160
Fish muscle	0.6–0.9 FW	160
Bird muscle	1.0–1.6 FW	160
Mink muscle	2.4 FW	160
Ringed seal		
Brain	0.2 FW	160
Kidney	0.2 FW	160
Liver	5.1 FW	160
Muscle	0.3 FW	160
Beluga whale		
Brain	2.7 FW	160
Liver	20.3 FW	160
Muscle	2.6 FW	160

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Cuba; 1985–87; chlor-alkali plant vicinity		
Terrestrial plant, <i>Mimosa pudica</i> vs. soils; distance from source, in km		
0.0–0.5	2.2 DW vs. 2.6 DW	161
0.6–1.0	0.28 DW vs. 0.12 DW	161
3.1–5.0	0.04 DW vs. 0.21 DW	161
21–180	0.03 DW vs. 0.10 DW	161
Sea urchin, <i>Lytechinus variegatus</i> ; gonads		
Near discharge	0.38 DW	161
Transition area	0.29 DW	161
Control area	0.07 DW	161
Florida; 1995; southern estuaries		
Sediments		
Total Hg	0.02 (0.001–0.22) DW	187
MethylHg	Max. 0.0005 DW	187
Water, filtered		
Total Hg	Max. 0.000007 FW	187
MethylHg	Max. 0.000002 FW	187
Fish muscle, 9 species		
Total Hg	1.4 (0.1–10.1) DW; 0.31 (0.03–2.2) FW	187
MethylHg	1.05 (0.06–4.5) DW; 0.23 (0.01–1.0) FW	187
Greenland; 1983–91		
Molluscs; 5 species; soft parts	0.01–0.02 FW	162
Crustaceans; 6 species; whole	Max. 0.33 FW	162
Fish; 10 species		
Liver	<0.01 FW–0.6 FW	162
Muscle	0.01 FW–0.3 FW	162
Seabirds; 10 species		
Kidney	0.1 FW–2.1 FW	162
Liver	0.04 FW–2.7 FW	162
Muscle	0.02 FW–0.67 FW	162
Marine mammals		
Seals, 4 species		
Kidney	0.09 FW–3.5 FW	162
Liver	0.3 FW–19.9 FW	162
Muscle	0.06 FW–3.6 FW	162
Baleen whales; 1 species		
Kidney	0.3 FW	162
Liver	0.4 FW	162
Muscle	0.16 FW	162
Toothed whales; 3 species		
Kidney	0.18 FW–1.4 FW	162
Liver	0.8 FW–8.2 FW	162
Muscle	0.15 FW–0.66 FW	162
Polar bear, <i>Ursus maritimus</i>		
Kidney	10.8 FW–23.2 FW	162
Liver	7.2 FW–21.6 FW	162
Muscle	0.06 FW–0.08 FW	162
Greenland; 1984–87; total mercury vs. organic mercury		
Birds		
Liver	Max. 2.3 FW vs. 0.45 (0.1–1.5) FW	163

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Seals		
Kidney	Max. 6.4 FW vs. Max. 0.98 FW	163
Liver	Max. 174.5 FW vs. 0.4 (0.1–2.1) FW	163
Muscle	Max. 1.4 FW vs. Max. 1.2 FW	163
Toothed whales		
Kidney	Max. 2.9 FW vs. Max. 0.4 FW	163
Liver	Max. 16.4 FW vs. Max. 1.6 FW	163
Muscle	Max. 1.3 FW vs. Max. 1.2 FW	163
Baleen whales		
Kidney	Max. 1.1 FW vs. Max. 0.11 FW	163
Liver	Max. 1.5 vs. Max. 0.4 FW	163
Muscle	Max 0.4 FW vs. Max. 0.24 FW	163
Polar bear		
Kidney	Max. 48.6 FW vs. Max. 0.2 FW	163
Liver	Max. 23.8 FW vs. Max. 0.6 FW	163
Muscle	Max. 0.1 FW vs. Max. 0.07 FW	163
India; Bombay		
Sediments	Max. 55–7.0 DW	164
Humans; blood		
Fish eaters	0.05–0.07 (0.02–0.13) FW	164
Non-fish eaters	0.019 (0.006–0.042) FW	164
Bombay vs. reference site		
Fish, <i>Arius</i> sp.; muscle	1.5–2.2 DW vs. 0.5 DW	164
Prawn, <i>Penaeus</i> sp.; muscle	0.0–2.1 DW vs. 0.3 DW	164
Italy; vicinity of Monte Amiata		
Near banks of roasted cinnabar		
Soils	1379.0 DW	165
Pine, <i>Pinus nigra</i>		
Needles	8.1 DW	165
Branches	1.8 DW	165
Roots	0.9 DW	165
Near geothermal plant		
Soils	18.7 DW	165
Pine, <i>Pinus nigra</i>		
Needles	0.5 DW	165
Branches, roots	0.2–0.3 DW	165
Reference site, 6–7 km from known sources		
Soils	0.5 DW	165
Pine, all samples	<0.07 DW	165
Italy; coast; summer; 1986–87		
Mussel, <i>Mytilus galloprovincialis</i> ; soft parts	0.01–0.07 FW	166
Snail, <i>Murex trunculus</i> ; soft parts	0.03–0.15 FW	166
Fish, <i>Serranus</i> spp.; muscle	0.09–0.63 FW	166
Spain; Catalonia; November 1992–February 1993; edible tissues		
Means		
Fish, 9 species	0.02–0.9 FW	167
Cephalopods, 3 species	0.003–0.27 FW	167
Crustaceans, 4 species	0.006–0.72 FW	167
Molluscs, 5 species	0.001–0.19 FW	167
Maximum values		
All species	0.001–1.8 FW	167
Taiwan; 1995–96; edible tissues		
Pacific oyster, <i>Crassostrea gigas</i>	0.2 (0.03–1.3) DW	183
Fish, 5 species	1.0–2.5 (0.1–6.8) DW	183

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Blue marlin, <i>Makaira nigricans</i>	10.3 (1.7–22.9) DW	183
Yellowfin tuna, <i>Thunnus albacares</i>	9.8 (8.8–10.4) DW	183
Shrimp, 2 species	2.2–2.4 (0.7–5.4) DW	183
United States		
New Jersey; Newark Bay		
Sediments	0.1–9.8 DW	168
Fish muscle	0.1–1.4 FW	168
Puerto Rico; estuaries; 1988		
Aquatic		
Blue crab, <i>Callinectes sapidus</i> ; Shrimp, <i>Palaemonetes</i> sp.	ND in any tissue or whole body	169
Fish muscle		
Tarpon, <i>Megalops atlantica</i>	0.09–0.24 FW	169
Tilapia, <i>Tilapia mossambica</i>	0.08–0.46 FW	169
Lizard, <i>Ameiva exsul</i>	ND	
Cattle egret, <i>Bubulcus ibis</i> ; pectoral muscle vs. liver	0.1 FW vs. 0.1 FW	169
Moorhen, <i>Gallinula chloropus</i>		
Liver	0.16 FW	169
Muscle	0.12 FW	169
Whole	0.08 FW	169
Tennessee; mercury-contaminated (1950–63) site vs. reference site; 1986–87		
Soil	269 FW vs. 0.2 FW	170
Vegetation	Max. 2.0 FW vs. Max. 0.02 FW	170
Earthworms	16 FW vs. 0.2 FW	170
Centipedes	3.4 FW vs. 0.1 FW	170
Termites	2.6 FW vs. 0.7 FW	170
White-footed mouse, <i>Peromyscus leucopus</i> ; kidney	1.2 FW vs. 0.5 FW	170
Short tail shrew, <i>Blarina brevicauda</i> ; kidney	39 FW vs. 1 FW	170

^a Concentrations are listed as not detectable (ND), mean, range, or maximum (Max.).

^b 1, Jenkins 1980; 2, Chigbo et al. 1982; 3, Lodenius and Tulisalo 1984; 4, Augier et al. 1978; 5, Huckabee et al. 1979; 6, Cooper 1983; 7, Windom and Kendall 1979; 8, Schreiber 1983; 9, Cappon and Smith 1982; 10, Iglesias and Panchaszadeh 1983; 11, Hornung et al. 1984; 12, Kiorboe et al. 1983; 13, Flegal et al. 1981; 14, Barber et al. 1984; 15, Busch 1983; 16, Bodaly et al. 1984; 17, Winger and Andreasen 1985; 18, Henderson and Shanks 1973; 19, Lowe et al. 1985; 20, Suckcharoen and Lodenius 1980; 21, NAS 1978; 22, Bycroft et al. 1982; 23, Wren and MacCrimmon 1984; 24, Alexander et al. 1973; 25, Miller and Jude 1984; 26, Lloyd et al. 1977; 27, Sloan and Schofeld 1983; 28, Lyle 1984; 29, Schreiber 1983; 30, Terhivuo et al. 1984; 31, Hall 1980; 32, Solonen and Lodenius 1984; 33, Lindsay and Dommick 1983; 34, Norheim et al. 1982; 35, Norheim and Kjos-Hanssen 1984; 36, Delbekke et al. 1984; 37, Ohlendorf and Harrison 1986; 38, Firreite 1979; 39, Broo and Odsjow 1981; 40, Lindberg 1984; 41, Wiemeyer et al. 1984; 42, Karlog and Clausen 1983; 43, Ohlendorf et al. 1985; 44, Bacher 1985; 45, Krynski et al. 1982; 46, Sheffy and St. Amant 1982; 47, Kucera 1983; 48, Edwards and Pumphrey 1982; 49, Itano et al. 1984a; 50, Itano et al. 1984b; 51, Beyer et al. 1997; 52, Wiener and Spry 1996; 53, Allard and Stokes 1989; 54, Beauvais et al. 1995; 55, Yanochko et al. 1997; 56, Bidwell and Heath 1993; 57, Chvojka et al. 1990; 58, Braune 1987b; 59, Krom et al. 1990; 60, Rask and Metsala 1991; 61, Lodenius 1991; 62, Falandysz and Kowalewska 1993; 63, Lange et al. 1993; 64, Haines et al. 1992; 65, Leah et al. 1992; 66, Leah et al. 1993; 67, Gutenmann et al. 1992; 68, Leah et al. 1991; 69, Chvojka 1988; 70, Gerstenberger et al. 1993; 71, Wiener et al. 1990; 72, Lathrop et al. 1991; 73, Munn and Short 1997; 74, Kai et al. 1988; 75, Monteiro and Lopes 1990; 76, Borgmann and Whittle 1991; 77, Hueter et al. 1995; 78, Lange et al. 1994; 79, Bloom 1992; 80, Saiki et al. 1992; 81, Parks et al. 1991; 82, Dixon and Jones 1994; 83, Halbrook et al. 1994; 84, Borgmann and Whittle 1992; 85, Joiris et al. 1997; 86, Stafford and haines 1997; 87, Goldstein et al. 1996; 88, Clark and Topping 1989; 89, Mathieson and McLusky 1995; 90, Schmitt and Brumbaugh 1990; 91, Wood et al. 1996b; 92, Littrell 1991; 93, Szefer et al. 1993; 94, Newton and Galbraith 1991; 95, Spalding et al. 1994; 96, Mullie et al. 1992; 97, Thompson et al. 1991; 98, Newton et al. 1993; 99, Burger et al. 1994; 100, Meyer et al. 1995; 101, Becker et al. 1993; 102, Thompson et al. 1993; 103, Wood et al. 1996a; 104, Wiemeyer et al. 1993; 105, Elliott et al. 1996; 106, Bowerman et al. 1994; 107, Kairu 1996; 108, Lewis et al. 1993; 109, Koster et al. 1996; 110, Braune

Table 5.6 (continued) Mercury Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg total Hg/kg fresh weight [FW], or dry weight [DW])

and Gaskin 1987; 111, Burger and Gochfeld 1996; 112, Honda et al. 1986; 113, Zicus et al. 1988; 114, Audet et al. 1992; 115, Wiemeyer et al. 1988; 116, Mason et al. 1997; 117, Henny and Herron 1989; 118, Wenzel et al. 1996; 119, Kim et al. 1996; 120, Barrett et al. 1996; 121, Luke et al. 1989; 122, Monteiro et al. 1995; 123, Lock et al. 1992; 124, Braune 1987a; 125, Thompson and Furness 1989; 126, Becker et al. 1994; 127, Bishop et al. 1995; 128, King et al. 1991; 129, Mora 1996; 130, Sanpera et al. 1993; 131, Honda et al. 1987; 132, Kacmar and Legath 1991; 133, Roelke et al. 1991; 134, PHS 1994; 135, Richardson et al. 1995; 136, Wheatley and Paradis 1995; 137, Szefer et al. 1993; 138, Wren et al. 1986; 139, Foley et al. 1988; 140, Holbrook et al. 1994; 141, Ropek and Neely 1993; 142, Mason and Madsen 1992; 143, Skaare et al. 1994; 144, Khan and Forester 1995; 145, Wagemann et al. 1988; 146, Watanabe et al. 1996; 147, Joiris et al. 1991; 148, Cannella and Kitchener 1992; 149, Khan et al. 1995; 150, Andre et al. 1991a; 151, Andre et al. 1991b; 152, Stevens et al. 1997; 153, Zilincar et al. 1992; 154, Lentfer and Galster 1987; 155, Born et al. 1991; 156, Buzina et al. 1989; 157, Malm et al. 1990; 158, Hylander et al. 1994; 159, Palheta and Taylor 1995; 160, Langlois et al. 1995; 161, Gonzalez 1991; 162, Dietz et al. 1996; 163, Dietz et al. 1990; 164, Srinivasan and Mahajan 1989; 165, Ferrara et al. 1991; 166, Giordano et al. 1991; 167, Schuhmacher et al. 1994; 168, Gillis et al. 1993; 169, Burger et al. 1992; 170, Talmage and Walton 1993; 171, Thompson et al. 1992; 172, Bargagli et al. 1998; 173, Hoffman et al. 1998; 174, Burger and Snodgrass 1998; 175, Elbert and Anderson 1998; 176, Wolfe and Norman 1998; 177, Cahill et al. 1998; 178, Evers et al. 1998; 179, Scheuhammer et al. 1998a; 180, Scheuhammer et al. 1998b; 181, Pokras et al. 1998; 182, Meyer et al. 1998; 183, Han et al. 1998; 184, Gariboldi et al. 1998; 185, DesGranges et al. 1998; 186, Watanabe et al. 1998; 187, Kannan et al. 1998.

5.6 LETHAL EFFECTS

5.6.1 General

For all organisms tested, early developmental stages were the most sensitive, and organomercury compounds — especially methylmercury — were more toxic than inorganic forms. Numerous biological and abiotic factors modify the toxicity of mercury compounds, sometimes by an order of magnitude or more, but the mechanisms of action are not clear. Lethal concentrations of total mercury to sensitive, representative organisms varied from 0.1 to 2.0 µg/L of medium for aquatic fauna; from 2.2 to 31.0 mg/kg body weight (acute oral) and 4.0 to 40.0 mg/kg (dietary) for birds; and from 0.1 to 0.5 mg/kg body weight (daily dose) and 1.0 to 5.0 mg/kg (dietary) for mammals.

5.6.2 Aquatic Organisms

Lethal concentrations of mercury salts ranged from less than 0.1 µg Hg/L to more than 200 µg/L for representative sensitive species of marine and freshwater organisms (Table 5.7). The lower concentrations (less than 2.0 µg/L) were usually associated with early developmental stages, long exposures, and flowthrough tests (Table 5.7). Females and larger fish were more resistant to lethal effects of mercury than males and smaller fishes (Diamond et al. 1989). Among metals tested, mercury was the most toxic to aquatic organisms, and organomercury compounds showed the greatest biocidal potential (Eisler 1981; Jayaprakash and Madhyastha 1987). In general, toxicity was higher at elevated temperatures (Armstrong 1979), at reduced salinities in marine organisms (McKenney and Costlow 1981), and in the presence of other metals such as zinc and lead (Parker 1979).

Signs of acute mercury poisoning in fish included flaring of gill covers, increased frequency of respiratory movements, loss of equilibrium, excessive mucus secretion, darkening coloration, and sluggishness (Armstrong 1979; Hilmy et al. 1987). Signs of chronic mercury poisoning included emaciation (due to appetite loss), brain lesions, cataracts, diminished response to change in light intensity, inability to capture food, abnormal motor coordination, and various erratic behaviors (Armstrong 1979; Hawryshyn et al. 1982). Mercury residues in severely poisoned fish that died soon after ranged (in mg/kg fresh weight) from 26 to 68 in liver, 16 to 20 in brain, and 5 to 7 in whole body (Armstrong 1979).

Table 5.7 Lethality of Inorganic and Organic Mercury Compounds to Selected Species of Aquatic Organisms

Chemical Species, Ecosystem, Taxonomic Group, Species, and Other Variables	Effect ^a	Concentration ($\mu\text{g Hg/L}$ medium)	Ref. ^b
INORGANIC MERCURY			
Freshwater			
Crustaceans			
Crayfish, <i>Orconectes limosus</i>	LC50 (30 d)	2.0	1
Daphnid <i>Daphnia magna</i>	LC50 (96 h)	5.0	1
Daphnid, <i>Daphnia magna</i>	LC50 (LT)	1.3–1.8	1
Scud, <i>Gammarus pseudolimnaeus</i>	LC50 (96 h)	10.0	1
Fish			
Zebrafish, <i>Brachydanio rerio</i>	No deaths	<2.0	16
Embryo-larvae			
Catfish, <i>Clarias batrachus</i>	LC50 (96 h)	507.0	18
Adults			
Catfish, <i>Clarias lazera</i>	LC50 (96 h)	720	17
Adults			
Mosquitofish, <i>Gambusia affinis</i>	LC50 (24 h)	960	17
Adults			
Channel catfish, <i>Ictalurus punctatus</i>	LC77 (10 d)	1000	19
Embryo-larva			
Static test	LC50 (10 d)	30.0	2
Flowthrough test	LC50 (10 d)	0.3	2
Largemouth bass, <i>Micropterus salmoides</i>			
Embryo-larva			
Static test	LC50 (8 d)	140.0	2
Flowthrough test	LC50 (8 d)	5.3	2
Rainbow trout, <i>Oncorhynchus mykiss</i>			
Juveniles	LC50 (96 h)	155.0–200.0	1
Embryo-larva			
Static test	LC50 (28 d)	4.7	2
Flowthrough test	LC50 (28 d)	<0.1	2
Subadults	LC50 (58 d)	64.0	20
Subadults	LC50 (24 h)	426.0	20
Brook trout, <i>Salvelinus fontinalis</i>	LC50 (LT)	0.3–0.9	1
Fish, <i>Notopterus notopterus</i>	LC50 (96 h)	440.0	3
Amphibians			
Narrow-mouthed toad, <i>Gastrophryne carolinensis</i>			
Embryo-larva	LC50 (96 h)	1.3	2
Treefrogs, <i>Hyla</i> spp.			
Embryo-larva, 5 spp.	LC50 (96 h)	2.4–2.8	2
Frog, <i>Microhyla ornata</i>			
Tadpoles			
Age 1 week	LC50 (96 h)	1112	13
Age 4 weeks	LC50 (96 h)	1430	13
Frog, <i>Rana cyanophlyctis</i>			
Adult females	LC50 (31–65 d)	960	14
Adult females	LC50 (96 h)	4800	14
River frog, <i>Rana heckscheri</i>			
Adult females	No deaths in 60 d	880	15
Adult females	LC50 (96 h)	4400	15
Leopard frog, <i>Rana pipens</i>			
Embryo-larva	LC50 (96 h)	7.3	2
Cricket frog, <i>Acris</i> sp.			
Embryo-larva	LC50 (96 h)	10.4	2

Table 5.7 (continued) Lethality of Inorganic and Organic Mercury Compounds to Selected Species of Aquatic Organisms

Chemical Species, Ecosystem, Taxonomic Group, Species, and Other Variables	Effect ^a	Concentration ($\mu\text{g Hg/L}$ medium)	Ref. ^b
Anurans, 4 spp.			
Embryo-larva	LC50 (96 h)	36.8–67.2	2
Marbled salamander, <i>Ambystoma opacum</i>			
Embryo-larva	LC50 (96 h)	107.5	2
Marine			
Protozoans			
Ciliate, <i>Uronema marinum</i>	LC50 (24 h)	6.0	4
Molluscs			
Softshell clam, <i>Mya arenaria</i>	LC50 (168 h)	4.0	5
Hardshell clam, <i>Mercenaria mercenaria</i>			
Larva	LC50 (48 h)	4.8	1
Larva	LC5 (9 d)	4.0	1
American oyster, <i>Crassostrea virginica</i>			
Embryo	LC5 (12 d)	3.3	1
Larva	LC50 (48 h)	5.6	1
Adults	LC50 (48 h)	5.5–10.2	1
Blue mussel, <i>Mytilus edulis</i>	LC50 (96 h)	5.8	6
Slipper limpet, <i>Crepidula fornicata</i>			
Larva	LC50 (96 h)	60.0	7
Adults	LC50 (96 h)	330.0	7
Bay scallop, <i>Argopecten irradians</i>			
Juveniles	LC50 (96 h)	89.0	8
Crustaceans			
Fiddler crab, <i>Uca pugilator</i>			
Zoea	LC50 (8 d)	1.8	1
Mysid shrimp, <i>Mysidopsis bahia</i>			
Juveniles	LC50 (96 h)	3.5	9
Egg to egg	LC50 (LT)	1.8	9
Dungeness crab, <i>Cancer magister</i>			
Larva	LC50 (96 h)	6.6	10
Copepod, <i>Acartia tonsa</i> , adult	LC50 (96 h)	10.0–15.0	1
Prawn, <i>Penaeus indicus</i>			
Postlarva	LC50 (48 h)	16.1	11
Postlarva	LC50 (96 h)	15.3	11
Annelids			
Polychaete, <i>Capitella capitata</i>			
Larva	LC50 (96 h)	14.0	1
Fish			
Haddock, <i>Melanogrammus aeglefinus</i>			
Larvae	LC50 (96 h)	98.0	1
ORGANIC MERCURY			
Freshwater			
Planarians			
Flatworm, <i>Dugesia dorotocephala</i>			
Adult	LC0 (10 d)	200.0	12
Adult	LC100 (5 d)	500.0	12
Crustaceans			
Daphnid, <i>Daphnia magna</i>	LC50 (LT)	0.9–3.2	1

Table 5.7 (continued) Lethality of Inorganic and Organic Mercury Compounds to Selected Species of Aquatic Organisms

Chemical Species, Ecosystem, Taxonomic Group, Species, and Other Variables	Effect ^a	Concentration ($\mu\text{g Hg/L}$ medium)	Ref. ^b
Fish			
Rainbow trout			
Larva	LC50 (96 h)	24.0	1
Juvenile	LC50 (96 h)	5.0–42.0	1
Subadults	LC50 (48 h)	34.0	20
Subadults	<50% dead in 100 d	4.0	20
Brook trout			
Yearling	LC50 (96 h)	65.0	1
Catfish, <i>Clarias batrachus</i> ; adults			
Methylmercury	LC50 (96 h)	430	18
Methoxyethyl mercury	LC50 (96 h)	4300	18
Blue gourami, <i>Trichogaster</i> sp.			
Adults	LC50 (96 h)	70	22
Marine			
Crustaceans			
Amphipod, <i>Gammarus duebeni</i>	LC50 (96 h)	150.0	1
Fish			
Mummichog, <i>Fundulus heteroclitus</i>			
Eggs, polluted creek (sediment content of 10.3 mg Hg/kg)	LC50 (20 min)	1700.0	21
Eggs, reference site	LC50 (20 min)	700	21

^a Abbreviations: LT = lifetime exposure; h = hours; d = days.

^b 1, USEPA 1980; 2, Birge et al. 1979; 3, Verma and Tonk 1983; 4, Parker 1979; 5, Eisler and Hennekey 1977; 6, USEPA 1985; 7, Thain 1984; 8, Nelson et al. 1976; 9, Gentile et al. 1983; 10, Glickstein 1978; 11, McClurg 1984; 12, Best et al. 1981; 13, Jayaprakash and Madhyastha 1987; 14, Kanamadi and Saidapur 1991; 15, Punzo 1993; 16, Dave and Xiu 1991; 17, Hilmy et al. 1987; 18, Kirubagaran and Joy 1988; 19, Diamond et al. 1989; 20, Niimi and Kissoon 1994; 21, Khan and Weis 1987; 22, Hamasaki et al. 1995.

Some fish populations have developed a resistance to methylmercury, but only in the gamete and embryonic stage. For example, eggs of the mummichog (*Fundulus heteroclitus*), an estuarine cyprinodontiform fish, from a mercury-contaminated creek, when compared to a reference site, were more than twice as resistant to methylmercury (LC50 values of 1.7 mg Hg/L vs. 0.7 mg Hg/L) when exposed for 20 min prior to combination with untreated sperm. Eggs from the polluted creek that were subjected to 1 or 2.5 mg $\text{CH}_3\text{HgCl}/\text{L}$ produced embryos with a 5 to 7% malformation frequency vs. 32% malformations at 1.0 mg/L and little survival at 2.5 mg/L in the reference group (Khan and Weis 1987). Genetic polymorphism in mosquitofish (*Gambusia* sp.) at specific enzyme loci are thought to control survival during mercury exposure (Diamond et al. 1989). In one population of mosquitofish during acute exposure to mercury, genotypes at 3 loci were significantly related to survival time, as was heterozygosity, but neither genotype of heterozygosity was related to survival in a different population of mosquitofish during acute mercury exposure (Diamond et al. 1991).

5.6.3 Birds

Signs of mercury poisoning in birds includes muscular incoordination, falling, slowness, fluffed feathers, calmness, withdrawal, hyporeactivity, hypoactivity, and eyelid drooping. In acute oral exposures, signs appeared as early as 20 min postadministration in mallards and 2.5 h in pheasants. Deaths occurred between 4 and 48 h in mallards and 2 and 6 days in pheasants; remission took up to 7 days (Hudson et al. 1984). In studies with coturnix (*Coturnix coturnix coturnix*), Hill (1981)

found that methylmercury was always more toxic than inorganic mercury and that young birds were usually more sensitive than older ones. Furthermore, some birds poisoned by inorganic mercury recovered after treatment was withdrawn, but chicks that were fed methylmercury and later developed toxic signs usually died, even if the treated feed was removed. *Coturnix* subjected to inorganic mercury, regardless of the route of administration, showed a violent neurological dysfunction that ended in death 2 to 6 h posttreatment. The withdrawal syndrome in *coturnix* poisoned by Hg^{2+} was usually preceded by intermittent, nearly undetectable tremors, coupled with aggressiveness toward cohorts; time from onset to remission was usually 3 to 5 days, but sometimes extended to 7 days. *Coturnix* poisoned by methylmercury appeared normal until 2 to 5 days posttreatment; then, ataxia and low body carriage with outstretched neck were often associated with walking. In advanced stages, *coturnix* lost locomotor coordination and did not recover; in mild to moderate clinical signs, recovery usually took at least 1 week (Hill 1981).

Mercury toxicity to birds varies with the form of the element, dose, route of administration, species, sex, age, and physiological condition (Fimreite 1979). For example, in northern bobwhite chicks fed diets containing methylmercury chloride, mortality was significantly lower when the solvent was acetone than when it was another carrier, such as propylene glycol or corn oil (Spann et al. 1986). In addition, organomercury compounds interact with elevated temperatures and pesticides, such as DDE and parathion, to produce additive or more-than-additive toxicity, and with selenium to produce less-than-additive toxicity (Fimreite 1979). Acute oral toxicities of various mercury formulations ranged between 2.2 and about 31.0 mg Hg/kg body weight for most avian species tested ([Table 5.8](#)). Similar data for other routes of administration were 4.0 to 40.0 mg/kg for diet and 8.0 to 15.0 mg/kg body weight for intramuscular injection ([Table 5.8](#)).

Residues of mercury in experimentally poisoned passerine birds usually exceeded 20 mg/kg FW and were similar to concentrations reported in wild birds that died of mercury poisoning (Finley et al. 1979). In one study with the zebra finch (*Poephila guttata*), adults were fed methylmercury in the diet for 76 days at dietary levels of <0.02 (controls), 1, 2.5, or 5 mg Hg/kg DW ration (Scheuhammer 1988). There were no signs of mercury intoxication in any group except the high-dose group, which experienced 25% dead and 40% neurological impairment. Dead birds from the high-dose group had 73 mg Hg/kg FW in liver, 65 in kidney, and 20 in brain; survivors without signs had 30 in liver, 36 in kidney, and 14 in brain; impaired birds had 43 mg Hg/kg FW in liver, 55 in kidney, and 20 in brain (Scheuhammer 1988). Mercury levels in tissues of poisoned wild birds were highest (45 to 126 mg/kg FW) in red-winged blackbirds (*Agelaius phoeniceus*), intermediate in starlings (*Sturnus vulgaris*) and cowbirds (*Molothrus ater*), and lowest (21 to 54) in grackles (*Quiscalus quiscula*). In general, mercury residues were highest in the brain, followed by the liver, kidney, muscle, and carcass. Some avian species are more sensitive than passersines (Solonen and Lodenius 1984; Hamasaki et al. 1995): liver residues (in mg Hg/kg FW) in birds experimentally killed by methylmercury ranged from 17 in red-tailed hawks (*Buteo jamaicensis*) to 70 in jackdaws (*Corvus monedula*); values were intermediate in ring-necked pheasants, kestrels (*Falco tinnunculus*), and magpies (*Pica pica*). Experimentally poisoned grey herons (*Ardea cinerea*) seemed to be unusually resistant to mercury; lethal doses produced residues of 415 to 752 mg Hg/kg dry weight of liver (Van der Molen et al. 1982). However, levels of this magnitude were frequently encountered in livers from grey herons collected during a massive die-off in the Netherlands during a cold spell in 1976; the interaction effects of cold stress, mercury loading, and poor physical condition of the herons are unknown (Van der Molen et al. 1982).

5.6.4 Mammals

Methylmercury affects the central nervous system in humans — especially the sensory, visual, and auditory areas concerned with coordination. The most severe effects lead to widespread brain damage, resulting in mental derangement, coma, and death (Clarkson and Marsh 1982; USPHS 1994). In mule deer (*Odocoileus hemionus hemionus*), after acute oral mercury poisoning was

Table 5.8 Lethality to Birds of Mercury Administered by Oral, Dietary, or Other Routes

Route of Administration (units), Organism, and Mercury Formulation	Concentration	Exposure Interval	Effect	Ref ^a
ACUTE ORAL (mg Hg/kg body weight)				
Chukar, <i>Alectoris chukar</i>				
Ethyl	26.9	Within 14 d after treatment	LD50	1
Mallard, <i>Anas platyrhynchos</i>				
Methyl	2.2–23.5	"	LD50	1
Ethyl	75.7	"	LD50	1
Phenyl	524.7	"	LD50	1
Northern bobwhite, <i>Colinus virginianus</i>				
Methyl	23.8	"	LD50	1
Coturnix, <i>Coturnix japonica</i>				
Methyl	11.0–33.7	"	LD50	1, 2, 3
Inorganic	26.0–54.0	"	LD50	2
Ethyl	21.4	"	LD50	1
Inorganic	31.1	"	LD50	3
Rock dove, <i>Columba livia</i>				
Ethyl	22.8	"	LD50	1
Fulvous whistling duck, <i>Dendrocygna bicolor</i>				
Methyl	37.8	"	LD50	1
Domestic chicken, <i>Gallus domesticus</i>				
Phenyl	60.0	"	LD50	4
House sparrow, <i>Passer domesticus</i>				
Methyl	12.6–37.8	"	LD50	1
Gray partridge, <i>Perdix perdix</i>				
Ethyl	17.6	"	LD50	1
Ring-necked pheasant, <i>Phasianus colchicus</i>				
Ethyl	11.5	"	LD50	1
Methyl	11.5–26.8	"	LD50	1
Phenyl	65.0–101.0	"	LD50	1, 4
Prairie chicken, <i>Tympanuchus cupido</i>				
Ethyl	11.5	"	LD50	1
DIETARY (mg Hg/kg diet)				
Mallard, hens				
Methyl	3.0	Two reproductive seasons	Reduced duckling survival	11
Coturnix				
Inorganic	32.0	Hatch to 9 weeks	LD0	2
Inorganic	2956–5086	5 d + 7 d observation period	LD50	2
Inorganic				
In dry salt	500	28 d	LD86	6
In ethanol, methanol, or water	500	28 d	LD55	6
In casein premix	500	28 d	LD33	6
Methyl	4.0	Hatch to 9 weeks	LD0	2
Methyl	8.0	5 d	Some deaths	3
Methyl	31.0–47.0	5 d plus 7 d observation period	LD50	2
Zebra finch, <i>Poephila guttata</i>				
Methyl	2.5	77 days	LD0	12
Methyl	5.0	77 days	LD25	12

Table 5.8 (continued) Lethality to Birds of Mercury Administered by Oral, Dietary, or Other Routes

Route of Administration (units), Organism, and Mercury Formulation	Concentration	Exposure Interval	Effect	Ref^a
Ring-necked pheasant				
Ethyl	4.2	70 d	LD0 ^b	5
Ethyl	12.5	70 d	LD50	5
Ethyl	37.4	28 d	LD50	5
Ethyl	112.0	15 d	LD50	5
Birds, 4 spp.				
Methyl	40.0	6–11 d	LD33	7
Birds, 3 spp.				
Methyl	33.0	35 d	LD8 to LD90	14
INTRAMUSCULAR INJECTION (mg Hg/kg body weight)				
Coturnix				
Methyl	8.0–33.0	Single dose	LD50	2
Inorganic	15.0–50.0	Single dose	LD50	2
Rock dove				
Inorganic	10.0	Daily, 17 d	Some deaths	8
YOLK SAC INJECTION (µg Hg/egg)				
Chicken				
Methyl	15.0	Single dose	Some deaths	13
Methyl	40.0–50.0	Single dose	LD50	13
APPLIED TO EGG SURFACE (µg Hg/egg)				
Mallard				
Methyl	3.0	Single dose	Some deaths	9
Methyl	9.0	Single dose	LD50	9
IN DRINKING WATER (mg Hg/L)				
Chicken				
Inorganic	500.0	3 d	Some deaths	10

^a 1, Hudson et al. 1984; 2, Hill 1981; 3, Hill and Soares; 4, Mullins et al. 1977; 5, Spann et al. 1972; 6, El-Begearmi et al. 1980; 7, Finley et al. 1979; 8, Leander et al. 1977; 9, Hoffman and Moore 1979; 10, Grissom and Thaxton 1985; 11, Heinz and Locke 1976; 12, Scheuhhammer 1988; 13, Greener and Kochen 1983; 14, Hamasaki et al. 1995.

^b 55 to 80% reduction in egg production; embryonic survival sharply reduced.

induced experimentally, additional signs included belching, bloody diarrhea, piloerection (hair more erect than usual), and loss of appetite (Hudson et al. 1984). The kidney is the probable critical organ in adult mammals due to the rapid degradation of phenylmercurials and methoxyethylmercurials to inorganic mercury compounds and subsequent translocation to the kidney (Suzuki 1979), whereas in the fetus the brain is the principal target (Khera 1979). Most human poisonings were associated with organomercury compounds used in agriculture as fungicides to protect cereal seed grain (Elhassani 1983); judging from anecdotal evidence, many wildlife species may have been similarly afflicted. Organomercury compounds, especially methylmercury, were the most toxic mercury species tested. Among sensitive species of mammals, death occurred at daily organomercury concentrations of 0.1 to 0.5 mg/kg body weight, or 1.0 to 5.0 mg/kg in the diet (Table 5.9). Larger animals such as mule deer and harp seals appear to be more resistant to mercury than smaller mammals such as mink, cats, dogs, pigs, monkeys, and river otters; the reasons for this difference are unknown, but may be related to differences in metabolism and detoxification rates. Tissue residues in fatally poisoned mammals (in mg Hg/kg fresh weight) were 6.0 in brain, 10.0 to 55.6 in liver,

Table 5.9 Lethality of Organomercury Compounds to Selected Mammals

Organism	Dose, Route of Administration, and Other Variables	Effects	Ref. ^a
Domestic dog, <i>Canis familiaris</i>	0.1 to 0.25 mg/kg body weight (BW) during entire pregnancy; oral route	High incidence of stillbirths	1
Domestic cat, <i>Felis domesticus</i>	0.25 mg/kg BW daily for 90 days (total 80–90 mg Hg); dietary route	Mean survival time 78 days. Convulsions starting at day 68; all with signs by day 90. Liver residues of survivors were 40.2 and 18.1 mg/kg FW for total mercury and inorganic mercury, respectively	2
Pig, <i>Sus</i> spp.	0.5 mg/kg BW during pregnancy; oral route	High incidence of stillbirths	1
Rhesus monkey, <i>Macaca mulatta</i>	0.5 mg/kg BW during days 20–30 of pregnancy	Maternally toxic, and abortive	1
Mink, <i>Mustela vison</i>	1.0 mg/kg in diet	Fatal to 100% in about 2 months	3
Mink	1.0 mg/kg diet daily for 4 months; then every other day for 4 months alternating with control diet	High mortality after 4 months when subjected to cold stress; significant placental transfer to the fetus	9
Mink	5.0 mg/kg in diet	All dead in 30 to 37 days. Elevated residues in kidney (37.7 mg/kg fresh weight) and liver (55.6) prior to death	3
River otter, <i>Lutra canadensis</i>	>2.0 mg/kg in diet	Fatal within 7 months	4, 8
Humans, <i>Homo sapiens</i>	Various	Lethal residues in tissues, in mg/kg fresh weight, were >6.0 in brain, >10.0 in liver, and >17.0 in whole body	1
Mule deer, <i>Odocoileus hemionus hemionus</i>	17.88 mg/kg BW; single oral dose	LD50	5
Harp seal, <i>Pagophilus groenlandicus</i>	25.0 mg/kg BW daily; oral route	Dead in 20 to 26 days. Blood Hg levels just before death were 26.8 to 30.3 mg/L	6
Rat, <i>Rattus</i> sp.	27 mg/m ³ air for 1–2 h	Fatal; death by asphyxiation; lung edema; necrosis of alveolar epithelium	7

^a 1, Khera 1979; 2, Eaton et al. 1980; 3, Sheffy and St. Amant 1982; 4, Kucera 1983; 5, Hudson et al. 1984; 6, Ronald et al. 1977; 7, PHS 1994; 8, Ropek and Neely 1993; 9, Wren et al. 1987a.

17.0 in whole body, about 30.0 in blood, and 37.7 in kidney (Table 5.9). Mercury interactions with other compounds should be considered. Adverse effects on growth and survival of mink kits are reported for diets containing 1.0 mg Hg/kg ration as methyl mercury and Aroclor 1254 — a polychlorinated biphenyl — at 1.0 mg/kg ration (Wren et al. 1987b).

5.6.5 Other Groups

Methylmercury compounds at concentrations of 25.0 mg Hg/kg in soil were fatal to all tiger worms (*Eisenia foetida*) in 12 weeks; at 5.0 mg/kg, however, only 21% died in a similar period (Beyer et al. 1985). Inorganic mercury compounds were also toxic to earthworms (*Octochaetus pattoni*); in 60 days, 50% died at soil Hg levels of 0.79 mg/kg, and all died at 5.0 mg/kg (Abbasi and Soni 1983).

5.7 SUBLETHAL EFFECTS

5.7.1 General

Mercury is a known mutagen, teratogen, and carcinogen. At comparatively low concentrations in birds and mammals, it adversely affects reproduction, growth and development, behavior, blood

and serum chemistry, motor coordination, vision, hearing, histology, and metabolism. It has a high potential for bioaccumulation and biomagnification, and is slow to depurate. Organomercury compounds were more effective in producing adverse effects than were inorganic mercury compounds; however, effects were significantly enhanced or ameliorated by numerous biotic and nonbiological modifiers. For sensitive aquatic species, adverse effects were observed at water concentrations of 0.03 to 0.1 µg Hg/L. For sensitive species of birds, harmful levels were 640 µg Hg/kg body weight daily, or 50 to 500 µg Hg/kg in the diet; for sensitive mammals, these levels were 250 µg Hg/kg body weight daily, or 1100 µg Hg/kg diet.

5.7.2 Carcinogenicity, Genotoxicity, and Teratogenicity

Mercury has been assigned a weight-of-evidence classification of D, which indicates that it is not classifiable as to human carcinogenicity (USPHS 1994). Beluga whales (*Delphinapterus leucas*) in the St. Lawrence estuary have a high incidence of cancer (Gauthier et al. 1998). Studies with isolated skin fibroblasts of beluga whales exposed to mercuric chloride or methylmercury induced a significant dose-response increase of micronucleated cells. Concentrations as low as 0.5 mg Hg²⁺/L and 50 µg CH₃Hg⁺/L — comparable to concentrations present in certain whales of this population — significantly induced proliferation (Gauthier et al. 1998).

Mercury is not genotoxic in humans. Dental amalgam has been used for more than 150 years, and it is well established that patients with amalgam dental fillings are chronically exposed to mercury and that the number of amalgam fillings correlates positively with mercury levels in blood and plasma (Loftenius et al. 1998). Amalgam removal, however, did not have a measurable effect on proliferation of peripheral blood lymphocytes, suggesting that mercury contributed by amalgams was not mitogenic to lymphocytes (Loftenius et al. 1998). Mercury does not adversely affect the number or structure of chromosomes in human somatic cells in workers occupationally exposed to mercury compounds by inhalation or accidentally exposed through ingestion (USPHS 1994). In the laboratory, however, mercury compounds often exerted genotoxic effects, especially by binding SH groups and acting as spindle inhibitors, resulting in abnormal chromosome numbers (De Flora et al. 1994). Chromosomal aberrations and sister chromatid exchanges have been produced by mercury compounds in larvae and embryos of amphibians and fishes; various species of bacteria, yeasts, and molds; and cultured somatic cells of fish, insects, echinoderms, and mammals — including somatic cells of rodents, dolphins, cats, and humans (Heagler et al. 1993; De Flora et al. 1994; Kramer and Newman 1994; USPHS 1994; Betti and Nigro 1996).

Toxicant stress to individuals may modify genetic characteristics of mosquitofish populations. Allozyme polymorphisms existing in mosquitofish populations with no history of contaminant stress can be subject to selection and provide the basis for adaptation to anthropogenic stress (Mulvey et al. 1995). For example, metabolic differences in glucosephosphatase isomerase genotypes, or closely related loci, may be expressed in degree of environmental stress or fluctuation (Mulvey et al. 1995). Allozyme genotypes could be responsible for transient genotype effects noted in electrophoretic surveys of mercury-stressed mosquitofish populations (Lee et al. 1992).

Methylmercury induces increased teratogenic and mutagenic effects in killifish (*Fundulus heteroclitus*) embryos after exposure to 50 µg Hg/L for up to 7 days postfertilization (Perry et al. 1988). Chromosomal aberrations were 13% in the treated group vs. 5.1% in controls. Mutagenic effects in killifish embryos occurred at levels below that measured in some marine sediments (Perry et al. 1988). In terms of ability to affect normal development of embryos of the horseshoe crab (*Limulus polyphemus*), mercury — as the acetate or chloride — was the most toxic metal tested, followed in decreasing order by tributyltin chloride, hexavalent chromium, cadmium, copper, lead, and zinc (Itow et al. 1998). Mercury was associated with a high frequency of segment-defective embryos and could be replicated with SH inhibitors, and by compounds inhibiting SH-SS exchange (Itow et al. 1998).

5.7.3 Aquatic Organisms

Sublethal concentrations of mercury are known to adversely affect aquatic organisms through inhibition of reproduction (Dave and Xiu 1991; Kanamadi and Saidapur 1991; Kirubagaran and Joy 1992; Khan and Weis 1993; Punzo 1993), reduction in growth rate (Kanamadi and Saidapur 1991; Punzo 1993), increased frequency of tissue histopathology (Kirubagaran and Joy 1988, 1989; Handy and Penrice 1993; Voccia et al. 1994), impairment in ability to capture prey (Weis and Weis 1995) and olfactory receptor function (Baatrup et al. 1990; Baatrup and Doving 1990), alterations in blood chemistry (Allen 1994) and enzyme activities (Nicholls et al. 1989; Kramer et al. 1992), disruption of thyroid function (Kirubagaran and Joy 1989), chloride secretion (Silva et al. 1992), and other metabolic and biochemical functions (Nicholls et al. 1989; Angelow and Nicholls 1991). In general, the accumulation of mercury by aquatic biota is rapid and depuration is slow (Newman and Doubet 1989; Angelow and Nicholls 1991; Wright et al. 1991; Handy and Penrice 1993; Pelletier and Audet 1995; Geffen et al. 1998). It is emphasized that organomercury compounds, especially methylmercury, were significantly more effective than inorganic mercury compounds in producing adverse effects and accumulations (Baatrup et al. 1990; Wright et al. 1991; Kirubagaran and Joy 1992; Odin et al. 1995).

Reproduction was inhibited among sensitive species of aquatic organisms at water concentrations of 0.03 to 1.6 µg Hg/L. In the planarian (*Dugesia dorotocephala*), asexual fission was suppressed at 0.03 to 0.1 µg organomercury/L (Best et al. 1981); in the slipper limpet (*Crepidula fornicate*), spawning was delayed and fecundity was decreased at 0.25 µg Hg²⁺/L (Thain 1984); in the zebrafish (*Brachydanio rerio*), hatching success was reduced at 0.1 µg Hg²⁺/L and egg deposition was reduced at 0.8 µg/L (Armstrong 1979); fathead minnows (*Pimephales promelas*) exposed to 0.12 µg methylmercury/L for 3 months failed to reproduce (Birge et al. 1979); the leopard frog (*Rana pipiens*) did not metamorphose during exposure to 1.0 µg methylmercury/L for 4 months (USEPA 1980); and in the mysid shrimp (*Mysidopsis bahia*), the abortion rate increased and population size decreased after lifetime (i.e., 28 days) exposure to 1.6 µg/L of mercury as mercuric chloride (Gentile et al. 1983). For sensitive marine invertebrates such as hydroids, protozoans, and mysid shrimp, reproduction was inhibited at concentrations between 1.1 and 2.5 µg Hg²⁺/L; this range was 5 to 71 µg/L for more resistant species of marine invertebrates (Gentile et al. 1983). Impairment of testicular lipid metabolism in catfish (*Clarias batrachus*) at sublethal concentrations of inorganic and organic mercury compounds may account for the mercury-induced inhibition of steroidogenesis and spermatogenesis (Kirubagaran and Joy 1992). Inorganic and organic mercury compounds produce different morphological effects on the micropyle of fish eggs. Reduced insemination success of killifish (*Fundulus heteroclitus*) eggs exposed to methylmercury was due to rupture of cortical vesicles and blockage of the micropyle. However, reduced insemination due to inorganic mercury was due to swelling of the micropylar lip and a decrease in micropyle diameter (Khan and Weis 1993).

Reduced growth of sensitive species of aquatic organisms has been recorded at water concentrations of 0.04 to 1.0 µg Hg/L. The rainbow trout (*Oncorhynchus mykiss*) was the most sensitive species tested; growth reduction was observed after 64 days in 0.04 µg Hg/L as methylmercury, or 0.11 µg Hg/L as phenylmercury (USEPA 1980). In adults of the marine mollusc *Crepidula fornicate*, growth was reduced after 16 weeks in 0.25 µg Hg²⁺/L (Thain 1984). Growth inhibition was recorded in freshwater algae after exposure of 24 h to 10 days to 0.3 to 0.6 µg organomercury/L, in brook trout (*Salvelinus fontinalis*) alevins after exposure for 21 days to 0.79 µg organomercury/L (USEPA 1980), and in the marine alga *Scripsiella faeroense* exposed to 1.0 µg Hg²⁺/L for 24 h (Kayser 1976).

Adverse effects of mercury on aquatic organisms, in addition to those listed on reproduction and growth, have been documented at water concentrations of 0.88 to 5.0 µg/L: enzyme disruption in brook trout (*Salvelinus fontinalis*) embryos immersed for 17 days in solutions containing

0.88 µg/L, as methylmercury (USEPA 1980); an increased incidence of frustule abnormalities and burst thecae in two species of marine algae during exposure to 1.0 µg Hg²⁺/L for 24 h (Kayser 1976; Saboski 1977); arrested development of sea urchin larvae at 3.0 µg Hg²⁺/L for 40 h (USEPA 1980); decreased rate of intestinal transport of glucose, fructose, glycine, and tryptophan in the murrel (*Channa punctatus*) at 3.0 µg Hg²⁺/L for 30 days (Sastry et al. 1982); altered blood chemistry in striped bass (*Morone saxitilis*) at 5.0 µg Hg²⁺/L in 60 days (Dawson 1982); and decreased respiration in striped bass 30 days postexposure after immersion for 30 to 120 days in 5.0 µg Hg²⁺/L (Armstrong 1979; USEPA 1980). In largemouth bass, elevated liver metallothioneins are indicative of elevated muscle mercury concentrations, suggesting that mercury-induced metallothioneins may be useful biomarkers of mercury exposure (Schlenk et al. 1995). In marine molluscs exposed to water concentrations of 6 to 10 µg Hg²⁺/L for 96 h, the feeding of adults ceased, and the swimming rate of larval stages declined (Thain 1984). At 44 µg Hg²⁺/L for 30 days, the freshwater fish *Notopterus notopterus* showed generalized metabolic derangement (Verma and Tonk 1983). In freshwater planarians exposed to 80 to 100 µg/L as methylmercury, behavior was modified and regeneration retarded (Best et al. 1981). And at high sublethal concentrations of methylmercury, rainbow trout were listless and darkly pigmented; appetite was reduced; and digestion was poor (Rodgers and Beamish 1982). Olfactory receptor function in Atlantic salmon is highly vulnerable to brief exposures of sublethal concentrations of mercuric chloride or methylmercury chloride. In both cases, mercury was deposited in the olfactory system along its whole length from receptor cell apices to the brain (Baatrup and Diving 1990). Inorganic mercury inhibited the olfactory response after exposure to 10 µg Hg/L for 10 min, with effects reversible; however, methylmercury-induced inhibition was not reversible (Baatrup et al. 1990).

At lower trophic levels, the efficiency of mercury transfer was low through natural aquatic food chains; however, in animals of higher trophic levels, such as predatory teleosts and fish-eating birds and mammals, the transfer was markedly amplified (Eisler 1978, 1981, 1987). High uptake and accumulation of mercury from the medium by representative species of marine and freshwater teleosts and invertebrates are documented (Kopfler 1974; Eisler 1978, 1981; Birge et al. 1979; Huckabee et al. 1979; USEPA 1980, 1985; Stokes et al. 1981; Rodgers and Beamish 1982; Hirota et al. 1983; Clarkson et al. 1984; McClurg 1984; Niimi and Lowe-Jinde 1984; Ramamoorthy and Blumhagen 1984; Ribeyre and Boudou 1984; Thain 1984; Newman and Doubet 1989; Angelow and Nicholls 1991; Wright et al. 1991; Handy and Penrice 1993). Accumulation patterns were enhanced or significantly modified by numerous biological and abiotic factors (NAS 1978; Eisler 1978, 1981, 1984, 1985; USEPA 1980, 1985; Stokes et al. 1981; Rodgers and Beamish 1982; Clarkson et al. 1984; Ramamoorthy and Blumhagen 1984; Ribeyre and Boudou 1984; Ponce and Bloom 1991; Odin et al. 1995; Choi et al. 1998). In general, the accumulation of mercury was markedly enhanced at elevated water temperatures, reduced water salinity or hardness, reduced water pH, increased age of the organism, and reduced organic matter content of the medium; in the presence of zinc, cadmium, or selenium in solution; after increased duration of exposure; and in the presence of increased nominal concentrations of protein-bound mercury. Uptake patterns were significantly modified by sex, sexual condition, prior history of exposure to mercury salts, the presence of complexing and chelating agents in solution, dietary composition, feeding niche, tissue specificity, and metabolism. However, trends were not consistent between species and it is difficult to generalize. In one example, Ribeyre and Boudou (1984) immersed rainbow trout in solutions containing 0.1 µg Hg/L as methylmercury: after 30 days, bioconcentration factors (BCF) ranged from 28,300 for brain to 238,000 for spleen; values were intermediate for muscle (30,000), whole fish (36,000), blood (102,000), liver (110,000), kidney (137,000), and gill (163,000). These values may have been higher if exposure had extended beyond 30 days. Rodgers and Beamish (1982) showed that whole body mercury residues in rainbow trout subjected to mercury insult continued to increase for the first 66 days before stabilizing. When mercury was presented as inorganic mercuric ion at 0.1 µg/L for 30 days, BCF values were usually lower than in trout exposed to methylmercury: 2300 for muscle; 6800 for brain; 7000 for whole trout; 14,300 for blood; 25,000

for liver; 53,000 for kidney; 68,600 for gill; and 521,000 for spleen (Ribeyre and Boudou 1984). The high BCF values recorded for rainbow trout were probably due to efficient uptake from water, coupled with slow depuration (Rodgers and Beamish 1982).

Total mercury concentrations, in mg/kg FW, in tissues of adult freshwater fishes with signs of methylmercury intoxication ranged from 3 to 42 in brain, 6 to 114 in liver, 5 to 52 in muscle, and 3 to 35 in whole body (Wiener and Spry 1996). Whole body levels up to 100 mg Hg/kg were reportedly not lethal to rainbow trout, although 20 to 30 mg/kg were associated with reduced appetite, loss of equilibrium, and hyperplasia of gill epithelium (Niimi and Lowe-Jinde 1984). However, brook trout showed toxic signs and death at whole body residues of only 5 to 7 mg/kg (Armstrong 1979). In another example, the marine copepod *Acartia clausi*, subjected to 0.05 µg/L of mercury and higher, reached equilibrium with the medium in only 24 h. In that study (Hirota et al. 1983), BCF values for whole *Acartia* after 24-h exposures were 14,360 for inorganic mercuric ion (0.05 µg/L) and, for methylmercury, 179,200 (0.05 µg/L) and 181,000 (0.1 µg/L).

Elimination of accumulated mercury, both organic and inorganic, from aquatic organisms is a complex multicompartmental process, but appears to be largely dependent on its rate of biological assimilation. This rate, in turn, varies widely (20 to 90%) between species, for reasons as yet unexplained (NAS 1978). For example, mercury associated with dietary components that are not assimilated is eliminated rapidly with feces. The rest is absorbed across the gut and incorporated into tissues. This assimilated fraction of mercury is depurated much more slowly, at a rate positively correlated with the organism's metabolism (NAS 1978; Rodgers and Beamish 1982). Route of administration is also important. Bioavailability estimates of methylmercury from orally administered doses to channel catfish (*Ictalurus punctatus*) tend to overestimate the true bioavailability (McCloskey et al. 1998) and indicate that data based on this route of administration need to be reexamined. Time to eliminate 50% of biologically assimilated mercury and its compounds (T_b 1/2) is variable. Among various species of freshwater teleosts, T_b 1/2 values (in days) were 20 for guppies *Poecilia reticulatus*, 23 for goldfish *Carassius auratus*, 100 for northern pike, and 1000 each for mosquitofish *Gambusia affinis*, brook trout, and rainbow trout (Huckabee et al. 1979). A similar range in T_b 1/2 values was recorded for invertebrates and marine fishes: 297 days for the crayfish *Astacus fluviatilis*, 435 days for mussel, 481 days for the clam *Tapes decussatus*, 1030 days for the eel *Anguilla vulgaris*, and 1200 days for the flounder *Pleuronectes flesus* (NAS 1978).

Mercury-tolerant strains of bacteria (Colwell et al. 1976), protozoa (Berk et al. 1978), crustaceans (Green et al. 1976; Weis 1976), and fish (Weis 1984) are reported. Mercury-resistant strains of bacteria are recommended as bioindicators of environmental mercury contamination and as markers of methylmercury in biological samples (Baldi et al. 1991). The mercury-resistant strains of bacteria that have been cultured or discovered may have application in mobilization or fixation of mercury from contaminated aquatic environments to the extent that polluted areas may become innocuous (Colwell et al. 1976). The marine protozoan *Uronema nigricans*, after feeding on mercury-laden bacteria, acquired mercury tolerance within a single generation (Berk et al. 1978). The white shrimp (*Penaeus setiferus*), preexposed for 57 days to 1 µg Hg/L, did not differ from controls during either exposure or subsequent mercury stress experiments (Green et al. 1976). These observations suggest that nonsensitization or adaptation mechanisms are involved. The fiddler crab (*Uca pugilator*) seemed unusually resistant and showed negligible uptake or effects during exposure to 100 µg Hg/L for 2 weeks (Weis 1976). Reasons to account for mercury adaptation of the estuarine cyprinodontiform teleost *Fundulus heteroclitus* to both methylmercury and inorganic mercury are under investigation (Weis 1984).

5.7.4 Birds

Sublethal effects of mercury on birds, administered by a variety of routes, included adverse effects on growth, development, reproduction, blood and tissue chemistry, metabolism, and behavior. Histopathology and bioaccumulation were also noted.

The dietary route of administration is the most extensively studied pathway of avian mercury intake. Domestic chickens fed diets containing as little as 50 µg/kg of mercury, as methylmercury, contained elevated total mercury (2.0 mg/kg fresh weight) residues in liver and kidney after 28 weeks; at 150 µg/kg, residues ranged from 1.3 to 3.7 mg/kg in heart, muscle, brain, kidney, and liver, in that general order. At 450 µg/kg in diets, residues in edible chicken tissues (3.3 to 8.2 mg/kg) were considered hazardous to human consumers, although no overt signs of mercury toxicosis were observed in the chickens (March et al. 1983). High inorganic mercury levels (500 mg/L) in drinking water of chickens decreased growth rate and food and water consumption, and elevated hemoglobin, hematocrit, and erythrocyte content within 3 days (Grissom and Thaxton 1985).

The dietary concentration of 0.5 mg Hg/kg dry weight (equivalent to about 0.1 mg/kg fresh weight) in the form of methylmercury was fed to three generations of mallards (Heinz 1979). Females laid a greater percentage of their eggs outside nest boxes than did controls, and also laid fewer eggs and produced fewer ducklings. Ducklings from parents fed methylmercury were less responsive than controls to tape-recorded maternal calls, but were hyperresponsive to a fright stimulus in avoidance tests (Heinz 1979). Mallard hens fed diets containing 3 mg Hg/kg ration as methylmercury for two reproductive seasons produced eggs with elevated mercury concentrations (5.5 to 7.2 mg Hg/kg FW); hatched ducklings from this group had brain lesions of the cerebellum and reduced survival (Heinz and Locke 1976).

Adult female mallards fed diets containing 1 or 5 mg Hg/kg ration, as methylmercury chloride, produced eggs that contained 1.4 mg Hg/kg FW (1.0 mg/kg ration) or 8.7 mg Hg/kg FW (5 mg Hg/kg diet); breast muscle had 1.0 or 5.3 mg Hg/kg FW; the addition of 5 mg DDE/kg diet did not affect mercury retention in breast muscle or eggs (Heinz 1987). Lesions in the spinal cord were the primary effect in adult female mallards fed diets containing 1.5 or 2.8 mg Hg/kg DW ration as methylmercury (Pass et al. 1975). The tissues and eggs of ducks and other species of birds collected in the wild have sometimes contained levels of mercury equal to, or far exceeding, those associated with reproductive and behavioral deficiencies in domestic mallards (e.g., 9 to 11 mg/kg in feathers; >2.0 mg/kg in other tissues); therefore, it is possible that reproduction and behavior of wild birds have been modified by methylmercury contamination (Heinz 1979). Tissue mercury residues of wild-strain mallards and game-farm mallards were not significantly different after the birds were fed diets containing 0.5 mg Hg/kg as methylmercury for extended periods — indicating that game-farm mallards are suitable substitutes for wild mallards in toxicological evaluations (Heinz 1980).

Interaction effects of mercury with other metals need to be considered. Pekin duck (*Anas platyrhynchos*), age 6 months, fed a diet containing 8 mg Hg/kg ration as methylmercury chloride for 12 weeks, had kidney histopathology; damage effects were exacerbated when diets also contained 80 mg lead acetate/kg, 80 mg cadmium chloride/kg, or both (Rao et al. 1989). Recent studies with mallard adults show significant interaction effects of mercury and selenium. In one 10-week study, mallard adults were fed diets containing 10 mg Hg/kg DW ration as methylmercury chloride, 10 mg Se/kg as seleno-DL-methionine, or a mixture containing 10 mg Hg/kg plus 10 mg Se/kg (Heinz and Hoffman 1998). One of the 12 adult mallards fed the 10 mg Hg/kg diet and 8 others suffered paralysis of the legs; however, none of the 12 males on the mixture diet became sick. Both selenium and mercury diets lowered duckling production through reduced hatching success and survival; the mixture diet was worse than either Hg or Se alone. Controls produced 7.6 ducklings/female, females fed 10 mg Se/kg produced 2.8, females fed 10 mg Hg/kg produced 1.1 young, and the mixture diet resulted in 0.2 ducklings/females. Deformity frequency was 6.1% in control ducklings, 16.4% for the mercury group, 36.2% for the selenium group, and 73.4% for the group fed the methylmercury and selenomethionine mixture. The presence of mercury in the diet enhanced selenium storage; however, Se did not enhance Hg storage (Heinz and Hoffman 1998). In another study with mallard adult males fed diets as outlined in the Heinz and Hoffman (1998) study, the investigators analyzed blood, liver, and brain samples for clinical and biochemical alterations after

10 weeks (Hoffman and Heinz 1998). The 10 mg Hg/kg ration group had decreased hematocrit and hemoglobin, and decreased activities of various enzymes involved in glutathione metabolism. Selenium in combination with methylmercury partially or totally alleviated effects of mercury on various glutathione activities. The ability of seleno-DL-methionine to restore the glutathione status involved in antioxidative defense mechanisms may be important in protecting against the toxic effects of methylmercury (Hoffman and Heinz 1998).

Dietary concentrations of 1.1 mg total Hg/kg have been associated with kidney lesions in juvenile starlings (*Sturnus vulgaris*) and with elevated residues in the liver (6.5 mg/kg dry weight and kidney (36.3 mg/kg), after exposure for 8 weeks (Nicholson and Osborn 1984). In American black ducks (*Anas rubripes*) fed diets containing 3.0 mg Hg/kg as methylmercury for 28 weeks, reproduction was significantly inhibited; tissue residues were elevated in kidney (16.0 mg/kg fresh weight) and liver (23.0 mg/kg); and brain lesions characteristic of mercury poisoning were present (Finley and Stendell 1978). Japanese quail (*Coturnix japonica*) fed diets containing 8 mg Hg/kg of inorganic mercury for 3 weeks had depressed gonad weights; those fed 3 mg/kg inorganic mercury or 1 mg/kg methylmercury for 9 weeks showed alterations in brain and plasma enzyme activities (Hill and Soares 1984). Grossly elevated tissue residues of 400 mg/kg in feathers and 17 to 130 mg/kg in other tissues were measured in gray partridge (*Perdix perdix*) after dietary exposure of 20 to 25 mg total Hg/kg for 4 weeks (McEwen et al. 1973).

Mercury exposure by immersion and oral administration have caused reproductive and behavioral modifications. Brief immersion of mallard eggs in solutions of methylmercury resulted in a significant incidence of skeletal embryonic aberrations at dosages of 1.0 µg Hg/egg, and higher; no increases in embryonic malformations were noted at 0.3 µg Hg/egg (Hoffman and Moore 1979). Reduced reproductive ability was noted in grey pheasants ingesting 640 µg Hg (as organomercury)/kg body weight daily for 30 days (McEwen et al. 1973); similar results were observed in ring-necked pheasants (Spann et al. 1972; Mullins et al. 1977). Behavioral alterations were noted in pigeons (*Columba livia*) given 3000 µg inorganic Hg/kg body daily for 17 days (Leander et al. 1977) or 1000 µg/kg body weight of methylmercury for 5 weeks (Evans et al. 1982). Observed behavioral changes in posture and motor coordination of pigeons were permanent after the brain accumulated >12,000 µg Hg/kg fresh weight, and were similar to the "spastic paralysis" observed in wild crows during the Minamata, Japan, outbreak of the 1950s, although both species survived for years with these signs (Evans et al. 1982).

Tissue concentrations >15,000 µg Hg/kg FW brain and >30,000 to 40,000 µg/kg FW liver or kidney are associated with neurological impairment (Scheuhammer 1988). Mercury residues of 790 to 2000 µg/kg in egg and 5000 to 40,000 µg/kg in feathers are linked to impaired reproduction in various bird species (Spann et al. 1972; NAS 1978; Heinz 1979; Fimreite 1979; Solonen and Lodenius 1984). Residues in eggs of 1300 to 2000 µg Hg/kg fresh weight were associated with reduced hatching success in white-tailed sea-eagles (*Haliaeetus albicilla*), the common loon (*Gavia immer*), and in several seed-eating species (Fimreite 1979). This range was 900 to 3100 µg/kg for ring-necked pheasant (Spann et al. 1972), and 790 to 860 µg/kg for mallards (Heinz 1979). Residues of 5000 to 11,000 µg Hg/kg in feathers of various species of birds have been associated with reduced hatch of eggs and with sterility (NAS 1978). Sterility was observed in the Finnish sparrow hawk (*Accipiter nisus*) at mercury concentrations of 40,000 µg/kg in feathers (Solonen and Lodenius 1984). Chicks of the common tern (*Sterna hirundo*) from a colony in Long Island, New York, with abnormal feather loss, had significantly elevated mercury levels in blood and liver (Gochfeld 1980); however, the linkage of feather loss to mercury contamination requires further examination.

Interaction effects of mercury with other contaminants, such as herbicides and pesticides, could intensify hazards to avian populations (Mullins et al. 1977). For example, a striking parallel exists between levels of Hg and of DDT and its metabolites in birds of prey, suggesting the existence of common ecotoxicological mechanisms (Delbeke et al. 1984; Wiemeyer et al. 1984); additional research is clearly needed.

5.7.5 Mammals

Mercury has no known physiological function (USEPA 1985). In humans and other mammals, it causes teratogenic, mutagenic, and carcinogenic effects; the fetus is the most sensitive life stage (NAS 1978; Chang 1979; Khera 1979; USEPA 1980, 1985; Elhassani 1983; Greener and Kochen 1983; Clarkson et al. 1984). Methylmercury irreversibly destroys the neurons of the central nervous system. Frequently, a substantial latent period intervenes between the cessation of exposure to Hg and the onset of signs and symptoms. This interval is usually measured in weeks or months, but sometimes in years (Clarkson et al. 1984). At high sublethal doses in humans, mercury causes cerebral palsy, gross motor and mental impairment, speech disturbances, blindness, deafness, microcephaly, intestinal disturbances, tremors, and tissue pathology (Chang 1979; USEPA 1980, 1985; Elhassani 1983; Clarkson et al. 1984; USPHS 1994). Pathological and other effects of mercury may vary from organ to organ, depending on factors such as the effective toxic dose in the organ, the compound involved and its metabolism within the organ, the duration of exposure, and the other contaminants to which the animal is concurrently exposed (Chang 1979). Many compounds — especially salts of selenium — protect humans and other animals against mercury toxicity, although their mode of action is not clear (NAS 1978; Chang 1979; USEPA 1980, 1985; Eisler 1985).

Adverse effects of organomercury compounds to selected species of mammals have been recorded at administered doses of 0.25 mg Hg/kg body weight daily, dietary levels of 1.1 mg/kg, and blood Hg levels of 1.2 mg/L ([Table 5.10](#)).

Mercury transfer and biomagnification through mammalian food chains is well documented (Galster 1976; NAS 1978; Eaton et al. 1980; Eisler 1981; Huckabee et al. 1981; Sheffy and St. Amant 1982; Kucera 1983; Clarkson et al. 1984; Wren 1986), but there is considerable variation. Among terrestrial mammals, for example, herbivores such as mule deer, moose (*Alces alces*), caribou (*Rangifer tarandus*), and various species of rabbits usually contained less than 1.0 mg Hg/kg fresh weight in liver and kidney, but carnivores such as the marten (*Martes martes*), polecat (*Mustela putorius*), and red fox (*Vulpes vulpes*) frequently contained more than 30 mg/kg (NAS 1978). The usually higher mercury concentrations in fish-eating furbearers than in herbivorous species seemed to reflect the amounts of fish and other aquatic organisms in the diet. In river otter and mink from the Wisconsin River drainage system, Hg levels paralleled those recorded in fish, crayfish, and bottom sediments at that location. Highest Hg levels in all samples were recorded about 30 km downstream from an area that supported 16 pulp and paper mills and a chloralkali plant. Residues were highest in the fur, followed by the liver, kidney, muscle, and brain (Sheffy and St. Amant 1982).

In marine mammals, more than 90% of the mercury content is inorganic; however, enough methylmercury occurs in selected tissues to result in the accumulation of high tissue concentrations of methylmercury in humans and wildlife consuming such meat (Clarkson et al. 1984). The liver of the ringed seal (*Phoca hispida*) normally contains 27,000 to 187,000 µg Hg/kg fresh weight, and is a traditional and common food of the coastal Inuit people (Eaton et al. 1980). Although levels of Hg in hair (109,000 µg/kg) and blood (37 µg/L) of Inuits were grossly elevated, no symptoms of Hg poisoning were evident in the coastal Inuits. Similar high concentrations have been reported for Alaskan Inuit mothers who, during pregnancy, ate seal oil twice a day, and seal meat or fish from the Yukon–Kuskokwim Coast every day (Galster 1976). Despite the extremely high total Hg content of seal liver, only the small organomercury component was absorbed and appeared in the tissues. Cats fed a diet of seal liver (26,000 µg Hg/kg fresh weight) for 90 days showed no neurologic or histopathologic signs (Eaton et al. 1980). It seems that the toxic potential of seal liver in terms of accumulated tissue levels in cats (up to 862 µg total Hg/L blood, and 7600 µg total Hg/kg hair) is better indicated by the organomercury fraction in seal liver than by the concentration of total Hg (Eaton et al. 1980).

Table 5.10 Sublethal Effects of Organomercury Compounds Administered to Selected Species of Mammals

Organism	Dose, and Other Variables	Effect	Ref. ^a
Cat, <i>Felis domesticus</i>	250 µg/kg BW daily on days 10 to 58 of gestation; oral route	Increased incidence of anomalous fetuses	1
Human, <i>Homo sapiens</i> ; adult	50 µg/day	Risk of paresthesia, 0.3% (burning-prickling sensation of skin)	2
Human, adult	200 µg/day	Risk of paresthesia, 8%	2
Human, adult	1000 µg/day	Risk of paresthesia, 50%	2
Human, adult	50 µg Hg/m ³ air for 8 h	Mercury content, in µg/L, of 100 in urine and 280 in blood	9
Human, adult	100 µg/m ³ air for 8 h	Mercury content, in µg/L, of 250 in urine and 500 in blood	9
Human, whole blood Hg concentration	<10–100 µg/L	Increased tremors	9
	10–20 µg/L	Increased prevalence of abnormal psychomotor scores	9
	>15 µg/L	Disturbances in tests on verbal intelligence and memory	9
Human, urine	0–510 µg/L	Short-term memory loss	9
	5–1000 µg/L	Increased tremor frequency and reaction time	9
	20–450 µg/L	Increased motor and sensory nerve latency	9
	>56 µg/L	Disturbances in tests on verbal intelligence and memory	9
Human, adult	Various	Symptoms of poisoning evident at residues of 1200 µg Hg/L blood, 2000 to 3000 µg/kg whole body, or 3400 µg/kg hair	6
Human, infant	Various	Severe effects at blood levels of 3000 µg Hg/L	8
Monkeys, <i>Macaca fascicularis</i> ; adults; age 7–10 years	Exposed <i>in utero</i> ; maternal doses of 0, 50, 70, or 90 µg methylmercury/kg BW daily resulted in blood mercury levels in treated infants of 1.0–2.5 mg/L; offspring were conditioned and tested for ability to respond to a lit button for an apple juice reward and other tasks	<i>In utero</i> exposure to mercury did not produce significant adverse effects on adult performance, although gender differences may interact with methylmercury on certain behaviors	11
Monkeys, <i>Macaca fascicularis</i> ; female adults	Daily dose of methylmercury chloride in apple juice for 150 days equivalent to daily doses of 0.0, 0.4, 4.0, or 50.0 µg methylmercury/kg BW	All groups seemed normal at day 150; no difference in blood or serum cholinesterase activity	12
Monkeys, <i>Macaca</i> spp.	Various	Visual upset at blood mercury levels of 1200 to 4000 µg/L or brain levels of 6000 to 9000 µg Hg/kg; tremors at blood levels of 2000 to 10,000 µg Hg/L; kidney pathology at brain levels of 1500 µg Hg/kg	6
Rhesus monkey, <i>Macaca mulatta</i>	16 µg/kg body weight (BW) daily on days 20 to 30 of pregnancy	No effect on reproduction	1
Mice, <i>Mus</i> spp.	Various	Residues of 2000 to 5000 µg/kg hair or >10,000 µg/kg brain associated with motor incoordination and decreased swimming ability; no observable effect at <2000 µg/kg hair	6
Mink, <i>Mustela vison</i>	1.0 µg/kg ration as methylmercury	Reproduction normal; growth rate of kits normal	10
Mink	1100 mg/kg in diet	Residues of 7100 to 9300 µg/kg in brain; signs of poisoning	5

Table 5.10 (continued) Sublethal Effects of Organomercury Compounds Administered to Selected Species of Mammals

Organism	Dose, and Other Variables	Effect	Ref. ^a
Harp seal, <i>Pagophilus groenlandicus</i>	250 µg kg BW daily for 90 days in diet	Increased incidence of anomalous fetuses	3, 4
Brown Norway rat, <i>Rattus norvegicus</i>	Adult males gavaged twice weekly for 19 weeks with methylmercury chloride equivalent to 0.8, 8, or 80 µg Hg/kg BW daily	Intratesticular testosterone in high dose group reduced 44% and sperm count 17%. Negative relation between fertility and testicular Hg content. Testicular Hg concentrations, in µg/kg FW, were 1 in controls, 10 in 0.8 µg/kg BW daily group, 107 in 8 µg/kg group, and 1670 in high dose group	13
Laboratory white rat, <i>Rattus</i> sp.	50 µg/m ³ air, 4 h daily for 7 days	Impaired spatial learning; increased locomotor activity	9
Rat	500 µg/kg BW daily; oral route	Reduced fertility	1
Rat	2000 µg/kg in diet (as Pacific blue marlin); gestation through postnatal day 16	Adverse behavioral changes in offspring	6
Rat	13,300 to 50,000 µg/kg BW daily for 5 days; subcutaneous injection	Impaired cutaneous sensitivity and hearing up to one year post-treatment	7

^a 1, Khera 1979; 2, Clarkson et al. 1984; 3, Ronald et al. 1977; 4, Ramprashad and Ronald 1977; 5, Kucera 1983; 6, Suzuki 1979; 7, Wu et al. 1985; 8, Elhassani 1983; 9, USPHS 1994; 10, Wren et al. 1987b; 11, Gilbert et al. 1994; 12, Petruccioli and Turillazzi 1991; 13, Friedmann et al. 1998.

Retention of mercury by mammalian tissues is longer for organomercury compounds (especially methylmercury) than for inorganic mercury compounds (NAS 1978; Clarkson and Marsh 1982; Elhassani 1983; Clarkson et al. 1984). Excretion of all mercury species follows a complex, variable, multicompartmental pattern; the longer-lived chemical mercury species have a biological half-life that ranges from about 1.7 days in human lung to 1.36 years in whole body of various pinnipeds. In humans, increased urinary excretion and blood levels of mercury were observed in volunteers who used phenylmercuric borate solutions or lozenges intended for treatment of throat infections (USPHS 1994).

5.7.6 Other Groups

Seedlings of rice (*Oryza sativa*) grown on mercury-contaminated waste soil from a chloralkali factory for 75 days showed increasing mercury concentrations over time with increasing soil mercury content. At 2.5% waste soil in garden soil, rice seedlings contained 8.0 mg Hg/kg FW; at 10%, 15.2 mg Hg/kg; and at 17.5% waste soil in garden soil, seedlings had 19.1 mg Hg/kg FW (Nanda and Misra 1997). Content of nucleic acids and proteins in rice shoot decreased with increasing mercury concentrations in waste soils and with time, but free amino acid content increased. An increase in the RNA/DNA ratio occurred, indicating an enhanced synthesis of RNA per molecule of DNA (Nanda and Mishra 1997). Seedlings of spruce (*Picea abies*) exposed to solutions containing up to 0.2 mg Hg/L as inorganic mercury or methylmercury showed a dose-dependent inhibition in root growth, especially for methylmercury. Dose-dependent decreases in concentrations of potassium, manganese, and magnesium were evident in roots and root tips, and increases in iron in root tips (Godbold 1991).

Methylmercury compounds have induced abnormal sex chromosomes in the fruit fly (*Drosophila melanogaster*) (NAS 1978; Khera 1979). Earthworms (*Eisenia foetida*) exposed to soil containing methylmercury concentrations of 5.0 mg Hg/kg — typical of soil Hg levels near chloralkali plants — showed a significant reduction in the number of segments regenerated after 12 weeks, and contained

85 mg Hg/kg on a whole-body fresh weight basis. Regeneration was normal at soil Hg levels of 1.0 mg/kg, although body burdens up to 27 mg/kg were recorded. It was concluded that soil contaminated with methylmercury posed a greater hazard to the predators of earthworms than to the earthworms (Beyer et al. 1985). Studies with a different species of earthworm (*Octochaetus pattoni*) and mercuric chloride demonstrated a progressive initial increase in reproduction as soil mercury levels increased from 0.0 to the 60-day lethal level of 5.0 mg/kg (Abbasi and Soni 1983).

5.8 RECOMMENDATIONS

Proposed mercury criteria for the protection of sensitive aquatic organisms, birds, and mammals, as well as human health, are shown in [Table 5.11](#). In almost every instance, these criteria are listed as concentrations of total mercury, with most, if not all, the mercury present as an organomercury species. In some cases the recommended criteria are routinely exceeded, as is the case for brown bears (*Ursus arctos*) in the Slovak Republic (Zilincar et al. 1992), and in Italian seafood products recommended for human consumption (Barghigiani and De Ranieri 1992).

In 1980, the U.S. Environmental Protection Agency's proposed mercury criteria for freshwater aquatic life protection were 0.00057 µg/L (24-h average), not to exceed 0.0017 µg/L at any time. These criteria seemed to afford a high degree of protection to freshwater biota, as judged by survival, bioconcentration, and biomagnification. Literature documented in this paper showed that mercury concentrations in water of 0.1 to 2.0 µg/L were fatal to sensitive aquatic species and that concentrations of 0.03 to 0.1 µg/L were associated with significant sublethal effects. The 1980 proposed freshwater criteria provided safety factors for acute toxicities of 175 to 3508 based on the 24-h average, and 58 to 1176 based on the maximum permissible concentration ([Table 5.11](#)). For

Table 5.11 Proposed Mercury Criteria for Protection of Various Resources and Human Health

Resource and Criterion (units in parentheses)	Mercury Concentration	Reference ^b
AQUATIC LIFE		
Freshwater (µg/L)	Total recoverable mercury less than 0.00057 (24 h average), not to exceed 0.0017 at any time	1
Freshwater (µg/L)	Less than 0.012, 4-day average (not to be exceeded more than once every 3 years; less than 2.4, one-h average (not to be exceeded more than once every 3 years) ^a	2
Freshwater (µg/L)	Less than 0.1	33, 34
	Less than 0.01	34
Freshwater (µg/L)	Less than 10.0 from point source discharge	3
Inland surface waters, India		
Public water supply, Wisconsin	Less than 0.079	42
Warmwater sport fish communities	Less than 0.079	42
Coldwater communities	Less than 0.079	42
Great Lakes communities	Less than 0.079	42
Saltwater (µg/L)	Total recoverable mercury less than 0.025 (24-h average), not to exceed 3.7 at any time	1
Saltwater (µg/L)	Less than 0.025, 4-day average (not to be exceeded more than once every 3 years); less than 2.1, one-h average (not to be exceeded more than once every 3 years) ^a	2

Table 5.11 (continued) Proposed Mercury Criteria for Protection of Various Resources and Human Health

Resource and Criterion (units in parentheses)	Mercury Concentration	Reference^b
Sediments (mg/kg dry weight)		
Canada, marine and freshwater		
Safe	<0.14	34
Severe effect level	>2.0	35
California		
Low toxic effect	>0.15	35
Acceptable	<0.51	35
Bivalve mollusc larval abnormalities	>0.51	35
Hazardous	>1.2–1.3	35
Washington state, safe	<0.41	35
Tissue residues, fish (µg Hg/kg fresh weight)		
Brook trout, <i>Salvelinus fontinalis</i>		
Whole body, nonlethal	Less than 5000	1, 2
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Lethal		
Eggs	More than 70	31
Muscle, adults	More than 10,000	31
Whole body	10,000–20,000	32
Adverse effects probable		
Whole body	1000–5000	32
Various species; freshwater; adults; adverse effects expected		
Brain	More than 3000	31
Muscle	More than 5000	31
Whole body	More than 3000	31
BIRDS		
Tissue residues (µg/kg FW)		
Safe		
Brain, muscle	Less than 15,000	27
Feather	Less than 5000	4
Kidney		
Nonmarine birds	Less than 20,000	27, 30
Seabirds	Less than 30,000	30
Liver		
Normal	1000–10,000	37
Toxic to sensitive species	More than 5000–6000	37, 55
Hazardous, possibly fatal	More than 20,000	37, 38
Egg (µg/kg FW), safe		
Mallard, <i>Anas platyrhynchos</i>	Less than 900	5
Ring-necked pheasant, <i>Phasianus colchicus</i>	Less than 900	6
Common tern, <i>Sterna hirundo</i>		
Normal reproduction	Less than 1000	36
Reduced hatching and fledging success	2000–4700	36
Various species, safe	Less than 500–less than 2000	7, 30
Waterbirds		
Adverse effects	1000–3600	55
Feather (µg/kg DW)		
Acceptable	Less than 9000	26
Diet (µg Hg/kg FW ration as methylmercury)	Less than 20 for fish-eating birds	56
Diet (µg/kg FW ration as methylmercury)	50 to less than 100	5, 8
Diet (µg/kg FW)	Less than 300 ^e	57, 59
Diet (µg/kg DW)	Less than 1000 to less than 3000	29, 30
Daily intake (µg/kg body weight)	Less than 640	6, 9, 10, 60
Daily intake (µg/kg body weight daily)	Less than 32 ^f	60

Table 5.11 (continued) Proposed Mercury Criteria for Protection of Various Resources and Human Health

Resource and Criterion (units in parentheses)	Mercury Concentration	Reference^b
CROPS		
Irrigation water ($\mu\text{g/L}$) Brazil	Less than 0.2	43
Land application of sludge and solid waste, maximum permissible concentration (mg Hg/kg waste)		
Iowa, Maine, Vermont	10.0	42
California	20.0	42
Soils (mg/kg DW)		
Germany	Less than 2.0	44
MAMMALS		
Daily dosage ($\mu\text{g/kg}$ body weight)	Less than 250	13, 14, 15
Diet ($\mu\text{g Hg/kg FW}$ ration as methylmercury)	Less than 100 for piscivorous mammals	56
Diet ($\mu\text{g/kg FW feed}$)	Less than 1100	12
Diet ($\mu\text{g/kg FW feed}$)	Less than 2000	30
Drinking water ($\mu\text{g/L}$)		
Wild and domestic animal supply, Wisconsin	Less than 0.002	42
Terrestrial vertebrate wildlife	0.0013 ^g	60
Soils (mg/kg DW), terrestrial ecosystem protection		
Agricultural and residential land use	Less than 2.0	34
Commercial and industrial use	Less than 30.0	34
Tissue residues ($\mu\text{g/kg FW}$)		
Kidney	Less than 1100	1
Liver, kidney	Less than 30,000	30
Blood	Less than 1200	11
Brain	Less than 1500	11
Hair	Less than 2000	11
Florida panther, <i>Felis concolor coryi</i> , blood		
Reproduction normal (1.46 kittens per female annually)	Less than 250	41
Reproduction inhibited (0.167 kittens per female annually)	More than 500	41
Otter, <i>Lutra lutra</i> , liver		
Normal	Less than 4000	39
Adverse sublethal effects possible	More than 10,000	39
Wildlife protection, Slovak Republic		
Fat	Less than 1	40
Muscle	Less than 50	40
Liver, kidney	Less than 100	40
HUMAN HEALTH		
Air		
Acceptable ($\mu\text{g/m}^3$)		
Arizona	1.5 for 1 h	42
California	<0.00	42
Connecticut	1.0 for 8 h	42
Kansas	0.0024 annually	42
Montana	0.008 for 24h	42
North Dakota	0.0005 for 8 h	42
New York	0.167 for 1 year	42
Texas	0.05 for 1 year	42
Virginia	1.7 for 24 h	42
Workplace		
Organic mercury	Less than 10	42
Metallic mercury vapor	Less than 50	42

Table 5.11 (continued) Proposed Mercury Criteria for Protection of Various Resources and Human Health

Resource and Criterion (units in parentheses)	Mercury Concentration	Reference^b
Short-term exposure limit, skin ($\mu\text{g}/\text{m}^3$)	Less than 30.0	42
Emissions, in grams of mercury daily		
From mercury ore processing facilities and mercury cell chlor-alkali plants	Max. 2300	42
From sludge incineration plants, sludge drying plants, or any combination that process wastewater treatment plant sludge	Max. 3200	42
Drinking water ($\mu\text{g}/\text{L}$)		
Total mercury		
Brazil	Less than 0.2	43
International	Less than 1.0	42
USA, most states	Less than 2.0	42
Bottled water	Less than 2.0	42
Effluent limitations from wastewater treatment plants ($\mu\text{g}/\text{L}$)		
Delaware, Oklahoma, Texas	Less than 5.0	42
Illinois, Wisconsin	Less than 0.5	42
New Jersey	Less than 2.0	42
Tennessee	Less than 50.0	42
Fish consumption advisory (mg total Hg/kg FW edible aquatic product)		
Florida	More than 0.5	53
Most states, USA	More than 1.0	53
Fish and seafood, edible portions		
Acceptable intake (μg)		
Daily, 60 kg adult	25	15
Weekly, 70 kg adult	200	15
Weekly, adult	500	17
Florida, consumption of contaminated fish with 2–3 mg methylmercury/kg FW muscle		
Nonpregnant adults (grams weekly)	Less than 454	45
Women of childbearing age and children less than 15 years of age (grams monthly)	Less than 454	45
Pregnant women ($\mu\text{g}/\text{kg FW}$)	Less than 250	15
Various locations ($\mu\text{g}/\text{kg FW}$)		
Japan	Less than 400	4
Canada, West Germany, United States	Less than 500	4, 42, 52
Australia	Less than 500 (mean), not to exceed 1500 in any sample	18
Brazil	Less than 500	49
Italy	Less than 700	51
Finland	Less than 1000	17
Israel	Less than 1000	48
Scandinavia	Less than 1000	19
Sweden	Less than 1000	4, 54
United States	Less than 1000	1, 2, 20, 21
United States	Max. of 1000 as methylmercury	42
Shark flesh ($\mu\text{g}/\text{kg FW}$)		
Consumption limited to once weekly by healthy nonpregnant adults	500–1500	41
Consumption prohibited	More than 1500	41
Foods of animal origin ($\mu\text{g}/\text{kg FW}$)		
Livestock tissues	Less than 500	22
Wildlife tissues	Less than 50	23
Breast muscle		
Domestic poultry	Less than 500	4
Ducks (wildlife)	Less than 1000	24

Table 5.11 (continued) Proposed Mercury Criteria for Protection of Various Resources and Human Health

Resource and Criterion (units in parentheses)	Mercury Concentration	Reference^b
Foods of vegetable origin		
Treated grain (µg/kg FW)	Less than 1000	42
Vegetables (µg/kg DW)	Less than 50	44
All foods		
Adult weekly intake (µg)		
As methylmercury	Less than 100	4
As total mercury	Less than 150	4
As methylmercury	Less than 200	50, 56
As total mercury	Less than 300	50, 51
Adult daily intake (µg/kg body weight daily)		
Nonpregnant adults	Less than 4.3	28
Pregnant adults	Less than 0.6 to less than 1.1 ^c	28
Diet (µg/kg FW ration)	Max. 500	46
Various locations (µg/kg FW)		
Australia	10 to 100	4
Benelux countries	Less than 30	4
Brazil	Less than 50	4
Canada	Less than 500	25
United States	Less than 1000	25, 58
Permissible tolerable weekly intake (µg/kg body weight weekly)		
Total mercury	Less than 5.0	42
Total mercury	Max. 4.28	51
Methylmercury	Less than 3.3	42, 47
Oral dose, maximum concentration, in mg Hg/kg	8.4 ^d	42
BW daily as phenylmercuric acetate		
Tissue residues (µg/kg FW)		
Blood	Less than 200	16
Hair	Less than 6000	17
Water (µg/L)		
Potable	Less than 2.0	4
Recreational, Brazil	Less than 0.2	43
Protection from toxic properties of Hg through consumption of contaminated aquatic organisms	Less than 0.146	1
Protection from toxic properties of Hg from ingestion of water plus consumption of resident aquatic organisms	Less than 0.144	1, 42

^a All mercury that passes through a 0.45-µm membrane filter after the sample is acidified to pH 1.5 to 2.0 with nitric acid.

^b 1, USEPA 1980; 2, USEPA 1985; 3, Abbasi and Soni 1983; 4, NAS 1978; 5, Heinz 1979; 6, Spann et al. 1972; 7, Fimreite 1979; 8, March et al. 1983; 9, McEwen et al. 1973; 10, Mullins et al. 1977; 11, Suzuki 1979; 12, Kucera 1983; 13, Ramprashad and Ronald 1977; 14, Ronald et al. 1977; 15, Khera 1979; 16, Galster 1976; 17, Lodenius et al. 1983; 18, Lyle 1984; 19, Suckcharoen and Lodenius 1983; 20, Barber et al. 1984; 21, Miller and Jude 1984; 22, Best et al. 1981; 23, Krynski et al. 1982; 24, Lindsay and Dimmick 1983; 25, Bodaly et al. 1984; 26, Beyer et al. 1997; 27, Heinz 1996; 28, Clarkson 1990; 29, Scheuhammer 1988; 30, Thompson 1996; 31, Wiener and Spry 1996; 32, Niimi and Kissoon 1994; 33, Dave and Xiu 1991; 34, Gaudet et al. 1995; 35, Gillis et al. 1993; 36, Mora 1996; 37, Wood et al. 1996; 38, Littrell 1991; 39, Mason and Madsen 1992; 40, Zilincar et al. 1992; 41, Roelke et al. 1991; 42, USPHS 1994; 43, Palhetta and Taylor 1995; 44, Zumbock 1997; 45, Fleming et al. 1995; 46, Holbrook et al. 1994; 47, Petruccioli and Turillazzi 1991; 48, Krom et al. 1990; 49, Hylander et al. 1994; 50, Buzina et al. 1989; 51, Bargigiani and De Ranieri 1992; 52, Lathrop et al. 1991; 53, Facemire et al. 1995; 54, Hakanson et al. 1990; 55, Zillioux et al. 1993; 56, Yeardley et al. 1998; 57, Scheuhammer et al. 1998a; 58, Kannan et al. 1998; 59, Gariboldi et al. 1998; 60, Wolfe and Norman 1998.

^c Assuming continuous exposure until steady-state balance for methylmercury is achieved. This process will take up to one year in most cases (Clarkson 1990).

^d Derived from lowest observable adverse effect level (LOAEL) of 42 µg Hg/kg BW daily of phenylmercuric acetate for detectable kidney damage in rats after 2 years and an uncertainty factor of 5 (USPHS 1994).

^e Loon (*Gavia immer*) reproduction declined when mercury in prey exceeded 300 µg total Hg/kg FW.

^f No observed adverse effect level with uncertainty factor of 20.

^g Based on food chain biomagnification in aquatic webs.

protection against sublethal effects, these values were 53 to 175 based on the 24-h mean, and 18 to 59 based on the maximum permissible concentration ([Table 5.11](#)). However, more recent freshwater criteria of 0.012 µg/L, not to exceed 2.4 µg/L ([Table 5.11](#); USEPA 1985), dramatically reduces the level of protection afforded aquatic biota: safety factors for acute toxicities are now 8 to 167 based on the 96-h average, and only 0.04 to 0.8 based on the maximum permissible concentration. For protection against sublethal effects, these values were 2 to 8 based on the 4-day average, and only 0.01 to 0.04 based on the maximum permissible concentration, or essentially no significant protection. The proposed saltwater criteria of USEPA (1980) for mercury and marine life were unsatisfactory. Proposed saltwater values of 0.025 µg/L (24-h average), not to exceed 3.7 µg/L at any time ([Table 5.11](#)), provided safety factors of 4 to 80 against acute toxicity (based on a 24-h average), but less than 0.5 based on the maximum permissible level. For protection against sublethal damage effects, the safety factors computed were 1.2 to 4 (based on a 24-h average) and less than 0.03 (based on maximum allowable concentration). The more recent saltwater criteria of 0.025 µg/L, not to exceed 2.1 µg/L ([Table 5.11](#); USEPA 1985), does not appear to offer a substantive increase in protection to marine life, when compared to criteria proposed 5 years earlier (USEPA 1980). It seems that some downward modification is needed in the proposed mercury saltwater criteria if marine and estuarine biota are to be provided even minimal protection.

The significance of elevated mercury residues in tissues of aquatic organisms is not fully understood. Induction of liver metallothioneins and increased translatability of mRNA are biochemical indicators of the response of fish to mercury exposure (Angelow and Nicholls 1991; Schlenk et al. 1995), and more research is recommended on this and other indicators of mercury stress. Concentrations exceeding 1000 µg Hg/kg fresh weight can occur in various tissues of selected species of fish and aquatic mammals eaten by humans, but it would be incorrect to assume that aquatic food chains — especially marine food chains — incorporate mercury exclusively from anthropogenic activities (Barber et al. 1984). Some organisms, however, do contain mercury tissue residues associated with known adverse effects to the organism and its predators. Thus, whole-body residues of 5000 to 7000 µg Hg/kg fresh weight in brook trout eventually proved fatal to that species (USEPA 1980). To protect sensitive species of mammals and birds that regularly consume fish and other aquatic organisms, total mercury concentrations in these food items should probably not exceed 100 µg/kg for avian protection, or 1100 µg/kg for small mammals ([Table 5.11](#)). By comparison, proposed mercury levels in fish and seafood, in µg/kg fresh weight, for human health protection should not exceed 250 for expectant mothers, and 400 to 1000 for adults worldwide ([Table 5.11](#)). In humans, methylmercury concentration in head hair during pregnancy is considered to be the most reliable indicator for predicting the probability of psychomotor retardation in the child. The minimum toxic intake for pregnant humans is estimated to range between 0.6 and 1.1 µg methylmercury/kg body weight daily (Clarkson 1990).

Since long-lived, slow-growing, high-trophic-position aquatic organisms usually contain the highest tissue mercury residues (Eisler 1981), some fisheries managers have proposed a legal maximum limit based on fish length or body weight, or alternatively, constraining the mean mercury concentration of the entire catch to a designated level. In the Australian shark fishery, for example, implementation of a maximum length restriction (to a designated level of 500 µg Hg/kg), would result in retention of less than half of the present catch of seven species (Lyle 1984). Also in Australia, a maximum total length of 92 cm is proposed for the taking of yellowtail kingfish (*Seriola grandis*) and would effectively remove 23% of the total weight of the catch and 9% of the numbers (Chvojka 1988). If the total length of the yellowtail kingfish is reduced to 73 cm, a length that ensures that almost all fish will contain less than 500 µg Hg/kg FW muscle, this would preclude 59% by weight and 30% by numbers (Chvojka 1988). Other strategies to control mercury concentrations in predatory fishes include control of forage fish, overfishing, and various chemical treatments. In lakes with pelagic forage fish, there is less than a 5% probability of finding elevated mercury levels in muscle of lake trout less than 30 cm in total length vs. 45 cm in lakes where pelagic forage fish were absent. In the case of lake trout lakes with no pelagic forage fish, every

effort should be made to avoid their introduction (Futter 1994). Overfishing of top-level predators is recommended as a means of lowering methylmercury levels in certain types of lakes and is attributed to the more rapid growth of the predators and by changes in the dietary intake of methylmercury (Verta 1990). The treatment of lakes with selenium compounds is one of the few known methods of lowering the mercury content of fish muscle to less than 1.0 mg Hg/kg FW (Paulsson and Lundbergh 1989). Treatments that have achieved partial success in reducing mercury content in fish tissues include liming of lakes, wetlands, and drainage areas (Lindqvist et al. 1991). More research is needed on mercury protectants because several are known to cause substantial reductions in tissue mercury concentrations in fishes and plants (Siegel et al. 1991). Thiamine and various group VI derivatives, including sulfur, selenium, and tellurium compounds, protect against organomercury poisoning by their antagonistic effects; thiamine was the most effective of the derivatives against the widest spectrum of organisms and test systems (Siegel et al. 1991).

Among sensitive avian species, adverse effects — predominantly on reproduction — have been reported at mercury concentrations (in µg/kg fresh weight) of 5000 in feather, 900 in egg, 50 to 100 in diet, and daily administered doses of 640 on a body weight basis ([Table 5.11](#)). Although low mercury concentrations (e.g., 50 µg/kg in the diets of domestic chickens) sometimes produced no adverse effects in chickens, the tissue residues of mercury were sufficiently elevated to pose a hazard to human consumers (March et al. 1983). In contrast, in eggs of the bald eagle (with 150 µg Hg/kg and low hatch), other contaminants present — especially organochlorine compounds — probably had a greater effect on hatchability than did mercury (Wiemeyer et al. 1984).

Mammals, such as the domestic cat and the harp seal, showed birth defects, histopathology, and elevated tissue residues at doses of 250 µg Hg/kg body weight daily ([Table 5.11](#)). The mink, at dietary levels of 1100 µg Hg/kg, had signs of mercury poisoning; mercury residues in mink brain at this dietary level ranged from 7100 to 9300 µg/kg (Kucera 1983). Tissue residues in kidney, blood, brain, and hair in excess of 1100 µg Hg/kg in other nonhuman mammals are usually considered presumptive evidence of significant mercury contamination ([Table 5.11](#)). Tissue residues of mercury, as methylmercury, considered harmful to adult inland mammals and birds ranged between 8 mg/kg FW in brain to 15 in muscle to 20 mg/kg FW in liver and kidney (Heinz 1996). In Canadian aboriginal peoples, a 20-year followup study on methylmercury levels has been initiated, with emphasis on age, sex, location, relation between maternal and fetal levels, and a reassessment of potential risk in communities where the highest known methylmercury levels have been found (Wheatley and Paradis 1995). Similar studies are recommended for avian and mammalian wildlife.

More research is needed on mercury removal technology. In the Florida Everglades, for example, using prototype wetlands of 1545 ha, removal of agricultural nutrients from stormwater reduced total mercury and methylmercury concentrations in water by as much as 70% in the first 2 years of operation; moreover, total mercury concentrations in largemouth bass were about 0.1 mg Hg/kg FW muscle throughout the project site vs. 0.5 mg Hg/kg FW in adjacent areas (Miles and Fink 1998).

At this point, it seems that four courses of action are warranted. First, toxic mercurials in agriculture and industry should be replaced by less toxic substitutes. In Sweden, for example, clinical mercury thermometers have been prohibited since January 1992 for import, manufacture, and sales (Gustafsson 1995). Since January 1993, the same prohibition was applied to other measuring instruments and electrical components containing mercury. By the year 2000, Sweden plans to prohibit mercury in all processes and products, including thermometers and sphygmomanometers, and to replace them with available substitutes (Gustafsson 1995). In Quebec hospitals, medical instruments containing mercury are being replaced with mercury-free instruments because of inadequate maintenance and disposal of existing instruments (Guerrier et al. 1995).

Second, controls should be applied at the point of origin to prevent the discharge of potentially harmful mercury wastes. Point sources need to be identified and regulated (Facemire et al. 1995). In Sweden, discharges from point sources in the 1950s and 1960s averaged 20 to 30 metric tons annually. Since the end of the 1960s, the annual emission of mercury in Sweden has been reduced

to about 3.5 tons through better emission control legislation, improved technology, and reduction of polluting industrial production (Lindqvist et al. 1991).

Third, continued periodic monitoring of fishery and wildlife resources is important, especially in areas with potential for reservoir development, in light of the hypothesis that increased flooding increases the availability of mercury to biota. The use of museum collections for mercury analysis is strongly recommended for monitoring purposes. For example, the Environmental Specimen Bank at the Swedish Museum of Natural History constitutes a base for ecotoxicological research and for spatial and trend monitoring of mercury and other contaminants in Swedish fauna (Odsjo et al. 1997).

And finally, additional research is needed on mercury accumulation and detoxification in comparatively pristine ecosystems. Key uncertainties in understanding the process of mercury uptake in aquatic ecosystems, for example, include relations between water chemistry and respiratory uptake, quantitative estimates of intestinal tract methylation and depuration, and degree of seasonal variability in mercury speciation and methylation–demethylation processes (Post et al. 1996).

5.9 SUMMARY

Mercury has been used by man for at least 2300 years, most recently as a fungicide in agriculture, in the manufacture of chlorine and sodium hydroxide, as a slime control agent in the pulp and paper industry, in the production of plastics and electrical apparatus, and in mining and smelting operations. Mercury burdens in some environmental compartments are estimated to have increased up to five times precultural levels, primarily as a result of human activities. The construction of artificial reservoirs, for example, which releases mercury from flooded soils, has contributed to the observed elevation of Hg concentrations in fish tissues from these localities. Elevated levels of Hg in living organisms in Hg-contaminated areas may persist for as long as 100 years after the source of pollution has been discontinued. One major consequence of increased mercury use, coupled with careless waste disposal practices, has been a sharp increase in the number of epidemics of fatal mercury poisonings in humans, wildlife, and aquatic organisms.

Most authorities agree on six points: (1) mercury and its compounds have no known biological function, and the presence of the metal in the cells of living organisms is undesirable and potentially hazardous; (2) forms of mercury with relatively low toxicity can be transformed into forms of very high toxicity, such as methylmercury, through biological and other processes; (3) mercury can be bioconcentrated in organisms and biomagnified through food chains; (4) mercury is a mutagen, teratogen, and carcinogen, and causes embryocidal, cytochemical, and histopathological effects; (5) some species of fish and wildlife contain high concentrations of mercury that are not attributable to human activities; (6) anthropogenic use of mercury should be curtailed, as the difference between tolerable natural background levels of mercury and harmful effects in the environment is exceptionally small.

Concentrations of total mercury lethal to sensitive, representative, nonhuman species range from 0.1 to 2.0 µg/L (ppb) of medium for aquatic organisms; from 2200 to 31,000 µg/kg body weight (acute oral) and 4000 to 40,000 µg/kg (dietary) for birds; and from 100 to 500 µg/kg body weight (daily dose) and 1000 to 5000 µg/kg diet for mammals. Organomercury compounds, especially methylmercury, are always more toxic than inorganic Hg compounds. Numerous biological and abiotic factors modify the toxicity of Hg compounds — sometimes by an order of magnitude or more — but the mechanisms of action are not clear. Significant adverse sublethal effects were observed among selected aquatic species at water concentrations of 0.03 to 0.1 µg Hg/L. For some birds, adverse effects (predominantly on reproduction) have been associated with total mercury concentrations (in µg/kg fresh weight) of 5000 in feather, 900 in egg, and 50 to 100 in diet; and with daily intakes of 640 µg/kg body weight. Sensitive nonhuman mammals showed significant

adverse effects of mercury when daily intakes were 250 µg/kg body weight, when dietary levels were 1100 µg/kg, or when tissue concentrations exceeded 1100 µg/kg.

Mercury criteria proposed by the U.S. Environmental Protection Agency for protection of freshwater aquatic life are 0.012 µg/L medium (4-day average), not to exceed 2.4 µg/L on an hourly average; however, these criteria offer only limited protection to freshwater ecosystems. The saltwater criteria of 0.025 µg Hg/L medium (4-day average), not to exceed 2.1 µg/L hourly, are unsatisfactory for the protection of marine life. For the protection of sensitive species of mammals and birds that regularly consume fish and other aquatic organisms, total Hg concentrations in these prey items should probably not exceed 100 µg/kg fresh weight for birds, and 1100 µg/kg for small mammals. The significance of elevated Hg levels in tissues of fish and wildlife is not fully understood; some species of marine pinnipeds, for example, normally contain high concentrations of Hg in various tissues without apparent adverse effects. Usually, however, concentrations in excess of 1100 µg/kg fresh weight of tissue (liver, kidney, blood, brain, hair) should be considered as presumptive evidence of an environmental mercury problem.

Four courses of action now seem warranted. First, toxic mercurials in agriculture and industry should be replaced by less toxic substitutes. Second, controls should be applied at the point of origin to prevent the discharge of potentially harmful mercury wastes. Third, continued periodic monitoring of mercury in fish and wildlife is needed for identification of potential problem areas, and for evaluation of ongoing mercury curtailment programs. And fourth, additional research is merited on mechanisms of mercury accumulation and detoxification in comparatively pristine ecosystems.

5.10 LITERATURE CITED

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CHAPTER 6

Nickel

6.1 INTRODUCTION

In Europe, nickel (Ni) is listed on European Commission List II (Dangerous Substances Directive) and regulated through the Council of European Communities because of its toxicity, persistence, and affinity for bioaccumulation (Bubb and Lester 1996). In Canada, nickel and its compounds are included in the Priority Substances List under the Canadian Environmental Protection Act (Hughes et al. 1994). The World Health Organization (WHO) classifies nickel compounds in Group 1 (human carcinogens) and metallic nickel in group 2B (possible human carcinogen; U.S. Public Health Service [USPHS] 1993). The U.S. Environmental Protection Agency (USEPA) classifies nickel refinery dust and nickel subsulfide as Group A human carcinogens (USPHS 1993) and nickel oxides and nickel halides as Class W compounds, that is, compounds having moderate retention in the lungs and a clearance rate from the lungs of several weeks (USEPA 1980). Nickel and its compounds are regulated by USEPA's Clean Water Effluent Guideline for many industrial point sources, including the processing of iron, steel, nonferrous metals, and batteries; timber products processing; electroplating; metal finishing; ore and mineral mining; paving and roofing; paint and ink formulating; porcelain enameling; and industries that use, process, or manufacture chemicals, gum and wood, or carbon black (USPHS 1993).

Nickel is ubiquitous in the biosphere. Nickel introduced into the environment from natural or human sources is circulated through the system by chemical and physical processes and through biological transport mechanisms of living organisms (National Academy of Sciences [NAS] 1975; Sevin 1980; WHO 1991). Nickel is essential for the normal growth of many species of microorganisms and plants and several species of vertebrates, including chickens, cows, goats, pigs, rats, and sheep (NAS 1975; USEPA 1980; WHO 1991; USPHS 1993, 1995).

Human activities that contribute to nickel loadings in aquatic and terrestrial ecosystems include mining, smelting, refining, alloy processing, scrap metal reprocessing, fossil fuel combustion, and waste incineration (NAS 1975; WHO 1991; Chau and Kulikovsky-Cordeiro 1995). Nickel mining and smelting in the Sudbury, Ontario, region of Canada is associated with denudation of terrestrial vegetation and subsequent soil erosion (Adamo et al. 1996), and gradual ecological changes, including a decrease in the number and diversity of species and a reduction in community biomass of crustacean zooplankton (WHO 1991). At nickel-contaminated sites, plants accumulate nickel, and growth is retarded in some species at high nickel concentrations (WHO 1991). However, nickel accumulation rates in terrestrial and avian wildlife near nickel refineries are highly variable; Chau and Kulikovsky-Cordeiro (1995) claim similar variability for plants, soils, and interstitial sediment waters.

The chemical and physical forms of nickel and its salts strongly influence bioavailability and toxicity (WHO 1991). In general, nickel compounds have low hazard when administered orally

Table 6.1 Nickel Chronology

Date	Event	Ref. ^a
220 BCE	Nickel alloys made by the Chinese	1
1500s	Toxicity observed in miners of nickel	2
1751	Nickel isolated and identified. The name nickel was derived from "Old Nick," a gremlin to whom miners ascribed their problems	3
Early 1800s	Purified nickel obtained	1
1826	Nickel toxicity in rabbits and dogs demonstrated experimentally. High doses of nickel sulfate given by stomach gavage caused gastritis, convulsions, and death; sublethal doses produced emaciation and conjunctivitis	1, 2, 4
1840s	Commercial nickel electroplating initiated	1
1850s	Commercial exploitation of nickel begins after development of technology to remove copper and other impurities	3
1850–1900	Nickel used therapeutically in human medicine to relieve rheumatism (nickel sulfate) and epilepsy (nickel bromide)	2, 5
1880s	Excess nickel found lethal to animals under controlled conditions	2
1889	Skin dermatitis in humans caused by chemicals used in nickel plating	5
1890	Extraordinary toxicity of nickel carbonyl ($\text{Ni}(\text{CO})_4$) established	1
1893	Excess nickel found lethal to plants	2
1912	Nickel dermatitis documented	1
1915–1960	Nickel applied as fungicide found to enhance plant growth and increase yield	2
1926	Nickel dust caused skin dermatitis, especially in hot industrial environments	5
1932	Increased frequency of lung and nasal cancers reported among English nickel refinery workers exposed to high concentrations of nickel carbonyl	1, 5, 6
1939–1958	Certain forms of nickel found to be carcinogenic to humans	2
1943	Certain forms of nickel found to be carcinogenic to animals	2
1965–1967	Nickel found beneficial to plants	2
1970s	Nickel deficiency leads to adverse effects in microorganisms and plants	2
1980s	Nickel found to be constituent of various essential plant enzymes	2

^a 1, Nriagu 1980b; 2, Hausinger 1993; 3, Sevin 1980; 4, Nielsen 1977; 5, USPHS 1977; 6, Benson et al. 1995.

(NAS 1975; USEPA 1980). In humans and other mammals, however, nickel-inhalable dust, nickel subsulfide, nickel oxide, and especially nickel carbonyl induce acute pneumonitis, central nervous system disorders, skin disorders such as dermatitis, and cancer of the lungs and nasal cavity (Graham et al. 1975; NAS 1975; USPHS 1977; Sevin 1980; Smialowicz et al. 1984; WHO 1991; Benson et al. 1995; Table 6.1). Nickel carbonyl is acutely lethal to humans and animals within 3 to 13 days of exposure; recovery is prolonged in survivors (Sevin 1980). An excess number of deaths from lung cancer and nasal cancer occurs in nickel refinery workers, usually from exposure to airborne nickel compounds (USPHS 1977). At one nickel refinery, workers had a fivefold increase in lung cancer and a 150-fold increase in nasal sinus cancer compared to the general population (Lin and Chou 1990). Pregnant female workers at a Russian nickel hydrometallurgy refining plant, when compared to a reference group, show a marked increase in frequency of spontaneous and threatening abortions and in structural malformations of the heart and musculoskeletal system in live-born infants with nickel-exposed mothers (Chashchin et al. 1994). Nickel is also a common cause of chronic dermatitis in humans as a result of industrial and other exposures, including the use of nickel-containing jewelry, coins, utensils, and various prostheses (NAS 1975; Chashchin et al. 1994). Additional information on ecological and toxicological aspects of nickel in the environment is presented in reviews and annotated bibliographies by Sunderman (1970), Eisler (1973), Eisler and Wapner (1975), NAS (1975), USEPA (1975, 1980, 1985, 1986), International Agency for Research on Cancer [IARC] (1976), Nielsen (1977), USPHS (1977, 1993), Eisler et al. (1978b, 1979), Norseth and Piscator (1979), Brown and Sunderman (1980), Nriagu (1980a), Sevin (1980), National Research Council of Canada [NRCC] (1981), Norseth (1986), Kasprzak (1987), Sigel and Sigel (1988), WHO (1991), Hausinger (1993), Outridge and Scheuhammer (1993), Chau and Kulikovsky-Cordeiro (1995), and Eisler (1998).

6.2 SOURCES AND USES

6.2.1 General

About 250,000 people in the United States are exposed annually to inorganic nickel in the workplace. This group includes workers in the mining, refining, smelting, electroplating, and petroleum industries and workers involved in the manufacture of stainless steel, nickel alloys, jewelry, paint, spark plugs, catalysts, ceramics, disinfectants, varnish, magnets, batteries, ink, dyes, and vacuum tubes (USPHS 1977). Nonoccupational exposure to nickel and its compounds occurs mainly by ingestion of foods and liquids and by contact with nickel-containing products, especially jewelry and coins (Sunderman et al. 1984; WHO 1991). Food processing adds to nickel already present in the diet through leaching from nickel-containing alloys in food-processing equipment made from stainless steel, milling of flour, use of nickel catalysts to hydrogenate fats and oils, and use of nickel-containing fungicides in growing crops (NAS 1975; USEPA 1980). Nickel contamination of the environment occurs locally from emissions of metal mining, smelting, and refining operations; from combustion of fossil fuels; from industrial activities, such as nickel plating and alloy manufacturing; from land disposal of sludges, solids, and slags; and from disposal as effluents (Cain and Pafford 1981; Chau and Kulikovsky-Cordeiro 1995). In Canada in 1988, the mining industry released a total of 11,664 tons of nickel into the air (9.4%), water (0.5%), and on land as sludges or solids (15.4%) and slags (74.7%). The global nickel cycle is unknown, but recent estimates suggest that 26,300 to 28,100 tons are introduced each year into the atmosphere from natural sources and 47,200 to 99,800 tons from human activities; airborne nickel is deposited on land at 50,800 tons and in the ocean at 21,800 tons annually (Chau and Kulikovsky-Cordeiro 1995).

6.2.2 Sources

More than 90% of the world's nickel is obtained from pentlandite ($(\text{FeNi})_9\text{S}_8$), a nickel-sulfitic mineral, mined underground in Canada and the former Soviet Union (Sevin 1980; IARC 1976; WHO 1991). One of the largest sulfitic nickel deposits is in Sudbury, Ontario (USPHS 1993). Nickeliferous sulfide deposits are also found in Manitoba, South Africa, the former Soviet Union, Finland, western Australia, and Minnesota (Norseth and Piscator 1979; USPHS 1993). Most of the rest of the nickel obtained is from nickel minerals such as laterite, a nickel oxide ore mined by open pit techniques in Australia, Cuba, Indonesia, New Caledonia, and the former Soviet Union (Sevin 1980). Lateritic ores are less well defined than sulfitic ores, although the nickel content (1 to 3%) of both ores is similar (USPHS 1993). Important deposits of laterite are located in New Caledonia, Indonesia, Guatemala, the Dominican Republic, the Philippines, Brazil, and especially Cuba, which holds 35% of the known reserves (USPHS 1993). Nickel-rich nodules are found on the ocean floor, and nickel is also present in fossil fuels (Sevin 1980).

Total world mine production of nickel is projected to increase steadily from 7500 metric tons in 1900 to 2 million tons by 2000 (Table 6.2). In 1980, nickel mine production in the United States was 14,500 tons or about 1.8% of the world total (Kasprzak 1987). In 1986, primary nickel production ceased in the United States. Secondary nickel production from scrap became a major source of nickel for industrial applications (USPHS 1993). In 1988, the United States imported 186,000 tons of primary nickel; Canada supplied 58% of the total and Norway 14% (USPHS 1993). In 1990, Canada produced 196,606 metric tons of nickel. About 63% of the total production was exported, mostly (56%) to the United States (Chau and Kulikovsky-Cordeiro 1995).

Natural sources of airborne nickel include soil dust, sea salt, volcanoes, forest fires, and vegetation exudates and account for about 16% of the atmospheric nickel burden (Kasprzak 1987; WHO 1991; Chau and Kulikovsky-Cordeiro 1995). Human sources of atmospheric nickel — which account for about 84% of all atmospheric nickel — include emissions from nickel ore mining, smelting, and refining activities; combustion of fossil fuels for heating, power, and motor vehicles;

Table 6.2 World Mine Production of Nickel

Year	Metric tons
1900	7500
1925	42,700
1950	141,000
1970	694,100
1975	753,000 ^a
1980	784,100
1985	821,000 ^b
2000 (projected)	>2,000,000

^a About 32% from Canada, 18% from New Caledonia, 17% from the former Soviet Union, 10% from Australia, 5% from Cuba, 4% from the Dominican Republic, 3% from the Republic of South Africa, 2% each from Greece, Indonesia, and the United States, and 5% from other countries.

^b Mostly from Canada, the former Soviet Union, Australia, and Cuba in that order. The United States produced 6900 tons in 1985.

Data from NAS 1975; International Agency for Research on Cancer 1976; Duke 1980; Kasprzak 1987; WHO 1991.

incineration of sewage sludges; nickel chemical manufacturing; electroplating; nickel–cadmium battery manufacturing; asbestos mining and milling; and cement manufacturing (NAS 1975; IARC 1976; USEPA 1986; Kasprzak 1987; WHO 1991; USPHS 1993). In Canada in 1975, human activities resulted in the release of about 3000 tons of nickel into the atmosphere, mostly from metallurgical operations (NRCC 1981). Between 1973 and 1981, atmospheric emissions of nickel from stacks of four smelters in the Sudbury Basin, Canada, averaged a total of 495 tons annually (WHO 1991). Industrial nickel dust emissions from a single Canadian stack 381 meters high averaged 228 tons annually (range 53 to 342) between 1973 and 1981. This stack accounted for 396 tons annually (range 53 to 896) between 1982 and 1989 (Chau and Kulikovsky-Cordeiro 1995). Three other emission stacks of Canadian nickel producers emitted an average of 226, 228, and 396 tons of nickel, respectively, each year between 1973 and 1989. Industrial emissions of nickel to the Canadian atmosphere in 1982 were estimated at 846 tons, mostly from nickel production in Ontario (48% of total) and Quebec (14%) and from industrial fuel combustion (17%). Nickel released into the air in Canada from smelting processes is likely in the form of nickel subsulfide (52%), nickel sulfate (20%), and nickel oxide (6%). Fuel combustion is also a major contributor of airborne nickel in Canada, mostly from combustion of petroleum (Chau and Kulikovsky-Cordeiro 1995). In the United States, yearly atmospheric emissions from coal and oil combustion are estimated at 2611 metric tons (WHO 1991).

Chemical and physical degradation of rocks and soils, atmospheric deposition of nickel-containing particulates, and discharges of industrial and municipal wastes release nickel into ambient waters (USEPA 1986; WHO 1991). Nickel enters natural waterways from wastewater because it is poorly removed by treatment processes (Cain and Pafford 1981). The main anthropogenic sources of nickel in water are primary nickel production, metallurgical processes, combustion and incineration of fossil fuels, and chemical and catalyst production (USEPA 1986). The primary human sources of nickel to soils are emissions from smelting and refining operations and disposal of sewage sludge or application of sludge as a fertilizer. Secondary sources include automobile emissions and emissions from electric power utilities (USEPA 1986). Weathering and erosion of geological materials release nickel into soils (Chau and Kulikovsky-Cordeiro 1995), and acid rain may leach nickel from plants into soils as well (WHO 1991).

6.2.3 Uses

Most metallic nickel produced is used to manufacture stainless steel and other nickel alloys with high corrosion and temperature resistance (Norseth and Piscator 1979; Norseth 1980; WHO 1991). These alloys are used in ship building, jet turbines and heat elements, cryogenic installations, magnets, coins, welding rods, electrodes, kitchenware, electronics, and surgical implants. Other nickel compounds are used in electroplating, battery production, inks, varnishes, pigments, catalysts, and ceramics (IARC 1976; Nriagu 1980b; Sevin 1980; Sunderman et al. 1984; USEPA 1986; Kasprzak 1987; USPHS 1993). Some nickel compounds are preferred for use in nickel electroplating (nickel sulfate, nickel ammonium sulfate, nickel chloride, nickel fluoborate, nickel sulfamate), refining (nickel carbonyl), nickel–cadmium batteries (nickel hydroxide, nickel fluoride, nickel nitrate), manufacture of stainless steel and alloy steels (nickel oxide), electronic components (nickel carbonate), mordant in textile industry (nickel acetate), catalysts and laboratory reagents (nickel acetate, nickel hydroxide, nickel nitrate, nickel carbonate, nickel monosulfide, nickelocene), and some, such as nickel subsulfide, are unwanted toxic by-products (IARC 1976).

In 1973, global consumption of nickel was 660,000 tons and that of the United States 235,000 tons (Sevin 1980). End uses of nickel in the United States in 1973 were transportation (21%), chemicals (15%), electrical goods (13%), fabricated metal products (10%), petroleum (9%), construction (9%), machinery (7%), and household appliances (7%; IARC 1976). A similar pattern was evident for 1985 (Table 6.3). In 1988, 40% of all nickel intermediate products consumed was in the production of steel; 21% was in alloys, 17% in electroplating, and 12% in super alloys (USPHS 1993). The pattern for 1985 was similar (Table 6.3). In Canada, nickel is the fourth most important mineral commodity behind copper, zinc, and gold. In 1990, Canada produced 197,000 tons of nickel worth 2.02 billion dollars and was the second largest global producer of that metal (Chau and Kulikovsky-Cordeiro 1995). Most of the nickel used in the United States is imported from Canada and secondarily from Australia and New Caledonia (USPHS 1977).

Table 6.3 Nickel Consumption in the United States by Intermediate Product and End-Use Industry in 1985^a

Index	Consumption (% of total)
Intermediate Product	
Stainless and alloy steels	42
Nonferrous alloys	36
Electroplating	18
Other	4
Total	100
End-use Industry	
Transportation	23
Chemicals	15
Electrical equipment	12
Construction	10
Fabricated metal products	9
Petroleum	8
Household appliances	8
Machinery	8
Other	7
Total	100

^a Nickel consumption in the United States, exclusive of scrap, was 160,000 tons.

Data from Kasprzak, K.S. 1987. Nickel. *Adv. Modern Environ. Toxicol.* 11:145-183; World Health Organization (WHO). 1991. *Nickel. Environ. Health Crit.* 108. 383 pp.

Various nickel salts — including the sulfate, chloride, and bromide — were used in human medicine during the mid- to late-1800s to treat headache, diarrhea, and epilepsy and as an antiseptic. Therapeutic use of nickel compounds was abandoned in the early 1900s after animal studies demonstrated acute and chronic toxicity of these salts (NAS 1975; Nriagu 1980b). Some nickel salts have been incorporated into fungicides to combat plant pathogens, although their use has not been approved by regulatory agencies (NAS 1975).

6.3 CHEMICAL AND BIOLOGICAL PROPERTIES

6.3.1 General

Nickel normally occurs in the 0 and +2 oxidation states, although other oxidation states are reported (NAS 1975; Nriagu 1980b; Higgins 1995). In natural waters Ni^{2+} is the dominant chemical species in the form of $(\text{Ni}(\text{H}_2\text{O})_6)^{2+}$ (WHO 1991; Chau and Kulikovsky-Cordeiro 1995). In alkaline soils, the major components of the soil solution are Ni^{2+} and $\text{Ni}(\text{OH})^+$; in acidic soils, the main solution species are Ni^{2+} , NiSO_4 , and NiHPO_4 (USPHS 1993). Most atmospheric nickel is suspended onto particulate matter (NRCC 1981).

Nickel interacts with numerous inorganic and organic compounds (Schroeder et al. 1974; Nielsen 1980a; USEPA 1980, 1985; USPHS 1993). Some of these interactions are additive or synergistic in producing adverse effects, and some are antagonistic.

Toxic and carcinogenic effects of nickel compounds are associated with nickel-mediated oxidative damage to DNA and proteins and to inhibition of cellular antioxidant defenses (Rodriguez et al. 1996). Most authorities agree that albumin is the main transport protein for nickel in humans and animals and that nickel is also found in nickeloplasmin — a nickel-containing alpha-macroglobulin — and in an ultrafilterable serum fraction similar to a nickel-histidine complex (Norseth and Piscator 1979; Sarkar 1980; Sevin 1980; USEPA 1980; Norseth 1986; Sigel and Sigel 1988; WHO 1991; USPHS 1993). Normal routes of nickel intake for humans and animals are ingestion, inhalation, and absorption through the skin (Mushak 1980; USEPA 1975, 1980, 1986; Sigel and Sigel 1988; WHO 1991; USPHS 1993). Nickel absorption is governed by the quantities inhaled or ingested and by the chemical and physical forms of the nickel. Following oral intake by mammals, nickel was found mainly in the kidneys after short-term or long-term exposure to various soluble nickel compounds; significant levels of nickel were also found in the liver, heart, lung, and fat. Nickel also crosses the placental barrier, as indicated by increases in the levels of nickel in the fetuses of exposed mothers (USPHS 1993). Inhaled nickel carbonyl results in comparatively elevated nickel concentrations in lung, brain, kidney, liver, and adrenals (USEPA 1980). Parenteral administration of nickel salts usually results in high levels in kidneys and elevated concentrations in endocrine glands, liver, and lung (USEPA 1980, 1986; WHO 1991). Nickel concentrations in whole blood, plasma, serum, and urine provide good indices of nickel exposure (Sigel and Sigel 1988).

6.3.2 Physical and Chemical Properties

Nickel was first isolated in 1751, and a relatively pure metal was prepared in 1804. In nature, nickel is found primarily as oxide and sulfide ores (USPHS 1977). It has high electrical and thermal conductivities and is resistant to corrosion at environmental temperatures between -20°C and $+30^\circ\text{C}$ (Chau and Kulikovsky-Cordeiro 1995). Nickel, also known as carbonyl nickel powder or C.I. No. 77775, has a CAS number of 7440-02-0. Metallic nickel is a hard, lustrous, silvery white metal with a specific gravity of 8.9, a melting point of about 1455°C , and a boiling point at about 2732°C . It is insoluble in water and ammonium hydroxide, soluble in dilute nitric acid or aqua regia, and slightly soluble in hydrochloric and sulfuric acid. Nickel has an atomic weight of 58.71. Nickel is

a composite of five stable isotopes: Ni-58 (68.3%), -60 (26.1%), -61 (1.1%), -62 (3.6%), and -64 (0.9%). Seven unstable isotopes have been identified: ^{56}Ni (half-life of 6 days), ^{57}Ni (36 h), ^{59}Ni (80,000 years), ^{63}Ni (92 years), ^{65}Ni (2.5 h), ^{66}Ni (55 h), and ^{67}Ni (50 sec). Radionickel-59 (^{59}Ni) and ^{63}Ni are available commercially. In addition to the 0 and +2 oxidation states, nickel can also exist as -1, +1, +3, and +4 (NAS 1975; IARC 1976; Kasprzak 1987; Nriagu 1980b; WHO 1991; Hausinger 1993; USPHS 1993; Foulds 1995; Higgins 1995).

Nickel enters surface waters from three natural sources: as particulate matter in rainwater, through the dissolution of primary bedrock materials, and from secondary soil phases. In aquatic systems, nickel occurs as soluble salts adsorbed onto or associated with clay particles, organic matter, and other substances. The divalent ion is the dominant form in natural waters at pH values between 5 and 9, occurring as the octahedral, hexahydrate ion $(\text{Ni}(\text{H}_2\text{O})_6)^{2+}$. Nickel chloride hexahydrate and nickel sulfate hexahydrate are extremely soluble in water at 2400 to 2500 g/L. Less soluble nickel compounds in water include nickel nitrate (45 g/L), nickel hydroxide (0.13 g/L), and nickel carbonate (0.09 g/L). Nickel forms strong, soluble complexes with OH^- , SO_4^{2-} , and HCO_3^- ; however, these species are minor compared with hydrated Ni^{2+} in surface water and groundwater. The fate of nickel in fresh water and marine water is affected by the pH, pE, ionic strength, type and concentration of ligands, and the availability of solid surfaces for adsorption. Under anaerobic conditions, typical of deep groundwater, precipitation of nickel sulfide keeps nickel concentrations low (IARC 1976; USEPA 1980; WHO 1991; USPHS 1993; Chau and Kulikovsky-Cordeiro 1995).

In alkaline soils, the major components of the soil solution are Ni^{2+} and $\text{Ni}(\text{OH})^+$; in acidic soils the main solution species are Ni^{2+} , NiSO_4 , and NiHPO_4 (USPHS 1993). Atmospheric nickel exists mostly in the form of fine respirable particles less than 2 μm in diameter (NRCC 1981), usually suspended onto particulate matter (USEPA 1986).

Nickel carbonyl ($\text{Ni}(\text{CO})_4$) is a volatile, colorless liquid readily formed when nickel reacts with carbon monoxide; it boils at 43°C and decomposes at more than 50°C. This compound is unstable in air and is usually not measurable after 30 min (NRCC 1981; Norseth 1986; USPHS 1993). The intact molecule is absorbed by the lung (USEPA 1980) and is insoluble in water but soluble in most organic solvents (WHO 1991).

Analytical methods for detection of nickel in biological materials and water include various spectrometric, photometric, chromatographic, polarographic, and voltammetric procedures (Sunderman et al. 1984; WHO 1991). Detection limits for the most sensitive procedures — depending on sample pretreatment, and extraction and enrichment procedures — were 0.7 to 1.0 ng/L in liquids, 0.01 to 0.2 $\mu\text{g}/\text{m}^3$ in air, 1 to 100 ng/kg in most biological materials, and 12 $\mu\text{g}/\text{kg}$ in hair (WHO 1991; Chau and Kulikovsky-Cordeiro 1995).

6.3.3 Metabolism

In mammalian blood, absorbed nickel is present as free hydrated Ni^{2+} ions, as small complexes, as protein complexes, and as nickel bound to blood cells. The partition of nickel among these four components varies according to the metal-binding properties of serum albumin, which is highly variable between species (NAS 1975; USEPA 1980, 1986; Kasprzak 1987). A proposed transport model involves the removal of nickel from albumin to histidine via a ternary complex composed of albumin, nickel, and L-histidine. The low-molecular-weight L-histidine nickel complex can then cross biological membranes (Sunderman et al. 1984; Kasprzak 1987; USPHS 1993). Once inside the mammalian cell, nickel accumulates in the nucleus and nucleolus (Sunderman et al. 1984), disrupting DNA metabolism and causing crosslinks and strand breaks (Kasprzak 1987; USPHS 1993; Hartwig et al. 1994). The observed redox properties of the nickel–histidine complex are crucial for maximizing the toxicity and carcinogenicity of nickel (Datta et al. 1992, 1994).

The acute toxicity and carcinogenicity of Ni_3S_2 and Ni_3S_2 -derived soluble nickel (Ni^{2+}) in mice depend, in part, on the antioxidant capacity of target organs, which varies among different strains

(Rodriguez et al. 1996). Experimental evidence now supports the conclusion that the nickel-dependent formation of an activated oxygen species — including superoxide ion, hydrogen peroxide, and hydroxy radical — is a primary molecular event in acute nickel toxicity and carcinogenicity (WHO 1991; Hausinger 1993; Tkeshelashvili et al. 1993; Novelli et al. 1995; Stohs and Bagchi 1995; Rodriguez et al. 1996; Zhang et al. 1998). For example, the superoxide radical (O_2^-) is an important intermediate in the toxicity of insoluble nickel compounds such as NiO and NiS (Novelli et al. 1995). One of the keys to the mechanism of nickel-mediated damage is the enhancement of cellular redox processing by nickel. Accumulated nickel in tissues elicits the production of reactive oxygen species, such as the superoxide radical, as the result of phagocytosis of particulate nickel compounds and through the interaction of nickel ions with protein ligands, which promote the activation of the Ni^{2+}/Ni^{3+} redox couple. Thus, NiS and NiO can elicit the formation of O_2^- (Novelli et al. 1995).

The most serious type of nickel toxicity is that caused by the inhalation of nickel carbonyl (Nielsen 1977). The half-time persistence of nickel carbonyl in air is about 30 min (Sevin 1980). Nickel carbonyl can pass across cell membranes without metabolic alteration because of its solubility in lipids, and this ability of nickel carbonyl to penetrate intracellularly may be responsible for its extreme toxicity (NAS 1975). In tissues, nickel carbonyl decomposes to liberate carbon monoxide and Ni^0 , the latter being oxidized to Ni^{2+} by intracellular oxidation systems. The nickel portion is excreted with urine, and the carbon monoxide is bound to hemoglobin and eventually excreted through the lungs (USEPA 1980; Kasprzak 1987). Nickel carbonyl inhibits DNA-dependent RNA synthesis activity, probably by binding to chromatin or DNA and thereby preventing the action of RNA polymerase, causing suppression of messenger-RNA-dependent induction of enzyme synthesis (Sunderman 1968; NAS 1975; USEPA 1980). The lung is the target organ in nickel carbonyl poisoning (USEPA 1980). Acute human exposures result in pathological pulmonary lesions, hemorrhage, edema, deranged alveolar cells, degeneration of bronchial epithelium, and pulmonary fibrosis. The response of pulmonary tissue to nickel carbonyl is rapid: interstitial edema may develop within 1 h of exposure and cause death within 5 days. Animals surviving acute exposures show lung histopathology (USEPA 1980).

Gastrointestinal intake of nickel by humans is high compared to some other trace metals because of contributions of nickel from utensils and from food processing machinery. Average human dietary values range from 300 to 500 μg daily with absorption from the gastrointestinal tract of 1 to 10% (USEPA 1980, 1986; Sigel and Sigel 1988). In humans, nearly 40 times more nickel was absorbed from the gastrointestinal tract when nickel sulfate was given in the drinking water (27%) than when it was given in the diet (0.7%). Uptake was more rapid in starved individuals (WHO 1991; USPHS 1993). Dogs and rats given nickel, nickel sulfate hexahydrate, or nickel chloride in the diet or by gavage rapidly absorbed 1 to 10% of the nickel from the gastrointestinal tract, while unabsorbed nickel was excreted in the feces (USPHS 1993).

During occupational exposure, respiratory absorption of soluble and insoluble nickel compounds is the major route of entry, with gastrointestinal absorption secondary (WHO 1991). Inhalation exposure studies of nickel in humans and test animals show that nickel localizes in the lungs, with much lower levels in liver and kidneys (USPHS 1993). About half the inhaled nickel is deposited on bronchial mucosa and swept upward in mucus to be swallowed; about 25% of the inhaled nickel is deposited in the pulmonary parenchyma (NAS 1975). The relative amount of inhaled nickel absorbed from the pulmonary tract is dependent on the chemical and physical properties of the nickel compound (USEPA 1986). Pulmonary absorption into the blood is greatest for nickel carbonyl vapor; about half the inhaled amount is absorbed (USEPA 1980). Nickel in particulate matter is absorbed from the pulmonary tract to a lesser degree than nickel carbonyl; however, smaller particles are absorbed more readily than larger ones (USEPA 1980). Large nickel particles ($>2 \mu\text{m}$ in diameter) are deposited in the upper respiratory tract; smaller particles tend to enter the lower respiratory tract. In humans, 35% of the inhaled nickel is absorbed into the blood from the respiratory tract; the remainder is either swallowed or expectorated. Soluble nickel compounds

were more readily absorbed from the respiratory tract than insoluble compounds (USPHS 1993). In rodents, the half-time persistence of nickel particles was a function of particle diameter: 7.7 months for particles 0.6 μm in diameter, 11.5 months for particles 1.2 μm in diameter, and 21 months for particles 4.0 μm in diameter (USPHS 1993). In rodents, a higher percentage of insoluble nickel compounds was retained in the lungs for a longer time than soluble nickel compounds, and the lung burden of nickel decreased with increasing particle size. Nickel retention was 6 to 10 times greater in rodents exposed to insoluble nickel subsulfide compared to soluble nickel sulfate. Lung burdens of nickel generally increased with increasing duration of exposure and increasing concentrations of various nickel compounds in the air (USPHS 1993). Animals exposed to nickel carbonyl by inhalation exhale some of the respiratory burden in 2 to 4 h. The remainder is slowly degraded to divalent nickel, which is oxidized, and carbon monoxide, which initially binds to hemoglobin, with nickel eventually excreted in the urine (NAS 1975; Norseth and Piscator 1979; USEPA 1980; Norseth 1986).

Dermal absorption of nickel occurs in animals and humans and is related to nickel-induced hypersensitivity and skin disorders (Samitz and Katz 1976; USEPA 1986). Absorption of nickel sulfate from the skin is reported for guinea pigs, rabbits, rats, and humans (Norseth and Piscator 1979). Nickel ions in contact with the skin surface diffuse through the epidermis and combine with proteins; the body reacts to this conjugated protein (Samitz and Katz 1976; Nielsen 1977). Nickel penetration of the skin is enhanced by sweat, blood and other body fluids, and detergents (Nielsen 1977; USEPA 1980). Absorption is related to the solubility of the compound, following the general relation of nickel carbonyl, soluble nickel compounds, and insoluble nickel compounds, in that order; nickel carbonyl is the most rapidly and completely absorbed nickel compound in mammals (WHO 1991). Anionic species differ markedly in skin penetration: nickelous ions from a chloride solution pass through skin about 50 times faster than do nickelous ions from a sulfate solution (USPHS 1993). Radionickel-57 (^{57}Ni) accumulates in keratinous areas and hair sacs of the shaved skin of guinea pigs and rabbits following dermal exposure. After 4 h, ^{57}Ni was found in the stratum corneum and stratum spinosum; after 24 h, ^{57}Ni was detected in blood and kidneys, with minor amounts in liver (USPHS 1993). As much as 77% of nickel sulfate applied to the occluded skin surface of rabbits and guinea pigs was absorbed within 24 h; sensitivity to nickel did not seem to affect absorption rate (USPHS 1993). In humans, some protection against nickel may be given by introducing a physical barrier between the skin and the metal, including fingernail polish, a polyurethane coating, dexamethasone, or disodium EDTA (Nielsen 1977).

Nickel retention in the body of mammals is low. The half-time residence of soluble forms of nickel is several days, with little evidence for tissue accumulation except in the lung (USEPA 1980, 1986). Radionickel-63 (^{63}Ni) injected into rats and rabbits cleared rapidly; most (75%) of the injected dose was excreted within 24 to 72 h (USEPA 1980). Nickel clears at different rates from various tissues. In mammals, clearance was fastest from serum, followed by kidney, muscle, stomach, and uterus; relatively slow clearance was evident in skin, brain, and especially lung (Kasprzak 1987). The half-time persistence in human lung for insoluble forms of nickel is 330 days (Sevin 1980).

The excretory routes for nickel in mammals depend on the chemical forms of nickel and the mode of nickel intake. Most (>90%) of the nickel that is ingested in food remains unabsorbed within the gastrointestinal tract and is excreted in the feces (NAS 1975; Sevin 1980; USEPA 1986; Kasprzak 1987; Hausinger 1993; USPHS 1993). Urinary excretion is the primary route of clearance for nickel absorbed through the gastrointestinal tract (USEPA 1976, 1986; USPHS 1993). In humans, nickel excretion in feces usually ranges between 300 and 500 μg daily, or about the same as the daily dietary intake; urinary levels are between 2 and 4 $\mu\text{g/L}$ (USEPA 1980, 1986). Dogs fed nickel sulfate in the diet for as long as 2 years excreted most of the nickel in feces and 1 to 3% in the urine (USPHS 1993). Biliary excretion occurs in rats, calves, and rabbits, but the role of bile in human metabolism of nickel is not clear (USEPA 1980). Absorbed nickel is excreted in the urine regardless of the route of exposure. The excretory route of inhaled nickel depends on the

solubility of the nickel compound. Inhalation studies show that rats excrete 70% of the nickel in soluble nickel compounds through the urine within 3 days and 97% in 21 days. Less soluble nickel compounds (nickel oxide, nickel subsulfide) are excreted in urine (50%) and feces (50%); 90% of the initial dose of nickel subsulfide was excreted within 35 days, and 60% of the nickel oxide — which is less soluble and not as rapidly absorbed as nickel subsulfide — was excreted in 90 days (USPHS 1993). The half-time persistence of inhaled nickel oxide is 3 weeks in hamsters (Sevin 1980). In addition to feces, urine, and bile, other body secretions, including sweat, tears, milk, and mucociliary fluids, are potential routes of excretion (WHO 1991). Sweat may constitute a major route of nickel excretion in tropical climates. Nickel concentrations in sweat of healthy humans sauna bathing for brief periods were 52 µg/L in males and 131 µg/L in females (USEPA 1980). Hair deposition of nickel also appears to be an excretory mechanism (as much as 4 mg Ni/kg dry weight [DW] hair in humans), but the relative magnitude of this route, compared to urinary excretion, is unclear (USEPA 1980, 1986). In the case of nickel compounds administered by way of injection, tests with small laboratory animals show that nickel is cleared rapidly from the plasma and excreted mainly in the urine (Norseth and Piscator 1979; USEPA 1980). About 78% of an injected dose of nickel salts was excreted in the urine during the first 3 days after injection in rats and during the first day in rabbits (Norseth 1986). Exhalation via the lungs is the primary route of excretion during the first hours following injection of nickel carbonyl into rats, and afterwards via the urine (Norseth and Piscator 1979).

In microorganisms, nickel binds mainly to the phosphate groups of the cell wall. From this site, an active transport mechanism designed for magnesium transports the nickel (Kasprzak 1987). In microorganisms and higher plants, magnesium is the usual competitor for nickel in the biological ion-exchange reactions. In lichens, fungi, algae, and mosses, the active binding sites are the carboxylic and hydroxycarboxylic groups fixed on the cell walls. Nickel in hyperaccumulating genera of terrestrial plants is complexed with polycarboxylic acids and pectins, although phosphate groups may also participate (Kasprzak 1987). In terrestrial plants, nickel is absorbed through the roots (USEPA 1975).

6.3.4 Interactions

In minerals, nickel competes with iron, cobalt, and magnesium because of similarities in their ionic radius and electronegativity (NRCC 1981). At the cellular level, nickel interferes with enzymatic functions of calcium, iron, magnesium, manganese, and zinc (Kasprzak 1987). Binding of nickel to DNA is inhibited by salts of calcium, copper, magnesium, manganese, and zinc (WHO 1991). In toads (*Bufo arenarum*), ionic nickel interferes with voltage-sensitive ionic potassium channels in short muscle fibers (Bertran and Kotsias 1997). Among animals, plants, and microorganisms, nickel interacts with at least 13 essential elements: calcium, chromium, cobalt, copper, iodine, iron, magnesium, manganese, molybdenum, phosphorus, potassium, sodium, and zinc (Nielsen 1980a). Nickel interacts noncompetitively with all 13 elements and also interacts competitively with calcium, cobalt, copper, iron, and zinc. Quantification of these relationships would help clarify nickel-essential mineral interactions and the circumstances under which these interactions might lead to states of deficiency or toxicity (Nielsen 1980a). Mixtures of metals (arsenic, cadmium, copper, chromium, mercury, lead, zinc) containing nickel salts are more toxic to daphnids and fishes than are predicted on the basis of individual components (Enserink et al. 1991). Additive joint action of chemicals, including nickel, should be considered in the development of ecotoxicologically relevant water-quality criteria (Enserink et al. 1991).

Nickel may be a factor in asbestos carcinogenicity. The presence of chromium and manganese in asbestos fibers may enhance the carcinogenicity of nickel (USEPA 1980), but this relation needs to be verified. Barium–nickel mixtures inhibit calcium uptake in rats, resulting in reduced growth (WHO 1991). Pretreatment of animals with cadmium enhanced the toxicity of nickel to the kidneys and liver (USPHS 1993). Simultaneous exposure to nickel and cadmium — an industrial situation

common in nickel and cadmium battery production — caused a significant increase in beta-2-macroglobulin excretion (Sunderman et al. 1984). Nickel or cadmium alone did not affect calcium kinetics of smooth muscle from bovine mesenteric arteries. However, mixtures of cadmium and nickel at greater than 100 Nm inhibited the calcium function and may explain the vascular tension induced by nickel and other cations (Stockard et al. 1993). Smooth muscle of the ventral aorta of the spiny dogfish (*Squalus acanthias*) contracted significantly on exposure to cadmium or nickel but not to other divalent cations. Cadmium-induced vasoconstriction of shark muscle (but not nickel) was inhibited by atropine (Evans and Walton 1990). Nickel toxicity in soybeans (*Glycine max*) was inhibited by calcium, which limited the binding of nickel to DNA (WHO 1991). Chromium–nickel mixtures were more-than-additive in toxicity to guppies (*Poecilia reticulata*) in 96-h tests (Khangarot and Ray 1990). Rabbits (*Oryctolagus* sp.) exposed by inhalation to both nickel and trivalent chromium had more severe respiratory effects than did rabbits exposed to nickel alone (USPHS 1993). In natural waters, the geochemical behavior of nickel is similar to that of cobalt (USEPA 1980). It is therefore not surprising that nickel–cobalt mixtures in drinking water of rats were additive in toxicity (WHO 1991) and that there is a high correlation between nickel and cobalt concentrations in terrestrial plants (Memon et al. 1980).

Copper–nickel mixtures have a beneficial effect on growth of terrestrial plants but are more-than-additive in toxic action to aquatic plants (NRCC 1981; WHO 1991). Nickel interacts with iron in rat nutrition and metabolism, but the interaction depends on the form and level of the dietary iron (Nielsen 1980b; USEPA 1985). Weanling rats fed diets containing nickel chloride and ferric sulfate had altered hematocrit, hemoglobin level, and alkaline phosphatase activity which did not occur when a mixture of ferric and ferrous sulfates were fed (Nielsen 1980b). In iron-deficient rats, nickel enhanced the absorption of iron administered as ferric sulfate (USPHS 1993), and nickel acted as a biological cofactor in facilitating gastrointestinal absorption of ferric ion when iron was given as ferric sulfate (USPHS 1993). Mice given a lead–nickel mixture in drinking water (57 mg Ni/L to 200 mg Pb/L) for 12 days had increased urinary excretion of delta aminolevulinic acid and increased delta aminolevulinic dehydratase activity in erythrocytes when compared to groups given lead alone or nickel alone (Tomokuni and Ichiba 1990).

Magnesium competes with nickel in isolated cell studies (WHO 1991). Treatment with magnesium reduces nickel toxicity, presumably through inhibition of nickel binding to DNA (USPHS 1993; Hartwig et al. 1994). Manganese also inhibits the binding of nickel to DNA (WHO 1991), and manganese administration reduces the accumulation of nickel in some organs (Murthy and Chandra 1979). Manganese dust inhibits nickel subsulfide-induced carcinogenesis in rats following simultaneous intramuscular injection of the two compounds (USPHS 1993). Also, nickel–manganese mixtures are less-than-additive in producing cytotoxicity of alveolar macrophages in rats (WHO 1991). Nickel compounds enhance the cytotoxicity and genotoxicity of ultraviolet radiation, X-rays, and cytostatic agents such as *cis*-platinum, *trans*-platinum, and mitomycin C (Hartwig et al. 1994). Nickel is less-than-additive in toxicity to aquatic algae in combination with zinc (WHO 1991). Treatment with zinc lessens nickel toxicity, presumably by competing with nickel in binding to DNA and proteins (USEPA 1985; WHO 1991; USPHS 1993; Hartwig et al. 1994). Zinc binding sites of DNA-binding proteins, known as “finger loop domains,” are likely molecular targets for metal toxicity. Ionic nickel has an ionic radius similar to Zn²⁺ and substitution is possible. Such substitution may disrupt nickel-induced gene expression by interfering with site-specific free radical reactions, which can result in DNA cleavage, formation of DNA protein crosslinks, and disturbance of mitosis (WHO 1991).

Nickel also interacts with chelating agents, phosphatases, viruses, vitamins, and polycyclic aromatic hydrocarbons (PAHs). Chelating agents mitigate the toxicity of nickel by stimulating the excretion of nickel (USPHS 1993). Chelators reduced the toxicity of nickel to aquatic plants, presumably by lowering nickel bioavailability (WHO 1991). Lipophilic chelating agents, such as triethylenetetramine and Cyclam (1,4,8,11-tetraazacyclotetradecane) are more effective in reducing toxicity than hydrophilic chelating agents such as EDTA, cyclohexanediamine tetraacetic acid,

diethylenetriamine pentaacetic acid, and hydroxyethylenediamine triacetic acid. The greater efficacy of the lipophilic agents may be due to their ability to bind to nickel both intracellularly and extracellularly, while the hydrophilic agents can only bond extracellularly (USPHS 1993). Nickel irreversibly activates calcineurin, a multifunctional intracellular phosphatase normally activated by calcium and calmodulin (Kasprzak 1987). With nickel present, Newcastle Disease virus suppresses mouse L-cell interferon synthesis, suggesting virus–nickel synergism (USEPA 1980). Nickel interacts with Vitamin C (USEPA 1985) and has a synergistic effect on the carcinogenicities of various PAHs (USEPA 1980). Rats given intratracheal doses of nickel oxide and 20-methylcholanthrene develop squamous cell carcinomas more rapidly than with 20-methylcholanthrene alone. Simultaneous exposure of rats to benzopyrene and nickel subsulfide reduced the latency period of sarcomas by 30% and induced lung histopathology at a higher frequency than either agent alone. Also, tissue retention of PAH carcinogens is prolonged with nickel exposure (USEPA 1980).

6.4 CARCINOGENICITY, MUTAGENICITY, AND TERATOGENICITY

6.4.1 General

Some forms of nickel are carcinogenic to humans and animals (IARC 1976; Smialowicz et al. 1984; USEPA 1986; WHO 1991; Hausinger 1993; USPHS 1993; Hartwig et al. 1994). Carcinogenicity of nickel compounds varies significantly with the chemical form of nickel, route of exposure, animal model used (including intraspecies strain differences), dose, and duration of exposure (USEPA 1980). In tests with small laboratory mammals, induction of carcinomas of the types found in humans has only been accomplished following exposures by the respiratory route (Sunderman 1968). Inhalation studies with nickel subsulfide and nickel oxide show evidence of carcinogenicity in mammals and humans. However, the evidence based on oral or cutaneous exposure to these and other nickel compounds is either negative or inconclusive (NAS 1975; IARC 1976; Norseth 1980; USEPA 1980, 1986; WHO 1991; USPHS 1993). Nickel carbonyl and metallic nickel are carcinogenic in experimental animals, but data regarding their carcinogenicity in humans are inconclusive (USEPA 1975; Norseth 1980; USPHS 1993).

Certain nickel compounds are weakly mutagenic in a variety of test systems, but much of the evidence is inconclusive or negative (USPHS 1977, 1993; USEPA 1986; Kasprzak 1987; WHO 1991; Outridge and Scheuhammer 1993). Mutagenicity — as measured by an increased frequency of sister chromatid exchange, chromosome aberrations, cell transformations, spindle disturbances, and dominant lethal effects — is induced by various nickel compounds at high concentrations in isolated cells of selected mammals including humans; however, these effects have not been observed *in vivo* (Sunderman 1981; USEPA 1986; WHO 1991; USPHS 1993). Nickel mutagenesis is thought to occur through inhibition of DNA synthesis and excision repair, resulting in an increased frequency of crosslinks and strand breaks (USEPA 1986; WHO 1991; USPHS 1993). DNA strand breaks occur in rat cells exposed to 5 to 40 mg Ni/kg medium as nickel carbonate; similar effects occur in hamster cells at 10 to 2000 mg Ni/kg medium as nickel chloride and nickel subsulfide, and in human cells with nickel sulfate (WHO 1991). The ability of a particular nickel compound to cause mutations is considered proportional to its cellular uptake; however, data on nickel bioavailability to cells is scarce (Niebuhr et al. 1980; USPHS 1993).

No teratogenic effects of nickel compounds occur in mammals by way of inhalation or ingestion except from nickel carbonyl (USEPA 1986; Outridge and Scheuhammer 1993). However, injection of low nickel doses results in consistent fetal malformations, particularly when nickel is administered during the organogenic stage of gestation of mammals or during the early development of domestic chick embryos (Outridge and Scheuhammer 1993). Injected doses causing teratogenic effects in rodents were as low as 1.0 to 1.2 mg Ni/kg body weight (BW), although more malformations resulted at higher dosages (2.3 to 4.0 mg/kg BW), which also increased fetal mortality

and toxicity in the dam (Mas et al. 1985; Outridge and Scheuhammer 1993). Possible causes of nickel-induced malformations include direct toxicity from high transplacental nickel levels, reduced availability of alpha-fetoprotein to fetuses, or an increase in maternal glucose levels, which induces hyperglycemia in fetuses (Mas et al. 1985; Outridge and Scheuhammer 1993).

6.4.2 Carcinogenicity

Epidemiological studies conducted some decades ago in England, Canada, Japan, Norway, Germany, Russia, New Caledonia, and West Virginia indicated that humans working in the nickel processing and refining industries — or living within 1 km of processing or refining sites — had a significantly increased risk of developing fatal cancers of the nose, lungs, larynx, and kidneys, and a higher incidence of deaths from nonmalignant respiratory disease (Sunderman 1968, 1981; NAS 1975; IARC 1976; USPHS 1977, 1993; Norseth and Piscator 1979; Norseth 1980; Sevin 1980; USEPA 1980; Kasprzak 1987; WHO 1991). Nasal cancers in nickel refinery workers were similar to those of the general population; however, lung cancers of nickel refinery workers had a higher frequency of squamous cell carcinomas (USPHS 1993). Smoking of tobacco contributed to the development of lung cancers in the nickel-exposed workers. Smoking about 15 cigarettes daily for one year adds about 1930 µg of nickel, as nickel carbonyl, to the human lung; this is equivalent to a carcinogenic dose of nickel for rats (Sunderman 1970, 1981). Symptoms of cancer in humans may occur 5 to 35 years after exposure (Furst and Radding 1980; Kasprzak 1987; USPHS 1993). The incidence of human lung and nasal cancers in occupationally exposed workers is related to nickel concentration and duration of exposure (USEPA 1986). Nickel compounds implicated as carcinogens include insoluble dusts of nickel subsulfide (Ni_3S_2) and nickel oxides (NiO , Ni_2O_3), the vapor of nickel carbonyl ($\text{Ni}(\text{CO})_4$), and soluble aerosols of nickel sulfate (NiSO_4), nickel nitrate (NiNO_3), and nickel chloride (NiCl_2 ; USEPA 1980; USPHS 1977). Soluble nickel compounds, though toxic, have relatively low carcinogenic activities (Ho and Furst 1973). In general, carcinogenicity of nickel compounds is inversely related to its solubility in water, the least soluble being the most active carcinogen (Sunderman 1968; Furst and Radding 1980; USEPA 1980; USPHS 1993). The highest risk to humans of lung and nasal cancers comes from exposure to respirable particles of metallic nickel, nickel sulfides, nickel oxide, and the vapors of nickel carbonyl (NAS 1975; USPHS 1977; Norseth and Piscator 1979; Norseth 1980; Sunderman 1981; Sunderman et al. 1984; USEPA 1986; Kasprzak 1987; WHO 1991; USPHS 1993). Cancers were most frequent when workers were exposed to soluble nickel compounds at concentrations greater than 1.0 mg Ni/m³ air and to exposure to less soluble compounds at greater than 10.0 mg Ni/m³ air (USPHS 1993). Nickel subsulfide appears to be the nickel compound most carcinogenic to humans, as judged by animal studies and epidemiological evidence (Furst and Radding 1980; Outridge and Scheuhammer 1993). The death rate of nickel workers from cancer has declined significantly since the mid-1920s because of improved safety and awareness (USPHS 1977, 1993).

The underlying biochemical mechanisms governing the carcinogenicity of various nickel compounds are imperfectly understood. There is general agreement that intracellular nickel accumulates in the nucleus, especially the nucleolar fraction (NAS 1975; USEPA 1980). Intracellular binding of nickel to nuclear proteins and nuclear RNA and DNA may cause strand breakage and other chromosomal aberrations, diminished RNA synthesis and mitotic activity, and gene expression (USEPA 1980; Kasprzak 1987). A key mechanism of the transformation of tumorous cells involves DNA damage resulting from mutation (Sigel and Sigel 1988) caused by hydroxy radical or other oxidizing species (Datta et al. 1994). Alterations in cytokine (also known as tumor necrosis factor) production is associated with fibrotic lung injury in rats. Inhaled nickel oxide is known to increase cytokine production in rats (Morimoto et al. 1995).

Nickel entering the digestive tract of mammals is likely to be noncarcinogenic. Chronic ingestion studies of various nickel compounds that lasted as long as 2 years using several species of mammals show no evidence of carcinogenesis (Outridge and Scheuhammer 1993). Inhalation is the dosing

route most relevant to human occupational exposure (Sunderman et al. 1984) and probably an important route for wildlife exposure in the case of nickel powder, nickel carbonyl, and nickel subsulfide (IARC 1976).

Inhalation of airborne nickel powder at 15 mg Ni/m³ air causes an increased frequency of lung anaplastic carcinomas and nasal cancers in rodents and guinea pigs, especially when the particles are less than 4 µm in diameter (USPHS 1977; USEPA 1980). Rats exposed to airborne dusts of metallic nickel at 70 mg Ni/m³ air for 5 h daily, 5 days weekly over 6 months had a 40% frequency of lung cancers; the latent period for tumor development was 17 months (Sunderman 1981). A similar case is made for nickel sulfide and nickel oxide (Sunderman 1981). In Canada, however, metallic nickel is considered "unclassifiable with respect to carcinogenicity" due to the limitations of identified studies (Hughes et al. 1994). Inhaled nickel carbonyl is carcinogenic to the lungs of rats, a species generally considered to be peculiarly resistant to pulmonary cancer (Sunderman and Donnelly 1965; NAS 1975; IARC 1976; USEPA 1980; WHO 1991). Pulmonary cancers developed in rats 24 to 27 months after initial exposure to nickel carbonyl, and growth and survival of rats during chronic exposure were markedly reduced (Sunderman and Donnelly 1965). Rats exposed to air containing 250 µg nickel carbonyl/L for only 30 min had a 4% incidence of lung cancer in 2-year survivors vs. 0% in controls; rats exposed to 30 to 60 µg/L air for 30 min, three times weekly for 1 year had a 21% incidence of lung cancer in 2-year survivors (Sunderman 1970; NAS 1975). Inhaled nickel oxides do not seem to be tumorigenic to hamsters at concentrations of 1.2 mg Ni/m³ air during exposure for 12 months (Outridge and Scheuhammer 1993). Hamsters did not develop lung tumors during lifespan inhalation exposure to nickel oxide; however, inhaled nickel oxide enhanced nasal carcinogenesis produced by diethylnitrosamine (USPHS 1977). Inhalation of nickel subsulfide produced malignant lung tumors and nasal cancers in rats in a dose-dependent manner (Ottolenghi et al. 1974; IARC 1976; USPHS 1977, 1993; WHO 1991; Benson et al. 1995; Rodriguez et al. 1996). Rats develop benign and malignant lung tumors (14% frequency vs. 0% in controls) after exposure for 78 weeks (6 h daily, 5 days weekly) to air containing 1.0 mg Ni/m³ (as nickel subsulfide; particles <1.5 µm in diameter) and during a subsequent 30-week observation period (IARC 1976; USPHS 1977; USEPA 1980; NRCC 1981).

Local sarcomas may develop in humans and domestic animals at sites of nickel implants and prostheses made of nickel. Latency of the implant sarcomas varies from 1 to 30 years in humans (mean, 10 years) and from 1 to 11 years in dogs (mean, 5 years). No cases of malignant tumors are reported at sites of dental nickel prostheses (Kasprzak 1987).

Injection site tumors are induced by many nickel compounds that do not cause cancer in animals by other routes of exposure (USPHS 1977). In fact, most of the published literature on nickel carcinogenesis concerns injected or implanted metallic nickel or nickel compounds. However, these data seem to be of limited value in determining carcinogenic exposure levels for avian and terrestrial wildlife (Outridge and Scheuhammer 1993). The applicability of these studies to a recommendation for human workplace exposure is also questionable (USPHS 1977). Nevertheless, injection- or implantation-site sarcomas have been induced by many nickel compounds after one or repeated injections or implantations in rats, mice, hamsters, guinea pigs, rabbits, and cats (NAS 1975; IARC 1976; USPHS 1977, 1993; Norseth and Piscator 1979; USEPA 1980; NRCC 1981; Sunderman 1981; WHO 1991). Nickel compounds known to produce sarcomas or malignant tumors by these routes of administration (implantation, intratracheal, intramuscular, intraperitoneal, subcutaneous, intrarenal, intravenous, intratesticular, intraocular, intraosseus, intrapleural, intracerebral, intrahepatic, intraarticular, intrasubmaxillary, intraadipose, intramedullary) include nickel subsulfide, nickel carbonyl, nickel powder or dust, nickel oxide, nickel hydroxide, nickel acetate, nickel fluoride, nickelocene, nickel sulfate, nickel selenide, nickel carbonate, nickel chromate, nickel arsenide, nickel telluride, nickel antimonide, nickel-iron matte, nickel ammonium sulfate and nickel monosulfide.

Some parenteral routes of administration were less effective than others in producing an increase in the frequency of benign or malignant tumors, including intravenous, submaxillary, and intrahepatic

injection routes (Sunderman 1981). Some nickel compounds are more effective at inducing tumors than others; for example, nickel sulfate and nickel acetate induce tumors in the peritoneal cavity of rats after repeated intraperitoneal injections but nickel chloride does not (WHO 1991). Likewise, some species are more sensitive to tumor induction by injection than others; rats, for example, are more sensitive than hamsters (USPHS 1977). Most nickel compounds administered by way of injection usually produce responses at the site of injection; however, nickel acetate injected intraperitoneally produced pulmonary carcinomas in mice (USEPA 1980). Some carcinogenic nickel compounds produce tumors only when a threshold dose is exceeded (IARC 1976; USPHS 1993), and some strains of animals are more sensitive than others. In one study, three strains of male mice (*Mus* sp.) were given a single intramuscular injection of 0.5, 2.5, 5.0, or 10.0 mg nickel subsulfide per mouse — equivalent to 19, 95, 190, or 380 mg Ni₃S₂/kg BW — and observed for 78 weeks for tumor development (Rodriguez et al. 1996). Nickel subsulfide is a water-insoluble compound suspected to damage cells through oxidative mechanisms. The highest dose injected was lethal (53 to 93% dead) within 7 days. The final incidence of sarcomas in the 5 mg/mouse groups ranged between 40 and 97%, with decreased survival and growth noted in all test groups. In the most sensitive strain tested, there was a dose-dependent increase in tumor frequency, with a significant increase in tumors at the lowest dose tested (Rodriguez et al. 1996).

Carcinogenic properties of nickel are modified by interactions with other chemicals (NAS 1975; USEPA 1985; WHO 1991). Nickel–cadmium battery workers exposed to high levels of both nickel and cadmium have an increased risk of lung cancer when compared to exposure from cadmium alone (WHO 1991). Some nickel compounds interact synergistically with known carcinogens (WHO 1991). Nickel chloride enhances the renal carcinogenicity of N-ethyl-N-hydroxyethyl nitrosamine in rats. Metallic nickel powder enhances lung carcinogenicity of 20-methylcholanthrene when both are administered intratracheally to rats. Nickel subsulfide in combination with benzo(a)pyrene shortens the latency time to local tumor development and produces a disproportionately higher frequency of malignant tumors. Nickel sulfate enhanced dinitrosopiperazine carcinogenicity in rats (WHO 1991), and nickel potentiated the specific effects of cobalt in rabbits by enhancing the formation of lung nodules (Johansson et al. 1991). Some chemicals inhibit nickel-induced carcinogenicity. Carcinogenicity induced by nickel subsulfide is reduced by manganese dust (Sunderman 1981; Sunderman et al. 1984; WHO 1991). Manganese protects male guinea pigs against tumorigenesis induced by nickel subsulfide, possibly due to the stimulating effect of manganese on macrophage response and by displacing nickel from the injection site (Murthy and Chandra 1979). Sodium diethyldithiocarbamate reduced tumor incidence in rats implanted with nickel subsulfide (WHO 1991), and magnesium acetate and calcium acetate inhibit lung adenoma formation in mice treated intraperitoneally with nickel acetate (WHO 1991). Nickel interactions with other suspected carcinogens, such as chromium, merit additional research (Norseth 1980). Nickel and other trace metals in asbestos fibers are responsible, in part, for the pulmonary carcinogenicity found in asbestos workers (Sunderman 1968). Nickel–sulfur mineral complexes may also have carcinogenic potential; a similar case is made for the corresponding arsenides, selenides, and tellurides (USEPA 1980).

6.4.3 Mutagenicity

Nickel salts gave no evidence of mutagenesis in tests with viruses (USPHS 1977), and bacterial mutagenesis tests of nickel compounds have consistently yielded negative or inconclusive results (USPHS 1977; Sunderman 1981; Sunderman et al. 1984; WHO 1991). However, nickel chloride and nickel sulfate were judged to be mutagenic or weakly mutagenic in certain bacterial eukaryotic test systems (USEPA 1985). Nickel subsulfide was positively mutagenic to the protozoan *Paramecium* sp. at 0.5 mg Ni/L (WHO 1991). Ionic Ni²⁺ was mutagenic to *Escherichia coli*; mutagenesis was enhanced by the addition of both hydrogen peroxide and tripeptide glycyl-L-histidine, suggesting

that short-lived oxygen free radicals are generated (Tkeshelashvili et al. 1993). Nickel chloride hexahydrate induced respiratory deficiency in yeast cells, but this may be a cytotoxic effect rather than a gene mutation (USPHS 1977; WHO 1991).

Nickel is weakly mutagenic to plants (USPHS 1977) and insects (WHO 1991). Abnormal cell divisions occur in roots of the broad bean (*Vicia faba*) during exposure to various inorganic nickel salts at nickel concentrations of 0.1 to 1000 mg/L (USPHS 1977). All nickel salts tested produced more abnormal cell divisions than did controls. In beans, nickel nitrate was the most effective inorganic nickel compound tested in producing deformed cells, abnormal arrangement of chromatin, extra micronuclei, and evidence of cell nucleus disturbances; however, nickel salts showed only weak mutagenic action on rootlets of peas (*Pisum* sp.; USPHS 1977). Nickel sulfate induced chromosomal abnormalities in root tip cells of onions, *Allium* sp. (Donghua and Wusheng 1997) and caused sex-linked recessive mutations in the fruit fly (*Drosophila melanogaster*) at 200 to 400 mg Ni/L culture medium (WHO 1991).

Human cells exposed to various nickel compounds have an increased frequency of chromosomal aberrations, although sister chromatid exchange frequency is unaffected. Cells from nickel refinery workers exposed to nickel monosulfide (0.2 mg Ni/m³) or nickel subsulfide (0.5 mg Ni/m³) showed a significant increase in the incidence of chromosomal aberrations (Boysen et al. 1980; WHO 1991; USPHS 1993). No correlation was evident between nickel exposure level and the frequency of aberrations (USPHS 1993).

In Chinese hamster ovary cells, nickel chloride increased the frequency of chromosomal aberrations and sister chromatid exchanges. The cells with aberrations increased from 8% at about 6 µg Ni/L to 21% at about 6 mg Ni/L in a dose-dependent manner (Howard et al. 1991). There is a large difference in the mutagenic potential of soluble and insoluble nickel compounds, which seems to reflect the carcinogenic potential of these forms of nickel (Lee et al. 1993). For example, insoluble particles less than 5 µm in diameter of crystalline nickel subsulfide — a carcinogen — produced a strong dose-dependent mutagenic response in Chinese hamster ovary cells up to 80 times higher than untreated cells. However, soluble nickel sulfate produced no significant increase in mutational response over background in Chinese hamster ovary cells (Lee et al. 1993). A similar response is reported for Syrian hamster embryo cells (USPHS 1993). Interactions of carcinogens and soluble nickel salts need to be considered. Benzo(a)pyrene, for example, showed a comutagenic effect with nickel sulfate in hamster embryo cells (USEPA 1985).

In rats, nickel carbonyl is reported to cause dominant lethal mutations (WHO 1991), but this needs verification. Nickel sulfate, when given subcutaneously at 2.4 mg Ni/kg BW daily for 120 days causes infertility; testicular tissues are adversely affected after the first injection (USEPA 1980). Nickel salts given intraperitoneally to rats at 6 mg Ni/kg BW daily for 14 days did not produce significant chromosomal changes in bone marrow or spermatogonial cells (Mathur et al. 1978).

In mice, nickel chloride produces a dose-dependent increase in abnormal lymphoma cells (WHO 1991). Mice given high concentrations of nickel in drinking water, equivalent to 23 mg Ni/kg BW daily and higher, have an increased incidence of micronuclei in bone marrow (USPHS 1993). However, mice injected once with 50 mg Ni/kg BW as nickel chloride show no evidence of mutagenicity (USPHS 1977).

6.4.4 Teratogenicity

Nickel carbonyl at high doses is a potent animal teratogen (Sunderman et al. 1984). Inhalation exposure to nickel carbonyl caused fetal death and decreased weight gain in rats and hamsters (WHO 1991) and eye malformations in rats (Sevin 1980; Sunderman et al. 1980). Studies on hamsters, rats, mice, birds, frogs, and other species suggest that some individuals are susceptible to reproductive and teratogenic effects when given high doses of nickel by various routes of administration (USPHS 1977; Sunderman et al. 1980; USEPA 1986; WHO 1991; Hausinger 1993). Intravenous injection of nickel sulfate to hamsters at 2 to 25 mg/kg BW on day 8 of gestation

produces developmental abnormalities (USPHS 1977; Norseth and Piscator 1979). Teratogenic malformations — including poor bone ossification, hydronephrosis, and hemorrhaging — occur in rats when nickel is administered during organogenesis, and these malformations are maximal at dose levels toxic for the dam (Mas et al. 1985). A dose of 4 mg/kg BW given intraperitoneally on day 12 or 19 of pregnancy is teratogenic in rats (Mas et al. 1985). Rats exposed continuously for three generations to drinking water containing 5 mg Ni/L produce smaller litters, higher offspring mortality, and fewer males (NAS 1975; USPHS 1977). An increase in the number of runts suggests that transplacental toxicity occurs (USPHS 1977; Norseth and Piscator 1979).

Divalent nickel is a potent teratogen for the South African clawed frog (*Xenopus laevis*). Frog embryos actively absorb Ni²⁺ from the medium and develop ocular, skeletal, craniofacial, cardiac, and intestinal malformations (Sunderman et al. 1990; Hopfer et al. 1991; Hausinger 1993; Luo et al. 1993; Hauptman et al. 1993; Plowman et al. 1994). A Ni²⁺-binding serpin, *pNiXa*, is abundant in clawed frog oocytes and embryos; binding of Ni²⁺ to *pNiXa* may cause embryotoxicity by enhancing oxidative reactions that produce tissue injury and genotoxicity (Beck et al. 1992; Haspel et al. 1993; Sunderman et al. 1996). Another Ni²⁺-binding protein, *pNiXc*, isolated from mature oocytes of the clawed frog, was identified as a monomer of fructose-1,6-biphosphate aldolase A and raises the possibility that aldolase A is a target enzyme for nickel toxicity (Antonijczuk et al. 1995).

Nickel is embryolethal and teratogenic to white leghorn strains of the domestic chicken (*Gallus* sp.), possibly due to the mitosis-inhibiting activity of nickel compounds (Gilani and Marano 1980). Fertilized chicken eggs injected with 0.02 to 0.7 mg Ni/egg as nickel chloride on days 1 through 4 of incubation show a dose-dependent response. All dose levels of nickel tested were teratogenic to chickens. Malformations include poorly developed or missing brain and eyes, everted viscera, short and twisted neck and limbs, hemorrhaging, and a reduction in body size. Toxicity and teratogenicity are highest in embryos injected on day 2 (Gilani and Marano 1980). Mallard (*Anas platyrhynchos*) ducklings from fertile eggs treated at age 72 h with 0.7 µg Ni as nickel mesotetraphenylporphine show a marked decrease in survival. Among survivors, there is a significant increase in the frequency of developmental abnormalities, a reduction in bill size, and a reduction in weight (Hoffman 1979).

Changes in employment practices in North America and Europe have increased the proportion of women among workers in nickel mines and refineries and in nickel-plating industries and have increased the concern regarding possible fetal toxicity associated with exposures of pregnant women to nickel during gestation (Sunderman et al. 1978). One preliminary report (Chashschin et al. 1994) strongly suggests that exposure to nickel of Russian female hydrometallurgy workers causes significantly increased risks for abortion, total defects, cardiovascular defects, and defects of the musculoskeletal system. Nickel was observed to cross the human placenta and produce teratogenesis and embryotoxicity, as judged by studies with isolated human placental tissues (Chen and Lin 1998). Nickel disrupts lipid peroxidative processes in human placental membranes, and this metabolic change may be responsible for the observed decrease in placental viability, altered permeability, and embryotoxicity (Chen and Lin 1998).

Nonteratogenic reproductive effects of nickel include increased resorption of embryos and fetuses, reduced litter size, testicular damage, altered rates of development and growth, and decreased fertility. Nickel compounds can penetrate the mammalian placental barrier and affect the fetus (USEPA 1980; Sunderman et al. 1984; Mas et al. 1985). Intravenous administration of nickel acetate (0.7 to 10.0 mg Ni/kg BW) to pregnant hamsters on day 8 of gestation resulted in dose-dependent increases in the number of resorbed embryos (USEPA 1980). Rats injected intramuscularly with nickel chloride on day 8 of gestation with 12 or 16 mg Ni/kg BW produced significantly fewer live fetuses than did controls (USPHS 1977). Three generations of rats given nickel in their diets at 250 to 1000 mg Ni/kg ration had increased fetal mortality in the first generation and reduced body weights in all generations at 1000 mg/kg (USPHS 1977). Litter sizes were reduced in pregnant rats fed nickel in various forms at 1000 mg Ni/kg ration (USEPA 1980). Rodents exposed to nickel

during gestation show a decline in the frequency of implantation of fertilized eggs, enhanced resorption of fertilized eggs and fetuses, an increased frequency of stillbirths, and growth abnormalities in live-born young (Hausinger 1993). Exposure of eggs and sperm of rainbow trout to 1.0 mg Ni/L as nickel sulfate for 30 min did not affect fertilization or hatchability; however, most exposed zygotes hatched earlier than the controls (NAS 1975). Nickel salts produced testicular damage in rats and mice given oral, subcutaneous, or intratesticular doses of 10 to 25 mg Ni/kg BW; nickel-treated male rats were unable to impregnate females (USPHS 1977). Nickel sulfate at 25 mg Ni/kg BW daily for 120 days via the esophagus selectively damaged the testes of rats (inhibition of spermatogenesis) and resulted in a reduced procreative capacity (USPHS 1977); males were permanently infertile after 120 days on this regimen (NAS 1975).

6.5 CONCENTRATIONS IN FIELD COLLECTIONS

6.5.1 General

Nickel is ubiquitous in the biosphere and is the 24th most abundant element in the earth's crust with a mean concentration of 75 mg/kg (Sevin 1980; Chau and Kulikovsky-Cordeiro 1995). Nickel enters the environment from natural and human sources and is distributed throughout all compartments by means of chemical and physical processes and biological transport by living organisms. Nickel is found in air, soil, water, food, and household objects; ingestion or inhalation of nickel is common, as is dermal exposure (USPHS 1977). In general, nickel concentrations in plants, animals, and abiotic materials are elevated in the vicinity of nickel smelters and refineries, nickel–cadmium battery plants, sewage outfalls, and coal ash disposal basins (NAS 1975; Kasprzak 1987; WHO 1991; USPHS 1993; Chau and Kulikovsky-Cordeiro 1995). A global inventory estimate of nickel shows that living organisms contain about 14 million metric tons of nickel, mostly (98.8%) in terrestrial plants ([Table 6.4](#)), but plants and animals account for only 0.00000031% of the total nickel inventory estimate of 4500 trillion metric tons, the vast majority of the nickel being present in the lithosphere and other abiotic materials ([Table 6.4](#)).

Table 6.4 Inventory of Nickel in Various Global Environmental Compartments

Compartment	Mean Concentration (mg/kg)	Nickel in Compartment (metric tons)
Lithosphere, down to 45 km	75	4,300,000,000,000,000
Sedimentary rocks	48	120,000,000,000,000
Soils, to 100 cm	16	5,300,000,000,000
Oil shale deposits	30	1,400,000,000,000
Dissolved oceanic	0.0006	840,000,000
Nickel ore reserves	>2000	160,000,000
Coal deposits	15	150,000,000
Terrestrial litter	15	33,000,000
Terrestrial plants	6	14,000,000
Suspended oceanic particulates	95	6,600,000
Crude oil	10	2,300,000
Terrestrial animals	2.5	50,000
Swamps and marshes	7	42,000
Lakes and rivers, total	0.001	34,000
Consumers/reducers (biological)	3.5	11,000
Atmosphere	0.3	1500
Oceanic plants	2.5	500
Lakes and rivers, plankton	4	230

Modified from Nriagu, J.O. 1980b. Global cycle and properties of nickel. Pages 1–26 in J.O. Nriagu (ed.). *Nickel in the Environment*. John Wiley, NY.

6.5.2 Abiotic Materials

Nickel concentrations are elevated in air, water, soil, sediment, and other abiotic materials in the vicinity of nickel mining, smelting, and refining activities; in coal fly ash; in sewage sludge; and in wastewater outfalls ([Table 6.5](#)). Maximum concentrations of nickel found in abiotic materials were 15,300 ng/L in air under conditions of extreme occupational exposure, 19.2 µg/L in seawater, 30 µg/L in rain, 240 µg/L in sewage liquids, 300 µg/L in drinking water near a nickel refinery, 500 µg/kg in snow, 183,000 µg/L in fresh water near a nickel refinery, 4430 µg/L in groundwater, 27,200 µg/L in waste water from nickel refineries, 1600 mg/kg in coal fly ash, 2000 mg/kg in ultramafic rocks, 24,000 mg/kg in soils near metal refineries, 53,000 mg/kg in sewage sludge, more than 100,000 mg/kg in lake sediments near a nickel refinery, and 500,000 mg/kg in some meteorites ([Table 6.5](#)).

Nickel in the atmosphere is mainly in the form of particulate aerosols (WHO 1991) resulting from human activities (Sevin 1980). Air concentrations of nickel are elevated near urbanized and industrialized sites and near industries that process or use nickel (USPHS 1993; Chau and Kulikovsky-Cordeiro 1995; Pirrone et al. 1996; [Table 6.5](#)). The greatest contributor to atmospheric nickel loadings is combustion of fossil fuels, in which nickel appears mainly as nickel sulfate, nickel oxide, and complex metal oxides containing nickel (USEPA 1986). Nickel concentrations in the atmosphere of the United States are highest in winter and lowest in summer, demonstrating the significance of oil and coal combustion sources (USPHS 1993; Pirrone et al. 1996). Nickel in the atmosphere is removed through rainfall and dry deposition, locating into soils and sediments; atmospheric removal usually occurs in several days. When nickel is attached to small particles, however, removal can take more than a month (USPHS 1993). Cigarette smoke contributes significantly to human intake of nickel by inhalation; heavy smokers can accumulate as much as 15 µg of nickel daily from this source (USEPA 1980).

Most unpolluted Canadian rivers and lakes sampled between 1981 and 1992 contained 0.1 to 10 µg Ni/L; however, natural waters near industrial sites may contain 50 to 2000 µg Ni/L (Chau and Kulikovsky-Cordeiro 1995). Nickel concentrations in snow from Montreal, Canada, are high compared with ambient air ([Table 6.5](#)); nickel burdens in Montreal snow are positively correlated with those of vanadium, strongly suggesting that combustion of fuel oil is a major source of nickel (USPHS 1993). In drinking water, nickel levels may be elevated due to the corrosion of nickel-containing alloys used in the water distribution system and from nickel-plated faucets (USPHS 1993). Nickel concentrations in uncontaminated surface waters are usually lower with increasing salinity or phosphorus loadings (USPHS 1993). Nickel tends to accumulate in the oceans and leaves the ocean as sea spray aerosols, which release nickel-containing particles into the atmosphere (USEPA 1986).

Sediment nickel concentrations are grossly elevated near the nickel–copper smelter at Sudbury, Ontario, and downstream from steel manufacturing plants. Sediments from nickel-contaminated sites have between 20 and 5000 mg Ni/kg DW; these values are at least 100 times lower at comparable uncontaminated sites (Chau and Kulikovsky-Cordeiro 1995). A decrease in the pH of water caused by acid rain may release some of the nickel in sediments to the water column (NRCC 1981). Transfer of nickel from water column to sediments is greatest when sediment particle size is comparatively small and sediments contain high concentrations of clays or organics (Bubb and Lester 1996).

In soils, nickel exists in several forms, including inorganic crystalline minerals or precipitates, as free ion or chelated metal complexes in soil solution, and in various formulations with inorganic cationic surfaces (USEPA 1986). Soil nickel is preferentially adsorbed onto iron and manganese oxides (USPHS 1993; Chau and Kulikovsky-Cordeiro 1995); however, near Sudbury, Ontario, soil nickel is mostly associated with inorganic sulfides (Adamo et al. 1996). The average residence time of nickel in soils is estimated at 3500 years, as judged by nickel concentrations in soils and estimates of the loss of nickel from continents (Nriagu 1980b). Natural levels of soil nickel are augmented by contamination from anthropogenic activities including atmospheric fallout near nickel-emitting industries, automobile traffic, and treatment of agricultural lands with nickel-containing phosphate

fertilizers or municipal sewage sludge (USEPA 1980; Munch 1993). Soils with less than 3 mg Ni/kg DW are usually too acidic to support normal plant growth (NAS 1975). Nickel availability to plants grown in sludge-amended soils is correlated with soil-solution nickel (USPHS 1993). Sewage-derived fertilizers from industrial areas may contain 1000 mg Ni/kg DW or more (NRCC 1981). In sewage sludge, a large percentage of the nickel exists in a form that is easily released from the solid matrix (USPHS 1993). Water solubility of nickel in soils and its bioavailability to plants are affected by soil pH, with decreases in pH below 6.5 generally mobilizing nickel (USPHS 1993; Chau and Kulikovsky-Cordeiro 1995).

Table 6.5 Nickel Concentrations in Selected Abiotic Materials

Material and Units of Concentration	Concentration ^a	Reference ^b
AIR, ng/m³		
Asbestos textile plants, 1961–65	8.8	1
Canada, 1987–90		
Arctic	0.38; Max. 0.68	2
Copper Cliff, Ontario	Max. 6100	2
Hamilton, Ontario	7; Max. 77	2
Quebec City	5; Max. 15	2
Toronto	3; Max. 11	2
Near nickel alloy plants	Max. 1200	3
Occupational exposure		
Miners	6–40	24
Mill area	Max. 2,800,000	24
Matte separation area	170,000–15,300,000	24
Converter furnace area	Max. 200,000	24
Particulate materials, United States		
Remote areas	0.0–6.0	4
Rural areas	0.6–78	4
Urban areas	1–328	4
Urban areas, North America		
Canada, 1971		
Sudbury, Ontario	Max. 2101	5
Toronto	Usually <59	5
United States		
1970–74; various locations	9–15	5
1982; 111 cities	8 (1–86)	4, 7
217 locations; summer vs. winter	17 (Max. 39) vs. 25 (Max. 112)	3, 4, 8, 9
All locales	Usually <20; Max. 328	10
Chicago, 1968–71	18	4
Detroit		
1971–82	21–51 (6–130)	10
1982–92	7–14 (4–32)	10
Houston, 1968–71	15	4
New York, 1968–71	42	4
Texas, 1978–82	1; Max. 49	4
Washington, D.C., 1968–71	23	4
Various locations		
Canadian Arctic	0.1–0.5	4
Continental	1–3	11
Europe	Usually <20; Max. 1400	10
Marine	<0.1–1	11
Nonurban areas	6 (2–11)	3, 6, 8, 9
Remote areas	<0.1–3	11
DRINKING WATER, µg/L		
Canada		
Ontario except Sudbury	0.2–7	2

Table 6.5 (continued) Nickel Concentrations in Selected Abiotic Materials

Material and Units of Concentration	Concentration^a	Reference^b
Sudbury		
Prior to 1972	200 (141–264)	5
1972–92	26–300	2
Current	Max. 72	4
Europe	1–11	4
United States		
All locations	Usually <10; sometimes 10–20; rarely 75; Max. 200	4, 8, 9
969 locations, 1964–70	4.8; <1% had >20; Max. 75	3, 4, 6, 12
Ten largest cities	Usually <5.6	6
Hartford, Connecticut	1	4, 5
Philadelphia	13	6
FOSSIL FUELS, mg/kg		
Coal		
Canadian	15 dry weight (DW)	11
Fly ash; particle diameter 1.1–2.1 µm vs. >11.3 µm	1600 DW vs. 460 DW	5
Crude oil		
Western Canadian	0.1–76 fresh weight (FW)	11
Various	10 FW; Max. 20 FW	5, 8
GROUNDWATER, µg/L		
Contaminated with nickel compounds from a nickel-plating factory	Max. 2500	4
Guelph, Ontario	2.5	2
Newfoundland	<0.2	2
New Jersey, 1977–79	3; Max. 600	4
United States; 1982; upper Mississippi River Basin vs. Ohio River Basin	3 vs. 4430	7
METEORITES, mg/kg		
Selected	50,000–500,000	5
RAIN, µg/L		
Bermuda	0.2	4
Delaware	0.8	4
Massachusetts	0.8 (0.5–1.5)	4
Ontario, Canada; 1982	0.5–0.6	4
Prince Edward Island, Canada	<0.5; Max. 30	2
Sweden	0.2–0.5	4
RIVERS AND LAKES (freshwater), µg/L		
Lake Huron, 1980	0.5; Max. 3.8	4
Lake Ontario, 1980 vs. 82	4 vs. 6 (<1–17)	4
Most locations	Usually <10; 4.8 (4–71)	4, 5, 12
Near Sudbury, Ontario	131 (8–2700)	2, 14
Near Sudbury refinery	Max. 183,000	13
New York state, Adirondacks region; summer, 1975		
Six lakes	0.4–1.1	16
Lake Champlain (contaminated)	12–15	16
River basins, United States; 1975; dissolved	0.5–0.6; Max. 56.0	4, 13
Smoking Hills, Northwest Territories	6300 (from atmospheric releases of combustion of bituminous shales)	2
United Kingdom		
River Ivel (receives municipal wastes) vs. River Yare (reference)	28 (11–84) vs. 3.7 (1.3–11.5)	15
United States; 1982; Great Basin of southern Nevada vs. Ohio River basin	Max. <5 vs. Max. >600	7

Table 6.5 (continued) Nickel Concentrations in Selected Abiotic Materials

Material and Units of Concentration	Concentration^a	Reference^b
ROCKS, mg/kg		
Acid	5–20	2
Mafic	130–160	2
Sandstone, limestone	5–20	2
Shales	50–70	2
Ultramafic	1400–2000	2
SEAWATER, µg/L		
Dissolved		
Atlantic Ocean; offshore; surface vs. 400 m	0.10 vs. 0.16	4
Eastern Arctic Ocean; surface vs. 2000 m	0.13 vs. 0.22	4
Most locations	0.1–0.7	4, 5, 9, 11
Dissolved plus particulate		
Caribbean Sea	2.1	12
Indian Ocean	5.4	12
Northwest Atlantic	3.1–3.5	12
Southwest Atlantic	4.8–19.2	12
Nearshore vs. open ocean	1.8 vs. 1.2	12
Estuaries, Greece		
Euripos Straits; 1980 vs. 1993		
Dissolved	2.5 vs. 1.8	18
Particulate	0.6 vs. 1.4	18
Louros estuary; summer, 1986		
Dissolved; surface vs. 5 m	0.5–7.4 vs. 3.1–9.2	17
Particulate; surface vs. 5 m	Max. 1 vs. Max. 36	17
SEDIMENTS, mg/kg DW		
Canada, lake sediments		
Uncontaminated vs. contaminated	<20 vs. >4000 (Max. 100,000)	2, 14
Precambrian Shield lakes	20–30	14
34% of all samples	<16	2
About 65% of all samples	16–74	2
0.1% of all samples	>75	2
50% of all samples	27	2
15% of all samples	>31	2
Sudbury, Ontario		
About 180 km from Sudbury smelters	<31	4
Within 10 km of smelters	2500–4490	4, 12, 13
Europe		
Ems estuary	21–42	12
Louros estuary, Greece; summer 1986	113–242	17
Euripos Straits, Greece; 1980 vs. 1993	59 vs. 64	18
Former West Germany	100–210	12
Rhine-Meuse estuary	19–59	12
United States		
Alaska, off northern coast	25–31	4
Casco Bay, Maine	18	4
Eastern Long Island	8	4
Great Lakes	0.1–500	12
Lake St. Clair	14 (9–31)	4
New England	4–58	4
New York; Adirondacks region; six lakes vs. Lake Champlain	0.1–3 vs. 3–5	16
Penobscot Bay, Maine	8–35	4

Table 6.5 (continued) Nickel Concentrations in Selected Abiotic Materials

Material and Units of Concentration	Concentration^a	Reference^b
Rocky Mountain lakes		
Four lakes	(10–18)	4
Five lakes	(6–38)	4
Washington; Puget Sound; near sewage treatment plant outfall	35–50	19
SEWAGE LIQUIDS, µg/L		
New York City, 1974		
Industrial	100 (70–240)	13
Municipal	50 (10–150)	13
Sewage recipients; harbor waters vs. adjacent marine waters	15 vs. 4	13
Wastewater treatment plants	200	11
SEWAGE SLUDGE, mg/kg DW		
Missouri; 74 publicly owned treatment works (POTW)	33 (10–13,000)	20
United States; 50 POTW	134	20
United States	Max. 53,000	7
SNOW, µg/kg DW		
Montreal, Canada	2–300	4
Snow particulates	100–500	4
SOILS, mg/kg DW		
Cultivated soils		
Canada	5–50; Max. 950	2, 4, 14
England and Wales	26 (4–80)	4
Farm soils, all locales	Usually 4–80 (<5–1000)	4, 9, 11, 20
Farm soils, United States; mean vs. too acidic to support plant growth	30 vs. <3	5
Forest soils; nine northeastern states vs. Idaho	11 vs. 12–23	4
Contaminated soils		
Near metal refineries	Max. 24,000 DW	14
Near nickel smelter	80–5100; Max. 9372	4, 14
Near nickel smelter, top 5 cm		
Mineral soils; 3 km from smelter vs. 11–18 km distant	500–1500 vs. 16	21
Organic soils; 1 km from smelter vs. reference site	600–6455 vs. 29	21
Near Sudbury smelter vs. site 10 km distant	580 (80–2149) vs. 210 (23–475)	22
Roadside soils, Germany; near road vs. site 5 m from road	32 vs. 8	23
Earth's crust		
Mean	60–90	14
Glacial till	>1000	4
Podzol soil	5000	4
United States	13 (<5–700)	4
WASTEWATERS, µg/L		
Canada; 1988–90; from nickel mining, smelting, and refinery operations	16–27,200	2

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).^b 1, Sunderman 1968; 2, Chau and Kulikovsky-Cordeiro 1995; 3, Sevin 1980; 4, USPHS 1993; 5, NAS 1975; 6, USEPA 1980; 7, USEPA 1986; 8, Norseth 1986; 9, Norseth and Piscator 1979 10, Pirrone et al. 1996; 11, WHO 1991; 12, Snodgrass 1980; 13, Kasprzak 1987; 14, NRCC 1981; 15, Bubb and Lester 1996; 16, Williams et al. 1977; 17, Scoullos et al. 1996; 18, Dassenakis et al. 1996; 19, Schell and Nevissi 1977; 20, Beyer 1990; 21, Frank et al. 1982; 22, Adamo et al. 1996; 23, Munch 1993; 24, USPHS 1977.

6.5.3 Terrestrial Plants and Invertebrates

Nickel is found in all terrestrial plants, usually at concentrations of less than 10 mg/kg DW (NRCC 1981; Kasprzak 1987). The majority of terrestrial plants are nickel-intolerant species and are restricted to soils of relatively low nickel content; some plants without specific nickel tolerance can accumulate anomalous levels of nickel, but at a cost of reduced metabolism (Rencz and Shilts 1980). Plants grown in nickel-rich soils can accumulate high concentrations of nickel (Sigel and Sigel 1988). Crops grown in soils amended with sewage sludge may contain as much as 1150 mg Ni/kg DW (USEPA 1986). Vegetation near point sources of nickel, such as nickel refineries, have elevated nickel concentrations that decline with increasing distance from the source (WHO 1991; Table 6.6). Fruits and vegetables grown near nickel smelters contain 3 to 10 times more nickel in edible portions than those grown in uncontaminated areas (NRCC 1981). Trees, ferns, and grasses near nickel smelters had elevated concentrations of nickel: as much as 174 mg/kg DW in trees and ferns and 902 mg/kg DW in wavy hairgrass (*Deschampsia flexuosa*; Table 6.6). Nickel concentrations in lichens and other vegetation were elevated when grown on nickeliferous rocks, serpentine soils, near nickel smelters (Jenkins 1980b), near urban and industrial centers (Richardson et al. 1980), and near roadsides treated with superphosphate fertilizers (NAS 1975).

Terrestrial vegetation within 3.5 km of one of the Sudbury, Ontario, smelters had as much as 140 mg Ni/kg DW; concentrations decreased with distance from the smelter, reaching a mean concentration of about 12 mg Ni/kg DW at a distance of 60 km (Chau and Kulikovsky-Cordeiro 1995). Some vegetation near a Sudbury smelter — including lawn grasses, timothy (*Phleum pratense*), and oats (*Avena sativa*) — showed signs of nickel toxicosis. Concentrations in these species ranged between 80 and 150 mg Ni/kg DW. Vegetables — beets (*Beta vulgaris*), radishes (*Raphanus* spp.), cabbages (*Brassica oleracea capitata*), and celery (*Apium graveolans*) — grown in soils about 1 km from a nickel refinery had 40 to 290 mg Ni/kg DW in their top portions. All of these vegetables had reduced yield, stunted growth, and chlorosis and necrosis, which is attributed to the high levels of nickel in local soils (Chau and Kulikovsky-Cordeiro 1995).

Mosses and lichens accumulate nickel readily and at least nine species are used to monitor environmental gradients of nickel (Jenkins 1980a). Maximum concentrations of nickel found in whole lichens and mosses from nickel-contaminated areas range between 420 and 900 mg/kg DW vs. 12 mg/kg DW from reference sites (Jenkins 1980a). Nickel concentrations in herbarium mosses worldwide have increased dramatically during this century. In one case, nickel concentrations in *Brachythecium salebrosum* from Montreal, Canada, rose from 6 mg/kg DW in 1905 to 105 mg/kg DW in 1971 (Richardson et al. 1980).

Nickel-tolerant or accumulator species of plants are likely to be found only on nickel-rich soils (Rencz and Shilts 1980). Hyperaccumulator species usually grow on relatively infertile nickel-rich serpentine soils and contain more than 10,000 mg Ni/kg DW (Jenkins 1980b; NRCC 1981; WHO 1991; Table 6.6). Leaves from some genera of nickel hyperaccumulator plants, including *Alyssum*, *Homalium*, and *Hybanthus*, growing on soils derived from volcanic rocks, which are rich in nickel, accumulate nickel to concentrations of 120,000 mg kg DW (Kasprzak 1987; Table 6.6). Nickel is bound as a citrate complex in hyperaccumulator plants from New Caledonia; however, nickel accumulator plants from other locations do not contain unusually high levels of citrate, and nickel is not present as a citrate complex but as a carboxylic acid complex (Lee et al. 1978).

Terrestrial plants take up nickel from soil primarily via the roots (NRCC 1981; WHO 1991). The nickel uptake rate from soil is dependent on soil type, pH, humidity, organic content, and concentration of extractable nickel (NAS 1975; WHO 1991). For example, at soil pH less than 6.5 nickel uptake is enhanced due to breakdown of iron and manganese oxides that form stable complexes with nickel (Rencz and Shilts 1980). The exact chemical forms of nickel that are most readily accumulated from soil and water are unknown; however, there is growing evidence that complexes of nickel with organic acids are the most favored (Kasprzak 1987). In addition to their uptake from the soils, plants consumed by humans may receive several milligrams of nickel per

kilogram through leaching of nickel-containing alloys in food-processing equipment, milling of flour, and catalytic hydrogenation of fats and oils by use of nickel catalysts (USEPA 1986). Nickel reportedly disrupts nitrogen cycling, and this could have serious ecological consequences for forests near nickel smelters (WHO 1991), although adverse effects of nitrogen disruption by nickel need to be verified.

Data are limited on nickel concentrations in terrestrial invertebrates. Earthworms from uncontaminated soils may contain as much as 38 mg Ni/kg DW, and workers of certain termite species may normally contain as much as 5000 mg Ni/kg DW (Table 6.6). Larvae of the gypsy moth (*Lymantria dispar*) near a nickel smelter had 20.4 mg Ni/kg DW; concentrations in pupae and adults were lower because these stages have higher nickel elimination rates than larvae (Bagatto et al. 1996).

6.5.4 Aquatic Organisms

Nickel concentrations are comparatively elevated in aquatic plants and animals in the vicinity of nickel smelters, nickel–cadmium battery plants, electroplating plants, sewage outfalls, coal ash disposal basins, and heavily populated areas (Kniep et al. 1974; Eisler et al. 1978a; Montgomery et al. 1978; Jenkins 1980a; Eisler 1981; Kasprzak 1987; Chau and Kulikovsky-Cordeiro 1995; Table 6.6). For example, at Sudbury, Ontario, mean nickel concentrations, in mg/kg DW, were 22 for larvae of aquatic insects, 25 for zooplankton, and 290 for aquatic weeds; maximum concentrations reported were 921 mg/kg DW in gut of crayfish (*Cambarus bartoni*) and 52 mg/kg fresh weight (FW) in various fish tissues (Chau and Kulikovsky-Cordeiro 1995; Table 6.6). For all aquatic species collected, nickel concentrations were highly variable between and within species; this variability is attributable, in part, to differential tissue uptake and retention of nickel, depth of collection, age of organism, and metal-tolerant strains (Bryan et al. 1977; Bryan and Hummerstone 1978; Jenkins 1980a; Eisler 1981; Chau and Kulikovsky-Cordeiro 1995; Table 6.6).

The bioaccumulation of nickel under field conditions varies greatly among groups. Bioconcentration factors (BCF, which equals the milligrams of nickel per kilogram fresh weight of the sample divided by the milligrams of nickel per liter in the medium) for aquatic macrophytes range from 6 in pristine areas to 690 near a nickel smelter; for crustaceans these values are 10–39; for molluscs, 2 to 191; and for fishes, 2 to 52 (Sigel and Sigel 1988). Bioconcentration factors of 1700 have been reported for marine plankton, 800 and 40 for soft parts and shell, respectively, of some marine molluscs, and 500 for brown algae, suggesting that some food chain biomagnification may occur (NAS 1975).

Concentrations of nickel in roots of *Spartina* sp. from the vicinity of a discharge from a nickel–cadmium battery plant on the Hudson River, New York, ranged between 30 and 500 mg/kg DW and reflected sediment nickel concentrations in the range of 100 to 7000 mg Ni/kg DW (Kniep et al. 1974). The detritus produced from dead algae and macrophytes is the major food source for fungi and bacteria, and in this way nickel can again enter the food chain (NRCC 1981; Chau and Kulikovsky-Cordeiro 1995). Nickel concentrations in tissues of sharks from British and Atlantic water range between 0.02 and 11.5 mg/kg FW; concentrations were highest in fish-eating, mid-water species such as the blue shark (*Prionace glauca*) andtope shark (*Galeorhinus galeus*) (Vas 1991). Concentrations of nickel in livers of tautogs (*Tautoga onitis*) from New Jersey significantly decreased with increasing body length in both males and females; however, this trend was not observed in bluefish (*Pomatomus saltatrix*) or tilefish (*Lopholatilus chamaeleonticeps*) (Mears and Eisler 1977).

6.5.5 Amphibians

In Maryland, nickel concentrations in tadpoles of northern cricket frogs (*Acrida crepitans*) and gray treefrogs (*Hyla versicolor*) increased with increasing soil nickel concentrations, with maximum nickel concentrations recorded of 7.1 mg/kg DW in gray treefrogs and 10.0 mg/kg DW in northern

cricket frogs (Sparling and Lowe 1996). In study sites 9 to 66 km from Sudbury, Ontario, populations of treefrogs (*Hyla crucifer*) and American toads (*Bufo americanus*) declined. Population abundance of adult treefrogs declined with increasing atmospheric deposition of nickel, and abundance of toad tadpoles declined as nickel concentrations in pond water rose from 3.3 µg Ni/L at more distant sites to 19.5 µg Ni/L at sites near Sudbury (Glooschenko et al. 1992).

6.5.6 Birds

Nickel concentrations in the organs of most avian wildlife species in unpolluted ecosystems range from about 0.1 to 2.0 mg/kg DW and occasionally reach 5.0 mg/kg DW (Eisler 1981; Outridge and Scheuhammer 1993). In nickel-contaminated areas, nickel concentrations were elevated in feathers, eggs, and internal tissues of birds when compared to conspecifics collected at reference sites (Darolova et al. 1989; Outridge and Scheuhammer 1993; [Table 6.6](#)). In contaminated ecosystems, mean nickel concentrations between 31 and 36 mg/kg DW occur in primary feathers of mallards (*Anas platyrhynchos*) collected 20 to 30 km from a nickel smelter, bone of the common tern (*Sterna hirundo*) from Hamilton Harbor, Ontario, and eggshell of the tree swallow (*Tachycineta bicolor*) from the Hackensack River, New Jersey ([Table 6.6](#)).

Waterfowl feeding in areas subjected to extensive nickel pollution — such as smelters and nickel–cadmium battery plants — are at special risk because waterfowl food plants in those areas contain 500 to 690 mg Ni/kg DW (Eastin and O’Shea 1981). Dietary items of the ruffed grouse (*Bonasa umbellus*) near Sudbury, Ontario, had 32 to 95 mg Ni/kg DW, whereas nickel concentrations in grouse body tissues usually contain less than 10% of the dietary level. Nickel concentrations in aspen (*Populus tremula*) from the crop of ruffed grouse near Sudbury ranged from 62 mg/kg DW in May to 136 mg/kg DW in September (Chau and Kulikovsky-Cordeiro 1995), which shows the role of season in dietary nickel composition.

6.5.7 Mammals

Mammalian wildlife from uncontaminated habitats usually contain less than 0.1 to about 5 mg Ni/kg DW in tissues; in nickel-contaminated areas, these same species have 0.5 to about 10 mg Ni/kg DW in tissues (Outridge and Scheuhammer 1993; Chau and Kulikovsky-Cordeiro 1995), with a maximum of 37 mg/kg DW in kidneys of the common shrew (*Sorex araneus*) ([Table 6.6](#)). Nickel accumulations in wildlife vary greatly between species. For example, tissues of mice have higher concentrations of nickel than rats and other rodents, while beavers and minks have higher nickel concentrations in their livers than birds in similar sites near Sudbury (Chau and Kulikovsky-Cordeiro 1995).

The highest concentrations in wildlife tissues from nickel-contaminated locales are associated with tissues exposed to the external environment, such as fur and skin. Nickel concentrations in internal organs are usually similar, regardless of degree of contamination (Outridge and Scheuhammer 1993; [Table 6.6](#)). However, nickel concentrations in bone, reproductive organs, and kidneys in certain herbivorous species of wildlife and livestock are elevated when compared to other internal tissues, especially in the vicinity of nickel smelters and other nickel point sources (Outridge and Scheuhammer 1993; Kalas et al. 1995). Trophic position in the food chain, sex, and reproductive state do not seem to significantly influence the nickel body burdens of mammals (Outridge and Scheuhammer 1993), but age is an important variable, and nickel generally increases in various organs with increasing age of terrestrial and marine mammals. Fetuses of a variety of wildlife and domestic species contain concentrations of nickel significantly lower than those in their mothers or in juveniles, suggesting that placental transfer of nickel is restricted. Nickel concentrations in aquatic macrophytes and lower plants in the vicinity of nickel smelters may approach or exceed dietary levels known to cause adverse effects in young animals. Sensitive species of wildlife ingesting this vegetation for extended periods could experience nickel-related toxicity or risk

alterations in community structure as nickel-sensitive taxa are eliminated or their abundance is reduced (Outridge and Scheuhammer 1993).

Elevated nickel concentrations in Norwegian wildlife are linked to emissions from Russian nickel smelters (Kalas et al. 1995). In Norway, nickel concentrations were elevated in livers and kidneys of moose (*Alces alces*) and caribou (*Rangifer tarandus*) because of atmospheric transport of wastes from nickel-processing plants of nearby Russian towns (Sivertsen et al. 1995). In Russia between 1974 and 1992, three species of voles (*Clethrionomys glareolus*, *Clethrionomys rutilus*, *Lemmus lemmus*) were eliminated from the immediate vicinity of a copper–nickel smelter that discharged 2700 metric tons of nickel annually to the atmosphere, and these species were scarce at a moderately contaminated area 28 km south of the smelter (Kataev et al. 1994). Declines were associated with a decrease of important food plants: lichens for *C. glareolus* and *C. rutilus*, mosses for *L. lemmus*, and seed plants for other species of *Clethrionomys*. Close to the smelter, direct toxic effects of accumulated nickel and other metals also may have reduced population densities (Kataev et al. 1994). Nickel concentrations are also elevated in rodents, shrews, soil, vegetation, and earthworms in the vicinity of roads with high automobile density (Pankakoski et al. 1993). In ruminant mammals, tissue nickel concentrations were higher in winter (WHO 1991), presumably because of increased combustion of fossil fuels.

Nickel is normally present in human tissues, and under conditions of high exposure, these levels may increase significantly (WHO 1991). Nickel enters the human body through the diet, through inhalation, by absorption through the skin, and in medications (NAS 1975). The diet accounts for about 97% of the total intake, and drinking water about 2.5% (Kasprzak 1987). Foods rich in nickel include tea (7.6 mg/kg DW), cereals (6.5), vegetables (2.6), and fish (1.7 mg/kg DW) (IARC 1976; Table 6.6). The daily dietary intake of nickel by humans in the United States ranges between 0.15 and 0.6 mg, almost all of which is excreted in the feces (NAS 1975; Norseth and Piscator 1979; USEPA 1980; NRCC 1981; Sunderman et al. 1984). Minor amounts are also excreted in sweat, urine, and hair (Kasprzak 1987). Residents of the Sudbury, Ontario, area who consume homegrown garden products ingest an average of 1.85 mg of nickel daily, of which 0.6 mg comes from the drinking water (NRCC 1981). Inhalation intake of nickel for residents of New York City is estimated at 2.4 µg daily; for Chicago, a maximum value of 13.8 µg daily is recorded; and 14.8 µg are inhaled daily by smokers of 40 cigarettes (NAS 1975; WHO 1991). Canadians in urban areas inhale 0.06 to 0.6 µg Ni daily; near nickel smelters, this may increase to 15 µg daily (NRCC 1981). In Connecticut, serum nickel levels in newborns were normal (3 µg/L) and similar to those of their mothers (Norseth and Piscator 1979). Nickel concentrations in human serum, however, are modified by disease and stress. Concentrations are usually elevated after strokes, pregnancy, and extensive burns, and are depressed in cases of cirrhosis, hypoalbuminemia, extremes of heat, and uremia (Mushak 1980; USEPA 1980, 1986).

About 727,000 workers were potentially exposed to nickel metal, nickel alloys, or nickel compounds during the period 1980 to 1983 (USPHS 1993). Worker exposure differs from that of the general population in that the major route of exposure for nickel workers is inhalation and for the general population it is dermal contact (Sevin 1980). Nickel workers with lung cancer had elevated concentrations of 1.97 mg/kg DW in their lungs when compared to the general population (0.03 to 0.15 mg/kg DW; USPHS 1977). Plasma concentrations of nickel quickly reflect current exposure history to nickel (USEPA 1980). Mean nickel concentrations in plasma of humans occupationally exposed to nickel have declined by about 50% since 1976, suggesting decreased exposure due to improved safety (Boysen et al. 1980).

6.5.8 Integrated Studies

Beaver ponds downstream from an abandoned copper–nickel ore roast yard near Sudbury, Ontario, were devoid of fish and had reduced macroinvertebrate taxon richness and diversity when compared to upstream ponds. Nickel water concentrations, in µg Ni/L, were 57 in upstream ponds,

82 in downstream ponds, and 1800 at the station directly on the roast pit (Rutherford and Mellow 1994). Beavers (*Castor canadensis*) near nickel smelters had elevated nickel concentrations in livers and kidneys when compared to conspecifics from a reference site; accumulations were attributed to food chain contamination (Hillis and Parker 1993).

Hutchinson et al. (1975) found nickel contamination in the Sudbury, Ontario, region to be the result of aerial transport and terrestrial drainage from mining and smelting activities. Nickel concentrations in soils were elevated as far as 52 km from the source. Erosion of soils following the death of vegetation was widespread and affected an area of more than 820 km². Soils increased in acidity, increasing the solubility of nickel. In aquatic ecosystems, nickel was accumulated from the water column by periphyton, rooted aquatic macrophytes, zooplankton, crayfish, clams, and fishes. However, there was no evidence of food chain biomagnification of nickel in the Sudbury ecosystem (Hutchinson et al. 1975). For example, in the nickel-contaminated Wanapitei River, bioconcentration factors during the summer of 1974 were highest for whole periphyton (19,667), followed by whole pondweeds (11,429), sediments (5333), whole crayfish (929), whole zooplankton (643), muscle of carnivorous fishes (329), soft tissues of clams (262), and muscle of omnivorous fishes (226) (Hutchinson et al. 1975). Higher BCF values are recorded for acid- and metal-tolerant flora (Outridge and Scheuhammer 1993).

There is little convincing evidence for the biomagnification of nickel in the food chain. Most authorities agree that nickel concentrations do not increase with ascending trophic levels of food chains and that predatory animals do not have higher concentrations (Jenkins 1980a; WHO 1991; Outridge and Scheuhammer 1993; Chau and Kulikovsky-Cordeiro 1995). The potential for biomagnification exists because algae and macrophytes have comparatively elevated concentrations of nickel; however, animals seem to be able to regulate the nickel content of their tissues by controlled uptake and increased excretion (Jenkins 1980a; Outridge and Scheuhammer 1993).

Table 6.6 Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
TERRESTRIAL PLANTS		
Red maple, <i>Acer rubrum</i> ; leaf; various distances from nickel smelter		
2 km	98 DW	1
20 km	57 DW	1
40 km	14 DW	1
Onion, <i>Allium cepa</i> ; spring vs. fall		
Leaf	9.4 DW vs. 3.8 DW	1
Root	18.4 DW vs. 10.9 DW	1
Celery, <i>Apium graveolans</i> ; spring vs. fall		
Leaf	36 DW vs. 5 DW	1
Root	32 DW vs. 3 DW	1
Paper birch, <i>Betula papyrifera</i> ; leaf; various distances from nickel smelter; June vs. August		
1.0 km	158 DW vs. 148 DW	1
4.6 km	82 DW vs. 111 DW	1
12.0 km	66 DW vs. 64 DW	1
Coffee, <i>Coffea arabica</i> ; green beans	0.1–0.3 FW	1
Sweet fern, <i>Comptonia peregrina</i> ; leaf; various distances from nickel smelter; August		
1.0 km	174 DW	1
6.5 km	46 DW	1
31.0 km	15 DW	1
Lichen, <i>Complum polyatum</i> ; whole; from serpentine soils	420 DW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Wavy hairgrass, <i>Deschampsia flexuosa</i> ; leaf; various distances from nickel smelter		
1.7 km	902 DW	1
2.1 km	242 DW	1
7.4 km	160 DW	1
20.4 km	43 DW	1
52.7 km	37 DW	1
Tall fescue, <i>Festuca</i> sp.; shoot; Maryland; various distances from highway		
8 m	(3.8–5.0) DW	1
16 m	(2.5–3.8) DW	1
32 m	(1.3–2.8) DW	1
Forest species; Nagoya University, Japan; leaves		
57 species	2–8 DW	2
3 species	10–16 DW	2
Grasses, various species; near roadside vs. >30 m from roadside	3.8 DW vs. 1.3 DW	3
Hypnum moss, <i>Hypnum cupressiforme</i> ; whole; U.K.; downwind of nickel industrial complex		
<3 km	All dead; no residues measured	1
8 km	193 DW	1
25 km	420 DW	1
Lettuce, <i>Lactuca sativa</i> ; spring vs. fall		
Leaf	28 DW vs. 3 DW	1
Root	15 DW vs. 4 DW	1
Lichens		
Industrial sites; 13 species	2–52 DW	4
Near nickel smelters; 3 species	220–846 DW	4
Rural sites		
Mineralized substrates; 19 species	1–115 DW	4
Nonmineralized substrates; 13 species	1–10 DW	4
Urban sites; 2 species	33–183 DW	4
Macrophytes, 4 species; 1.6 km from nickel smelter (soil had 2679 mg Ni/kg DW)	109–902 DW	5
Mosses, 4 species; isolated areas	0.2–5.0 DW	4
Nickel hyperaccumulator plants		
<i>Allysum</i> spp.; various locations		
Flowers	Max. 5400 DW	1
Fruits	Max. 5800 DW	1
Leaves	2590–9330 DW; Max. 20,400 DW	1, 6
Roots	Max. 3100 DW	1
Seeds	Max. 6100 DW	1
Stems	Max. 13,500 DW	1
<i>Geissosoma prainosa</i> ; New Caledonia; leaves	6720 DW	6
<i>Homalium</i> spp.; New Caledonia; 9 species; leaves		
3 species	3730–9580 DW	6
3 species	446–662 DW	6
3 species	15–75 DW	6
<i>Hybanthus</i> spp.; New Caledonia; 2 species; leaves	6820–14,900 DW	6
<i>Pearsonia metallifera</i> ; Rhodesia; leaves	10,600 DW	6
<i>Planchonella oxyedra</i> ; southeast Asia; leaves	1600 (50–19,600) DW	1
<i>Psychotria douarrei</i> ; New Caledonia; leaf	13,400 DW; Max. 47,000 DW	1, 6
<i>Sebertia acuminata</i> ; New Caledonia		
Latex	112,000 FW; 167–257,000 DW	1, 6
Leaves	10,200–11,700 DW	1, 6
Rice, <i>Oryza sativa</i> ; Japan; polished vs. unpolished grain	0.50–0.65 FW vs. 1.8 FW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Moss, <i>Pleurozium schreberi</i>		
Near nickel smelter	Max. 195 DW	4
Rural sites	1–34 DW	4
Urban sites	Max. 100 DW	4
Red oak, <i>Quercus rubra</i> ; leaf; 1.6 km vs. 10.6 km from nickel smelter	(79–108) DW vs. (12–57) DW	1
Spinach, <i>Spinacia oleracea</i> ; leaf		
Alabama	2.3 DW	1
New Jersey	2.2 DW	1
World, 44 varieties	4.2 DW	1
United States	0.35 FW	1
Lichen, <i>Umbilicaria</i> sp.; whole; 16 km vs. 90 km from nickel smelter	220 DW vs. 37 DW	1
Terrestrial vegetation		
Hyperaccumulator plants	>1000 DW	5
Most species	0.05–5.0 DW (>50 DW is toxic)	5
Vegetables		
Grown on soils containing 558 mg Ni/kg DW through sewage sludge application		
Beans and peas	42–65 DW	5
Green vegetables, cabbage, onions	11–65 DW	5
Root vegetables	8–27 DW	5
Grown on nickel-contaminated soils (>1500 mg Ni/kg DW surface soils) vs. reference site		
Heads and tops	15–400 DW vs. Max. 5.0 DW	8
Roots	24–280 DW vs. Max. 5.0 DW	8
Near nickel smelter vs. reference site; edible portions		
Cabbage, <i>Brassica oleracea capitata</i>	4.7 DW vs. 1.2 DW	7
Lettuce, <i>Lactuca sativa</i>	11.0 DW vs. 3.5 DW	7
Corn, <i>Zea mays</i>	2.8 DW vs. 1.1 DW	7
Wheat, <i>Triticum aestivum</i> ; from sludge-amended soil (19.4 mg Ni/kg DW soil) vs. nonsludge amended soil	0.98 DW vs. 0.40 DW	9
Lowbush blueberry, <i>Vaccinium angustifolium</i> ; leaf; various distances from nickel smelter		
1.7 km	92 DW	1
7.4 km	45 DW	1
52.7 km	14 DW	1
Corn, <i>Zea mays</i>		
Grain vs. root	(0.1–5.0) DW vs. 28.0 DW	1
Grown on soil containing 745 mg Ni/kg DW		
Kernels	2.3–4.3 DW	5
Leaves	6.7–10.7 DW	5
Stems	4.3–5.5 DW	5
AQUATIC PLANTS		
Algae and macrophytes: nickel-contaminated areas vs. reference sites	About 150 DW vs. usually <15 DW	5
Brown alga, <i>Ascophyllum nodosum</i>		
Norway	(1–22) DW	1
Nova Scotia	0.6 DW	1
Former Soviet Union	0.4 DW	1
Scotland	0.9 FW; (1.5–6.3) DW	1
Alga, <i>Cymodocea</i> sp.; Puerto Rico	2.1 (1.5–2.6) FW; 24 (19–29) DW	1
Bladder wrack, <i>Fucus vesiculosus</i>		
England	(1.2–29.6) DW	1
Greenland	(0.6–2.3) DW	1
Norway	(2–7) DW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Nova Scotia	2 DW	1
Scotland	1.4 FW; 4.9 DW	1
Duckweed, <i>Lemna minor</i> ; from ponds (27 µg Ni/L) in southern Ontario, Canada	5.4–35.1 DW	5
Marine algae and macrophytes		
England, 14 species	2.7–10.3 DW	10
India, 27 species	3.5–39.1 DW	10
Japan, 60 species	0.2–31.0 DW	10
Texas, Harbour Island, 14 species	0.2–2.6 DW	10
Pond lily, <i>Nuphar</i> sp.; Ontario, Canada; nickel-contaminated areas		
Leaf	8–62 FW	1
Peduncle	3–9 FW	1
Petiole	5–35 FW	1
Root	5–14 FW	1
Laver, <i>Porphyra umbilicalis</i> ; whole	0.2–9.7 DW	1
Sargassum, <i>Sargassum</i> spp.; Gulf of Mexico; whole	0.9–15.6 DW	10
Smooth cordgrass, <i>Spartina alterniflora</i> ; leaves	5.3 DW	1

TERRESTRIAL INVERTEBRATES

Earthworm, <i>Allolabophora</i> sp.; whole; Maryland	12.9–37.5 DW	1
Beach flies, 2 species; whole; California	Max. 7.0 DW	1
Gypsy moth, <i>Pophetria dispar</i> ; near ore smelter at Sudbury, Ontario, Canada vs. reference site		
Adult males; whole	8.8 DW vs. 2.9 DW	11
Larvae		
Feces	28 DW (reflects nickel content of leaf diet) vs. <2 DW	11
Whole	20.4 DW vs. 0.4–7.2 DW	11
Pupae	1.5 DW vs. 1.6 DW	11
Termites, <i>Odontotermes transvaalensis</i> , <i>Trinervitermes dispar</i> ; whole		
Queen	20 DW	1
Soldier	100 DW	1
Worker	5000 DW	1

AQUATIC INVERTEBRATES

Protozoans, marine		
Foraminiferan tests	15.4–23.0 DW	10
Radiolarians, whole	3.7 DW	10
Sponge, <i>Halichondria</i> sp.; whole; Sweden	22.0 DW	1
Corals; open ocean species vs. shallow coastal zone species	<2.0–23.0 DW vs. Max. 3.0 DW	10
Molluscs		
Duck mussel, <i>Anodonta anatina</i> ; Thames River, England; soft parts; near sewage outfall	Max. 46.0 DW	12
Ocean quahog, <i>Arctica islandica</i> ; soft parts		
Long Island, New York; 1974–75; offshore	1.1–7.0 FW	13
New England; offshore; February vs. March	5–29 DW vs. 4–18 DW	10
Waved whelk, <i>Buccinum undatum</i> ; soft parts; near sludge dump site vs. reference site	8.5 DW vs. 0.6 DW	1
Scallop, <i>Chlamys opercularis</i>		
Digestive gland	4.3 DW	10
Kidneys	78.2 DW	10
Shell	(0.2–7.6) DW	10
Other tissues	0.2–1.6 DW	10

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Pacific oyster, <i>Crassostrea gigas</i> ; soft parts		
South Africa	Max. 2.0 DW	1
United Kingdom	(1–10) DW	1
United States	Max. 0.2 FW	1
World	0.1–1.6 DW	10
Eastern oyster, <i>Crassostrea virginica</i> ; shell vs. soft parts	<1.0 DW vs. (0.9–5.4) DW; 0.19 (0.08–1.8) FW	1, 10
Common Atlantic slippersnail, <i>Crepidula fornicata</i> ; United Kingdom; shell vs. soft parts	1.6 DW vs. 127.0 FW; 850.0 DW	1, 10
Red abalone, <i>Haliotis rufescens</i> ; California		
Digestive gland	(3–11) DW	1, 10
Foot	(0.2–1.6) DW	1, 10
Gills	(69–112) DW	1, 10
Mantle	(19–57) DW	1, 10
Abalone, <i>Haliotis tuberculata</i> ; soft parts; England	13.6–15.9 DW	14
Marine molluscs; 21 species; soft parts	Max. 3.4 FW	10
Northern quahog, <i>Mercenaria mercenaria</i> ; soft parts		
United Kingdom	2.2 FW; (6.5–19.2) DW	1
United States	1.2 (0.1–2.4) FW	1
Common mussel, <i>Mytilus edulis</i> ; soft parts		
France	0.5 FW; 2.4 DW	1
The Netherlands, 1985–90	0.33–0.52 FW	15
Norway	(6–43) DW	1
United Kingdom	0.4 FW; Max. 53.0 FW; 3.7 (5–12) DW	1
United States	(11–14) DW	1
Mud snail, <i>Nassarius</i> sp.; soft parts; Los Angeles, California	36 DW	1
Common limpet, <i>Patella vulgata</i> ; soft parts		
Israel; near sewage discharge vs. control site	12 DW vs. 5–9 DW	1
Norway	(4–11) DW	1
United Kingdom	7.3 (2.5–24.0) DW	1
Pen shell, <i>Pinna nobilis</i> ; contaminated area		
Byssus gland	200 DW	10
Gonads	74 DW	10
Nervous system	18 DW	10
Soft parts	21 DW	10
Stomach plus intestines and hepatopancreas	170 DW	10
Sea scallop, <i>Placopecten magellanicus</i>		
Long Island, New York; 1974–75; soft parts	(<0.5–3.3) FW	13
North Atlantic coast, 42 stations		
Gonads	0.2–2.5 FW	16
Muscle	<0.3–0.7 FW	16
Viscera	0.3–1.6 FW	16
Vicinity ocean disposal sites; soft parts	4.4 DW	17
Clam, <i>Scrobicularia plana</i>		
Contaminated estuary, soft parts	Max. 11.9 DW	18
United Kingdom; digestive gland		
Camel estuary	10.6 DW	10
Gannel estuary	43.1 DW	10
Tamar estuary	(6.6–25.0) DW	10
Arthropods		
Amphipods; whole; Antarctica	2.2 DW	19
Green crab, <i>Carcinus maenas</i> ; all tissues	6.2–12.3 FW	1
Sand shrimp, <i>Crangon allmani</i> ; Scotland; soft parts; reference site vs. waste dump site	15 DW vs. 92 DW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Seaskaters (oceanic insects), <i>Halobates</i> spp., <i>Rheumobates</i> sp.; whole; from mangrove swamps	6–18 DW	20
American lobster, <i>Homarus americanus</i> ; serum	0.012 (0.008–0.020) FW	3, 21
Marine crustaceans		
Muscle, 10 species	0.2–0.9 FW	10
Whole, various species	6.5–9.8 FW	10
Aesop shrimp, <i>Pandalus montagui</i> ; soft parts; Scotland; reference site vs. waste dump site	25 DW vs. 70 DW	1
Caribbean spiny lobster, <i>Panulirus argus</i> ; soft parts; Puerto Rico		
Anasco Bay	1.3 (1–2) FW; 4.5 (8–9) DW	1
West coast	4.6 (1.4–5.0) FW; 36 (22–60) DW	1
Brown shrimp, <i>Penaeus aztecus</i> ; Texas		
Exoskeleton	6.2 DW; Max. 17.9 DW	1
Muscle	1.4 DW; Max. 1.9 DW	1
Viscera	5.7 DW; Max. 5.8 DW	1
Zooplankton; New York Bight vs. Long Island Sound	1.7–4.6 DW vs. 0.9–4.5 DW	22
Annelids, marine		
Sandworm, <i>Nereis diversicolor</i> ; whole; British Columbia; various locations	2.1–5.2 DW	10
Polychaete worms, 3 species; whole; California	(3.8–18.7) DW	1
Echinoderms		
Starfish, <i>Asterias rubens</i>		
Gonad	2.4 DW	10
Pyloric caeca	4.1 DW	10
Other tissues	0.7–1.5 DW	10
Rock boring sea urchin, <i>Echinometra lucunter</i> ; Puerto Rico; skeleton vs. whole	51 (42–78) DW vs. 37 DW	1
Sea urchin, <i>Tripneustes esculentus</i> ; Puerto Rico		
Ovary	1.4 FW	1
Skeleton	35 (18–54) DW	1
Testes	22 FW	1
Tunicate, <i>Halocynthia roretzi</i> ; whole	0.1 FW	10

FISHES AND ELASMOBRANCHS

Rock bass, <i>Ambloplites rupestris</i> ; near smelter; Sudbury, Ontario, Canada		
Gills	31.7 FW	1
Kidneys	17.3 FW	1
Livers	17.0 FW	1
Muscle	12.5 FW	1
Whitetip shark, <i>Carcharhinus longimanus</i>		
Liver	0.05 FW; 0.1 DW	1
Skin	1.9 FW; 7.3 DW	1
Vertebrae	1.6 FW; 4.9 DW	1
White sucker, <i>Catostomus commersoni</i> ; muscle; near smelter vs. reference site	13.2 FW vs. 0.1 FW	1
Blackfin icefish, <i>Chaenocephalus aceratus</i> ; Antarctica; muscle vs. liver	0.2 DW vs. 0.3 (0.2–0.5) DW	19
Lake whitefish, <i>Coregonus clupeaformis</i> ; muscle; northern Quebec; 1989–90	<0.01 FW	23
Lumpfish, <i>Cyclopterus lumpus</i> ; United Kingdom; all tissues	3.2–5.2 FW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Northern pike, <i>Esox lucius</i> ; muscle Canada		
Ontario; near smelter	13.3 FW	1
Northern Quebec, 1989–91	<0.05–0.05 FW	23
Illinois vs. New York	0.15 (0.08–0.19) FW vs. (0.2–3.8) FW	1
Muskellunge, <i>Esox masquinongy</i> ; muscle; New York	0.2–1.3 FW	1
Chain pickerel, <i>Esox niger</i> ; muscle; New York	0.1–0.25 FW	1
Pickerel, <i>Esox</i> sp.; near smelter; Sudbury, Ontario		
Gills	16.0 FW	1
Kidneys	51.6 FW	1
Livers	14.4 FW	1
Muscle	13.8 FW	1
Skipjack tuna, <i>Euthynnus pelamis</i> ; muscle Peru	2.0 FW; 5.0 DW	1
Puerto Rico	0.5 FW; 2.2 DW	1
Fishes, 10 species; muscle; Bay of Bengal, India	0.7–6.1 DW	24
Atlantic cod, <i>Gadus morhua</i> ; all tissues	1.6–4.6 FW	1
Brown bullhead, <i>Ameiurus nebulosus</i> ; near smelter; Canada		
Gills	11.1 FW	1
Kidneys	11.8 FW	1
Livers	10.7 FW	1
Muscle	9.5 FW	1
Yellowtail flounder, <i>Pleuronectes ferruginea</i> ; New York Bight; liver vs. muscle	0.2–1.1 FW vs. <0.2–0.4 FW	1
Marine fishes		
Liver; 5 species; New York Bight; 1971–73	<0.2–1.7 FW	25
Most species; all tissues	Usually <0.3 FW; rarely >3.0 FW in uncontaminated areas; Max. 16.0 DW	10
Muscle		
New Zealand, 9 species	0.02–0.07 FW	1
United Kingdom, 8 species	2.1–3.5 DW	1
Atlantic croaker, <i>Micropogonias undulatus</i> ; Texas; muscle vs. skin	2.7 DW vs. 3.8 DW	1
Smallmouth bass, <i>Micropterus dolomieu</i> ; muscle; New York vs. Illinois	(0.16–1.2) FW vs. 0.13 (0.08–0.19) FW	1
Largemouth bass, <i>Micropterus salmoides</i> ; muscle; New York vs. Illinois	(0.18–1.9) FW vs. 0.11 (0.05–0.23) FW	1
Dover sole, <i>Microstomus pacificus</i> ; California; muscle vs. liver	0.2 (0.1–0.3) FW vs. 1.4–2.6 FW	1
Hump rock cod, <i>Notothenia gibberifrons</i> ; muscle; Antarctica	0.22 DW	19
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Kidney, liver	Usually <1.5 FW	5
Muscle	Usually <0.5 FW	5
Kelp bass, <i>Paralabrax clathratus</i> ; California		
Gonad	1.5–2.2 DW	1
Liver	3.9–7.6 DW	1
Muscle	5.0–6.4 DW	1
Skin	9.0–10.2 DW	1
Winter flounder, <i>Pleuronectes americanus</i>		
New York Bight; muscle vs. skin	<0.3–0.5 FW vs. <0.3–1.0 FW	1
Texas; muscle vs. skin	3.3 (0.6–7.4) DW vs. 4.4 (2.9–7.4) DW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Lake trout, <i>Salvelinus namaycush</i> ; whole less head and viscera; New York		
Ages 1–4 years	Max. 0.009 FW	1
Ages 5–8 years	Max. 0.022 FW	1
Ages 9–12 years	Max. 0.022 FW	1
Sharks, 10 species; British and Atlantic waters; 1984–88; inshore species vs. offshore species		
Gills	0.3–1.8 FW vs. 1.7–1.9 FW	26
Gonads	<0.02–8.3 FW vs. 1.7 FW	26
Heart	No data vs. 2.8 FW	26
Jaws	5.7 FW vs. 0.3 FW	26
Kidneys	0.07–1.2 FW vs. 1.6 FW	26
Liver	<0.02–0.8 FW vs. 1.9–3.2 FW	26
Muscle	<0.02–1.8 FW vs. 1.4–2.6 FW	26
Pancreas	0.9 FW vs. No data	26
Skin	<0.02–3.4 FW vs. 1.0–2.0 FW	26
Spleen	<0.02–0.8 FW vs. 1.3 FW	26
Vertebrae	0.5–2.4 FW vs. 0.2–10.8 FW	26
South Carolina; gamefish; 1990–93; whole		
Spotted seatrout, <i>Cynoscion nebulosus</i>	Max. 12.6 FW	27
Southern flounder, <i>Paralichthys lethostigma</i>	Max. 8.2 FW	27
Red drum, <i>Sciaenops ocellatus</i>	Max. 2.9 FW	27
Scup, <i>Stenotomus chrysops</i> ; Texas		
Muscle	1.0 (0.5–2.0) DW	1
Skin	4.9 (2.8–7.4) DW	1
Viscera	3.5 DW	1
AMPHIBIANS		
Maryland; 1991; tadpoles		
Northern cricket frog, <i>Acris crepitans</i> ; whole	2.4–10.0 DW	28
Gray treefrog, <i>Hyla versicolor</i> ; whole	2.0–7.1 DW	28
Green frog, <i>Rana clamitans</i> ; body vs. gut coil	4.7 DW vs. 16.4 DW	28
BIRDS		
Wood duck, <i>Aix sponsa</i> ; ducklings; liver; Ontario, Canada; polluted area	0.2 FW	29
Mallard, <i>Anas platyrhynchos</i>		
Canada; nickel-contaminated areas vs. reference site		
Liver	0.1–1.4 FW vs. 0.2 FW	29
Muscle (breast)	0.1–0.8 FW vs. 0.6 FW	29
New Jersey; Raritan Bay; contaminated environment; liver vs. salt gland	0.1–2.5 FW vs. 9.7 FW	30, 31
Primary flight feathers; 1975; various distances from nickel smelter		
20–30 km	2.0–12.5 DW; Max. 36.7 DW	32
50–60 km	0.2–3.8 DW	32
85 km	0.2–1.5 DW	32
95–140 km	0.0–4.3 DW	32
Reference site	0.0–0.4 DW	32
Black duck, <i>Anas rubripes</i>		
Canada; ducklings; nickel-contaminated vs. reference site		
Kidney	0.3 FW vs. 0.3 FW	29
Liver	0.6 FW vs. 0.4 FW	29
Canada; primary feathers; contaminated vs. noncontaminated areas	2.5–3.7 DW vs. 0.2–1.5 DW	32
Raritan Bay, New Jersey; liver vs. salt gland	0.2–2.7 FW vs. 15.2 FW	30, 31

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Gadwall, <i>Anas strepera</i> ; Canada; muscle; contaminated area	0.3 FW	29
Antarctica; February-March 1989		
Gentoo penguin, <i>Pygoscelis papua</i> ; muscle vs. liver	<0.03 DW vs. 0.09 DW	19
Adelie penguin, <i>Pygoscelis adeliae</i> ; muscle vs. liver	<0.03 DW vs. 0.06 DW	19
Chinstrap penguin, <i>Pygoscelis antarctica</i>		
Feces	3.5 (3.2–3.7) DW	19
Liver	0.07 DW	19
Muscle	<0.03 DW	19
Blue eyed cormorant, <i>Phalacrocorax atriceps</i> ; muscle	0.29 DW	19
South giant petrel, <i>Macronectes giganteus</i> ; muscle	0.06 DW	19
Redhead, <i>Aythya americana</i> ; Texas and Louisiana; liver; winter 1987–88	<4.0 DW	33
Ring-necked duck, <i>Aythya collaris</i> ; ducklings; contaminated vs. reference location		
Kidney	0.3 FW vs. 0.1 FW	29
Liver	0.5 FW vs. 0.2 FW	29
Greater scaup, <i>Aythya marila</i> ; contaminated areas		
Ontario; muscle	0.2 FW	29
New Jersey; liver vs. salt gland	0.3–3.6 FW vs. 2.7 FW	30, 31
Canvasback, <i>Aythya valisineria</i> ; Louisiana; winter 1987–88; liver	Usually <1.0 DW; Max. 2.0 DW	34
Ruffed grouse, <i>Bonasa umbellus</i>		
Canada; nickel-contaminated vs. reference areas		
May		
Feathers, primaries	7.3 DW vs. 2.9 DW	35
Dung	19.4 DW vs. <0.5 DW	35
Kidney	2.8 DW vs. 1.7 DW	35
Liver	1.0 DW vs. 0.9 DW	35
Muscle	1.4 DW vs. <0.5 DW	35
September		
Feathers, primaries	4.8 DW vs. 0.8 DW	35
Dung	47.7 DW vs. <0.5 DW	35
Kidney	2.1 DW vs. <0.5 DW	35
Liver	3.5 DW vs. 0.7 DW	35
Muscle	0.2 DW vs. 0.2 DW	35
New England		
Kidney	5.0 DW	1
Liver	1.1–2.4 DW	1
Common goldeneye, <i>Bucephala clangula</i> ; ducklings; Canada; contaminated vs. reference areas		
Kidney	0.3 FW vs. 0.1 FW	29
Liver	0.5 FW vs. 0.8 FW	29
Turkey vulture, <i>Cathartes aura</i> ; California; kidney vs. liver	<0.1–0.4 FW vs. <0.1 FW	36
Common raven, <i>Corvus corax</i> ; California; kidney vs. liver	<0.1–0.12 FW vs. <0.1 FW	36
American coot, <i>Fulica americana</i> ; Ontario; muscle	1.5 FW	37
Domestic chicken, <i>Gallus</i> sp.; serum; United States	0.0036 (0.0033–0.0053) FW	3, 21
Common loon, <i>Gavia immer</i> ; Ontario; muscle	1.1 FW	37
California condor, <i>Gymnogyps californianus</i> ; feathers	0.5–2.0 DW	36
Willow ptarmigan, <i>Lagopus lagopus</i> ; near nickel smelter; 1990–93; Norway; kidney	Max. 2.3 DW	38
Herring gull, <i>Larus argentatus</i> ; Ontario; muscle	1.0 (0.6–1.3) FW	37
Lesser black-backed gull, <i>Larus fuscus</i> ; Norway		
Kidney	5.0 DW	1
Liver	2.0 DW	1
Muscle	5.0 DW	1

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Hooded merganser, <i>Lophodytes cucullatus</i> ; ducklings; nickel-contaminated vs. reference areas		
Kidney	1.2 FW vs. 1.0 FW	29
Liver	0.07 FW vs. 0.14 FW	29
Turkey, <i>Meleagris gallopavo</i> ; liver vs. muscle	0.002 FW vs. 0.015 FW	39
Black-crowned night-heron, <i>Nycticorax nycticorax</i> ; liver; northeastern United States; nickel-contaminated vs. reference areas	<0.1–9.2 DW vs. <0.1 DW	40
Owl (species unidentified); Germany; polluted area vs. reference site; tail feathers		
Lower feather	2.0 FW vs. 1.6 FW	41
Upper feather	14.3 FW vs. 2.0 FW	41
Osprey, <i>Pandion haliaetus</i> ; liver	<0.2–0.3 FW	42
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg	Max. 0.072 FW	1
Liver	Max. 0.078 FW	1
Common eider, <i>Somateria mollissima</i> ; Norway		
Egg, liver	1.0 DW	1
Muscle, kidney	2.0 DW	1
Common tern, <i>Sterna hirundo</i>		
Rhode Island; 1981; immatures; liver vs. diet	Max. 1.0 DW vs. 0.8–2.1 DW	43
Hamilton Harbor, Ontario vs. Long Island Sound, New York		
Bone	Max. 19 DW vs. Max. 36 DW	44
Kidney	Max. 9 DW vs. Max. 26 DW	44
Liver	<5 DW vs. < 5 DW	44
Muscle	<2 DW vs. <2 DW	44
Tree swallow, <i>Tachycineta bicolor</i> ; Hackensack River, New Jersey (contaminated area)		
Brain, prefledgling	27.6 FW	45
Eggshell	31.4 FW	45
Embryo, whole	1.6 FW	45
Feather	4.3 FW	45
Gizzard	9.4 FW	45
Liver	23.8 FW	45
Muscle	7.6 FW	45
American robin, <i>Turdus migratorius</i> ; New England; kidney vs. liver	1.7 FW vs. 0.9 FW	1

TERRESTRIAL MAMMALS

Cow, <i>Bos</i> sp.		
Blood, whole	0.011 FW	39
Blood, plasma	0.0017–0.0044 FW	39
Bone	0.58 FW	1
Feces	0.75 FW	1
Kidney	0.01–0.66 FW	1
Liver	0.13 FW	39
Muscle	Not detectable	1
Pancreas	0.14 FW	39
Goat, <i>Capra hircus</i> ; serum; England	0.0035 (0.0027–0.0044) FW	21
Common beaver, <i>Castor canadensis</i>		
Ontario, Canada; 1986–87; adults; near nickel smelter vs. reference site		
Kidney	2.6 DW vs. 1.5 DW	46
Liver	1.5 DW vs. 1.1 DW	46
Ontario; uncontaminated site		
Intestine	0.4 FW	47
Kidney	0.4 FW	47

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Liver	0.5 FW	47
Muscle	0.9 (0.6–1.3) FW	48
Least shrew, <i>Cryptotis parva</i> ; Virginia; whole body; polluted areas vs. reference sites	1.3–1.6 DW vs. 0.8 DW	49
Horse, <i>Equus caballus</i> ; serum; United States	0.002 (0.0013–0.0025) FW	21
Human, <i>Homo sapiens</i>		
Adrenal gland	0.13 (0.05–0.34) DW	50
Average daily intake, in mg Ni/kg body weight (BW) daily; Canada		
General population; age >12 years vs. age <12 years		
Air	Max. 0.000007 vs. Max. 0.000009	51
Water	Max. 0.00016 vs. Max. 0.00077	51
Food	0.0044–0.0057 vs. Max. 0.022	51
Soil	Max. 0.000018 vs. Max. 0.00025	51
Tobacco smoking	Max. 0.00015 vs. no data	51
Canadians living near nickel point sources; age >12 years vs. age <12 years		
Air	Max. 0.000008 vs. Max. 0.000009	51
Water	Max. 0.0025 vs. Max. 0.012	51
Food	Max. 0.0057 vs. Max. 0.022	51
Soil	Max. 0.00013 vs. Max. 0.0019	51
Blood, plasma		
Workers from nickel refinery	0.0064–0.0119 FW	52
Occupationally exposed workers vs. same workers after 2-week vacation	0.0102–0.0111 FW vs. 0.0053 FW	3
Normal	0.0016–0.0020 FW	3
Blood, whole; normal	0.003–0.007 FW	52, 53
Blood, serum		
Near nickel mine	0.0046 FW	52
Normal	0.0026 (0.0011–0.0046) FW	3, 21, 52, 53, 54
Diet		
Condiments		
Most	<1.0 FW	3
Baking powder	13.4 FW	54
Nutmeg	1.2 FW	54
Pepper, black	3.9 FW	54
Fish and seafoods		
Most	<0.3 FW	3, 55
Salmon, muscle	1.7 FW	3, 39
Oysters, soft parts	1.5 FW	3, 39
Shrimp, muscle	0.03 FW	39
Swordfish	0.02 FW	39
Fruits and vegetables	Usually 0.02–0.65 FW; Max. 2.6 FW	3, 55
Grains and grain products	Usually 0.2–1.3 FW; Max. 2.7–6.4 FW	3, 39, 55
Liquids		
Beer, wine, soft drinks	0.01–0.2 FW	3, 39
Cocoa	5.0 FW	54
Coffee	1.0 FW	39
Drinking water	0.0048 (0.001–0.2) FW	39
Tea, orange pekoe	7.6 FW	54
Meats		
Beef, pork	0.06–0.4 FW	39
Chicken	0.14–0.24 FW	39
Feces, normal	3.3 (2.1–4.4) FW; 14.2 (10.8–18.7) DW	54

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Hair		
Near refineries	3.6 (1.1–32.0) DW	3
Rural areas	2.1 (1.6–17.0) DW	3
Urban areas	2.4 (1.2–20.0) DW	3
Heart, normal	0.0061 FW; 0.023 DW	54
Kidney, normal	1.82 DW	3
Liver, normal	1.85 DW	3
Lung		
Bituminous coal miners vs. controls	2.5 DW vs. 0.6 DW	56
Normal	0.17 (0.07–0.37) DW	50
Perspiration; males vs. females	0.052 (0.007–0.182) FW vs. 0.131 (0.039–0.270) FW	53, 54
Spleen, normal	1.72 DW	3
Thyroid, normal	0.14 (0.04–0.24) DW	50
Urine		
Normal	0.001–0.005 FW	3, 52, 53
Nickel battery workers	0.0117 FW	3
Nickel plate workers	0.0275 FW	3
Nickel refinery workers (atmospheric nickel = 489 µg/m ³)	0.222 FW	3
Near nickel refinery vs. reference location; Russia; 1994–95	0.0034 FW vs. 0.0027 FW	83
Near nickel refinery	0.045–0.129 FW	52
Snowshoe hare, <i>Lepus americanus</i> ; whole; Wisconsin	0.2 FW	57
River otter, <i>Lutra canadensis</i> ; Ontario, Canada; reference areas vs. nickel-contaminated areas		
Kidney	0.7 FW vs. 0.44 FW	47, 58
Liver	0.4–0.5 FW vs. 0.5 FW	47, 58
Muscle	0.9 (0.6–1.0) FW vs. no data	47, 48
Mammals; serum; healthy adults		
Normal levels for horses, humans, cattle, dogs, and rats	0.0020–0.0027 (0.0009–0.0046) FW	3
Normal levels for goats, cats, guinea pigs, hamsters, and swine	0.0035–0.0053 (0.0015–0.0083) FW	3
Normal for rabbits	0.0093 (0.0065–0.0140) FW	3
Meadow vole, <i>Microtus pennsylvanicus</i> ; whole		
Virginia; contaminated area vs. reference site	Max. 2.5 DW vs. Max. 1.8 DW	49
Wisconsin; near undeveloped ore deposits	Max. 2.6 FW	57
House mouse, <i>Mus musculus</i>		
Kidney	0.46–0.52 FW	1, 39
Liver	(0.02–0.62) FW	1, 39
Lung	(0.32–0.61) FW	1, 39
Mink, <i>Mustela vison</i>		
Illinois; 1984–89; trapped		
Kidney	1.1 (0.4–0.6.6) FW	59
Liver	0.9 (0.3–2.6) FW	59
Muscle	0.7 (0.3–1.5) FW	59
Ontario, Canada; nickel-contaminated area vs. reference area		
Kidney	0.6 FW vs. 0.6 FW (same)	58
Liver	0.7 FW vs. 0.7 FW (same)	58
Norway; 1990–91; near nickel processing plants vs. reference site		
Moose, <i>Alces alces</i>		
Kidney	0.19 FW vs. 0.12 FW	60
Liver	0.02 FW vs. <0.01 FW	60
Domestic sheep, <i>Ovis aries</i>		
Kidney	0.03 FW vs. 0.03 FW (same)	60
Liver	0.01 FW vs. 0.01 FW (same)	60

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Caribou, <i>Rangifer tarandus</i>		
Kidney	0.28 FW vs. 0.13 FW	60
Liver	0.09 FW vs. 0.02 FW	60
Mule deer, <i>Odocoileus hemionus</i> ; Montana; kidney and liver	Max. 3 DW	61
White-tailed deer, <i>Odocoileus virginianus</i> ; kidney vs. liver	0.0–2.9 FW vs. 0.0–2.5 FW	1
Rabbit, <i>Oryctolagus</i> sp.; serum; New Zealand	0.0093 (0.0065–0.0140) FW	21
White-footed mouse, <i>Peromyscus leucopus</i> ; Virginia; whole; contaminated area vs. reference site	Max. 1.5 DW vs. Max. 3.1 DW	49
Raccoon, <i>Procyon lotor</i> , Ontario, Canada		
Kidney	0.7 FW	47
Muscle	1.0 (0.9–1.3) FW	48
Laboratory white rat, <i>Rattus</i> sp.		
Fur	0.16 FW	62
Kidney	0.32 FW	62
Muscle	0.17 FW	62
Shrews; southern Finland		
Common shrew, <i>Sorex araneus</i> ; nickel-contaminated vs. reference site		
Liver	Max. 7.2 DW vs. <0.1 DW	63
Kidney	Max. 23.0 DW vs. Max. 37.5 DW	63
Long-tailed shrew, <i>Sorex minutus</i> ; kidney vs. liver	Max. 0.7 DW vs. 3.4 DW; Max. 68.1 DW	63
Gray squirrel, <i>Sciurus carolinensis</i> ; New England		
Heart	3.7 FW	1
Kidney	3.2 FW	1
Liver	1.5 FW	1
Masked shrew, <i>Sorex cinereus</i> ; whole; nickel-contaminated area vs. reference site	Max. 0.9 FW vs. Max. 4.2 DW	63
Swine, <i>Sus</i> sp.		
Heart	Max. 0.43 FW	39
Kidney	Max. 3.4 FW	1
Muscle	Max. 0.02 FW	1
Serum	(0.0035–0.0083) FW	21, 39
Mole, <i>Talpa europaea</i> ; rural areas; Finland; liver	0.13 DW; Max. 0.25 DW	63
Red squirrel, <i>Tamiasciurus hudsonicus</i>		
New England; liver and kidney	<0.2 FW	1
Canada; fur; polluted area vs. reference site		
Spring (premoult)	3–9 DW vs. 2.2 DW	64
Fall (postmoult)	1–3 DW vs. 0.6 DW	64
MARINE MAMMALS		
British Isles; 8 species; 1988–89; livers	All values below detection limit of 0.5 FW	65
Welsh coast and Irish Sea; 8 species; 1989–91; livers	Usually <0.5 FW; Max. 2.1 FW	66
Vaquita (porpoise), <i>Phocoena sinus</i> ; Baja California, Mexico		
Heart	0.7 FW	67
Kidney	0.5 FW	67
Liver	<0.4 FW	67
Sperm whale, <i>Physeter macrocephalus</i> ; North Sea; 1994–95; found stranded; livers	0.39 FW; Max. 2.1 FW	68
Sweden, 3 species (harbor seal, <i>Phoca vitulina</i> ; gray seal, <i>Halichoerus grypus</i> ; ringed seal, <i>Phoca hispida</i>); livers and kidneys	Usually <0.0006 FW; maximum concentrations were 0.17 FW in livers and 0.08 FW in kidneys	69

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
INTEGRATED STUDIES		
Arctic; Spitsbergen, Svalbard; July-August 1988		
Surface water	0.0015 FW	70
Glacier ice	0.00725 FW	70
Algae, <i>Zygnema</i> sp.	3.25 DW	70
Lichen, <i>Cetraria nivalis</i>	1.6 DW	70
Mosses, <i>Tomentypnum</i> sp., <i>Rhacomitrium</i> sp.	2.4–6.4 DW	70
Vascular plant, <i>Cassiope</i> sp.	4.1 DW	70
Herring gull, <i>Larus argentatus</i> ; feathers	1.9–9.9 DW	70
Caribou, <i>Rangifer tarandus</i> ; fur	4.8 DW	70
Canada; Wanapitei River (near nickel smelter) vs. Pickerel River (reference site); Ontario; 1974		
Water	0.042 FW vs. 0.002 FW	71
Sediments	224 FW vs. 13 FW	71
Pondweed, <i>Potamogeton</i> sp.		
Leaves	480 FW vs. 39 FW	71
Stems	255 FW vs. 7 FW	71
Periphyton, whole	826 FW vs. 43 FW	71
Zooplankton, whole	27 FW vs. 7 FW	71
Crayfish, whole	39 FW vs. 9 FW	71
Clams, soft parts	11 FW vs. 4 FW	71
Fishes, 6 species		
Gill	11.1–31.7 FW vs. no data	71
Kidney	11.8–51.6 FW vs. no data	71
Liver	10.7–17.0 FW vs. no data	71
Muscle	9.5–13.8 FW vs. no data	71
Florida; near sewage outfall; exposure for 120 days		
Turtle grass, <i>Thalassia testudinum</i> ; leaves	45 DW	72
Mangrove, <i>Rhizophora mangle</i> ; roots	10 DW	72
Sea urchin, <i>Lytechinus variegatus</i> (consumes <i>Thalassia</i>); whole	30 DW	72
Sea cucumber, <i>Holothuria mexicana</i> ; whole	40 DW	72
Florida; stormwater ponds in Orlando vs. reference sites; 1991–92		
Sediments	2.4 FW vs. 0.07 FW	73
Fishes, whole		
Redear sunfish, <i>Lepomis microlophus</i>	5.3 FW vs. 0.6 FW	73
Bluegill, <i>Lepomis macrochirus</i>	0.2 FW vs. 0.08 FW	73
Largemouth bass, <i>Micropterus salmoides</i>	2.5 FW vs. 1.2 FW	73
French-Spanish border; Bidason estuary; 4 sites; April 1993		
Sediments	35 (22–44) DW	74
Clam, <i>Scrobicularia plana</i> ; soft parts	4.1 (2.9–5.7) DW	74
Sandworm, <i>Nereis diversicolor</i> ; whole	5.4 (3.2–8.5) DW	74
Israel, Mediterranean coast; 1974		
Water	0.0028–0.0036 FW	75
Sediments	4.8 DW	75
Algae	5.2–5.8 DW	75
Fishes, 10 species; whole	0.1–10.8 DW	75
Lake Erie; near coal ash disposal basin; 1983–84		
Sediment	Max. 26.4 DW (vs. 19.8 DW in reference site)	76
Coal ash	65.0 DW	76
Oligochaetes	Max. 32.5 DW	76
Chironomids	<9.1 DW	76

Table 6.6 (continued) Nickel Concentrations (milligrams of nickel per kilogram fresh weight [FW] or dry weight [DW]) in Field Collections of Representative Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration (mg/kg) ^a	Reference ^b
Fishes, whole		
Brown bullhead, <i>Ameiurus nebulosus</i> ; adults vs. yearlings	<9.1 DW vs. Max. 26.6 DW	76
Yellow perch, <i>Perca flavescens</i> ; white bass, <i>Morone chrysops</i>	<9.1 DW	76
Lebanon; near Ras Beirut		
Seawater	Max. 0.027 FW	77
Molluscs, 3 species; soft parts	27.4–40.1 DW	77
Mississippi River delta and northwest Gulf of Mexico		
Sargassum weed, <i>Sargassum</i> spp. plus mixed phytoplankton; whole	0.9–15.6 DW	78
Zooplankton	<0.5–8.2 DW	78
New York; Hudson River; near nickel-cadmium battery plant; 1972		
Water; insoluble vs. soluble	0.043 FW vs. 0.068 FW	79
Sediments	Max. 7000 DW	79
Cordgrass, <i>Spartina</i> sp.; roots	Max. 500 DW	79
New Guinea; Upper Fly River; September 1974		
Water	<0.001–0.005 FW	80
Sediments	24–38 DW	80
Gastropod, <i>Melanoides</i> sp.; soft parts	8–18 DW	80
Prawn, <i>Macrobrachium</i> sp.; whole	5–17 DW	80
Fishes, various species; liver and muscle	3–93 DW	80
Texas; outer continental shelf		
Sargassum weed, <i>Sargassum</i> spp.	5.2 DW	81
Squid, muscle	2.5 DW	81
Zooplankton, whole	4.6 DW	81
Shrimp, 2 species; whole	1.4–1.6 DW	81
Fish, various species; muscle	0.6–4.9 DW	81
Turkey; Tigris River (contaminated by wastes from smelter)		
Water	0.5–0.8 FW	82
Sediments with living organisms	41–305 DW	82
Sediments with no living organisms	403 DW	82
Fish, <i>Cyprinodon macrostomus</i>		
Liver	105–502 FW	82
Muscle	8–95 FW	82
Fish, <i>Garra rufa</i>		
Liver	Max. 380 FW	82
Muscle	Max. 43 FW	82

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).

^b 1, Jenkins 1980b; 2, Memon et al. 1980; 3, USEPA 1980; 4, Richardson et al. 1980; 5, WHO 1991; 6, Lee et al. 1978; 7, Anke et al. 1980a; 8, Frank et al. 1982; 9, Stoewsend et al. 1984; 10, Eisler 1981; 11, Bagatto and Shorthouse 1996; 12, Manly and George 1977; 13, Palmer and Rand 1977; 14, Bryan et al. 1977; 15, Stronkhorst 1992; 16, Greig et al. 1978; 17, Pesch et al. 1977; 18, Bryan and Hummerstone 1978; 19, Szefer et al. 1993; 20, Cheng et al. 1976; 21, Mushak 1980; 22, Greig et al. 1977; 23, Langlois and Langis 1995; 24, Sharif et al. 1993; 25, Greig and Wenzloff 1977; 26, Vas 1991; 27, Mathews 1994; 28, Sparling and Lowe 1996; 29, Outridge and Scheuhammer 1993; 30, Burger and Gochfeld 1985; 31, Gochfeld and Burger 1987; 32, Ranta et al. 1978; 33, Michot et al. 1994; 34, Custer and Hohman 1994; 35, Rose and Parker 1983; 36, Wiemeyer et al. 1986; 37, Wren et al. 1988; 38, Kalas et al. 1995; 39, Kasprzak 1987; 40, Custer and Mulhern 1983; 41, Ahmed and Stoeppeler 1994; 42, Wiemeyer et al. 1987; 43, Custer et al. 1986; 44, Connors et al. 1975; 45, Kraus 1989; 46, Hillis and Parker 1993; 47, Wren 1984; 48, Wren et al. 1983; 49, Scanlon 1987; 50, Hausinger 1993; 51, Hughes et al. 1994; 52, Norseth 1986; 53, NRCC 1981; 54, NAS 1975; 55, Norseth and Piscator 1979; 56, Sevin 1980; 57, Smith and Rongstad 1981; 58, Wren et al. 1988; 59, Halbrook et al. 1996; 60, Sivertsen et al. 1995; 61, Munshower and Neuman 1979; 62, Kirchgessner and Schnegg 1980; 63, Pankakoski et al. 1994; 64, Lepage and Parker 1988; 65, Law et al. 1991; 66, Law et al. 1992; 67, Villa et al. 1993; 68, Law et al. 1996; 69, Frank et al. 1992; 70, Drbal et al. 1992; 71, Hutchinson et al. 1975; 72, Montgomery et al. 1978; 73, Campbell 1994; 74, Saiz-Salinas et al. 1996; 75, Roth and Hornung 1977; 76, Hatcher et al. 1992; 77, Shiber and Shatila 1978; 78, Trefry and Presley 1976; 79, Kniep et al. 1974; 80, Boyden et al. 1978; 81, Horowitz and Presley 1977; 82, Gumgum et al. 1994; 83, Smith-Sivertsen et al. 1998.

6.6 NICKEL DEFICIENCY EFFECTS

6.6.1 General

Nickel is reportedly an essential micronutrient for maintaining health in certain species of plants, invertebrates, birds, and mammals, including humans (NAS 1975; Spears et al. 1979; Sunderman et al. 1984; Norseth 1986; USEPA 1986; Sigel and Sigel 1988; Hausinger 1993; USPHS 1993; Stangl and Kirchgessner 1996, 1997). However, it has not yet been proven that nickel is essential for humans (Norseth and Piscator 1979; USPHS 1993), and the evidence for marine tunicates and land snails is inconclusive (Hausinger 1993). To prevent nickel deficiency in rats and chickens, diets should contain at least 50 µg Ni/kg ration; cows and goats require more than 100 µg Ni/kg ration, perhaps reflecting the increased use of nickel by rumen bacteria (USPHS 1993). In humans, nickel deficiency is not a public health concern because daily oral intake normally exceeds 170 µg of nickel (USPHS 1993).

Nickel is considered essential to animals because it is present in the fetus or newborn, is homeostatically regulated, the metabolic pool of nickel is specifically influenced by hormonal substances or pathologic processes, certain metalloproteins contain nickel, and because nickel deficiency has been induced experimentally in certain species of birds and animals (NAS 1975; USPHS 1977; Kirchgessner and Schnegg 1980). In general, the nickel deficiency syndrome can be cured or prevented by trace amounts of nickel (NAS 1975). However, nickel administration may not be successful in reversing all abnormalities produced by nickel deprivation (USPHS 1977).

Nickel deficiency effects from dietary deprivation of nickel is now documented in at least 17 animal species, including chickens, cows, goats, pigs, rats, and sheep (USPHS 1977, 1993; Norseth and Piscator 1979; USEPA 1985; Norseth 1986; WHO 1991). According to Kirchgessner and Schnegg (1980), nickel deficiency can be induced only by very low nickel concentrations in the diet — not by its bioavailability. Signs of nickel deficiency include delayed gestation periods and fewer offspring; decreased growth and sometimes dwarfism; anemia; skin eruptions; brittle hair; reduced oxygen consumption; decreased levels of serum proteins; enhanced urinary nitrogen excretion; reduced tissue iron and zinc concentrations; reduced hemoglobin and hematocrit values; abnormal liver morphology and lipid metabolism; reduced liver glucose, lipids, glycogen, and triglycerides; and reduced activity of several enzymes, including dehydrogenases, transaminases, and alpha-amylases (USEPA 1980, 1985, 1986; WHO 1991; USPHS 1993; Stangl and Kirchgessner 1996).

6.6.2 Bacteria and Plants

Nickel is essential for the active synthesis of urease in plant cells and of various hydrogenases in bacteria (Thauer et al. 1980; USEPA 1986; WHO 1991; Hausinger 1993). In several species of higher plants, including jack beans (*Canavalia* sp.), soybeans (*Glycine max*), rice (*Oryza sativa*), and tobacco (*Nicotiana tabacum*), nickel is required for effective urea metabolism and urease synthesis (Kasprzak 1987; Sigel and Sigel 1988). Root growth of onions (*Allium* sp.) is stimulated at 60 to 600 µg/Ni²⁺/L culture solution (Donghua and Wushing 1997). Some terrestrial plants, such as *Alyssum* spp., accumulate nickel and require it for growth (Thauer et al. 1980). In bacteria, nickel is required for the growth of *Oscillatoria* sp. and *Alcaligenes* sp., for the synthesis of carbon monoxide dehydrogenase in *Clostridium posterianum*, and as a component of coenzyme F₄₃₀ in *Methanobacterium* spp. (Babich and Stotzky 1982a; Kasprzak 1987). Nickel deficiency in bacteria may adversely affect reproductive processes, such as endospore formation, and cause a decrease in nickel-containing intracellular pigments in strains of *Bacillus cereus* (Thauer et al. 1980); however, both of these observations require verification.

6.6.3 Birds

All studies demonstrating nickel deficiency in birds were conducted on a single species; specifically, chicks of the domestic chicken, *Gallus* sp. The relevance of these results to avian wildlife species is unknown. Chicks grew normally when fed nickel-deficient diets (2 to 15 µg Ni/kg ration) for 3 to 4 weeks, but these chicks had liver histopathology, decreased concentrations of yellow lipochrome pigments in liver, low hematocrit, skin dermatitis, leg thickening, altered lengths of leg bones, and decreased plasma cholesterol (Nielsen et al. 1975a; Hausinger 1993). Adverse effects of nickel-deficient diets (<20 µg Ni/kg ration) were reversed by the addition of nickel to the diet (Ling and Leach 1979). Chicks fed diets containing 25 to 2500 µg Ni/kg ration for 3 to 4 weeks grew normally and all organs appeared normal (Nielsen et al. 1975a). Nickel-deficient chicks (40 to 80 µg Ni/kg ration), when compared to controls (3 to 5 mg Ni/kg ration), had swollen hock joints, reduced length-to-width ratios of tibias, scaly dermatitis of the legs, orange-yellow discoloration of the legs, fat-depleted livers, altered liver metabolism, and elevated concentrations of nickel in liver, spleen, and aorta (Sunderman et al. 1972; NAS 1975; USEPA 1980; USEPA 1985). Chicks fed nickel-deficient diets of 44 µg Ni/kg ration for 30 days had markedly lower nickel concentrations in serum and livers than did controls fed diets containing 3.4 mg Ni/kg ration; nickel deficient chicks had 1.6 µg Ni/L in serum vs. 4.2 in controls and 64 µg Ni/kg DW liver vs. 82 in controls (Sunderman et al. 1972). Livers of nickel-deficient chicks had an altered gross appearance, reduced oxidative ability, and decreased lipid phosphorus concentrations (Nielsen et al. 1975a). Nickel deficiency in chicks may be associated with thyroid hormone imbalance (Nielsen et al. 1975a), but this needs verification.

6.6.4 Mammals

In humans, there is no evidence of a nickel deficiency syndrome (USEPA 1985) or proof that nickel is essential (Norseth and Piscator 1979; Norseth 1986).

Cows (*Bos* sp.) fed nickel-deficient diets containing less than 100 µg Ni/kg ration had reduced growth and survival (Hausinger 1993). Nickel-deficiency in cows was exacerbated when diets were also low in protein, but effects were lessened when diets were supplemented with 5 mg Ni/kg ration (Spears et al. 1979). Lambs from domestic sheep (*Ovis aries*) fed a low nickel diet (30 µg Ni/kg ration) for 97 days had lower growth, higher mortality, and altered blood and tissue chemistry when compared to controls fed a diet containing 5 mg Ni/kg ration (Spears et al. 1979). Lambs given diets containing 65 µg Ni/kg DW ration had disrupted metabolism (USEPA 1980).

Adults and offspring of breeding goats (*Capra hircus*) and swine (*Sus* sp.) fed nickel-deficient diets (<100 µg Ni/kg ration) or control diets (10 mg Ni/kg ration) for 6 years had normal conception and abortion rates. However, nickel-deficient goats and pigs had delayed pregnancies, reduced litter sizes, lower birth rates, lower weight gains during suckling, and significant increases in mortality during the suckling period; mortality was 41% higher than controls in kids and 51% higher than controls in piglets (Anke et al. 1978). Nickel-deficient adult goats had lower nickel concentrations in kidneys, liver, and other tissues than did controls, specifically, 0.2 to 0.6 mg Ni/kg DW tissue vs. 0.6 to 1.2 mg Ni/kg DW in controls (Anke et al. 1980a). Kids of nickel-deficient ewes (100 µg Ni/kg DW ration for 6 years vs. control diet of 300 µg Ni/kg ration) had inhibited growth starting at age 8 weeks and reduced survival (Anke et al. 1980b). During lactation, hemoglobin concentrations and hematocrits of nickel-deficient goats were significantly lower than control values (Anke et al. 1980b). Nickel-deficient pigs had rough coats, decreased growth, and impaired reproduction (USEPA 1980; Hausinger 1993).

Signs of nickel deficiency in the laboratory white rat (*Rattus* sp.) include retarded growth, anemia, a reduction in hematocrit and hemoglobin values, decreased enzyme activities (malate dehydrogenase, glucose-6-phosphate dehydrogenase, alpha amylase), a reduction in liver total lipids

and phospholipids, and altered tissue concentrations of fatty acids, iron, copper, and zinc (Nielsen et al. 1975b; Norseth and Piscator 1979; Nielsen 1980b; Norseth 1986; Hausinger 1993; Stangl and Kirchgessner 1996, 1997). Nickel concentrations in fur, kidneys, and muscle of rats fed nickel-deficient diets (15 µg Ni/kg DW ration) were about 66% lower than those of controls given 20 mg Ni/kg ration (Kirchgessner and Schnegg 1980). Signs of nickel deficiency in rats were usually reversed by supplementing the diet with nickel (Ling and Leach 1979) at more than 50 µg Ni/kg ration (USEPA 1985). Rats fed nickel-deficient diets (<5 µg Ni/kg ration) for three generations produced offspring that were anemic and grew poorly in the first two generations and that had impaired reproduction in all generations (USEPA 1980; Sevin 1980). In another three-generation study, rats fed nickel-deficient diets containing 2 to 15 µg Ni/kg ration had increased perinatal mortality, unthrifty appearance of young rats, decreased physical activity, decreased liver cholesterol, and liver histopathology compared to controls fed diets containing 3 mg Ni/kg ration (Nielsen et al. 1975b).

6.7 LETHAL AND SUBLETHAL EFFECTS

6.7.1 General

Nickel toxicity reduces photosynthesis, growth, and nitrogenase activity of algae; fermentative activity of a mixed rumen microbiota; growth rate of marine bacteria; metabolism of soil bacteria; and mycelial growth, spore germination, and sporulation of fungi (Babich and Stotzky 1982a). Adverse effects of excess nickel have also been observed with yeasts, higher plants, protozoans, molluscs, crustaceans, insects, annelids, echinoderms, fishes, amphibians, birds, and mammals (USEPA 1975). As discussed later, sensitive species of aquatic organisms are adversely affected at nominal concentrations of 11 to 113 µg Ni²⁺/L.

In birds, mortality occurred in young individuals of sensitive species when rations contained more than 500 mg Ni/kg (Outridge and Scheuhammer 1993). Nickel accumulated in avian tissues at dietary loadings as low as 0.7 to 12.5 mg Ni/kg ration (Cain and Pafford 1981; Eastin and O’Shea 1981; Stoewsand et al. 1984); however, nickel intoxication in some species tested was not always reflected by elevated tissue nickel concentrations (Outridge and Scheuhammer 1993).

In mammals, the toxicity of nickel is a function of the chemical form of nickel, dose, and route of exposure. Exposure to nickel by inhalation, injection, or cutaneous contact is more significant than oral exposure. Toxic effects of nickel to humans and laboratory mammals are documented for respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, immunological, developmental, neurological, and reproductive systems (NAS 1975; Nielsen 1977; USEPA 1980, 1986; WHO 1991; USPHS 1993).

6.7.2 Terrestrial Plants and Invertebrates

In general, the effects of long-term, low-level exposure to nickel are shown in growth inhibition with no other visible signs (WHO 1991). However, many species of plants growing on soils contaminated with excess nickel show stunted and discolored roots and tops, wilting, chlorosis, necrosis, twisted stalks, thickening of leaf tissues, and failure of leaves to fold to form compact heads (NAS 1975; Frank et al. 1982; WHO 1991; Barman and Bhargava 1997; Donghua and Wusheng 1997). In solution culture, 1 mg of soluble nickel/L is toxic to sensitive plants (NRCC 1981; Outridge and Scheuhammer 1993; Donghua and Wusheng 1997). Accumulations of 50 mg Ni/kg DW plant and higher are toxic to most plants (NAS 1975; NRCC 1981; WHO 1991). Depending on soil conditions and chemical form, nickel in soil is toxic when concentrations exceed 500 mg Ni/kg DW soil with more than 25 mg Ni/L extractable in a 2.5% acetic acid solution

(NRCC 1981). Accumulation and toxic effects occur in vegetables grown on soils treated with sewage sludge and in vegetation close to nickel-emitting sources (WHO 1991). Nickel was shown experimentally to decrease growth of soybeans (*Glycine max*) when administered as particulate nickel through the atmosphere or in the rooting medium (Ormrod et al. 1986). Crop plants are the most sensitive group of terrestrial vegetation tested against nickel. Adverse effects on chlorophyll metabolism and growth occur at soil water concentrations as low as 1 mg Ni/L (Outridge and Scheuhammer 1993). Radishes, beets, cabbages, celery, and lettuce planted in organic soils contaminated by aerial fallout from a nearby nickel smelter and containing between 1570 and 6550 mg Ni/kg DW soil have decreasing yields with increasing soil nickel concentrations (Frank et al. 1982). No radishes or cabbages were suitable for marketing. Celery, lettuce, and beets were reduced from a normal yield on soil with 1300 mg Ni/kg to zero on soils with 4800 mg/kg. Dried cabbage heads and celery tops had as much as 400 mg Ni/kg (Frank et al. 1982). Decreased yields of alfalfa (*Medicago sativa*) occur when plant nickel content exceeds 44 mg/kg DW (NAS 1975). Decreased yield of oats (*Avena sativa*) was associated with nickel concentrations more than 60 mg/kg DW grain, more than 28 mg/kg DW oat straw, or more than 500 mg Ni/kg DW soil (NAS 1975). Signs of nickel toxicity in oats decrease in severity with increasing magnesium concentrations in culture solution during exposure for 35 days (Proctor and McGowan 1976).

Temperature, pH, chlorophyll, and various metals all modify the toxicity of nickel to fungi (Babich and Stotzky 1982b). A reduction in the toxicity of nickel to the mycelial growth rates of five species of filamentous fungi occurs when pH increases from acidic to alkaline (*Achyla* sp., *Saprolegnia* sp.); at elevated concentrations of magnesium, zinc, or lead (*Achyla* sp.); at chlorophyll or humic acid contents equivalent to 1% (*Saprolegnia* sp., *Cunninghamella blakesleean*a, *Aspergillus clavatus*); and at increased temperatures of 33°C vs. 23°C (*Aspergillus flavus*; Babich and Stotzky 1982b). Growth of sensitive species of filamentous fungi is inhibited at 10 mg Ni/L and abnormal mycelia occur at 50 mg/L (Babich and Stotzky 1982a). Histidine may govern nickel accumulation in the approximately 400 known species of nickel-hyperaccumulating plants. Nickel hyperaccumulator plants, including 48 of 170 species of *Alyssum* spp., contain as much as 3% of the dry leaf biomass as nickel (Kramer et al. 1996). Exposing hyperaccumulator species of *Alyssum* to nickel elicits a large and proportional increase in the levels of free histidine, which is shown to be coordinated with nickel in vitro. Supplying histidine to a nonaccumulating species greatly increases both nickel tolerance and capacity for nickel transport to the shoot, indicating that enhanced production of the amino acid histidine is responsible for the nickel hyperaccumulation phenotype in *Alyssum* (Kramer et al. 1996).

Data on nickel toxicity to terrestrial invertebrates are scarce. A soil concentration of 757 mg/kg DW soil is lethal to 50% of earthworms (*Eisenia foetida*) in 14 days, and higher concentrations of 1200 to 12,000 mg/kg DW soil for shorter periods produced reduced growth and survival in the same species (WHO 1991). Earthworms are less sensitive to nickel if the medium is rich in microorganisms and organic matter, thus, making the nickel less bioavailable (WHO 1991).

6.7.3 Aquatic Organisms

Signs of nickel poisoning in fishes include surfacing, rapid mouth and opercular movements, and, prior to death, convulsions and loss of equilibrium (Khangarot and Ray 1990). Destruction of the gill lamellae by ionic nickel decreases the ventilation rate and may cause blood hypoxia and death (Ellgaard et al. 1995). Other signs of nickel poisoning in fishes include decreased concentrations of glycogen in muscle and liver with simultaneous increases in levels of lactic acid and glucose in blood (Ghazaly 1992), depressed hydrogen peroxide production in tissues and a reduction in superoxide dismutase (Bowser et al. 1994), and contractions of vascular smooth muscle — signs similar to those associated with hypertension in mammals (Evans et al. 1990). Ionic nickel is lethal to sensitive species of aquatic organisms at 11 to 113 µg/L. Deaths occur among embryos of rainbow

trout at 11 to 90 µg/L, daphnids at 13 µg/L, embryos of channel catfish at more than 38 µg/L, embryos of the narrow-mouthed toad at 50 µg/L, and embryos of largemouth bass at 113 µg/L (Table 6.7). Species intermediately resistant to nickel died at 150 to 410 µg Ni/L, including mysid shrimp at 150 µg/L, freshwater snails at 237 µg/L, clam embryos at 310 µg/L, and embryos of salamanders at 410 µg/L (Table 6.7). Aquatic bacteria and yeasts are comparatively tolerant to nickel. Sensitive species of freshwater eubacteria and actinomycetes show reduced growth at 5 mg Ni/L; for marine eubacteria, growth inhibition begins at 10 to 20 mg/L (Babich and Stotzky 1982a). Sensitive species of yeasts show growth inhibition at 1.0 mg Ni/L (*Torulopsis glabrata*); resistant species of yeasts (*Rhodotorula* sp., *Cryptococcus terrens*) show a reduction in growth at 5 to 20 mg Ni/L (Babich and Stotzky 1982a; WHO 1991).

The biocidal properties of nickel are modified by many variables. For example, nickel is most lethal at pH 8.3 and least lethal to freshwater crustaceans and fishes at pH 6.3 (Schubauer-Berigan et al. 1993); less toxic to algae when copper is reduced or absent (NRCC 1981) and chelating agents, such as EDTA, are present (Lee and Lustigman 1996); most lethal to echinoderm embryos prior to gastrulation (Timourian and Watchmaker 1972); and more toxic to estuarine amphipods and clams under conditions of decreased salinity in the 0.5 to 3.5% range and increased temperature in the 5 to 15°C range (WHO 1991).

Representative nickel-sensitive aquatic species show sublethal effects at 11.7 to 125 µg Ni/L. These effects include altered immunoregulatory mechanisms in tissues of the rainbow trout at 11.7 µg/L (Bowser et al. 1994), inhibited reproduction of daphnids at 30 µg/L, growth inhibition of freshwater and marine algae at 30 to 125 µg/L, reduced growth of rainbow trout at 35 µg/L, accumulation from the medium by mussels at 56 µg/L, and abnormal development of sea urchin embryos at 58 µg/L (NRCC 1981; WHO 1991; Outridge and Scheuhammer 1993; Table 6.7).

Bioconcentration factors (BCF) for nickel vary among organisms under laboratory conditions. For freshwater species, typical BCF values for nickel are about 10 for algae, 61 for fathead minnows, and 100 for cladocerans; for marine mussels and oysters, typical BCF values range between 299 and 414 (USEPA 1980). The alga *Thalassiosira rotula* can accumulate as much as 90 mg Ni/kg DW (Dongmann and Nurnberg 1982). Other species of aquatic plants can extract nickel from water and concentrate it to as much as 10,000 mg/kg DW (NRCC 1981). The alga *Anacystis nidulans* can develop tolerance to nickel and other metals under laboratory conditions (Whitton and Shehata 1982), and this may account for high BCF values in this species. Nickel at 50 µg/L was accumulated from seawater by softshell clams (*Mya arenaria*) more rapidly during summer at water temperatures of 16° to 22°C than during winter at 0° to 10°C. No accumulations occurred at 10 µg Ni/L in winter, but clams accumulated twice as much nickel over controls in summer (Eisler 1977a). Embryos of sea urchins actively accumulate nickel from seawater at all dose levels tested (Timourian and Watchmaker 1972). Bioconcentration factors for rainbow trout after exposure for 6 months to 1.0 mg Ni/L were 0.8 for muscle, 2.9 for liver, and 4.0 for kidneys (Calamari et al. 1982). Fish can accumulate nickel from food and water. Levels up to 13 mg Ni/kg DW occurred in northern pike (*Esox lucius*) and pickerel (*Esox* sp.) from a contaminated river (NRCC 1981). Common carp (*Cyprinus carpio*) and tilapia (*Tilapia nilotica*) exposed for 16 days to 1.0 mg Ni/L had elevated concentrations in livers of 49 to 77 mg Ni/kg DW (Canli and Kargin 1995). Goldfish (*Carassius auratus*) that died during immersion in solutions containing more than 35 mg Ni/L showed elevated concentrations in tissues, but most of the nickel was washed off with water, and it is not clear if accumulation occurred after death (Kariya et al. 1968). Nickel accumulates in fish tissues and causes alterations in gill structure, including hypertrophy of respiratory and mucus cells, separation of the epithelial layer from the pillar cell system, cauterization and sloughing, and necrosis of the epithelium (Nath and Kumar 1989). Although aquatic organisms can accumulate nickel from their surroundings, there is little evidence of significant biomagnification of nickel levels along food chains (NRCC 1981; Sigel and Sigel 1988; WHO 1991).

Table 6.7 Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
ALGAE AND MACROPHYTES		
Alga, <i>Anabaena inequalis</i>		
125 µg/L	Growth inhibited	1
10.0 mg/L	Photosynthesis inhibited	1
20.0 mg/L	Nitrogenase activity inhibited	1
Blue-green alga, <i>Anacystis nidulans</i>		
160 µg/L	Growth of wild strains inhibited 50%	2
1.3 mg/L	Growth of nickel-tolerant strain inhibited 50%	2
10.0 mg/L	Decreased growth in 14 days	3
50.0 mg/L	No growth in 14 days	3
Freshwater algae, 4 species		
100–700 µg/L	Reduced growth at 50 mg CaCO ₃ /L	4
Green algae, 4 species		
100 µg/L	Growth inhibition at 20°C	1
Giant kelp, <i>Macrocystis pyrifera</i>		
2.0 mg/L	Photosynthesis inhibited 50%	4
Diatom, <i>Navicula pelliculosa</i>		
100 µg/L	Growth inhibited 50% in 14 days	1
Alga, <i>Phaeodactylum tricornutum</i>		
1.0 mg/L	Reduced growth	4
Alga, <i>Scenedesmus acutiformis</i> ; from lake containing 2.5 mg Ni/L		
1.9 mg/L	Growth reduced 47%	1
3.0 mg/L	Growth reduced 82%	1
Marine diatom, <i>Thalassiosira rotula</i>		
30 µg/L	Growth inhibited	5
300 µg/L	Toxic threshold	5
ROTIFERS		
Rotifer, <i>Philodina acuticornis</i>		
2.9–7.4 mg/L	LC50 (96 h) at 25 mg CaCO ₃ /L	4
MOLLUSCS		
Eastern oyster, <i>Crassostrea virginica</i>		
100 µg/L, embryos	None dead in 48 h	6
1.18 mg/L embryos	LC50 (48 h)	6
3.0 mg/L, embryos	All dead in 48 h	6
12.0 mg/L, larvae	LC50 (12 days); normal growth in survivors	7
Freshwater snail, <i>Juga plicifera</i>		
124 µg/L	No adverse effects in 96 h	1
237 µg/L	LC50 (96 h)	1
Freshwater mussel, <i>Lamellidens marginalis</i>		
Exposed for 15 days to 22 mg Ni/L; tissue concentrations, in mg/kg fresh weight (FW), experimental vs. controls		
Foot	218 vs. 122	8
Gills	570 vs. 153	8
Hepatopancreas	327 vs. 160	8
Mantle	277 vs. 145	8
Muscle	186 vs. 130	8
110 mg/L	LC50 (96 h)	8
Northern quahog, <i>Mercenaria mercenaria</i>		
100 µg/L, embryos	No deaths in 48 h	6
310 µg/L, embryos	LC50 (48 h)	6

Table 6.7 (continued) Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
600 µg/L, embryos	All dead in 48 h	6
5.7 mg/L, larvae	LC50 (8–10 days); survivors had reduced growth	7
Softshell clam, <i>Mya arenaria</i> ; adults		
10.0–50.0 mg/L	No deaths in 168 h	9, 11
112.0 mg/L	LC50 (168 h)	9
200.0 mg/L	All dead in 168 h	9
320.0 mg/L	LC50 (96 h)	9
Common mussel, <i>Mytilus edulis</i>		
Exposed to 0, 13, 25, 30, 56 or 107 µg Ni/L for 4 weeks	No accumulations in soft parts at 30 µg/L and lower. After 4 weeks, the 56 µg/L group had 32 mg Ni/kg dry weight (DW) soft parts, and the 107 µg/L group had 41 mg Ni/kg DW soft parts vs. 12 mg/kg DW in controls	10
Exposed to 0, 20.0, 40.0, or 80.0 mg/L for 96 h	No deaths in any group. No byssal thread secretion in 40 and 80 mg/L groups. Nickel concentrations, in mg/kg DW soft parts, were 12 in controls, 400–420 in intermediate dose groups, and 820 in the high dose group	10
Mud snail, <i>Nassarius obsoletus</i> ; adults		
10.0 mg/L	No deaths in 168 h	9
25.0 mg/L	All dead in 168 h	9
72.0 mg/L	LC50 (96 h)	9
ARTHROPODS		
Aquatic insects, 5 species		
4.0–33.5 mg/L	LC50 (96 h) at 42–50 mg CaCO ₃ /L	4
Caddisfly, <i>Clistoronia magnifica</i>		
295–734 µg/L	MATC ^b at 50 mg CaCO ₃ /L	4
Copepods, 4 species		
600–9700 µg/L	LC50 (96 h)	4
Copepod, <i>Cyclops abyssorum prealpinus</i>		
15.0 (8.0–26.0) mg/L	LC50 (48 h)	12
Daphnid, <i>Ceriodaphnia dubia</i>		
13 µg/L	LC50 (48 h) at pH 8.0–8.5	13
>200 µg/L	LC50 (48 h) at pH 6.0–6.5	13
Daphnid, <i>Daphnia hyalina</i>		
1.9 (1.5–2.5) mg/L	LC50 (48 h)	12
Daphnid, <i>Daphnia magna</i>		
10.2–21.4 µg/L	MATC ^b at 51 mg CaCO ₃ /L	4
30–95 µg/L	Reproduction impaired in 21 days	4
100 µg/L	Growth inhibited in 9 days	4
101–150 µg/L	MATC ^b at 105 mg CaCO ₃ /L	4
220–570 µg/L	MATC ^b at 205 mg CaCO ₃ /L	4
360 (330–400) µg/L	LC50 (21 days)	14
500 µg/L	LC50 (9 days) at 60 mg CaCO ₃ /L	4
510 µg/L	LC50 (96 h) at 45 mg CaCO ₃ /L	4
540 µg/L	Population biomass reduced 10% in 21 days	14
950 (670–1300) µg/L	Population biomass reduced 50% in 21 days	14
2.34 mg/L	LC50 (96 h) at 100 mg CaCO ₃ /L	4
4.96 mg/L	LC50 (96 h) at 206 mg CaCO ₃ /L	4
Daphnid, <i>Daphnia pulicaria</i>		
1.8–2.2 mg/L	LC50 (48 h) at 44–48 mg CaCO ₃ /L	4
2.4–3.8 mg/L	LC50 (48 h) at 194–244 mg CaCO ₃ /L	4
Copepod, <i>Eudiaptomus padanus</i>		
3.6 (2.8–4.6) mg/L	LC50 (48 h)	12
Amphipod, <i>Gammarus</i> sp.		
13.0 mg/L	LC50 (96 h)	4

Table 6.7 (continued) Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
Amphipod, <i>Hyalella azteca</i>		
890 µg/L	LC50 (96 h) at pH 8.0–8.5	13
2.0 mg/L	LC50 (96 h) at pH 6.0–6.5	13
Mysid shrimp, <i>Mysidopsis bahia</i>		
61–141 µg/L	MATC ^b	4
Mysid shrimp, <i>Mysidopsis bigelowi</i>		
510–640 µg/L	LC50 (96 h)	4
Mysid shrimp, <i>Mysidopsis formosa</i>		
150 µg/L	LC50 (96 h)	4
Copepod, <i>Nitocra spinipes</i>		
6.0 mg/L	LC50 (96 h)	15
Hermit crab, <i>Pagurus longicarpus</i>		
10.0 mg/L	No deaths in 168 h	9
47.0 mg/L	LC50 (96 h)	9
50.0 mg/L	All dead in 168 h	9
ANNELIDS		
Oligochaete, <i>Lumbriculus variegatus</i>		
26.0 mg/L	LC50 (96 h) at pH 8.0–8.5	13
100.0 mg/L	LC50 (96 h) at pH 6.0–6.5	13
Sandworm, <i>Nereis diversicolor</i> ; adults		
10.0 mg/L	No deaths in 168 h	9
25.0 mg/L	LC50 (96–168 h)	9
50.0 mg/L	All dead in 168 h	9
Polychaete annelids, 3 species		
17.0–49.0 mg/L	LC50 (96 h)	4
Oligochaete, <i>Tubifex tubifex</i>		
80–61,400 µg/L; various water hardnesses	LC50 (48 h) range; most sensitive in soft waters; survivors had increased respiration rate	16, 17
ECHINODERMS		
Sea urchin, <i>Arbacia punctulata</i> ; embryos		
17.0 mg/L	More than 50% dead in 42 h	4
Starfish, <i>Asterias forbesi</i> ; adults		
5.0 mg/L	No deaths in 168 h	9
13.0 mg/L	LC50 (168 h)	9
50.0 mg/L	All dead in 168 h	9
150.0 mg/L	LC50 (96 h)	9
Sea urchin, <i>Lytechinus pictus</i> ; embryos; exposed continuously from fertilization through hatching to 5.8, 58, 580, 5800, 58,000, or 580,000 µg Ni/L, as nickel chloride		
5.8 µg/L group	Normal growth and development	18
58 and 580 µg/L groups	Normal development through gastrulation, but larvae developed abnormally (no dorsoventral symmetry)	4, 18
58.0 mg/L and higher	Normal cleavage, but gastrulation unsuccessful	18
Sea urchin, <i>Strongylocentrotus purpuratus</i>		
Sperm held in 0.6, 5.9, 59, 590, or 5900 µg Ni/L for 50 min	0.6 and 5.9 µg/L had no effect on sperm motility; 59 µg/L had initial depressing effect followed by increased motility; 590 µg/L had initial depressing effect in motility with recovery; 5900 µg/L caused significant depression in sperm motility	19
Sea urchins, various species; embryos		
180 µg/L	No adverse effects on development	20
370–1470 µg/L	Embryonic development inhibited	20

Table 6.7 (continued) Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
FISHES		
Rock bass, <i>Ambloplites rupestris</i> 2.48 mg/L	LC50 (96 h) at 26 mg CaCO ₃ /L	4
Climbing perch, <i>Anabas testudineus</i> 146.0 mg/L for 30 days	No deaths; significant depletion of glycogen and total proteins in liver and gonads	21
American eel, <i>Anguilla rostrata</i> 13.0 mg/L	LC50 (96 h)	4
Zebradanio, <i>Brachydanio rerio</i> ; exposed from 2 h after fertilization through hatching and larval stages until day 16; 11 different doses as nickel sulfate hexahydrate 40 µg/L >40 µg/L 80 µg/L 1024 µg/L	No effect on hatching time Delayed hatching time No effect on larval survival No effect on embryonic survival	22 22 22 22
Goldfish, <i>Carassius auratus</i> 500 µg/L for 2 weeks 25 mg/L 75 mg/L 100 mg/L	Some accumulation in scales and otoliths, but not statistically significant Swimming activity reduced 31% in 96 h LC25 (96 h) LC88 (96 h)	23 24 24 24
Giant gourami, <i>Colisa fasciata</i> ; adults 64 mg/L as nickel sulfate (equivalent to 0.8 times the LC50 [96 h] value); gonads examined after 96 h	Testicular degeneration (spermatogonial activity reduced, germ cells in testicular lobules degenerating, congested blood vessels); ovaries histologically different, oocytes resorbed	25
Common carp, <i>Cyprinus carpio</i> 750 µg/L, larvae 1.0 mg/L for 16 days (in mixture containing 1.0 mg/L each of Cd, Cr, and Pb salts); adults 1.3–40.0 mg/L 8.0 mg/L for 15 days, adults 8.0 mg/L for 15 days (sublethal exposure); nickel concentrations (in mg/kg FW) in tissues of experimentals at end of exposure vs. controls Brain Gill Kidney Liver Muscle 10.4–10.6 mg/L	LC50 (257 h) at 128 mg CaCO ₃ /L Maximum nickel concentrations, in mg/kg DW, were 77 in liver, 49 in gill, 39 in brain, and 19 in muscle; other metals tested showed time-dependent increases in tissues LC50 (96 h) No deaths. Disrupted protein metabolism in gills and kidneys 41 vs. 25 103 vs. 31 80 vs. 50 97 vs. 32 58 vs. 30 LC50 (96 h) at 55 mg CaCO ₃ /L	4 26 4, 27 8 29 29 29 29 29 4
Carp, <i>Cyprinus carpio communis</i> Fingerlings; exposed to 2.5, 5, 7.5, or 10 mg Ni/L for 30 days	No deaths; protein content significantly decreased over time in dose-dependent pattern in brain, intestine, and muscle	30
Orange chromite, <i>Etroplus maculatus</i> Exposed to 10, 30, 60, 80, or 100 mg Ni/L for 96 h at 3 salinities (2.5, 5, or 15 ppt)	At 2.5 ppt salinity, whole body nickel concentrations increased from 19 to 232 mg/kg DW in a dose-dependent manner (vs. control of 12.5 mg/kg DW); at 15 ppt salinity, nickel increased from 20 to 113 mg/kg DW; in combination with copper salts, nickel uptake increased at intermediate salinities	31

Table 6.7 (continued) Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
Fishes; most species; adults		
4–14 mg/L	LC50 (96 h), soft water	1
24–44 mg/L	LC50 (96 h), hard water	1
Banded killifish, <i>Fundulus diaphanus</i>		
46.1 mg/L	LC50 (96 h) at 53 mg CaCO ₃ /L	4
Mummichog, <i>Fundulus heteroclitus</i>		
50 mg/L	No deaths in 168 h	9
150 mg/L	LC50 (96 h)	9
250 mg/L	All dead in 168 h	9
Channel catfish, <i>Ictalurus punctatus</i> ; from fertilization through day 4 posthatch		
38 (18–68) µg/L	LC10	28
710 (490–1010) µg/L	LC50	28
Spot, <i>Leiostomus xanthurus</i>		
70 mg/L	LC50 (96 h), adults	1
Pumpkinseed, <i>Lepomis gibbosus</i>		
5.2 mg/L	LC50 (96 h) at 20 mg CaCO ₃ /L	4
8.0 mg/L	LC50 (96 h) at 55 mg CaCO ₃ /L	4
Bluegill, <i>Lepomis macrochirus</i>		
5.4 mg/L	LC50 (96 h) at 20 mg CaCO ₃ /L	4
39.6 mg/L	LC50 (96 h) at 360 mg CaCO ₃ /L	4
Atlantic silverside, <i>Menidia menidia</i>		
8.0 mg/L	LC50 (96 h)	4
Tidewater silverside, <i>Menidia peninsulae</i> ; larvae		
38.0 mg/L	LC50 (96 h)	1
Largemouth bass, <i>Micropterus salmoides</i>		
113 (61–185) µg/L; exposed from fertilization through day 4 after hatching	LC10	28
2.02 mg/L, embryos	LC50 (8 days) at 93–105 mg CaCO ₃ /L	4
2.06 (1.48–2.84) mg/L; exposed from fertilization through day 4 after hatching	LC50	28
White perch, <i>Morone americana</i>		
13.6 mg/L	LC50 (96 h) at 55 mg CaCO ₃ /L	4
Striped bass, <i>Morone saxatilis</i>		
6.2 mg/L	LC50 (96 h) at 54 mg CaCO ₃ /L	4
Coho salmon, <i>Oncorhynchus kisutch</i>		
16.7 mg/L	LC50 (96 h), alevins	32
18.0 mg/L	LC50 (96 h), juveniles	32
Rainbow trout, <i>Oncorhynchus mykiss</i>		
11 µg/L; embryos exposed from fertilization through day 4 after hatching	LC10	28
23.9 µg/L	Avoidance by adults	33
<35 µg/L; chronic exposure; newly fertilized eggs	No adverse effects	33
50 µg/L; embryos exposed from fertilization through day 4 after hatching	LC50 (28 days) at 93–105 mg CaCO ₃ /L	4, 28
60 µg/L; fertilization through day 4 after hatching	LC50 at 125 mg CaCO ₃ /L	1
90 µg/L; fertilization through day 4 after hatching	LC50 at 174 mg CaCO ₃ /L	1
134 µg/L; chronic exposure of eyed eggs and larvae	No adverse effects	33
230–535 µg/L	MATC ^b at 50 mg CaCO ₃ /L	4
1.0 mg/L, as hexahydrate nickel chloride; exposure for 6 months plus 3-month postexposure observation period in uncontaminated media; juveniles	All fish appeared outwardly normal at all times. After 6 months of exposure, tissue concentrations, in mg Ni/kg FW, were 4.0 in kidneys, 2.9 in liver, and 0.8 in muscle. Nickel concentrations following the 3-month	34

Table 6.7 (continued) Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
7.8–10.9 mg/L	postexposure period (vs. controls), in mg/kg FW, were 2.5 (1.5) in kidneys, 1.8 (1.5) in liver, and 0.6 (0.5) in muscle	32, 33
25.1 mg/L	LC50 (96 h), juveniles	32
31.7 mg/L	LC50 (96 h), alevins	35
35.7 mg/L, adults	LC50 (96 h); adults; hard water	4
Fed diet containing 61 mg Ni/kg DW ration (and other metals found in activated sewage sludge) for 10 weeks	LC50 (48 h) at 42 mg CaCO ₃ /L	36
Isolated R1 liver cells exposed to culture media containing 84 mg Ni/L	Whole body nickel concentration increased from 0.33 mg/kg DW to 0.63 mg/kg DW	
Isolated liver cells in 116 mg Ni/L	50% inhibition of neutral red dye uptake	35
Tilapia, <i>Oreochromis niloticus</i> 1.5 or 3.0 mg/L for 10 days	Cytotoxic	35
Fathead minnow, <i>Pimephales promelas</i> 109–433 µg/L 380–730 µg/L 730–1600 µg/L; lifetime exposure	Significant depletion in liver and muscle glycogen; significant increase in plasma glucose; differences more pronounced at higher dose MATC ^b at 44 mg CaCO ₃ /L MATC ^b at 210 mg CaCO ₃ /L No adverse effects on growth or survival; reproduction inhibited	37 4 4, 38
3.1 mg/L >4.0 mg/L 4.6–9.8 mg/L 25.0–32.2 mg/L 42.0–44.5 mg/L	LC50 (96 h) at pH 8.0–8.5 LC50 (96 h) at pH 6.0–6.5 LC50 (96 h) at 20 mg CaCO ₃ /L LC50 (96 h) at 210 mg CaCO ₃ /L LC50 (96 h) at 360 mg CaCO ₃ /L	13 13 4 4 4
Guppy, <i>Poecilia reticulata</i> 31.0 mg/L 36.0 Mg/L	LC50 (10 days) LC50 (96 h)	39 39
Brook trout, <i>Salvelinus fontinalis</i> 54.4 mg/L	LC50 (48 h) at 42 mg CaCO ₃ /L	4
Lake trout, <i>Salvelinus namaycush</i> 16.7 mg/L	LC50 (48 h) at 42 mg CaCO ₃ /L	4
Spiny dogfish, <i>Squalus acanthias</i> 6.0–11.0 mg/L	Nickel causes <i>in vitro</i> contraction of vascular smooth muscle of ventral aorta	40
Nile tilapia, <i>Tilapia nilotica</i> 1.0 mg/L for 16 days	Maximum nickel concentrations, in mg/kg DW, were 49 in liver, 42 in brain, 37 in gill, and 14 in muscle	26
Exposed to 19, 32 or 51 mg/L for up to 96 h	Dose- and time-dependent increase in blood glucose and lactic acid concentrations; liver glycogen decreased at all nickel levels and muscle glycogen decreased at the two higher levels; high nickel concentrations were associated with elevated erythrocyte number, hemoglobin, and hematocrit. Nickel accumulated in blood, liver, muscle, and especially in kidney	41
65 mg/L	LC50 (96 h)	41
Arctic grayling, <i>Thymallus arcticus</i> 8.2 (5.6–12.0) mg/L 8.7 (6.7–11.4) mg/L	LC50 (96 h), alevins LC50 (96 h), juveniles	32 32
AMPHIBIANS		
Marbled salamander, <i>Ambystoma opacum</i> 410 µg/L as nickel chloride; fertilization through day 4 after hatching 420 µg/L, embryos	LC50 LC50 (8 days) at 93–105 mg CaCO ₃ /L	28 4

Table 6.7 (continued) Nickel Effects on Selected Aquatic Plants and Animals

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Ref. ^a
Fowler's toad, <i>Bufo fowleri</i> 11.03 mg/L as nickel chloride; fertilization through day 4 after hatching	LC50	28
Egyptian toad, <i>Bufo regularis</i> Females given single subcutaneous injection of nickel sulfate of 30, 40, 60, 80, 88, 92, 96, 100, 120, or 160 mg Ni/kg BW 73 mg/kg BW 120 mg/kg BW Concentrations of nickel in selected tissues of nickel-exposed survivors (all groups) vs. controls at 96 h Whole blood Kidney Liver Serum Skin Urine	Calculated LD50 (96 h) Calculated LD50 (24 h)	42 42
Narrow-mouthed toad, <i>Gastrophryne carolinensis</i> 50 µg/L as nickel chloride; fertilization through day 4 after hatching 50 µg/L; embryos	320 µg/FW (Max. 1420 µg/L at 24 h) vs. 40 µg/L 1.82 mg/kg FW (Max. 3.6 mg/kg FW at 24 h) vs. 0.11 mg/kg FW 0.54 mg/kg FW (Max. 2.02 mg/kg FW at 48 h) vs. 0.3 mg/kg FW 0.3 mg/L vs. 0.05 mg/L 0.6 mg/kg FW (Max. 1.56 mg/kg FW at 24 h) vs. 0.01 mg/kg FW 2.12 mg/L (Max. 70.0 mg/L at 24 h) vs. not detectable	42 42 42 42 42 42
	LC50 (7 days) at 195 mg CaCO ₃ /L	4

^a 1, WHO 1991; 2, Whitton and Shehata 1982; 3, Lee and Lustigman 1996; 4, USEPA 1980; 5, Dongmann and Nurnberg 1982; 6, Calabrese and Nelson 1974; 7, Calabrese et al. 1977; 8, Sreedevi et al. 1992a; 9, Eisler and Hennekey 1977; 10, Friedrich and Felice 1976; 11, Eisler 1977b; 12, Baudouin and Scoppa 1974; 13, Schubauer-Berigan et al. 1993; 14, Enserink et al. 1991; 15, Bengtsson 1978; 16, Brkovic-Povic and Popovic 1977a; 17, Brkovic-Povic and Popovic 1977b; 18, Timourian and Watchmaker 1972; 19, Timourian and Watchmaker 1977; 20, Kobayashi and Fujinaga 1976; 21, Jha and Jha 1995; 22, Dave and Xiu 1991; 23, Mugiya et al. 1991; 24, Ellgaard et al. 1995; 25, Nath and Kumar 1990; 26, Canli and Kargin 1995; 27, Alam and Maughan 1992; 28, Birge and Black 1980; 29, Sreedevi et al. 1992b; 30, Thatheyus et al. 1992; 31, Patterson and Fernandez 1995; 32, Buhl and Hamilton 1991; 33, Nebeker et al. 1985; 34, Calamari et al. 1982; 35, Segner et al. 1994; 36, Singh and Ferms 1978; 37, Alkahem 1995; 38, Pickering 1974; 39, Khangarot and Ray 1990; 40, Evans et al. 1990; 41, Ghazaly 1992; 42, Daabees et al. 1991.

^b MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair is highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value is lowest concentration tested producing a measurable effect.

6.7.4 Birds

In mallards (*Anas platyrhynchos*), nickel accumulates in tissues when diets contain as little as 12.5 mg Ni/kg DW ration (Table 6.8). Metabolic upset and altered bone densities occur in mallards fed diets containing 800 mg Ni/kg ration for 90 days (Cain and Pafford 1981; Eastin and O'Shea 1981). Inhibited growth and reduced survival occur in mallards at dietary loadings of 1200 mg Ni/kg ration (Table 6.8). Dietary nickel concentrations of 0.074 mg Ni/kg ration have no adverse effects on Coturnix quail (*Coturnix risoria*). However, Japanese quail (*Coturnix japonica*) fed diets containing 0.71 mg Ni/kg ration — when compared to controls fed diets containing 0.48 mg Ni/kg — have significantly elevated nickel concentrations in liver (Table 6.8). Increased concentrations of nickel in the diets of domestic chickens (*Gallus* sp.) were associated with decreased growth and survival and increased nickel concentrations in bone and kidney (Ling and Leach 1979). Dietary loadings of 500 mg Ni/kg ration and higher were associated with reduced growth and high mortality in some strains of chickens, but not others (Table 6.8). No developmental abnormalities

Table 6.8 Nickel Effects on Birds

Organism, Dose, and Other Variables	Effect	Ref. ^a
MALLARD, <i>Anas platyrhynchos</i>		
Breeding adults 20-months old fed diets containing 0, 12.5, 50, 200, or 800 mg Ni/kg ration for 90 days. All birds killed at day 90 and examined		
All groups	No effect on egg production, hatchability, or survival of ducklings; adults had normal blood chemistry and no organ histopathology; nickel accumulated in kidneys at all doses and in feathers, blood, and livers of birds fed high doses	1, 9
50 mg/kg group	Feathers contained 5.2 mg Ni/kg dry weight (DW) vs. 0.9 mg/kg DW in controls	1
800 mg/kg group	Abnormal black, tarry feces in test birds. Mean nickel concentrations, in mg/kg fresh weight (controls), were 1.9 (0.09) in kidneys, 0.52 (0.12) in livers, and 0.14 (0.005) in blood. Newly grown feathers had 68 (range 8–558) mg Ni/kg DW vs. 0.9 (0.5–1.6) mg/kg DW in controls	1
Ducklings age 1 day fed diets containing 0, 200, 800, or 1200 mg Ni/kg fresh weight (FW) ration, as nickel sulfate, for 90 days		
800 mg/kg group and lower	No effect on growth or survival	2
800 mg/kg group	Lower bone density in females at day 60	2
1200 mg/kg group	Tremors and paresis beginning at day 14; 71% dead by day 60. Survivors weighed less at day 28 than did birds fed other diets. Lower bone density evident at day 30. Livers and kidneys of survivors had <1.0 mg Ni/kg FW; dead birds had as much as 22.7 mg Ni/kg FW liver and 74.4 mg Ni/kg FW kidney	2
JAPANESE QUAIL, <i>Coturnix japonica</i>		
For 2 generations quail ate diets containing wheat (<i>Triticum aestivum</i>) grown on sludge-amended soils (980 µg Ni/kg DW wheat) or control wheat (400 µg Ni/kg DW). Total diets contained 710 µg Ni/kg DW (sludge-grown wheat) or 480 µg Ni/kg DW (controls)	Nickel concentrations in livers of birds fed sludge-grown wheat were significantly elevated in males (210 µg Ni/kg DW vs. 130 in controls) and females (120 vs. 80 µg Ni/kg DW); mixed function oxidase activities were elevated in livers of both sexes when compared to controls	3
COTURNIX QUAIL, <i>Coturnix risoria</i>		
Fed diets containing 74 µg Ni/kg ration for 4 generations	No observed adverse effects	4
DOMESTIC CHICKEN, <i>Gallus</i> sp.		
Chicks given single intraperitoneal injection of 10 mg Ni (as nickel chloride)/kg body weight (BW)	Initial increase in plasma glucose after 15 min followed by hypoglycemia 60–120 min after injection. Starved chicks remained hyperglycemic during 120 min postinjection observation period	5
Day-old Plymouth Rock males fed semipurified diets for 3 weeks		
300 mg Ni/kg diet	Reduced growth rate; elevated kidney nickel concentration of 4.2 mg/kg FW vs. 0.13 in controls	6, 9
500 mg Ni/kg diet	Some deaths. Kidneys had 7.6 mg Ni/kg FW and bone had 1.9 mg Ni/kg FW vs. 0.1 mg Ni/kg bone FW in controls. Addition of 100 mg copper, iron, zinc, or cobalt/kg ration did not reverse adverse effects	6

Table 6.8 (continued) Nickel Effects on Birds

Organism, Dose, and Other Variables	Effect	Ref. ^a
700 mg/kg diet	Growth retardation; kidneys had 9.7 mg Ni/kg FW	6
1100 mg Ni/kg diet	High mortality and anemia; kidneys had 11.5 mg Ni/kg FW; possible breakdown in urinary excretion mechanisms	6
Broiler chicks fed diets for 4 weeks containing 500 mg Ni (as nickel sulfate or nickel acetate)/kg ration	Normal growth in body weight	4, 5, 7
As above at 700 mg Ni/kg ration	Decreased growth in body weight	4, 5, 7
As above at 900 or 1300 mg Ni/kg ration	Marked reduction in growth; nitrogen retention decreased in 1300 mg/kg group	4, 7
Embryos; age 4 or 8 days; white leghorn strain; injected into yolk or onto the chorioallantoic membrane; 3.6 mg Ni/kg FW embryo (0.2 mg nickel as nickel chloride hexahydrate/egg)	LD50 (18 days postinjection); no developmental abnormalities in survivors	8

^a 1, Eastin and O'Shea 1981; 2, Cain and Pafford 1981; 3, Stoewsand et al. 1984; 4, NAS 1975; 5, Nielsen 1977; 6, Ling and Leach 1979; 7, Weber and Reid 1968; 8, Ridgway and Karnofsky 1952; 9, Outridge and Scheuhammer 1993.

occurred in chicks from survivors challenged by nickel during embryogenesis (USPHS 1977). Chick embryos receiving a single injected dose of 3.6 mg Ni/kg embryo, however, experienced 50% mortality within 18 days (Ridgway and Karnofsky 1952). Chicks are more resistant than embryos to injected nickel. Chicks injected with 10 mg Ni/kg BW survived but had disrupted glucose metabolism; effects were exacerbated by starvation (Nielsen 1977).

6.7.5 Mammals

Outridge and Scheuhammer (1993), in their excellent review of nickel hazards, draw six major conclusions regarding nickel toxicity in mammals:

1. Lifetime exposure of resistant species of mammals to diets containing 2500 mg Ni/kg DW or to drinking water containing 10,000 mg Ni/L are not lethal.
2. Lethal nickel doses in mammals are usually derived from studies with laboratory animals injected with nickel and its compounds, not from realistic exposure regimens.
3. Inhaled nickel is at least 100 times more toxic than ingested nickel because it is more readily absorbed from the lungs than from the gastrointestinal tract, and death is more often the result of respiratory failure than of nervous system effects. For example, oral ingestion of 0.05 mg Ni/kg BW and inhalation at 0.005 Ni/m³ are equally effective threshold doses in rats (USPHS 1977).
4. Large differences in sensitivity to nickel exist between closely-related taxonomic species, such as rats and mice.
5. Threshold effects on lung function or morphology in several species of laboratory mammals occur at airborne nickel concentrations of 0.1 to 0.2 mg/m³, depending on nickel compound and duration of exposure.
6. Juveniles were usually more sensitive to nickel than adults.

Nickel salts administered by intravenous or subcutaneous injection are comparatively toxic. For all routes of parenteral administration, the LD50 (lethal dose to 50% of the sample) range for injected nickel salts is 6 mg Ni/kg BW for dogs given nickel oxide intravenously to 600 mg Ni/kg BW for mice given nickel disodium EDTA intraperitoneally (Nielsen 1977).

Several trends were evident among sensitive species of mammals tested against nickel through administration routes other than injection ([Table 6.9](#)).

1. Nickel carbonyl is lethal to mice, rats, and cats at 0.067–0.24 mg Ni/L.
2. Inhalation of nickel compounds other than nickel carbonyl causes significant effects in humans, rats, mice, rabbits, and dogs, with respiratory effects being most common.
3. Nickel-contaminated drinking water has adverse effects on rat reproduction and may neurologically affect the eyes of humans, although this needs to be verified.
4. Diets containing nickel carbonate, nickel chloride, or nickel sulfate cause reduced growth, disruptions of food intake and thyroid function, and emphysema and pneumonia in calves, dogs, mice, or rats.
5. Dermal application of nickel sulfate hexahydrate causes skin and testicular damage.
6. Single oral doses of 136 to 410 mg Ni/kg BW as nickel acetate are lethal to mice.

Nickel carbonyl ($\text{Ni}(\text{CO})_4$) is the only nickel compound known to cause severe acute effects, such as pulmonary damage and death; acute toxic effects of other nickel compounds to mammals are a minor risk (Norseth and Piscator 1979; Sevin 1980; WHO 1991). In fatal cases, death occurs 3 to 13 days after exposure. Recovery from nickel carbonyl poisoning usually occurs within 70 days after exposure, but sometimes may take up to 6 months (Sunderman 1970; Sevin 1980; WHO 1991). Nickel carbonyl is a volatile, colorless liquid formed when finely divided nickel or its compounds come into contact with carbon monoxide. It is unstable under atmospheric conditions, and if inhaled, nickel is deposited in highly active form on the respiratory mucosa on contact. Nickel carbonyl is widely used commercially as a catalyst but is one of the most toxic gases encountered in industrial operations (Sunderman 1970; Norseth and Piscator 1979; USEPA 1980, 1986). Exposure to air containing more than 50 mg $\text{Ni}(\text{CO})_4/\text{m}^3$ for 0.5 to 2.0 h may be fatal to humans (WHO 1991). Intraperitoneal injection of nickel carbonyl was the most toxic route of administration; for all routes of administration, LD₅₀ values for various test mammals ranged between 13 and 65 mg/kg BW (WHO 1991; [Table 6.9](#)). Nickel carbonyl toxicity is due, in part, to its volatility and lipophilicity (Sigel and Sigel 1988). Signs of nickel carbonyl poisoning, which strongly resemble those of viral pneumonia, include headache, vertigo, nausea, vomiting, insomnia, and irritability followed by an asymptomatic interval and then the onset of insidious, persistent signs that include chest pains, dry coughing, cyanosis, sweating, visual and gastrointestinal disturbances, severe weakness, paralysis of the hind limbs, and convulsions. The lungs are the primary target organs in all animals tested, although the liver, kidneys, adrenal glands, spleen, and brain are also affected (Sunderman 1970; Nielsen 1977; Mushak 1980; USEPA 1980, 1986; Norseth 1986; WHO 1991).

Adverse effects in mammals by inhalation of nickel compounds other than nickel carbonyl occur with aerosols of both soluble and insoluble nickel compounds (USEPA 1980). Inhalation of nickel by humans and other mammals produces respiratory, hepatic, renal, dermal, immune system, and body weight effects (WHO 1991; USPHS 1993). Respiratory effects of nickel include asthma, nasal septal perforations, chronic rhinitis and sinusitis, and increased risk of chronic respiratory tract infections (USPHS 1977; USEPA 1986; WHO 1991; Zhang et al. 1998); immunological, genotoxic, and carcinogenic effects were also observed (USPHS 1993). Lung reactions in the form of asthma were attributed to sensitization by nickel (Norseth and Piscator 1979). Insoluble forms of inhaled nickel are more persistent in lungs than are soluble forms, as judged by 90-day studies with nickel chloride (soluble) and nickel oxide (insoluble) given to rodents by intratracheal administration (English et al. 1981). Severity of respiratory toxicity was higher with increasing solubility of the nickel compound tested and not with increasing burden of nickel on the lung; insoluble nickel oxide had the lowest toxicity but the highest lung burden. Nickel sulfate was more toxic than nickel subsulfide, which was more toxic than nickel oxide (USPHS 1993).

Local effects noted in guinea pigs, rats, mice, and hamsters caused by inhalation of metallic nickel powder (15 mg/m³), nickel subsulfide (0.97 mg/m³), or nickel oxide (53 mg/m³) include nasal sinus inflammations, ulcers, lung irritation, nickel accumulations in lungs, emphysema, and

increased viral respiratory infections (Norseth 1986; WHO 1991). Rats inhaling nickel subsulfide at 2.5 mg/m³ for 22 days had nasal and lung histopathology within 4 days and disrupted enzyme activities and elevated nickel accumulations within 7 days (Benson et al. 1995). Repeated inhalation of nickel subsulfide by rats for 3 months resulted in chronic inflammation in the lung and atrophy of the olfactory epithelium (Benson et al. 1995). Rats exposed via inhalation of nickel sulfate hexahydrate of 635 µg Ni/m³ for 6 h daily over 16 days had no outward signs of toxicity; however, internal examination revealed lesions on the olfactory epithelium (Evans et al. 1995). Rats and mice died following inhalation exposure for 16 days to equal doses of nickel sulfate or nickel subsulfide, but not nickel oxide (USPHS 1993). Rats showed epithelial hyperplasia after inhalation exposure to aerosols of nickel chloride or nickel oxide and pulmonary fibrosis after inhalation exposure to nickel subsulfide; a similar syndrome was reported in rabbits after high-level inhalation exposure to nickel-graphite dust (WHO 1991). Dogs exposed to nickel powder for 6 months by way of inhalation developed lung pneumosclerosis causing cardiac insufficiency (USPHS 1977). Rats exposed to airborne nickel dusts (100 µg Ni/m³, 12 h daily for 2 months) had respiratory irritation (NRCC 1981). Single exposures of mice to 250 µg Ni/m³ for 2 h depressed the humoral immune response (NRCC 1981). Rats exposed to 1000 µg Ni dust/m³ (5 days/week for 3 to 6 months) had high accumulations of nickel in the lungs and kidneys and interstitial fibrosis (NRCC 1981).

Nickel and nickel salts are comparatively nontoxic when taken orally because of homeostatic mechanisms that control nickel metabolism and limited intestinal absorption (Nielsen 1977). In cattle, young calves fed nickel carbonate at concentrations as high as 1000 mg Ni/kg ration for 8 weeks had nephritic kidneys, with degree of severity increasing with dietary nickel level. However, dietary nickel did not affect growth or food consumption of calves or cause histopathology of the rumen, abomasum, duodenum, liver, or testes (O'Dell et al. 1970). Human and animal data indicate that death is unlikely from oral nickel exposure except when exposed accidentally to high levels (USPHS 1993). Oral exposure studies for humans were limited to acute intoxication and include death (due to cardiac arrest) and the effects of gastrointestinal (nausea, cramps, diarrhea, vomiting), hematological (increase in reticulocytes), hepatic (increase in serum bilirubin), renal (albuminuria), and neurological damage. A child who accidentally ingested 20.36 grams of Ni/kg BW as crystals of nickel sulfate died from heart failure (USPHS 1993). Oral LD₅₀ doses of nickel chloride to rats produced depression of the nervous system, edema of the mucous membranes of the mouth and nose, diffusions from the oral cavity, lacrimation, bleeding from the nose, and diarrhea (USPHS 1977). Prior to death, rats were lethargic, ataxic, and with irregular breathing and cool body temperatures (USPHS 1993).

Nickel is a reproductive toxicant in animals. Specific effects of nickel on reproduction include degenerative changes in the testes, epididymis, and spermatozoa of rats; adverse effects on embryo viability of rats and hamsters; and delayed embryonic development of rodents (Smialowicz et al. 1984; USEPA 1986; USPHS 1993). Nickel salts given by injection cause intrauterine mortality and decreased weight gain in rats and mice (WHO 1991). Inhibited testosterone and reduced growth occur in male rats given 2.32 mg Ni/kg BW as nickel acetate via intramuscular injection. Females given the same treatment had increased uterine weights (USPHS 1977). Nickel given in drinking water of rats for three generations at concentrations which do not interfere with growth or survival (i.e., 5 mg/L) was intolerable for normal reproduction (Schroeder and Mitchener 1971). All generations of rats given nickel in drinking water had increased proportions of runts and increased neonatal mortality when compared to controls. In the third generation of nickel-treated rats, there were reductions in litter size and a reduction in the proportion of males (Schroeder and Mitchener 1971). Excess nickel inhibits prolactin secretion in rats. Because prolactin influences milk production, the observation that suckling pups from nickel-exposed dams were most severely affected lends support to the concept that nickel plays a role in lactation at the pituitary level (Nielsen et al. 1975b).

Table 6.9 Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
COW, <i>Bos</i> sp.		
Diet		
63 mg Ni/kg ration for 8 weeks as nickel carbonate; male calves	Normal growth and food consumption	1, 2
250 mg Ni/kg ration for 42 days; lactating cows	Negligible transfer of nickel from diet to milk	3
250 mg Ni/kg DW ration for 8 weeks as nickel carbonate; male calves; equivalent to daily intake of 1218 mg nickel	No accumulations in tissues; slight (13%) reduction in food intake and growth rate (11%)	1, 2
1000 mg Ni/kg dry weight (DW) ration for 8 weeks as nickel carbonate; male calves; equivalent to daily intake of 1410 mg nickel	Abnormal rumen fluid composition; nickel accumulations in tissues; marked reduction in food intake and growth rate. During a 6-week postexposure recovery period, growth rate was same as in controls	1, 2
1750 mg Ni/kg ration; adult females	No detectable nickel in milk	2
<i>In vitro</i> culture; isolated brain cells exposed for 20 h to graded concentrations of nickel chloride up to 116 mg Ni/L	Time- and dose-dependent effects on kinetics of brain microtubule polymerization; effects reversed on removal of Ni ²⁺ from culture media	4
DOMESTIC DOG, <i>Canis familiaris</i>		
Diet		
0, 100, 1000, or 2500 mg Ni/kg ration for 2 years as nickel sulfate hexahydrate	No significant adverse effects at 1000 mg Ni/kg ration and lower. At 2500 mg Ni/kg, adverse effects observed on growth and blood chemistry; livers and kidneys enlarged; lung lesions; hyperplasia of bone marrow	5
Equivalent to 25 or 63 mg Ni/kg BW daily, as nickel sulfate, for 2 years	No serious adverse effects at low dose; high dose group had emphysema, pneumonia, low hematocrit, increased liver and kidney weight, and a 40% decrease in body weight gain	6
Inhalation		
2.7 mg Ni/L, as nickel carbonyl (Ni(CO) ₄), for 75 min	LC80 (1–5 days postexposure)	8
5 to 6 mg Ni powder/m ³ , 10 min daily for 6 months; observed for additional 19 months following treatment	No change in weight or general condition. At 3 months after treatment, leukocyte and primary neutrophil counts were low, and nickel was elevated in liver and kidneys. At 12 months, blood flow was reduced in small vessels of lungs. At 19 months, survivors had increased pulse and respiration rates	7
Intravenous injection, single dose		
6 to 7 mg Ni/kg BW, as nickel oxide	Lethal	2
10 to 20 mg Ni/kg BW as colloidal nickel	Death preceded by gastroenteritis, tremors, and paralysis	2, 9
10 to 20 mg Ni/kg BW as nickel chloride	Some deaths	2, 9
Oral		
12 mg/kg BW daily for 200 days	Tolerated without ill effects	10
1000–3000 mg Ni/kg BW as powdered nickel	Tolerated	9
Subcutaneous injection; single dose of 500 mg Ni/kg BW as nickel sulfate hexahydrate	Some deaths	2
DOMESTIC GOAT, <i>Capra hircus</i>		
Pulmonary macrophages cultured <i>in vitro</i> for 20 h with media containing 14.5–58.0 mg Ni/kg as nickel chloride	Concentration-dependent decrease in viability of alveolar macrophages; highest dose had survival of <50%. Death associated with release of superoxide anions	11

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
GUINEA PIG, <i>Cavia</i> sp.		
Drinking water; 2.5 mg Ni/L for 4 months	No accumulations in hair; all values were between 3.4 and 4.6 mg Ni/kg DW hair	12
Inhalation; 15 mg Ni/m ³ as elemental nickel; lifetime exposure	Excess blood, swelling, hemorrhage, and increased frequency of lesions in the pharyngeal area	7
Intravenous injection; 62 mg Ni/kg BW as nickel sulfate; single injection	LD50	2
Subcutaneous injection; males given 0.0001, 0.001 or 1.0 mg Ni/kg BW daily as nickel chloride for 15 days were mated with fertile females	No effect on female gestation period, number of litters or offspring, weight of offspring, or offspring development	7
HAMSTER, <i>Cricetus</i> sp.		
Gavage; 5 mg of nickel oxide	After 24 h, no increase in nickel content of lungs, liver, kidney or carcass	7
Inhalation Exposed to nickel oxide aerosols at concentrations of 2–160 µg/L (2 to 160 mg/m ³) and particle size of 1 to 2.5 µm 15 mg Ni/m ³ as elemental nickel; lifetime exposure 39 mg Ni/m ³ as nickel oxide for 3 weeks 48.4 mg/m ³ as nickel oxide for 61 days	45 days after exposure about 50% of the original dose remained in lungs with no significant accumulations in other tissues	10
	No significant effect on survival or health	7
	Inflammation and congestion of lungs; emphysema	7
	No deaths	6
DOMESTIC CAT, <i>Felis domesticus</i>		
Inhalation; nickel carbonyl 0.19 mg/L for 30 min 3.0 mg/L for 75 min	LC50 (0.2 h-6 days after exposure)	8
	LC50 (1–5 days after exposure)	8
	Tolerated, with no apparent ill effects	2, 9, 10
HUMAN, <i>Homo sapiens</i>		
Dermal; <59 µg Ni/L; nickel-sensitive persons	No contact allergic reaction	14
Dialysis; 23 patients; nickel leached into dialysate from a nickel-plated stainless steel water heater tank	At plasma nickel concentrations of about 3 mg/L, patients had adverse effects including headaches, nausea, vomiting, and weakness; recovery occurred 3 to 13 h after cessation of dialysis	8
Drinking water Equivalent to 0.012 or 0.05 mg Ni/L as nickel sulfate 250 mg Ni/L in contaminated drinking water 32 workers in an electroplating plant drank water accidentally contaminated with nickel sulfate and nickel chloride at 1630 mg Ni/L; estimated intake of 0.5–2.5 g, equivalent to 8.3–41.6 mg/kg BW	Neurological effect on eyes at high dose; no adverse effects at low dose	6
	Stomach ache, increased red blood cell number, increased protein in urine	6
	Symptoms included nausea, vomiting, abdominal discomfort, diarrhea, giddiness, lassitude, headache, cough, and shortness of breath, and persisted for at least 2 h and sometimes 2 days. Serum nickel concentrations on day 1 after exposure were 286 (13–1340) µg/L vs. 50 µg/L in nonaffected workers; for urine these concentrations were 5.8 (0.2–37.0) mg/L vs. 4.0 µg/L	8
Inhalation >0.04 mg Ni/m ³ air, usually as nickel oxide or metallic nickel	Chronic bronchitis, emphysema, reduced lung capacity, and increased incidence of deaths from respiratory disease among workers occupationally exposed	6

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
30 mg Ni/L air as nickel carbonyl for 30 min	Lethal	13
Chronic exposure		
Nickel aerosols, occupational exposure	Lung cancer, nasal sinusitis, chronic rhinitis	10
Nickel particulates	Chronic respiratory infections	10
Oral		
Low nickel diet fed to patients with chronic nickel dermatitis	Significant improvement in 6 weeks; adverse effects when placed on normal diet	10
Accidental ingestion of nickel sulfate crystals (15–20 grams) by 2.5 year-old female child	Death in 4 h of heart failure; blood had 7.5 mg Ni/kg, urine 50 mg/L, and liver 25 mg Ni/kg FW	6, 8
Placental tissue incubated for as long as 24 h in media containing 145 mg Ni/L	When compared to controls, treated tissues had increased permeability, lipid peroxidation, and nickel concentration over time. Treatment with ascorbic acid or zinc decreased nickel-induced placental lipid peroxidation and permeability, but had no effect on nickel tissue concentrations	43
MONKEYS		
Various species; different forms of nickel in diet; as much as 1000 mg Ni/kg ration for 24 weeks	No adverse effects on growth, behavior, or blood chemistry	10, 13
DOMESTIC MOUSE, <i>Mus</i> spp.		
Diet		
Young mice fed diets containing 0, 1100 or 1600 mg Ni/kg ration as the acetate salt for 4 weeks	Food consumption and growth reduced in the male 1600 mg/kg group and the female 1100 and 1600 mg/kg groups. All nickel groups had significant decreases in liver cytochrome oxidase and isocitric dehydrogenase activities; in heart and kidney homogenates, malic dehydrogenase activity decreased in the high nickel groups	15, 16
Equivalent to >1.4 mg Ni/kg BW daily for 2 years as nickel chloride or nickel sulfate	Decreased liver weight	6
Equivalent to 108 mg Ni/kg BW daily for 180 days as nickel sulfate	Renal tubular damage at the corticomedullary junction	6
Drinking water		
Equivalent to >23 mg Ni/kg BW for 6–30 h as nickel chloride, nickel sulfate, or nickel nitrate	Abnormal sperm in mature males	6
150 mg/L as nickel sulfate for 6 months	No deaths	6
160 mg/L as nickel chloride in drinking water of pregnant females from gestation day 2 to day 7	Increased incidence of spontaneous abortions	6
Inhalation		
Nickel carbonyl		
0.01 mg/L for 120 min	All dead	8
0.067 mg/L for 30 min	LC50 (0.2 h–6 days after exposure)	8, 9
Nickel oxide		
>3.9 mg/m ³ for as long as 13 weeks	Adverse respiratory effects including chronic inflammation, fibrosis, macrophage hyperplasia, interstitial infiltrates, and increased lung weight	6
23.6 mg/m ³ for 16 days	No deaths	6
Nickel subsulfide		
>0.11 mg/m ³ for 16–91 days	Adverse respiratory effects	6
7.3 mg/m ³ for 16 days	All dead	6

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
Nickel sulfate		
>0.1 mg/m ³ for 16–91 days	Adverse respiratory effects	6
1.6 mg/m ³ for 16 days	All dead	6
Isolated Leydig cells incubated with 3.6–58.0 mg Ni/L for 48 h; testosterone production measured in testicular interstitial cells	A dose-related depression in testosterone production at doses not producing any general toxic or significant cytotoxic action	44
Single intramuscular injection of 18.3 mg Ni/kg BW as nickel chloride	Involution of thymus and suppression of cellular and humoral activity and transient immunosuppressive effects within 2 days of injection with responses returning to normal within a few days	17
Single intraperitoneal injection		
Nickel acetate		
11 mg/kg BW	Adverse effects	21
32 mg/kg BW	LD50 (48 h)	7
39–50 mg/kg BW; adult males; age 9–15 weeks	LD50 (5 days postinjection)	20
48–54 mg/kg BW; adult females; age 9–15 weeks	LD50 (5 days postinjection)	20
89–97 mg/kg BW; juveniles; age 3 weeks	LD50 (5 days postinjection)	20
Nickel chloride		
Pregnant females given 1.2, 2.0, 3.0, 3.5, 4.6, 5.7, or 6.9 mg Ni/kg BW between days 7 and 11 of gestation	Dose-related increase in fetal deaths and malformations	8
3.1 mg Ni/kg BW	Normal spleen lymphocyte function	18
Pregnant mice given 4.6 mg Ni/kg BW on day 16 of gestation and killed 2 to 48 h after injection	Maximum nickel concentrations in tissues (in mg/kg FW) were reached in blood (19.8) and placentas (3.9) 2 h following injection; those in liver (4.9), spleen (1.3), and kidneys (56.2) were reached 4 h after injection; and maximum concentration in fetal tissues (1.1) was reached after 8 h. Authors estimate that all nickel is excreted in 42 to 84 h	19
9.3–12.3 mg Ni/kg BW	Immunosuppression in spleen lymphocyte function	18
26 mg Ni/kg BW	LD50 (48 h)	7
Nickel chloride hexahydrate; 48 mg Ni/kg BW	LD50 (48 h)	7
Nickelocene; 27 mg Ni/kg BW	Adverse sublethal effects	21
Nickel oxide; >744 mg/kg BW	LD50 (72 h)	7
Nickel perchlorate heptahydrate; 100 mg Ni/kg BW	LD50 (12 h)	7
Nickel sulfate; 21–38 mg Ni/kg BW	LD50 (10–30 days)	7
Oral, single dose		
Nickel acetate; 136–410 mg Ni/kg BW	LD50 (72–120 h)	7, 21
Nickelocene; 186 mg/kg BW	LD50	21
Single subcutaneous injection of 10, 20, or 40 mg Ni/kg BW every 3 days for 4 treatments	Depressed testosterone production of Leydig cells at 20 mg/kg BW and higher; normal histology	44
RABBIT, <i>Oryctolagus</i> sp.		
Inhalation		
Metallic nickel dust		
>0.2 mg/m ³ for about 8 months	Alterations in alveolar macrophages; impaired cellular function	6
1.0 mg/m ³ for 3 or 6 months, 5 days weekly, 6 h daily; lungs examined	At both 3 and 6 months, there was a two- to threefold increase in volume density of alveolar Type II cells; after 6 months, lungs had foci of pneumonia, suggesting a higher susceptibility to pulmonary	

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
Nickel carbonyl; 1.4 mg/L for 50 min	Infections due to a decrease in function of alveolar macrophages	22
Nickel chloride; >0.2 mg/m ³ for about 8 months	Alveolar cell degeneration within 5 days; LC80 (120 h)	8, 10
Single intravenous injection; nickel chloride	Alterations in alveolar macrophages	6
10 mg/kg BW	Transient hyperglycemia 1–4 h after injection	7
15 mg/kg BW	Pronounced hyperglycemia 1–4 h after injection, returning to normal after 24 h	7
15–20 mg/kg BW	Pancreas histopathology	7
Single subcutaneous injection; various nickel salts; 1300 mg/kg Ni/BW	Lethal	9
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Dermal; nickel sulfate hexahydrate; dose equivalent to 40, 60, or 100 mg Ni/kg BW daily for 30 days (rats licked skin so exposure route may be oral in part)	No adverse effects in 40 mg/kg BW group. High dose groups had skin damage (atrophy, acanthosis, hyperkeratinization) and testicular damage (abnormal seminiferous tubules, tubular lumens filled with degenerated sperm)	6, 8, 10
Diet		
Weanlings fed rations containing 0, 100, 500, or 1000 mg Ni/kg, as nickel acetate, for 6 weeks	At high doses (500, and 1000 mg/kg), rats had depressed growth, low hematocrit and hemoglobin, and low tissue cytochrome oxidase and alkaline phosphatase activities; the 1000 mg/kg group (vs. controls) had elevated nickel concentrations — in mg Ni/kg DW — of 2.1 (0.9) in heart, 40.7 (5.0) in kidney, 4.0 (0.7) in liver, and 7.2 (1.6) in testes	38
0, 100, 1000, or 2500 mg Ni/kg ration, as nickel sulfate hexahydrate, for 2 years	No histopathology in any group; at 1000 and 2500 mg Ni/kg ration, rats had depressed growth, lower liver weights, and increased heart weights	5
0, 250, 500, or 1000 mg Ni/kg ration, as nickel sulfate hexahydrate, for 3 generations; equivalent to 0.7, 12.5, 25, or 50 mg Ni/kg BW daily; reproductive study	Higher incidence of stillborns and fetal mortalities noted only in the first generation at all nickel dietary levels; weanling body weight was lower at 1000 mg Ni/kg ration in all generations	5, 6, 21
0.08 mg Ni/kg ration for 55 days	No adverse effects	2
250 mg Ni/kg ration for 16 months	Normal growth	16
1000 mg Ni/kg ration (as nickel carbonate or nickel catalysts) for 8 weeks	Normal growth	10
1000 mg Ni/kg ration for 13 days; juveniles	Altered blood chemistry, diminished food intake, and reduced growth within a few days	39
Dietary equivalent of 1, 25, or 100 mg/kg BW daily for 4 months; nickel chloride	Thyroid function affected; decreased iodine uptake at 1 mg/kg BW, increased at 25 mg/kg BW, and decreased at 100 mg/kg BW	7
Dietary equivalent of >1.4 mg Ni/kg BW daily for 2 years; nickel chloride or nickel sulfate	Decreased liver weight	6
Drinking water		
5 mg/L; lifetime exposure	No effect on growth or survival	35, 36
5 mg/L for 3 generations; diets contained 0.31 mg Ni/kg FW ration	Significant increase in mortality of young rats in all generations; significant increase in runts in first and third generations; litter size decreased with each generation; total number of rats reduced; few males were born in the third generation	35
225 mg/L for 4 months as nickel chloride	Depressed growth rate; lower serum triglyceride and cholesterol concentrations	13, 40

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
Inhalation		
Nickel carbonyl ($\text{Ni}(\text{CO})_4$)		
0.1 mg/L for 20 min	Some deaths after exposure	8
0.24 mg/L for 30 min	LC50 (0.2 h-6 days)	2, 8, 9
0.24–1.0 mg/L for 30 min	Lung histopathology within 10 days	10
0.9 mg/L for 30 min	LC80 (2 h–several months)	8
100 mg/L for 15 min	About 26% of the inhaled nickel was excreted in urine within 4 days; absorption estimated at 50%	10
160 mg/m ³ on days 7–8 of gestation or 300 mg/m ³ on day 7	Increased fetal mortality; reduced body weight in live pups; 16% incidence of fetal malformations (anophthalmia, microphthalmia, cystic lungs, hydronephrosis)	8
Nickel chloride (NiCl_2); 0.05–5.0 mg/m ³ for 2 to 4 weeks	Significant decrease in iodine uptake by thyroid	10
Nickel dust; 15 mg/m ³ ; lifetime exposure	Increased frequency of adenoidal lesions and chronic sinus inflammation and ulceration	7
Nickel oxide (NiO)		
0.06 mg/m ³ ; lifetime exposure	Survival time decreased from 125 weeks in controls to 88 weeks; body weight loss after 13 months; alveolar proteinosis and marked lung enlargement	6
0.2 mg/m ³ for 1 year	Pneumonia and bronchial epithelial metaplasia	6
0.5 mg/m ³ for 1 month	Bronchial gland hyperplasia 20 months after exposure	6
1.6 mg/m ³ on gestation days 1–21	Decrease in fetal body weight	6
>3.9 mg/m ³ for as long as 13 weeks	Adverse respiratory effects	6
11.7 mg/m ³ , 8 h daily, 5 days weekly, for 4 weeks	Significant increase in tumor necrosis factor for alveolar macrophages	24
23.6 mg/m ³ for 16 days	No deaths	6
Nickel subsulfide (Ni_3S_2)		
Equivalent to 0, 0.4, or 1.8 mg Ni/m ³ ; 6 h daily for as long as 22 days	The high dose group had reduced survival, nose and lung histopathology, and disrupted enzyme activity levels; survivors were lethargic and grew poorly. At day 22, nickel concentrations in lungs, in mg/kg FW, were <1.8 in controls, 12 in the low dose group and 34.0 in the high dose group	26
Equivalent to 0.11, 0.44, or 1.8 mg Ni m ³ for as long as 13 weeks; exposures were 6 h daily and 5 days weekly	Dose-dependent increase in pulmonary lesions; atrophy of the nasal olfactory epithelium at 0.44 mg/m ³ and higher	26
Equivalent to 0.73 mg/m ³ for 78 weeks plus 30 weeks of postexposure observation; exposure for 6 h daily and 5 days weekly	Pulmonary tumor growth (14% incidence in lung tumors vs. 1% in controls) and increased mortality (95% dead vs. 69% in controls)	6, 25
7.3 mg/m ³ for 16 days	LC20	6
Nickel sulfate (NiSO_4)		
50 µg/rat	Half-time persistence in lung of 32 h; lung inflammatory responses disrupted lung enzyme activity	29
>0.1 mg/m ³ for as long as 13 weeks	Adverse respiratory effects	6
0.635 mg/m ³ for 16 days, 6 h daily	Induced lesions of olfactory epithelium but no measurable changes in olfactory function	31
1.6 mg/m ³ for 16 days	No deaths	6
Single intramuscular injection, unless noted otherwise		
Metallic nickel; 110 mg/kg BW	Lowest toxic dose	2
Nickel acetate		
Males and females given 2.32 mg Ni/kg BW daily for 4 days	Males had inhibited testosterone levels and reduced growth, while females had increased uterine weights	7
420 mg/kg BW	Lowest toxic dose	2

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
Nickel chloride		
Females given 1.5–2.0 mg/kg BW daily on days 6–10 of gestation	Significant intrauterine mortality, but body weight of live pups was normal	8
Females given 2.0 mg/kg BW twice daily on days 6–10 of gestation	No congenital abnormalities	34
12 mg/kg BW to pregnant and nonpregnant females; tissues analyzed 24 h following injection	Relative tissue concentrations were kidney > serum > adrenal=lung=ovary > spleen=heart=liver > muscle. Nickel concentration in pituitary gland was significantly higher in pregnant rats	34
16 mg Ni/kg BW on day 8 of gestation	Reduction in number of live pups and diminished body weight of fetus on day 20 of gestation and of weanlings 4 to 8 weeks after birth; no developmental abnormalities	34
23–98 mg/kg BW	LD50 (7 days)	7, 21, 23, 80
Nickel oxide		
7 mg Ni/kg BW	Significantly increased levels of serum alkaline phosphatase, amylase, aspartate transaminase, and lipoperoxide. Daily injections of copper-zinc superoxide dismutase prevented these changes	28
180 mg/kg BW	Toxic	2
Nickel subsulfide		
80 mg Ni/kg BW on day 6 of gestation	Reduction in mean number of live pups	34
90 mg/kg BW	Lowest toxic dose	2
Nickel sulfate; 12–16 mg/kg BW on day 8 of gestation	Reduction in mean number of live pups; reduced body weight in fetuses on day 20 of gestation and in pups 4–8 weeks after birth	8
Nickel sulfide; 7 mg/kg BW	Disrupted serum enzyme activity	28
Single intraperitoneal injection, unless indicated otherwise		
Nickel acetate		
8 mg/kg BW	Toxic	21
24 (19–28) mg/kg BW	LD50 (48 h)	7, 8
Nickel carbonyl; 13 mg/kg BW	LD50	8
Nickel chloride		
4 mg/kg BW	Tissue concentrations at 24 h (and at 15 min) after injection, in mg/kg FW, were 2.7 (16.1) in kidney, 0.3 (4.7) in liver, 1.2 (5.9) in blood, and 0.9 (1.4) in placenta	33
6.0 (5.5–6.5) mg/kg BW	LD50 (7 days) for females pregnant 19 days	33
6.3 (5.6–7.1) mg/kg BW	LD50 (7 days) for females pregnant 12 days	33
8.0 mg/kg BW	Rapid transient increase in serum glucose and decrease in serum insulin	40
9.3 (8.5–10.2) mg/kg BW	LD50 (7 days) for virgin females	33
11–19 mg/kg BW	LD50 (7 days)	2, 7, 8
Nickelocene; 16–59 mg/kg BW	LD50, usually within 14 days	8, 21
Nickel oxide; >690 mg/kg BW	LD50 (3 days)	7
Nickel sulfate; 3 or 6 mg/kg BW daily for 7 or 14 days; killed 48 h after last injection	Highest nickel concentrations were in myocardium (5.7 mg/kg FW vs. 2.2 in controls) and spleen (2.1 vs. 0.6), followed by kidney, bone, and other tissues	37
Single intrarenal injection of nickel subsulfide equivalent to 39 mg/kg BW	Pronounced erythrocytosis; increased hematocrit and reticulocyte count	30
Intratracheal injection		
Single injection of ultrafine particles of nickel metal (20 nm diameter) at 5 mg Ni/kg BW and examined 1–30 days later	Severe lung inflammation, cytotoxicity, and increased epithelial permeability	42

Table 6.9 (continued) Nickel Effects on Selected Mammals

Organism, Route of Exposure, Dose, and Other Variables	Effect	Reference ^a
Nickel chloride; 1.0 mg/kg BW; examined 6 and 72 h after injection	At 6 h, tissue nickel concentrations were elevated in kidneys, lungs, adrenals, liver, pancreas, spleen, heart, and testes, in that order; by 72 h, 90% of the nickel was excreted, mostly (75%) in the urine	7
Nickel oxide; >110 mg/kg BW	LD50 (72 h)	7
Single intravenous injection of nickel carbonyl		
11 mg/kg BW; day 7 of gestation	High incidence of fetal deaths and malformations; reduced body weight in live pups	8
22 mg/kg BW	LD50, usually within 14 days	8
65 mg/kg BW	Massive lung histopathology within 6 days	10
Single oral exposure, unless indicated otherwise		
Nickel acetate		
116–120 mg/kg BW	Toxic	21
304–410 mg/kg BW	LD50 (7 days)	7, 8
Nickel chloride		
0.35 mg/kg BW daily for 28 days	Hyperglycemia, decreased body weight, reduced food and water intake	6
8.6 mg/kg BW daily for 91 days	LD25; decreased body weight in survivors	6
116 mg/kg BW	Toxic	6, 21
285 mg/kg BW	LD50, usually within 14 days	7
Nickel fluoborate ($\text{Ni}(\text{BF}_4)_2$); 500 mg/kg BW	Lethal	2
Nickel hexahydrate; 8.5 mg/kg BW daily for 91 days	Death preceded by lethargy, ataxia, irregular breathing, hypothermia, salivation, squinting, and loose stools	6
Nickel nitrate ($\text{Ni}(\text{NO}_3)_2$); 1620 mg/kg BW	LD50, usually within 14 days	2
Nickelocene		
154 mg/kg BW	Toxic	21
471–525 mg/kg BW	LD50, usually within 14 days	8
Nickel sulfate		
25 mg/kg BW daily for 120 days	Infertility	8
66 mg/kg BW	LD50, usually within 14 days	6
Single subcutaneous injection		
Nickel carbonyl; 21 mg/kg BW	LD50 within several days	8
Nickel chloride		
10 or 20 mg/kg BW; young males; observed for 7 days	Increased prolactin levels that persisted for 4 days; increased insulin levels on days 1 and 2	8
11.9 mg/kg BW	5% dead	27
59.5 mg/kg BW given 16 h prior to sacrifice	Significant increase in hepatic glutathione S-transferase activity	32

^a 1, O'Dell et al. 1970; 2, NAS 1975; 3, Stevens 1991; 4, Lin and Chou 1990; 5, Ambrose et al. 1976; 6, USPHS 1993; 7, USPHS 1977; 8, WHO 1991; 9, Sunderman 1970; 10, USEPA 1980; 11, Waseem et al. 1993; 12, Scheiner et al. 1976; 13, Nielsen 1977; 14, USEPA 1975; 15, Weber and Reid 1969; 16, Ling and Leach 1979; 17, Smialowicz et al. 1984; 18, Graham et al. 1975; 19, Lu et al. 1981; 20, Hogan 1985; 21, USEPA 1985; 22, Hohansson et al. 1981; 23, Sunderman et al. 1983; 24, Morimoto et al. 1995; 25, Ottolenghi et al. 1974; 26, Benson et al. 1995; 27, Iscan et al. 1992; 28, Novelli et al. 1995; 29, Hirano et al. 1994; 30, Oskarsson et al. 1981; 31, Evans et al. 1995; 32, Iscan et al. 1993; 33, Mas et al. 1985; 34, Sunderman et al. 1978; 35, Schroeder and Mitchener 1971; 36, Schroeder et al. 1974; 37, Mathur et al. 1978; 38, Whanger 1973; 39, Schnegg and Kirchgessner 1976; 40, Clary 1975; 41, Ho and Furst 1973; 42, Zheng et al. 1998; 43, Chen and Lin 1998; 44, Forgacs et al. 1998.

The most commonly observed toxic reaction to nickel and nickel compounds in the general human population is nickel dermatitis and skin sensitivity arising from dermal contact with metals containing nickel (Sunderman 1970; NAS 1975; Norseth and Piscator 1979; USEPA 1980, 1986; WHO 1991; USPHS 1993). Studies on occupational dermatitis, which is the most prevalent

occupational disease, show that 8% of the cases are due to nickel (Sunderman et al. 1984). Nickel dermatitis in occupational exposure begins as an itching or burning in the web of the fingers, spreading to the fingers, the wrists, and the forearms; the eruption is similar to atopic dermatitis (NAS 1975; USEPA 1980, 1986). Once an individual is dermally sensitized to nickel, even minimal contact (i.e., 0.007 to 0.04 mg Ni/kg BW daily) by any route of exposure may elicit a reaction (USEPA 1980; WHO 1991; USPHS 1993; Hughes et al. 1994). Nickel, in fact, is the most common allergen tested in North America; about 1 to 5% of human males and 7 to 14% of females are contact sensitized to nickel (NAS 1975; Nielsen 1977; Sevin 1980; USEPA 1980, 1986; Sunderman et al. 1984; USPHS 1993; Ikarashi et al. 1996). Nickel contact hypersensitivity has been documented worldwide, with 10% of the female population and 1% of the male population affected. Of these, 40 to 50% have vesicular hand eczema that, in some cases, can be severe and lead to loss of working ability (WHO 1991). Nickel contact dermatitis is decreasing in occupational exposure, but increasing elsewhere due to increasing contact with nickel alloys in jewelry, coins, zippers, tools, pots and pans, stainless steel, detergents, prostheses, and certain hair dressings (NAS 1975; Nielsen 1977; USEPA 1980; Sunderman et al. 1984; WHO 1991; USPHS 1993). Nickel is a major allergen for women, and between 1970 and 1980 there was a two- to threefold increase in the number of cases (Sunderman et al. 1984). In recent years, the incidence of nickel allergy has increased disproportionately in young females due to an increased frequency of ear piercing by this group to accommodate nickel-plated jewelry (Ikarashi et al. 1996).

Although contact allergy to nickel is common in humans, experimental sensitization in animals is only successful under special conditions (WHO 1991). Dermal studies with nickel salts and small laboratory mammals show that primary nickel sensitization typically takes place beneath nickel-containing metal objects that are in contact with the skin for hours and exposed to friction and sweating; nickel is released from nickel-containing objects by the action of blood, sweat, or saliva; ionic nickel diffuses through the skin at sweat-duct and hair-follicle openings, with a special affinity for keratin; and nickel subsequently binds to proteins, including amino and carboxyl groups of keratin and serum albumin (NAS 1975; USEPA 1980; USPHS 1993). Rats, guinea pigs, and rabbits absorbed and subsequently distributed 55 to 77% of nickel applied dermally (USPHS 1977, 1993). Dermal effects in animals after dermal exposure to nickel include distortion of the dermis and epidermis, hyperkeratinization, atrophy of the dermis, and biochemical changes (USPHS 1993; Ikarashi et al. 1996). For example, in rats treated dermally with more than 40 mg Ni/kg BW daily as nickel hexahydrate for 30 days, distortion of the epidermis and dermis occurred by day 15, and hyperkeratinization, vacuolization, hydropic degeneration of the basal layer, and atrophy of the epidermis occurred by day 30 (USPHS 1993). Skin irritation and death from nickel salts is reported in rabbits when nickel was applied dermally to abraded skin; no negative effects occurred in rabbits when the same dose was applied to intact skin (USPHS 1977). As was the case for humans, allergic reactions occur in laboratory animals after oral nickel challenge in sensitized individuals (USPHS 1993).

Nickel affects endocrine and enzymatic processes. Nickel-induced endocrine effects include inhibition of insulin production in pancreas, prolactin in hypothalamus, amylase excretion in parotid gland, and iodine uptake in thyroid (Mushak 1980; USEPA 1980, 1986; USPHS 1977; WHO 1991). Inhibition of enzyme activity by nickel is reported for RNA polymerase, ATPase, dialkyl fluorophosphate, and aspartase (NAS 1975). Inhibition of ATPase is associated with neurological abnormalities, such as tremors, convulsions, and coma; altered hormone release or action; and internal rearrangement of calcium ions in muscle that might cause paralysis and abnormal heart rhythm (Nielsen 1977). Nickel increases the duration of the action potential of excitable membranes of nerve and muscle tissues; this effect is competitive with and imitative of those of calcium (NAS 1975). Nickel hexahydrate at 14.8 mg Ni/kg BW disrupts hepatic monooxygenases; mice were more sensitive to this disruption than rats or guinea pigs (Iscan et al. 1992). Nickel is also reported to activate various enzymes, including bovine pancreatic ribonuclease, pancreatic deoxyribonuclease, carboxypeptidase, arginase, phosphoglucomutase (Sevin 1980), and calcineurin — a calmodulin-dependent phosphoprotein phosphatase (USEPA 1986). Nickel affects the activity of heme

oxygenase, thereby affecting the absorption of hemoglobin iron. Nickel, like many other metals and metalloids, induces heme oxygenase activity in tissues of mice, hamsters, and guinea pigs in a dose-related manner (Sunderman et al. 1983).

Systemic effects of nickel exposure include hyperglycemia, increased levels of plasma glucagon, damage to the pancreatic islet cells, decreased body weight, reduced food and water intake, and hypothermia (NAS 1975; USEPA 1980; USPHS 1993). Acute administration of nickel salts caused prompt hyperglucagonemia and subsequent hyperinsulinemia in rats, rabbits, and guinea pigs (WHO 1991). Nickel chloride given orally to young male rabbits at 500 µg daily for 5 months produced a decrease in liver glycogen and an increase in muscle glycogen, with prolonged hyperglycemia (NAS 1975). Nickel increased glucose metabolism in rats injected intratracheally with 0.5 mg ionic nickel. This phenomenon probably reflected the influence of nickel on the production or secretion of insulin through decreased production of pituitary hormone secretions — specifically, prolactin — which control insulin concentrations (USPHS 1977). Nickel significantly affects the activity of hepatic glutathione S-transferases (GST); these compounds play important roles in the detoxification of electrophilic xenobiotics, such as nickel, epoxides, and diolepoxydes (Iscan et al. 1993), and readily eliminate the cytotoxic products of lipid peroxidation, particularly the organic peroxides (Coban et al. 1996). The influence of nickel chloride on hepatic GST activity levels depends on the animal species tested, being depressed in mice, unchanged in rats, and increased in guinea pigs (Iscan et al. 1992). In humans, nickel toxicity is not related to GST depletion or increased lipid peroxidases *in vitro*, whereas in rat kidney, nickel toxicity may be due to GST depletion and stimulation of lipid peroxidases (Coban et al. 1996).

Nickel affects the immune, cardiac, and excretory systems. Nickel adversely affects the immune system by reducing host resistance to bacterial and viral infections, suppressing phagocytic activity of macrophages, reducing the number of T-lymphocytes (thereby suppressing the natural kill cell activity) and increasing susceptibility to allergic dermatitis (WHO 1991; USPHS 1993). In mice, nickel chloride suppresses the activity of natural killer cells within 24 h of a single intramuscular injection (USEPA 1986). Nickel-induced cardiovascular effects include vasoconstriction, inhibition of contraction by myocardial muscle, and a reduction in coronary vascular flow (USEPA 1986; WHO 1991; USPHS 1993). Nickel salts are demonstrably cardiotoxic in dogs (Sigel and Sigel 1988). Cats injected intravenously with NiCl₂ had altered heart rhythms, conductivity, and calcium metabolism (Nielsen 1977). Nickel is a nephrotoxin with greatest adverse effect on the glomerular epithelium of the kidney. Kidneys from mammals exposed to nickel showed renal tubular damage, protein loss, and weight changes (USPHS 1993).

Nickel accumulations in tissues and organs of mammals vary significantly with species, route of administration, sex, and general health. No significant accumulations of nickel were observed in liver or kidney of Holstein calves fed diets containing 1000 mg Ni/kg ration for 21 weeks (Stevens 1992). In lactating dairy cows, no transfer of soluble nickel was observed from diet to tissues (Stevens 1992). In rats, guinea pigs, rabbits, sheep, dogs, and other species of mammals, nickel tends to accumulate in kidneys and other tissues after nickel exposure (as quoted in Eastin and O'Shea 1981). Nickel-poisoned rats had elevated accumulations primarily in myocardium (5.7 mg/kg FW vs. 2.2 in controls) and spleen (2.1 mg/kg FW vs. 0.6), followed by kidney, bone, and other tissues (Mathur et al. 1978). In rats, nickel accumulated mainly in lung and secondarily in heart tissues after intratracheal administration of nickel chloride; nickel was retained for at least 40 days after dosing (Novelli and Rodrigues 1991). In rodents, nickel accumulates in endocrine tissues, including the pituitary, adrenals, and pancreas (Mushak 1980; USEPA 1980). High nickel concentrations in the pituitary gland of rodents were associated with inhibition of insulin release and decreased prolactin secretion (Clary 1975). Rat weanlings fed diets containing 500 mg Ni/kg ration as nickel acetate show elevated nickel accumulations in plasma, erythrocytes, heart, liver, testes, and especially kidneys. High accumulations were associated with reductions in growth, hematocrit, hemoglobin, cytochrome oxidase, and alkaline phosphatase (Whanger 1973; Nielsen 1977). Male guinea pigs accumulated higher concentrations of nickel in hair than did females after

exposure for 4 months to drinking water containing 2.5 mg Ni/L (Scheiner et al. 1976). Invading microorganisms can change the distribution of ^{63}Ni in mice infected with coxsackie B3 virus. Infected mice had high accumulations of ^{63}Ni in the pancreas and the wall of the ventricular myocardium. Healthy mice had almost no ^{63}Ni accumulations in these tissues, but residues were elevated in blood, kidney, and lung (Ilback et al. 1992).

Excretion of ingested nickel by rats, regardless of amount ingested, usually occurs through the feces within 48 h (Ho and Furst 1973). Most nickel administered to rats through a variety of routes, and irrespective of chemical form, is usually excreted within a few days; however, excretion is slower for nickel powder and from lungs (USPHS 1977). Nickel caused a twofold increase in urinary corticoid excretion in guinea pigs (USPHS 1977), increased urinary excretion of protein in rats (USPHS 1977), and increased urinary excretion of B-2-macroglobulin in nickel refinery workers (USPHS 1993). Nickelemia was associated with increased urinary B-2-macroglobulin levels, and 5 of 11 workers with urinary nickel concentrations more than 100 $\mu\text{g}/\text{L}$ had increased urinary B-2-macroglobulin ($>240 \mu\text{g}/\text{L}$; (USPHS 1993).

6.8 PROPOSED CRITERIA AND RECOMMENDATIONS

While nickel may be carcinogenic, perhaps in all forms, there is little or no detectable risk in most sectors of the nickel industry at current exposure levels, including some processes that had previously been associated with very high lung and nasal cancer risks (WHO 1991). Research is ongoing to clarify the hazards of nickel to humans, including chronic inhalation carcinogenicity studies of nickel subsulfide, nickel oxide, and nickel sulfate hexahydrate in rats and mice (USPHS 1993). Nevertheless, additional research on nickel-induced cancer has been proposed, including research on (1) route of administration (USPHS 1993); (2) oxidative state of nickel (Kasprzak 1987); (3) effect of nickel on nucleic acid synthesis (Sunderman 1981); (4) interaction effects with asbestos (USEPA 1980), zinc and magnesium (Furst and Radding 1980), tobacco smoke (NRCC 1981), and agents thought to inhibit nickel carcinogenesis, such as manganese, copper, and aluminum (Furst and Radding 1980); (5) role of diet in nickel carcinogenesis (Furst and Radding 1980) and specificity and mechanism of uptake of nickel ion from the gastrointestinal tract (Hausinger 1993); and (6) nickel immunosuppressive mechanisms, especially effects of nickel on natural killer cell activity and the relation between suppression of these cells and the known carcinogenesis of nickel compounds (Smialowicz et al. 1984). Large-scale studies are needed to establish the upper limits of cancer risk from nickel (WHO 1991).

Humans have been shown to develop sensitivity to nickel (USPHS 1993). The use of nickel in products that may release the metal when in contact with the skin should be regulated (WHO 1991). Among various subgroups of the U.S. population who may be at special risk for adverse effects of nickel are those who have nickel hypersensitivity and suffer chronic flare-ups of skin disorders with frank exposure (USEPA 1986). The role of oral nickel exposure in dermatic responses by sensitive individuals suggests that nickel-limited diets resulted in marked improvement of hand eczema and that nickel added to the diets appeared to aggravate the allergic response (USEPA 1986). More research is needed on the role of nickel in contact dermatitis, including the role of oral nickel exposure, and the pathogenesis and therapy of nickel dermatitis (NAS 1975; Sunderman et al. 1984; USEPA 1986). Additional dermal exposure studies are needed to determine if testicular effects result from both oral and dermal exposure to nickel (USPHS 1993).

Animal experimental models of nickel-induced skin sensitivity are few and have been conducted only under very specialized conditions (USEPA 1986). Studies examining the mechanism of nickel contact sensitization and its extent in wildlife are needed (USPHS 1993). The importance of the surface properties and crystalline structure of nickel compounds in relation to their reactivity and protein-binding activities is well documented. It is therefore necessary to identify clearly the nickel compounds to which exposure occurs (Sunderman et al. 1984). Acute and chronic dermal and

inhalation studies using all nickel compounds would determine if certain compounds are more effective in eliciting allergic dermatitis (USPHS 1993).

To protect terrestrial vegetation against decreased growth and other toxic effects, nickel residues in leaves should contain less than 44 to less than 50 mg/kg DW; soils should contain less than 50 to less than 250 mg Ni/kg DW; and sewage sludge applied to agricultural soils should be limited to 30 to 140 kg Ni/surface ha at the low end and 50 to 560 kg/ha at the high end ([Table 6.10](#)). Research is needed on the direct effects on vegetation of nickel from airborne deposition, the effects of soil acidification on mobility and toxicity of nickel in soil, differences in nickel metabolism between tolerant and nickel-sensitive plants (NRCC 1981), and on the interactions of nickel and organic acids in nickel-accumulating plants and in the surrounding soils (Lee et al. 1978).

To protect freshwater plants and animals against nickel, a proposed range of less than 25 to 96 µg total recoverable Ni/L is recommended by various authorities ([Table 6.10](#)). This range will protect most species of freshwater biota. However, certain species have reduced survival within this range, including embryos of rainbow trout (*Oncorhynchus mykiss*) at 11 µg/L (Birge and Black 1980), daphnids (*Ceriodaphnia dubia*) at 13 µg/L (Schubauer-Berrigan et al. 1993), and embryos of the narrow-mouthed toad (*Gastrophryne carolinensis*) at 50 µg/L (Birge and Black 1980; USEPA 1980). Mixtures of metals are additive or more-than-additive in toxicity and, in some cases, will exceed the recommended water-quality criteria based on the individual metals. Such additive effects were demonstrated for daphnids and rainbow trout using water-quality criteria developed in the Netherlands for mixtures of nickel salts and those of arsenic, cadmium, chromium, copper, lead, mercury, or zinc (Enserink et al. 1991). To protect marine life, the 24-h average for total recoverable Ni/L should not exceed 7.1 µg/L, and the maximum concentration should not exceed 140 µg/L at any time ([Table 6.10](#)). The maximum concentration level for marine life protection needs to be reexamined because 30 µg Ni/L adversely affects growth of marine diatoms (Dongmann and Nurnberg 1982), 56 µg/L results in nickel accumulations in mussels (Friedrich and Filice 1976), 58 µg/L causes abnormal sea urchin development (Timourian and Watchmaker 1972), and 59 µg/L has adverse effects on motility of sperm of sea urchins (Timourian and Watchmaker 1977). In aquatic systems, research is needed to determine the mechanisms of nickel toxicity to biota, the transport of nickel, its interaction with other inorganic and organic chemicals, and its mobility in sediments under various environmental conditions (NRCC 1981).

To protect birds, diets should contain at least 50 µg Ni/kg ration to prevent nickel deficiency, but less than 200 mg Ni/kg ration in the case of young birds and less than 800 mg/kg ration in the case of adults to prevent adverse effects on growth and survival ([Table 6.10](#)). Nickel residues in avian kidneys in excess of 10 mg/kg DW or in liver in excess of 3 mg/kg DW are sometimes associated with adverse effects (Outridge and Scheuhammer 1993); however, nickel accumulates in kidneys of mallards (*Anas platyrhynchos*) at dietary concentrations as low as 12.5 mg Ni/kg ration (Eastin and O’Shea 1981). In general, tissue concentrations of nickel were not reliable indicators of potential toxicity in mammals and birds because adverse effects, including death, frequently occurred in the absence of elevated tissue nickel concentrations (Outridge and Scheuhammer 1993). For monitoring birds, analysis of kidneys, bone, and feathers is the most likely to reveal elevated exposure to environmental nickel contamination; nickel concentrations in liver and spleen often do not reflect elevated exposure (Outridge and Scheuhammer 1993).

To protect humans and other mammals, proposed air-quality criteria range from 0.01 to less than 1.0 mg/m³ for metallic nickel and slightly soluble nickel compounds, 0.015–0.5 mg/m³ for water soluble nickel compounds, and 0.005 to 0.7 mg/m³ for nickel carbonyl ([Table 6.10](#)). Inhalation of nickel subsulfide concentrations (0.11 to 1.8 mg Ni/m³) near the current threshold limit value of 1 mg Ni/m³ can produce detrimental changes in the respiratory tract of rats after only a few days of exposure (Benson et al. 1995). Additional animal studies are recommended to identify minimally effective inhalation exposure levels for the various nickel compounds (USPHS 1993). Continued monitoring of nickel refining, nickel-cadmium battery manufacture, and nickel powder metallurgy installations is recommended because ambient air levels of bioavailable nickel at these

installations in excess of 1 mg/m³ can sometimes still be found (NAS 1975; Sevin 1980; Sunderman et al. 1984; Chau and Kulikovsky-Cordeiro 1995).

Most species of mammals had normal growth and survival during chronic exposure to diets equivalent to 0.8 to 40 mg Ni/kg BW daily (Outridge and Scheuhammer 1993). Reduced growth and survival sometimes occurred when sensitive species of wildlife were fed diets containing 500 to 2500 mg Ni/kg ration, equivalent to 10 to 50 mg Ni/kg BW daily (Outridge and Scheuhammer 1993). Proposed criteria for nickel by way of the diet or drinking water range from 2 µg total Ni/kg BW daily (USPHS 1993) to 443 µg total Ni/kg BW daily (USEPA 1980) for soluble nickel compounds, less than 1.0 mg Ni/kg FW diet, and less than 350 µg Ni/L drinking water ([Table 6.10](#)). Further research is needed to clarify the role of nickel in mammalian nutrition, including dietary requirements of nickel and identification of the chemical forms of nickel present in foods and their bioavailability (NAS 1975; Sunderman et al. 1984; Hausinger 1993). Studies are needed on the absorption and cellular uptake, transport, and metabolism of well-characterized nickel species following different routes and types of administration (NAS 1975; WHO 1991; Hausinger 1993) and on the transfer of dietary nickel to tissues of lactating dams and juveniles (Stevens 1992). Because young female laboratory mice were more susceptible to dietary nickel than were adults, it is possible that no-observable-adverse-effect-levels (NOAELs) derived from adult animals may be inappropriately high for neonates and juveniles (Outridge and Scheuhammer 1993). Studies that compare the toxicokinetics of humans and animals concurrently could be helpful in determining which species of animal is the most appropriate model for assessing the effects of nickel in human health (USPHS 1993). Animal studies designed to examine neurological effects after inhalation or oral exposure are needed to determine, in part, if human exposure to nickel will cause permanent neurological damage (USPHS 1993).

Nickel affects reproduction of selected mammals. Drinking water containing 5 mg Ni/L — equivalent to 0.2 to 0.4 mg Ni/kg BW daily — had adverse effects on rat reproduction and iron metabolism (Outridge and Scheuhammer 1993). Dogs given the equivalent of 1.3 mg Ni/kg BW daily had decreased litter survival (Hughes et al. 1994). Nickel is known to cross the placental barrier and reach the fetus in mammals and humans. More information is needed on the effects of *in utero* nickel exposure in pregnant women (USEPA 1986; Chashchin et al. 1994). Such information may be obtained using appropriate animal models (USPHS 1977). Multigenerational inhalation studies are recommended to determine if developmental effects result from both inhalation and oral exposure (USPHS 1993).

Biomarkers of nickel exposure and effects include nickel concentrations in feces and urine and changes in serum antibodies and serum proteins (USPHS 1993). Levels of carnosine, a dipeptide, seem to reflect the extent of nickel-induced damage to olfactory mucosa of rats, although the rodent olfactory system is more resilient than the human's (Evans et al. 1995). Studies on the availability of trace levels of nickel in food and water and in air would be helpful to relate levels of nickel found in the hair, nails, blood, and urine to levels of nickel in internal organs (USPHS 1993). Nickel concentrations in human tissues now considered elevated include 4.6 µg/L in serum, 11.9 µg/L in plasma, and 100 to 129 µg/L in urine ([Table 6.10](#)). Treatment of mammals suffering from nickel poisoning is usually through administration of various classes of chelating agents, including dithiocarb (sodium diethyl-dithiocarbamate — the drug of choice in the management of nickel carbonyl poisoning), EDTA salts, BAL (2,3-dimercaptopropanol), and penicillamine (Norseth and Piscator 1979; Norseth 1986). In all cases, the agents accelerate urinary excretion of absorbed nickel before extensive tissue injury occurs (USEPA 1980).

The nomenclature of nickel compounds should be further standardized (WHO 1991). Analytical methods must be developed and standardized in order to facilitate speciation of nickel compounds in atmospheric emissions, biological materials, and in other environmental samples (NAS 1975; WHO 1991). Studies are needed to elucidate the biogeochemical nickel cycle on a global scale and determine its potential for long-range transport (WHO 1991).

Table 6.10 Proposed Nickel Criteria for Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Nickel Concentration	Reference ^a
AQUATIC LIFE, FRESHWATER		
Sediments		
Great Lakes		
Safe	Less than 20 mg/kg dry weight (DW)	1
Moderately polluted	20–50 mg/kg DW	1
Heavily polluted	More than 50 mg/kg DW	1
Wisconsin; for disposal in water	Less than 100 mg/kg DW	1
Water		
Canada; safe level	Less than 25 µg/L	2
Rainbow trout, <i>Oncorhynchus mykiss</i> ; safe level	Less than 29 µg/L	3
Toxic effects expected	30–50 µg/L	4
Ontario, Canada; from sediment disposal in water; final water concentration	Less than 50 µg/L	1
The Netherlands; safe level	Less than 50 µg/L	5
United States; water hardness of 50 mg CaCO ₃ /L	24-h average not to exceed 56 µg total recoverable nickel/L; maximum concentration not to exceed 1100 µg/L at any time	6
Sweden; safe level	Less than 80 µg/L	7
United States; water hardness of 100 mg CaCO ₃ /L	24-h average not to exceed 96 µg total recoverable Ni/L; maximum concentration not to exceed 1800 µg/L at any time	6
United States; water hardness of 200 mg CaCO ₃ /L	24-h average not to exceed 160 µg total recoverable Ni/L; maximum concentration not to exceed 3100 µg/L at any time	6
AQUATIC LIFE, MARINE		
Water	24-h average not to exceed 7.1 µg total recoverable Ni/L; maximum concentration not to exceed 140 µg/L at any time	6
BIRDS		
Diet		
Domestic chicken, <i>Gallus</i> sp.; to prevent nickel deficiency in chicks	More than 50 µg/kg ration	8, 9, 10
Mallard, <i>Anas platyrhynchos</i>		
Ducklings; no adverse effects	Less than 200 mg/kg ration	4
Adults; no adverse effects	Less than 800 mg/kg ration	4
Adults; adverse effects	More than 800 mg/kg fresh weight (FW) ration	11
Tissue concentrations		
Adverse effects expected; most species		
Kidney	More than 10 mg/kg DW	4
Liver	More than 3 mg/kg DW	4
Internal organs, most species		
Normal	Less than 3 mg/kg DW	4
Nickel-contaminated environments	As much as 30 mg/kg DW	4
Mallard; liver or kidney; significant exposure to dietary nickel that may be harmful	More than 1.0 mg/kg FW	11

Table 6.10 (continued) Proposed Nickel Criteria for Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Nickel Concentration	Reference ^a
CROPS AND OTHER TERRESTRIAL VEGETATION		
Plant residues		
Alfalfa, <i>Medicago sativa</i>		
Normal	0.3–3.2 mg/kg DW	12
Decreased growth	44.0 mg/kg DW	12
Terrestrial vegetation		
Hyper-accumulator plants	More than 1000 mg/kg DW	13
Most species		
Normal	0.05–5.0 mg/kg DW	13
Toxic	More than 50 mg/kg DW	13
Sewage sludge; maximum addition to agricultural soils		
Europe	30–75 kg sludge/ha soil	1
South Africa	200 mg/kg DW sludge	24
United States; soils with low exchange capacity vs. soils with high exchange capacity		
Maryland	140 kg/ha vs. 280 kg/ha	1
Massachusetts	56 kg/ha vs. 112 kg/ha	1
Minnesota and Vermont	56 kg/ha vs. 112–224 kg/ha	1
Missouri	140 kg/ha vs. 280–560 kg/ha	1
New York, all soils	34–50 kg/ha	1
Oregon	50 kg/ha vs. 100–200 kg/ha	1
Wisconsin	50–100 kg/ha vs. 150–200 kg/ha	1
Soils; suitability for crop production		
Canada; Alberta; acidic soils; acceptable	Less than 250 mg/kg DW	1
The Netherlands		
Background	50 mg/kg DW	1
Moderate contamination	100 mg/kg DW	1
Unacceptable and requires cleanup	More than 500 mg/kg DW	1
Russia; maximum acceptable concentration; extractable by ammonium acetate buffer at pH 4.6	4.0 mg/kg soil	1
South Africa, no phytotoxicity or elevated nickel concentrations in crops	38 mg/kg DW soil	24
United States; New Jersey; acceptable	Less than 100 mg/kg DW soil	1
MAMMALS, EXCEPT HUMANS		
Air		
Laboratory white rat, <i>Rattus</i> sp.		
Adverse effects; nickel sulfate	More than 0.1 mg/m ³	9
No adverse effects		
Nickel refinery dust	Equivalent to less than 0.84 mg/kg BW daily	9
Nickel subsulfide	Equivalent to less than 1.7 mg/kg BW daily	9
Nickel sulfate	Less than 0.1 mg/m ³	9
Rodents, <i>Mus</i> spp., <i>Rattus</i> spp.		
Adverse effects; nickel oxide, nickel sulfate	More than 0.02 mg/m ³	14
No adverse effects; nickel chloride, nickel subsulfide	Less than 0.1 mg/m ³	4
Diet		
To prevent deficiency		
Rats, <i>Rattus</i> spp.	More than 50 µg/kg ration	9, 10, 15
Ruminants (<i>Bos</i> spp.), swine (<i>Sus</i> spp.)	More than 100 µg/kg DW ration ^b	9, 10

Table 6.10 (continued) Proposed Nickel Criteria for Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Nickel Concentration	Reference ^a
No observable adverse effects during chronic exposure		
Cattle, <i>Bos</i> spp.	Less than 0.5 mg/kg DW ration	10
Dogs (<i>Canis</i> sp.), rats (<i>Rattus</i> spp.), monkeys (<i>Macaca</i> spp.)	Less than 1.0 mg/kg ration	4
Rat	Equivalent to 16.7 µg/kg BW daily ^c	9
Various species	Less than 100 mg/kg ration, equivalent to 0.8 to less than 40.0 mg/kg BW daily	4
Adverse effects expected		
Cattle		
Adults	More than 50 mg/kg ration	16
Calves	More than 5 mg/kg ration, equivalent to more than 0.16 mg/kg BW daily	4, 16
Dogs	Equivalent to more than 1.3 mg/kg BW daily	14
Mammals, most species	More than 500 to 2500 mg/kg diet, equivalent to 10–50 mg Ni/kg BW daily	4
Drinking water		
Adverse effects observed		
Rat	5 mg/L, equivalent to 0.35 mg/kg BW daily	4
Most species	200–225 mg/L	4
Tissue residues		
Evidence of significant nickel exposure		
Kidney	More than 10 mg/kg DW	4
Liver	More than 3 mg/kg DW	4
HUMAN HEALTH		
Air		
Cancer risk		
Increased risk; soluble nickel compounds	More than 1 to 2 mg/m ³	13
No increased risk; metallic nickel	Less than 0.5 mg/m ³	13
Industrial plant; United States; nickel carbonyl		
Safe	Daily average less than 1.0 µg/L; single air sample less than 40 µg/L	17
Discontinue operations	More than 1 to 5 µg/L daily average; single air sample more than 200 to 2000 µg/L	17
Shut down plant	Daily average more than 5 µg/L; single air sample more than 2000 µg/L	17
Outside industrial plant; nickel carbonyl		
Acceptable	Less than 0.3 µg/L monthly average	17
Shut down plant	More than 1.0 µg/L monthly average	17
Safe		
Canada		
Soluble nickel compounds	Less than 0.1 mg/m ³	18
Sparingly soluble nickel compounds	Less than 1.0 mg/m ³	18
Nickel carbonyl	Less than 0.12 mg/m ³ (equivalent to less than 0.35 mg Ni(CO) ₄ /m ³)	18
Former Soviet Union		
Nickel metal, nickel monoxide and sulfide dust, soluble nickel compounds	Less than 0.5 mg/m ³	19
Nickel carbonyl	Less than 0.005 mg/m ³	19
Germany; nickel carbonyl	Less than 0.7 mg/m ³	19
Sweden; nickel metal	Less than 0.01 mg/m ³	19

Table 6.10 (continued) Proposed Nickel Criteria for Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Nickel Concentration	Reference^a
United States		
Nickel carbonyl	Less than 0.007 mg/m ³	19
Nickel metal and relatively insoluble nickel compounds; 8 h daily, 40 h weekly	Less than 1.0 mg/m ³	6, 9, 19
Inorganic nickel in workplace (elemental and all nickel compounds except organonickel compounds with a covalent C-Ni bond, such as nickel carbonyl); 10-h work shift, 40-h workweek, over a working lifetime	Less than 0.015 mg/m ³	20, 25
Water soluble nickel compounds; 8 h daily, 40 h weekly	Less than 0.1 mg/m ³	9, 19
Oral, via diet and drinking water		
Safe chronic exposure via diet or drinking water; soluble nickel compounds	Less than 0.002 mg/kg BW daily	9
Diet; Australia; marine fish muscle; acceptable concentration	Less than 1.0 mg/kg FW	21
Drinking water		
Acceptable daily intake for 70-kg person (with a safety factor of 1000)	0.031 mg daily (equivalent to 0.443 µg/kg BW daily)	6
Concentrations developed for noncarcinogenic effects		
Daily intake, lifetime exposure, 70-kg adult (safety factor of 100)	Less than 350 µg/L	15
Daily intake, 10-day health advisory for 10-kg child (with safety factor of 100)	Less than 1.0 mg/L	15, 25
Daily intake, 10-day health advisory for 70-kg adult (with safety factor of 100)	Less than 3.5 mg/L	15, 25
Water containing edible fishery products		
From ingestion through water and nickel-contaminated fishery products	Less than 13.4 µg total recoverable Ni/L	6
From consumption of fish and shellfish products alone	Less than 101.0 µg/L	6
Tissue residues		
Plasma; total nickel; nickel workers; considered elevated	More than 11.9 µg/L	22
Serum; total nickel		
Normal	Less than 2.6 µg/L, excretion of 2.6 µg daily	22
Elevated (near nickel mine)	More than 4.6 µg/L, excretion of 7.9 µg daily	22
Urine; nickel carbonyl		
Mild exposure	Less than <0.1 mg/L during the first 8 h after exposure	22, 23
Significant exposure	More than 0.1 mg/L during the first 8 h after exposure	23
Urine; total nickel; nickel workers; considered elevated	More than 129 µg/L	22

^a 1, Beyer 1990; 2, Rutherford and Mellow 1994; 3, Nebeker et al. 1985; 4, Outridge and Scheuhammer 1993; 5, Enserink et al. 1991; 6, USEPA 1980; 7, Sreedevi et al. 1992a; 8, Nielsen et al. 1975a; 9, USPHS 1993; 10, Hausinger 1993; 11, Cain and Pafford 1981; 12, Jenkins 1980b; 13, WHO 1991; 14, Hughes et al. 1994; 15, USEPA 1985; 16, Stevens 1991; 17, NAS 1975; 18, NRCC 1981; 19, Sevin 1980; 20, USPHS 1977; 21, Sharif et al. 1993; 22, Norseth and Piscator 1979; 23, Norseth 1986; 24, Steyn et al. 1996; 25, USPHS 1995.

^b Elevated requirement may reflect increased use by rumen bacteria.

^c Based on no observable adverse effects during chronic exposure to diets containing 100 mg Ni (as soluble salts) per kg ration (= 5 mg Ni/kg BW daily) divided by uncertainty factor of 300.

6.9 SUMMARY

Nickel is found in air, soil, water, food, and household objects; ingestion or inhalation of nickel is common, as is dermal exposure. Recent estimates suggest that as much as 28,100 tons of nickel are introduced into the atmosphere each year from natural sources and as much as 99,800 tons from human activities. In the atmosphere, nickel is mostly suspended onto particulate matter. In natural waters, the dominant chemical species is Ni^{2+} in the form of $(\text{Ni}(\text{H}_2\text{O})_6)^{2+}$. In alkaline soils, the major components of the soil solution are Ni^{2+} and Ni(OH)^+ ; in acidic soils, the main solution species are Ni^{2+} , NiSO_4 , and NiHPO_4 .

Nickel is an essential micronutrient for maintaining health in certain species of plants and animals. Its deficiency effects from dietary deprivation have been induced experimentally in many species of birds and mammals. To prevent nickel deficiency in rats and chickens, diets should contain at least 50 μg Ni/kg ration, while cows and goats require more than 100 μg Ni/kg rations, perhaps reflecting the increased use by rumen bacteria. Nickel deficiency is not a public health concern for humans because daily oral intake is sufficient to prevent deficiency effects.

Nickel contamination from anthropogenic activities occurs locally from emissions of metal mining, smelting, and refining operations; combustion of fossil fuels; nickel plating and alloy manufacturing; land disposal of sludges, solids, and slags; and disposal as effluents. Nickel concentrations in living organisms and abiotic materials tend to be elevated in the vicinity of nickel smelters and refineries, nickel–cadmium battery plants, sewage outfalls, and coal ash disposal basins.

Adverse effects of excess nickel are documented for bacteria, algae, yeasts, higher plants, protozoans, molluscs, crustaceans, insects, annelids, echinoderms, fishes, amphibians, birds, and mammals. To protect terrestrial vegetation against decreased growth and other toxic effects, nickel concentrations in leaves should contain less than 50 mg Ni/kg DW (and in some cases less than 44 mg Ni/kg DW), growing soils should contain less than 250 mg Ni/kg DW (and in some cases <50 mg Ni/kg DW), and sewage sludge applied to agricultural soils should be limited to 30 to 140 kg Ni/surface ha at the low end and 50 to 560 kg/surface ha at the high end. To protect freshwater plants and animals against nickel, a proposed range of less than 25 to 96 μg total recoverable Ni/L is recommended by various authorities; however, certain species have reduced survival within this range. To protect marine organisms, the 24-h average for total recoverable nickel per liter should not exceed 7.1 $\mu\text{g}/\text{L}$ and the maximum concentration should not exceed 140 $\mu\text{g}/\text{L}$ at any time. However, certain marine organisms show adverse effects to as little as 30 μg Ni/L.

To protect young birds against adverse effects of excess nickel on their growth and survival, diets should contain less than 200 mg Ni/kg ration; diets of older birds should contain less than 800 mg Ni/kg ration. Nickel concentrations in avian tissues in excess of 10 mg/kg DW kidney or 3 mg/kg DW liver are sometimes associated with adverse effects.

Toxic effects of nickel to humans and laboratory mammals are documented for respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, dermal, ocular, immunological, developmental, neurological, and reproductive systems. Nickel toxicity in mammals is governed by the chemical form of nickel, dose, and route of exposure. Mammalian exposure to nickel by inhalation or cutaneous contact was more significant than oral exposure. To protect humans and other mammals against respiratory effects, proposed air-quality criteria are 0.01 to less than 1.0 mg/m³ for metallic nickel and sparingly soluble nickel compounds and 0.005 to 0.7 mg/m³ for nickel carbonyl. Most species of mammals tested had normal growth and survival during chronic exposure to dietary nickel (equivalent to 0.8 to 40 mg Ni/kg BW daily) and reduced growth and survival when fed diets containing 500 to 2500 mg Ni/kg ration (equivalent to 10 to 50 mg Ni/kg BW daily). Proposed nickel criteria for sensitive species by way of the diet or drinking water now range from 2 to less than 443 μg total Ni/kg BW daily for soluble nickel compounds, less than 1.0 mg Ni/kg FW diet, and less than 350 μg Ni/L in drinking water. Nickel concentrations in human tissues now considered elevated include 4.6 $\mu\text{g}/\text{L}$ serum, 11.9 $\mu\text{g}/\text{L}$ plasma, and 100 to 129 $\mu\text{g}/\text{L}$ urine; comparable data for mammalian wildlife are lacking.

Some forms of nickel are carcinogenic to humans and animals, but only when exposure is by the respiratory route. Toxic and carcinogenic effects of nickel compounds are associated with nickel-mediated oxidative damage to DNA and proteins and to inhibition of cellular antioxidant defenses. Some nickel compounds are weakly mutagenic in a variety of test systems, but much of the evidence is inconclusive or negative. In mammals, no teratogenic effects of nickel compounds occur by way of inhalation or ingestion, except from nickel carbonyl. Inhaled nickel carbonyl results in comparatively elevated nickel concentrations in lung, brain, kidney, liver and adrenals, and is the most hazardous form of nickel.

Overall, nickel is not an immediate threat to the health of plants, animals, and humans at environmentally encountered levels, except in the case of nickel carbonyl, and progress has been made toward minimizing or eliminating occupational nickel exposure.

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CHAPTER 7

Silver

7.1 INTRODUCTION

Silver (Ag) found in the body of mammals (including humans) has no known biological purpose and is suspected of being a contaminant (Smith and Carson 1977). Silver, as ionic Ag⁺, is one of the most toxic metals known to aquatic organisms in laboratory testing, although large industrial losses to the aquatic environment are probably infrequent because of its economic value as a recoverable resource (National Association of Photographic Manufacturers [NAPM] 1974; Nebeker et al. 1983). Silver, however, is of concern in various aquatic ecosystems because of the severity of silver contamination in the water column, sediments, and biota. San Francisco Bay, for example, is affected by discharges of silver in wastewater outfalls and by the diagenic remobilization of silver from contaminated sediments in the estuary (Luoma and Phillips 1988; Rivera-Duarte and Flegal 1993).

The principal industrial use of silver is as silver halide in the manufacture of photographic imaging materials; other products include jewelry, coins, indelible inks, and eating utensils (Klaassen et al. 1986). In medicine, silver salts are used as caustics, germicides, antiseptics, and astringents; the use of silver nitrate for prophylaxis of ophthalmia neonatorum in the eyes of newborn infants is a legal requirement in some states (Klaassen et al. 1986). Long-term industrial or medical exposure to silver and its compounds may increase blood concentrations of silver to levels which can have toxic effects, such as induction of sarcomas, anemia, and enlargement of the heart (Aoki et al. 1993). Repeated occupational handling of silver objects, especially after repeated minor injuries, may result in localized argyria — a bluish-gray discoloration of the skin at the exposed site (Fowler and Nordberg 1986). In humans, the most common noticeable effects of chronic exposure to silver and its compounds are generalized argyria, localized argyria, and argyrosis (argyria of the eye, usually; Smith and Carson 1977). Generalized argyria consists of a slate-gray pigmentation of the skin and hair caused by deposition of silver in the tissues, a silver coloration of the hair and fingernails, and a blue halo around the cornea and in the conjunctiva. Acute toxic effects in humans have resulted only from accidental or suicidal overdoses of medical forms of silver (Smith and Carson 1977).

Ecological and toxicological aspects of silver are reviewed by Smith and Carson (1977), the U.S. Environmental Protection Agency [USEPA] (1980, 1987), Lockhart (1983), the U.S. Public Health Service [USPHS] (1990), Andren et al. (1993, 1994), Andren and Bober (1995), Eisler (1996), Mukherjee (1997), and Ratte (1999).

7.2 SOURCES AND USES

7.2.1 General

About 2.47 million kg of silver are lost each year to the domestic biosphere, mostly (82%) as a result of human activities. As discussed later, the photography industry accounts for about 47% of all silver discharged into the environment from anthropogenic sources. In 1990, about 50% of the refined silver consumed domestically was used to manufacture photographic products; 25% in electrical and electronic products; 10% in electroplated ware, sterlingware, and jewelry; 5% in brazing alloys; and 10% in other products and processes.

7.2.2 Sources

Silver is a rare but naturally occurring metal, often found deposited as a mineral ore in association with other elements (USPHS 1990). Argentite is the main ore from which silver is extracted by cyanide, zinc reduction, or electrolytic processes (Fowler and Nordberg 1986). Silver is frequently recovered as a by-product from smelting of nickel ores in Canada, from lead-zinc and porphyry copper ores in the United States, and from platinum and gold deposits in South Africa (Smith and Carson 1977). About 12 to 14% of the domestic silver output is recovered from lead ores and about 4% from zinc ores. Secondary sources of silver comprise new scrap generated in the manufacture of silver-containing products; coin and bullion; and old scrap from electrical products, old film and photoprocessing wastes, batteries, jewelry, silverware, and bearings (Smith and Carson 1977).

Silver is produced in 68 countries, but most (75%) of the world's silver (excluding the former Soviet bloc) is mined in the United States, Mexico, Canada, Australia, and Japan. The United States produces about 50% of the world's supply of refined silver (Smith and Carson 1977). The primary silver mines of the United States are in the Coeur d'Alene mining district in the northern Idaho panhandle (USPHS 1990). Between 1949 and 1970, the United States consistently accounted for less than 15% of the global silver production and consumed 34 to 64% (Heyl et al. 1973). Since 1951, silver consumption in the United States has exceeded its extraction from ore (USPHS 1990). In 1979, about 95% of the silver in domestic production was from Idaho, Nevada, Arizona, Colorado, Utah, Montana, and Missouri (U.S. Bureau of Mines 1980). End-use categories of silver consumed domestically in 1979 included photography (39%), electrical and electronic components (25%), sterlingware and electroplated materials (15%), and brazing alloys and solders (8%). In 1979, the photographic industry was located mainly in New York, and most other end-use manufacturers were in Connecticut, New York, Rhode Island, and New Jersey (U.S. Bureau of Mines 1980).

World production of silver increased from 7.4 million kg in 1964 to 9.06 million kg in 1972 and to 9.67 million kg in 1982 (Fowler and Nordberg 1986). In 1986, 13.06 million kg of silver was produced globally; the United States produced 1.06 million kg in 1986 but consumed 3.94 million kg (USPHS 1990). In 1990, the estimated world mine production of silver was 14.6 million kg; major producers were Mexico with 17% of the total, the United States with 14%, Peru with 12%, the former Soviet Union with 10%, and Canada with 9% (Reese 1991). In the United States during 1990, about 160 mines produced silver worth an estimated value of \$320 million; most (71%) of the 1990 mine production was in Nevada (32%), Idaho (21%), Montana (11%), and Arizona (7%). In 1990, 22 major refiners of commercial grade silver and more than 5000 silver fabricating and manufacturing firms were located primarily in the northeastern states. Of the silver imported into the United States in 1990, 44% came from Mexico, 34% from Canada, 5% from Peru, and 4% from Chile. Most was exported after transformation to sterlingware, coinage, and other finished products. Melting and refining old scrap silver in 1990 accounted for 500,000 kg of silver (Reese 1991).

Table 7.1 Estimated Release of Silver to the Environment in the United States in 1978

Compartment and Source Category	Metric Tons ^a
ATMOSPHERE	
Metals production	30
Urban refuse combustion	10
Coal and petroleum combustion	9
Iron and steel production	7
Cloud seeding	3
Cement manufacture	2
Other	29.7
AQUATIC	
Soil erosion (natural source)	438
Urban runoff	72
Sewage treatment plants	70
Photographic developing	65
Photographic manufacture	54
Other	6
TERRESTRIAL	
Photographic industry	630
Urban refuse	445
Sewage treatment	220
Metals production	165
Electrical contacts and conductors	150
Alloys and solders	60
Other	5

^a Of the total silver released to the domestic environment in 1978 (2,470,700 kg), about 3.7% entered the atmosphere, 28.5% the aquatic environment, and 67.8% the terrestrial ecosystem.

Data from U.S. Public Health Service (USPHS). 1990. Toxicological profile for silver. *Agen. Toxic Subs. Dis. Reg.* TP-90-24. 145 pp.; Purcell, T.W. and J.J. Peters. 1998. Sources of silver in the environment. *Environ. Toxicol. Chem.* 17:539-546.

Emissions from smelting operations, manufacture and disposal of certain photographic and electrical supplies, coal combustion, and cloud seeding are some of the anthropogenic sources of silver in the biosphere (Freeman 1979). Fallout from cloud seeding with silver iodide is not always confined to local precipitation; silver residuals have been detected several hundred kilometers downwind of seeding events (Freeman 1979). In 1978, the estimated loss of silver to the environment in the United States was 2.47 million kg, mostly to terrestrial and aquatic ecosystems; the photography industry alone accounted for about 47% of all silver discharged into the environment from anthropogenic sources (Smith and Carson 1977; Table 7.1). In California, anthropogenic sources contributed 50% more silver to sediments of coastal basins than natural sources, as judged by sedimentary basin fluxes of $0.09 \mu\text{g}/\text{cm}^2$ in anthropogenic sources of silver and $0.06 \mu\text{g}/\text{cm}^2$ in natural sources (Bruland et al. 1974). Sometimes, liquid effluents from the nuclear industry contained significant quantities of radiosilver-110m (Berthet et al. 1992). In Lake Michigan, storms contribute a large fraction of the annual load of tributary-derived silver; concentrations of particle-bound silver in many rivers during storms were more than $0.1 \mu\text{g}/\text{L}$ (Shafer et al. 1995).

Most of the silver lost to the environment each year enters terrestrial ecosystems, where it is immobilized in the form of minerals, metal, or alloys; agricultural lands may receive as much as 80,000 kg of silver from photoprocessing wastes in sewage sludge. An estimated 150,000 kg of silver enter the aquatic environment every year from the photography industry, mine tailings, and electroplaters (Smith and Carson 1977). During processing of photographic paper and film, silver is generally solubilized as the tightly bound thiosulfate complex. Silver thiosulfate in secondary biological waste treatment plants is converted to insoluble silver sulfide, which is removed in the sludge; only trace amounts of complexed and adsorbed silver are discharged into the aquatic environment. The silver incorporated into the sludge is immobile and should not restrict the use of sludge for the enrichment of soils (Dagon 1973; Bard et al. 1976; Cooley et al. 1988). The atmosphere receives 300,000 kg of silver each year from a variety of sources, but atmospheric concentrations are not known to exceed the occupational threshold limit value of 10 µg total Ag/m³ (Smith and Carson 1977).

Daily intake of total silver from all sources by humans in the United States ranged from 70 to 88 µg; diet accounted for 35 to 40 µg daily (USEPA 1980). Sources of elevated dietary silver include seafood from areas near sewage outfalls or industrial sources and crops grown in areas with high ambient levels of silver in the air or soil (USPHS 1990). Most occupational exposures to silver occur through inhalation of silver-containing dusts or dermal exposure to photographic compounds. Dermal routes of human exposure to silver include handling of silver-containing processing solutions used in radiographic and photographic materials, dental amalgams, and silver sulfadiazine cream and solutions for treating burns (USPHS 1990).

7.2.3 Uses

Silver was used for ornaments and utensils for almost 5000 years, and as a precious metal, a monetary medium, and a basis of wealth for more than 2000 years. Until the late 1960s, it was used extensively for coinage (Heyl et al. 1973). Since 1970, U.S. coinage has not contained silver, although minting of as many as 45 million silver-clad subsidiary coins has been authorized (Smith and Carson 1977). Industrial consumption of silver in the United States between 1966 and 1972 totaled 4.67 million kg, primarily in the manufacture of photographic materials, electrical contacts and conductors, and sterlingware (Table 7.2). In 1973, silver was used mainly in photographic materials (29%), electrical and electronic components (22%), sterlingware (20%), electroplated ware (10%), brazing wares (20%), dental and medical products, catalysts, bearings, and jewelry (9%; Heyl et al. 1973). In 1986, photographic materials accounted for 45% of the silver consumption in the United States; electrical and electronic components, 25%; jewelry, sterlingware, and electroplated ware, 11%; alloys and solders, 5%; and mirrors, dental amalgam, medical supplies, chemicals, water purification, and cloud seeding, 14% (USPHS 1990). Silver, as silver iodide, is used in the United States for weather modification including rain and snow making and hail suppression; as much as 3110 kg of silver is used for this purpose annually (Smith and Carson 1977). Silver nitrate in hair dyes has been in use regularly for almost 200 years (USEPA 1980), even though its use may lead to argyria (Smith and Carson 1977). In 1990, about 50% of the refined silver consumed domestically was used to manufacture photographic and X-ray products; 25% in electrical and electronic products; 10% in electroplated ware, sterlingware, and jewelry; 5% in brazing alloys; and 10% in other uses (Reese 1991).

Because of its bacteriostatic properties, silver compounds are used in filters and other equipment to purify the water in swimming pools and drinking water, and in the processing of foods, drugs, and beverages (Smith and Carson 1977; USEPA 1980; USPHS 1990). Activated charcoal filters coated with metallic silver to yield water concentrations of 20 to 40 µg Ag/L are used in filtering systems of swimming pools to control bacteria (USEPA 1980). Silver may also function as an algicide in swimming pools if chlorine, bromine, and iodine are absent; it prevents growth of blue-green algae at 80 to 140 µg Ag/L (Smith and Carson 1977). Aboard orbiting Russian space stations

Table 7.2 Industrial Domestic Use of Silver During 1966–72 (Total silver used was 4.67 million kg)

Category	Percent of Total
Photographic materials	28.1
Contacts and conductors	20.2
Sterling ware	17.1
Brazing alloys and solders	10.1
Electroplated wares	10.0
Batteries	5.1
Jewelry	3.3
Miscellaneous	2.4
Dental and medical supplies	1.5
Mirrors	1.2
Bearings	0.4

Smith, I.C. and B.L. Carson. 1977. *Trace Metals in the Environment*. Volume 2. *Silver*. Ann Arbor Sci. Publ., Ann Arbor, MI. 469 pp.

and spaceships, potable water is routinely treated with 100 to 200 µg Ag/L to eliminate microorganisms; sterilization is usually complete in 20 min (Smith and Carson 1977). Silver-containing ceramic water filters are used to purify potable water in Swiss ski resorts, German breweries, British ships, oil tankers, drilling rigs, U.S. home consumption, and more than half the world's airlines. Monovalent and metallic silver compounds are considered excellent disinfectants; however, Ag²⁺ and Ag³⁺ are about 50 to 200 times more effective than Ag⁺ or Ag⁰ (Antelman 1994), possibly because of their higher oxidation states (Kirschenbaum 1991).

Silver nitrate was used for many years as eye drops in newborns to prevent blindness caused by gonorrhea (USPHS 1990). Laws in many states still require that a few drops of a 1 to 2% silver nitrate solution be applied to the conjunctiva of the eyes of newborn infants to prevent ophthalmia neonatorum by transmittal of gonorrhea from the mother (USEPA 1980; USPHS 1990). This treatment is still required in Denmark but no longer in Japan or Australia (USEPA 1980). Silver nitrate is not used in many U.S. hospitals because of the dangers of chemical conjunctivitis and has been replaced by antibiotics (USEPA 1980). In the United States, several silver-containing pharmaceuticals were used topically on skin or mucous membranes to assist in healing burn patients and to combat skin ulcers (Smith and Carson 1977; USEPA 1980). Oral medicines containing silver include silver acetate-containing antismoking lozenges; breath mints coated with silver; and silver nitrate solutions for treating gum disease (USPHS 1990). The widespread medical use of silver compounds for topical application to mucous membranes and for internal use has become nearly obsolete in the past 50 years because of the fear of argyria and the development of sulfonamide and antibiotic microbials (Smith and Carson 1977).

7.3 CHEMISTRY AND METABOLISM

7.3.1 General

Silver occurs naturally in several oxidation states, the most common being elemental silver (Ag⁰) and the monovalent ion (Ag⁺). Soluble silver salts are, in general, more toxic than insoluble salts. In natural waters, the soluble monovalent species is the form of environmental concern. Sorption is the dominant process that controls silver partitioning in water and its movements in soils and sediments. As discussed later, silver enters the animal body through inhalation, ingestion, mucous membranes, and broken skin. The interspecies differences in the ability of animals to accumulate, retain, and eliminate silver are large. Almost all of the total silver intake is usually

Table 7.3 Some Properties of Silver and Silver Nitrate

Variable	Silver	Silver Nitrate
Alternate names	Argentum, argentum crede Cl 77820, shell silver, silver atom, silver colloidal, silflake, silpowder, silver	Lunar caustic fused silver nitrate, molded silver nitrate argenti, nitratas, nitric acid silver (I) salt, nitric acid silver (1+) salt, silver (1+) nitrate
CAS number	7440-22-4	7761-88-8
Chemical formula	Ag	AgNO_3
Molecular weight	107.87	169.89
Physical state	Solid metal	Solid crystalline
Boiling point	2212°C	Decomposes at 440°C
Solubility	Insoluble in water; soluble in nitric acid but not sulfuric acid	Soluble in water to 1220 g/L; soluble in ethanol and acetone
Density	10.5	4.35

Data from Lockhart, H.B., Jr. 1983. Silver compounds. Pages 16–32 in *Encyclopedia of Chemical Technology*, 3rd ed. John Wiley & Sons, NY. U.S. Public Health Service (USPHS). 1990. Toxicological profile for silver. *Agen. Toxic Subs. Dis. Reg.* TP-90-24. 145 pp.

excreted rapidly in feces; less than 1% of the total silver intake is absorbed and retained in tissues, primarily liver, through precipitation of insoluble silver salts. In mammals, silver usually interacts antagonistically with selenium, copper, and Vitamin E; in aquatic environments, ionic or free silver interferes with calcium metabolism in frogs and marine annelids and with sodium and chloride uptake in gills of fishes.

7.3.2 Physical and Chemical Properties

Silver is a white, ductile metal occurring naturally in its pure form and in ores (USEPA 1980). Silver has the highest electrical and thermal conductivity of all metals. Some silver compounds are extremely photosensitive and are stable in air and water, except for tarnishing readily when exposed to sulfur compounds (Heyl et al. 1973). Metallic silver is insoluble in water, but many silver salts, such as silver nitrate, are soluble in water to more than 1220 g/L (Table 7.3). In natural environments, silver occurs primarily in the form of the sulfide or is intimately associated with other metal sulfides, especially those of lead, copper, iron, and gold, which are all essentially insoluble (USEPA 1980; USPHS 1990). Silver readily forms compounds with antimony, arsenic, selenium, and tellurium (Smith and Carson 1977). Silver has two stable isotopes (^{107}Ag and ^{109}Ag) and 20 radioisotopes; none of the radioisotopes of silver occurs naturally, and the radioisotope with the longest physical half-life (253 days) is $^{110\text{m}}\text{Ag}$. Several compounds of silver are potential explosion hazards: silver oxalate decomposes explosively when heated; silver acetylide (Ag_2C_2) is sensitive to detonation on contact; and silver azide (AgN_3) detonates spontaneously under certain conditions (Smith and Carson 1977).

Silver occurs naturally in several oxidation states, usually as Ag^0 and Ag^+ ; other possible oxidation states of silver are Ag^{2+} and Ag^{3+} (USPHS 1990). In surface freshwater, silver may be found as the monovalent ion; in combination with sulfide, bicarbonate, or sulfate; as part of more complex ions with chlorides and sulfates; and adsorbed onto particulate matter (USPHS 1990). In the aqueous phase, silver at the lowest concentrations exists as either a simple AgSH or as a simple polymer $\text{HS}-\text{Ag}-\text{S}-\text{Ag}-\text{SH}$ (Bell and Kramer 1999). At higher concentrations, colloidal Ag_2S or polysulfide complexes are formed. Silver^+ binds strongly with sulfur $^{2-}$ in inorganic and organic species, resulting in ng/L aqueous dissolved concentrations (Bell and Kramer 1999). Trace levels of dissolved silver in the presence of ferric sulfide are rapidly adsorbed and silver remaining in solution remains as acanthite (Ag_2S); however, silver thiolate complexes can be the dominant dissolved species in highly contaminated waters near urban centers or in waters with high levels of natural organic matter (Adams and Kramer 1998). The most important and crucial aspect of silver thiolate chemistry is the rapid exchange of Ag^+ among thiolates whereby Ag^+ can transfer

onto, or off, particulate materials or the cells of an organism. Silver thiolates also react rapidly with H_2S or HS^- as ligands to form Ag_2S , although the reverse process is slow (Bell and Kramer 1999). Soluble silver salts are more toxic than insoluble salts, and soluble silver ion (Ag^+) is the most toxic chemical species. In natural waters, the soluble monovalent species is the form of environmental concern (USEPA 1980). The argentous ion (Ag^+) does not hydrolyze appreciably in solution and is considered to be a mild oxidizing agent (Smith and Carson 1977). Hypervalent silver species, such as Ag^{2+} and Ag^{3+} , are significantly more effective as oxidizing agents than Ag^0 and Ag^+ (Kouadio et al. 1990; Kirschenbaum 1991; Sun et al. 1991) but are unstable in aqueous environments, especially at water temperatures near 100°C (Smith and Carson 1977). In natural waters, silver may exist as metalloorganic complexes or be adsorbed to organic materials (USEPA 1980). In freshwater and soils, the primary silver compounds under oxidizing conditions are bromides, chlorides, and iodides; under reducing conditions, the free metal and silver sulfide predominates (USPHS 1990). In river water, one study showed silver present as the monovalent ion (Ag^+) at 53 to 71% of the total silver, as silver chloride (AgCl) at 28 to 45%, and as silver chloride ion (AgCl_2^-) at 0.6 to 2.0% (USPHS 1990). Increasing salinity of brackish and marine waters increased concentrations of silver chloro complexes (AgCl^0 , AgCl_2^- , AgCl_3^{2-} , AgCl_4^{3-}); these chloro complexes retain some silver in dissolved form, and relatively small anthropogenic quantities can substantially enrich the environment (Luoma 1994; Andren et al. 1995). In the open ocean, the principal dissolved form of silver is AgCl_2^- , but the most bioavailable form may be the neutral monochloro complex AgCl (Bryan and Langston 1992).

Sorption is the dominant process that controls silver partitioning in water and its movement in soils and sediments (USEPA 1980; USPHS 1990). Silver may leach from soils into groundwater; the leaching rate increases with decreasing pH and increasing drainage (USPHS 1990). Silver adsorbs to manganese dioxide, ferric compounds, and clay minerals, and these compounds are involved in silver deposition into sediments; sorption by manganese dioxide and precipitation with halides reduce the concentration of dissolved silver, resulting in higher concentrations in sediments than in the water column (USEPA 1980). Under reducing conditions, adsorbed silver in sediments may be released and subsequently reduced to metallic silver, or it may combine with reduced sulfur to form the insoluble silver sulfide (USEPA 1980). Sediments may be a significant source of silver to the water column. In one study, anoxic sediments containing 1.0 to 27.0 grams of silver/kg DW and 10 mmoles of acid volatile sulfide/kg DW were resuspended in oxygenated seawater for several hours to days. The seawater in contact with sediment containing 10.8 g/kg had 20 µg Ag/L; seawater in contact with sediments containing 27 g Ag/kg had about 2000 µg Ag/L, which seems to be the solubility of silver in seawater (Crecelius and Phillips 1995).

The global biogeochemical movements of silver are characterized by releases to the atmosphere, water, and land by natural and anthropogenic sources, long-range transport of fine particles in the atmosphere, wet and dry deposition, and sorption to soils and sediments (USPHS 1990). The chief source of silver contamination of water is silver thiosulfate complexes in photographic developing solutions that photofinishers discard directly to sewers (Smith and Carson 1977). Secondary waste treatment converts most of the silver thiosulfate complex to insoluble silver sulfide and forms some metallic silver (Lytle 1984). About 95% of the total silver is removed in publicly owned treatment works from inputs containing municipal sewage and commercial photoprocessing effluents; effluents usually contained less than 0.07 µg ionic silver/L and concentrations were independent of the influent silver concentration (Lytle 1984; Shafer et al. 1998). Silver in sewage treatment plant effluents may be associated with suspended particles or be present as thiosulfate complex, colloidal silver complex, colloidal silver chloride, silver sulfide, or soluble organic complexes (Smith and Carson 1977). Silver on suspended matter and in colloidal forms and insoluble salts ultimately settles out in the sediments. At the water treatment plant, most of the silver is precipitated after treatment with lime or adsorbed after treatment with alum-flocculent. Chlorination converts some silver to silver chloride or to a soluble silver chloride complex (Smith and Carson 1977). Aerobic biodegradation of a photoprocessing wastewater containing 1.85 mg total Ag/L did not adversely

affect the activated sludge process (Pavlostathis and Maeng 1998). Practically all silver became associated with the sludge solids at 1840 mg Ag/kg mixed liquor suspended solids. When fresh sludge and aerobically digested sludge solids were subjected to leaching procedures, the resulting silver concentration was at least 40 times lower than the regulatory limit of 5 mg/L (Pavlostathis and Maeng 1998).

Forms of silver in atmospheric emissions are probably silver sulfide, silver sulfate, silver carbonate, silver halides, and metallic silver (Smith and Carson 1977). About 50% of the silver released into the atmosphere from industrial operations is transported more than 100 km and is eventually deposited in precipitation (USPHS 1990). Minute amounts of ^{110m}Ag have been detected in natural waters and are attributed to atmospheric fallout from nuclear explosions (Smith and Carson 1977).

A variety of spectrographic, colorimetric, polarographic, and other analytical techniques are used for routine measurement of silver in biological and abiotic samples. The detection limit of silver in biological tissues with scanning electron microscopy and X-ray energy spectrometry is 0.02 $\mu\text{g}/\text{kg}$ and sometimes as low as 0.005 $\mu\text{g}/\text{kg}$. In air, water, and soil samples, the preferred analytical procedures include flame and furnace atomic absorption spectrometry, plasma emission spectroscopy, and neutron activation (Fowler and Nordberg 1986; USPHS 1990). Sensitive anodic stripping voltammetry techniques have recently been developed to measure free silver ion in surface waters at concentrations as low as 0.1 $\mu\text{g}/\text{L}$ (Schildkraut 1993; Song and Osteryoung 1993; Schildkraut et al. 1998).

7.3.3 Metabolism

The acute toxicity of silver to aquatic species varies drastically by the chemical form and correlates with the availability of free ionic silver (Wood et al. 1994). In natural aquatic systems, ionic silver is rapidly complexed and sorbed by dissolved and suspended materials that are usually present. Complexed and sorbed silver species in natural waters are at least one order of magnitude less toxic to aquatic organisms than the free silver ion (Rodgers et al. 1994; Ratte 1999). Thus, silver nitrate — which is strongly dissociated — is extremely toxic to rainbow trout (*Oncorhynchus mykiss*); the 7-day LC₅₀ value is 9.1 $\mu\text{g}/\text{L}$. Silver thiosulfate, silver chloride, and silver sulfide were relatively benign (7-day LC₅₀ values >100,000 $\mu\text{g}/\text{L}$), presumably due to the abilities of the anions to remove ionic silver from solution (Wood et al. 1994, 1996b; Hogstrand et al. 1996).

For freshwater fish, the acute toxicity of silver is caused solely by Ag^+ , interacting at the gills, inhibiting basolateral Na^+ , K^+ -ATPase activity. Disruption of this enzyme inhibits active Na^+ and Cl^- uptake and, therefore, osmoregulation by the fish (Wood et al. 1999). The primary toxic mechanism of silver in rainbow trout is the interruption of ionic regulation at the gills, stopping active Na^+ and Cl^- uptake without increasing passive efflux, thereby causing net ion loss (Webb and Wood 1998). However, concentrations of silver in the gills of rainbow trout did not correlate to Ag^+ concentrations in the medium, and no correlation was found between gill silver levels and either Na^+ influx rates or gill Na^+/K^+ ATPase activity (Bury et al. 1999b). Morgan et al. (1995) suggest that the sites of action of silver toxicity in rainbow trout may be inside the cells of the gill epithelium rather than at the external surface and linked to carbonic anhydrase — a gill enzyme involved in Na^+ and Cl^- transport. Silver concentrations and metallothionein levels in gills and livers of rainbow trout increased with increasing exposure to silver; internal toxicity associated with increased silver accumulations may be lessened by the formation of silver-induced metallothioneins (Hogstrand et al. 1996). A key toxic effect of Ag^+ in freshwater is the inhibition of branchial Na^+ , K^+ -ATPase activity, which leads to blockade of active Na^+ and Cl^- across the gills; increased metabolic ammonia production and internal buildup occur as part of this acute stress syndrome (Hogstrand and Wood 1998). The probable cause of hyperventilation in rainbow trout exposed to silver nitrate was a severe metabolic acidosis manifested in decreased arterial plasma pH and HCO_3^- levels. Lethality of ionic silver to trout is probably due to surface effects at the gills — disrupting Na^+ , Cl^- , and H^+ — causing secondary fluid volume disturbance, hemoconcentration, and eventual cardiovascular collapse (Wood et al. 1994, 1995, 1996a, 1996b). Acidosis in rainbow

trout — due to a net uptake of acidic equivalents from the water — in the intracellular compartment accounts for the continual loss of K⁺ to the water in the absence of any change in plasma K⁺ (Webb and Wood 1998).

In seawater, silver nitrate is less toxic than in freshwater (Wood et al. 1995; Wood et al. 1999). This difference is probably due to the low concentration of free Ag⁺ (the toxic moiety in freshwater) in seawater, the high levels of chloride, and the predominance of negatively charged silver-chloro complexes. However, high levels of silver nitrate are toxic to marine invertebrates despite the absence of Ag⁺, and this is attributed to the bioavailability of stable silver-chloro complexes (Wood et al. 1995; Ratte 1999). In seawater, in contrast to freshwater, plasma Na⁺ and Cl⁻ rise rather than fall, and death may result from the elevated Na⁺ and Cl⁻ concentrations combined with dehydration (Hogstrand and Wood 1998). Osmoregulatory failure occurs in marine teleosts exposed to high concentrations of Ag⁺, and the intestine is the main toxic site of action (Wood et al. 1999).

Ionic silver interferes with calcium metabolism of frogs and marine polychaete worms. Silver ions cause muscle fibers of frogs (*Rana* spp.) to deteriorate by allowing excess calcium to enter the cell. Studies with frog skeletal muscle fibers exposed to 1.08 mg/L showed that silver activated the calcium ion channel by acting on sulfhydryl groups in a calcium ion channel protein (Aoki et al. 1993). In marine polychaetes contaminated with silver, the calcium content of nephridial cells was reduced, although silver was not detected in the calcium vesicles (Koechlin and Grasset 1988). Silver binds with protein sulfhydryl groups, and this process protects the worm against silver poisoning (Koechlin and Grasset 1988). In marine molluscs, however, sulfide anion was the ligand of silver (Truchet et al. 1990). In marine gastropods (*Littorina littorea*), silver was stored in the basement membranes of the digestive system; in clams (*Scrobicularia plana*), it was stored in the basement membrane of the outer fold of the mantle edge and in the amoebocytes (Truchet et al. 1990). The availability of free silver in marine environments was strongly controlled by salinity because of the affinity of silver for the chloride ion (Sanders et al. 1991). Silver sorbs readily to phytoplankton and to suspended sediments. As salinity increases, the degree of sorption decreases. Nearly 80% of silver sorbed to suspended sediments at low salinities desorb at higher salinities, but desorption does not occur when silver is associated with phytoplankton. Thus, silver incorporation in or on cellular material increases the retention of silver in the estuary, reducing the rate of transport (Sanders and Abbe 1987).

Silver may enter the body of mammals through inhalation, ingestion, mucous membranes, or broken skin (Smith and Carson 1977; USEPA 1980; Klaassen et al. 1986; USPHS 1990). In most cases of occupational argyrosis, absorption occurs via the respiratory tract or at the eyes (Smith and Carson 1977; USEPA 1980). Silver is retained by all body tissues; tissue concentrations are related to the dose, form of administered silver, and route of exposure. Silver also accumulates in mammalian tissues with increasing age of the individual, even if none is administered intentionally. Inside the body, silver is transported mainly in the protein fractions of plasma, presumably as silver albuminate or silver chloride (Smith and Carson 1977; USEPA 1980). In mammals, the highest concentrations of silver are usually found in the liver and spleen and to some extent in the muscles, skin, and brain (Fowler and Nordberg 1986). The primary sites of silver deposition in the human body are the liver, skin, adrenals, lungs, muscle, pancreas, kidney, heart, and spleen. Silver is also deposited in blood vessel walls, the trachea, and bronchi (Smith and Carson 1977). Dogs exposed to silver by inhalation accumulated most of the administered dose in the liver; concentrations in the lung, brain, skin, and muscle were lower (USEPA 1980; Fowler and Nordberg 1986). Intravenous injection of silver produces accumulations in the spleen, liver, bone marrow, lungs, muscle, and skin (Klaassen et al. 1986). Intestinal absorption of silver by rodents, canids, and primates has been recorded at 10% or less after ingestion of radioactive silver; a value of 18% was estimated in a single human given radiosilver acetate (USEPA 1980; Klaassen et al. 1986), and about 3 to 10% of the absorbed silver is retained in the tissues (Smith and Carson 1977). In a human given radioactive silver, more than 50% of the whole-body burden of silver was found in the liver after 16 days (Fowler and Nordberg 1986).

Deposition of silver in tissues of warm-blooded animals results from precipitation of relatively insoluble silver salts, such as silver chloride and silver phosphate (USPHS 1990). These insoluble salts may be transformed into soluble silver sulfide albuminates that bind or complex with RNA, DNA, and proteins, or they may be reduced to metallic silver by ascorbic acid or catecholamines. In humans with argyria, the blue or gray skin discoloration is caused by the photoreduction of silver chloride to metallic silver during exposure to ultraviolet light. Metallic silver, in turn, is oxidized and bound as black silver sulfide (USPHS 1990). Silver sulfide (Ag_2S) is localized in extracellular structures such as basement membranes and in macrophageous cells (Baudin et al. 1994). Before storage as a stable mineral combination, silver binds to proteins that contain a large proportion of sulfhydryl groups such as metallothioneins (Fowler and Nordberg 1986). The last stage in the catabolic pathway of these proteins leads to storage of silver after reaction with a sulfur ligand (Baudin et al. 1994). These mechanisms explain why liver, the most important organ for protein synthesis, shows the highest capacity for silver accumulation. High concentrations of silver in the digestive tract are linked to the numerous basement membranes contained in its tissues. Interspecies differences in the ability to accumulate, retain, and eliminate silver are large (Baudin et al. 1994).

The enzyme-inhibiting action of silver ions may be due to the binding of sulfhydryl groups of some enzymes. Binding, in certain enzymes, is probably at a histidine imidazole group; in the case of glucose oxidase, silver ions compete with molecular oxygen as a hydrogen acceptor (Smith and Carson 1977). About 60% of the silver in liver and kidneys of silver-injected rats were in the cytosol fractions bound to the high-molecular-weight proteins and metallothionein fractions; however, in spleen and brain only 30% of the total tissue silver was found in the cytosol fractions (Fowler and Nordberg 1986). At moderate doses (0.4 mg Ag/kg BW) in rats, the liver handles most of the absorbed silver from the body in the bile; at higher doses, silver deposits are markedly increased in the skin (USEPA 1980). In house sparrows (*Passer domesticus*), a silver-binding protein was identified in liver after radiosilver-110m injection; the protein was heat-stable, resistant to low pH, and of low molecular weight (Kumar and Bawa 1979). The properties of the hepatic silver-binding protein in birds were similar to other studied metallothioneins, but more research is needed to distinguish differences from mammalian metallothioneins (Kumar and Bawa 1979).

Most absorbed silver is excreted into the intestines by way of the liver into the bile and subsequently excreted in feces; urinary excretion of silver is generally very low (USEPA 1980; Fowler and Nordberg 1986; Klaassen et al. 1986; USPHS 1990). Rodents, monkeys, and dogs given radioactive silver salts by oral and other routes excreted more than 90% of the absorbed dose in the feces (Fowler and Nordberg 1986). Rats injected intravenously with radioactive silver nitrate excreted silver in bile mainly bound to a low-molecular-weight complex similar to glutathione (Fowler and Nordberg 1986). Excretion was faster, and percentages excreted by mice, rats, monkeys, and dogs were larger when silver was administered orally than by intravenous or intraperitoneal injection (Smith and Carson 1977).

Among mammals, low doses of ingested silver were eliminated from the body within 1 week (USPHS 1990). In rats, mice, and rabbits, about 99% of a single oral dose of silver was eliminated within 30 days (USEPA 1980). Time for 50% clearance of silver in rats, mice, monkeys, and dogs after oral ingestion was about 1 day; this short half-time is due, in part, to fecal elimination of unabsorbed silver. The half-times were longer (1.8 to 2.4 days) after intravenous injection (Fowler and Nordberg 1986). Rodents dosed with silver accumulated high initial concentrations in the liver, which greatly decreased within 10 days; however, silver concentrations in spleen and brain were retained for longer periods. The biological half-time of radiosilver in rats given a single intraperitoneal injection was 40 h in whole blood, plasma, kidney, and liver; 70 h in spleen; and 84 h in brain. After exposure by inhalation, dogs cleared 59% of an administered dose of radiosilver-110m from the lungs in 1.7 days and from the liver in 9 days (Fowler and Nordberg 1986). The mean daily intake of silver in humans is about 88 µg; about 60 µg is excreted daily in the feces (Smith and Carson 1977). In humans, the whole-body effective half-time of persistence was 43 days.

(USEPA 1980). The biological half-time of silver in the lungs of an exposed person was about 1 day; in liver it was 52 days (Fowler and Nordberg 1986). In humans, 80% of the retained silver in lung was cleared in about 1 day; 50% of the remainder was usually cleared in 3 days (USEPA 1980). In persons who had accidentally inhaled radiosilver-110m, most of the inhaled silver had a half-time persistence of about 1 day, probably because of rapid mucociliary clearance, swallowing, and fecal excretion; most of the absorbed radiosilver translocated to the liver (USEPA 1980).

Silver interacts competitively with selenium, Vitamin E, and copper and induces signs of deficiency in animals fed adequate diets or aggravates signs of deficiency when diets were lacking one or more of these nutrients; antagonistic effects of silver have been described in dogs, pigs, rats, sheep, chicks, turkey poult, and ducklings (USEPA 1980). Conversely, the addition of selenium, copper, or Vitamin E to diets of turkey poult decreased the toxicity of diets containing 900 mg Ag/kg (Fowler and Nordberg 1986). Dietary administration of silver acetate antagonized selenium toxicity; silver prevented growth depression and death in chicks fed diets containing excess selenium (USEPA 1980). The addition of selenium to the diets of rats exposed to silver in drinking water prevented growth retardation but increased the concentration of silver in liver and kidneys (Fowler and Nordberg 1986). Silver deposits in rat liver, kidneys, and other internal organs were in the form of sulfides; under high selenium exposure, the sulfur can be replaced with selenium (USPHS 1990) and formation of silver selenide deposits in the liver may be considered a silver detoxification process (USEPA 1980).

7.4 CONCENTRATIONS IN FIELD COLLECTIONS

7.4.1 General

Silver is comparatively rare in the earth's crust — 67th in order of natural abundance of the elements; the crustal abundance is an estimated 0.07 mg/kg and predominantly concentrated in basalt (0.1 mg/kg) and igneous rocks (0.07 mg/kg; Heyl et al. 1973). Silver concentrations in nonbiological materials tend to be naturally elevated in crude oil and in water from hot springs and steam wells. Anthropogenic sources associated with the elevated concentrations of silver in nonliving materials include smelting, hazardous waste sites, cloud seeding with silver iodide, metals mining, sewage outfalls, and especially the photoprocessing industry. Silver concentrations in biota were greater in organisms near sewage outfalls, electroplating plants, mine wastes, and silver-iodide seeded areas than in conspecifics from more distant sites.

7.4.2 Nonbiological Materials

Maximum concentrations of total silver recorded in selected nonbiological materials were 36.5 ng/m³ in air near a smelter in Idaho; 2 µg/m³ in atmospheric dust; 0.1 µg/L in oil well brines; 6 µg/L in groundwater near a hazardous waste site; 8.9 µg/L in seawater from Galveston Bay, Texas; 260 µg/L in the Genesee River, New York — the recipient of photoprocessing wastes; 300 µg/L in steam wells; 300 µg/L in treated photoprocessing wastewaters; 4500 µg/L in precipitation from clouds seeded with silver iodide; 31 mg/kg in some Idaho soils; 43 mg/L in water from certain hot springs; 50 mg/kg in granite; as much as 100 mg/kg in crude oils; 150 mg/kg in some Genesee River sediments; and 27,000 mg/kg in some solid wastes from photoprocessing effluents ([Table 7.4](#)). It is emphasized that only a small portion of the total silver in each of these compartments is biologically available. For example, typical publicly owned treatment works receiving photoprocessing effluents show silver removal efficiencies greater than 90%; the mean concentration of free silver ion present in the effluents from these plants ranged from 0.001 to 0.07 µg/L (Lytle 1984; Bober et al. 1992).

Table 7.4 Silver Concentrations in Representative Nonbiological Materials

Material, Units of Concentration, and Other Variables	Concentration ^a	Reference ^b
AIR, ng/m³		
Chicago, 1969	4.3	1
Heidelberg, Germany; April, 1971	4.2	1
Indiana, industrialized area	1–5	2
Industrialized areas	7.0	3
Kellogg, Idaho; near smelter, 1977	10.5; Max. 36.5	1, 2
Niles, Michigan; June, 1969	1.0	1
Rural areas		
Silver-iodide cloud-seeding area	1.0	1
Non-cloud seeded area	0.04–0.17	2, 3
San Francisco, 1970	0.15	1
U.S. National Parks	0.012–0.19	2
Vicinity of lead smelters	Max. 175	3
Vicinity of silver iodide ground-based cloud-seeding generator		
At generator site	>10,000	1
>50 m from site	0.1	1
Washington, D.C., 1974	1.1	1
ATMOSPHERIC DUST, µg/m³		
Northern hemisphere	2.0	4
DRINKING WATER, SOLID RESIDUES, mg/kg		
USA	0.08 (0.01–0.20)	1
FOSSIL FUELS, mg/kg		
Coal fly ash	Max. 10–15	2, 5
Crude oil	Max. 100	3
Fuel oil, residual	Max. 0.12	3
FRESHWATER, µg/L		
Amazon River, South America	0.23	3
Genesee River, New York; receives photoprocessing wastes; 1973		
June	90–260	1
Winter	20	1
Patuxent River, Maryland	0.08–0.1	6
Rhone River, Europe	0.38	3
United States		
Dissolved	Usually <0.2	1, 3
Rivers	0.3 (0.09–0.55)	1, 3, 5
Surface waters	2.6	3
Tap water	2.2 (0.3–5.0)	1, 5
Tap water	Max. 26	3
GROUNDWATER, µg/L		
Near hazardous waste site	6.0	2
Noncontaminated site	<0.5	4
HOT SPRINGS, µg/L		
	Max. 43,000	1
OIL WELL BRINES, µg/L		
	0.1	1

Table 7.4 (continued) Silver Concentrations in Representative Nonbiological Materials

Material, Units of Concentration, and Other Variables	Concentration^a	Reference^b
PRECIPITATION, ng/L		
From seeding clouds with silver iodide	Usually 10–300; Max. 4500	1, 2
From non-seeded clouds	Usually 0.0–20; Max. 216	1, 2
ROCK, mg/kg		
Granite, igneous	Max. 50	5
SEAWATER, µg/L		
Near shore	0.25 (0.06–2.9)	1, 2, 5
Open ocean	0.00004–0.0025	3, 7
Galveston Bay, Texas, 1989		
Dissolved	3.2 (0.2–8.9)	8
Particulate	2.8 (0.7–5.9)	8
SEDIMENTS, mg/kg		
Ireland, Cork Harbour; intertidal sites, February 1990	<0.05	9
United Kingdom		
19 estuaries	0.07–4.1	7
Contaminated vs. uncontaminated estuaries	>1 vs. <0.1	7
United States		
Marine sediments, near Pacific coast cities	1.5–3.5	4
New York, Genesee River; 1973; receives photoprocessing effluents	150	1
Puget Sound, Washington; August, 1982		
0–20 cm depth	Max. 0.67	10
51–75 cm depth	Max. 0.55	10
110–175 cm depth	Max. 0.27	10
195–265 cm depth	Max. 0.07	10
San Francisco Bay	Max. >10	7
Southern California coastal basins, contaminated by wastewater	14–20	5
SOILS, mg/kg		
Canada	0.13	2
Earth's crust	0.1	2
Hazardous waste site	4.5	2
Kellogg, Idaho	20.0 (3.2–31.0)	2
Michigan		
Agricultural	0.19	2
Industrial	0.37	2
Residential	0.13	2
SOLID WASTES, mg/kg		
Municipal wastes	3.0 (<3–7)	2
Municipal and industrial wastes	15–120	2
Photoprocessing effluents	450–27,000	2
Sewage sludge	225–960	2

Table 7.4 (continued) Silver Concentrations in Representative Nonbiological Materials

Material, Units of Concentration, and Other Variables	Concentration ^a	Reference ^b
STEAM WELLS		
Water, µg/L	Max. 300	1
Residue, mg/L	Max. 13,000	1
WASTEWATER, µg/L		
Agricultural drainage water	Max. 1	1
Entering southern California coastal basins	Max. 30	5
Municipal wastewater	0.05–45.0	1
Sewage sludge, USA	5–150	5
Photoprocessing wastes, treated	70.0 (20–300)	2, 11

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).

^b 1, USEPA 1980; 2, USPHS 1990; 3, Smith and Carson 1977; 4, Freeman 1979; 5, Fowler and Nordberg 1986; 6, Connell et al. 1991; 7, Bryan and Langston 1992; 8, Morse et al. 1993; 9, Berrow 1991; 10, Bloom and Crecelius 1987; 11, NAPM 1974.

Silver is usually found in extremely low concentrations in natural waters because of its low crustal abundance and low mobility in water (USEPA 1980). One of the highest silver concentrations recorded in freshwater (38 µg/L) occurred in the Colorado River at Loma, Colorado, downstream of an abandoned gold–copper–silver mine, an oil shale extraction plant, a gasoline and coke refinery, and a uranium processing facility (USEPA 1980). The maximum recorded value of silver in tapwater in the United States was 26 µg/L — significantly higher than finished water from the treatment plant (maximum of 5.0 µg/L) — because of the use of tin–silver solders for joining copper pipes in the home, office, or factory (USEPA 1980).

In general, silver concentrations in surface waters of the United States decreased between 1970–74 and 1975–79, although concentrations increased in the north Atlantic, Southeast, and lower Mississippi basins (USPHS 1990). About 30 to 70% of the silver in surface waters may be ascribed to suspended particles (Smith and Carson 1977), depending on water hardness or salinity. For example, sediments added to solutions containing 2 µg Ag/L had 74.9 mg Ag/kg DW sediment after 24 h in freshwater, 14.2 mg/kg DW at 1.5% salinity and 6.9 mg/kg DW at 2.3% salinity (Sanders and Abbe 1987). Riverine transport of silver to the ocean is considerable: suspended materials in the Susquehanna River, Pennsylvania — that contained as much as 25 mg silver/kg — resulted in an estimated transport of 4.5 metric tons of silver to the ocean each year (USEPA 1980). The most recent measurements of silver in rivers, lakes, and estuaries using clean techniques show levels of about 0.01 µg/L for pristine, nonpolluted areas and 0.01 to 0.1 µg/L in urban and industrialized areas (Ratte 1999).

Emissions of silver from coal-fired power plants may lead to accumulations in nearby soils (Fowler and Nordberg 1986). Silver in soils is largely immobilized by precipitation to insoluble salts and by complexation or adsorption by organic matter, clays, and manganese and iron oxides (Smith and Carson 1972).

Silver can remain attached to oceanic sediments for about 100 years under conditions of high pH, high salinity, and high sediment concentrations of iron, manganese oxide, and organics (Wingert-Runge and Andren 1994). Estuarine sediments that receive metals, mining wastes, or sewage usually have higher silver concentrations (>0.1 mg/kg DW) than noncontaminated sediments. Silver is tightly bound by sewage sludge, and elevated silver concentrations in sediments are often characteristic of areas near sewage outfalls. In the absence of sewage, silver in oxidized sediments is associated with oxides of iron and with humic substances (Bryan and Langston 1992). Sediments

in the Puget Sound, Washington, were significantly enriched in silver, in part, from human activities; concentrations were higher in fine-grained particles (Bloom and Crecilius 1987). Marine annelids and clams accumulate dissolved and sediment-bound forms of silver. Uptake of silver from sediments by marine polychaete annelids decreased in sediments with high concentrations of humic substances or copper but increased in sediments with elevated concentrations of manganese or iron (Bryan and Langston 1992).

7.4.3 Plants and Animals

Maximum concentrations of total silver recorded in field collections of living organisms ([Table 7.5](#)), in mg Ag/kg DW, were 1.5 in liver of marine mammals, 2 in liver and 6 in bone of trout from ecosystems receiving precipitation from silver-iodide seeded clouds, 7 in kidneys and 44 in liver of birds from a metals-contaminated area, 14 in marine algae and macrophytes, 30 in whole annelid worms from San Francisco Bay, 72 in skin of humans afflicted with argyria, 110 in whole mushrooms, 133 to 185 in soft parts of clams and mussels near sewage and mining waste outfalls, and 320 in whole gastropods from South San Francisco Bay. Silver concentrations in conspecifics from areas remote from anthropogenic contamination were usually lower by one or more orders of magnitude ([Table 7.5](#)). The strong bioaccumulation of silver in marine benthic organisms from sediments is a major cause for concern, and one with potential for adverse effects on reproduction (Ratte 1999). High accumulation of silver from marine sediments is attributed, in part, to the formation of stable chlorocomplexes of silver with chlorine which, in turn, favor the distribution and accumulation of silver (Ratte 1999).

Silver is a normal trace constituent of many organisms (Smith and Carson 1977). In terrestrial plants, silver concentrations are usually less than 1.0 mg/kg ash weight (equivalent to less than 0.1 mg/kg DW) and are higher in trees, shrubs, and other plants near regions of silver mining. Seeds, nuts, and fruits usually contain higher silver concentrations than other plant parts (USEPA 1980). Silver accumulations in marine algae (max. 14.1 mg/kg DW) are due mainly to adsorption rather than uptake; bioconcentration factors of 13,000 to 66,000 are not uncommon (USPHS 1990; Ratte 1999).

Silver concentrations in molluscs vary widely between closely related species and among conspecifics from different areas (Bryan 1973; Eisler 1981; [Table 7.5](#)). The inherent differences in ability to accumulate silver among bivalve molluscs are well documented (oysters \gg scallops \gg mussels; Brooks and Rumsby 1965; Eisler 1981). The highest silver concentrations in all examined species of molluscs were in the internal organs, especially in the digestive gland and kidneys (Eisler 1981; Miramand and Bentley 1992; [Table 7.5](#)). Elevated concentrations of silver (5.3 mg/kg DW) in shells of limpets from uncontaminated sites suggest that silver may actively participate in carbonate mineral formation (Navrot et al. 1974), but this needs verification. In general, silver concentrations were elevated in molluscs collected near port cities and in the vicinities of river discharges (Fowler and Oregoni 1976; Berrow 1991), electroplating plant outfalls (Eisler et al. 1978; Stephenson and Leonard 1994), ocean dumpsites (Greig 1979), and urban point sources, including sewage outfalls (Alexander and Young 1976; Smith and Carson 1977; Martin et al. 1988; Anderlini 1992; Crecilius 1993), and from calcareous sediments rather than detrital organic or iron oxide sediments (Luoma and Jenne 1977).

Season of collection (Fowler and Oregoni 1976; Sanders et al. 1991) and latitude (Anderlini 1974) also influenced silver accumulations. Seasonal variations in silver concentrations of Baltic clams (*Macoma balthica*) were associated with seasonal variations in soft tissue weight and frequently reflected the silver content in the sediments (Cain and Luoma 1990). Oysters from the Gulf of Mexico vary considerably in whole-body concentrations of silver and other trace metals. Variables that modify silver concentrations in oyster tissues include the age, size, sex, reproductive stage, general health, and metabolism of the animal; water temperature, salinity, dissolved oxygen,

and turbidity; natural and anthropogenic inputs to the biosphere; and chemical species and interactions with other compounds (Presley et al. 1990). Silver concentrations in whole American oysters (*Crassostrea virginica*) from the Chesapeake Bay were reduced in summer and at increasing water salinities, and elevated near sites of human activity. Chemical forms of silver taken up by oysters included the free ion (Ag^+) and the uncharged AgCl^0 (Sanders et al. 1991; Daskalakis 1995). Declines in tissue silver concentrations of the California mussel (*Mytilus californianus*) were significant between 1977 and 1990; body burdens decreased from 10 to 70 mg/kg DW to less than 2 mg/kg DW and seem to be related to the termination of metal-plating facilities in 1974 and the decreased mass emission rates by wastewater treatment facilities (Stephenson and Leonard 1994).

Among arthropods, pyrophosphate granules isolated from barnacles have the capability to bind and effectively detoxify silver and other metals under natural conditions (Pullen and Rainbow 1991). In a Colorado alpine lake, silver concentrations in caddisflies and chironomid larvae usually reflected silver concentrations in sediments; seston, however, showed a high correlation with lake water silver concentrations from 20 days earlier (Freeman 1979).

Silver concentrations in fish muscle rarely exceeded 0.2 mg/kg DW and usually were less than 0.1 mg/kg FW; livers contained as much as 0.8 mg/kg FW, although values greater than 0.3 mg/kg FW were unusual; and whole fish contained as much as 0.225 mg/kg FW (Table 7.5). Livers of Atlantic cod (*Gadus morhua*) contained significantly more silver than muscles or ovaries; a similar pattern was evident in other species of marine teleosts (Hellou et al. 1992; Szefer et al. 1993; Table 7.5). Accumulations of silver in offshore populations of teleosts is unusual, even among fishes collected near dump sites impacted by substantial quantities of silver and other metals. For example, of 7 species of marine fishes from a disposal site in the New York Bight and examined for silver content, concentrations were highest (0.15 mg/kg FW) in muscle of blue hake (*Antimora rostrata*; Greig et al. 1976). Similarly, the elevated silver concentration of 0.8 mg/kg FW in liver of winter flounder (*Pleuronectes americanus*) was from a specimen from the same general area (Greig and Wenzloff 1977b).

Silver concentrations in muscle of Antarctic birds were low (0.01 mg/kg DW) when compared to livers (0.02 to 0.46 mg/kg DW) or feces (0.18 mg/kg DW; Szefer et al. 1993). Silver concentrations in avian tissues, especially in livers, were elevated in the vicinity of metals-contaminated areas and in diving ducks from the San Francisco Bay (Table 7.5). Birds with elevated concentrations of silver in tissues — as much as 44 mg/kg DW in liver in the common eider (*Somateria mollissima*) — seemed outwardly unaffected (Bryan and Langston 1992).

Silver in mammalian tissues is usually present at low or nondetectable concentrations (Klaassen et al. 1986). The concentration of silver in tissues of 3 species of seals collected in the Antarctic during 1989 was highest in liver (1.55 mg/kg DW) and lowest in muscle (0.01 mg/kg DW); intermediate in value were kidney (0.29 mg/kg DW) and stomach contents (0.24 mg/kg DW; Szefer et al. 1993). The mean concentration of silver in livers from normal female California sea lions (*Zalophus californianus*), having normal pups, was 0.5 mg/kg DW (Martin et al. 1976). Mothers giving birth to premature pups had only 0.4 mg Ag/kg DW liver. In general, *Zalophus* mothers delivering premature pups had lower concentrations in liver of silver, cadmium, copper, manganese, mercury, and zinc than mothers delivering normal pups (Martin et al. 1976). Silver concentrations in tissues of Antarctic seals were related to, and possibly governed by, concentrations of other metals (Szefer et al. 1994). In muscle, silver inversely correlated with zinc; in liver, silver positively correlated with nickel, copper, and zinc; and in kidney, correlations between silver and zinc and between silver and cadmium were negative (Szefer et al. 1994). In humans, USEPA (1980) states that silver is present in placentas and fetal livers, that silver concentrations in tissues increase with age, and that variations in tissue concentrations of silver are wide. The average daily intake of silver from all sources by humans is 88 μg , but very little of the silver ingested from nontherapeutic sources is retained (Smith and Carson 1977).

Table 7.5 Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
ALGAE, MACROPHYTES, AND HIGHER PLANTS		
Marine algae and macrophytes, 24 species		
9 species	<0.1–2.0 DW	1
11 species	2.1–10.0 DW	1
4 species	10.1–14.1 DW	1
Higher terrestrial plants	0.2–<1.0 AW	2, 3
CNIDARIANS		
Corals, 34 species	<1.0 DW	1
Various, 10 species	Max. 0.1 DW	1
MOLLUSCS		
Cephalopods, 7 species; digestive gland	3.0–46.0 DW	4
Cephalopods, French coast of English Channel, October 1987		
Octopus, <i>Eledone cirrhosa</i>		
Digestive gland	2.0–4.4 DW	4
Digestive tract	0.5 DW	4
Other tissues	<0.3 DW	4
Whole	0.8 DW	4
Cuttlefish, <i>Sepia officinalis</i>		
Digestive gland	4.9–7.4 DW	4
Kidney	0.7 DW	4
Other tissues	<0.3 DW	4
Whole	0.7 DW	4
Clam, <i>Corbicula</i> sp.; San Francisco Bay, 1983–86; soft parts	0.07–0.2 DW	5
American oyster, <i>Crassostrea virginica</i> ; soft parts		
Connecticut	6.1 FW	6
East coast	0.3–5.0 DW	7, 55
Georgia	28.0–82.0 DW	8
Gulf coast	0.6–6.0 DW; Max. 7.0 DW	7, 9, 10
Louisiana	5.5 DW	11
Maryland, Chesapeake Bay, 1986–88	2.0–6.0 DW	12
Northeast coast	0.8–2.3 FW	13
Red abalone, <i>Haliotis rufescens</i> ; California		
Digestive gland	14.0–60.0 DW	14
Foot	1.0–44.0 DW	14
Gills	13.0–129.0 DW	14
Mantle	16.0–54.0 DW	14
Periwinkle, <i>Littorina littorea</i> ; soft parts; Looe estuary, UK vs. uncontaminated site; 1988	10.7 (3.1–17.4) DW vs. 4.1 (3.4–5.0) DW	15
Baltic clam, <i>Macoma balthica</i> ; soft parts; San Francisco Bay		
Near sewage outfall	32.0–133.0 DW	11, 16
Reference site	<1.0 DW	11
Molluscs, marine; edible tissues; 18 species		
10 species	<0.1 FW	17
5 species	0.1–0.3 FW	17
3 species	0.3–0.7 FW	17
Molluscs; south San Francisco Bay, 1982; soft parts		
Mud snail, <i>Nassarius obsoletus</i>	Max. 320.0 DW	16
Clam, <i>Macoma nasuta</i>	Max. 5.1 DW	16
Softshell clam, <i>Mya arenaria</i>	Max. 34.0 DW	16
Clam, <i>Tapes japonica</i>	Max. 65.0 DW	16

Table 7.5 (continued) Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
California mussel, <i>Mytilus californianus</i> ; soft parts Bodega Bay, California; 1976–78 vs. 1986–88	0.15 DW vs. 0.1 DW	18
California coast, 1977–81 vs. 1989–91	Max. 10.0–70.0 DW vs. <2.0 DW	19
San Diego Bay near municipal wastewater outfall vs. references sites in Baja California and northern California	59.0 DW vs. 0.08–0.22 DW	20
San Francisco Bay, 1982; North Bay vs. South Bay	0.04–0.16 DW vs. 0.7–2.9 DW	16
Common mussel, <i>Mytilus edulis</i>		
Shell	0.1–6.3 DW	21, 22, 23
Soft parts		
Europe	0.1–6.0 DW	1
Ireland, February 1990; contaminated sites (Cork Harbour) vs. reference sites (east coast of Ireland)	0.8–4.3 DW vs. <0.05–1.0 DW	24
Rhode Island, Narragansett Bay, 1976–78 vs. 1986–88	0.20 DW vs. 0.22 DW	18
United States		
East coast; rural sites vs. urban areas	0.04–2.3 DW	1
West coast; rural sites vs. urban areas	0.3 DW vs. Max. 2.0 DW	55
West coast; rural sites vs. urban areas	0.1 DW vs. Max. 5.0 DW	55
Mussel, <i>Mytilus edulis aoteanus</i> ; soft parts; New Zealand, 1986–87; various distances from sewage outfall		
50 m	5.3–7.7 DW	25
100 m	4.2 DW	25
200 m	3.9 DW	25
750 m	3.5–4.1 DW	25
1500 m	2.9 DW	25
3000 m	2.7–3.4 DW	25
Oyster, <i>Ostrea equestris</i> ; soft parts, USA		
East coast	18.9 DW	7
Gulf coast	0.7–1.6 DW	7
Oyster, <i>Ostrea sinuata</i>		
Foot, gills, soft parts	0.7–1.1 DW	26
Gonad, mantle	0.2 DW	26
Intestine	2.9 DW	26
Kidney	4.8 DW	26
Muscle, shell	<0.1 DW	26
Limpet, <i>Patella vulgata</i> ; Israel, 1973; soft parts vs. shell		
Near sewage outfall	6.7 DW vs. 5.7 DW	27
Reference site 80 km north of outfall	1.2 DW vs. 5.3 DW	27
Mussel, <i>Perna canaliculus</i> ; soft parts; New Zealand, 1986–87; distance from sewage outfall		
200 m	35.0–113.0 DW	25
750 m	49.0–85.0 DW	25
1500–3000 m	8.0–13.0 DW	25
Widgeon clam, <i>Pitar morrhuanus</i> ; soft parts; near Rhode Island electroplating plant	1.2–4.6 DW	28
Giant scallop, <i>Placopecten magellanicus</i> ; soft parts		
Ocean disposal site	Max. 9.1 DW	11
Reference site	<0.1 DW	11
Clam, <i>Potamocorbula amurensis</i> ; San Francisco Bay (0.006 µg Ag/L); 1991–92; soft parts	2.2 (0.3–7.0) DW; BCF of about 366,000	57
Oysters, <i>Saccostrea</i> spp.; Australia, 1980–83; soft parts	Max. 0.4 FW	29
Clam, <i>Scrobicularia plana</i>		
Digestive gland	0.8 DW	4
Kidney	0.4 DW	4
Soft parts		
Reference sites	0.2–1.5 (0.03–2.1) DW	15, 30
Silver-contaminated estuary	4.0–5.8 (1.1–185.0) DW	15, 31

Table 7.5 (continued) Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
BRYOZOANS		
Bryozoan, <i>Victorella</i> sp; whole; Chesapeake Bay, Maryland	11.5 DW	32
CRUSTACEANS		
Amphipods, whole; Antarctica, February–March 1989	1.2 (0.7–1.4) DW	33
Rock crab, <i>Cancer irroratus</i>		
Digestive gland	2.1–3.4 FW; 6.3 DW	34, 35
Muscle	0.2–0.8 FW; 0.2 DW	34, 35
Crustaceans, edible tissues, 16 species		
8 species	<0.1 FW	17
5 species	0.1–0.2 FW	17
3 species	0.3–0.5 FW	17
Barnacle, <i>Elminius modestus</i> ; pyrophosphate granules	10.5 (9.7–11.3) DW	36
American lobster, <i>Homarus americanus</i> ; muscle	0.4–0.5 DW	37
Shrimps, unidentified		
Exoskeleton	1.1 DW	38
Muscle	0.2 DW	38
ANNELIDS		
Polychaete annelid, <i>Marpheysa sanguinea</i> ; whole; San Francisco Bay, 1982	Max. 5.5 DW	16
Sandworm, <i>Nereis diversicolor</i> ; whole	5.2 (0.7–30.0) DW	31
ECHINODERMS		
Various, 9 species	Usually <0.3 DW; Max. 0.6 DW	1
Starfish, <i>Luidia clathrata</i> ; Tampa Bay, Florida vs. Gulf of Mexico; 1992		
Body wall	0.26–0.84 DW vs. 0.67 DW	39
Pyloric caeca	0.4–1.1 DW vs. 0.17 DW	39
TUNICATES		
Whole, 2 species	Max. 0.03 DW; Max. 0.005 FW	1
Tunicate, <i>Cynthia claudicans</i> ; soft parts	0.9 FW; 4.8 DW	1
FISHES AND ELASMOBRANCHS		
Blackfin icefish, <i>Chaenocephalus aceratus</i> ; Antarctica, February–March 1989		
Liver	0.05 (0.04–0.05) DW	33
Muscle	0.01 (0.008–0.012) DW	33
Freshwater fishes, whole; USA, 1975–79	0.225 (0.004–1.9) FW	11
Atlantic cod, <i>Gadus morhua</i> ; Newfoundland, November 1990–March 1991; females		
Liver	Max. 1.49 DW; Max. 0.44 FW	40
Muscle	Max. 0.3 DW; Max. 0.02 FW	40
Ovaries	Max. 0.32 DW; Max. 0.04 FW	40
Marine fishes		
Liver		
66 species	<0.01 FW	17
12 species	(0.1–0.3) FW	17
4 species	(0.3–0.6) FW	17
Muscle		
158 species	<0.1 FW	17
1 species	(0.1–0.2) FW	17

Table 7.5 (continued) Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Scales, 7 species	(0.1–0.3) DW	41
Whole		
10 species	<0.1 FW	17
7 species	(0.1–0.2) FW	17
Striped bass, <i>Morone saxatilis</i>		
Liver	0.08 FW	42
Muscle	0.003 FW	42
Smooth dogfish, <i>Mustelus canis</i> ; New York Bight		
Liver	Max. 0.3 FW	43
Muscle	<0.1 FW	43
Hump rock cod, <i>Nothothenia gibberifrons</i> ; Antarctica, February–March 1989; muscle	0.014 (0.012–0.016) DW	33
Winter flounder, <i>Pleuronectes americanus</i>		
Liver	<0.1–0.8 FW	43
Muscle	<0.1 FW	43
Windowpane flounder, <i>Scophthalmus aquosus</i>		
Liver	<0.1–0.5 FW	35
Muscle	<0.1 FW	35
BIRDS		
Antarctica, February–March 1989		
Southern giant petrel, <i>Macronectes giganteus</i> ; muscle	0.018 (0.017–0.02) DW	33
Blue-eyed cormorant, <i>Phalacrocorax atriceps</i> ; muscle	0.01 DW	33
Adelie penguin, <i>Pygoscelis adeliae</i>		
Liver	0.02 DW	33
Muscle	0.01 DW	33
Chinstrap penguin, <i>Pygoscelis antarctica</i>		
Feces	0.18 (0.13–0.22) DW	33
Liver	0.05 DW	33
Muscle	0.009 DW	33
Gento penguin, <i>Pygoscelis papua</i>		
Liver	0.43 (0.41–0.46) DW	33
Muscle	0.01 DW	33
Greater scaup, <i>Aythya marila</i>		
San Francisco Bay, March–April 1982; liver	1.0 (0.4–3.1) DW	44, 45
British Columbia, Canada		
Diet	0.006–0.029 FW	46
Liver	0.04–0.32 FW	46
Ruffed grouse, <i>Bonasa umbellus</i> ; primary feathers; Virginia, 1977–79		
Adults	<0.01 DW	47
Immatures	<0.01 DW	47
Lesser black-backed gull, <i>Larus fuscus</i> ; Norway; metals-contaminated area		
Kidney	1.0 DW	22
Liver	2.0 DW	22
Muscle	3.0 DW	22
Surf scoter, <i>Melanitta perspicillata</i>		
British Columbia		
Diet	0.004–0.026 FW	46
Liver	0.03–0.14 FW	46
San Francisco Bay, March–April 1982		
Kidney	Max. 3.7 DW	44
Liver	0.9 (0.3–3.7) DW	44
Seabirds		
Liver, 11 species	0.04–0.6 DW; Max. 7.8 DW	58

Table 7.5 (continued) Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
3 species, Max. values		
Most tissues	<0.1 DW	58
Liver, gonad, fat	0.1–0.2 DW	58
Common eider, <i>Somateria mollissima</i> ; Norway; metals-contaminated area		
Eggs	1.0 DW	22
Kidneys	7.0 DW	22
Liver	44.0 DW	22
Muscle	2.0 DW	22
MAMMALS		
Human, <i>Homo sapiens</i>		
Daily intake, 70 kg individual, whole body		
All sources (35–88 µg)	0.0005–0.00125 FW	11
Air (0.023 µg)	0.0000033 FW	11
Drinking water (20–100 µg)	0.00285–0.00143 FW	11
Food (4.5 µg)	0.000064 FW	11
Diet		
Beef liver	0.005–0.194 FW	3
Beef muscle	0.004–0.024 FW	3, 11
Cereals and grains	0.008 (0.0–140.0) FW	11
Cigarettes; filter vs. nonfilter	0.27 FW vs. 0.18 FW	11
Crustaceans	2.0 DW	3
Dairy products	<0.06 FW	11
Fruits	<0.05 FW	11
Leafy vegetables	0.007 (0.0–0.04) FW	11
Meat, fish, poultry	0.01 (0.0–87.0) FW	11
Milk (cow)	0.027–0.059 FW	3, 11
Mushrooms	"Up to several hundred" DW	3
Oils and fats	<0.03 FW	11
Pork and mutton	0.006–0.012 FW	3, 11
Sugar	0.002–0.03 FW	3
Tea	0.2–2.0 DW	3, 11
Trout	0.48–0.68 DW	3
Typical diet	0.0091 DW	11
Wheat	0.5 DW	3
Tissues and organs		
Abnormal (argyria)		
Skin	63.0–72.0 DW	48
Normal		
Kidney	0.001 FW; 0.4 DW	48
Liver	0.006 FW; 0.7 DW	48
Lung	0.0001 FW	48
Skin	0.035 DW	48
Spleen	2.7 DW	48
Whole body	0.05 FW; <10.0 DW	2
Leopard seal, <i>Hydrurga leptonyx</i> ; Antarctic, February–March 1989		
Kidney	0.15 DW; Max. 0.24 DW	49
Liver	0.99 DW; Max. 1.55 DW	49
Muscle	0.01 DW; Max. 0.017 DW	49
Stomach contents	0.22 (0.20–0.24) DW	49
Weddell seal, <i>Leptonychotes weddelli</i> ; Antarctic, February–March 1989		
Kidney	0.10 DW; Max. 0.29 DW	49
Liver	0.73 DW; Max. 0.94 DW	49
Muscle	Max. 0.012 DW	49

Table 7.5 (continued) Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Crabeater seal, <i>Lobodon carcinophagus</i> ; Antarctic, February–March 1989		
Kidney	0.06 DW; Max. 0.17 DW	49
Liver	0.81 DW; Max. 1.36 DW	49
Muscle	0.01 DW; Max. 0.022 DW	49
Mammals, various species, liver	<50.0 AW	2
Polar bear, <i>Ursus maritimus</i> ; Northwest Territories, Canada, 1984; liver	0.21–0.54 DW	50
California sea lion, <i>Zalophus californianus</i> ; recent mothers; liver		
Mothers with normal pups	0.5 DW	51
Mothers giving birth to premature pups	0.4 DW	51
INTEGRATED STUDIES		
Alpine lake, Colorado, 1973–74. Silver iodide (43 kg), equivalent to 19.7 kg silver, released into system from local cloud seeding practices between 1963 and 1973		
Lake water, 1973 vs. 1974		
Bottom	0.00022 (Max. 0.00063) FW vs. 0.00044 (Max. 0.00122) FW	52
Surface	0.00031 (Max. 0.0009) FW vs. 0.00071 (Max. 0.00134) FW	52
Cutthroat trout, <i>Oncorhynchus clarkii</i> ; age 1 year vs. age 3 years		
Bone	5.8 DW vs. 2.6 DW	52
Liver	2.3 DW vs. 1.4 DW	52
Muscle	0.1 DW vs. 0.4 DW	52
Skin	0.2 DW vs. 0.4 DW	52
Arabian Sea, near Pakistan, 1987–88		
Sediments	0.53 DW	53
Water	0.000015 FW; Max. 0.000033 FW	53
Seaweeds, whole, 4 species	0.40–0.76 FW	53
Shrimps, edible portions, 2 species	0.25–0.29 FW	53
Fish, muscle, 3 species	0.29–0.53 FW	53
Calcasieu River, Louisiana		
Periphyton, whole	2.1 DW	54
Hooked mussel, <i>Ischadium exustus</i> (formerly <i>Brachidontes exustus</i>); soft parts	0.4 DW	54
American oyster, <i>Crassostrea virginica</i> ; soft parts	1.0 DW	54
Zooplankton, whole	0.8 DW	54
Blue crab, <i>Callinectes sapidus</i> ; muscle	0.1 DW	54
Shrimps, 2 species; muscle	0.04 DW	54
Fish, 7 species; muscle	0.1 DW	54
Poland, 1989–92		
Mushrooms, <i>Agaricus campestris</i> , whole	9–62 (6–110) DW	56
Soils	0.1–0.95 DW; Max. 1.4 DW; BCF values for silver by mushrooms from soils ranged between 60 and 330	56

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).

^b 1, Eisler 1981; 2, Smith and Carson 1977; 3, USEPA 1980; 4, Miramand and Bentley 1992; 5, Luoma et al. 1990; 6, Thurberg et al. 1974; 7, Goldberg et al. 1978; 8, Windom and Smith 1972; 9, Morse et al. 1993; 10, Presley et al. 1990; 11, USPHS 1990; 12, Sanders et al. 1991; 13, Greig and Wenzloff 1978; 14, Anderlini 1974; 15, Truchet et al. 1990; 16, Luoma and Phillips 1988; 17, Hall et al. 1978; 18, Lauenstein et al. 1990; 19, Stephenson and Leonard 1994; 20, Martin et al. 1988; 21, Segar et al. 1971; 22, Lande 1977; 23, Graham 1972; 24, Berrow 1991; 25, Anderlini 1992; 26, Brooks and Rumsby 1965; 27, Navrot et al. 1974; 28, Eisler et al. 1978; 29, Talbot 1985; 30, Bryan and Uysdal 1978; 31, Bryan and Hummerstone 1977; 32, Connell et al. 1991; 33, Szefer et al.

Table 7.5 (continued) Silver Concentrations (milligrams of silver per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW]) in Field Collections of Selected Plants and Animals

1993; **34**, Greig et al. 1977a; **35**, Greig et al. 1977b; **36**, Pullen and Rainbow 1991; **37**, Greig 1975; **38**, Bertine and Goldberg 1977; **39**, Lawrence et al. 1993; **40**, Hellou et al. 1992; **41**, Papadopoulou and Kassimati 1977; **42**, Heit 1979; **43**, Greig and Wenzloff 1977; **44**, Ohlendorf et al. 1986; **45**, Bryan and Langston 1992; **46**, Vermeer and Peakall 1979; **47**, Scanlon et al. 1980; **48**, Fowler and Nordberg 1986; **49**, Szefer et al. 1994; **50**, Braune et al. 1991; **51**, Martin et al. 1976; **52**, Freeman 1979; **53**, Tariq et al. 1993; **54**, Ramelow et al. 1989; **55**, Crecelius 1993; **56**, Falandysz and Danisiewicz 1995; **57**, Brown and Luoma 1995; **58**, Kim et al. 1998.

7.5 LETHAL AND SUBLETHAL EFFECTS

7.5.1 General

As discussed later, free silver ion is lethal to representative species of sensitive aquatic plants, invertebrates, and teleosts at water concentrations of 1.2 to 4.9 µg/L. Adverse effects occur on development of trout at concentrations as low as 0.17 µg/L and on phytoplankton species composition and succession at 0.3 to 0.6 µg/L. Aquatic organisms accumulate silver from environmental sources. No data were found on effects of silver on avian or mammalian wildlife, and all studied effects were on poultry and small laboratory mammals. Silver was not mutagenic, carcinogenic, or teratogenic to tested animals by normal routes of exposure. Adverse effects of silver on poultry occur at 1.8 mg/kg FW whole egg by way of injection (reduced survival), 10 mg/kg in diets (reduced hemoglobin with copper-deficient diet), 200 mg/kg in diets (growth suppression with copper-adequate diet), or when given drinking water containing 100 mg Ag/L (liver necrosis). Effects of silver on sensitive species of mammals include death at 13.9 to 20.0 mg/kg BW by intraperitoneal injection, histopathology of kidney and brain at 250 to 450 µg Ag/L drinking water, tissue accumulations at 6 mg/kg diet, and liver necrosis when fed diets containing more than 130 mg/kg. In humans, generalized argyria seems to be declining, which may be due to improved work conditions.

7.5.2 Terrestrial Plants

In general, accumulation of silver by terrestrial plants from soils is low, even if the soil is amended with silver-containing sewage sludge or the plants are grown on tailings from silver mines — where silver accumulates mainly in the root systems (Ratte 1999). Germination was the most sensitive stage to plants grown in solutions containing various concentrations of silver nitrate. Adverse effects on germination were expected at concentrations greater than 0.75 mg Ag/L for lettuce, and 7.5 mg/L for ryegrass (*Lolium perenne*) and other plants tested (Ratte 1999). Smith and Carson (1977) report that sprays containing 9.8 mg dissolved Ag/L kill corn (*Zea mays*), and sprays containing 100 to 1000 mg dissolved Ag/L kill young tomato (*Lycopersicon esculentum*) and bean (*Phaseolus* spp.) plants. Seeds of corn, lettuce (*Lactuca sativa*), oat (*Avena sativa*), turnip (*Brassica rapa*), soybean (*Glycine max*), spinach (*Spinacia oleracea*), and Chinese cabbage (*Brassica campestris*) were planted in soils amended with silver sulfide and sewage sludge to contain as much as 106 mg Ag/kg DW soil (Hirsch et al. 1993; Hirsch 1998c). All plants germinated and most grew normally at the highest soil concentration of silver tested. Yields of lettuce, oat, turnip and soybean were higher on soils amended with silver-laden, waste-activated sludge than control soils, but growth of Chinese cabbage and lettuce was adversely affected at 14 mg Ag/kg DW soil and higher. Silver concentrations in edible portions from all plants at all soil levels of silver tested, except lettuce, were less than 80 µg/kg DW, suggesting that availability of sludge-borne silver sulfide to most agricultural crops is negligible. Lettuce grown in soil containing 5 mg Ag/kg DW had about 0.5 mg Ag/kg DW leaves, and in 120 mg/kg DW soil as much as 2.7 mg Ag/kg DW leaves vs. 0.03 mg/kg DW in controls (Hirsch et al. 1993; Hirsch 1998c).

7.5.3 Aquatic Organisms

In fish and amphibian toxicity tests with 22 metals and metalloids, silver was the most toxic element as judged by acute LC₅₀ values (Birge and Zuiderveen 1995). In solution, ionic silver is extremely toxic to aquatic plants and animals (Nehring 1976; Nelson et al. 1976; Calabrese et al. 1977a; Gould and MacInnes 1977; Smith and Carson 1977; USEPA 1980; Buhl and Hamilton 1991; Bryan and Langston 1992), and water concentrations of 1.2 to 4.9 µg/L killed sensitive species of aquatic organisms, including representative species of insects, daphnids, amphipods, trout, flounders, sticklebacks, guppies, and dace (Table 7.6). At nominal water concentrations of 0.5 to 4.5 µg/L, accumulations in most species of exposed organisms were high and had adverse effects on growth in algae, clams, oysters, snails, daphnids, amphipods, and trout; molting in mayflies; and histology in mussels (Table 7.6).

In general, silver ion was less toxic to freshwater aquatic organisms under conditions of low dissolved Ag⁺ concentration, increasing water pH, hardness, sulfides, and dissolved and particulate organic loadings; under static test conditions when compared to flowthrough regimens; and when animals were adequately nourished when compared to starvation (Erickson et al. 1998; Bury et al. 1999a, 1999b; Karen et al. 1999; Ratte 1999; Wood et al. 1999). It is now agreed that increasing concentrations of dissolved organic carbon affords the highest protective effects (Berry et al. 1999; Karen et al. 1999). Among all tested species, the individuals most sensitive to silver were the young and those exposed to low water hardness or salinity (Smith and Carson 1977; USEPA 1980; Le Blanc et al. 1984; Erickson et al. 1998; Shaw et al. 1998; Table 7.6). In the case of seawater-acclimatized rainbow trout, silver-induced mortality was greater at higher salinities, but the increased toxicity with salinity was linked to an incomplete hypoosmoregulatory ability and not to an increase in a more toxic AgCl_n species (Ferguson and Hogstrand 1998). Sediment chemistry can affect toxicity of silver to marine amphipods (*Ampelisca abdita*) exposed for 10 days to sediments supplemented with various concentrations of silver (Berry et al. 1999). In general, sediments with an excess of acid volatile sulfide (AVS) relative to simultaneously extracted metal (SEM) were generally not toxic to marine amphipods. Sediments with an excess of SEM relative to AVS, and no measurable AVS, were generally toxic. Sediments with measurable AVS were not toxic (Berry et al. 1999). It is emphasized that silver-induced stress syndromes vary widely among animal classes. Among marine organisms, for example, silver ion was associated with respiratory depression in marine gastropods and cunners (*Tautogolabrus adspersus*), a teleost. However, silver ion increased oxygen consumption in 6 species of bivalve molluscs (Gould and MacInnes 1977).

Sensitive aquatic plants accumulated silver from water containing as little as 2 µg Ag/L to whole-cell burdens as high as 58 mg Ag/kg DW; grew poorly at 3.3 to 8.2 µg Ag/L during exposure for 5 days; and died at concentrations greater than 130 µg Ag/L (Table 7.6). Some metals seem to protect aquatic plants against adverse effects of silver. Algae in small lakes that contained elevated concentrations of metals, especially copper and nickel, had higher tolerances to silver than conspecifics reared in the laboratory under conditions of depressed concentrations of heavy metals (USEPA 1980). Species composition and species succession in Chesapeake Bay phytoplankton communities were significantly altered in experimental ecosystems continuously stressed by low concentrations (0.3 to 0.6 µg/L) of silver (Sanders and Cibik 1988; Sanders et al. 1990). At higher concentrations of 2 to 7 µg/L for 3 to 4 weeks, silver inputs caused disappearance of *Anacystis marina*, a mat-forming blue-green alga; increased dominance by *Skeletonema costatum*, a chain-forming centric diatom; and cell burdens of 8.6 to 43.7 Ag mg/kg DW (Sanders and Cibik 1988). Dissolved silver speciation and bioavailability were important in determining silver uptake and retention by aquatic plants (Connell et al. 1991). Silver availability was controlled by the concentration of free silver ion (Ag⁺) and the concentrations of other silver complexes, such as AgCl (Sanders and Abbe 1989). Silver uptake by phytoplankton was rapid in proportion to silver concentration and inversely proportional to water salinity. Silver incorporated by phytoplankton was not lost as the salinity increased, and silver associated with cellular material was largely retained

in the estuary (Sanders and Abbe 1989). Diatoms (*Thalassiosira* sp.), for example, readily accumulated silver from the medium. Once incorporated, silver was tightly bound to the cell membrane, even after the cells were mechanically disrupted (Connell et al. 1991).

The ability to accumulate dissolved silver from the medium ranges widely between species. Some reported bioconcentration factors (mg Ag per kg FW organism/mg Ag per liter of medium) are 210 in diatoms, 240 in brown algae, 330 in mussels, 2300 in scallops, and 18,700 in oysters (USEPA 1980). Silver is the most strongly accumulated of all trace metals by marine bivalve molluscs (Luoma 1994). Studies with radiosilver-110m suggest that the half-time persistence of silver is 27 days in mussels, 44 to 80 days in clams, and more than 180 days in oysters (Fisher et al. 1994). In oysters and other bivalve molluscs, the major pathway of silver accumulation was from dissolved silver; uptake was negligible from silver adsorbed onto suspended sediments or algal cells, and oysters eliminated adsorbed silver in the feces (Abbe and Sanders 1990; Sanders et al. 1990). Sometimes, benthic bivalve molluscs accumulated silver from certain sediments. Sediment-bound silver was taken up by the Baltic clam (*Macoma balthica*) at 3.6 to 6.1 times the concentration in calcite sediments but less than 0.85 times from manganeseous, ferrous, and biogenic CaCO_3 sediments (USEPA 1980). In oysters, silver associated with food was unavailable for incorporation, which may be due to the ability of silver to adsorb rapidly to cell surfaces and to remain tightly bound despite changes in pH or enzymatic activity (Connell et al. 1991). Silver concentrations in American oysters (*Crassostrea virginica*) held in seawater solutions containing 1.0 mg Ag/L for 96 h rose from 6.1 mg/kg FW soft parts to 14.9 mg/kg FW. In gills, these values were 5.9 and 33.9 mg/kg FW (Thurberg et al. 1974). A similar pattern was evident in common mussels (*Mytilus edulis*) and quahog clams (*Mercenaria mercenaria*; Thurberg et al. 1974). Adult surf clams (*Spisula solidissima*) immersed for 96 h in seawater containing 10 μg Ag/L had 1.0 mg Ag/kg FW soft tissues vs. 0.08 mg/kg in controls (Thurberg et al. 1975). Oysters accumulated radiosilver-110m from the medium by factors of 500 to 32,000 (Pouvreau and Amiard 1974). Uptake of dissolved silver by oysters was higher at elevated temperatures in the range of 15 to 25°C (Abbe and Sanders 1990). American oysters maintained near a nuclear power plant in Maryland that discharged radionuclides on a daily basis into the Chesapeake Bay accumulated radiosilver-110m; accumulations were higher in summer and fall than in winter and spring (Rose et al. 1988).

Marine gastropods exposed to concentrations as low as 1.0 μg Ag/L for as long as 24 months showed histopathology and accumulations as high as 34 mg Ag/kg FW soft parts; higher exposure concentrations of 5 and 10 μg Ag/L were associated with inhibited reproduction and whole-body burdens as high as 87 mg Ag/kg FW (Nelson et al. 1983). Histopathological findings in silver-exposed mussels (*Mytilus edulis*) were typical of argyria in humans and other mammals that have absorbed organic or inorganic silver compounds (Calabrese et al. 1984). Juvenile Pacific oysters (*Crassostrea gigas*) exposed for 2 weeks to solutions containing 20 μg Ag/L had high silver accumulations in tissues and a reduced capacity to store glycogen; however, after 30 days of depuration, glycogen storage capacity was restored and 80% of the soluble silver and 27% of the insoluble forms were eliminated, suggesting recovery to a normal physiological state (Berthet et al. 1990). About 70% of the insoluble silver in Pacific oysters was sequestered as Ag_2S , a stable mineral form that is not degradable, thereby limiting the risk of silver transfer through the food chain (Berthet et al. 1990). Most (69 to 89%) of the silver accumulated from the medium in soft tissues of oysters and clams was sequestered in amoebocytes and basement membranes. In scallops and mussels, silver was stored in basement membranes and pericardial gland. In all species of bivalve molluscs, sequestered silver was in the form of silver sulfide (Berthet et al. 1992). American oysters excreted about 60% of their accumulated silver in soft tissues within 30 days of transfer to silver-free seawater; soluble forms were preferentially eliminated, and insoluble forms retained (Berthet et al. 1992). Interspecies differences in ability to retain silver among bivalve molluscs are large, even among closely related species of crassostreid oysters. For example, the half-time persistence of silver was about 149 days in American oysters but only 26 days in Pacific oysters (USPHS 1990).

Table 7.6 Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
BACTERIA, ALGAE, AND MACROPHYTES		
Bacteria, freshwater <i>Escherichia coli</i> 1000–2000 (as Ag^{+3})	All dead in 0.5–5.0 min	1
<i>Streptococcus faecalis</i> 1000–2000 (as Ag^{+3})	All dead in 0.5–5.0 min	1
Various species 100–200	All dead in 15–20 min	2
Bacteria, marine Isolated from tubes of deep-sea polychaete annelids		
3000	Lowest concentration tested that inhibited growth in 50% of strains during 10-day exposure	3
20,000	Silver-resistant strains (55% of all strains tested) survived at least 24 h	3
40,000	Some strains survived during 10-day exposure	3
Alga, <i>Chlorella</i> spp. 50–100	Growth inhibition	4
Waterweed, <i>Eloea canadensis</i> 100	Respiration inhibited	4
Freshwater algae and macrophytes, 13 species 30–7500	Adverse effects	4
Freshwater plants 26	Bioconcentration factor (BCF) of 200	2
Duckweed, <i>Lemna minor</i> 270	Phytotoxic	4
Marine algae, 3 species 2	After 24 h algae contained 27.8–58.6 mg silver/kg dry weight (DW) at 1% salinity, 16.4–33.4 mg/kg at 1.5% salinity, and 9.8–25.2 mg Ag/kg DW at 2.0% salinity BCF between 13,000 and 66,000 at equilibrium	5
Marine algae, 4 species; various concentrations Blue-green alga, <i>Phormidium inundatum</i> 80–140	Controls growth in swimming pools	2
Marine alga, <i>Prorocentrum mariae-lebouriae</i> 3.3 6.7 8.2	50% growth reduction in 5 days at 0.75% salinity 50% growth reduction in 5 days at 1.5–2.25% salinity 50% growth reduction in 5 days at 3% salinity	6 6 6
Marine algae, various species Radiosilver-110m at 3 microcuries/L	BCF of 1600 to 2800 in 38 days	7
Marine plants 60	BCF of 200	2
Alga, <i>Scenedesmus</i> spp. 100–200	100% growth inhibition	4
Marine alga, <i>Skeletonema costatum</i> 5.9 15.4 20.0 130–170	50% growth reduction in 5 days at 0.75% salinity 50% growth reduction in 5 days at 1.5% salinity 50% growth reduction in 5 days at 2.25–3.0% salinity 50% reduction in cell numbers in 96 h	6 6 6 4
PROTOZOANS		
Ciliate, <i>Fabrea salina</i> ; held in seawater solution containing radiosilver-110m	Bioconcentration factor (volume/volume basis) of 7000 to 40,000 within 24 h	39

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
Protozoan, <i>Spirostomum ambiguum</i>		
8.8	LC50 (24 h) at 2.8 mg CaCO_3/L	8
15.3	LC50 (24 h) at 250 mg CaCO_3/L	8
NEMATODES		
Free-living nematode, <i>Caenorhabditis elegans</i>		
102 (95% confidence interval [CI] of 10 to 4980)	LC50 (96 h)	9
5000 (95% CI of 3000 to 10,000)	LC50 (24 h)	9
MOLLUSCS		
Bay scallop, <i>Argopecten irradians</i> , juveniles		
22	Oxygen consumption elevated after 96 h	10
33	LC50 (96 h); survivors with elevated silver concentrations	10
Freshwater snails; <i>Australorbis</i> sp., <i>Taphius</i> sp.		
30–100	Inhibited feeding and coordination	2
Bivalves, 4 species		
10	Elevated oxygen consumption after exposure for 30–90 days	10, 11
Scallop, <i>Chlamys varia</i> , adults		
20	After 14 days soft parts contained 18 mg Ag/kg DW vs. 1.7 in controls	12
100	LC50 (115 h)	12
Asiatic clam, <i>Corbicula fluminea</i>		
4.5	Adverse effects on growth after exposure for 21 days; residues of 1.65 mg Ag/kg FW soft parts were associated with reduced growth	13
7.8	No deaths in 21 days	13
26.0	Some deaths in 21 days	13
155 (116–208); exposed for 96 h then transferred to uncontaminated media for 96 h	LC50 for juveniles at end of observation period	13
Pacific oyster, <i>Crassostrea gigas</i>		
2–10	5 to 8% of embryos exposed for 48 h were abnormal (retarded shell growth, reduced size, erratic swimming behavior) vs. 1% in controls; no significant effect on embryogenesis	14
13.5–15.5	Significant effect on embryogenesis; 25–37% of embryos developed abnormally	14
18–32	95–98% of embryos exposed for 48 h were abnormal	14
20	Soft parts of adults exposed for 28 days contained 188.0 mg Ag/kg DW vs. 3.0 mg/kg DW in controls	12
Juveniles held in 20 μg Ag/L for 14 days then transferred to uncontaminated seawater for 23 days	No histopathology. During exposure, but not depuration, glycogen storage capacity was diminished. During depuration, silver concentrations decreased from 31.3 mg/kg DW soft parts to 12.8 vs. <10.0 in controls. Most of the insoluble accumulated silver was sequestered as Ag_2S in amoebocytes and basement membranes	15
100	LC50(209 h), adults	12

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
American oyster, <i>Crassostrea virginica</i>		
0.1 (controls) vs. 2; adults exposed for 14 days in large enclosures with natural phytoplankton assemblages	In controls, phytoplankton had 0.03 mg Ag/kg DW and oyster soft parts 0.8 mg/kg DW. In the 2.0 $\mu\text{g/L}$ group, phytoplankton had 8.6 mg Ag/kg DW and oysters 2.8 mg/kg DW; oyster growth rate significantly reduced	16
5 or 7; conditions as above	Phytoplankton had 24–44 mg Ag/kg DW and oysters 4.8–6.6 mg Ag/kg DW	16, 17
5.8	LC50 (48 h), embryos	10, 48
10	LC100 (48 h), embryos	4
25	LC50 (12 days), juveniles	10
500–1000	Adults exposed for 96 h had 12.4–14.9 mg Ag/kg FW in body and 34–38 mg Ag/kg FW in gills	11
Slipper limpet, <i>Crepidula fornicata</i>		
1, 5, or 10; exposed for 24 months and observed for effects on growth, reproduction, histology and accumulations	Growth reduced in the 5 and 10 $\mu\text{g/L}$ groups and reproduction inhibited in the 10 $\mu\text{g/L}$ group. All test groups showed deposition of silver in connective tissues and basement membranes. Maximum silver concentrations (mg/kg FW soft parts) were recorded for the controls at 12 months (2.8), for the 1.0 $\mu\text{g/L}$ group at 12 months (34.0), for the 5.0 $\mu\text{g/L}$ group at 6 months (54.1), and for the 10.0 $\mu\text{g/L}$ group at 6 months (86.7). After 24 months, silver-exposed groups contained between 5.4 and 8.0 mg Ag/kg FW soft parts	18
Zebra mussel, <i>Dreissena polymorpha</i> , adults		
400	No deaths in 28 days; soft parts at 28 days contained 147–184 mg Ag/kg DW vs. 0.02–1.8 mg/kg DW in controls	12
Hardshell clam, <i>Mercenaria mercenaria</i>		
21.0	LC50 (48 h), embryos	10
32.4	LC50 (10 days), juveniles	10
500–1000	Adults exposed for 96 h had 0.8–1.0 mg Ag/kg FW in soft parts and 6.9–7.6 mg Ag/kg FW in gills. Controls (<1.5 $\mu\text{g/L}$) had 0.4 mg Ag/kg FW soft parts and 1.6 mg/kg FW in gills	11
Softshell clam, <i>Mya arenaria</i>		
100	Increased oxygen consumption after 96 h	11
500	After exposure for 96 h adults had 10.4 mg Ag/kg FW soft parts vs. 0.3 mg Ag/kg FW in controls	11
1000	All adults died within 96 h	11
Common mussel, <i>Mytilus edulis</i>		
Exposed continuously for 21 months to 0.0 (control), 1, 5, or 10 $\mu\text{g Ag/L}$ from age 2.5 months (4.5 mm in shell length) and observed for growth, accumulations, and histopathology	No effect on growth. Silver concentrations (mg/kg FW soft parts) for controls ranged between 0.2 and 0.7; maximum concentrations in the 1 $\mu\text{g/L}$ group (9.1) occurred at 18 months; for the 5 $\mu\text{g/L}$ group, residues were highest (11.9) at 18 months; for the 10 $\mu\text{g/L}$ group, concentrations were highest (15.3) at 12 months. All silver-exposed groups had histopathology of basement membranes and connective tissues	19
Juveniles (16.1 mm shell length) and adults (53.4 mm shell length) were continuously exposed for 12 months to 0.0 (control), 5, 25, or 50 $\mu\text{g Ag/L}$ and observed for growth and accumulations	Growth inhibition of the 50 $\mu\text{g/L}$ group after 6 months but growth normal after 12 months; growth of other groups as in controls. At 12 months residues, in mg Ag/kg FW soft parts, for juveniles (adults) were 0.2 (0.1) in controls, 9.9 (2.0) in the 5 $\mu\text{g/L}$ group, 8.0 (2.0) in the 25 $\mu\text{g/L}$ group, and 10.7 (3.0) in the 50 $\mu\text{g/L}$ group	19

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
100	Increasing oxygen consumption with increasing water salinity	11
500 or 1000	Adults exposed for 96 h had 3.7–5.2 mg Ag/kg FW soft parts	11
Radiosilver-110m	BCF after 1 day were 860 in soft parts and 8 in shell; after 9 days these values were 2550 in soft parts and 11 in shell	20
Mussel, <i>Mytilus galloprovincialis</i> , adults		
10	Growth normal after 21-month exposure	12
20	After 28 days soft parts contained 15 mg Ag/kg DW vs. 0.08 mg Ag/kg DW in controls (<0.1 μg Ag/L)	12
25	Growth depressed after 21-month exposure	12
50	Severe tissue histopathology after 14 days	12
100	LC50 (110 h)	12
Mud snail, <i>Nassarius obsoletus</i>		
1.0	Inhibition of embryonic development	21
Clam, <i>Potamocorbula amurensis</i> ; exposed for 14 days at 1.8% salinity to 0.1, 0.2, 0.5, 1.0, or 2.0 μg Ag^+/L	Silver concentrations in soft parts rose in a dose-dependent manner from <1.0 mg Ag/kg DW to about 14.0 mg Ag/kg DW	42
Clam, <i>Scrobicularia plana</i> , adults		
20	Normal after 14 days	12
50	No deaths in 16 days; severe histopathology	12
100	LC50 (250 h)	12
200	LC50 (96 h)	12
Surf clam, <i>Spisula solidissima</i>		
10	Elevated oxygen consumption in juveniles after 96 h	10
14; 1-h exposure 60 min after fertilization	50% of embryos developed abnormally in 48 h	21
100	Lethal to juveniles in 96 h	10

BRYOZOANS

Bryozoan, <i>Victorella</i> sp.		
0.18 (control), 2, or 10	Silver concentrations, in mg/kg DW whole animal, after 24 h were 11.5 in controls, 38.3 in the 2 $\mu\text{g}/\text{L}$ group, and 180.0 in the 10 $\mu\text{g}/\text{L}$ group	22

ARTHROPODS

Copepod, <i>Acartia tonsa</i>		
36	LC50 (96 h)	4
Amphipod, <i>Ampelisca abdita</i>		
Controls	15% dead in 10 days	50
30	LC50 (10 days)	50
Chironomid, <i>Chironomus tentans</i> ; larvae		
57	LC50 (10 days)	49
Sediments supplemented with silver nitrate, in g Ag/kg DW sediment		
0.03 (1 μg Ag/L in overlying water = OW; 3 μg Ag/L in pore water = PW)	All survived exposure for 10 days	49
0.2 (16 $\mu\text{g}/\text{L}$ OW, 34 $\mu\text{g}/\text{L}$ PW)	87% survival in 10 days	49
0.5 (13 $\mu\text{g}/\text{L}$ OW, 127 $\mu\text{g}/\text{L}$ PW)	83% survival in 10 days	49
1.1–2.7	LC50 (10 days)	49
1.2 (156 $\mu\text{g}/\text{L}$ OW, 7979 $\mu\text{g}/\text{L}$ PW)	53% survival in 10 days	49
3.1 (34,600 $\mu\text{g}/\text{L}$ OW, 1,389,000 $\mu\text{g}/\text{L}$ PW)	All died within 10 days	49

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
Daphnid, <i>Daphnia magna</i>		
0.4–15.0	LC50 (96 h) at 38–75 mg CaCO_3/L	4
0.9	50% of starved daphnids immobilized in 48 h	23
1.6–19.4	MATC ^b	23
3.5	50% reduction in growth of nonstarved daphnids in 21 days	23
4.1	Reduced survival during 21-day exposure	23
10.5	Reproduction inhibited during 21-day exposure	23
12.5	50% of nonstarved daphnids immobilized in 48 h	23
45–49	LC50 (96 h) at 255 mg CaCO_3/L	4
Daphnids, <i>Daphnia</i> spp.		
10 (0.25–49.0)	LC50 (96 h)	9
Mayfly, <i>Ephemerella grandis</i>		
<1.0	LC50(14 days), naiads	24
4.0–8.8	LC50(7–15 days), adults	4
60 or 120	On death, whole mayflies contained 25.3 and 28.7 mg $\text{Ag}/\text{kg DW}$	24
Scud (amphipod), <i>Gammarus pseudolimnaeus</i>		
4.5 (3.7–5.5)	LC50 (96 h) at 44 mg CaCO_3/L	25
American lobster, <i>Homarus americanus</i>		
6.0	Altered enzyme activity after 30 days but no effect on survival, oxygen consumption, or osmoregulation	10
Amphipod, <i>Hyalella azteca</i>		
0.95	No observable effects after 21-day exposure	13
1.4	Reduced growth after 20 days	13
1.9 (1.4–2.3)	LC50 (96 h)	13
Mayfly, <i>Isonychia bicolor</i>		
1.6	Molting inhibited after 20 days	13
6.8 (5.5–7.8)	LC50 (96 h)	13
Stonefly, <i>Leuctra</i> sp.		
0.69	Adverse effects after 12 days	13
2.5 (1.7–3.2)	LC50 (96 h)	13
Mysid shrimp, <i>Mysidopsis bahia</i>		
250.0	LC50 (96 h)	4
Grass shrimp, <i>Palaemonetes pugio</i>		
2.0	After 2 weeks whole shrimps contained 0.5 mg $\text{Ag}/\text{kg DW}$ vs. 0.36 in controls	22
5.0	After 2 weeks whole shrimps had 3.7 mg $\text{Ag}/\text{kg DW}$	22
10.0	Whole shrimps contained 4.5 mg $\text{Ag}/\text{kg DW}$ after exposure for 2 weeks	22
For 2 weeks shrimp ate <i>Artemia</i> nauplii containing 0.72 mg $\text{Ag}/\text{kg DW}$, or bryozoans (<i>Victorella</i> sp.) containing elevated silver burdens (38–180 mg $\text{Ag}/\text{kg DW}$), or control bryozoans (11.5 mg $\text{Ag}/\text{kg DW}$)	Silver concentration (mg/kg DW whole body) in shrimp on <i>Artemia</i> diet was 0.19 vs. 0.09 in silver-free <i>Artemia</i> diet; 0.26–0.62 in the high-silver bryozoan diet and 0.36 in the control bryozoan diet	22
Stonefly, <i>Pteronarcys californica</i>		
4.0–9.0	LC50 (96 h)	24
50.0	On death, whole stoneflies contained 9.1 mg $\text{Ag}/\text{kg DW}$	24
105.0	Dead stoneflies had 13.2 mg $\text{Ag}/\text{kg DW}$	24
Mayfly, <i>Stenonema</i> sp.		
3.9 (2.5–5.7)	LC50 (96 h)	13

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
Midge, <i>Tanytarsus dissimilis</i> 3160 (2490–4010)	LC50 (48 h) at 44 mg CaCO_3/L	25
ANNELIDS		
Marine polychaete, <i>Sabellav. pavonina</i> Adults immersed in seawater containing 50 $\mu\text{g Ag/L}$ for 8 weeks then transferred to silver-free media for 8 weeks	During immersion, the maximum whole body silver concentration was 22.1 mg/kg DW vs. 0.8 in controls; main sites of accumulation were the connecting tissues of nephridia and gut. No histopathology. A constant elimination of silver in urine occurs simultaneously with silver accumulation. During depuration, new connective tissue formed and silver concentrations were reduced by 88%	26
ECHINODERMATA		
Sea urchin, <i>Arbacia lixula</i> 0.5	Reduced embryo development after 52 h	4
FISHES		
Mottled sculpin, <i>Cottus bairdi</i> 5.3 14.0	LC50 (96 h) at 30 mg CaCO_3/L LC50 (96 h) at 250 mg CaCO_3/L	4 4
Sheepshead minnow, <i>Cyprinodon variegatus</i> 1400	LC50 (96 h), juveniles	4
Common carp, <i>Cyprinus carpio</i> Held in radiosilver-110m solutions for 41 days then transferred to uncontaminated media for 42 days	Whole body BCF during immersion rose rapidly and progressively to 51 at day 19, then more slowly to 73 at day 41. At day 41, BCF for liver was 866, for digestive tract 560, for kidneys 299, for spleen 155, and for air bladder 109. During depuration, 68% of the silver was eliminated — about 31% during the first 3 days and 37% in the next 39 days. In both uptake and depuration phases, 71–77% of all radiosilver was present in liver and digestive tract	27
Mummichog, <i>Fundulus heteroclitus</i> 30–40	Inhibited liver enzyme activity after 4 days	2, 4
Mosquitofish, <i>Gambusia affinis</i> 23.5 (17.2–27.0)	LC50 (96 h), juveniles	13
Threespine stickleback, <i>Gasterosteus aculeatus</i> 3 4 10	Lethal in 10–30 days Lethal in 7 days Lethal in 96 h	2 2 2
Flagfish, <i>Jordanella floridae</i> 9.2 (8.0–10.7)	LC50 (96 h) at 44 mg CaCO_3/L	25
Bluegill, <i>Lepomis macrochirus</i> 31.7 (24.2–48.4) 70.0	LC50 (96 h) Survival as in controls after 6 months; whole body contained 0.3 mg Ag/kg ash weight	13 28
Atlantic silverside, <i>Menidia menidia</i> 110.0 400.0	LC50 (96 h), larvae LC50 (96 h), juveniles	4 4

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
Largemouth bass, <i>Micropterus salmoides</i>		
7.0	Survival of young of year as in controls after continuous exposure for 6 months. After 4 months, viscera contained 0.6 mg Ag/kg ash weight, gills 0.38, and carcass 0.016 mg Ag/kg ash weight	28
70.0	All dead within 24 h. Prior to death, bass had reddened gills, body tremors, and erratic swimming	28
Tidepool sculpin, <i>Oligocottus maculosus</i>		
119.0	LC50 (168 h); 2.5% salinity	46
331.0	LC50 (96 h); 2.5% salinity	46
472.0	LC50 (168 h); 3.2% salinity	46
664.0	LC50 (96 h); 3.2% salinity	46
Chum salmon, <i>Oncorhynchus keta</i>		
Eggs were exposed in freshwater to 4 µg Ag/L for 14 days prior to hatch. After hatching, larvae were exposed to 4 µg Ag/L in salt water for 14 days during yolk-sac resorption. Fry were then transferred to uncontaminated salt water and fed a high metals diet for 64 days (diet contained — in µg metal/kg feed DW — 2 Ag, 255 Cd, 6670 Cu, 1320 Pb, and 96,000 Zn)	At end of study, experimentals had a small, but significant, decline in survival. Just prior to transfer to uncontaminated salt water, experimentals contained 62 µg Ag/kg whole body DW vs. 4 in controls. After 64 days in uncontaminated salt water, whole alevins contained 18 µg Ag/kg DW vs. 4 in controls	29
Coho salmon, <i>Oncorhynchus kisutch</i>		
11.1 (7.9–15.7)	LC50 (96 h), alevins	30
12.5 (10.7–14.6)	LC50 (96 h), juveniles	30
Rainbow trout, <i>Oncorhynchus mykiss</i>		
0.03–0.06	MATC ^b after 13-month exposure beginning at eyed embryo stage	4
0.09–0.17	MATC ^b after exposure of eyed eggs and subsequent developmental stages for 18 months in soft water	31
0.18–0.40	MATC ^b ; 10-month exposure starting with newly-fertilized embryos	4
0.6	All eyed eggs survived 10-week exposure	31
1.2	40% of eyed eggs dead in 39 days	31
2.0	Inhibition of Na^+ and Cl^- influx across gills in mature trout after 72 h	44
2.2	All eyed eggs dead in 60 days	31
4.8–8.9	LC50 (144 h); juveniles	13, 44
5.3–8.1	LC50 (96 h); water hardness 20–31 mg CaCO_3/L	31
7.6–10.9	LC50 (96 h)	4, 23, 41
10.0	LC50 (28 days) at 93–105 mg CaCO_3/L	4
13.0	LC50 (96 h); water hardness 350 mg CaCO_3/L	31
16.1 (12.8–20.2)	LC50 (96 h); alevins	30
19.2 (16.0–23.1)	LC50 (96 h); juveniles	30
Juveniles fed diets containing 0, 3, 30, 300, or 3000 mg Ag/kg DW ration for 58 days as silver sulfide (Ag_2S)	At day 43, the 3000 mg/kg diet had 4 times more silver in livers than did controls; however, there was no significant elevation in silver burdens of kidneys, gills or intestine. Daily food consumption rates were lowered by 14–22% in groups receiving 30 mg Ag/kg ration and higher, possibly because of decreased palatability of the silver-laden diets. Growth rates, however, were the same for all groups.	51
Steelhead trout, <i>Oncorhynchus mykiss</i>		
0.1–1.1	Growth reduced during chronic exposure from egg through swimup fry	23

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
0.5 and 1.3	Survival reduced at low dose when exposed continuously from egg through swimup; all dead at high dose	23
9.2	LC50 (96 h)	23
100.0	LC50 (62 h); eyed embryos	32
200.0	LC50(96 h); eyed embryos	32
401.0; seawater acclimatized	No deaths in 96 h at 1.5 or 2.0% salinity; LC50 (96 h) at 2.5% salinity and LC67 (96 h) at 3.0% salinity	47
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
33.0	Fry survived exposure for 48 h	2
40.0–44.0	Lethal to fry in 48 h	2
Summer flounder, <i>Paralichthys dentatus</i>		
4.7	LC50 (96 h); larvae	4
8.0–48.0	LC50 (96 h); embryos	4
Fathead minnow, <i>Pimephales promelas</i>		
5.3–20.0	LC50 (96 h) at water hardness of 25–75 mg CaCO_3/L	4
5.6–7.4	LC50 (96 h); flow-through tests	23
9.4–9.7	LC50 (96 h); static tests	23
10.7 (10.6–10.8)	LC50 (96 h) at 44 mg CaCO_3/L	25
29.0	LC100 (96 h)	33
110.0–270.0	LC50 (96 h) at water hardness of 255 mg CaCO_3/L	4
Guppy, <i>Poecilia reticulata</i>		
4.3	Lethal	2
Winter flounder, <i>Pleuronectes americanus</i>		
10.0	Depressed liver transaminase activity after 60 days	10
54, 92, 180, or 386	No significant effect of lowest dose on growth or survival during exposure for 18 days of embryo through yolk-sac absorption. At 92 $\mu\text{g}/\text{L}$, 31% died; at 180 $\mu\text{g}/\text{L}$, 97% died; at 386 $\mu\text{g}/\text{L}$, hatch was reduced 24% and all larvae died	34
200.0–450.0	LC50 (96 h); embryos	4
Speckled dace, <i>Rhinichthys osculus</i>		
4.9	LC50 (96 h) in soft water	4
14.0	LC50 (96 h) in hard water	4
Brown trout, <i>Salmo trutta</i>		
Fingerlings exposed to radiosilver-110m for 57 days then transferred to clean freshwater for 28 days	After 57 days the whole body BCF was 2.7 with about 70% of total radiosilver concentrated in the liver (BCF for liver was 282); during depuration, 23% of whole fish radiosilver was excreted but concentration in liver was unchanged	35
Fingerlings were fed a diet containing radiosilver-110m for 34 days then fed a clean diet for 27 days	After 34 days, about 12% of the silver fed was retained; liver contained 63% of the total radioactivity. After 27 days of depuration 31% of the radiosilver was lost from whole trout, but liver contained 79% of the total radioactivity	36
Cunner, <i>Tautogolabrus adspersus</i>		
120, 250, or 500; after 96 h, gill tissues were excised and gill oxygen consumption monitored for 4 h	Gill tissue oxygen consumption was significantly lower than controls at all silver concentrations tested in a dose-dependent manner	37
500	After 96 h, gill tissue respiration was reduced and liver enzyme activity altered. Similar effects seen for silver nitrate and silver acetate	38
>500	Lethal after 96 h	37
Arctic grayling, <i>Thymallus arcticus</i>		
6.7 (5.5–8.0)	LC50 (96 h); alevins	30
11.1 (9.2–13.4)	LC50 (96 h); juveniles	30

Table 7.6 (continued) Effects of Silver on Representative Aquatic Plants and Animals (Concentrations are in micrograms of free silver (Ag^+) per liter of medium added at start unless indicated otherwise.)

Taxonomic Group, Organism, Silver Concentration (ppb), and Other Variables	Effects	Reference ^a
AMPHIBIANS		
Early life stages exposed to silver nitrate from fertilization through 4 days after hatching		
Leopard frog, <i>Rana pipiens</i>		
0.7–0.8	10% mortality or abnormal development of embryos and larvae	43
10.0	50% mortality or gross terata of embryos and larvae	43
5 species		
1–34	10% mortality or gross terata of embryos and larvae	43
10–240	50% mortality or abnormal development of embryos and larvae	43

^a 1, Antelman 1994; 2, Smith and Carson 1977; 3, Jeanthon and Prieur 1990; 4, USEPA 1980; 5, Sanders and Abbe 1987; 6, Sanders and Abbe 1989; 7, Eisler 1981; 8, Nalecz-Jawecki et al. 1993; 9, Williams and Dusenbery 1990; 10, Calabrese et al. 1977b; 11, Thurberg et al. 1974; 12, Berthet et al. 1992; 13, Diamond et al. 1990; 14, Coglianese and Martin 1981; 15, Berthet et al. 1990; 16, Sanders et al. 1990; 17, Abbe and Sanders 1990; 18, Nelson et al. 1983; 19, Calabrese et al. 1984; 20, Nolan and Dahlgaard 1991; 21, Bryan and Langston 1992; 22, Connell et al. 1991; 23, Nebeker et al. 1983; 24, Nehring 1976; 25, Lima et al. 1982; 26, Koechlin and Grasset 1988; 27, Baudin et al. 1994; 28, Coleman and Cearly 1974; 29, Buell 1991; 30, Buhl and Hamilton 1991; 31, Davies et al. 1978; 32, Rombaugh 1985; 33, LeBlanc et al. 1984; 34, Klein-MacPhee et al. 1984; 35, Garnier et al. 1990; 36, Garnier and Baudin 1990; 37, Thurberg and Collier 1977; 38, Gould and MacInnes 1977; 39, Fisher et al. 1995; 40, Fisher et al. 1984; 41, Hogstrand et al. 1996; 42, Brown and Luoma 1995; 43, Birge and Zuiderveen 1995; 44, Morgan et al. 1995; 45, Fisher and Reinfelder 1995; 46, Shaw et al. 1998; 47, Ferguson and Hogstrand 1998; 48, Ratte 1999; 49, Call et al. 1999; 50, Berry et al. 1999; 51, Galvez and Wood 1999.

^b MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable adverse effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Among arthropods, grass shrimp (*Palaemonetes pugio*) rapidly incorporate silver dissolved in brackish water in proportion to its concentration but not from planktonic or detrital food sources containing elevated silver burdens (Connell et al. 1991). Variations in ability of decapod crustaceans to accumulate radiosilver-110m from seawater are large, as judged by concentration factors that ranged from 70 to 4000 (Pouvreau and Amiard 1974). The reasons for this variability are unknown but may be associated with hepatopancreas morphology. It is generally acknowledged that hepatopancreas or digestive gland is the major repository of silver in decapods (Greig 1975; Greig et al. 1977a, 1977b). Aquatic insects concentrate silver in relative proportion to environmental levels (Nehring 1976), and more efficiently than most fish species (Diamond et al. 1990). Whole-body bioconcentration factors (BCF) of silver in 3 species of aquatic insects ranged from 21 to 240 in water containing 30 to 65 mg CaCO₃/L during exposure of 3 to 15 days; in bluegill sunfish (*Lepomis macrochirus*), this value was less than 1 after exposure for 28 days (USEPA 1980). Molt frequency of the stonefly (*Isonychia bicolor*) was a sensitive indicator of silver stress over time, and 1.6 µg total Ag/L over a 20-day period inhibited molting (Diamond et al. 1990). In freshwater sediments supplemented with silver nitrate, a high proportion of the dissolved silver fraction was not readily bioavailable to cause lethality to dipteran insect larvae (Call et al. 1999). Porewater concentrations of dissolved silver that killed 50% of the dipteran larvae were up to 275 times greater than the 10-day water-only LC50 value of 57 µg/L, indicating that most of the dissolved fraction was not readily bioavailable to cause death. Concentrations of silver in these sediments that caused significant adverse effects — 200 to 500 mg Ag/kg DW — in dipteran larvae were markedly above silver concentrations usually reported in the environment (Call et al. 1999).

Silver ion (Ag⁺) was the most toxic chemical species of silver to fishes. Silver ion was 300 times more toxic than silver chloride to fathead minnows (*Pimephales promelas*), 15,000 times more

toxic than silver sulfide, and more than 17,500 times more toxic than silver thiosulfate complex. In all cases, toxicity reflected the free silver ion content of tested compounds (Le Blanc et al. 1984); a similar pattern was noted in rainbow trout (Hogstrand et al. 1996). Silver was less toxic to fathead minnows under conditions of increasing water hardness between 50 and 250 mg CaCO₃/L, increasing pH between 7.2 and 8.6, and increasing concentrations of humic acid and copper. Starved minnows were more sensitive to ionic silver than minnows fed regularly (Brooke et al. 1994). Eggs of rainbow trout (*Oncorhynchus mykiss*) exposed continuously to silver concentrations as low as 0.17 µg/L had increased embryotoxicity and hatched prematurely; resultant fry had a reduced growth rate (Davies et al. 1978). Removal of the egg capsule of eyed embryos of steelhead trout (*O. mykiss*) significantly lowered the resistance of the embryos to salts of silver, copper, and mercury but not zinc and lead (Rombaugh 1985). Silver accumulation in gills of juvenile rainbow trout exposed to 11 µg Ag/L for 2 to 3 h was significantly inhibited by various cations (Ca²⁺, Na⁺, H⁺) and complexing agents (dissolved organic carbon, thiosulfate, chloride). These variables must be considered when constructing predictive models of silver binding to gills (Janes and Playle 1995).

Largemouth bass (*Micropterus salmoides*) and bluegills accumulated silver from the medium; accumulations increased with increasing concentrations of ionic silver and increasing duration of exposure (Coleman and Cearly 1974). Dietary silver sulfide exposure at or below 3000 mg Ag/kg ration is physiologically benign to juvenile rainbow trout over a 58-day period, although other forms of silver at dietary concentrations as low as 3 mg/kg DW ration can accumulate in liver of juvenile trout at concentrations 12-fold greater than controls after 3 months (Galvez and Wood 1999). Bioconcentration factors of radiosilver-110m and various species of teleosts were as high as 40 after 98 days (Pouvreau and Amiard 1974). However, flounders (*Pleuronectes platessa*) and rays (*Raja clavata*) fed nereid polychaete worms labeled with radiosilver-110m retained about 4.2% of the ingested dose after 3 days (Pentreath 1977), which suggests that the high silver concentration factors reported by Pouvreau and Amiard (1974) may have been due to loosely bound adsorbed silver. Flounders (*Pleuronectes* sp.) held in seawater solutions containing 40 µg Ag/L for 2 months had elevated silver concentrations in the gut (0.49 mg Ag/kg FW) but less than 0.05 mg/kg in all other examined tissues (Pentreath 1977). Similarly exposed rays (*Raja* sp.) contained 1.5 mg Ag/kg FW in liver, 0.6 in gut, 0.2 in heart, and 0.05 to 0.18 mg/kg FW in spleen, kidney, and gill filament (Pentreath 1977). Liver is usually considered the major repository of silver in teleosts (Garnier et al. 1990). In tidepool sculpins (*Oligocottus maculatus*), ionic silver was more toxic at lower salinities, longer exposure durations, and increasing medium ammonia concentrations; however, there was no correlation between whole-body silver burden and toxicity at 2.5% salinity, and no uptake at 3.2% salinity (Shaw et al. 1998).

At concentrations normally encountered in the environment, food chain biomagnification of silver in aquatic systems is unlikely (Connell et al. 1991; Ratte 1999), although regular ingestion of fish from contaminated waters may significantly affect dietary silver intake (USEPA 1980). Silver — as thiosulfate-complexed silver at nominal concentrations of 500 or 5000 µg Ag/L — was concentrated and magnified over a 10-week period in freshwater food chains of algae, daphnids, mussels, and fathead minnows (Terhaar et al. 1977), although the mechanisms of accumulation in this study were imperfectly understood. Sediments contaminated with silver sulfide (Ag₂S), however, do not seem to pose a major route of entry into the aquatic food web. Juvenile amphipods (*Hyalella azteca*) held on sediments containing as much as 753 mg Ag/kg DW, as silver sulfide, for 10 days had normal growth and survival (Hirsch 1998a). Aquatic oligochaetes (*Lumbriculus variegatus*) held on sediments containing 444 mg Ag/kg DW, as silver sulfide, for 28 days had a low bioconcentration factor of 0.18 (Hirsch 1998b). Fisher and Wang (1998) show that trophic transfer of silver in marine herbivores, especially mussels, is dependent on the silver assimilation efficiency from ingested food particles, feeding rate, and silver efflux rate. Silver assimilation efficiency is usually less than 30% and lower for sediment than for phytoplankton. Silver assimilation efficiency and distribution from ingested phytoplankton particles is modified by gut passage time, extracellular and intracellular digestion rates, and metal desorption at lowered pH. The kinetic

model of Fisher and Wang (1998) for mussels predicts that either the solute or particulate pathway can dominate and is dependent on silver partition coefficients for suspended particles, and silver assimilation efficiency.

7.5.4 Birds and Mammals

No data were found on the effects of silver compounds on avian or mammalian wildlife. All controlled studies with silver were with domestic poultry, livestock, or small laboratory mammals. Signs of chronic silver ion intoxication in tested birds and mammals included cardiac enlargement, vascular hypertension, hepatic necrosis, anemia, lowered immunological activity, altered membrane permeability, kidney pathology, enzyme inhibition, growth retardation, and a shortened life span (Smith and Carson 1977; Freeman 1979; Fowler and Nordberg 1986; USPHS 1990).

Silver affects turkeys (*Meleagris gallopavo*) and domestic chickens (*Gallus* spp.). Turkey poult on diets containing 900 mg Ag/kg of feed for 4 weeks had reduced growth, hemoglobin, and hematocrit and an enlarged heart (USEPA 1980). Chicken eggs injected with silver nitrate at 0.1 mg Ag/egg (equivalent to about 1.8 mg Ag/kg egg FW) had a 50% reduction in survival but no developmental abnormalities (Ridgway and Karnofsky 1952). Adverse effects of silver were reported in normal chicks fed diets containing 200 mg Ag/kg ration (growth suppression) or given drinking water containing 100 mg Ag/L (liver necrosis; Smith and Carson 1977). Chicks on copper-deficient diets had adverse effects at 10 mg Ag/kg ration (reduced hemoglobin; reversible when fed copper-adequate diet) and at 50 to 100 mg Ag/kg ration (growth suppression and increased mortality). Chicks deficient in Vitamin E experienced reduced growth when given drinking water containing 1500 mg Ag/L. Chickens infected with *Salmonella pullorum-gallinarum* and *Escherichia coli* were cured with aerosol treatments containing 10 µg Ag/L air (Smith and Carson 1977).

Studies with small laboratory mammals (which require verification) show that long-term exposure to high levels of silver nitrate in drinking water may result in sluggishness and enlarged hearts; however, these effects have not been observed in silver-exposed humans (USPHS 1990). Concentrations as high as 200 µg Ag/L in drinking water of test animals for 5 months had no significant effect on animal health or metabolism (USEPA 1990), but 400 µg Ag/L for 5 months caused kidney damage, and 500 µg/L for 11 months was associated with impaired conditioned-reflex activities, immunological resistance, and altered brain nucleic acid content (USEPA 1980). Diets deficient in Vitamin E or selenium caused rapidly fatal hepatocellular necrosis and muscular dystrophy in rats if they contained the dietary-intake equivalent of 130 mg Ag/kg BW daily, a comparatively high silver ion intake (Smith and Carson 1977; USPHS 1990).

The extent of absorption of an administered dose of silver depends on silver speciation, the presence and extent of silver-binding proteins, and other variables. But absorption depends mainly on the transit time through the gastrointestinal tract; the faster the transit time, the less silver is absorbed. Transit times ranged from about 8 h in mice and rats to about 24 h in monkeys, dogs, and humans (USPHS 1990). Route of administration affected the excretion rate of silver. Clearance of silver from mammals 2 days after silver was administered intravenously ranged from 15% in dogs to 82% in mice; clearance rates were intermediate in monkeys and rats. When silver was administered orally, clearance was more rapid, and extended from 90.4% in dogs to 99.6% in mice. The half-time persistence of silver administered orally to mice was 0.1 day for the short-lived component and 1.6 days for the long-lived component. Other species of tested laboratory animals had biphasic or triphasic whole-body silver-excretion profiles that differed significantly from mice. Monkeys, for example, had a biphasic excretion profile with peaks at 0.3 and 3.0 days; rats had a triphasic profile with peaks at 0.1, 0.7, and 5.9 days; and dogs had half-time persistence peaks at 0.1, 7.6, and 33.8 days (USPHS 1990).

Ionic silver is lethal to mice (*Mus* spp.) at 13.9 mg/kg BW by intraperitoneal injection, to rabbits (*Oryctolagus* spp.) at 20 mg/kg BW intraperitoneally, to dogs (*Canis familiaris*) at 50 mg/kg BW

by intravenous injection, to humans at greater than 166 mg/kg BW in a single dose, and to rats (*Rattus* spp.) at 1586 mg/L drinking water for 37 weeks (Table 7.7). Sublethal effects are reported in rabbits given 250 µg Ag/L drinking water (brain histopathology), in rats given 400 µg Ag/L drinking water for 100 days (kidney damage), in mice given 95 mg Ag/L drinking water for 125 days (sluggishness), in guinea pigs (*Cavia* sp.) given 81 mg Ag/cm² skin applied daily for 8 weeks (reduced growth), and in rats given diets containing 6 mg Ag/kg for 3 months (high accumulations in kidneys and liver) or 130 to 1110 mg/kg diet (liver necrosis; Table 7.7).

The connections between human cancers and silver as a causal agent are tenuous (USEPA 1980). All available evidence is negative or inconclusive on silver's ability to induce cancer, mutagenicity, or birth defects in animals by normal routes of exposure (USEPA 1980; USPHS 1990). Silver pellets, however, implanted under the skin of rodents, have caused sarcomas, malignant fibrosarcomas, fibromas, fibroadenomas, and invasions of muscle with connective tissue; in these cases, silver seems to act as a nonspecific irritant rather than as a specific carcinogen (Smith and Carson 1977; USEPA 1980). Intratumoral injections of colloidal silver promotes cancer growth in rats, possibly by producing an area of lowered tissue resistance that allows resistant cancer cells to grow freely (Smith and Carson 1977). However, silver nitrate seems to be a tumor inhibitor in mice (USEPA 1980).

In humans, acute toxic effects of silver have resulted only from accidental or suicidal overdoses of medical forms of silver. Symptoms of acute silver poisoning in patients dying after intravenous administration of Collargo (silver plus silver oxide) included gastrointestinal disturbances, pulmonary edema, tissue necrosis, and hemorrhages in bone marrow, liver, and kidney (Smith and Carson 1977; USEPA 1980). High sublethal doses of silver nitrate taken orally cause some patients to experience violent abdominal pain, abdominal rigidity, vomiting, and severe shock. Systemic effects among recovering patients are unlikely, although degenerative liver changes may occur (USEPA 1980). In humans, skin contact with silver compounds may cause mild allergic reactions such as rash, swelling, and inflammation (USPHS 1990); industrial and medicinal exposures to silver may cause lesions of the kidneys and lungs, and arteriosclerosis (Klaassen et al. 1986); colloidal silver compounds may interfere with nasal ciliary activity (Smith and Carson 1977); and exposure to dust containing high levels of silver compounds, such as silver nitrate or silver oxide, may cause breathing problems, lung and throat irritation, and stomach pain (USPHS 1990).

Chronic exposure of humans to silver or silver compounds frequently resulted in generalized argyria (slate-gray pigmentation of the skin and hair caused by deposition of silver), localized argyria (limited areas of pigmentation usually associated with medicinal silver applications), or argyrosis (argyria of the eye). Every silver compound in common chemical use has caused generalized argyria, usually from medical and occupational exposures (Smith and Carson 1977; USEPA 1980). In generalized argyria, skin pigmentation was highest in light-exposed areas, although silver concentrations in light-exposed and dark-exposed skin were the same (USEPA 1980). In severe cases of argyria, the skin can become black with a metallic luster, the eyes can be affected to the point that vision is disturbed, and the respiratory tract can be impaired (Klaassen et al. 1986). Individual variability in susceptibility to argyria is great and this is probably explained by the variability in absorption and retention of silver (Smith and Carson 1977). Generalized argyria as an occupational disease is unusual but has been reported in workers who make silver nitrate or are involved in mirror plating, glass bead silverying, silver Christmas cracker manufacturing, photographic plate manufacturing, and silver mining. Generalized argyria was also associated with chronic inhalation or ingestion of silver fulminate, silver nitrate, silver albuminate, and silver cyanide (Smith and Carson 1977). Improved workplace ventilation and sanitation among silver nitrate workers effected a decline in general argyria (USEPA 1980).

Localized argyria is rare and usually occurs when silver compounds contact broken skin or mucous membranes (Smith and Carson 1977). Localized argyria has been reported in workers who handle metallic silver in filing, drilling, polishing, turning, engraving, forging, soldering, or smelting

Table 7.7 Effects of Silver on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effects	Reference ^a
DOMESTIC DOG, <i>Canis familiaris</i>		
Inhalation route. Anesthetized dogs exposed to metallic silver particles about 0.5 µm in diameter; total dose deposited of 25 µg	About 3% (0.8 µg) of the deposited silver was found in liver and blood 6h after exposure. Clearance from the lung to the blood was triphasic, with half-times of 1.7, 8.4, and 40 days	1
Intratracheal route. Elemental silver deposited in lungs	After 6 h, 96.9% remained in the lung, 2.4% in liver, 0.35% in blood, 0.14% in gall bladder and bile, 0.1% in intestines, 0.06% in kidneys, and 0.02% in stomach. After 225 days, 0.49% of the initial dose was detected in liver, and 0.01–0.03% each in brain, gall bladder, intestines, lungs and trachea, bone, stomach and contents, heart, and muscle. If lung is excluded, liver contained 77% of the total silver body burden between 6 h and 225 days postexposure	1
Intravenous injection route 0.003 µg/kg body weight (BW) daily 500 mg (estimated at 50 mg/kg BW), single injection Oral route; 0.005 µg/kg BW daily	15% cleared in 2 days All dead within 24 h with hemolysis and lung edema 90.4% cleared in 2 days	1 2 1
GUINEA PIG, <i>Cavia</i> sp.		
Dermal application of 81 mg silver nitrate to 3.1 cm ² of skin daily for 8 weeks	Growth rate reduced 10–20%	1
HUMANS, <i>Homo sapiens</i>		
External route 0.25% silver nitrate solution in eyes for 3 weeks 3 to 5% colloidal silver compounds in eyes for 5–10 weeks	Argyrosis Argyrosis	2 2
Inhalation route 0.25 mg/m ³ air 1–2 mg/m ³ air; occupational exposure	Possibility of generalized argyria in 20 years Argyrosis of cornea and conjunctiva	2 3
Clearance half-time Feces Lung Urine	>300 days Biexponential profile; 1 day and 52 days <54 days	1 1 1
Oral route 80 µg/kg BW, single dose 0.7 mg silver weekly in diet 2–30 grams of silver nitrate, single dose 50–260 grams of metallic silver >600 grams over 1.2 years; given as silver nitrate to treat epilepsy and GI symptoms	21% of dose retained in body after 1 week Possibility of generalized argyria At dosages >10 grams death usually occurs within a few hours to a few days Gastric fullness, anorexia, gastric pain, diarrhea Generalized argyria evident 2 years after last dose	1 2 2, 3 2, 3 2
MONKEYS, Various		
Intravenous administration of 0.01 µg/kg BW daily Oral administration of 0.01 µg/kg BW daily	44.1% excreted in 2 days 94.3% cleared in 2 days	1 1

Table 7.7 (continued) Effects of Silver on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effects	Reference ^a
DOMESTIC MOUSE, <i>Mus</i> spp.		
Drinking water route; 95 mg/L for 125 days	Sluggishness	1
Intraperitoneal route		
13.9 mg/kg BW, single injection	LD50(30 days)	3
35.0 mg/kg BW, single injection; pretreated with single injection of 3.5 mg Ag/kg BW 24 h earlier	Only 3 of 10 pretreated mice died within 7 days vs. 8 of 10 nonpretreated mice	3
Intravenous injection; 1.0 µg/kg BW daily	82% cleared in 2 days	1
Oral route; 1.1 µg/kg BW daily	99.6% cleared in 2 days	1
RABBIT, <i>Oryctolagus</i> sp.		
Drinking water route		
Equivalent to 2.5 µg Ag/kg BW daily	No observable adverse effects	2
Equivalent to 25 or 250 µg Ag/kg BW daily for 11 months	Brain histopathology; altered conditioned reflexes	2
Equivalent to 500 or 5000 µg Ag/kg BW daily for 11 months	Lowered immunological activity; pathology of vascular, nerve, brain, and spinal cord tissues	3
Intraperitoneal injection route; 20 mg/kg BW, single injection	All dead within 2 h. Silver granules in liver parenchyma and kidney tubules	3
LABORATORY WHITE RAT, <i>Rattus</i> spp.		
Diet		
Equivalent to 6 mg/kg BW daily	After 12 weeks, kidneys and liver were impregnated with silver	2
130–1110 mg/kg ration	Liver necrosis which could be prevented by adding Vitamin E	2
Drinking water route		
50 µg/L (equivalent to 0.0025 mg Ag/kg BW daily) for 11 months	Normal in all variables measured (conditioned reflex activity, gastric secretion, blood serum enzymes, histology)	3
200 µg/L for 6 months	Normal conditioned reflex activity	3
<400, 400, 700, or 1000 µg/L for 100 days	At <400 µg/L, rats seemed healthy with normal tissuey histology. At 400 µg/L, hemorrhages noted in kidney. At 700 µg/L, kidney and liver histopathology was evident. At 1000 µg/L, spleen was pigmented and kidney and liver damage more pronounced	3
500 µg/L (equivalent to 0.025 mg Ag/kg BW daily) for 6 to 11 months	Abnormal conditioned reflex activity; increased liver weight and liver RNA concentration	3
5 mg/L for 6 months	Signs of intoxication beginning at days 25–27	3
20 mg/L for 3 months	Decreased growth; abnormal liver; increased levels of blood amino acids	3
20 mg/L for 5 months	Pathology in stomach, small intestine, and liver; altered blood serum enzyme activity; growth depressed 36%	3
20 mg/L for 6 months	Increased brain DNA and RNA	2
129 mg/L (about 18 mg/kg BW daily) for 17.8 weeks	Silver accumulations in brain and CNS; reduced motor activity	1
634 mg/L (89 mg Ag/kg BW daily) for 2 years	No effect on male fertility; no silver deposits in testes	1
635–660 mg/L; lifetime exposure beginning shortly after weaning	Lifespan normal; hypertrophy of left ventricle, suggesting vascular hypertension; skin normal but internal organs and eyes darkened by silver deposits	3
1200 mg/L for several months	Degenerative kidney changes	3

Table 7.7 (continued) Effects of Silver on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effects	Reference ^a
1500 mg/L for 2–4 weeks; Vitamin E-deficient rats	Liver necrosis and death. Prevented by adding Vitamin E	2
1586 mg/L for 37 weeks	Some deaths beginning at week 23; survivors weighed about 50% less than controls	1
2500 mg/L for 3 months, then silver-free water for 16 months	At end of exposure livers had 6.7–7.0 mg Ag/kg FW and kidneys 3.7–7.1 mg/kg FW; 16 months after exposure livers had 1.6 mg/kg FW and kidneys 6.0 mg/kg FW	3
2589 mg/L, (equivalent to 362 mg Ag/kg BW daily) for 2 weeks	25% died; water intake decreased beginning at day 1; survivors poorly groomed and listless	1
Intramuscular injection route		
Given radiosilver-110m alone or in combination with 4.0 mg Ag/kg BW daily for 6 days. Percent of tracer dose recovered vs. percent tracer plus 4.0 mg/kg BW		
Blood	0.5 vs. 3.0	1
Bone	0.2 vs. 2.2	1
Feces	96.6 vs. 37.3	1
GI tract	1.1 vs. 8.2	1
Heart, lungs	0.06 vs. 0.6	1
Kidney	0.07 vs. 0.6	1
Liver	0.4 vs. 33.7	1
Muscle	0.2 vs. 2.4	1
Skin	0.2 vs. 7.4	1
Spleen	0.01 vs. 2.7	1
Urine	0.6 vs. 1.8	1
Intravenous injection route		
0.2 µg/kg BW daily	70.7% excreted in 2 days vs. 98.4% in 2 days when administered orally	1
Isolated hepatocytes exposed for 20 h		
<275 µg/L	Not cytotoxic	4
500, 2000, or 5000 µg/L	Silver accumulated in nuclear fraction of hepatocytes at all concentrations; DNA repair synthesis was stimulated at 2000 µg/L; moderately cytotoxic at 5000 µg/L	5
1100 µg/L	Protein synthesis activity inhibited 50%	4
1980 µg/L	Almost complete inhibition of protein synthesis activity	4
Subcutaneous injection route		
7 mg/kg BW, single injection	Adverse effects on spermatogenesis and on testes histology	2, 3
Oral route		
123 mg/kg BW, as silver cyanide	Acute oral LD50	6
200–400 mg/kg BW, as silver arsenate	Acute oral LD50	6
500–800 mg/kg BW, as silver nitrate	Acute oral LD50	6
CARIBOU, <i>Rangifer tarandus</i>		
Ratio of silver concentration (mg/kg FW) in tissues to silver concentration (mg/kg FW) in lichen diet		
Bone	Bioconcentration factor (BCF) of 3.0	3
Kidney	BCF of 1.3	3
Liver	BCF of 80.0	3
Muscle	BCF of 0.3	3

^a 1, USPHS 1990; 2, Smith and Carson 1977; 3, USEPA 1980; 4, Denizeau et al. 1990; 5, Denizeau and Marion 1989; 6, Lockhart 1983.

operations. Silver polishers exposed for 25 years or more (range 2 to 38 years) sometimes exhibit increased densities in their lung X-rays due to silver impregnation of the elastic membranes of the pulmonary vessels. In one case, an Italian physician who dyed his facial hair with a silver dye for 25 years developed argyria in the conjunctiva of both eyes (Smith and Carson 1977).

7.6 RECOMMENDATIONS

Most measurements of silver concentrations in natural waters prior to the use of clean techniques are considered inaccurate. Until analytical capabilities that exceed the dissolved-particulate classification are developed, it will be necessary to rely on laboratory and theoretical modeling studies to fully understand chemical speciation of silver in natural waters (Andren et al. 1995).

Factors governing the environmental fate of silver are not well characterized, including silver transformations in water and soil and the role of microorganisms (USPHS 1990). The toxic potential of silver chloride complexes in seawater and the role of sediments as sources of silver contamination for the food web needs more research (Ratte 1999). Food chain transfer of silver requires more current information on sources and forms of silver and data on concentrations in field collections of flora and fauna, especially near hazardous waste sites (USPHS 1990). Although silver in sewage sludge is mostly immobilized, data are limited on silver concentrations in flesh and milk of livestock pastured or fed grains raised on soils amended with sewage sludge (Smith and Carson 1977). Data are needed on partition coefficients and vapor pressures of silver compounds (USPHS 1990) and on silver concentrations in emissions from cement producers and smelters and refineries of copper, lead, zinc, silver, iron, and steel (Smith and Carson 1977). Also, technology to recapture silver from waste media before it reaches the environment must be improved (USPHS 1990).

Silver criteria in aquatic ecosystems are under constant revision by regulatory agencies. For example, total recoverable silver is no longer recommended by the U.S. Environmental Protection Agency in silver criteria formulation and should be replaced by dissolved silver (USEPA 1995a). Dissolved silver more closely approximates the bioavailable fraction of silver in the water column than does total recoverable silver (USEPA 1995b). Dissolved silver criteria recommended are about 0.85 times those of total recoverable silver under certain conditions but may vary considerably depending on other compounds present in solution (USEPA 1995b).

The proposed human drinking water criteria of 50 to <200 µg total Ag/L do not seem to represent a hazard to human health, although much lower concentrations adversely affect freshwater and marine organisms (Smith and Carson 1977; [Table 7.8](#)). Proposed silver criteria for the protection of freshwater aquatic life during acute exposure now range from 1.2 to 13.0 µg total recoverable silver per liter ([Table 7.8](#)). If all total recoverable silver were in the ionic form, these proposed criteria would overlap the 1.2 to 4.9 µg/L range found lethal to sensitive species of aquatic plants and animals, and this indicates that the proposed freshwater acute silver criteria need to be reexamined. For freshwater aquatic life protection during chronic exposure, the proposed criterion of less than 0.13 µg total recoverable silver per liter ([Table 7.8](#)) is probably protective, but the proposed silver criterion of 2.3 µg total silver/L to protect marine life ([Table 7.8](#)) needs to be reconsidered because phytoplankton species composition and succession are significantly altered at 0.3 to 0.6 µg total silver/L and because some species of marine algae and molluscs show extensive accumulations at 1.0 to 2.0 µg total silver/L. Limited but insufficient data were available on correlations between tissue residues of silver with health of aquatic organisms ([Table 7.8](#)); additional research seems needed on the significance of silver residues in tissues.

In aquatic environments, more research is needed on the chemical speciation of silver to evaluate risk to the organism and its consumers (USEPA 1987; Berthet et al. 1992). Most silver criteria formulated for the protection of aquatic life are now expressed as total recoverable silver per liter ([Table 7.8](#)), but total silver measurements do not provide an accurate assessment of potential hazard. Silver ion (Ag⁺), for example, is probably the most toxic of all silver chemical species and must

Table 7.8 Proposed Silver Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Silver Concentration	Reference ^b
AGRICULTURAL CROPS		
Soils	<100 mg total silver/kg dry weight soil for most species; <10 mg/kg for sensitive species	7
FRESHWATER AQUATIC LIFE PROTECTION		
Acute exposure		
Total recoverable silver	<1.32 µg/L	1
Acid-soluble silver ^a	Four-day average shall not exceed 0.12 µg/L more than once every three years; 1-h average not to exceed 0.92 µg/L more than once every three years	8
Acute exposure		
Total recoverable silver, in µg/L, should not exceed $e^{(1.72[\ln(\text{hardness})]-6.52)}$ at any time.		
Examples follow:		
50 mg CaCO ₃ /L	<1.2 µg/L	2
100 mg CaCO ₃ /L	<4.1 µg/L	2
200 mg CaCO ₃ /L	<13.0 µg/L	2
Chronic exposure	<0.12 to <0.13 µg total recoverable silver/L	1, 2
Tissue residues		
Adverse effects on growth of the Asiatic clam, <i>Corbicula fluminea</i>	>1.65 mg total silver/kg soft tissues, fresh weight basis	1
MARINE LIFE PROTECTION		
Acute exposure		
Total recoverable silver	<2.3 µg/L at any time	2
Acid-soluble silver ^a	Four-day average concentration not to exceed 0.92 µg/L more than once every three years on average and the 1-h concentration not to exceed 7.2 µg/L more than once every three years	8
Tissue residues		
Marine clams, soft parts		
Normal	<1 mg total silver/kg dry weight	3
Stressful or fatal	>100 mg total silver/kg dry weight	3
HUMAN HEALTH		
Air, United States		
Current level of exposure, nationwide	100 µg total silver daily per person	2
Short-term exposure limit (15 min; up to 4 times daily with 60 min intervals at <0.01 mg Ag/m ³ air)	<0.03 mg total silver/m ³	2
Threshold limit value (8 h daily, 5 days weekly)		
Aerosol silver compounds	<0.01 mg total silver/m ³	2, 4, 5
Metallic silver dust	<0.1 mg total silver/m ³	5
Diet, United States		
Current level of exposure	35 to 40 µg daily per person	2
Drinking water		
United States		
Long-term exposure (>10 days)	<50 µg total silver/L	2, 5, 6
Proposed long-term exposure	<90 total silver µg/L	5
Short-term exposure (1–10 days)	<1142 µg total silver/L	5
California	<10 µg/L	2
Germany	<100 µg/L	2
Space vehicles		
Former Soviet Union	Max. 200 µg total silver/L	2

Table 7.8 (continued) Proposed Silver Criteria for the Protection of Natural Resources and Human Resource, Criterion, and Other Variables

Resource, Criterion, and Other Variables	Effective Silver Concentration	Reference ^b
United States	100 to Max. 200 µg total silver/L	2
Switzerland	<200 µg total silver/L	2
Groundwater	<50 µg total silver/L	5

^a Silver that passes through a 0.45 µm membrane after the sample has been acidified to a pH between 1.5 and 2.0 with nitric acid.

^b 1, Diamond et al. 1990; 2, USEPA 1980; 3, Bryan and Langston 1992; 4, Smith and Carson 1977; 5, USPHS 1990; 6, Fowler and Nordberg 1986; 7, Hirsch et al. 1993; 8, USEPA 1987.

be accurately measured in the assessment of silver risks in aquatic environments (Le Blanc et al. 1984; Hogstrand and Wood 1998; Bury et al. 1999b; Ratte 1999), perhaps as acid-soluble silver (USEPA 1987). Little is known of the biocidal properties of Ag²⁺ and Ag³⁺, which are the active ingredients in disinfectants and used increasingly in water purification systems of drinking water and swimming pools (Antelman 1994). The effects of these silver species on organism health clearly must be researched (USPHS 1990). Silver interactions with other metals and compounds in solution are not well defined. For example, mixtures of salts of silver and copper markedly increased the survival of oyster embryos, but only when copper concentrations were less than 6 µg/L and total silver less than 11 µg/L (Coglianese and Martin 1981).

The current freshwater acute ambient water-quality criterion for silver in the United States recognizes that water calcium levels may modify toxicity; however, studies with rainbow trout suggest that calcium and sodium were not as important as chloride or dissolved organic carbon in ameliorating adverse effects of silver (Bury et al. 1999b; Karen et al. 1999). Dissolved organic carbon was considered more important than hardness for predicting the toxicity of ionic silver in natural waters to daphnids and fishes (Karen et al. 1999). Incorporating an organic carbon coefficient into the silver criterion equation will enhance the criterion values for site specificity (Karen et al. 1999). The present proposed silver criteria for aquatic life protection could be further improved by taking into account the important geochemical modifiers of silver (Hogstrand and Wood 1998). For example, complexation of Ag⁺ by chloride, dissolved organic carbon and sulfide are important in reducing silver toxicity, and AgNO₃ as Ag⁺ is less toxic in seawater (LC50 [96 h] range of 320 to 2700 µg/L) than in freshwater (5 to 70 µg/L). More research is needed on the buildup of ammonia in Ag⁺-poisoned teleosts and its effects on their ability to swim. In any event, it is debatable whether silver discharges into the freshwater environment ever result in Ag⁺ levels high enough to cause acute toxicity (Hogstrand and Wood 1998). Laboratory tests with AgNO₃ reportedly overestimate acute silver toxicity because of the abundance in the field of natural ligands which bind Ag⁺ and reduce its toxicity. Also, there is little credible evidence that internal silver accumulations in freshwater biota play any role in acute toxicity or that dietary silver causes toxicity. In marine environments, current acute silver criteria seem overly stringent for aquatic life protection, with more research needed on chronic toxicity to euryhaline fishes — including the toxic potential of accumulated silver (Hogstrand and Wood 1998).

No studies have been conducted with silver and avian or mammalian wildlife, and it is unreasonable to extrapolate the results of limited testing with domestic poultry and livestock to wildlife to establish criteria or administratively enforced standards. Research on silver and avian and terrestrial wildlife merits the highest priority in this subject area. No silver criteria are available for the protection of avian and mammalian health, and all criteria now proposed are predicated on human health (Table 7.8). As judged by the results of controlled studies with poultry and small laboratory mammals, safe concentrations of silver ion were less than 250 µg/L in drinking water of mammals, less than 100 mg/L in drinking water of poultry, less than 6 mg/kg in diets of mammals, less than 10 mg/kg in copper-deficient diets of poultry, less than 200 mg/kg in copper-adequate diets of poultry, and less than 1.8 mg/kg in chicken eggs. The proposed short-term (10-day) allowable limit of 1142 µg Ag/L in drinking water for human health protection (Table 7.8) should

be reconsidered because it is 4.6 times higher than the value that produced adverse effects in sensitive laboratory mammals. Additional animal studies are needed to elucidate the effects of silver and silver compounds on reproduction, development, immunotoxicity, neurotoxicity, absorption, distribution, metabolism, and excretion; and on oral, dermal, and inhalation routes of exposure (USPHS 1990). In animals, there is also the need to establish a target organ for intermediate exposures to silver; to establish suitable biomarkers of silver exposures and effects; and to measure effects of chronic silver exposures on carcinogenicity (USPHS 1990). These studies should be implemented with suitable sentinel organisms including waterfowl, aquatic mammals, and other species of wildlife.

It is emphasized that silver and its compounds do not pose serious environmental health problems to humans from 50 µg/L in drinking water and 10 µg/m³ in air (Smith and Carson 1977). The only proven effect of chronic exposure to silver is argyria from occupational or therapeutic exposure to much larger amounts of silver (minimum necessary absorption of 910 µg, equivalent to about 15 µg/kg BW) than can feasibly be ingested or inhaled from environmental sources. Regular ingestion of fish, meat, and plants from silver-contaminated areas probably does not cause argyria (Smith and Carson 1977). Humans at special risk for argyria include those treated with silver-containing medicinals and people marginally deficient or deficient in copper, selenium, or Vitamin E (USEPA 1980). There is no recognized effective treatment for argyria, although the condition seems to be relatively stationary when exposure to silver is discontinued (Fowler and Nordberg 1986). Absorption and retention of silver from food and medicinals is imperfectly understood (Smith and Carson 1977), suggesting the need for additional animal studies.

Finally, alternatives exist to the use of silver in various materials and processes. These include substitution of aluminum and rhodium for silver in mirrors and other reflecting surfaces; tantalum replacement of silver in surgical plates, pins, and sutures; stainless steel as an alternative material to silver in the manufacture of table flatware; and, in photography, film with reduced silver content (Reese 1991).

7.7 SUMMARY

Ecological and toxicological aspects of silver (Ag) and silver salts in the environment are briefly summarized with an emphasis on natural resources. Subtopics include sources and uses, chemistry and metabolism, concentrations in field collections, lethal and sublethal effects, and recommendations for the protection of natural resources. Elevated silver concentrations in biota occur in the vicinities of sewage outfalls, electroplating plants, mine waste sites, and silver-iodide seeded areas; in the United States, the photography industry is the major source of anthropogenic silver discharges into the biosphere. Maximum concentrations recorded in field collections, in mg total silver/kg dry weight (tissue), were 1.5 in mammals (liver), 6 in fish (bone), 14 in plants (whole), 30 in annelid worms (whole), 44 in birds (liver), 110 in mushrooms (whole), 185 in bivalve molluscs (soft parts), and 320 in gastropods (whole). Humans afflicted with silver poisoning (argyria) contained 72 mg total Ag/kg dry weight skin and 1300 mg total Ag/kg fresh weight whole body. Silver and its compounds are not known to be mutagenic, teratogenic, or carcinogenic. Under normal routes of exposure, silver does not pose serious environmental health problems to humans at less than 50 µg total Ag/L drinking water or 10 µg total Ag/m³ air. Free silver ion, however, was lethal to representative species of sensitive aquatic plants, invertebrates, and teleosts at nominal water concentrations of 1.2 to 4.9 µg/L; at sublethal concentrations, adverse effects were significant between 0.17 and 0.6 µg/L. No data were found on effects of silver on avian or mammalian wildlife; all studied effects were on poultry, small laboratory animals, and livestock. Silver was harmful to poultry at concentrations as low as 1.8 mg total Ag/kg whole egg fresh weight by way of injection, 100 mg total Ag/L in drinking water, or 200 mg total Ag/kg in diets; sensitive mammals were

adversely affected at total silver concentrations as low as 250 µg/L in drinking water, 6 mg/kg in diets, or 13.9 mg/kg whole body. Proposed criteria for the protection of living organisms from silver are listed and discussed.

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CHAPTER 8

Tin

8.1 INTRODUCTION

Interest in the toxicity of tin compounds dates to the early 1800s when investigators demonstrated that inorganic tin compounds produced muscular weakness, loss of pain sensation, and immobility in dogs (Reiter and Ruppert 1984; Idemudia and McMillan 1986b). In humans, organotins can be assimilated by inhalation, absorption through the skin, and from food and drinking water (Zuckerman et al. 1978). The first documented case of organotin poisoning of humans was in 1880 when workers complained of headaches, general weakness, nausea, and diarrhea after exposure to triethyltin acetate vapors (Reiter and Ruppert 1984). Renewed interest in the toxicity of organotin compounds resulted from a medical tragedy in France in 1954. “Stalinon,” a proprietary compound of diethyltin diiodide plus linoic acid used to treat furuncles and other skin infections, caused 217 poisonings and 111 deaths (Piver 1973; Duncan 1980; Idemudia and McMillan 1986b). The identified toxic components in Stalinon were triethyltin contaminants; victims received a total dose of 3 grams over a 6- to 8-week period. Symptoms included constant severe headache, rapid weight loss, vomiting, urine retention, vertigo, hypothermia, abdominal pain, and visual and psychic disturbances. Some of the more severely affected patients had convulsions. Death usually occurred in coma or from respiratory or cardiac failure. In survivors, headaches and diminished visual acuity remained for at least 4 years.

World production of organotin compounds is about 30,000 tons, although relatively few organotin compounds, perhaps only 25, are produced and used to any great extent (Laughlin and Linden 1985). Diorganotins are used in the manufacture of antioxidants, whereas triorganotins are used as general biocides against microbial and invertebrate pests and in marine antifouling paints (Laughlin and Linden 1985). The first antifouling paints incorporating an organotin compound as a biocide were developed in 1961. Because of their effectiveness and availability in a variety of colors, tributyltin antifouling paints are the most commonly used type, replacing copper-, mercury-, and lead-based paints (Stebbing 1985). Worldwide synthesis of tributyltin compounds is about 900 metric tons annually for all applications (Laughlin et al. 1986a). Tributyltins are highly toxic to aquatic plants and animals, readily accumulate in fish and molluscs from contaminated localities, and are present in some harbors where their release from antifouling paints — found usually on small boats and recreational craft — is the putative source (Walsh et al. 1985; U.S. Environmental Protection Agency [USEPA] 1986; Laughlin et al. 1986a). Tributyltin is a contributory factor and probably a major cause for the reproductive failure of the European flat oyster (*Ostrea edulis*) in some locations (Thain and Waldock 1986). In fact, tributyltins are capable of causing adverse biological effects at levels far below those of any previously reported marine pollutant (Lawler and Aldrich 1987; van Slooten and Tarradellas 1994; Matthiessen and Gibbs 1998).

The widespread agricultural applications of trialkyltin biocidal agents have greatly increased the relative exposure risks to workers handling these materials (Rosenberg et al. 1985). Internationally, tin was recognized as a potential environmental contaminant at the Paris and Helsinki conventions in 1974; in later conventions, organotin compounds were moved to the “black list” (Vrijhof 1985). Due to the increasing use of organotin compounds as a class, the Canadian government, in 1979, placed organotins on Canada’s Category III Contaminant List. Category III indicates that additional data are needed on the occurrence, persistence, and toxicity of organotins for preparation of informed environmental and human health risk assessments (Chau et al. 1984). In 1982, the use of tributyltin paints was curtailed in France, and in 1985 the United Kingdom introduced regulations to limit sales of tributyltin paints that released the biocide at high rates (Huggett et al. 1992).

Many reviews and bibliographies are available on the environmental impacts of inorganic and organic tin compounds (Barnes and Stoner 1959; Piver 1973; Kimbrough 1976; CEC 1978; Zuckerman et al. 1978; Duncan 1980; Watanabe 1980; WHO 1980; Blunden and Chapman 1982; Blunden et al. 1984, 1985; Krigman and Silverman 1984; Reiter and Ruppert 1984; Reuhl and Cranmer 1984; Wilkinson 1984; Hall and Pinkney 1985; Laughlin and Linden 1985; McMillan and Wenger 1985; Thompson et al. 1985; Blunden and Chapman 1986; Cardwell and Sheldon 1986; Chang 1986; Maton 1986; Sylph 1986a, 1986b; USEPA 1987; Snoeij et al. 1987; Eisler 1989; Maguire 1991; U.S. Public Health Service [USPHS] 1992; Fent 1996). These authorities agree that inorganic tin compounds are comparatively harmless and that many organotin compounds are potentially very hazardous to natural resources — especially tributyltin compounds to aquatic biota. One rare exception to this generalization involved 113 cases of acute gastrointestinal illness in Washington and Oregon in 1969 associated with ingestion of canned tomato juice contaminated by inorganic tin; detinning in many cans resulted in tin levels as high as 477 mg inorganic tin per liter of juice. It seems that excessive use of nitrate fertilizer on one tomato crop was the ultimate cause of the detinning (Barker and Runte 1972).

8.2 CHEMICAL AND BIOCHEMICAL PROPERTIES

8.2.1 General

The chemical, physical, and biochemical properties of inorganic tin compounds differ dramatically from those of representative organotin compounds. There is general agreement that inorganic tins are not highly toxic due to their poor absorption and rapid turnover rate in tissues and to their being essential for growth in at least one species (rat). Of the 260 known organotin compounds, all but a few are manufactured, and 36 are listed as toxic (Watanabe 1980). Most authorities agree on several points regarding organotin compounds:

- Information concerning the mechanism of toxic action is incomplete
- There is no evidence of carcinogenicity
- Trialkyltin compounds are the most toxic
- There are large differences in resistance between and within species.

8.2.2 Inorganic Tin

Elemental tin has an atomic number of 50, an atomic mass of 118.69, and exists in three allotropic forms: white tin at room temperature, nonmetallic grey tin at <13.3°C, and brittle tin at >161°C. White tin is a stable silver-white, lustrous, soft metal with a density of 7.27, a melting point of 231.9°C, and a boiling point of 2507°C. Tin has 10 stable isotopes (^{112}Sn , ^{114}Sn , ^{115}Sn , ^{116}Sn , ^{117}Sn , ^{118}Sn , ^{119}Sn , ^{120}Sn , ^{122}Sn , and ^{124}Sn), more than any other element. Inorganic tin

compounds exist in the $+2$ (stannous) and $+4$ (stannic) oxidation states. Stannous compounds are generally more polar than stannic compounds, are unstable in dilute aqueous solutions, are easily oxidized, and normally contain some Sn^{+4} . Stannic oxide occurs naturally as the mineral cassiterite, has a melting point of 1127°C , and has wide application in industry. Additional information on inorganic tin chemistry is listed in Zuckerman et al. (1978), WHO (1980), Davies and Smith (1982) and USPHS (1992).

Signs of inorganic tin poisoning in mammals include local effects such as vomiting, diarrhea, and eye and nose irritation; however, these vary considerably among species (WHO 1980). The major systemic effects include ataxia, twitching of limbs, weakness of limbs, paralysis, growth retardation, decreased hemoglobin levels, and — at extremely high doses — testicular degeneration, pancreatic atrophy, formation of spongy brain white matter, and kidney necrosis. In humans, symptoms of inorganic tin intoxication include nausea, vomiting, diarrhea, stomach ache, fatigue, and headache. The lowest concentration producing outbreaks was about 250 mg Sn per liter in canned orange and apple juice. Ingestion of 50 mg of tin through eating canned peaches that contained Sn concentrations of about 450 mg/kg caused acute symptoms in 2 of 7 human volunteers (WHO 1980). Inhalation of SnO_2 dust is a hazard in the deep-mining of tin; deposits in lungs are easily detectable as “stannosis” (Krigman and Silverman 1984).

Inorganic tin and its salts are not highly toxic due to their poor absorption, relative insolubility of their oxides, and rapid tissue turnover (WHO 1980; Hassett et al. 1984; Krigman and Silverman 1984; Blunden and Chapman 1986). The absorption of ingested inorganic tin is usually less than 5%, although up to 20% has been reported. Stannous compounds are more readily absorbed from the gastrointestinal tract than stannic compounds, but absorbed tin leaves the vascular system rapidly. Bone is the main site of tin deposition, followed by lung, liver, and kidney. Penetration of the blood-brain and placental barriers by inorganic tin seems to be very slight. Except for lung, inorganic tin does not accumulate in organs with increasing age. Absorbed inorganic tin is excreted mainly in the urine, although excretion through the bile may account for up to 15% of the total. Tin and its inorganic compounds do not produce significant dermatitis or allergic reactions to skin epithelium, and results of all long-term studies of carcinogenicity, teratogenicity, and mutagenicity have been negative to date (WHO 1980).

WHO (1980) reviewed the half-time ($T_{1/2}$) of inorganic tins in animals. Studies with Sn^{+2} in mouse, rat, monkey, and dog show that in all species elimination is a four-compartment process regardless of the route of administration (i.e., intraperitoneal or intravenous). The $T_{1/2}$ for the longest-lived tin component was >3 months. In studies with rats, for example, radiotin-113 in skeleton following intramuscular administration had a $T_{1/2}$ of 3 to 4 months, but for oral administration of Sn^{+2} and Sn^{+4} it was only 28 to 40 days in bone and 10 to 20 days in liver and kidney. Inorganic tin can be biomethylated by microorganisms in the aquatic environment and subsequently mobilized in the ecosystem (Tugrul et al. 1983; Yemencioglu et al. 1987). The process is slow and usually does not proceed beyond the monomethyltin stage (Zuckerman et al. 1978), although dimethyltin formation by *Pseudomonas* bacteria has been reported (Smith 1978b). Tin is an essential nutrient for growth in the rat, and a tin-deficient diet leads to reduced growth (WHO 1980; Krigman and Silverman 1984). The mechanism of action is unclear, but involves increasing metabolic activity of liver lysosomes and liver hydrolytic enzymes during regeneration (Dwivedi et al. 1985a, 1985b).

8.2.3 Organotins

Organotins are compounds with at least one tin–carbon bond. In most organotin compounds, tin is in the tetravalent oxidation state. Four series of organotin compounds are known: R_4Sn , R_3SnX , R_2SnX_2 , and RSnX_3 wherein R is usually a butyl, octyl, or phenyl group, and X is commonly chloride, fluoride, oxide, hydroxide, carboxylate, or thiolate (CEC 1978). The possible molecular composition and structure of the R groups are virtually unlimited (Laughlin et al. 1985). At least 260 organotin compounds are known, of which 36 are listed as toxic chemicals (Watanabe 1980).

Except for some methyltin compounds, all organotins are manufactured (Laughlin et al. 1985). Most commercially used organotins are characterized by low mobility in the environment because of low aqueous solubility, low vapor pressure, and high affinity for soils and organic sediments (Blunden and Chapman 1986). Solubility data for organotin compounds are incomplete. In general, their solubility in water is limited to about 5 to 50 mg/L, but they are very soluble in many common organic solvents (WHO 1980). The presence of chloride in seawater reduces the solubility of tributyltin and triphenyltin compounds, probably by association with the hydrated cation to form the covalent organotin chloride (Blunden et al. 1985). Organotin compounds are analyzed in aqueous media by spectrophotometric, fluorometric, and electrochemical techniques. However, if picomole per liter concentrations are required, additional techniques must be used. More work needs to be done on analytical detection methods of organotins in sediments and biota (Thompson et al. 1985).

Methylation of inorganic and methyltin compounds has been reported with the formation of mono-, di-, tri-, and tetramethyltin compounds. In addition, tributylmethyltin and dibutylmethyltin species have been found in harbor sediments, which suggests that some butyltin compounds may be methylated in aquatic systems (Guard et al. 1981; Thompson et al. 1985; Donard et al. 1987). Methyltin formation in the environment is due mainly to methyl donation from methylcobalamin and methyl iodide (Hamasaki et al. 1995). Photochemical reaction and transalkylation of inorganic tins produce methyltins; methylation of tin increases the toxicity of their original metal form, due in part to their higher volatility and lipophilicity. Methyltins are ubiquitous in the environment and have been measured in seawater, freshwater, rain, wastewaters, sediments, fish, invertebrates, birds, and humans (Hamasaki et al. 1995).

Abiotic and biological degradation of organotins generally occurs through sequential dealkylation or dearylation (Zuckerman et al. 1978; WHO 1980; Smith 1981b; Chau et al. 1984; Blunden et al. 1985). Organotin compounds undergo successive cleavage of tin–carbon bonds to ultimately produce inorganic tin as follows: R_4Sn (via k_4) to R_3SnX (k_3) to R_2SnX_2 (k_2) to $RSnX_3$ (k_1) to SnX_4 . The reaction rate, k , usually proceeds as $k_4 > k_3 > k_2 = k_1$. The breaking of a Sn–C bond can occur by a number of different processes, including ultraviolet irradiation (UV), biological cleavage, chemical cleavage, gamma irradiation, and thermal cleavage (WHO 1980; Blunden and Chapman 1982, 1986; Blunden et al. 1985; Thompson et al. 1985). In general, UV and biological cleavage are the most important processes. The main abiotic factors that seem to limit organotin persistence in the environment are elevated temperatures, increased intensity of sunlight, and aerobic conditions (Table 8.1). A probable environmental degradation scheme for tributyltin and triphenyltin compounds is shown in Figure 8.1.

The tendency of an organotin compound to be concentrated by an organism depends on its partition behavior between lipid and aqueous phases. In general, compounds highly soluble in octanol and only slightly soluble in water have high K_{ow} values. K_{ow} values of organotins increase with number and molecular weight of organic groups attached to the tin atom, with significant bioaccumulation potential for organotins with R groups of butyl and larger (Thompson et al. 1985). K_{ow} values for tributyltins in seawater vary from 5500 to 7000, but can be significantly modified by salinity and speciation products (Laughlin et al. 1986b). Thus, organotins would be expected to accumulate in lipid-rich surface microlayers of natural waters (Cardwell and Sheldon 1986) and in biota (as discussed later). However, the ability of microorganisms, algae, and higher organisms to reduce various organotins to less toxic metabolites that can be excreted rapidly seems to preclude food chain biomagnification and to lessen the potential hazards to natural resources from consumption of organisms with elevated organotin residues (Table 8.1; Cardwell and Sheldon 1986).

Most authorities now agree on five points: (1) information concerning the mechanism of the toxic action of organotin compounds is inadequate; (2) results of all studies with various organotins for possible carcinogenicity are negative; (3) triorganotin compounds are the most toxic group of organotins; (4) large inter- and intraspecies differences exist in resistance to organotin compounds; and (5) organotins can alter enzyme activity levels in many organs and tissues including brain, liver, and kidney (Piver 1973; Duncan 1980; WHO 1980; Davies and Smith 1982; Maguire et al. 1982; Arakawa and Wada 1984; Dwivedi et al. 1985b; Blunden and Chapman 1986; Maguire 1991).

Table 8.1 Biological and Abiotic Degradation Times of Selected Organotins

Degradation Route, Organism or Compartment, and Tin Compound	Time for 50% Degradation and Other Variables (reference)
BIOLOGICAL	
Microorganisms	
Tributyltin	1 to 2 weeks in aerated medium in dark, 6 to 13 weeks in aerated medium in light, <1 year in anaerobic medium (Cardwell and Sheldon 1986)
Triphenyltin	60 to 140 days under aerobic, light conditions (Smith 1981b)
Algae, <i>Ankistrodesmus falcatus</i>	
Tributyltin	25 days (Maguire et al. 1984)
Bivalve molluscs, 3 species	
Tributyltin	10 to 14 days (Cardwell and Sheldon 1986; Laughlin et al. 1986a)
Sheepshead minnow, <i>Cyprinodon variegatus</i>	
Tributyltin	14 to 28 days (Cardwell and Sheldon 1986)
ABIOTIC	
Distilled water	
Tributyltin	>89 days at initial concentration of 0.7 mg Sn/L, 18 days at 2.0 to 4.0 mg Sn/L (Walsh et al. 1986a)
Freshwater	
Tributyltin	3 to 89 days (Duncan 1980; Smith 1981b; Ward et al. 1981; Maguire and Tkacz 1985; Walsh et al. 1985)
Triphenyltin	8 months at 1.0 to 2.5 mg/L, 100 days at 0.5 mg/L (Duncan 1980)
Diphenyltin	2 to 3 days (Soderquist and Crosby 1980)
Seawater	
Tributyltin	6 to 19 days; most rapid at low initial concentrations under high illumination (Seligman et al. 1986; Harino et al. 1998)
Triphenyltin	About 140 days (Duncan 1980)
Sediments	
Trimethyltin	About 80 days at 16°C to form the more volatile $(CH_3)_4Sn$ (Guard et al. 1981)
Tributyltin	At least 10 months at 20°C (Maguire and Tkacz 1985)
Tributyltin	360–775 days (Harino et al. 1998)

In aquatic systems, triorganotins were the most toxic group of organotins tested, followed in decreasing order of toxicity by diorganotins, tetraorganotins, and monoorganotins (Argese et al. 1998). Within each series, butyltin and phenyltin compounds seemed most toxic. Organotin toxicity increases with an increase in the length of the linear carbon chain; degradation processes, which involve the gradual breaking of Sn–C bonds, lead to the formation of compounds of low toxicity. Different biochemical mechanisms can account for the toxic effects of each structural class of organotins. For triorganotins, the derangement of energy-coupled processes, which occur at the membrane level, seems to be the most probable mode of action in aquatic organisms (Argese et al. 1998).

The monoorganotin compounds, $RSnX_3$, have a generally low toxicity and do not seem to have any important biological action in mammals (Duncan 1980; Davies and Smith 1982; Krigman and Silverman 1984; Blunden and Chapman 1986). Dialkylorganotins, R_2SnX_2 , are associated with hepatotoxicity (ethyl, propyl, butyl, and pentyltins), immunotoxic effects to T-cells (butyl and octyltins), and skin and eye irritation (methyl, ethyl, propyl, butyl, and octyltins; Watanabe 1980; Krigman and Silverman 1984). The diorganotins combine with coenzymes or enzymes possessing dithiol groups and exert their toxic action by inhibiting alpha-keto acid oxidation and blocking mitochondrial respiration (Duncan 1980; WHO 1980; Davies and Smith 1982). Resistance to diorganotin toxicity varies widely among species. For example, dibutyltins and dioctyltins — unlike other organotins tested — were toxic to rat thymocytes but did not induce similar effects on lymphoid atrophy in mice, guinea pigs, or Japanese quail (Seinen et al. 1977b). Selected dibutyltins

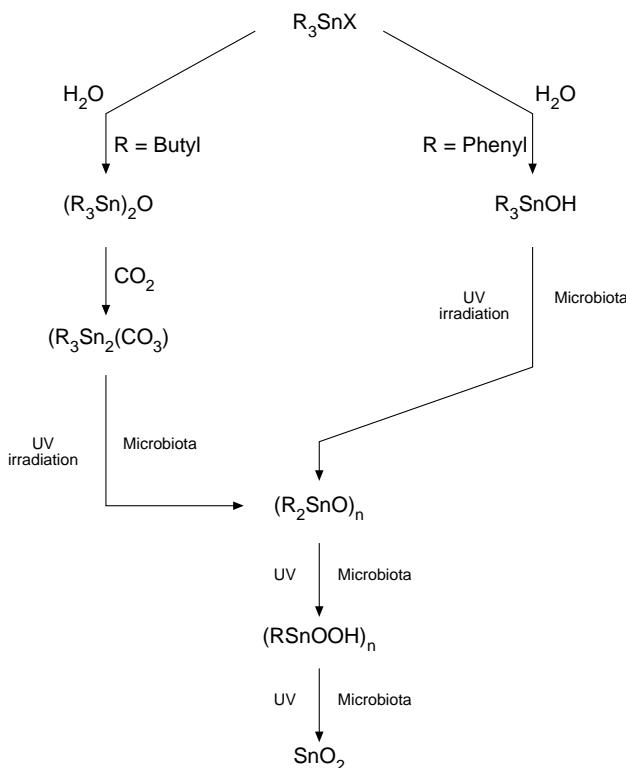


Figure 8.1 Environmental degradation scheme for tributyltin and triphenyltin compounds. (Modified from Smith, P.J. 1978b. *Structure/Activity Relationships for Di- and Triorganotin Compounds*. I.T.R.I. Rep. 569. 16 pp. Avail. from International Tin Research Institute, Greenford, Middlesex, U.K.; and Eisler, R. 1989. Tin hazards to fish, wildlife, and invertebrates: a synoptic review. *U.S. Fish Wildl. Serv. Biol. Rep.* 85(1.15). 83 pp.)

are effective as antihelminthics and are used to kill parasitic worms in chickens and turkeys without harm to host birds (Davies and Smith 1982).

In any member of the organotin series R_nSnX_{4-n} , progressive substitution of organic groups at tin produces a maximum biological activity for the triorganotin derivatives, R_3SnX (Davies and Smith 1982). Among triorganotin compounds, trimethyltins are highly toxic to insects, birds, and mammals; triethyltins to mammals; tripropyltins to Gram-negative bacteria; tributyltins to fish, molluscs, fungi, and Gram-positive bacteria; triphenyltins to fish, fungi, and molluscs; and tricyclohexyltins to mites (Duncan 1980; Davies and Smith 1982; Blunden and Chapman 1986; Maguire 1991). In mammals, the lower triorganotin homologues (trimethyltins, triethyltins) are essentially neurotoxic, the intermediate trialkyltins and triphenyltins are primarily immunotoxic, and the higher homologues are only slightly toxic or not toxic (Krigman and Silverman 1984; Snoeij et al. 1985). The toxicity of triorganotin compounds is probably due to their ability to bind to proteins and to inhibit mitochondrial oxidative phosphorylation (Smith 1978b; Duncan 1980; WHO 1980; Davies and Smith 1982; Blunden and Chapman 1986). Triorganotins also interfere with phagocytosis and exocytosis and other pathways where sulfhydryl groups play a pivotal role (Elferink et al. 1986), and inhibit uptake of gamma-aminobutyric acid and Na^+/K^+ -ATPase in brain (Costa 1985). Impairment of phagocytosis and related activities of polymorphonuclear leukocytes may enhance susceptibility for infection (Elferink et al. 1986).

Trimethyltins are the most toxic trialkyltins to mammals, regardless of the nature of the substituent (X group), according to Smith (1978b). They induce pathological lesions in brain and overt neurological and behavioral changes in rodents (Chang 1986). Trimethyltins are neurotoxins

that damage the limbic system, cerebral cortex, and brain stem and can traverse the placenta and accumulate in the fetus (Reuhl and Cranmer 1984). Trimethyltins (but not inorganic, monomethyl, or dimethyltins) inhibit brain protein synthesis by 47% and can cause a decrease of 4.2°C in body temperature of mice within 1 hour postadministration of 3.0 mg/kg body weight (Costa and Sulaiman 1986). Raising the ambient temperature to 35°C prevented hypothermia in treated mice and resulted in only a 20% inhibition in protein synthesis. More research is needed on the role of protein synthesis in organotin-induced neurotoxicity.

Triethyltins modify phosphorylation processes in subcellular fractions of rat brain proteins (Piver 1973; Neumann and Taketa 1987). Signs of triethyltin poisoning in rodents include weakness of hind limbs, dyspnea, and peripheral vasodilation (Watanabe 1980). Internally, acute triethyltin intoxication is characterized by a transient edema of the central and peripheral nervous systems manifested by extensive intramyelinic vacuolation due to splitting of myelin lamellae. Changes are reversible (Watanabe 1980; Reuhl and Cranmer 1984). Neuronal death is reported following triethyltin intoxication during the neonatal period, possibly as a result of elevated intracranial pressure (Reuhl and Cranmer 1984). In rabbit brain, triethyltins alter activity of pyruvate dehydrogenase (Neumann and Taketa 1987).

Studies on tributyltin uptake and depuration from food or water by rats, crabs, oysters, and fish showed that in all species it was accumulated and metabolized, at least partly, within 48 h to dibutyltins, monobutyltins, and more polar metabolites. However, oysters (*Crassostrea virginica*) metabolized significantly less tributyltin than other species tested (Lee 1985). The accumulation of tributyltin compounds in different tissues correlated well with lipid content and supports a partitioning mode of uptake (Laughlin et al. 1986a). The mixed function oxygenase system from hepatic tissues was able to metabolize tributyltins by forming hydroxylated metabolites (Lee 1985). Tributyltins are also potent cytotoxicants in rabbit erythrocyte and skin cultures (Gray et al. 1985).

The potential of tricyclohexyltins to modify the inducibility of cytochrome P-450 by various substances, such as 3-methylcholanthrene, is of considerable toxicological importance (Rosenberg et al. 1985). Significant metabolic interactions can result from a combination of environmental chemicals and drugs that produce alterations in heme and mixed function oxygenase activity (Rosenberg et al. 1985), suggesting that more research is needed on interaction effects of organotins with other environmental substances or contaminants.

The biological effects of the tetraorganotin compounds, R_4Sn , seem to be caused entirely by the R_3SnX derivative that is produced by their rapid *in vivo* dealkylation (Duncan 1980; Davies and Smith 1982; Blunden and Chapman 1986). Increasing toxicity of tetra- and triorganotins in mammals has been shown to be associated with decreasing length of their ligands, as reflected by solubility in biological fluids (Arakawa et al. 1981). It is not known if damage is produced by the metal or by its alkyl derivative, but the presence of trialkyl groups seems to enhance the toxicity of tin — probably by increasing its partition into lipids, thus aiding the absorption of the metal and speeding its distribution to the site of action (Arakawa et al. 1981).

8.3 SOURCES AND USES

Metallic tin is derived mainly from the mineral cassiterite (SnO_2) and to a lesser extent from the sulfide ore stannite $Cu_2S-FeS-SnS_2$, although it can be derived from rarer minerals such as malayaite, $CaSnSiO_5$ (Blunden et al. 1985). Tin is one of the earliest metals known and has influenced our lives through the ages. Tin alloy artifacts dating from about 5000 years ago have been unearthed at Ur, the site of ancient Babylonia (Zuckerman et al. 1978). Today we are exposed to tin on a daily basis through the use of tin-plated food cans; of alloys such as pewter, bronze, brass, and solder; and from toothpaste containing stannous fluoride (Zuckerman et al. 1978). Inorganic tin compounds are also used in a variety of industrial processes such as the strengthening

of glass, as a base for colors, as catalysts in various chemical reactions, as stabilizers in perfumes and soaps, and as dental anticariogenic agents (WHO 1980; Crowe 1987; USPHS 1992). The use of organotin is extensive in antifouling marine paints, in molluscicides, and in agriculture, which sometimes causes serious adverse effects on nontarget biota (Crowe 1987). In Italy, however, use of organotin products in agriculture at recommended application levels had no adverse effects and did not accumulate in tissues in European hares, *Lepus europaeus*, sampled over a 12-month period (Anfossi et al. 1990a). Some treated plants of the family Chenopodiaceae had 3.4 mg Sn/kg FW in August (range 0.9 to 13.4), but mean values in other families of plants in August were lower and ranged between 0.3 and 1.2 mg Sn/kg FW (Anfossi et al. 1990a).

In 1975, the total world tin production was 236,000 tons, of which 72% was produced by China (10%), Indonesia (8%), Malaysia (35%), Thailand (7%), and 6% each by the U.K. and the former Soviet Union (WHO 1980). Annual mine production of tin in the United States is a comparatively low 3300 metric tons (USPHS 1992). The world production of recycled tin was about 20,000 tons, of which France produced about half (WHO 1980). About 25% of the tin used in the United States is recovered from scrap materials containing tin. This secondary production occurs in the United States at 7 detinning plants and 162 processing plants (USPHS 1992). The production and consumption of tin chemicals, especially organotins, has increased markedly in the past several decades ([Table 8.2](#)).

The United States is the major consumer of tin and organotin compounds, followed by Japan, the U.K., Germany, and France (WHO 1980). In 1976, for example, the United States consumed 11,000 tons of organotins, or about 39% of the world organotin production (Chau et al. 1984). The projected total demand for primary tin up to the year 2000 is estimated at 7.5 million tons. Total reserves currently are about 6.5 million tons; however, it is likely that new discoveries and increases in known reserves will result in sufficient new tin to meet the demand for this period (WHO 1980).

The uses of inorganic and organotin compounds are numerous and increasing (Crowe 1987; [Table 8.3](#)). Industrial consumption of organotins, for example, rose from about 5000 tons in 1965 to about 35,000 tons in 1985. The uses of nontoxic organotin compounds (R_2SnX_2 and $RSnX_3$ types) account for about 67% of the total world production, although use of R_3SnX types as selective biocides has increased disproportionately (Davies and Smith 1982). Tin now has more of its organometallic derivatives in commercial use than any other element (Blunden et al. 1985).

Biocidal applications of organotins to control marine fouling communities, agricultural pests, and as selective molluscicides merit additional comment. The use of antifoulants on ships is necessitated by the damage some organisms can cause to wooden structures and by the reduced fuel efficiency and speed due to drag when vessels become heavily fouled (Laughlin et al. 1984). Until recently, the most widely used antifouling paint contained a copper base that is biocidally active when copper leaches as an ion from the paint (Hall et al. 1987). However, short effective lifetimes and high costs have limited the usefulness of copper-based paints. Organocompounds of arsenic, mercury, or lead have also been used in antifouling paints, but these paints have been removed from the commercial market because of the toxicological risks during preparation and application and to their hazards to the environment (Blunden et al. 1985; Hall et al. 1987). Organotin coatings are promoted because of their excellent antifouling action, long lifetime (up to 4 years), and lack of corrosion (Messiha and Ikladious 1986). Organotin coatings, especially tributyltins, present potential environmental problems to nontarget aquatic biota due to their extreme toxicity (Eisler 1989; Maguire 1991).

Use of organotin antifouling paints on recreational and commercial water craft has increased markedly in recent years. In Maryland, for example, 50% to 75% of the recreational boats used in Chesapeake Bay are covered with organotin paints (Hall et al. 1988). The organotin biocide released by hydrolysis from the surface of the paint film into seawater provides the antifoulant action. In consequence, the depleted outer layer of paint film, containing hydrophilic carboxylate groups, is easily eroded by moving seawater exposing a fresh surface layer of organotin acrylate polymer. In continuing tests by the U.S. Navy, ablative organotin fouling coatings have demonstrated more than 48 months of protection (Blunden et al. 1985). As discussed later, the use of organotin

Table 8.2 Annual Tin Production and Consumption

Chemical Group and Other Variables	Amount (metric tons)	Reference ^a
ORGANOTINS		
Production		
Worldwide		
Total		
1950	<5000	1
1955	~5000	2
1976	24,000–28,000	3, 4, 5, 6
1986	30,000	2
Triorganotins	8000	2
Tributyltins	900	7
Di- and monoorganotins	27,000	2
USA		
1965	2300	8
1976	10,400	8
1986	25,000	8
Consumption		
Worldwide		
Total		
1965	5000	9
1967	8000	10
1975	25,000	10
1980	30,000–35,000	9
Biocidal applications		
1975	10,000	10
1985	35,000	11
TOTAL TIN		
Production, worldwide		
1975, Total	236,000	4
1975, Primary tin	217,000	4
1976, Total	180,000–200,000	2, 3, 5
1976, Total	155,000	1
Tinplate	52,700	1
Solder	48,100	1
Chemicals	20,000	1
Other uses	34,200	1
1976, Total	225,000	4
Ores	157,500	4
Scrap metal	67,500	4
1985, Total	51,000	11

^a 1, Blunden et al. 1985; 2, Blunden and Chapman 1986; 3, Zuckerman et al. 1978; 4, WHO 1980; 5, Chau et al. 1984; 6, Guard et al. 1981; 7, Laughlin et al. 1986a; 8, Walsh et al. 1985; 9, Davies and Smith 1982; 10, CEC 1978; 11, Crowe 1987.

compounds in antifouling paints has been severely curtailed. Antifouling paints containing triphenyltin (TPT) will not be a suitable substitute for tributyltin (TBT) in paints designed to inhibit microbial biofilms (Pain and Cooney 1998). Up to 80% of bacteria resistant to six organotins, including TBT, isolated from estuarine sediments of Boston Harbor in Massachusetts were also resistant to TPT. All bacteria were resistant to at least six of eight metals tested, suggesting that resistance to metals — including nickel, cadmium, lead, copper, zinc, and mercury — may be associated with resistance to organotins (Pain and Cooney 1998).

Table 8.3 Major Uses of Inorganic and Organic Tin Compounds

Compounds, uses, and references (in parentheses)

Inorganic Tin Compounds: Tin plate, solder, brass, bronze, and other alloys; heat stabilizers for polyvinyl chloride manufacture; tin and tin alloy electroplating baths; catalysts for silicone and polyurethane foam production; in glass manufacture; flame retardants for woolen fabrics; in toothpastes and dentifrices; for control of parasitic worms in sheep; radiopharmaceuticals; in ceramic glazes and pigments; in fluorescent phosphors, in weighting and dying silk; stone polishing; corrosion inhibitors; color and perfume stabilizers in soaps (WHO 1980; Blunden et al. 1985; USPHS 1992).

Monoorganotins: Polyvinyl chloride stabilizers, catalysts, SnO_2 precursors (CEC 1978; WHO 1980; Chau et al. 1984; Blunden et al. 1985; Blunden and Chapman 1986).

Diorganotins: Catalysts for silicones, polyurethane foams; polyvinyl chloride stabilizers; precursor for forming SnO_2 films on glass; antihelmintics for poultry; lubricating oil additives (Piver 1973; CEC 1978; WHO 1980; Chau et al. 1984; Blunden et al. 1985; Blunden and Chapman 1986; USPHS 1992).

Triorganotins: Agrochemical fungicides, herbicides, miticides, insecticides, nematocides, acaracides, antifeedants; biocide in marine paints; slimicide in paper pulp mills and cooling towers; rodent repellent; molluscicides; wood preservative fungicides; disinfectants; stone preservation; textile, paper, and leather protection (Piver 1973; Hunter 1976; Kumpulainen and Koivistoinen 1977; CEC 1978; WHO 1980; Davies and Smith 1982; Chau et al. 1984; Subramanian 1984; Wilkinson 1984; Blunden et al. 1985; Maguire and Tkacz 1985; Thompson et al. 1985; Blunden and Chapman 1986; USPHS 1992).

Tetraorganotins: Used in manufacture of $\text{R}_n\text{SnX}_{4-n}$ compounds from SnCl_4 ; catalysts for olefin polymers; stabilizers for transformer oils; corrosion inhibitor in lubricating oils (CEC 1978; WHO 1980; Davies and Smith 1982)

Several organotins have been used extensively as agricultural pesticides, especially tricyclohexyltin and triphenyltin compounds (Hunter 1976; Kumpulainen and Koivistoinen 1977; Blunden et al. 1985). In general, these compounds showed low phytotoxicity, low toxicity to nontarget organisms, no evidence of development of resistant insect strains, and degradation to form harmless tin residues. It is probable that agricultural uses of organotins will increase. The toxicity of triorganotin compounds to aquatic invertebrates, especially slow release formulations of tributyltins, is usually high, and this property has been used advantageously to eradicate certain species of freshwater snails that are intermediate vectors of schistosomiasis, i.e., *Biomphalaria* spp., *Bulinus* spp. (Chliamovitch and Kuhn 1977; CEC 1978; Duncan 1980; Seinen et al. 1981). Unfortunately, nontarget biota, including some sensitive species of fishes, are killed at recommended application levels (USEPA 1987; Eisler 1989; Maguire 1991).

Organotins enter air, soil, and water primarily as a result of routine agricultural, industrial, municipal, and biocidal operations (Table 8.4). Deposition rates of organotins from air into soils and water are unknown at present, but may be significant around urban and industrialized areas. Total tin concentrations — primarily inorganic tin — in the atmosphere of the northern hemisphere are significantly higher than those in the southern hemisphere and are dominated by anthropogenic sources (Table 8.5). The most important of these seems to be the incineration of municipal wastes, which accounts for most of the tin flux to the atmosphere (Byrd and Andreae 1986a). Riverine fluxes of tin to the oceans vary between 36 and 71 million kg annually, almost all of it in particulate fractions (Byrd and Andreae 1986b).

8.4 CONCENTRATIONS IN FIELD COLLECTIONS

8.4.1 General

In aquatic environments, organotin concentrations were elevated in sediments, biota, and surface water microlayers collected near marinas, aquaculture rearing pens, and other facilities where organotin-based antifouling paints were used. In some cases, organotin concentrations in the water

Table 8.4 Possible Modes of Entry of Organotins into Air, Soil, and Water

Environmental Compartment and Organotin Group	Sources
AIR	
R ₃ SnX	Agricultural spraying, volatilization from biocidal treatments, antifouling paint sprays
R ₃ SnX, R ₂ SnX ₂ , RSnX ₃	Incineration of organotin-treated or -stabilized waste materials.
R ₂ SnX ₂ , RSnX ₃	Glass coating operations to produce SnO ₂ films
SOIL	
R ₃ SnX	Agricultural applications, wood preservation
R ₃ SnX, R ₂ SnX ₂ , RSnX ₃	Burial of waste materials containing organotins
WATER	
R ₃ SnX	Antifouling coatings, molluscicides, overspray from agricultural operations, land runoff from agricultural use, industrial processes (i.e., slimicides in paper manufacture)
R ₂ SnX ₂ , RSnX ₃	Leaching from organotin stabilized polyvinyl chloride

Modified from Blunden, S.J., P.A. Cusack, and R. Hill. 1985. *The Industrial Uses of Tin Chemicals*. Royal Soc. Chem., London. 337 pp.

Table 8.5 Total Tin Flux to the Atmosphere and Hydrosphere

Environmental Compartment and Other Variables	Annual Flux, in millions of kilograms
ATMOSPHERE	
Northern hemisphere	
Anthropogenic	16.6
Natural	1.2
Total	17.8
Southern hemisphere	
Anthropogenic	1.6
Natural	0.7
Total	2.3
HYDROSPHERE	
Riverine flux to oceans	
Dissolved fraction	0.09
Particulate fraction	35.6–71.2

Modified from Byrd, J.T. and M.O. Andreae. 1986a. Concentrations and fluxes of tin in aerosols and rain. *Atmos. Environ.* 20:931–939; Byrd, J.T. and M.O. Andreae. 1986b. Geochemistry of tin in rivers and estuaries. *Geochim. Cosmochim. Acta* 50:835–845.

column were high enough to pose a substantial risk to sensitive species. Data are limited on concentrations of organotins in environmental samples, especially in samples from terrestrial ecosystems, and this may be attributed, in part, to limitations in routine chemical analytical capabilities.

8.4.2 Nonbiological Samples

Tin concentrations in water, air, soils, sediments, and other nonbiological materials are documented, but information is scarce except for aquatic systems (Maguire 1991; Table 8.6). In aquatic systems, several trends were evident. First, tin and organotin compounds tend to concentrate in

surface microlayers by factors up to 10,000 relative to subsurface water; in the case of organotins, this may be due to partitioning into the film of petroleum hydrocarbons commonly present on water surfaces (Maguire et al. 1982; Cleary and Stebbing 1987; Hall et al. 1987; Maguire 1991). Second, organotin concentrations, especially tributyltins, were highest in the vicinity of marinas and harbors, and this is consistent with its use as an antifouling agent in some paints for boats, ships, and docks (Chau et al. 1984; Maguire et al. 1986; Randall et al. 1986; Valkirs et al. 1986; Maguire 1991; Dawson et al. 1992; Harino et al. 1998). Peak tributyltin concentrations occurred in late spring and early summer in association with postwinter launching of freshly painted boats (Hall et al. 1987). Third, organotin levels throughout the water column of marinas in numerous freshwater and marine locations were sufficiently elevated to cause chronic toxic effects in sensitive organisms including algae, copepods, oysters, mussel larvae, and fish (Maguire et al. 1982, 1986; Waldock and Thain 1983; Chau et al. 1984; Maguire and Tkacz 1985; Beaumont and Newman 1986; Cardwell and Sheldon 1986; Thain and Waldock 1986; Cleary and Stebbing 1987; Hall et al. 1987; Stromgren and Bongard 1987). Fourth, methyltin species were infrequently detected. Their occurrence was positively correlated with the presence of relatively high concentrations of inorganic tin and was due primarily to biotic and abiotic methylation of both organotin and inorganic tin compounds (Chau et al. 1984; Maguire et al. 1986; Maguire 1991). Finally, butyltin species were detected in harbor sediments at concentrations that were toxicologically hazardous to benthic fauna (Waldock and Thain 1983; Chau et al. 1984; Maguire et al. 1986). Tributyltin species can be accumulated from the sediments by oligochaetes (*Tubifex tubifex*, *Limnodrilus hoffmeisteri*), thus making it potentially available to bottom-feeding fish; oligochaetes can also degrade tributyltins by a sequential debutylation, with Tb 1/2 estimates of 5 months in water and 4 months in water-sediment mixtures (Maguire and Tkacz 1985; Maguire 1991).

Tributyltin antifouling paints were banned for use in tin-based paints in the U.K. in 1987. Field work on the River Crouch Estuary showed that sediments from areas most contaminated with TBT in 1987 contained 0.16 mg TBT/kg DW; however, by 1992 this had declined to 0.02 mg TBT/kg DW. TBT declines were accompanied by increases in abundance and diversity of benthic fauna, especially bivalve molluscs and amphipod crustaceans (Rees et al. 1999; Waldock et al. 1999).

Table 8.6 Tin Concentrations in Nonbiological Materials

Sample (units), Tin Species, and Other Variables	Concentration ^a	Reference ^b
SALINE WATERS (µg/L)		
Total tin		
Chesapeake Bay	Max. 0.46	1
San Diego Bay	Max. 0.07	1
Southwest U.K., 1984	Max. 3.2	2
France, Arcachon Bay		
1982	5.05	3
1983	2.20	3
1985	1.00	3
Northeastern Mediterranean	Max. 0.32	4
Open ocean	0.2–0.3	19
Total organotin		
England		
Subsurface		
Southwest	Max. 0.29	1
Southeast	Max. 0.06	1
Surface microlayer		
Southwest	Max. 1.1	1
Southeast	Max. 0.06	1
France, Arcachon Bay		
1982	0.20	3
1983	<0.15	3
1985	<0.15	3

Table 8.6 (continued) Tin Concentrations in Nonbiological Materials

Sample (units), Tin Species, and Other Variables	Concentration ^a	Reference ^b
Inorganic tin		
San Diego Bay, California	Max. 0.009	5
Northeastern Mediterranean	Max. 0.24	6
Methyltin		
Western Florida	<0.009	7
Gulf of Mexico	<0.015	7
Dimethyltin		
Western Florida	<0.005	7
Gulf of Mexico	<0.007	7
Baltimore Harbor, Maryland	Max. 0.1	7
Trimethyltin		
Western Florida	<0.0005	7
Gulf of Mexico	<0.001	7
Baltimore Harbor, Maryland	Max. 0.02	7
Tetramethyltin		
Baltimore Harbor, Maryland	Max. 0.3	7
Butyltin		
Tejo estuary, Portugal	0.0011	7
Baltimore Harbor	Max. 0.3	7
San Diego Bay	Max. 0.05	5
Dibutyltin		
San Diego Bay	Max. 0.46	5
San Diego Bay, 1988	0.04	21
Chesapeake Bay, 1985–86		
Surface microlayer	Max. 1.16	8
Water column		
Marinas	(0.02–0.15)	8
Other locations	<0.04	8
Tributyltin		
Coastal waters, U.K.	Max. 0.43	7
Japan; Osaka Bay; 1996	0.004–0.04	25
Marinas, U.K.	Max. 2.3	7
San Diego Bay, California	0.05; Max. 0.93	5, 21
Main channel	Max. 0.06	7
Boat basin	Max. 0.55	7
Surface microlayer	(0.06–0.25)	8
Water column	(0.01–0.18)	8
Chesapeake Bay, 1985–86		
Surface microlayer	Max. 1.2	8
Water column		
Marinas	(0.05–1.0), Max. 1.8	8, 17
Other locations	0.02–0.05	8, 17
Southwest U.K., 1984		
Maryland	Max. 0.88	2
Baltimore Harbor		
Surface microlayer	Max. 4.57	8
Annapolis, water column	0.07	8
Tetrabutyltin		
Chesapeake Bay	ND	8
FRESHWATER (µg/L)		
Total tin		
Drinking water	Usually <1.0, Max. 30.0	9
42 cities, USA	1.1–2.2	19
32 of 175 water supplies, Arizona	0.8–3.0	19
Great Lakes		
Subsurface	Max. 1.2	1
Surface microlayer	Max. 24.9	1

Table 8.6 (continued) Tin Concentrations in Nonbiological Materials

Sample (units), Tin Species, and Other Variables	Concentration ^a	Reference ^b
Inorganic tin		
Canadian marinas, 1982–84		
Lake St. Clair	6.7	10
Whitby	37.2	10
Port Hope	9.9	10
Monomethyltin		
Canada		
Marina	1.2	11
Harbors, lakes, rivers	(0.06–1.0)	7
USA rivers	<0.002	7
German rivers	<0.08	7
Florida lakes, ponds, rivers	<0.012	7
Dimethyltin		
Canadian marina	Max. 0.4	11
USA rivers	0.004	7
German rivers	Max. 0.26	7
Florida lakes, ponds, rivers	<0.008	7
Trimethyltin		
Canadian marina	Max. 0.05	11
Lake Superior	0.05	7
USA rivers	0.002	7
German rivers	0.002	7
Florida lakes, ponds, rivers	<0.008	7
Butyltin		
Canada		
Marinas		
Whitby	0.62	10
Port Hope	0.42	10
Lake St. Clair	8.5	11
Hamilton Harbor	0.02	7
Subsurface waters		
33 locations	detectable	12
188 locations	ND	12
Dibutyltin		
Canada		
Marinas		
Whitby	1.46	10
Port Hope	0.08	10
Lake St. Clair		
Subsurface	7.3	11
Surface microlayer	107.0	11
Harbor areas, lakes, rivers	(0.01–0.3)	7
Surface microlayer	(0.7–2600)	7
Subsurface waters		
27 locations	detectable	12
194 locations	ND	12
Surface waters	(0.01–7.3)	8
Lake Tahoe, 1987 vs. 1988	0.07 vs. 0.16	21
Tributyltin		
Canada		
Marinas		
Lake St. Clair		
Subsurface	0.18	10
Surface microlayer	50.9	11
Whitby	4.2	10
Port Hope	5.7	10
Harbor areas, lakes, rivers	(0.01–1.0)	7
Surface microlayer	(0.2–60.0)	7

Table 8.6 (continued) Tin Concentrations in Nonbiological Materials

Sample (units), Tin Species, and Other Variables	Concentration ^a	Reference ^b
Subsurface waters		
1 location	2.34	12
7 locations	(0.4–1.8)	12
13 locations	(0.07–0.4)	12
22 locations	detectable	12
178 stations	ND	12
Surface waters	(0.01–2.9)	8
Lake Tahoe, 1987 vs. 1988	0.73 vs. 0.25	21
AIR (µg/m³)		
USA cities	Usually <0.01 (0.003–0.3); Max. 0.8 (Boston)	9
Japan		
Near furnaces	(10–640)	9
700 m distant	(3.8–4.4)	9
SEWAGE SLUDGE (mg/kg)		
23 cities, USA	11–1300	19
SOILS (mg/kg)		
In mineral soils containing tin	>1000	9
In unmineralized soils	(2.0–<200)	9
United States	0.89	19
SEDIMENTS (mg/kg)		
Inorganic tin		
Toronto Harbor	Max. 0.62	13
Sault St. Marie	15.5	10
Lake Superior	0.7	10
Wabigoon River	(0.3–1.2)	10
Turkey	(0.5–1.1)	14
Northeast Mediterranean	Max. 2.3	6
Great Bay, New Hampshire	(0.40–0.63)	15
Monomethyltin		
Lake Superior	ND	10
Wabigoon River	0.1	10
Turkey	0.3	14
Mainz, Germany	Max. 0.08	20
Northeast Mediterranean	Max. 0.01	6
Great Bay, New Hampshire	Max. 0.08	15
San Diego Bay	Max. 0.003	7
Chesapeake Bay	Max. 0.0008	7
U.K., 5 rivers, East Anglia, June 1989	Max. 0.011	18
Dimethyltin		
Turkey	Max. 0.01	14
Mainz, Germany	Max. 0.04	20
Great Bay, New Hampshire	Max. 0.05	15
San Diego Bay	Max. 0.003	7
U.K., 5 rivers, East Anglia, June 1989	Max. 0.005	18
Trimethyltin		
Turkey	Max. 0.02	14
Mainz, Germany	Max. 0.03	20
Great Bay, New Hampshire	ND	15
San Diego Bay	Max. 0.0002	7
U.K., 5 rivers, East Anglia, June 1989	Max. 0.0006	18
Monobutyltin		
Toronto Harbor	Max. 0.08	13

Table 8.6 (continued) Tin Concentrations in Nonbiological Materials

Sample (units), Tin Species, and Other Variables	Concentration ^a	Reference ^b
Sault St. Marie	0.15	10
Wabigoon River	(0.04–0.11)	10
Great Bay, New Hampshire	(0.003–0.03)	15
Canada		
Marinas	0.02	7
Other locations	(0.014–0.58)	7
San Diego Bay	Max. 0.007	7
Mission Bay, California	Max. 0.011	7
U.K., 5 rivers, East Anglia, June 1989	Max. 0.044	18
Dibutyltin		
Toronto Harbor	Max. 0.26	13
Great Bay, New Hampshire	(0.001–0.015)	15
Canada		
Marinas	0.074	7
Harbors, lakes, rivers	(0.05–0.35)	7
U.K., 5 rivers, East Anglia, June 1989	Max. 0.22	18
Lake Tahoe, 1987 vs. 1988	0.6 vs. 0.5	21
San Diego Bay, 1988	0.24	21
Tributyltin		
Toronto Harbor	Max. 1.28	13
Osaka Bay; Japan; 1996	0.01–2.1	25
Great Bay, New Hampshire	(0.012–0.044)	15
Lake St. Clair, marina	0.125	7
Canadian harbors, lakes, and rivers	(0.11–0.54)	7
U.K., 5 rivers, East Anglia, June 1989	<0.004–1.3	18
Lake Tahoe, 1987 vs. 1988	0.78 vs. 0.83	21
San Diego Bay, 1988	0.16	21
MINERALS (mg/kg)		
Total tin		
Shale	4.1	16
Igneous rock	2.5	16
Oceanic clay	2.4	16
Oceanic carbonate	0.4	16
Sandstone	0.12	16
WASTEWATER PLANT (µg/L)		
Influent vs. primary effluent; maximum concentrations		
Monomethyltin	0.14 vs. 0.07	20
Dimethyltin	0.24 vs. 0.07	20
Trimethyltins	0.14 vs. 0.04	20

^a Concentrations are expressed as mean, (minimum-maximum), maximum (Max.), and nondetectable (ND).

^b 1, Cleary and Stebbing 1987; 2, Cleary and Stebbing 1985; 3, Alzieu et al. 1986; 4, Salihoglu et al. 1987; 5, Valkirs et al. 1986; 6, Yemenicioglu et al. 1987; 7, Hall and Pinkney 1985; 8, Hall et al. 1987; 9, WHO 1980; 10, Chau et al. 1984; 11, Maguire et al. 1982; 12, Maguire et al. 1986; 13, Maguire and Tkacz 1985; 14, Tugrul et al. 1983; 15, Randall et al. 1986; 16, Thompson et al. 1985; 17, Pinkney et al. 1990; 18, Dawson et al. 1992; 19, USPHS 1992; 20, Hamasaki et al. 1995; 21, Harrington 1991.

8.4.3 Biological Samples

Information on background concentrations of total tin in tissues of field populations of animals and plants was comparatively abundant when compared to organotin species (Table 8.7). Tin

concentrations in marine algae and macrophytes varied between 0.5 and 101 mg total Sn/kg dry weight and clearly demonstrated that most species of aquatic flora bioconcentrate tin from seawater (Table 8.7). Marine plants are also important in the cycling of tin. Living algae are effective in immobilizing tin from seawater and regulating the formation and degradation of toxic methyltin compounds (Donard et al. 1987). Dead and decaying algae accumulate inorganic and organotin compounds, release them, and ultimately remove tin from the estuary to the atmosphere by formation of tetramethyltins (Donard et al. 1987).

Organotin content in fish tissues is quite variable, ranging from a low of 3% to 6% of the total tin body burden (Tugrul et al. 1983) to 18% for goatfish (*Upeneus moluccensis*) to 5% for *Mullus barbatus*, another species of goatfish (Salihoglu et al. 1987). By contrast, the limpet (*Patella caerulea*) contains 35% to 75% of its total tin body burden as organotin (Tugrul et al. 1983).

In January 1982, France banned organotin compounds for use in antifouling paints. By 1985, tin and organotin concentrations in seawater and Pacific oysters (*Crassostrea gigas*) were 5 to 10 times lower than those found in 1982 (Alzieu et al. 1986). In Arcachon Bay, France, a decrease in the incidence and extent of anomalies in oyster calcification mechanisms was noted that seemed to be correlated with decreases in tin contamination (Alzieu et al. 1986). Crassostreid oysters can accumulate radiotin (Sn-113) to a higher degree than other species of bivalve molluscs, a characteristic that may be useful as a bioindicator in the event of contamination by this isotope (Patel and Ganguly 1973). Tributyltin and its degradation products continue to be detected in tissues of American oysters (*Crassostrea virginica*) from the Gulf of Mexico 10 years after the use of TBT-based paints was regulated. The likely sources for the tributyltin compounds include sediments, TBT-based paints on vessels longer than 25 meters, and shipyard wastes (Sericano et al. 1999). Fish, shellfish, and sediment samples from southwestern British Columbia in 1992/93 contained tributyltin and its metabolites dibutyltin and monobutyltin, strongly suggesting that tributyltin is a widespread contaminant in this geographic area and a continuing cause for concern despite restrictions on the use of organotin-based marine antifouling paints imposed in 1989 (Stewart and Thompson 1994).

Antifouling paints containing tributyltin compounds are used widely on netting panels of sea cages at fish and shellfish aquaculture units to minimize the obstruction of water exchange through the cages (Davies et al. 1987). Under these conditions, tributyltin paints were detrimental to the growth and survival of juvenile scallops and to calcium metabolism and growth of adult oysters (Paul and Davies 1986) and resulted in elevated concentrations of tributyltin in salmon tissues (Short and Thrower 1986; Davies and McKie 1987). Scallops (*Pecten maximus*) reared in sea pens for 31 weeks on nets coated with tributyltin oxide contained 2.5 mg total Sn/kg fresh weight soft parts (1.9 mg tributyltin/kg), but lost up to 40% during a 10-week depuration period. Scallop adductor muscle contained 0.53 mg tributyltin/kg, suggesting that this tissue (the one consumed by humans) is a probable tin storage site (Davies et al. 1986). Pacific oysters (*Crassostrea gigas*) reared for 31 weeks on tributyltin-exposed nets contained a maximum of 1.4 mg tributyltin/kg FW at week 16 (controls 0.12 mg/kg), but lost 90% during a 10-week depuration period (Davies et al. 1986). Atlantic salmon (*Salmo salar*) held for 3 months during summer in cages with tributyltin-treated net panels contained 0.75 to 1.5 mg tributyltin/kg fresh weight muscle vs. 0.28 mg/kg at the start (Davies and McKie 1987). Based on laboratory studies, it is probable that Atlantic salmon were exposed to approximately 1.0 µg tributyltin/L during this interval (Davies and McKie 1987). Chinook salmon (*Oncorhynchus tshawytscha*), reared in sea pens treated with tributyltin paints, contained <0.013 mg tributyltin/kg muscle fresh weight when introduced into the pens. Concentrations were 0.3 mg/kg after 3 months, 0.8 mg/kg at 13 months, and 0.9 mg/kg at 19 months. Cooking did not destroy or remove organotins from salmon muscle tissues (Short and Thrower 1986). Pink salmon (*Oncorhynchus gorbuscha*) and chum salmon (*Oncorhynchus keta*) fry cultured in TBT-treated marine net pens for 20 to 68 days prior to ocean release contained mean concentrations of 1.5 mg Sn/kg FW fry (chum) and 2.7 mg/kg FW (pinks) vs. <0.1 in controls; however, growth and survival were normal and returning adults 1 to 3 years later had no detectable TBT (Thrower and Short 1991).

Table 8.7 Tin Concentrations in Field Collections of Living Flora and Fauna (Unless indicated otherwise, all values are in mg total Sn/kg fresh weight [FW] or dry weight [DW] tissue.)

Taxonomic Group, Organism, and Other Variables	Concentration, (mg/kg) ^a	Reference ^b
ALGAE AND HIGHER PLANTS		
Algae, marine		
Whole, 10 species	(11–49) DW	1
Whole, 2 species	(96–101) DW	1
Swiss chard, whole, <i>Beta vulgaris cicla</i>		
Grown in soil at pH		
5.5	(12–51) DW	2
6.0	8 DW	2
6.5	<0.5 DW	2
Mangrove, <i>Bruguiera caryophylloides</i> , leaf		
Controls	1.3 DW	2
On tin drainage	9.4 DW	2
Green alga, <i>Enteromorpha</i> spp.		
Inorganic tin	0.4 FW; 4.4 DW	3
Monomethyltins	0.5 FW	3
Dimethyltins	0.5 FW	3
Trimethyltins	<0.001 FW	3
Tetramethyltins	ND	3
Monobutyltins	0.006 FW; 0.4 DW	3
Tributyltins	0.05 FW; 0.6 DW	3
Seaweeds, whole, 5 species		
May	(0.5–1.8) DW	1
June	(0.5–2.2) DW	1
June	(0.1–0.5) FW	1
Wheat, <i>Triticum vulgare</i>		
Japan	0.5 FW	2
USA	(5.6–7.9) FW	2
Elm, <i>Ulmus americana</i>		
Wood, Vermont		
40 years old	1.7 FW; 1.8 DW	2
80 years old	1.4 FW; 1.5 DW	2
Vegetation		
Near tin smelter	(338–2165) DW	2
Corn, <i>Zea mays</i>	0.1 FW	2
INVERTEBRATES		
Pacific oyster, <i>Crassostrea gigas</i>		
Soft parts		
Arcachon Bay, France, July 1982		
Total tin	Max. 7.0 DW	4
Organotin	Max. 1.6 DW	4
1983		
Total tin	Max. 4.0 DW	4
Organotin	Max. 0.8 DW	4
1985		
Total tin	Max. 0.9 DW	4
Organotin	Max. 0.4 DW	4
Soft parts		
Controls	0.1 FW	5
Reared in sea cages painted with tributyltin for 16 weeks		
Total tin	1.4 FW	5
Tributyltin	0.9 FW	5

Table 8.7 (continued) Tin Concentrations in Field Collections of Living Flora and Fauna (Unless indicated otherwise, all values are in mg total Sn/kg fresh weight [FW] or dry weight [DW] tissue.)

Taxonomic Group, Organism, and Other Variables	Concentration, (mg/kg) ^a	Reference ^b
Soft parts, coastal U.K. estuaries tributyltin		
1986	0.2–6.4 DW	19
1987	0.3–3.7 DW	19
1988	0.1–5.6 DW	19
1989	0.1–1.3 DW	19
Soft parts, Korea, January 1995		
Tributyltin	0.1–0.9 DW; 28% of total in gonads	23
Triphenyltin	0.16–0.7 DW; 19% of total body burden in gonads	23
American oyster, <i>Crassostrea virginica</i> ; Gulf of Mexico, 1989–91; soft parts		
Monobutyltins	Max. 0.15 DW	19
Dibutyltins	Max. 0.2 DW	19
Tributyltins	Max. 1.2 DW	19
Crustaceans, marine		
Edible tissues		
5 species	(0.6–0.7) FW	6
8 species	(0.7–0.9) FW	6
3 species	(0.9–2.0) FW	6
Zebra mussel, <i>Dreissena polymorpha</i> , soft parts		
Held in cages in freshwater marina contaminated with tributyltin (0.07 µg/L) for 35 days	Soft parts had 63 mg TBT/kg DW; BCF of 900,000; no adverse effects on growth or survival	16
As above. Held for 105 days then transferred to uncontaminated environment (0.004 µg Sn/L) for 105 days	Half-time of 26 days; no equilibrium reached after 105 days	16
American lobster, <i>Homarus americanus</i>		
Muscle	0.6 FW	2
Molluscs, marine		
Edible tissues		
3 species	(0.3–0.5) FW	6
7 species	(0.5–0.7) FW	6
4 species	(0.7–0.9) FW	6
4 species	(0.9–2.0) FW	6
Common mussel, <i>Mytilus edulis</i>		
Soft parts, total	(1.3–7.1) DW	7
Soft parts		
Lisbon, Portugal		
Monomethyltins	Max. 0.007 DW	20
Dimethyltins	Max. 0.01 DW	20
Trimethyltins	Max. 0.023 DW	20
Tokyo Bay, 1989		
Monobutyltins	Max. 0.12 FW	19
Dibutyltins	Max. 0.15 FW	19
Tributyltins	Max. 0.24 FW	19
Osaka Bay, Japan 1996		
Tributyltin	0.02–0.39 DW	25
British Columbia, 1990		
Monobutyltins	Max. 0.05 DW	19
Dibutyltins	Max. 0.08 DW	19
Tributyltins	Max. 0.31 DW	19
Tributyltins		
USA, 1986–87	<0.005–1.4 FW	19
Maine, 1989	2.4 DW	19

Table 8.7 (continued) Tin Concentrations in Field Collections of Living Flora and Fauna (Unless indicated otherwise, all values are in mg total Sn/kg fresh weight [FW] or dry weight [DW] tissue.)

Taxonomic Group, Organism, and Other Variables	Concentration, (mg/kg) ^a	Reference ^b
Perth, Australia, 1991	<0.001–0.33 FW	19
San Diego Bay, 1988	0.86 FW	21
Hepatopancreas		
San Diego harbor	(1.9–3.5) DW	8
Offshore	(<0.7–2.0) DW	8
Fraser River, British Columbia, Canada, 1992–93, soft parts		
Tributyltin	Max. 0.31 DW	17
Total tin	Max. 0.44 DW	17
Common dogwhelk, <i>Nucella lapillus</i>		
Soft parts, uncontaminated		
Total tin	Max. 0.3 FW	9
Total tin	(0.1–0.2) DW	10
Tributyltin	(0.1–0.2) DW	10
Dibutyltin	(0.01–0.05) DW	10
European oyster, <i>Ostrea edulis</i>		
Uncontaminated area		
All tissues	<0.1 FW	11
River Crouch, U.K.		
Flesh	(0.27–0.33) FW	11
Eggs	0.33 FW	11
Larvae	0.30 FW	11
Limpet, <i>Patella caerulea</i> N.E. Mediterranean, 1980		
Shell		
Total tin	0.013 DW	12
Methyltin	0.0004 DW	12
Dimethyltin	0.0002 DW	12
Trimethyltin	0.0009 DW	12
Soft parts		
Reared in sea pens with tributyltin-coated netting for 3 weeks		
Total tin		
Gonad	0.6 FW	5
Adductor muscle	0.6 FW	5
Gills	0.6 FW	5
Digestive gland	1.0 FW	5
Tributyltin		
Gonad	0.4 FW	5
Digestive gland	0.5 FW	5
Adductor muscle	0.5 FW	5
Gills	0.6 FW	5
Green mussel, <i>Perna viridis</i> ; soft parts		
Thailand, 1994–95		
Monobutyltins	0.014 (0.003–0.045) FW	19
Dibutyltins	0.013 (0.001–0.08) FW	19
Tributyltins	0.1 (0.004–0.8) FW	19
Tributyltins		
Hong Kong, 1989	0.06–0.12 FW	19
Malaysia, 1992	0.01–0.02 FW	
Plankton; Osaka Bay, Japan; 1996; whole; tributyltins	0.3–4.2 DW	25

FISH

Pacific herring, *Clupea harengus pallasi*

Whole, Vancouver, Canada 1984

Inorganic tin	0.04 FW	13
Butyltin	0.06 FW	13

Table 8.7 (continued) Tin Concentrations in Field Collections of Living Flora and Fauna (Unless indicated otherwise, all values are in mg total Sn/kg fresh weight [FW] or dry weight [DW] tissue.)

Taxonomic Group, Organism, and Other Variables	Concentration, (mg/kg) ^a	Reference ^b
Dibutyltin	0.05 FW	13
Tributyltin	0.24 FW	13
Lake whitefish, <i>Coregonus clupeaformis</i> , muscle	(0.8–3.6) FW	2
Northern pike, <i>Esox lucius</i> , muscle		
Manitoba, Canada	(0.7–5.4) FW	2
Lake Erie	0.5 FW	
Fish, marine		
Liver		
27 species	(<0.1–0.4) FW	6
45 species	(0.4–0.8) FW	6
10 species	(0.8–2.0) FW	6
Muscle		
8 species	(0.2–0.4) FW	6
110 species	(0.4–0.6) FW	6
34 species	(0.6–0.8) FW	6
7 species	(0.8–2.0) FW	6
Whole		
2 species	(0.3–0.6) FW	6
12 species	(0.8–2.0) FW	6
3 species	(2.0–9.0) FW	6
Atlantic cod, <i>Gadus morhua</i> , muscle	(0.5–3.7) FW	2
Tui chub, <i>Gila bicolor</i>		
Lake Tahoe, California; whole; 1987 vs. 1988		
Dibutyltins	0.12 FW vs. 0.55 FW	21
Tributyltins	1.3 FW vs. 1.3 FW	21
Atlantic halibut, <i>Hippoglossus hippoglossus</i> , muscle	1.2 FW	2
Rainbow smelt, <i>Osmerus mordax</i> , muscle	1.2 FW	2
Yellow perch, <i>Perca flavescens</i> , muscle	0.6 FW	2
Starry flounder, <i>Platichthys stellatus</i> , Fraser River, British Columbia, muscle, 1992–93	0.04–0.06 DW	17
Winter flounder, <i>Pleuronectes americanus</i> , muscle	3.2 FW	2
Atlantic salmon, <i>Salmo salar</i>		
Muscle	0.07 FW	14
Gonad	0.15 FW	14
Gill	0.03 FW	14
Kidney	0.06 FW	14
Liver	0.04 FW	14
Lake trout, <i>Salvelinus namaycush</i>		
Whole, Canada, 1982–84		
Methyltin	(0.2–0.9) FW	15
Dimethyltin	(ND–0.2) FW	15
Trimethyltin	ND	15
Inorganic tin	(0.2–0.3) FW	15
Inorganic tin	Max. 0.9 FW	13
Spiny dogfish, <i>Squalus acanthias</i> , muscle	2.0 DW	2
BIRDS		
Ruffed grouse, <i>Bonasa umbellus</i> , liver	0.5 FW	2
Chicken, <i>Gallus gallus</i>		
Muscle	1.7 FW	2
Egg	0.9 FW	2
Waterfowl; livers; 1995; butyltins		
Lake Huron	<0.03 FW	24
Maine	Max. 0.09 FW	24
British Columbia, west coast	Max. 1.1 FW	24

Table 8.7 (continued) Tin Concentrations in Field Collections of Living Flora and Fauna (Unless indicated otherwise, all values are in mg total Sn/kg fresh weight [FW] or dry weight [DW] tissue.)

Taxonomic Group, Organism, and Other Variables	Concentration, (mg/kg) ^a	Reference ^b
MAMMALS		
Cow, <i>Bos bovis</i>		
Muscle	Max. 2.8 FW	2
Milk	Max. 0.9 FW	2
Beaver, <i>Castor canadensis</i> , heart	7.3 FW	2
Humans, <i>Homo sapiens</i>		
Adipose tissue, USA, 1982	8.7–15.0 FW	18
European hare, <i>Lepus europaeus</i> ; Italy; in vicinity of agricultural use of organotin products		
Liver	Max. 0.2 DW	22
Kidney	Max. 0.02 DW	22
Woodchuck, <i>Marmota monax</i> , liver	1.8 FW	2
White-tailed deer, <i>Odocoileus virginianus</i>		
Liver	0.8 FW	2
Kidney	Max. 2.2 FW	2
Heart	ND	2
Muskrat, <i>Ondatra zibethicus</i> , liver	0.3 FW	2
Sheep, <i>Ovis aries</i>		
Liver	0.3 FW	2
Muscle	1.4 FW	2
Harbor seal, <i>Phoca vitulina</i>		
All tissues	<0.1 FW	2
Fox, <i>Vulpes</i> sp., liver	3.5 FW	2

^a Concentrations are expressed as mean, (minimum-maximum), maximum (Max.), and nondetectable (ND).

^b 1, Eisler 1981; 2, Jenkins 1980; 3, Donard et al. 1987; 4, Alzieu et al. 1986; 5, Davies et al. 1986; 6, Hall et al. 1978; 7, Karbe et al. 1977; 8, Young et al. 1979; 9, Davies et al. 1987; 10, Bryan et al. 1986; 11, Thain and Waldock 1986; 12, Tugrul et al. 1983; 13, Maguire et al. 1986; 14, Davies and McKie 1987; 15, Chau et al. 1984; 16, van Slooten and Tarradellas 1994; 17, Stewart and Thompson 1994; 18, USPHS 1992; 19, Kanatreklap et al. 1997; 20, Hamasaki et al. 1995; 21, Harrington 1991; 22, Anfossi et al. 1990a; 23, Shim et al. 1998; 24, Kannan et al. 1998a; 25, Harino et al. 1998.

Diet and proximity to tributyltin affect butyltin concentrations in waterfowl (Kannan et al. 1998a). Seaducks that fed mainly on molluscs had higher concentrations of butyltins than predatory birds feeding on fish, other birds, and small mammals. Continued exposure of birds to butyltin compounds occurs in harbors and marinas where tributyltin is used on vessels >25 m in length (Kannan et al. 1998a).

8.5 EFFECTS

8.5.1 General

Inorganic tin compounds are of low toxicologic risk due largely to their low solubility, poor absorption, low accumulations in tissues, and rapid excretion. By contrast, some organotin compounds — especially trialkyltins — produce a variety of harmful effects resulting in impaired behavior and lowered growth, survival, and reproduction. Among aquatic organisms, tributyltin compounds were especially potent. Adverse effects were noted in molluscs at water concentrations of 0.001 to 0.06 µg/L and in algae, fish, and other species of invertebrates at 0.1 to 1.0 µg/L. Bioconcentration of organotins was high, but degradation was sufficiently rapid to preclude food chain biomagnification. Birds seem to be relatively resistant to organotins, and data suggest that diets containing 50 mg of tin as trimethyltin chloride/kg are fatal to ducklings in 75 days; however,

no deaths occurred in 75 days at 50 mg/kg of eleven other mono-, di-, tri-, and tetraalkyltin compounds. Trimethyltin was lethal to other species of birds tested at doses of 1 to 3 mg/kg body weight. Trimethyltins and triethyltins were the most toxic organotin compounds tested on small laboratory mammals. Neurotoxicological effects of trimethyltins were usually not reversible, while those caused by triethyltins were reversible after exposure. Adverse effects of trimethyltins were produced at concentrations as low as 0.15 mg/L in drinking water (learning deficits), 0.625 mg/kg BW (diet aversion), and 1.25 mg/kg BW (death).

8.5.2 Aquatic Organisms

Studies on lethal and sublethal effects of tin compounds to representative species of aquatic organisms demonstrate that organotin compounds are more toxic than inorganic tin compounds; triorganotin compounds are more toxic than mono-, di-, or tetraorganotin forms; and tributyltin compounds are the most toxic triorganotin compounds tested (Argese et al. 1998; [Table 8.8](#)). Adverse effects of tributyltins were noted at water concentrations of 0.001 to 0.06 µg/L in marine gastropod and bivalve molluscs, and at 0.1 to 1 µg/L in algae, echinoderms, fish, crustaceans, and coelenterates ([Table 8.8](#)). In order of toxicity, tributyltins were followed by tripropyltins (harmful effects recorded at 0.001 to 10 µg/L to gastropods, fish, and algae), triphenyltins (0.6 to 1 µg/L to diatoms and annelids), triethyltins (3.8 to 10 µg/L to fish and algae), trimethyltins (20 µg/L to algae and crustaceans), and tripentyltins (50 to 100 µg/L to gastropods). Because many organotin compounds are slow-acting poisons, short-term toxicity tests seriously underestimate the toxicity of these compounds (Laughlin and Linden 1985). Tributyltin chloride was more toxic to larvae of the horseshoe crab (*Limulus polyphemus*) than were salts of other metals tested — mercury, cadmium, chromium, zinc, copper, and lead — as judged by effects on survival, molting, and limb regeneration (Itow et al. 1998).

Table 8.8 Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium (µg/L)	Effect	Ref ^a
INORGANIC TINS			
Dab (fish), <i>Limanda limanda</i>	35	No deaths in 96 h	1
Marine diatoms, 2 species	316–325	50% growth inhibition in 72 h	2
Freshwater cyanobacterium, <i>Synechocystis aquatilis</i>	1000–10,000 of Sn ²⁺ or Sn ⁴⁺	Inhibited growth and chlorophyll a content in 96 h, but only under alkaline conditions; Sn ²⁺ was more toxic than Sn ⁴⁺ ; toxicity of both tin species increased with increased tin concentration, increased exposure, and increased pH of the medium; humic acid reduced the toxicity of tin	43
MONOMETHYLTINS			
Marine diatom, <i>Skeletonema costatum</i>	78	50% growth inhibition in 72 h	2
DIMETHYLTINS			
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
TRIMETHYLTINS			
Alga, <i>Scenedesmus quadricauda</i>	20	LC87 (30 days)	3
Alga, <i>Chlorella vulgaris</i>	20	LC100 (30 days)	3
Alga, <i>Asteromonas gracilis</i>	20	LC100 (12 days)	3
Cladoceran, <i>Daphnia magna</i>	20	LC61 (30 days)	3

Table 8.8 (continued) Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium ($\mu\text{g/L}$)	Effect	Ref ^a
Marine diatoms, 2 species	214	50% growth inhibition in 72 h	2
TETRAMETHYLTINS			
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
DIETHYLTINS			
Snail, <i>Biomphalaria glabrata</i>	50–100	LC50 (24 h)	4
Marine diatoms, 2 species	500	No effect on growth in 72 h	2
TRIETHYLTINS			
Marine diatom, <i>Thalassiosira pseudonana</i>	3.8	LC50 (72 h)	2
Sevyuga sturgeon, <i>Accipenser stellatus</i> , larvae	10	LC100 (48 h)	3
Common carp, <i>Cyprinus carpio</i>	10	BCFs after 45 days ranged between 5 in muscle and 88 in blood	3
Marine diatom, <i>Skeletonema costatum</i>	40.2	LC50 (72 h)	2
TETRAETHYLTINS			
Marine diatoms, 2 species	127–142	50% growth inhibition in 72 h	2
TRIPROPYLTINS			
Snail, <i>Lymnaea stagnalis</i>	0.001–1.0	Fecundity reduced after exposure for three months	3
Sheep sturgeon, <i>Accipenser nudiventris</i>	0.001	Larvae die on exposure from fertilization	3
<i>A. nudiventris</i>	0.01	Polarvae die when exposed continuously from fertilization	3
Loach (fish), <i>Misgurnis fossilis</i> , larvae	<1	Normal development	3
<i>M. fossilis</i>	10	No development	3
Algae, Lake Ontario	4	50% reduction in primary productivity in 4 h	3
Alga, <i>Ankistrodesmus falcatus</i>	14	50% growth reduction in 8 days	3
Snail, <i>B. glabrata</i>	40–280	LC50 (24 h)	4
MONOBUTYLTINS			
Golden orfe (fish), <i>Leuciscus idus melanotus</i>	>45,000	LC50 (48 h)	5
DIBUTYLTINS			
Duck mussel, <i>Anodonta anatina</i>	15	After 7 months, tin localized exclusively in epithelial cells of kidney, accompanied by significant decrease in cellular glycogen content	6, 29
Marine diatom, <i>S. costatum</i>	35–56	50% growth inhibition in 72 h	2
Golden orfe	1000	LC50 (48 h)	5
TRIBUTYLTINS			
Dogwhelk, <i>Nucella lapillus</i>	0.001–0.02	Development of male characteristics in 13% of female snails after 31 days, 27% in 91 days and 41% in 120 days. Whole body BCF values about 19,000 in 31 days, 36,000 in 91 days, 78,000 in 120 days	7

Table 8.8 (continued) Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium ($\mu\text{g/L}$)	Effect	Ref ^a
<i>N. lapillus</i>	<0.002	No effect on imposex after exposure for 6 months	44
<i>N. lapillus</i>	0.002–0.128	Dose-related increase in frequency of imposex during exposure for 6–12 months. No effect on feeding rate (predation on <i>Mytilus edulis</i>) or activity patterns. Growth rate of females — but not males — reduced with increasing concentration. BCF values ranged from 7400 to 25,000 and decreased with increasing TBT exposure concentration; mussels accounted for about 40% of the accumulated TBT in whelks; the maximum concentration of TBT recorded in soft tissues of the 0.128 $\mu\text{g/L}$ group was 1.04 mg/kg FW after 12 months	44
Snail, <i>B. glabrata</i>	0.001	Reduction in egg deposition on continuous exposure from hatching	8
<i>B. glabrata</i>	0.1	Exposure for 34 days followed by 50-day recovery period produced 60% mortality, 80% reduction in egg deposition, and reduced growth	3
<i>B. glabrata</i>	0.4	LC99 (30 days)	9
<i>B. glabrata</i>	1.0	50% reduction in egg laying after exposure for 2–3 weeks	3
<i>B. glabrata</i>	3	BCF of 48 in muscle after 120 h	3
<i>B. glabrata</i>	7	LC100 (20 days)	9
<i>B. glabrata</i>	15	LC100 (5 days)	9
<i>B. glabrata</i>	75	LC100 (24 h)	4
Pacific oyster, <i>Crassostrea gigas</i>	0.01–0.02	Spat show reduced growth and hypoxia compensation after 2 weeks	10
<i>C. gigas</i>	0.15	Reduced growth and shell thickening after 8 weeks	11
<i>C. gigas</i>	0.2	BCF of about 6000 in adult soft tissues in 21 days, 11,400 in whole spat in 56 days	3
<i>C. gigas</i> , larvae	1.0	LC100 (12 days)	8
<i>C. gigas</i> , larvae	1.6	LC100 (48 h)	12
<i>C. gigas</i>	1.6	No growth. BCF after 8 weeks varied from 2300 to 3100	11
Copepod, <i>Eurytemora affinis</i>	0.0125	No adverse effects in 13 days	34
<i>E. affinis</i>	0.1	LC74 (13 days)	34
<i>E. affinis</i>	0.5	Reduction in brood size in 48 h	34
<i>E. affinis</i>	0.6	LC50 (72 h)	34
<i>E. affinis</i>	2.2	LC50 (48 h)	34
Common mussel, <i>Mytilus edulis</i>	0.05	Some larval deaths in 96 h	13
<i>M. edulis</i> , larvae	0.1	LC50 (15 days)	14
<i>M. edulis</i> , larvae	0.24	Growth reduction after 45 days	12, 14
<i>M. edulis</i>	0.31	No shell growth in 66 days	14
<i>M. edulis</i>	0.4	Reduction in shell growth rate in 7 days	15
<i>M. edulis</i> , adults	0.97	LC50 (66 days)	14, 16
<i>M. edulis</i> , larvae	0.5	LC100 (96 h)	13
European oyster, <i>Ostrea edulis</i>	0.06	Reduced growth rate in 10 days	14
<i>O. edulis</i>	0.24	No larval release after exposure for 74 days; BCF of 875	17
<i>O. edulis</i>	2.6	Reduced growth in 74 days; BCF of 397	17
<i>O. edulis</i> , larvae	3.4	LC50 (48 h)	17
Striped bass, <i>Morone saxatilis</i>			
Larvae, 13-days old	0.067	Body morphometry altered after exposure for 6 days	38
Larvae, 16-days old	0.44	After exposure for 7 days, no adverse effects on survival, growth, or morphometry	38

Table 8.8 (continued) Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium (µg/L)	Effect	Ref ^a
Larvae, 21-days old	0.51	Notochord development inhibited during exposure for 7 days	38
Larvae, 13-days old	0.77	Survival reduced after exposure for 6 days	38
Larvae, 16-days old	1.5	All dead in 6 days	38
Copepod, <i>Temora longicarpus</i> ; held in outdoor enclosures containing plankton for 28 days	0.09	Inhibited reproduction	52
<i>T. longicarpus</i> , as above	0.15	50% reduction in numbers	52
<i>T. longicarpus</i> , as above	0.32	50% reduction in biomass	52
Marine algae, 3 species	0.1	Reduced growth rate in 48 h	18
Brittle star, <i>Ophioderma brevispinosa</i>	0.1	Arm regeneration inhibited	19
Three-spined stickleback, <i>Gasterosteus aculeatus</i>	0.1 or 1.0	After exposure in seawater for 7.5 months, hepatocytes were abnormal in the high dose group; reproduction normal in both groups	45
<i>G. aculeatus</i>	10.0	Exposure as above; 80% dead in 2 months. Survivors had gill histopathology and abnormal gill chloride cells and liver hepatocytes	45
Goldfish, <i>Carassius auratus</i>	0.13	BCF of 1934 during 21–28 days of exposure via gill intake	40
Daphnid, <i>Daphnia magna</i> ; gravid females exposed for 21 days	0.3–1.25	No adverse effects on survival or molting	51
<i>D. magna</i> , as above	1.25	Enhanced ability to metabolize testosterone	51
<i>D. magna</i> , as above	2.6	LC60 (21 days)	51
<i>C. auratus</i>	75,000	LC50 (24 h)	40
Sheepshead minnow, <i>Cyprinodon variegatus</i>	0.18–1.0	Maximum BCFs after 167 days were 1600 in muscle, 3900 in viscera, 52,000 in liver; no adverse effects on growth or reproduction	20
<i>C. variegatus</i>	0.96	LC50 (21 days)	8
<i>C. variegatus</i>	1.6	Maximum BCFs after 58 days were 1810 in muscle, 2120 in head, 4580 in viscera, and 2600 in whole fish. Loss after 28 days depuration ranged from 64% to 80%	20
<i>C. variegatus</i>	3.2	LC100 (21 days)	20
<i>C. variegatus</i>	5–8	LC50 (96 h)	3
<i>C. variegatus</i>	18	LC50 (7 days)	8
Oysters, several species	0.2	LC70 (113 days)	8
Rainbow trout, <i>Oncorhynchus mykiss</i>	0.2–1.0	Exposure of yolk-sac fry for 110 days produced liver dysfunction, reduced growth, and altered blood chemistry; no deaths	8, 21
<i>O. mykiss</i>	0.5 or 2.0	Exposure of 3-week-old hatchlings for 21 days. Dose-dependent increase in TBT accumulation and growth reduction. Treated fish had greater swimming stamina than controls but lacked circular orientation typical of controls. TBT tissue concentrations in head and body at 21 days ranged from 1.5–2.0 mg/kg FW vs. 0.05–0.11 in controls	46
<i>O. mykiss</i>	0.5 or 2.0	Age and exposure as above. Brain histopathology, especially optic system. In high dose group, myelin alterations in CNS where optic nerve enters the midbrain	47,48
<i>O. mykiss</i>	0.6–4.0	TBT concentrations in whole trout after exposure for 28 days were 2.5 mg/kg FW at 0.6 µg/L, 3.0 at 1.0 µg/L, 5.8 at 2.0 µg/L, and 7.4 mg/kg FW at 4.0 µg/L	50

Table 8.8 (continued) Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium ($\mu\text{g/L}$)	Effect	Ref ^a
<i>O. mykiss</i>	1–6	Dose-related lymphocytic depletion and histopathology after exposure for 14 days of trout age 5 months	50
<i>O. mykiss</i>	1.4–20.0	LC50 (96 h)	5,22,49
<i>O. mykiss</i>	5	Kidney degeneration in 12 days, some deaths	21
<i>O. mykiss</i>	11.7	Bile duct pathology after 5 days; destruction of corneal epithelium after 7 days	3
<i>O. mykiss</i>	21	LC50 (48 h)	9
<i>O. mykiss</i>	28	LC50 (24 h)	23
Baltic amphipod, <i>Gammarus oceanicus</i> , larvae	0.3	Reduced survival after 5 weeks	24
<i>G. oceanicus</i>	3	LC100 (16 days)	3
Alga, <i>Skeletonema costatum</i>	0.33–0.36	50% growth inhibition in 72 h	2
Copepod, <i>Acartia tonsa</i>	0.4	50% immobilization in 144 h	25
<i>A. tonsa</i>	0.55	LC50 (6 days)	8
<i>A. tonsa</i>	1.0	LC50 (96 h)	25
Axolotl, <i>Ambystoma mexicanum</i> ; larvae with amputated forelimbs	0.5–50.0 for up to 49 days	All larvae in the 50 $\mu\text{g/L}$ group died within 24 h; 80% dead in the 15 $\mu\text{g/L}$ group within 7 days and 90% in 49 days; no deaths in other groups. TBT was slightly teratogenic to developing axolotl hindlimbs but had no measurable effect on skeletal patterns in regenerating forelimbs in the 0.5, 1.5, and 5 $\mu\text{g/L}$ groups	42
Fiddler crab, <i>Uca pugilator</i>	0.5	Limbs regenerated during 19 days showed a variety of deformities and retardation of regenerative growth	26, 35
<i>U. pugilator</i>	0.5–50	Non-dose dependent reduction in burrowing activity in 15 to 60 min; hyperactivity in 1 to 3 weeks	36
Mysid shrimp, <i>Metamysidopsis elongata</i> , juveniles	0.5–1.0	LC50 (96 h)	3
Freshwater minnow, <i>Phoxinus phoxinus</i> . Eggs and newly hatched larvae, exposed at 16°C or 21°C	0.69–0.82	All survived exposure for 6 days at 21°C, but 50% of larvae were abnormal (deformations, erratic swimming, paralysis)	41
As above	0.82–19.5	After 3–10 days, degenerative alterations of skin, muscle, kidney, eye, and spinal cord; effects more pronounced at higher doses and temperature	39
As above	4.3 and higher	In larvae, increased mortality, deformation of body axis, paralysis, and opaque eyes	39
As above	9.2	All dead in 4 days at 21°C; no sediments in assay containers	41
As above	10.4	90% dead in 9 days at 16°C; no sediments in assay containers	41
American oyster, <i>Crassostrea virginica</i>	0.73–1.9	Reduced larval growth in 66 days	16
<i>C. virginica</i> , larvae	0.9	50% immobilization in 48 h	12
Hydroid, <i>Campanularia flexuosa</i>	1.0	100% growth inhibition in 11 days	3
Cladoceran, <i>D. magna</i>	1.0	Reduced survival and impaired reproduction in 15 days	14
<i>D. magna</i>	1.7	LC50 (48 h)	12
<i>D. magna</i>	3	LC50 (24 h)	23
American lobster, <i>Homarus americanus</i>	1.0	No effect on larval metamorphosis in 6 days	8
<i>H. americanus</i> , larvae	5	LC100 (6 days)	25
<i>H. americanus</i> , larvae	20	LC100 (24 h)	3

Table 8.8 (continued) Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium ($\mu\text{g/L}$)	Effect	Ref ^a
Shrimp, <i>Crangon crangon</i> , larvae	1.5	LC50 (96 h)	12
<i>C. crangon</i> , adults	41	LC50 (96 h)	12
Copepod, <i>Nitroca spinipes</i>	2	LC50 (96 h)	25
Round Crucian carp, <i>Carassius carassius grandoculis</i>	2	BCF after 7 days of about 500 in vertebra, 630 in muscle, 3160 in kidney, and 5020 in liver	27
Sole, <i>Solea solea</i> , larvae	2	LC50 (96 h)	3
Lugworm, <i>Arenicola cristata</i>	2	LC0 (168 h)	28
<i>A. cristata</i> , larvae	4	LC100 (96 h)	23
Algae, various species	3–16	50% reduction in primary productivity in 4 h to 8 days	3
Barnacle, <i>Balanus amphitrite</i>	4	LC50 (24 h) nauplii	3
Freshwater clam, <i>Anodonta anatina</i>	5	LC100 (6 weeks)	29
Mud snail, <i>Nassarius obsoletus</i>	5–6	Induced male characteristics in females in 64 days	3
<i>N. obsoletus</i>	8	LC50 (61 days)	3
Lake trout, <i>Salvelinus namaycush</i>	5.2	LC50 (96 h)	49
Tubifex worm, <i>Tubifex tubifex</i>	6	LC50 (48 h)	9
Amphipod, <i>Orchestia traskiana</i>	6	LC47 (9 days)	3
<i>O. traskiana</i>	10	LC80 (9 days)	3
<i>O. traskiana</i>	15	LC93 (9 days)	3
Mud crab, <i>Rithropanopeus harrisii</i>	6	BCFs after 4 days were 650 in muscle, 4400 in hepatopancreas, and 1300 in gill	37
<i>R. harrisii</i>	15	Weight loss after 15 days	3, 37
Bluegill, <i>Lepomis macrochirus</i>	7.6	LC50 (96 h)	12
<i>L. macrochirus</i>	33	LC50 (48 h)	8
Mysid shrimp, <i>Mysis dopsis bahia</i>	8	LC50 (96 h)	30
Mummichog (fish), <i>Fundulus heteroclitus</i>	9	Avoidance	3
<i>F. heteroclitus</i>	24	LC50 (96 h)	12
Crab, <i>Carcinus maenus</i>	10	LC50 (96 h)	3
Amphioxus, <i>Branchiostoma caribaeum</i>	10	LC100 (96 h)	30
Snail, <i>Neritina</i> sp.	10	LC100 (6 days)	3
Snails, <i>Biomphalaria</i> spp.	10–30	LC50 (24 h)	8
Channel catfish, <i>Ictalurus punctatus</i>	12	LC50 (96 h)	8
Marine diatom, <i>S. costatum</i>	14.7	LC50 (72 h)	2
Snail, <i>Lymnaea</i> sp.	15	LC100 (5 days)	3
Atlantic menhaden, <i>Brevoortia tyrannus</i>	15	Avoidance by juveniles	3
Speckled sanddab, <i>Citharichthys stigmaeus</i>	20	LC50 (96 h)	3
Grass shrimp, <i>Palaemonetes pugio</i>	20	LC50 (96 h)	30
Green alga, <i>Ankistrodesmus falcatus</i>	20	BCF of 30,000 at day 7	23
<i>A. falcatus</i>	40	BCF of 8600 at day 7	23
Guppy, <i>Poecilia reticulata</i>	21–30	LC50 (96 h)	8
<i>P. reticulata</i>	26 to 34	LC50 (48 h)	5
Mozambique tilapia, <i>Tilapia mossambica</i>	28	LC50 (24 h)	8
Duckweed, <i>Lemna media</i>	30	Reduced growth in 10 days	31
Snail, <i>Australorbis glabratus</i>	30	LC100 (5 days)	31

Table 8.8 (continued) Lethal and Sublethal Effects of Inorganic and Organic Tin Compounds in Ambient Medium to Selected Species of Aquatic Organisms

Compound and Organism	Medium (µg/L)	Effect	Ref ^a
European frog, <i>Rana temporaria</i> , tadpole	30	LC50 (5 days)	32
<i>R. temporaria</i> , tadpole	75	LC100 (24 h)	9
Harlequin fish, <i>Rasbora heteromorpha</i>	42	LC50 (48 h)	8
Jewelfish, <i>Hemichromis bimaculatus</i>	45	LC70 (48 h)	8
Fathead minnow, <i>Pimephales promelas</i>	45	LC50 (96 h)	8
Golden orfe	50	LC50 (48 h)	5
Cladoceran, <i>Daphnia longispina</i>	60	LC100 (72 h)	31
Bleak (fish), <i>Alburnus alburnus</i>	70–400	LC50 (96 h)	5
Goldfish, <i>Carassius auratus</i>	75	LC100 (24 h)	31
Duckweed, <i>Lemna media</i>	500	LC100 (10 days)	31
TETRABUTYLTINS			
Golden orfe	10,000	LC50 (48 h)	5
TRIPENTYLTINS			
Snail, <i>B. glabrata</i>	50–100	LC50 (24 h)	4
TRIPHENYLTINS			
Goldfish, <i>Carassius auratus</i>	0.14	BCF of 1384 during exposure for 21–28 days via gill intake	40
Marine diatoms, 2 species	0.6–1.1	50% growth inhibition in 72 h	2
Lugworm, <i>A. cristata</i>	0.75–1.0	Abnormal larval development	28
<i>A. cristata</i> , larvae	1.5–2.5	LC0 (168 h)	28
<i>A. cristata</i> , larvae	4–10	LC100 (96 h)	23
Rainbow trout, age 6 months	1–6	Exposure for 4 weeks produced myelin alterations in the CNS at 4 and 6 µg/L, but not at lower doses	48
Algae, various species	2–20	50% growth inhibition in 4 h to 8 days	3
Marine diatom, <i>S. costatum</i>	4.3–13.8	LC50 (72 h)	2
Copepod, <i>Nitroca spinipes</i>	8	LC50 (96 h)	3
Snail, <i>B. glabrata</i>	10–1000	LC50 (24 h)	4
Rainbow trout	15	LC50 (96 h)	30
Snail, <i>Biomphalaria sudanica</i>	17	LC50 (24 h)	3
Cladoceran, <i>D. magna</i>	20	LC100 (30 days)	3
Cladoceran, <i>D. longispina</i>	50	LC100 (48 h)	33
Snail, <i>Australorbis glabratus</i>	50	LC100 (7 days)	33
<i>A. glabratus</i>	200	LC100 (72 h)	33

^a 1, Taylor et al. 1985; 2, Walsh et al. 1985; 3, Hall and Pinkney 1985; 4, Duncan 1980; 5, Blunden and Chapman 1986; 6, Herwig and Holwerda 1986; 7, Bryan et al. 1986; 8, Thompson et al. 1985; 9, Chliamovitch and Kuhn 1977; 10, Lawler and Aldrich 1987; 11, Waldock and Thain 1983; 12, Champ 1986; 13, Dixon and Prosser 1986; 14, Cardwell and Sheldon 1986; 15, Stromgren and Bongard 1987; 16, Valkirs et al. 1987; 17, Thain and Waldock 1986; 18, Beaumont and Newman 1986; 19, Walsh et al. 1986b; 20, Ward et al. 1981; 21, Seinen et al. 1981; 22, Douglas et al. 1986; 23, Maguire et al. 1984; 24, Laughlin et al. 1984; 25, U'ren 1983; 26, Weis et al. 1987; 27, Tsuda et al. 1986; 28, Walsh et al. 1986a; 29, Holwerda and Herwig 1986; 30, Clark et al. 1987; 31, Floch et al. 1964; 32, Laughlin and Linden 1982; 33, Floch and Deschiens 1962; 34, Hall et al. 1988; 35, Weis and Kim 1988; 36, Weis and Perlmutter 1987; 37, Evans and Laughlin 1984; 38, Pinkney et al. 1990; 39, Fent and Meier 1992; 40, Tsuda et al. 1991; 41, Fent 1992; 42, Scadding 1990; 43, Pawlik-Skowronska et al. 1997; 44, Davies et al. 1997; 45, Holm et al. 1991; 46, Triebeskorn et al. 1994a; 47, Triebeskorn et al. 1994b; 48, Triebeskorn et al. 1994c; 49, Martin et al. 1989; 50, Schwaiger et al. 1992; 51, Oberdorster et al. 1998; 52, Jak et al. 1998.

Results of acute toxicity tests with several organotin compounds and *Daphnia magna* indicated several distinct trends: toxicity increased with length of alkyl group from methyl to butyl; the anion substituents are relatively unimportant; and bioavailability is correlated with increasing solubility in lipids, which is a direct function of K_{ow} , the n-octanol/water partition coefficient (Vighi and Calamari 1985). Structure–activity relations seem to have high predictive capacity in hazard assessment, and those for organotins seem particularly promising (Vighi and Calamari 1985). For example, studies on the biocidal properties of structurally distinct diorganotins (R_2SnX_2) and triorganotins (R_3SnX) to zoeae of a marine crab show, within a homologous series, that diorganotins are less toxic than the corresponding triorganotins (Table 8.9). It was concluded that the toxicity of organotins to crab zoeae seems to be a function of the hydrophobic characteristics conferred by the number and structure of the organic ligands (Laughlin et al. 1985). Studies with yolk sac fry of the rainbow trout also demonstrate that triorganotins are at least two orders of magnitude more toxic than diorganotins (de Vries et al. 1991). The no-observable-effect-concentration (NOEC) for rainbow trout fry during exposure for 110 days was 40 µg/L for dibutyltin chloride, 60 µg/L for diphenyltin chloride, and 0.04 to 0.05 µg/L for various tributyltin compounds (de Vries et al. 1991). Alterations of steroid mechanisms, such as ability to metabolize testosterone, by TBT may be a more sensitive indicator of sublethal exposure in *Daphnia magna* than reproductive endpoints (Oberdorster et al. 1998).

Signs of tributyltin poisoning in rainbow trout and other freshwater fishes include sluggishness, loss of appetite, altered body pigmentation, air gulping, loss of positive rheotaxis, increased rate of opercular movements, increases in blood hemoglobin and hematocrit, damaged gills and cornea, increases in erythrocyte number, damage to epithelial cells of the bile duct, (Chliamovitch and Kuhn 1977; Thompson et al. 1985; Holm et al. 1991), decreased resistance to bacterial pathogens (de Vries et al. 1991), and peripheral blood neutrophilia and impaired antibody secreting mechanisms (Rice et al. 1995). These changes were consistent with the known inhibitory effects on

Table 8.9 Toxicity of Selected Diorganotin and Triorganotin Compounds to Zoeae of the Marine Mud Crab (*Rithropanopeus harrisi*) Exposed from Hatching to Age 14 Days

Compound Tested	Lowest Concentrations Tested (mg/L) Producing			
	Some Deaths, but <50% Mortality		At Least 50% Mortality	
	Total Product	Tin Only	Total Product	Tin Only
DIORGANOTINS				
Dimethyltin dichloride, $(CH_3)_2SnCl_2$	10.0	5.4	20.0	10.8
Diethyltin dichloride, $(C_2H_5)_2SnCl_2$	2.5	1.2	5.0	2.4
Dipropyltin dichloride, $(C_3H_7)_2SnCl_2$	2.5	1.1	5.0	2.2
Dibutyltin dichloride, $(C_4H_9)_2SnCl_2$	0.25	0.097	2.0	0.78
Diphenyltin dichloride, $(C_6H_5)_2SnCl_2$	0.5	0.18	0.75	0.27
Dicyclohexyltin dichloride, $(C_6H_{13})_2SnCl_2$	0.125	0.041	0.25	0.082
TRIORGANOTINS				
Trimethyltin hydroxide, $(CH_3)_3SnOH$	0.075	0.05	0.1	0.067
Triethyltin hydroxide, $(C_2H_5)_3SnOH$	0.075	0.04	0.1	0.053
Tripropyltin oxide, $(C_3H_7)_3Sn_2O$	0.025	0.015	0.05	0.03
Tributyltin oxide, $((C_4H_9)_3Sn)_2O$	0.01	0.005	0.02	0.011
Triphenyltin hydroxide, $(C_6H_5)_3SnOH$	0.01	0.003	0.02	0.007
Tricyclohexyltin bromide, $(C_6H_{13})_3SnBr$	0.006	0.0016	0.009	0.0023

Modified from Laughlin, R.B., Jr., R.B. Johannesen, W. French, H. Guard, and F.E. Brinckman. 1985. Structure–activity relationships for organotin compounds. *Environ. Toxicol. Chem.* 4:343–351.

mitochondrial and oxidative phosphorylation of triorganotin compounds. Exposure to tributyltin may alter both cytochrome P-450 dependent metabolism, and induction response to other environmental pollutants (Fent and Stegeman 1993). Studies with scup (*Stenotomus chrysops*), a marine fish, show that a single intraperitoneal injection of 3.3, 8.1, or 16.3 mg tributyltin/kg BW results in a dose-dependent decrease in hepatic microsome ethoxyresorufin O-deethylase activity, cytochrome P-450 degradation to P420, and increase in liver concentrations from 8 to 202 mg Sn/kg FW (Fent and Stegeman 1993). Organotins also act on the microsomal electron transport system, the hemoprotein P-450, and the flavoproteins of freshwater fishes (Fent and Bucheli 1994). Cytopathological changes in trout brain induced by tributyltin or triphenyltin resemble the reactions observed in brains of mammals after triethyltin insult and are similar to symptoms in the brains of patients affected by a disease known as central pontine myelinosis (in which tin is detected in intramyelin vacuoles) or by multiple sclerosis (Triebeskorn et al. 1994c). In rainbow trout erythrocytes, tributyltin inhibits the uptake of Na^+ and Cl^- ions and interacts with the activity of the Na^+/H^+ exchanger (Virki and Nikinmaa 1993). Tributyltin compounds modify calcium flux across the plasma membrane in a dose-dependent manner in oyster toadfish (*Opsanus tau*), a marine species (Rice and Weeks 1990). At 50 $\mu\text{g}/\text{L}$, tributyltin facilitated an inward flux of calcium. At 500 $\mu\text{g}/\text{L}$ calcium mobilization was inhibited, resulting in impaired macrophage function (Rice and Weeks 1990). In trout hepatocytes, tributyltin mobilizes Ca^{+2} from intracellular stores. The cytoplasmic acidification following tributyltin exposure seems to be caused by the combination of intracellular Ca^{+2} and by direct action of tributyltin (Reader et al. 1994). Suppression of regeneration in echinoderms, and presumably other aquatic groups by organotins, may be due primarily to neurotoxicological action of organotins, or secondarily by direct action on tissue at the breakage point (Walsh et al. 1986b). In freshwater minnows (*Phoxinus phoxinus*) the toxicity of tributyltin compounds to early life stages is based on its eye- and skin-irritative activity, and on its activity against muscular, renal, and neuronal tissues (Fent and Meier 1992).

Imposex — the superimposition of male characteristics onto a functionally normal female reproductive anatomy — is a phenomenon documented in populations of marine gastropod molluscs in the vicinity of yacht basins and marinas and is a sensitive indicator of tributyltin contamination. A female with imposex displays one or more male characteristics, such as a penis, a vas deferens, or convolution of the normally straight gonadal oviduct. It is measured by frequency of occurrence in the adult females and by the intensity of expression of all male characteristics in bearer females. Imposex is prevalent in mud snails (*Nassarius obsoletus*) near estuarine marinas and has been induced experimentally in that species by exposure for 60 days to three tributyltin compounds at concentrations of 4.5 to 5.5 $\mu\text{g}/\text{L}$ (Smith 1981a, 1981b). Imposex has been documented extensively in declining populations of the common dogwhelk (*Nucella lapillus*), especially in southwestern England (Bryan et al. 1986, 1987; Gibbs and Bryan 1986; Davies et al. 1987; Gibbs et al. 1987). These authorities agree on six points: (1) dogwhelk populations near centers of boating and shipping activity show the highest degrees of imposex, coinciding with the introduction and increasing use of antifouling paints containing tributyltin compounds; (2) imposex is not correlated with tissue burdens of arsenic, cadmium, copper, lead, silver, or zinc, but with increasing concentrations of tributyltin and dibutyltin fractions; (3) transplantation of dogwhelks from a locality with little boating activity to a site near a heavily used marina causes a marked increase in the degree of imposex and in tissue accumulations of tributyltins; (4) imposex can be induced in female dogwhelks by exposure to 0.02 μg Sn/L leached from a tributyltin antifouling paint; after exposure for 120 days, 41% of the females had male characteristics and whole-body residues of 1.65 mg Sn/kg dry weight soft parts (vs. 0.1 in controls), of which almost all was tributyltin (1.64 vs. 0.08 mg/kg in controls). Concentrations as low as 0.0015 μg tributyltin/L can initiate imposex in immature females; (5) declining dogwhelk populations were characterized by a moderate to high degree of imposex, relatively fewer functional females, few juveniles, and a general scarcity of laid egg

capsules. Many females in late imposex contained aborted capsules as a result of oviduct blockage, resulting in sterility and premature death; and (6) there was no evidence that loss of tin leads to any remission of imposex; in fact, all evidence indicates that gross morphological changes that occur in late imposex are irreversible.

Signs of imposex were severe in some populations of whelks (*Thais* spp., *Vasum turbinellus*) sampled in eastern Indonesia in 1993 and are attributed to unrestricted use of paints containing tributyltin (Evans et al. 1995). Studies indicate that imposex in gastropod molluscs is caused by elevated testosterone titers that masculinize TBT-exposed females as a result of competitive inhibition of cytochrome P450-mediated aromatase (Matthiessen and Gibbs 1998). TBT-induced masculinization in gastropods (imposex and intersex) is a convincing example of endocrine disruption described in invertebrates that is unequivocally linked to an environmental contaminant (Matthiessen and Gibbs 1998). It is clear that additional research is needed on the imposex phenomenon in molluscs and on its implications for vertebrates and other taxonomic groups.

Biological factors known to modify lethal and sublethal effects of organotins include age of the organism, inherent interspecies resistance, and tissue specificity. Abiotic modifiers include exposure route, and physicochemical regimen. Early developmental stages were more sensitive to organotins than later developmental stages in marine annelids (Walsh et al. 1986a), mysid shrimp (Hall and Pinkney 1985), and rainbow trout (Thompson et al. 1985). Mortality of zoeae of fiddler crabs (*Uca pugilator*) to trimethyltins was greatest at elevated temperatures and low salinities (Thompson et al. 1985). Mussels exposed through a diet of algae showed slow accumulation of organotins when compared to exposure from the medium; the reverse was observed for crabs (Evans and Laughlin 1984; Hall and Pinkney 1985; Laughlin et al. 1986a). A marine diatom (*Thalassiosira pseudonana*) showed no adaptation or resistance to triphenyltins or tributyltins (Walsh et al. 1985), but another diatom (*Amphora coffeaeformis*) was extremely resistant (Thomas and Robinson 1986, 1987). Benthic fauna are probably capable of transferring organotins from sediments to bottom-feeding teleosts. For example, sediments spiked with 0.98 mg Sn/kg dry weight, as tributyltin, resulted in concentrations of 4.41 mg/kg whole-body dry weight in oligochaete annelid worms after 22 weeks, up from 0.38 at the start (Maguire and Tkacz 1985). Mortality was substantially higher when organisms were exposed simultaneously to organotins through water and sediments; in the case of grass shrimp (*Palaemonetes pugio*), the addition of contaminated sediments increased mortality by up to 1000 times (Clark et al. 1987). However, the addition of uncontaminated sediments to assay containers reduced the bioavailability of tributyltin to freshwater fishes by as much as 84% (Fent 1992).

Aside from direct toxic effects that antifouling paint residues may have on marine life, there is no evidence of any risk from cytogenetic damage. Tributyltins, for example, were not genotoxic to larvae of the mussel (*Mytilus edulis*), based on results of sister chromatid exchange and analysis of chromosomal aberrations (Dixon and Prosser 1986). Teratogenic effects, however, were detected in larvae of the lugworm (*Arenicola cristata*) at sublethal concentrations of tributyltins (Walsh et al. 1986a), and algae (*Nitzschia liebenthutii*) exposed to 15 mg inorganic Sn/L for 14 days had frustule abnormalities (Saboski 1977).

Bioconcentration of inorganic and organic tin compounds from the medium is considerable. Bioconcentration factors (BCFs) for inorganic tin and marine algae were about 1900; moreover, tin-resistant bacteria contained a remarkable 3.7 to 7.7 grams Sn/kg dry weight (Maguire et al. 1984; Eisler 1989; Maguire 1991). Partitioning or binding may control bioaccumulation of tributyltin by marine phytoplankton. A linear relation is documented for external concentrations of tributyltin compounds and cell burdens in the marine microalgae *Nannochloris* sp., *Chaetoceros gracilis*, and the cyanobacterium *Synechococcus* sp. However, the relation was not linear for the alga *Isochrysis galbana* (Chiles et al. 1989). BCFs for organotin compounds varied from about 400 to 30,000 among various species of molluscs, algae, and crustaceans and were highest when ambient tin concentrations were <1.0 µg/L, when exposure times were comparatively lengthy, and when organism lipid content was elevated (Thompson et al. 1985; Champ 1986; Laughlin et al. 1986a; Thain and Waldock 1986). Studies with freshwater minnows (*Phoxinus phoxinus*) demon-

strate a high potential for tributyltin bioconcentration in early life stages, and slow metabolism in embryo and yolk-sac larvae (Fent 1991). Sheepshead minnows (*Cyprinodon variegatus*) were unable to reach equilibrium with a medium containing 1.61 µg tributyltin/L after 58 days of exposure, and maximum BCF values recorded were 2600 in whole fish, 1810 in muscle, 4580 in viscera, and 2120 in the remainder of the carcass; however, whole-body loss was 52% after depuration for 7 days and 74% after 28 days (Ward et al. 1981). Sheepshead minnows were able to metabolize tributyltins into lower alkyl moieties, which were less toxic. Thus, even though significant bioconcentration occurred, the chronic toxicity of tributyltins to sheepshead minnow was not significantly greater than its acute toxicity (Ward et al. 1981).

Uptake of organotins through the medium is a more effective route than the diet, and triphenyltin compounds are more readily accumulated through dietary uptake than are tributyltin compounds. Tributyltin and triphenyltin compounds show BCF values of 1384 to 1974 in whole goldfish (*Carassius auratus*) after exposure for 21 to 28 days in media containing 0.13 to 0.14 µg Sn/L. But goldfish fed diets containing these same compounds at 1.7 to 1.9 µg Sn/kg ration for 28 to 35 days had BCF values of 0.04 to 0.1 (Tsuda et al. 1991). A nearly identical pattern was reported for willow shiner (*Gnathopodion caerulescens*), another freshwater teleost (Tsuda et al. 1992). Red sea bream (*Pagrus major*) fed tributyltin or triphenyltin compounds in the diet (8 to 1000 µg Sn/kg ration) for 8 weeks and simultaneously challenged with seawater containing 0.067 to 0.083 µg/L of triorganotin compounds accumulated 25% of their whole-body tin burden from the diet, regardless of tin concentration or chemical species in the ration. Tributyltin assimilation in red sea bream was 10% and retention 24%; for triphenyltin, assimilation was 13% and retention 60% (Yamada et al. 1994). American plaice (*Hippoglossoides platessoides*) given a single oral dose of ¹¹³Sn-tributyltin showed ¹¹³Sn distribution over the entire body — especially liver and gallbladder — with steady state achieved in 5 to 10 days; average retention efficiency of TBT over a 6-week period was 44%, with half-time persistence of 15 to 77 days (Rouleau et al. 1998).

8.5.3 Birds

Information is scarce on the effects of tin and organotin compounds on birds. Limited data suggest that triorganotin compounds, especially trimethyltins (and to a lesser extent triethyltins) are the most toxic (Table 8.10). Fleming et al. (1991), in a 75-day feeding study with mallard ducklings (*Anas platyrhynchos*) and 12 organotin compounds, concluded that (1) trimethyltin was the most toxic compound tested, (2) a dietary level of 50 mg of tin as trimethyltin chloride/kg food was fatal to all ducklings, (3) 5 mg trimethyltin chloride/kg ration killed 40%, but all survived at 0.5 mg/kg diet, (4) death was preceded by mild to severe tremors, progressing to ataxia and lethargy, (5) trimethyltin-stressed ducklings exhibited degeneration of the large neurons of the pons, medulla oblongata, gray matter of the spinal cord, and pyramidal cells of the cerebral cortex, (6) all ducklings survived exposure to 50 mg/kg ration of tetraethyltin, tetrabutyltin, tetraphenyltin, triethyltin chloride, tripropyltin chloride, tributyltin chloride, tributyltin oxide, triphenyltin chloride, tricyclohexyltin chloride, dimethyltin chloride, and dibutyltin chloride. Sublethal effects were recorded at 50 mg triethyltin chloride/kg ration (low body weight, vacuolization of spinal cord and brain white matter), at 50 mg tributyltin chloride/kg (enlarged liver), and at 50 mg tetrabutyltin/kg (elevated kidney weight; Fleming et al. 1991).

Dietary studies with Japanese quail (*Coturnix japonica*) showed that tributyltin oxide affected reproduction at a dose where no overt toxicity was observed. Dietary levels as low as 60 mg tributyltin oxide/kg ration for 6 weeks was associated with decreased hatchability and decreased survival of chicks, although adults fed and behaved normally (Coenen et al. 1992).

8.5.4 Mammals

Inorganic tin compounds and some heterocyclic organic tin compounds are of low toxicologic risk to mammals (Table 8.11), due largely to their low solubility, poor absorption, low tissue accu-

Table 8.10 Lethal and Sublethal Effects of Selected Organotin Compounds to Birds

Compound and Organism	Effect (reference)
DIALKYLTINS	
Japanese quail, <i>Coturnix japonica</i>	No measurable effect at dietary levels of 150 mg/kg ration for 2 weeks (Seinen et al. 1977b)
TRIALKYLTINS	
Mallard, <i>Anas platyrhynchos</i>	Ducklings fed diets containing 50 mg trimethyltin chloride/kg died within 60 days (Fleming et al. 1991)
Pigeon, <i>Columba</i> sp.	Trimethyltin injections (3 intramuscular injections, 2 weeks apart) at 1.0 mg/kg body weight (BW) interfered with ability to perform motor tasks; no evidence of cumulative effects (Idemudia and McMillan 1986b)
Domestic chicken, <i>Gallus</i> sp.	Single oral dose of 3 mg trimethyltin/kg BW produced tremors, convulsions, and death within 24 h (Stoner et al. 1955)
Pigeon	Triethyltin injections (4 intramuscular injections, 2 weeks apart) at 1.75 mg/kg BW resulted in total suppression of pecking behavior for 3 h; recovery underway by 27 h postinjection (Idemudia and McMillan 1986a)
Domestic chicken	Single oral dose of 3 mg triethyltin sulfate/kg BW resulted in immediate collapse, salivation, convulsions, and death in a few min; at 2 mg/kg, bird was unconscious for 1–1.5 h postadministration, with recovery beginning in 1 day (Stoner et al. 1955)
Domestic chicken	Feeding of 160 mg triethyltin hydroxide/kg diet for 15 weeks was not fatal, but caused muscular weakness and some diet avoidance (Stoner et al. 1955)
Japanese quail	Acute oral LD50 of tricyclohexyltin hydroxide varies between 255 and 390 mg/kg BW; dietary levels of 20 mg/kg had no measurable effect on growth, survival, or reproduction (Zuckerman et al. 1978)
Japanese quail; fed diets containing 0, 24, 60 or 150 mg tri- <i>n</i> -butyltin oxide for 6 weeks. Eggs produced and chicks hatched were observed	Food concentration normal with no overt adverse signs of TBTO exposure noted in adults. Decreased hatchability and increase in percent of chicks found dead in the shell were noted at 60 and 150 mg/kg food. Egg production and eggshell thickness normal. Abnormal blood chemistry and hepatic EROD noted in parent birds treated with TBTO (Coenen et al. 1992)
Domestic chicken	Acute oral LD50 of 654 mg of tricyclohexyltin hydroxide (Smith 1978a)
TETRAALKYLTINS	
Domestic chicken	Daily doses >0.0001 mg tetraethyltin/kg BW produced adverse effects on blood chemistry and CNS (Duncan 1980)

mulations, and rapid tissue excretion (Hiles 1974; Kimbrough 1976). Inorganic tin compounds accumulate mostly in liver and kidney, rarely in brain, in proportion to dose and regardless of the exposure route (Hassett et al. 1984). Noncyclic organotin compounds, by contrast, have produced adverse effects on the skin, eyes, gastrointestinal tract, liver, bile duct, kidney, hematopoietic system, central nervous system, reproduction, growth, and chromosomes of small laboratory animals (Table 8.11). Effects of diorganotin compounds can be distinguished from those of tri- and tetraorganotin compounds. The chief toxicological difference is that some trialkyltins have a specific effect on the central nervous system resulting in cerebral edema, whereas diorganotins do not produce this effect but are potent irritants that induce inflammatory reactions. The tetraorganotins resemble triorganotins, which are usually more toxic than either mono- or diorganotins (WHO 1980; Table 8.11).

Diorganotin compounds cause cerebral edema and inhibit mitochondrial respiration by preventing the oxidation of keto acids, presumably through inhibition of alpha-keto oxidase activity (Piver 1973; WHO 1980). Large interspecies variability exists in the capacity of diorganotins to induce lymphoid atrophy. For example, dioctyltins and dibutyltins were selectively cytotoxic to rat thymocytes after dietary exposures of 50 to 150 mg/kg diet for 2 weeks; in contrast, no lymphoid atrophy occurred in mice, guinea pig, or Japanese quail given similar dosages and exposures (Seinen et al. 1977a, 1977b). Route of exposure can also modify effects of diorganotins. Oral exposure to dibutyltin compounds, for example, produces inflammatory changes in bile duct of the rat and

necrotic changes in liver of mice and rats; dermal exposure causes bile duct injury in rats and rabbits; and intravenous administration produces pulmonary edema in rats (WHO 1980). Intratesticular administration of high doses of some dibutyltins produced marked degeneration in rat testes within 7 days, including atrophy of seminiferous tubules and complete arrest of spermatogenesis; however, similar results have been reported for cadmium, zinc, and copper salts (Saxena et al. 1985).

Trimethyltin, triethyltin, and tributyltin compounds are highly toxic to animals and man. Trimethyltin and triethyltin compounds are more toxic to mammals than the higher triorganotin homologues, probably because of poorer absorption of higher trialkyltin compounds from the gastrointestinal tract (Kimbrough 1976; WHO 1980). Trimethyltin and triethyltin compounds are potent inhibitors of oxidative phosphorylation in the mitochondria for which these compounds have a high binding affinity (WHO 1980). Different triorganotin compounds cause different neuronal patterns of toxicity in adult animals (Reiter and Ruppert 1984). Trimethyltins, for example, produce largely irreversible behavioral impairments, such as hyperactivity and impaired learning and performance, and these are consistent with reported neuronal cell death in limbic system structures. Triethyltins, with their direct effect on muscle — consistent with reports of myelin vacuolation and cerebral edema — produce largely reversible effects (Reiter and Ruppert 1984). Differences in chronic toxicity between triethyltins and trimethyltins have resulted in different strategies in assessment of hazard. Evaluations of triethyltin have focused on repeated testing throughout dosing, followed by a recovery period. However, evaluations of trimethyltin-induced behavioral impairments have generally focused on testing weeks to months after exposure (Reiter and Ruppert 1984).

Symptoms of trimethyltin intoxication in humans include irritability, headache, depression, aggressiveness, disorientation, appetite loss, memory deficits, and decreased libido; changes were largely reversible following cessation of exposure (Reiter and Ruppert 1984; Reuhl et al. 1985). At high doses, trimethyltins cause death in primates and humans, preceded by seizures, anorexia, and emotional lability (Brown et al. 1984). Trimethyltin produced adverse effects in laboratory animals over an unusually narrow dose range, with differences of tenfold or less between doses producing no observable effects and those producing 100% mortality in all species tested (McMillan and Wenger 1985). Trimethyltin effects in small laboratory animals are usually not reversible. Signs of trimethyltin poisoning include tremors, hyperexcitability, aggressive behavior, weight loss, neuronal destruction in hippocampus and other portions of the brain, seizures, learning and memory impairment, self-mutilation, altered sensitivity to stimuli, and disrupted patterns of drinking and eating (Aldridge et al. 1981; Brown et al. 1984; Hassett et al. 1984; Reiter and Ruppert 1984; Bushnell and Evans 1985; McMillan and Wenger 1985; Reuhl et al. 1985).

Trimethyltin-induced behavioral disruptions usually peak 3 to 5 days after exposure, but effects persist for extended periods and seem to be irreversible (Reiter and Ruppert 1984; McMillan and Wenger 1985). Rats sometimes survive the trimethyltin behavior syndrome and appear outwardly normal, although later neuropathological examination shows extensive bilateral damage, including hippocampus shrinkage and cell loss (Aldridge et al. 1981).

Triethyltins were the most potent organotins tested on mammals, although other organotins produced similar signs of poisoning (Table 8.11). Mammals poisoned by triethyltin compounds showed muscle weakness within hours of dosing; after a short period of recovery, tremors developed, leading to convulsions and death 2 to 5 days after dosing. Although toxicity produced by triethyltins becomes more pronounced with continued exposure, reversal of behavioral deficits occurs within weeks after dosing is terminated (Reiter and Ruppert 1984). Initial reaction to triethyltin exposure in rats was fluid accumulation in white matter of the central nervous system, which persisted for as long as the compound was administered; after administration the effects reversed (Piver 1973). There is general agreement that triethyltin-induced behavioral changes are accompanied by cerebral edema, neurodegenerative disorders, interference with oxidative phosphorylation, and disrupted metabolism of glucose and enzyme activity (Kimbrough 1976; Hassett et al. 1984; Reiter and Ruppert 1984; McMillan and Wenger 1985; Reuhl et al. 1985; Linee and Hennon 1986).

Triphenyltins are skin and eye irritants to rats and rabbits (WHO 1980). They do not accumulate in rats, dogs, and guinea pigs, although some triphenyltin acetate was partly absorbed by cattle and sheep — with most excreted in 6 to 8 weeks (Duncan 1980). Thymus atrophy was associated with a lymphocyte depletion in the thymic cortex and is the predominant effect of the intermediate trialkyltins. Intermediate trialkyltin homologues caused a dose-related reduction of thymus weight in male rats after 2 weeks on diets containing 150 mg organotin/kg; decreases were 19% for triphenyltin, 47% for tripropyltin, and 61% for tributyltin (Snoeij et al. 1985).

Phenyltin compounds significantly inhibit natural killer cell function and possible natural killer cell-mediated immunotoxic potential of these compounds in humans (Whalen et al. 1999). The toxic potential followed the order of triphenyltin > diphenyltin > monophenyltin; however, phenyltins were less toxic than butyltins to human natural killer cells (Whalen et al. 1999).

Tributyltins and other organotins induce chromosomal aberrations in mammals, although this was not observed in tests with aquatic invertebrates (Dixon and Prosser 1986). Studies with isolated rat hepatoma cells, TBT, and PCB 126, show that TBT inhibits cytochrome P-4501A activity, and PCB 126 induces EROD activity. However, PCB-induced EROD activity was potentiated by coexposure to low noncytotoxic concentrations of TBT (Kannan et al. 1998b). Authors concluded that TBT does not interfere with Ah receptor binding and that potentiation of EROD activity and cytotoxicity as a result of coexposure to PCB 126 and TBT is significant because they coaccumulated in a variety of marine organisms.

Tetraorganotin compounds produce muscular weakness, paralysis, respiratory failure, tremors, and hyperexcitability as acute effects in mice and dogs; latent effects are similar to those seen in triorganotin poisoning (WHO 1980). Tetramethyltin, for example, produces the same toxic syndrome as trimethyltin in rats because it is rapidly dealkylated *in vitro* to the latter compound (Aldridge et al. 1981). Signs of triorganotin poisoning in rabbits were evident shortly after administration of tetraorganotin compounds, suggesting that triorganotins were soon distributed to the site of action in amounts sufficient to produce signs of poisoning (Arakawa et al. 1981). The dealkylation and distribution of tetraorganotins are related to alkyl chain length and to their accumulations in tissues, including brain. In 3-hour studies with rabbits, at intravenous dosage rates of 2 to 3 mg/kg BW, tetraethyltin was quickly distributed to liver, but tetrapropyltin and tetrabutyltin were slowly distributed (Arakawa et al. 1981). Tetraethyltin was more readily converted into the corresponding trialkyltin than was tetrapropyltin. About 20% of the tetraethyltin, 4% of the tetrapropyltin, and 1% of the tetrabutyltin were converted to their corresponding trialkyltins. Thus, the extent of formation of triorganotins decreased as the size and stability of the ligand increased. There was poor distribution of tetraorganotins to brain, but the amounts of triorganotin metabolites found in brain increased over time. Particularly, the transfer of triethyltin to the brain was significant and compatible with the appearance of signs of toxicity. It was concluded that the extent of the dealkylation and the toxicity of organotin compounds depends on the length of their alkyl group, which was associated with their rate of absorption and ultimate distribution (Arakawa et al. 1981).

Organotin compounds are not mutagenic, teratogenic, or carcinogenic, as judged by largely negative but incomplete evidence (Duncan 1980; WHO 1980; Cardarelli et al. 1984b). It has been suggested that some organotins retard the onset and growth of cancer in laboratory animals and that the anticarcinogenic action is mediated through the thymus gland (Cardarelli et al. 1984b). The absence of tin in tissues may also be associated with tumor development (Cardarelli et al. 1984)). In one study, mice with cancer-prone mammary glands and transplanted mammary tumors had significantly reduced tumor growth rates after oral dosing with tributyltin fluoride (Cardarelli et al. 1984b). In another study, tumor growth rates were significantly reduced in mice continuously exposed to various diorganotin compounds in drinking water at 1 and 10 mg/L (Cardarelli et al. 1984a). It is hypothesized that the unknown thymic organotins are antagonistic to cancers in mice and possibly man (Cardarelli et al. 1984a, b). Additional research on potential anticarcinogenic properties of organotins is clearly indicated.

Table 8.11 Effects of Tin Compounds on Selected Species of Mammals

Tin Compound, Organism	Dose	Effect	Ref. ^a
INORGANIC TINS			
Rat, <i>Rattus</i> sp.	6.7 mg/kg body weight (BW)	Single intraperitoneal (ip) injection caused deficits in auditory startle habituation tests	1
Dog, <i>Canis familiaris</i>	54 mg/kg BW	LD100, single oral dose	2
Rat	20–30 mg/kg BW, or 1.0 g/kg diet	No observed effect level after 13 weeks	3
Rat	188 mg/kg BW	LD50, single oral dose of tin fluoride	4
Rat	700 mg/kg BW	LD50, single oral dose of tin chloride	4
Rat	2275 mg/kg BW	LD50, single oral dose of Sn ⁺²	3
Rat	10 g/kg diet	Normal growth after 4 weeks	3
Rat	>10 g/kg BW	LD50, single oral dose of SnO	4
Mouse, <i>Mus</i> sp.	Radiotin-113	50% clearance after 29 days following ip injection	5
METHYLTINS			
Rat	120 mg/L drinking water	Impaired learning of pups when dam consumed Sn-laced water throughout 21-day gestation	6
Rat	575 to 1370 mg/kg BW	LD50, single oral dose	7, 8
Rat	600 mg/L	LC50, aerosol dose for 1 h	7
ETHYLTINS			
Rat	200 mg/kg BW	LD50, single oral dose	7
BUTYLTINS			
Mouse	1400–>6000 mg/kg BW	LD50, single oral dose	3
Rat	2220–2300 mg/kg BW	LD50, single oral dose	7
OCTYLTINS			
Rat	2400–3800 mg/kg BW	LD50, single oral dose	7
Mouse	4600 mg/kg BW	LD50, single oral dose	3
DIMETHYLTINS			
Rat	74–237 mg/kg BW	LD50, single oral dose	7
Rat	1070 mg/L	LC50, aerosol dose for 1 h	7
DIETHYLTINS			
Rat	40–100 mg/kg BW	LD50, single oral dose	9
DIBUTYLTINS			
Rat	0.1 and 1.0 mg/kg BW	Kidney damage after 12-month dietary exposure	3
Mouse	1–10 mg/L drinking water	Reduction in tumor growth rates	10
Rat	2 mg/kg BW daily or 40 mg/kg diet	No observable effect level after 90 days	9
Rat, mouse	10 mg/kg BW	Dermal application daily for 10 days causes severe effect on skin and bile duct	3
Mouse	35–112 mg/kg BW	LD50, single oral exposure	9
Rat	80 mg/kg diet	Slight reduction in growth rate and food intake; mild anemia after 90 days	9
Rat	100–520 mg/kg BW	LD50, single oral dose	8

Table 8.11 (continued) Effects of Tin Compounds on Selected Species of Mammals

Tin Compound, Organism	Dose	Effect	Ref. ^a
DIOCTYLTINS			
Rat	50 or 150 mg/kg ration	After 6 weeks altered immune function as evidenced by inhibition of T-lymphocyte activity	11
Guinea pig, <i>Cavia</i> sp.; mouse	50 or 150 mg/kg diet	No evidence of altered immune function	11
Rat	945–7000 mg/kg BW	LD50, single oral exposure	7, 8, 9
Mouse	1140–4000 mg/kg BW	LD50, single oral exposure	9
TRIMETHYLTINS			
Rat	0.15–1.0 mg/L in drinking water	Dams consuming contaminated water throughout 21-day gestation produced pups with decreased learning ability at age 11 days	6
Rat	0.625 mg/kg BW	3 ip doses resulted in flavor aversion	12
Cynomolgus monkey, <i>Macaca fascicularis</i>	0.75 mg/kg BW	Single intravenous (iv) injection produced reduced appetite 7 days postexposure	13
Cynomolgus monkey	1.1 mg/kg BW	Single iv injection resulted in tremors, hyperactivity, ataxia, stupor, unconsciousness	13
Cynomolgus monkey	1.25 mg/kg BW	Single iv injection is fatal within 4 days	13
Cynomolgus monkey	1.5 mg/kg BW	Single iv injection is fatal within 2 days	13
Cynomolgus monkey	3.0 mg/kg BW	Single iv injection is fatal within 24 h	13
Hamster, <i>Cricetus</i> sp.	About 3.0 mg/kg BW	LD100, single oral dose	14, 15
Rat	3.0 mg/kg BW	Loss in body weight and disrupted diurnal pattern of drinking and in rearing young after single oral dose, 2-week observation period	16
Mouse	3.0 mg/kg BW	Single ip dose produced hypoactivity and impaired motor activity	12
Marmoset, <i>Callithrix jacchus</i>	About 3.0 mg/kg BW	LD50, single oral dose	14, 15
Gerbil, <i>Gerbillus</i> sp.	About 3.0 mg/kg BW	LD50, single oral dose	14, 15
Human, <i>Homo sapiens</i>	About 3.0 mg/kg BW	LD50, single oral dose	14, 15
Rat	<4 mg/kg BW	No effect following stomach gavage route of administration	1
Rat	5 mg/kg BW	Single oral dose produces hyperactivity	12
Rat	6 mg/kg BW	No significant effect on behavior	17
Rat	7 mg/kg BW	Significantly altered behavior	17
Rat	>8 mg/kg BW	Lethal within 4 days after stomach gavage	1
Rat	9.1–30 mg/kg BW	LD50, single oral dose	9, 18
Rat	15 mg/kg diet	Neuronal degradation in 2 weeks	19
Rat	16 mg/kg BW	LD50, single ip dose	2
Rat	30 mg/kg BW	LD100, single oral dose	7
TRIETHYLTINS			
Rat	0.25 mg/kg BW	Impaired response to pain after 14 subcutaneous (sc) injections	12
Rat	0.38 mg/kg BW	Flavor aversion after 2 ip doses	12
Rat	1.0 mg/kg BW	Reduced amplitude startle response after 3 oral doses	12
Rat	1.5 mg/kg BW	Hypoactivity, single sc injection	12
Mouse	2.0 mg/kg BW	Hypoactivity, 27 days after single ip injection	12
Rat	4.0–9.0 mg/kg BW	LD50, single oral dose	8

Table 8.11 (continued) Effects of Tin Compounds on Selected Species of Mammals

Tin Compound, Organism	Dose	Effect	Ref. ^a
Guinea pig	5–10 mg/kg BW	LD50, single oral dose	9
Rat	5 mg/L in drinking water for 15 days followed by 10 mg/L for 15 days	Brain edema	20
Rat	10 mg/kg BW	LD50, single ip dose	2
Rat	10 mg/kg BW	LD100, single oral dose	7
Rabbit, <i>Lepus</i> sp.	10 mg/kg BW	LD50, single ip dose	2
Rabbit	10 mg/kg BW	LD50, single oral dose	8
Rabbit, rat, guinea pig	10 mg/kg BW	LD100, single oral dose	21
Rat	15 mg/kg diet	Cerebral edema in 2 weeks	19
Rat	20 mg/kg diet	After 7 days, decreased food intake; after 3 to 4 weeks, hind limb weakness and some deaths; on return to normal diet, signs of poisoning gone in 7 days with normal weight in 4 weeks	21
Rabbit	40 mg/kg diet	Muscular weakness after chronic exposure	21
TRIPROPYLTINS			
Rat	44–120 mg/kg BW	LD50, single oral dose	4, 8
TRIBUTYLTINS			
Rabbit	0.04 mg/kg BW	After 16 weeks, central nervous system dysfunction	20
Rat	Isolated H411E hepatoma cells exposed to various concentrations of TBT	TBT was cytotoxic at >98 nM and inhibited EROD activity in a dose-dependent manner	26
Guinea pig	0.2 mg/L air	Ocular and nasal irritation, asphyxic convulsions, death within 1 h	20
Mouse	0.2 mg/kg BW	Reduces mammary tumor growth rate; adversely affects thymus gland growth	22
Rat	0.36–0.95 mg/kg BW	Single dermal application causes skin irritation	3
Rat	Pregnant females given oral doses of 8, 16, or 32 mg tributyltin chloride on days 0–3 of pregnancy or 8, 16, 32, or 65 mg/kg BW on days 4–7 of pregnancy	On day 20 of pregnancy, 16 mg/kg BW and higher produced increase in rate of implantation failure for both gestation periods. No increase in fetal malformations in any group	25
Rat	10 mg/kg BW	LD50, single ip dose	2
Rabbit	12 mg/kg BW	Daily doses for 6 months were not fatal; signs of intoxication disappeared within a few weeks after withdrawal	20
Guinea pig	20 mg/kg BW	LD50, single oral dose	9
Rat	32 mg/kg diet	Impaired growth after 30 days	20
Mouse	46–230 mg/kg BW	LD50, single oral dose. LD50 values were lowest for tributyltin acetate (46 mg/kg BW) followed by benzoate (108), chloride (117), laurate (180), and oleate (230)	9
Rat	50–380 mg/kg BW	LD50, single oral dose	7, 8, 9
Rabbit	60 mg/kg BW	LD50, single oral dose	9
Rat	150 mg/kg diet	61% reduction in thymus weight after 2 weeks	19
Rat	320 mg/kg diet	Some deaths in 30 days	20
TRIPHENYLTINS			
Rat	0.6 mg/kg BW daily	After 6 weeks, diminished exploratory behavior in maze and significantly more errors in maze learning	23

Table 8.11 (continued) Effects of Tin Compounds on Selected Species of Mammals

Tin Compound, Organism	Dose	Effect	Ref. ^a
Guinea pig	3.7 mg/kg BW	LD50, single ip dose	2
Guinea pig	10–24 mg/kg BW	LD50, single oral dose	2, 9
Guinea pig	25–50 mg/kg diet	At 25 mg/kg, 83% dead in 77 days; at 50 mg/kg, all dead by day 29	7
Rat	25–300 mg/kg diet	No measurable effect at 25 mg/kg in 170 days; some lesions at 50 mg/kg in 105 days; impaired growth at 200 mg/kg in 70 days; weight loss and some deaths at 300 mg/kg in 117 days	7
European hare, <i>Lepus europaeus</i>	Fed diets with 25, 50, or 100 mg triphenyltin acetate/kg ration for 15 days, then 5 days on clean feed, 15 days on test diet, 5 days on clean feed then 22 days on diets	Normal food consumption, blood chemistry, and growth in all groups. Tissue concentrations were elevated only in the 100 mg/kg group: 3.0 mg/kg DW in liver, 2.8 in kidney, and 2.4 in caecum (vs. <1–<2 in all other groups)	24
Rat	34 mg/kg BW	LD50, single ip dose	23
Mouse	81–245 mg/kg BW	LD50, single oral dose	3
Rat	118–268 mg/kg BW	LD50, single oral dose	7, 8
TRIHEXYLTINS			
Rat	1000 mg/kg BW	LD50, single oral dose	8
TRICYCLOHEXYLTINS			
Dogs, rats	6–12 mg/kg diet	Some weight loss in 2 years, but no other toxic effects	20
Rat	13 mg/kg BW	LD50, single ip dose	2
Sheep, <i>Ovis</i> sp.	15–150 mg/kg BW	No observed effect at injected dose of 15 mg/kg BW; adverse effects at 25 to 50 mg/kg; death at 150 mg/kg	8
Rat	25 mg/kg BW	Gastroenteritis after 19 days	3
Rat	235–650 mg/kg BW	LD50, single oral dose	20
Rabbit	500–1000 mg/kg BW	LD50, single oral dose	7
White-footed mice, <i>Peromyscus leucopus</i>	710 mg/kg BW	LD50, single oral dose	3
Guinea pig	780 mg/kg BW	LD50, single oral dose	7
Dogs, monkeys, cats (<i>Felis domesticus</i>)	>800 mg/kg BW	LD50, single oral dose	8
Mouse	1070 mg/kg BW	LD50, single oral dose	3
TRIOCTYLTINS			
Rat	29,200 mg/kg BW	LD50, single oral dose	7
TETRAMETHYLTINS			
Rat	195–331 mg/kg BW	LD50, single oral dose	7
TETRAETHYLTINS			
Rabbit	7 mg/kg BW	LD50, single oral dose	8
Rat	9–16 mg/kg BW	LD50, single oral dose	8
Mouse	40 mg/kg BW	LD50, single oral dose	3
Guinea pig	40 mg/kg BW	LD50, single oral dose	3
TETRABUTYLTINS			
Rat	6000 mg/kg BW	LD50, single oral dose	7

Table 8.11 (continued) Effects of Tin Compounds on Selected Species of Mammals

^a 1, Hassett et al. 1984; 2, Kimbrough 1976; 3, WHO 1980; 4, Blunden et al. 1985; 5, Brown et al. 1977; 6, Noland et al. 1982; 7, Smith et al. 1978a; 8, Zuckerman et al. 1978; 9, Piver 1973; 10, Cardarelli et al. 1984a; 11, Seinen et al. 1977a; 12, Reiter and Ruppert 1984; 13, Reuhl et al. 1985; 14, Aldridge et al. 1981; 15, Brown et al. 1984; 16, Bushnell and Evans 1985; 17, McMillan and Wenger 1985; 18, Watanabe 1980; 19, Snoeij et al. 1985; 20, Duncan 1980; 21, Stoner et al. 1955; 22, Cardarelli et al. 1984b; 23, Lehotzky et al. 1982; 24, Anfossi et al. 1990b; 25, Harazono et al. 1998; 26, Kannan et al. 1998b.

8.5.5 Terrestrial Invertebrates

Resistance to organotin acaricides has been reported in several populations of spider mites. After cyhexatin and fenbutatin oxide were used for 10 to 17 years on pears and apples to control mites, populations of McDaniel spider mite (*Tetranychus mcdanieli*), two-spotted spider mite (*T. urticae*), and European red mite (*Panonychus ulmi*) slowly began to develop strains that were resistant to these chemicals (Croft et al. 1987).

8.6 RECOMMENDATIONS

Proposed organotin criteria for the protection of aquatic life, domestic animals, and human health, vary substantially (Table 8.12). The most stringent criteria now proposed are for triorganotins and aquatic life; these vary from 0.002 to 0.008 µg/L (Table 8.12). But even these comparatively low concentrations will not protect certain species of gastropod molluscs or larvae of the sheep sturgeon (*Accipenser nudipectoralis*) from tributyltin impacts, as discussed earlier. No criteria are currently proposed for protection of mammals against trimethyltins and triethyltins, the most toxic organotins tested in this group. Trimethyltins, for example, produce nonreversible neurotoxicological effects to certain species of small laboratory animals at concentrations as low as 0.15 mg/L drinking water or 0.625 mg/kg BW and are fatal at 1.25 mg/kg BW.

Hazard evaluation posed by organotin compounds to natural resources is predicated partly on their chemical composition, partly on their concentration and persistence in abiotic materials and diet items, and partly on their availability to organisms. In each of these areas, key data are missing for promulgation of effective regulations. It seems that additional research is needed in eight areas to acquire these data:

1. The development of sensitive and rapid analytical schemes for the extraction and separation of inorganic tin and organic tin compounds and their chemical speciation products from water, sediments, and biological materials (WHO 1980; Reuhl and Cranmer 1984; Hall and Pinkney 1985; Laughlin and Linden 1985; Thompson et al. 1985; Blunden and Chapman 1986; USPHS 1992).
2. Elucidation of mechanisms and modes of toxicity for organotin compounds, especially those involving sublethal chronic exposures and cellular and subcellular impacts (WHO 1980; Reuhl and Cranmer 1984; Hall and Pinkney 1985; Thompson et al. 1985; Vrijhof 1985).
3. Acquisition of data on organotin toxicokinetics, including data on routes of exposure, uptake, retention, and translocation. Studies should emphasize whole organisms to determine if food chain biomagnification is a potential problem; reproductive organs, in which organotin burdens may affect proliferation; and edible tissue, especially muscle and liver, which are selectively consumed by humans and various animal species (WHO 1980; Reuhl and Cranmer 1984; Wilkinson 1984; Hall and Pinkney 1985; Thompson et al. 1985).
4. Determination of the persistence and mobility of organotin compounds — especially in aquatic abiotic materials, such as sediments, sediment interstitial waters, suspended particulates, and the water column — and on the partitioning of these compounds between the surface microlayer and subsurface waters (Wilkinson 1984; Thompson et al. 1985).
5. Determination of the extent of tin methylation and the biotransformation and pharmacodynamics of organotins (WHO 1980).

Table 8.12 Proposed Organotin Criteria for Protection of Natural Resources and Human Health

Resource, Organotin Compound	Criterion or Effective Tin Concentration	Reference ^a
AQUATIC LIFE		
Freshwater		
Triorganotins		
North Carolina	<0.008 µg/L	1
Triethyltins		
Max. permissible concentration	<100 µg/L	2
Tributyltins		
Acute value	<0.97 µg/L	3
Chronic value	<0.30 µg/L	3
Safe level	0.12 to <0.27 µg/L	2
Safe level	<0.026 µg/L	18
Saltwater		
Triorganotins		
North Carolina	<0.002 µg/L	1, 4
Safe level, USA	<0.05 µg/L	5
Tributyltins		
4-day average	<0.017 µg/L (not to be exceeded more than once in 3 years)	6
Chronic value	<0.064 µg/L	3
Acute value	<0.22 µg/L	3
1-h average	<0.43 µg/L (not to be exceeded more than once in 3 years)	6
Safe level		
U.K.	<0.02 µg/L	4
USA	<0.01-<0.02 µg/L	16, 18
USA	<0.002 µg/L	15
Water		
Dibutyltin dichloride, Former Soviet Union	<2000 µg/L	7
Dibutyltin disulfide, Former Soviet Union	<20,000 µg/L	7
Tributyltins		
USA, Canada	<0.2 µg/L	8
In schistosomiasis control	<0.1 µg/L	9
Tetraethyltin, FSU	<200 µg/L	7
Marine Antifouling Paints		
Organotins	<4 grams/L	4
Tributyltin	<4.0 µg/cm ² daily	15, 17
Sediments		
Freshwater		
Tributyltins		
4-day average	<30 µg/kg	3
1-h average	<48 µg/kg	3
Saltwater		
Tributyltins		
4-day average	<7 µg/kg	3
1-h average	<1 µg/kg	3
No effect level on annelids, mysids, clams	<610 µg/kg	3

Table 8.12 (continued) Proposed Organotin Criteria for Protection of Natural Resources and Human Health

Resource, Organotin Compound	Criterion or Effective Tin Concentration	Reference ^a
DOMESTIC AND LABORATORY ANIMALS		
Diet		
Dibutyltins		
Rat, age 3 months	<40 mg/kg diet	10
Rat, age 6 months	<20 mg/kg diet	10
Triphenyltins		
Guinea pig, daily intake	<0.1 mg/kg body weight (BW)	10
Rat, daily	<3 mg/kg BW	10
Drinking water		
Rat	<0.007 µg/L	11
HUMAN HEALTH		
Air		
Total tin		
Connecticut	<40 µg/m ³ , 8-h daily	17
Virginia	<1.6 µg/m ³ , 24-h daily	17
Inorganic tin compounds	<2000 µg/m ³	17
Organotins	<100 µg/m ³	7, 12, 17
Organotins, daily	<200 µg/kg BW	7
Triethyltins, occupational exposure	<100 µg/m ³	13
Tricyclohexyltins	<1200 µg/m ³	7
Diet		
Total tin		
Daily intake	0.2-<8.8 mg	7
Daily intake		
Total	4.003 mg	17
Diet	4.000 mg	17
Air	0.003 mg	17
Daily intake		
From fresh foods	1 to 4 mg	10
From water	<0.03 mg	10
Daily intake, adult	0.003 to <0.13 mg/kg BW	7
Daily intake, adult	0.2 to <17 mg/kg BW	10
Composition of diet		
Inorganic tin	About 1 mg/kg	10
Organic tin	<2 mg/kg	10
Tricyclohexyltins		
Peaches	<4 mg/kg	8
Apples, pears	<2 mg/kg	7
Meat	<0.2 mg/kg	7
Milk	<0.05 mg/L	7
Total daily intake	<0.0075 mg/kg BW	7, 14

^a 1, Anonymous 1985; 2, Duncan 1980; 3, Cardwell and Sheldon 1986; 4, Side 1987; 5, USN 1984; 6, Hall et al. 1987; 7, Zuckerman et al. 1978; 8, Thompson et al. 1985; 9, Chliamovitch and Kuhn 1977; 10, WHO 1980; 11, Simmonds 1986; 12, Blunden and Chapman 1986; 13, Watanabe 1980; 14, CEC 1978; 15, Huggett et al. 1992; 16, Pinkney et al. 1990; 17, USPHS 1992; 18, Harrington 1991.

6. Measurement of biological interaction effects of organotins with other toxic chemicals under stressful environmental conditions of temperature, oxygen, and other variables (Thompson et al. 1985).
7. Development of quantitative structure activity relations for use in evaluating toxicity of organotin compounds (Hall and Pinkney 1985; Laughlin and Linden 1985; Laughlin et al. 1985; Laughlin 1987).
8. Initiation of long-term environmental monitoring studies in terrestrial and aquatic ecosystems to establish appropriate baseline concentrations and to separate these from contaminant effects (Kumplainen and Koivistoninen 1977; WHO 1980; Hall and Pinkney 1985; Thompson et al. 1985).

Antifouling paints containing organotin compounds have been associated with a number of adverse effects to marine biota, including reductions in natural bacterial assemblages (Prior and Riemann 1998), contamination of salmon farmed in sea cages with treated net panels (Side 1987), and reduced growth of oysters (Cleary and Stebbing 1985). The United States Navy, however, has implemented fleetwide use of organotin antifouling paints that contain tributyltin as a biocide. This procedure will result in a 15% fuel consumption reduction, and will increase the interval between cleaning ship hulls from 2 years (with cuprous oxide-based antifouling paints) to about 7 years, and will also increase ship speed up to 40% as a direct result of reduced drag (U.S. Navy [USN] 1984). Since naval vessels rarely remain moored for extended periods in coastal areas, hazard effects to the environment are minimal — despite the size of the vessel — when compared to boating practices at local marinas (USN 1984).

Accordingly, civilian use of marine paints containing organotin compounds has been severely restricted in recent years. France banned tributyltin compounds in antifouling paints in January 1982 for use on vessels under 25 m (82 feet) in length (Waldock and Thain 1983; Side 1987; Huggett et al. 1992). The State of Virginia enacted legislation that prohibits the use of tributyltin paints on nonaluminum vessels under 25 m (Anonymous 1987). Also in Virginia, tributyltin paints applied on large ships and aluminum craft should not exceed a daily leach rate of 4.0 µg/cm² (Huggett et al. 1992). Similar legislation is proposed in at least 12 coastal and Great Lakes states (Anonymous 1988). In April 1987, England banned the retail sale of antifouling paints containing organotin compounds at concentrations greater than 4 grams of total tin per liter (Side 1987). Because of their hazards, use of the more toxic triorganotin biocides should be curtailed to prevent their entry into the environment (Piver 1973). Continued monitoring of tributyltin levels is recommended, especially in areas of extensive boating activity (Simmonds 1986).

8.7 SUMMARY

Tin (Sn) has influenced our lives for the past 5000 years. Today we are exposed to tin on a daily basis: tin-plated baby food cans; alloys such as pewter, bronze, brass, and solder; and toothpaste containing stannous fluoride. These inorganic tin compounds are not highly toxic due to their low solubility, poor absorption, low accumulation, and rapid excretion. Synthetic organotin compounds, however, first manufactured commercially in the 1960s, may present a variety of problems to animals, including impaired behavior and reduced growth, survival, and reproduction. Some triorganotins (for example, in antifouling marine paints, in molluscicides, and in agricultural pesticides) can be harmful to sensitive species of nontarget biota at recommended application protocols.

Background concentrations of organotin compounds are frequently elevated — occasionally to dangerous levels — in aquatic organisms collected near marinas and other locales where organotin-based antifouling paints are used extensively. But more information is needed on background concentrations of organotins, especially those from terrestrial ecosystems.

Tributyltin compounds are especially toxic to aquatic organisms. Adverse effects were noted at concentrations of 0.001 to 0.06 µg/L on molluscs and at 0.1 to 1.0 µg/L on algae, fish, and crustaceans. In general, bioconcentration of organotins from seawater was high, especially by algae, but degradation was sufficiently rapid to preclude food chain biomagnification. In contrast, current

environmental concentrations of some organotins are not likely to be directly toxic to birds and mammals. Birds seem to be relatively resistant to organotins, although data are scarce. Preliminary studies of 75 days' duration suggest that diets containing 50 mg tin as trimethyltin chloride/kg were fatal to ducklings; 5 mg/kg killed 40%, and 0.5 mg/kg was not lethal. Trimethyltin compounds were lethal to other species of birds tested at doses of 1 to 3 mg/kg body weight. Other tests with ducklings and 11 other mono-, di-, tri-, and tetraalkyltin compounds at dietary levels equivalent to about 50 mg Sn/kg showed no adverse effects on survival. Small laboratory mammals were adversely affected by trimethyltin compounds at doses as low as 0.15 mg/L in drinking water (learning deficits), 0.63 mg/kg body weight (diet aversion), and 1.25 mg/kg body weight (death); neurotoxicological effects of trimethyltins were usually not reversible. Triethyltins were also toxic to small mammals, but effects (which were similar to those of trimethyltins) were usually reversible after cessation of exposure. All evidence to date indicates that organotin compounds are not carcinogenic.

Methodologies and data necessary for the promulgation of effective criteria and standards to protect natural resources seem to be deficient in eight key areas: (1) routine analytical chemical methodologies for extraction, separation, and identification of inorganic and organic tin compounds and their chemical speciation products in biological and other samples; (2) mechanisms of toxicity for organotin compounds; (3) rates of uptake, retention, and translocation of organotins in biota; (4) persistence and mobility rates of organotins in nonbiological materials; (5) rates of tin methylation and biotransformation in biological and abiotic samples; (6) organotin interactions with other toxic chemicals; (7) quantitative structure-activity relation for use in evaluating organotin toxicity; and (8) long-term environmental monitoring studies in terrestrial and aquatic ecosystems for establishment of baseline concentrations.

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CHAPTER 9

Zinc

9.1 INTRODUCTION

Zinc is an essential trace element for all living organisms. As a constituent of more than 200 metalloenzymes and other metabolic compounds, zinc assures stability of biological molecules, such as DNA, and of biological structures, such as membranes and ribosomes (Vallee 1959; National Academy of Sciences [NAS] 1979; Casey and Hambidge 1980; Llobet et al. 1988b; Mason et al. 1988; Leonard and Gerber 1989). Plants do not grow well in zinc-depleted soils, and deficiency has resulted in large losses of citrus in California and pecans in Texas (Vallee 1959). Clinical manifestations of zinc deficiency in animals include growth retardation, testicular atrophy, skin changes, and poor appetite (Prasad 1979). The ubiquity of zinc in the environment would seem to make human deficiencies unlikely; however, reports of zinc-associated dwarfism and hypogonadism in adolescent males are now confirmed (Casey and Hambidge 1980) and reflect the fact that much of their dietary zinc is not bioavailable. Zinc deficiency was a major factor in the syndrome of nutritional dwarfism in adolescent males from rural areas of Iran and Egypt in 1961; about 3% of the population in these areas were affected, and a similar syndrome was found in Turkey, Tunisia, Morocco, Portugal, and Panama (Casey and Hambidge 1980). The use of unleavened bread as a major staple food contributed to severe zinc deficiency in the Middle East. Even though unleavened bread may contain adequate amounts of zinc for nutrition and intakes may exceed recommended allowances by a wide margin, zinc is largely unavailable for absorption due to the high levels of fiber and phytic acid esters in unleavened bread (Casey and Hambidge 1980). Marginal deficiency of zinc in man is probably widespread and common throughout the world, including the United States (Prasad 1979). Dietary zinc replacement usually will reverse the pathologic events of zinc depletion in humans and animals (NAS 1979). But zinc repletion seems to be of little value in rat offspring with congenital malfunctions or behavioral abnormalities associated with zinc depletion (NAS 1979).

Zinc poisoning has been documented in dogs, cats, ferrets, birds, cattle, sheep, and horses, usually as a result of ingesting galvanized metal objects, certain paints and fertilizers, zinc-containing coins, and skin and sunblock preparations containing zinc oxide (Wentink et al. 1985; Lu and Combs 1988a; Ogden et al. 1988; Binnerts 1989; Robinette 1990). Signs of acute poisoning include anorexia, depression, enteritis, diarrhea, decreased milk yield, excessive eating and drinking and, in severe cases, convulsions and death (Ogden et al. 1988). Emissions from zinc smelters at Palmerton, Pennsylvania, have destroyed wildlife habitat, reduced prey abundance, poisoned deer, songbirds, and shrews, and eliminated terrestrial amphibians from the mountainside at Lehigh Gap (Beyer et al. 1985; Sileo and Beyer 1985; Beyer 1988). Aquatic populations are frequently decimated in zinc-polluted waters (Solbe and Flook 1975; Everall et al. 1989a). Zinc in the aquatic

environment is of particular importance because the gills of fish are physically damaged by high concentrations of zinc (NAS 1979).

Zinc toxicosis in humans is not a common medical problem, although it may appear in some metal workers and others under special conditions (NAS 1979). Industrial processes, such as welding, smelting, or fabrication of molten metals can produce ultrafine metal oxides at harmful concentrations. Inhalation of these metal oxides, including oxides of zinc, causes the industrial malady known as *metal fume fever* (Lam et al. 1985; Llobet et al. 1988b; Lu and Combs 1988a). Symptoms occur several hours after exposure and include fever, chills, perspiration, tachycardia, dyspnea, and chest pains. Recovery is normally complete within 24 h, but susceptible workers can have persistent pulmonary impairment for several days after exposure (Lam et al. 1985). Most reports of human zinc intoxication have been in response to food poisoning incidents arising from lengthy storage of acidic foods or beverages in galvanized containers (Llobet et al. 1988b; Fosmire 1990).

Historically, zinc has been used for industrial, ornamental, or utilitarian purposes for nearly 2000 years, and may have been used as an ointment to treat skin lesions by the ancient Egyptians and other Mediterranean peoples (NAS 1979). In biblical times, the Romans were known to have produced brass by mixing copper with a zinc ore (Elinder 1986). In its isolated form, zinc was not recognized until the 15th century when smelting occurred accidentally (NAS 1979). The Chinese probably were the first to extract zinc metal, although its first description in 1597 by an occidental traveler, Liborius, related that the process was observed in India (Vallee 1959). Commercial smelting began in the 18th century, when it was realized that zinc could be obtained from the calamine ore used to make brass; no reports of zinc toxicosis in any form were recorded from these early accounts (NAS 1979). The first documented use of zinc administered orally was in 1826 to treat discharges from various body orifices (NAS 1979). Zinc was recognized as an essential nutrient for plants and animals in 1869. Its occurrence in biological matter, e.g., human liver, was first described in 1877 (Vallee 1959). In 1934, zinc was conclusively demonstrated to be essential to normal growth and development in animals (Prasad 1979).

Zinc composes 0.004% of the earth's crust and is 25th in order of abundance of the elements (Vallee 1959). Uses of zinc include production of noncorrosive alloys, galvanizing steel and iron products, and in the therapeutic treatment of zinc deficiency (Elinder 1986). Zinc is found in coal and many manufactured products such as motor oils, lubricants, tires, and fuel oil (NAS 1979). Ecological and toxicological aspects of zinc in the environment have been reviewed by many authorities, including Vallee (1959), Skidmore (1964), NAS (1979), Prasad (1979, 1980), U.S. Environmental Protection Agency [USEPA] (1980, 1987), Nriagu (1980), Weatherley et al. (1980), Eisler (1981, 1993, 1997), Spear (1981), Apgar (1985), Elinder (1986), Vymazal (1986), Greger (1989), U.S. Public Health Service [USPHS] (1989), and Sorensen (1991).

9.2 SOURCES AND USES

World production of zinc increased from 0.5 million metric tons in 1900 to 6.1 million tons in 1978 (Elinder 1986) to 7.1 million tons in 1987 (USPHS 1989). The principal ores of zinc are sulfides, such as sphalerite and wurtzite (Elinder 1986). The major world producers include Canada, the former Soviet Union, and Japan — which collectively account for about half the production — and, secondly, the United States, Australasia, Mexico, and Peru (Weatherley et al. 1980; Elinder 1986). Zinc is now available as ingots, lumps, sheets, wire, shot, strips, granules, and powder (USPHS 1989). The United States produced 240,000 tons of zinc in 1987 — mostly from Tennessee, Mississippi, and New York, but also 16 other states — and imported an additional 774,000 metric tons, thus consuming 14% of world zinc production while producing 3.4% (USPHS 1989).

Zinc is mainly used in the production of noncorrosive alloys, brass, and in galvanizing steel and iron products. Zinc undergoes oxidation on the surface, thus protecting the underlying metal from degradation. Galvanized products are widely used in construction materials, automobile parts, and

household appliances (Elinder 1986). Zinc oxide is used to form white pigments, in rubber processing, and to coat photocopy paper (USEPA 1987; USPHS 1989). Zinc sulfate is used as a cooperative agent in fungicides and as a protective agent against zinc deficiency in soils. When incorporated with copper compounds or arsenic-lead wettable powders and applied by spraying, it can minimize the toxic effects of these metals on fruits, such as plum, apple, and peach; in Japan alone, about 250 tons of zinc sulfate is sprayed in fields each year (Maita et al. 1981). Zinc is used therapeutically in human medicine in the treatment of zinc deficiency, various skin diseases, wound healing, and to reduce pain in sickle cell anemia patients (Prasad 1979; Spear 1981; USEPA 1987; Warner et al. 1988).

Zinc is discharged into the global environment at a yearly rate estimated at 8.8 million tons; 96% of the total is a result of human activities (Leonard and Gerber 1989). Major sources of anthropogenic zinc discharges to the environment include electroplaters, smelting and ore processors, drainage from active and inactive mining operations, domestic and industrial sewage, combustion of fossil fuels and solid wastes, road surface runoff, corrosion of zinc alloys and galvanized surfaces, and erosion of agricultural soils (Weatherley et al. 1980; Spear 1981; Mirenda 1986; Llobet et al. 1988a; Buhl and Hamilton 1990). During smelting, large amounts of zinc are emitted into the atmosphere. In the United States alone during 1969, about 50,000 metric tons of zinc were discharged into the atmosphere during smelting operations (Elinder 1986). Another 20,000 metric tons are discharged annually into U.S. estuaries (Table 9.1). Zinc is also dispersed from corroded galvanized electrical transmission towers for at least 10 km by runoff, and by wind-driven spray and water droplets from the towers (Jones and Burgess 1984). Discharges from placer mining activities usually contain 75 to 165 µg Zn/L, sometimes up to 882 µg Zn/L in active mines, and these concentrations may represent acute hazards to salmonids in areas downstream of placer mine effluents (Buhl and Hamilton 1990). In Maine, galvanized culverts significantly increased zinc concentrations in stream waters, particularly in newer culverts. Highest zinc concentrations in culverts were found during conditions of elevated temperatures and low flow; levels of zinc sometimes exceeded the avoidance threshold (0.05 mg/L) of Atlantic salmon (*Salmo salar*); invertebrates seemed unaffected, except for a freshwater sponge, *Spongilla* sp. (Gregory and Trial 1975). Zinc sources implicated in livestock poisonings include galvanized iron wire and troughs, and zinc-containing fertilizers and fungicides (Allen et al. 1983; Reece et al. 1986). Zinc toxicosis in man has been reported from consumption of milk stored in galvanized vessels, and from food contaminated with particles of zinc from a zinc pigment plant (Zee et al. 1985). Zinc toxicity will be discussed in greater detail later.

Table 9.1 Estimated Annual Zinc Inputs to United States Coastal Marine Ecosystems (study area comprised 116,000 km²)

Source	Metric Tons Per Year
Rivers	5950
Atmosphere	4300
Barged wastes	3490
Storm channels	3060
Municipal wastewater	2500
Direct industrial discharges	710
Vessel protection	360
Dredging release	10
Thermal discharges	2
Groundwater	1
Total	20,383

Data from Young, D.R., T.K. Jan, and G.P. Hershelman. 1980. Cycling of zinc in the nearshore marine environment. Pages 297-335 in J.O. Nriagu (ed.), *Zinc in the Environment. Part I: Ecological Cycling*. John Wiley, NY.

9.3 CHEMICAL AND BIOCHEMICAL PROPERTIES

9.3.1 General

Most of the zinc introduced into aquatic environments is eventually partitioned into the sediments. Zinc release from sediments is enhanced under conditions of high dissolved oxygen, low salinity, and low pH. Dissolved zinc usually consists of the toxic aquo ion ($Zn(H_2O)_6^{2+}$) and various organic and inorganic complexes. Aquo ions and other toxic species have their greatest biological impacts under conditions of comparatively low pH, low alkalinity, low dissolved oxygen, and elevated temperatures. Zinc has its primary metabolic effect on zinc-dependent enzymes that regulate RNA and DNA. Low-molecular-weight proteins, metallothioneins, play an important role in zinc homeostasis and in protection against zinc poisoning in animals; zinc is a potent inducer of metallothioneins. The pancreas seems to be a primary target organ of zinc intoxication in birds and mammals, followed by bone; in fish, gill epithelium is the primary target site. Biological effects of excess zinc are modified by numerous variables, especially by interactions with other chemicals. Interactions frequently produce radically altered patterns of accumulation, metabolism, and toxicity. Some are beneficial to the organism, while others are harmful.

9.3.2 Chemical Properties

Zinc is a bluish-white metal which dissolves readily in strong acids. In nature it occurs as a sulfide, oxide, or carbonate. In solution, it is divalent and can form hydrated Zn^{2+} cations in acids, and zinctated anions — probably $Zn(OH)_4^{2-}$ — in strong bases (USEPA 1980, 1987). Zinc dust and powder are sold commercially under a variety of trade names: Asarco, Blue powder, CI 77949, CI pigment metal 6, Emanay zinc dust, granular zinc, JASAD Merrillite, L15, and PASCO (USPHS 1989). Selected physical and chemical properties of zinc, zinc chloride, and zinc sulfate are listed in [Table 9.2](#).

Zinc ligands are soluble in neutral and acidic solutions, so that zinc is readily transported in most natural waters (USEPA 1980, 1987), but zinc oxide, the compound most commonly used in industry, has a low solubility in most solvents (Elinder 1986). Zinc mobility in aquatic ecosystems is a function of the composition of suspended and bed sediments, dissolved and particulate iron and manganese concentrations, pH, salinity, concentrations of complexing ligands, and the concentration of zinc (USEPA 1980). In freshwater, zinc is most soluble at low pH and low alkalinity: 10 mg Zn/L of solution at pH 6 that declines to 6.5 at pH 7, 0.65 at pH 8, and 0.01 mg/L at pH 9 (Spear 1981). Dissolved zinc rarely exceeds 40 $\mu\text{g}/\text{L}$ in Canadian rivers and lakes; higher concentrations are usually associated with zinc-enriched ore deposits and anthropogenic activities. Marine

Table 9.2 Some Properties of Zinc, Zinc Chloride, and Zinc Sulfate

Property	Zinc	Zinc chloride	Zinc sulfate
Formula	Zn	$ZnCl_2$	$ZnSO_4$
CAS number	7440-66-6	7646-85-7	7733-02-0
Molecular weight	65.38	136.29	161.44
Melting point, °C	419.5	290	Decomposes at 600
Boiling point, °C	908	732	—
Density	7.14	2.907	3.54
Physical state	Bluish-white lustrous solid	Solid white granules	Colorless solid
Solubility	Insoluble in water, soluble in acetic acid and alkali	61.4 g/L water, 769 g/L alcohol, 500 g/L glycerol	Soluble in water, slightly soluble in alcohol

From U.S. Public Health Service (USPHS). 1989. Toxicological profile for zinc. U.S. Publ. Health Serv., *Agen. Toxic Subst. Dis. Regis.*, Atlanta, GA. 121 pp.

waters usually contain <10 µg Zn/L, most adhering to suspended solids; however, saturated seawater may contain 1.2 to 2.5 mg Zn/L (Spear 1981).

In water, the free zinc ion is thought to coordinate with six water molecules to form the octahedral aquo ion ($Zn(H_2O)_6^{2+}$) in the absence of other complexing or adsorbing agents (Spear 1981). In freshwater, zinc exists almost exclusively as the aquo ion at pH >4 and <7 (Campbell and Stokes 1985). In freshwater at pH 6, the dominant forms of dissolved zinc are the free ion (98%) and zinc sulfate (2%); at pH 9 the dominant forms are the monohydroxide ion (78%), zinc carbonate (16%), and the free ion (6%; USEPA 1987). In typical river waters, 90% of the zinc is present as aquo ion, and the remainder consists of $ZnHCO_3^+$, $ZnCO_3$, and $ZnSO_4$ (Spear 1981).

Zinc bioavailability and toxicity to aquatic organisms are highest under conditions of low pH, low alkalinity, low dissolved oxygen, and elevated temperatures (Weatherley et al. 1980). Soluble chemical species of zinc are the most bioavailable and most toxic (Spear 1981). The aquo ion predominates over other dissolved species and is suspected of being most toxic; however, aquo ion concentrations decrease under conditions of high alkalinity, at pH >7.5, and increasing salinity (Spear 1981). Under conditions of high alkalinity and pH 6.5, the most abundant species are $ZnHCO_3^+$, Zn^{2+} , and $ZnCO_3$; at low alkalinity and an elevated pH of 8.0, the order of abundance was $Zn^{2+} > ZnCO_3 >$ zinc humic acid $> ZnOH^+ > ZnHCO_3^+$ (Spear 1981). Water hardness is the principal modifier of acute zinc toxicity. Increased alkalinity or water hardness results in decreased toxicity to freshwater organisms when all zinc is dissolved; this effect is associated with decreased concentration of aquo ions and is heightened by increased pH. Increased water hardness at pH <8.5 when zinc is in suspension results in increased toxicity associated with increased suspended $ZnCO_3$. Increased water hardness at pH >8.5 when zinc is in suspension produces decreased toxicity and increased suspended $Zn(OH)_2$. Suspended zinc carbonate may also be toxic, although its toxicity decreases under conditions suitable to zinc hydroxide formation; suspended $Zn(OH)_2$ is relatively nontoxic. Thus, $ZnCO_3$ composes <1% of the dissolved zinc at low pH and low alkalinity but is the predominant chemical species at high pH and high alkalinity. Organozinc complexes are not stable and may dissociate under reducing conditions, liberating Zn^{2+} (Spear 1981).

In seawater, zinc exists in a dissolved state, as a solid precipitate, or is adsorbed to particle surfaces. Soluble zinc in seawater exists as uncomplexed free (hydrated) ions, as inorganic complexes (the primary form in the open sea), or as organic complexes (Young et al. 1980). In seawater at pH 8.1, the dominant species of soluble zinc are zinc hydroxide (62%), the free ion (17%), the monochloride ion (6.4%), and zinc carbonate (5.8%). At pH 7, the percentage of dissolved zinc present as the free ion increases to 50% (USEPA 1987). In the presence of dissolved organic materials, most of the dissolved zinc is present as organozinc-complexes (USEPA 1987). In estuaries and other marine environments, the relative abundance of zinc species changes with increasing salinity. At low salinities, $ZnSO_4$ and $ZnCl^+$ predominate; at higher salinities, the aquo ion predominates (Spear 1981). But as salinity decreases, the concentration of free zinc ion increases and the concentration of zinc-chloro complexes decreases, resulting in increased bioavailability of the free metal ion and increased bioconcentration by resident organisms (Nugegoda and Rainbow 1989b).

In solution, zinc is adsorbed by organic agents such as humic materials and biogenic structures (i.e., cell walls of plankton), and by inorganic adsorbing agents, such as mineral particles, clays, and hydrous oxides of manganese, iron, and silicon (Spear 1981). Particulate materials in the medium may contain as little as 2% and as much as 100% of the total zinc (Sprague 1986). Formation of zinc-ligand complexes increases the solubility of zinc and probably increases the tendency for zinc to be adsorbed (USEPA 1980). Sorption to particulates was lower at higher salinities due to displacement of sorbed zinc ions by alkali and alkaline earth cations (USEPA 1987). Increased pH increases zinc sorption to particulates, and seems to be independent of water salinity or hardness (USEPA 1987).

Most of the zinc introduced into aquatic environments is sorbed onto hydrous iron and manganese oxides, clay minerals, and organic materials, and eventually is partitioned into the sediments (USEPA 1987). Zinc is present in sediments as precipitated zinc hydroxide, ferric and manganic

oxyhydroxide precipitates, insoluble organic complexes, insoluble sulfides, and other forms. As the sediments change from a reduced to an oxidized state, soluble zinc is mobilized and released; however, the bioavailability of different forms of sediment zinc varies substantially, and the mechanisms of transfer are poorly understood (USEPA 1987). Sorption to sediments was complete at pH >7, but was negligible at pH <6 (USEPA 1987). Zinc is dissolved from sediments at low salinities due to displacement of adsorbed zinc ions by alkali and alkaline earth cations, which are abundant in brackish waters (USEPA 1980). Sulfide precipitation in sediments is an important control on zinc mobility in reducing environments, and precipitation of the hydroxide, carbonate or sulfate may occur when zinc is present in high concentrations (USEPA 1980).

Extractable concentrations of sediment-bound zinc were positively correlated with zinc concentrations in deposit feeding clams (Luoma and Bryan 1979). Availability of sediment zinc to bivalve molluscs was higher at increased sediment concentrations of amorphous inorganic oxides or humic substances, and lower at increased concentrations of organic carbon and ammonium acetate-soluble manganese. Zinc uptake by euryhaline organisms was enhanced at low water salinity (Luoma and Bryan 1979).

9.3.3 Metabolism

Zinc is ubiquitous in the tissues of plants and animals (Rosser and George 1986) and is essential for normal growth, reproduction, and wound healing (Prasad 1979; Stahl et al. 1989a). More than 200 different enzymes require zinc for maximum catalytic activity, including carbonic anhydrase, alkaline phosphatase, alcohol dehydrogenase, acid phosphatase, lactic dehydrogenase, carboxypeptidase, and superoxide dismutase (Prasad 1979, 1980; Casey and Hambidge 1980; Rosser and George 1986; Blesbois and Mauger 1989; Thompson et al. 1989). Zinc has its primary effect on zinc-dependent enzymes that regulate the biosynthesis and catabolic rate of RNA and DNA (Prasad 1979; Casey and Hambidge 1980; Gipouloux et al. 1986; Sternlieb 1988). Zinc exerts a protective effect on liver by inhibiting lipid peroxidation and stabilizing lysosomal membranes (Sternlieb 1988); aids neurotransmission in brain of fish, birds, reptiles, and mammals (Smeets et al. 1989); prolongs muscular contractions, increases oxygen affinity of myoglobin, and is necessary for the growth and differentiation of muscle fiber types (Rosser and George 1986); increases numbers and birth weights of lambs of zinc-supplemented ewes; is essential for wound healing in most organisms studied (Ireland 1986); and is used therapeutically in treating patients with skin diseases, zinc deficiency, and other symptoms (Mooradian et al. 1988; Sternlieb 1988).

Zinc enters the gastrointestinal tract as a component of low-molecular-weight proteins secreted by the salivary glands, intestinal mucosa, pancreas, and liver (Goyer 1986). Usually, only dissolved zinc is sorbed or bound, but zinc dissolution probably occurs in the alimentary tract of animals after ingestion of particulates containing undissolved zinc (USEPA 1987). After ingestion, zinc is absorbed across several physiologically active membranes: gut mucosa, alveocapillary membranes, and tissue and organ membranes. The exact transport mechanisms are unknown but may be associated with formation of a tetrahedral quadradentate ligand with a small organic molecule (NAS 1979). Some of the zinc taken up by the intestinal epithelial cells is rapidly transferred to the portal plasma where it associates with albumin, α_2 macroglobulin, and amino acids. About 67% of the zinc in plasma is bound to albumin, and about 3% is stored in liver (Sternlieb 1988). Soluble organozinc complexes are passively absorbed across the plasma membrane of the mucosa of the intestinal villi; the soluble, nondiffusible complexes are transported in the intestinal products and excreted in feces (NAS 1979). Zinc loss from urine and sweat is usually small (Casey and Hambidge 1980). In a normal human adult, about 2 g of zinc is filtered by the kidneys daily and about 0.3 to 0.6 mg is actually excreted each day (Goyer 1986). Zinc homeostasis in rats, unlike most mammals, is maintained by zinc secretion from the intestines rather than by regulation of zinc absorption (Elinder 1986). Initial uptake of zinc from the rat gastrointestinal tract involves binding to albumin and transport of the zinc-albumin complex from intestine to liver (Hoadley and Cousins 1988).

Foods rich in zinc include red meat, milk, gelatin, egg yolks, shellfish, liver, whole grain cereals, lentils, peas, beans, and rice (Sternlieb 1988). About 20 to 30% of zinc in the diet is absorbed, but this is highly variable and ranges from <10% to >90% (Prasad 1979; Casey and Hambridge 1980; Elinder 1986). Increased zinc absorption, for example, was associated with low body weight, poor zinc status, and various prostaglandins; decreased absorption was caused by excess dietary calcium or phytate, and by a deficiency of pyridoxine or tryptophan (Elinder 1986; Goyer 1986). The half-time persistence of zinc in most mammalian tissues ranges between 100 and 500 days; it is longer in bone and muscle, and shorter in liver (Elinder 1986).

Metallothioneins play an important role in metal homeostasis and in protection against heavy-metal toxicity in vertebrates and invertebrates (Engel 1987; Overnell et al. 1987a; Andersen et al. 1989; Olsson et al. 1989; Richards 1989a; Eriksen et al. 1990). Metallothioneins are cysteine-rich (>20%), low (about 6000)-molecular-weight proteins, with high affinity for copper, silver, gold, zinc, copper, and mercury. These heat-stable, metal-binding proteins are found in all vertebrate tissues and are readily inducible by a variety of agents, to which they bind through thiolate linkages. Zinc is a potent inducer of metallothioneins, and a redistribution of zinc from enzymes to metallothioneins is one way to maintain low intracellular zinc concentrations. Metallothioneins also serve as temporary storage proteins for zinc and other metals during early development and may function by maintaining the pool of available zinc at an appropriate concentration. Metallothioneins are quite similar among organisms; that is, all metallothioneins are small proteins of molecular weight 6000 to 10,000, rich in sulfur and cysteine, and lacking aromatic amino acids (Sprague 1986). Metallothioneins isolated from cattle, sheep, horses, pigs, and other livestock, contain 61 amino acids; thioneine, the metal-free protein, is a single-chain polypeptide with a molecular weight of about 6000 (Richards 1989a). Chicken thioneine consists of 63 amino acids, including histidine, an amino acid not present in mammalian metallothioneins. The unusually high cysteine content enables metallothioneins to selectively bind up to 7 zinc and 12 copper atoms per mole of protein (Richards 1989a).

Metallothioneins are involved in zinc homeostasis in chick, rat, and calf. When zinc is present at high dietary concentrations, a temporary zinc storage protein aids in counteracting zinc toxicity (Oh et al. 1979). Zinc absorption in mice is directly proportional to intestinal metallothionein levels and implies a significant role for metallothionein in zinc absorption (Starcher et al. 1980). Chick embryo hepatic metallothionein is highly responsive to exogenous zinc introduced into the yolk, and increases in a dose-dependent manner; a similar pattern is evident in turkey development (Fleet and McCormick 1988). Zinc protects against subsequent exposure to zinc insult, and protection is believed to be mediated by metallothioneins (Woodall et al. 1988). For example, preexposure of South African clawed frog (*Xenopus laevis*) tadpoles to 5 mg ZnSO₄ (7H₂O)/L for 96 h resulted in no deaths during subsequent exposure to 15 mg Zn/L for 90 h vs. 45% dead in the nontreated group. At 20 mg Zn/L, 15% died in the pretreated group vs. 50% in the nontreated group (Woodall et al. 1988). Metallothioneins are an important factor in zinc regulation during the period of exogenous vitellogenesis in rainbow trout (*Oncorhynchus mykiss*). In female rainbow trout, for example, metallothioneins maintain homeostasis of hepatic zinc during egg formation (Olsson et al. 1989). In plaice (*Pleuronectes platessa*), a marine fish, intraperitoneal injection of zinc raised hepatic metallothionein-like species by a factor of 15; metallothionein levels remained elevated for the next 4 weeks (Overnell et al. 1987a).

In marine molluscs and crustaceans, excess zinc is usually sequestered by metal-binding proteins and subsequently transported to storage or detoxification sites; soluble proteins and amino acids may contain 20 to 70% zinc (Sprague 1986). Metallothioneins are actively involved in zinc regulation during normal growth processes in blue crab (*Callinectes sapidus*), as judged by a decrease in zinc content in hemolymph and digestive gland during molting (Engel 1987).

Elevated metallothionein levels are not necessarily indicative of heavy-metal insult. Starcher et al. (1980) show that liver metallothionein levels in mice are elevated following acute stress or starvation, and that this effect is blocked by actinomycin D, a protein synthesis inhibitor. It is further emphasized that not all zinc-binding proteins are metallothioneins (Webb et al. 1985;

Andersen et al. 1989; Richards 1989; Eriksen et al. 1990). Low-molecular-weight metal-binding proteins — not metallothioneins — were induced in snails and polychaete annelids in metals-contaminated environments (Andersen et al. 1989). A high-molecular-weight protein fraction was detected in the plasma of laying turkey (*Meleagris gallopavo*) hens, which bound significant amounts of zinc and which coeluted with vitellogenin; vitellogenin, a metalloprotein, from laying hens contained 0.54 mg Zn/kg protein (Richards 1989). In rock oysters (*Saccostrea cucullata*) collected near an iron-ore shipping terminal, some of the tissue zinc was bound to a high molecular weight (around 550,000) iron-binding protein called ferritin (Webb et al. 1985). Ferritin accounts for about 40% of the protein-bound zinc in rock oysters, and most probably in other bivalves containing elevated tissue levels of zinc (Webb et al. 1985). This requires verification, however. In four species of sediment-feeding marine polychaete annelids, zinc was mainly associated with high-molecular-weight proteins, suggesting that metallothionein-like proteins may not be satisfactory for monitoring purposes and that other cytosolic components should be studied (Eriksen et al. 1990).

High zinc levels induce copper deficiency in rats and interfere with metabolism of calcium and iron (Goyer 1986). Excess zinc interferes with normal metabolism of pancreas, bone, gall bladder, and kidney in mammals, and gill in fishes. The pancreas is a target organ for zinc toxicity in birds and mammals. Pancreatic alterations are documented from experimentally produced zinc toxicosis in cats, sheep, dogs, calves, chickens, and ducklings, and naturally in sheep and calves. Pancreatic changes were limited to acinar cells, specifically cytoplasmic vacuolation, cellular atrophy, and eventually cell death (Lu and Combs 1988a; Kazacos and Van Vleet 1989). Zinc excess may cause stimulation of bone resorption and inhibition of bone formation in chicks, dogs, monkeys, and rats (Kaji et al. 1988). By preferentially accumulating in bone, zinc induces osteomalacia — a softening of the bone caused by deficiency of calcium, phosphorus, and other minerals (Kaji et al. 1988). Zinc plays a role in bone metabolism of aging rats (Yamaguchi et al. 1989a). Normally, the femoral zinc diaphysis content in rats increases from 50 to 150 mg/kg FW during the first three weeks of life and remains constant thereafter. Oral administration of zinc (5 to 20 mg/kg body weight [BW] daily for 3 days to 28-week-old rats) increased alkaline phosphatase activity and calcium content in femur, and delayed bone deterioration in aging rats (Yamaguchi et al. 1989a). Its high affinity for electrons causes zinc to bind covalently to proteins, mostly at imidazole and cysteine residues. In mud puppy (*Necturus maculosus*), zinc blocks apical membrane anion exchange in gallbladder epithelium and blocks chloride channels in nerve and muscle cells. The slow onset and reversal of the effects suggest a covalent modification of the exchanger, or an effect requiring Zn²⁺ transport to the cell interior (Kitchens et al. 1990).

Zinc toxicity to aquatic organisms depends on the physical and chemical forms of zinc, the toxicity of each form, and the degree of interconversion among them. Aquatic plants and fish are relatively unaffected by suspended zinc, but many aquatic invertebrates and some fishes may be adversely affected if they ingest enough zinc-containing particulates (USEPA 1987). Zinc toxicosis affects freshwater fishes by destruction of gill epithelium and consequent tissue hypoxia. Signs of acute zinc toxicosis in freshwater fishes includes osmoregulatory failure, acidosis and low oxygen tensions in arterial blood, and disrupted gas exchange at the gill surface and at internal tissue sites (Spear 1981). Zinc exerts a critical influence on mammalian and piscine immune systems (Ghanmi et al. 1989). Lymphocytes from the pronephros of common carp (*Cyprinus carpio*) were transformed by various mitogenetic agents; zinc added to lymphocyte cultures enhanced thymidine incorporation, and inhibited the response of the mitogenetic agents — although Zn²⁺ was in itself toxic at these concentrations (650 µg Zn²⁺/L; Ghanmi et al. 1989).

9.3.4 Interactions

Zinc interacts with numerous chemicals, sometimes producing greatly different patterns of accumulation, metabolism, and toxicity when compared to zinc alone. Recognition of these interactions is essential to the understanding of zinc kinetics in the environment.

Cadmium

Cadmium-zinc interactions are typical in that sometimes they act to the organism's advantage and sometimes not, depending on the organism, its nutritional status, and other variables.

Dietary cadmium accentuates signs of zinc deficiency in turkeys, chicks, rodents, and pigs (NAS 1979). Chicks on a zinc-deficient diet showed an increased frequency of muscle and feather abnormalities when 40 mg of cadmium/kg of diet was added; however, supplementing the diet with 200 mg Zn/kg for 14 to 15 days lessened or reversed the adverse effects of cadmium (Supplee 1963). Cadmium promotes the growth of zinc-limited phytoplankton (Price and Morel 1990). Substitution of trace metals or metalloenzymes could be a common strategy for phytoplankton in trace-metal impoverished environments, such as the ocean, and could result in an effective colimitation of phytoplankton growth by several bioactive elements (Price and Morel 1990). Zinc-deficient marine diatoms (*Thalassiosira weissflogii*), for example, can grow at 90% of their maximum rate when supplied with cadmium (which substitutes for Zn in certain macromolecules); cobalt can also substitute for zinc, although less efficiently than cadmium (Price and Morel 1990).

Zinc diminishes or negates the toxic effects of cadmium. Specifically, zinc protected embryos of the toad (*Bufo arenarum*) and other amphibian embryos against cadmium-induced developmental malformations (Herkovits et al. 1989; Herkovits and Perez-Coll 1990; Rivera et al. 1990). Zinc counteracted adverse effects of cadmium on limb regeneration and growth of the fiddler crab (*Uca pugilator*; Weis 1980). Preexposure of a freshwater amphipod (*Gammarus pulex*) to 10 µg Zn/L for 2 weeks increased whole-body zinc content from 74 to 142 mg/kg DW and protected against the toxic effects of subsequent cadmium exposure of 500 µg Cd/L for 96 h (Howell 1985). In crickets (*Acheta domesticus*), excess zinc in diets of larvae protected against cadmium toxicity (Migula et al. 1989). Zinc protected rats (*Rattus* sp.) against the toxic effects of cadmium, such as testicular lesions, reduced sperm counts, hepatotoxicity, and lung damage (Sato and Nagai 1989; Saxena et al. 1989a). Zinc also protected mouse (*Mus* sp.) embryos against cadmium toxicity (Yu and Chan 1988). An effective protection ratio was 1 Cd: 1 Zn for mouse embryos, but for free-living embryos of the toads (*B. arenarum*), this ratio was 1 Cd: 8 Zn (Belmonte et al. 1989). Zinc reversed the toxic action of cadmium on natural killer cells of mice: 500 mg Zn/L drinking water negated the toxic action of 50 mg Cd/L (Chowdhury and Chandra 1989). The mechanisms of zinc protection against cadmium were variously attributed to metallothionein induction (Sato and Nagai 1989), enhanced detoxification rates of cadmium (Rivera et al. 1990), and competition with cadmium for the same metalloenzyme sites (Yu and Chan 1988; Rivera et al. 1990).

Waterborne solutions of zinc–cadmium mixtures were usually additive in toxicity to aquatic organisms, including freshwater fishes (Skidmore 1964) and amphipods (de March 1988), and to marine fishes (Eisler and Gardner 1973), copepods (Verriopoulos and Dimas 1988), and amphipods (Ahsanullah et al. 1988). However, mixtures of zinc and cadmium were less toxic than expected to *Daphnia magna*, as judged by acute lethality studies (Attar and Maly 1982).

Zinc exerted antagonistic effects on the uptake of cadmium by gills of the freshwater clam (*Anodonta cygea*), but accelerated cadmium transport from gills toward internal organs (Hemelraad et al. 1987). Cadmium uptake in tissues of *Anodonta* was reduced by about 50% during exposure for 16 weeks to water containing 25 µg Cd/L and 2.5 mg Zn/L (Hemelraad et al. 1987). In a marine prawn (*Pandalus montagui*), cadmium exposure had no effect on tissue zinc levels, but zinc enhanced cadmium uptake in hepatopancreas at the expense of carcass (Ray et al. 1980). In marine fishes, cadmium was taken up more rapidly at elevated seawater zinc levels; however, zinc concentrations in fish tissues decreased with increasing tissue cadmium burdens, suggesting competition between these two metals for the same physiologically active site (Eisler 1981). Zinc concentrations in larval shrimp (*Palaemon serratus*), within its threshold regulation range of 75 to 525 µg Zn/L, were not affected by the addition of 100 µg of cadmium/L (Devineau and Amiard Triquet 1985). In zebrafish (*Brachydanio rerio*), zinc did not affect cadmium uptake by whole body or gills, but did inhibit intestinal uptake and tended to increase gill cadmium elimination rates (Wicklund et al. 1988).

Among marine vertebrates, cadmium is selectively accumulated over zinc (Eisler 1984). In ducks, zinc selectively competes with cadmium on high- and low-molecular-weight protein pools in kidney and liver. Once the high-molecular-weight protein pool is Zn-saturated, excess Zn is stored on metal-binding proteins, with serious implications for waterfowl simultaneously stressed with cadmium and zinc (Brown et al. 1977). On the other hand, a cadmium-induced disease in bone collagen of chicks was prevented by zinc because of preferential accumulation of Zn (Kaji et al. 1988).

Copper

Mixtures of zinc and copper are generally acknowledged to be more-than-additive in toxicity to a wide variety of aquatic organisms, including oyster larvae (Sprague 1986), marine fishes (Eisler and Gardner 1973; Eisler 1984), freshwater fishes (Skidmore 1964; Hilmy et al. 1987b) and amphipods (de March 1988), and marine copepods (Sunda et al. 1987; Verriopoulos and Dimas 1988). But Zn–Cu mixtures were less-than-additive in toxicity to marine amphipods (*Allorchestes compressa*; Ahsanullah et al. 1988).

Zinc added to the ambient water depressed copper accumulations in tissues of juvenile catfish (*Clarias lazera*), but copper added to the medium depressed zinc uptake (Hilmy et al. 1987b). A similar situation was reported in barnacles (*Elminius modestus*); however, simultaneous exposure to copper and zinc resulted in enhanced uptake of both metals (Elliott et al. 1985).

In higher organisms zinc is a copper antagonist and potentiates the effects of nutritional copper deficiency in rats and chicks. This effect only occurs at extremely high Zn:Cu dietary ratios. The addition of copper to the diet of chicks or rats in physiological amounts counteracted all observed signs of zinc intoxication (Tom et al. 1977). No antagonism was evident between dietary copper and zinc fed to channel catfish (*Ictalurus punctatus*) fingerlings; therefore, the high levels of supplemental zinc required in practical feeds should not impair copper status, provided that normal dietary copper levels are present (Gatlin et al. 1989).

High levels of administered zinc limits copper uptake in humans and certain animals (Sammon and Roberts 1988) and provides protection against toxicosis produced by copper in pigs and sheep (Allen et al. 1983). Excessive zinc in humans interferes with copper absorption from the intestine, resulting in copper deficiency and eventually cardiovascular diseases; high zinc intakes also decrease iron bioavailability, leading to a 67% reduction in erythrocyte life span (Saxena et al. 1989b). Copper deficiency induced by excess dietary zinc is associated with lameness in horses, donkeys, and mules (NAS 1979; Bridges 1990; Ostrowski et al. 1990).

Lead

Lead–zinc mixtures were more-than-additive in toxicity to marine copepods (Verriopoulos and Dimas 1988) and significantly delayed development of mud crab (*Rithropanopeus harrissii*) larvae (USEPA 1987). Lead is accumulated up to 10 times more rapidly by marine fishes at elevated zinc concentrations in seawater (Eisler 1981).

Among terrestrial animals, zinc protects against lead toxicosis. Dietary zinc reduced the toxic effects of dietary lead to larvae of the house cricket (*Acheta domesticus*) by inhibiting assimilation and stimulating fecal excretion (Migula et al. 1989). Zinc at 100 to 200 µg/egg (1 mg Zn/kg egg) significantly protected developing white leghorn chicks against lead (50 µg/egg)-induced deformities and death when injected into the yolk sac on the 7th day of incubation (Anwer et al. 1988). Zinc also protects against lead toxicity in horses (Anwer et al. 1988), and against testicular injury induced by lead in rats (Saxena et al. 1989a).

Nickel

Nickel–zinc mixtures were additive in toxicity to marine copepods (Verriopoulos and Dimas 1988) and to the three-spined stickleback (*Gasterosteus aculeatus*; Skidmore 1964).

Oral nickel toxicity in chicks was prevented by increased dietary zinc (Warner et al. 1988).

Nickel is a leading cause of allergic contact dermatitis (ACD) in many industrial nations; about 6% of the general public is sensitive to nickel and about 11% of dermatology clinic patients (Warner et al. 1988). Zinc prevents nickel sulfate-induced ACD in guinea pigs (*Cavia* spp.) through addition of 100 to 200 mg Zn/L drinking water for 4 weeks prior to nickel insult (Warner et al. 1988). Nickel and other metals that cause ACD penetrate the skin, complex with selected ligands, and stimulate a delayed hypersensitivity. Zinc is thought to block the sites where nickel complexes to the protein (Warner et al. 1988).

Other Chemicals

Zinc interacts with a wide variety of inorganic, organic, and biological agents, but in most cases the available information is fragmentary, and the mechanisms of action are unknown. Mice pre-treated with zinc at 6.5 mg Zn/kg BW for 9 days showed increased resistance to arsenic toxicosis over a 30-day observation period (Kreppel et al. 1988). Oral zinc therapy was effective in treating biological agents, such as infectious pododermatitis in cattle, ovine foot rot in sheep, sporidesmin in sheep, cattle, and rodents, and the toxins of the fungus *Phomopsis leptostromiformis* in sheep (Allen et al. 1983). However, juvenile channel catfish (*Ictalurus punctatus*) fed zinc in the diet for 16 weeks at concentrations as high as 60 mg Zn/kg ration as zinc methionine or zinc sulfate were not protected against bacterial infections of *Edwardsiella ictaluri* (Lim et al. 1996). Elevated testicular zinc concentrations in bank voles (*Clethrionomys glareolus*) protect the testes from fluoride-induced histopathology caused by 200 mg F/L drinking water for 4 months (Krasowska and Wlostowski 1996). Calcium modifies zinc toxicity to freshwater aquatic organisms, with increased calcium associated with decreased acute toxicity (Everall et al. 1989a; Handy et al. 1989). Zinc absorption in rat gut is decreased after ingestion of phosphorus as polyphosphate or orthophosphate plus high levels of calcium (Greger 1989). Zinc cytotoxicity is blocked by increased calcium or iron, but not magnesium (Borovansky and Riley 1989). Zinc reportedly protects rats against carbon tetrachloride poisoning (Allen et al. 1983).

Various chelating agents protect mice against zinc acetate poisoning, including disodium ethylene diamine tetraacetic acid (EDTA), disodium calcium cyclohexanediamine tetraacetate, D-penicillamine, 2,3-dimercapto-1-propane sulfonic acid, and 2,3-dimercaptosuccinic acid (Llobet et al. 1988b). Zinc protects toad embryos against agents known to produce malformations, including excess Vitamin A, acetazolamide, calcium-EDTA, and acetaminophen (Herkovits et al. 1989). Venom of the jararaca (*Bothrops jararaca*), a venomous Brazilian serpent, contains a zinc metalloprotease called J protease; the proteolytic activity of J protease is inactivated by EDTA and other sequestering agents (Tanizaki et al. 1989).

Chromium-zinc mixtures were more-than-additive in toxicity to *Tisbe holothuriae*, a marine copepod. Zinc in combination with chromium was more toxic to copepods than were mixtures of zinc with copper, lead, nickel, or cadmium (Verriopoulos and Dimas 1988).

Renal tubular absorption of zinc in mice was impaired by certain diuretics and was further influenced by dietary proteins (Goyer 1986). Zinc absorption in rats was depressed after consumption of high levels of inorganic iron; absorption was normal with organoiron (Greger 1989).

Mercury-zinc mixtures were more-than-additive in toxicity to oyster larvae (Sprague 1986). Preexposure of mussels (*Mytilus edulis*) to 50 µg Zn/L for 28 days conferred increased tolerance to 75 µg inorganic mercury/L (Roesijadi and Fellingham 1987). Zinc inhibited the accumulation of mercury in marine snails and crustaceans (Andersen et al. 1989).

Zinc deficiency places an increased demand on selenium (Se) pools in daphnids. As little as 5 µg Se/L in zinc-free water eliminated overt cuticle damage and substantially increased reproduction, but did not alter the shortened life span. Cladocerans at the threshold of Se deficiency will become overtly Se deficient when zinc supplies are lacking (Keating and Caffrey 1989). Insufficient copper introduces cuticle problems in daphnids similar to those introduced by insufficient zinc or

selenium, increasing the likelihood of a proposed relation between glutathione peroxidase (which contains Se), and copper-zinc superoxide dismutase (Keating and Caffrey 1989).

High levels of dietary tin increased zinc loss from rats (Greger 1989). Zinc prevented toxic effects of vanadium (10 mg/kg BW) on bone metabolism of weanling rats (Yamaguchi et al. 1989).

9.4 CARCINOGENICITY, MUTAGENICITY, AND TERATOGENICITY

9.4.1 General

Zinc can induce testicular sarcomas in birds and rats when injected directly into the testes, but zinc has not been shown to be tumorogenic by any other route. Zinc promotes tumor growth after conditions of zinc deficiency, but excess zinc may suppress or inhibit tumor proliferation, although the mechanisms of action are imperfectly understood. Chromosomal aberrations were observed under conditions of zinc deficiency, but excess zinc was not mutagenic in most tests. Organozinc compounds are effective mutagens when presented to susceptible cell populations in an appropriate form, but the evidence for inorganic zinc is incomplete. Zinc is teratogenic to frog and fish embryos, but conclusive evidence of teratogenicity in mammals is lacking. Zinc may protect against the effects of some mammalian teratogens. Under conditions of mild zinc deficiency, however, diabetes and effects of various teratogens are exacerbated.

9.4.2 Carcinogenicity

Carbamate esters of zinc, zineb, and ziram are carcinogenic and teratogenic in animals, but this is attributed to the action of the carbamate esters and not to zinc (Elinder 1986). Results of studies with small mammals showed zinc to be cocarcinogenic with 4-nitroquinoline-N-oxide on oral cancer, and with N-ethyl-N-nitrosourea on brain cancer (Leonard and Gerber 1989).

There is conclusive evidence that repeated intratesticular injections of zinc salts can induce testicular sarcomas in birds and rats (NAS 1979; Elinder 1986; Goyer 1986; USPHS 1989). Testicular teratomas in roosters were first produced experimentally in 1926 when zinc salts were injected into the testes as a method of practical castration; tumors could be induced only by intratesticular injection during the spring period of gonadal growth (Guthrie 1971). Teratomas of the testes were observed in fowl given testicular injections of 2 mL of 10% ZnSO₄ solution (USPHS 1989). Teratomas were induced in Japanese quail (*Coturnix coturnix japonica*) by intratesticular injections of 3% zinc chloride solutions during a period of testicular growth stimulated by increased photoperiod. Tumors were similar to those of domestic fowl and had histological features in common with spontaneous testicular teratomas in humans (Guthrie 1971). Testicular tumors in rats were produced by direct intratesticular injection of zinc; no other carcinogenic effects were produced by any other route, regardless of dose (Goyer 1986). It is emphasized that zinc and zinc compounds are not conclusively carcinogenic except when injected directly into the testes; no field or experimental evidence exists showing zinc to be tumorogenic through any other route (NAS 1979; Phillips and Kindred 1980; Elinder 1986; Leonard and Gerber 1989; USPHS 1989).

Zinc is essential for the growth of rapidly proliferating cells, such as tumors. The high zinc requirements of these cells in tumor disease can result in latent zinc deficiency. Accordingly, growth of animal tumors is stimulated by zinc and retarded by zinc deficiency (Prasad 1979; Leonard and Gerber 1989). In mouse fibrosarcoma cells, zinc inhibits endonucleases, subsequently blocking DNA fragmentation and tumor cell lysis, allowing tumors to grow (Flieger et al. 1989). There is no evidence that zinc deficiency causes cancer (NAS 1979), although deficiency was associated with decreasing tumor growth (Prasad 1979; Phillips and Kindred 1980). Malignant human tissues, for example, frequently contained less zinc than normal tissue, i.e., 78 mg/kg FW normal liver vs. 18 in cancerous liver (Phillips and Kindred 1980).

Zinc can also inhibit tumor growth (NAS 1979), although the mechanisms of zinc suppression of carcinomas are imperfectly understood (Phillips and Kindred 1980). Zinc inhibits the growth of mouse melanoma cells at concentrations between 8.2 and 9.9 mg Zn/L culture medium (Borovansky and Riley 1989). The addition of 100 mg ZnSO₄/L to drinking water of hamsters inhibited formation of dimethylbenzanthracene-induced carcinomas (Phillips and Kindred 1980). Rats fed high zinc diets of 500 mg/kg ration had reduced growth of a chemically induced hepatoma (Phillips and Kindred 1980). Intramuscular injections of zinc oxide or zinc acetate administered together with nickel sulfide — a potent muscle carcinogen — delayed, but did not prevent, 100% tumor incidence in rats over a 66-week observation period (Kasprzak et al. 1988). Administration of zinc slows the carcinogenic process induced by nickel due to the production of water-soluble and water-insoluble zinc compounds, despite markedly different retention times in muscle of zinc compounds (T_b 1/2 of ZnO = 24 days; Zn acetate = 2.5 days; Ni₃S₂ = 21 days). Zinc in either form exerted no measurable influence on nickel retention at the injection site or early local cellular reactions to nickel (Kasprzak et al. 1988). Testicular tumors in rats caused by injection of cadmium were suppressed by zinc injection (Leonard and Gerber 1989), provided that the Zn:Cd molar ratio was about 100:1 (Phillips and Kindred 1980). Zinc inhibition of cadmium carcinogenesis is a complex phenomenon, depending on dose, route, and target site (Waalkes et al. 1989). For example, the number of cadmium-induced testicular tumors in rats was reduced by 50% over a 2-year period after three subcutaneous injections of 65.4 mg Zn/kg BW given within 18 h of initial cadmium insult, even though this group had a marked elevation in prostatic tumors when compared to controls. Tumor number was reduced by 92% when rats were given 100 mg Zn/L in drinking water (Waalkes et al. 1989).

9.4.3 Mutagenicity

Results of mutagenicity studies with whole organisms were usually negative because homeostatic controls of absorption and protein binding preclude the likelihood of zinc being genotoxic under standard feeding conditions (Thompson et al. 1989). However, zinc is an effective mutagen and clastogen when presented to a susceptible cell population in an appropriate form (Thompson et al. 1989). Zinc acetate produced dose-related positive responses in the mouse lymphoma assay, and also in a cytogenetic assay with Chinese hamster ovary cells; however, results of mutagenicity assays with inorganic zinc were negative in the *Salmonella* mutation assay, and in unscheduled DNA synthesis on primary cultures of rat hepatocytes (Thompson et al. 1989). Organozinc compounds have mutagenic potential, as judged by the positive responses with zinc 2,4-pentanedione and *Salmonella* (Thompson et al. 1989).

Structural chromosome aberrations, particularly chromatid gaps and increased frequency of fragment exchange, were observed in rat bone marrow cells after 14 days of exposure to 240 mg Zn/L drinking water (Kowalska-Wochna et al. 1988). Chromosomal aberrations were observed in bone marrow cells of mice fed diets equivalent to 650 mg Zn/kg BW daily, in mice exposed to zinc oxide by inhalation, and in mice maintained on a low-calcium diet (USPHS 1989). Aberrations in bone marrow of mice given 5000 mg Zn/kg diet may be associated with calcium deficiency (Leonard and Gerber 1989). Calcium is displaced by zinc in calcium-depleted conditions, leading to chromosomal breaks and interference in the repair process (USPHS 1989).

Zinc chloride induces chromosomal aberrations in human lymphocytes *in vitro* (Elinder 1986). A higher incidence of chromosome anomalies in leukocytes occurs among workers exposed to zinc (Elinder 1986), but these aberrations are likely due to other (unspecified) mutagenic factors in the work environment (Leonard and Gerber 1989).

Zinc inhibits the mutagenic action of some carcinogens because it is a constituent of mutagen detoxifying enzymes, or because it acts directly on the microsomal monooxygenases forming the ultimate carcinogen (Leonard and Gerber 1989). Zinc significantly reduced a genotoxic effect of lead in rat bone marrow cells (500 mg Pb/L drinking water followed by 240 mg Zn/L for 2 weeks), and also protected against lead accumulations in erythrocytes and Pb-induced inhibition of delta-amino

levulinic acid dehydratase (Kowalska-Wochna et al. 1988). Zinc deficiency can lead to chromosomal aberrations, but excess zinc was not mutagenic in the majority of tests for DNA damage — except for zinc-containing fungicides wherein the organic dithiocarbamate constituents were the mutagenic agents, and for zinc chromate wherein the chromate ion was the active agent (Leonard and Gerber 1989). Frequencies of sister chromatid exchanges (SCE) in calves with hereditary zinc deficiency, also known as lethal trait A46, are lower than in healthy normal cows, suggesting a fundamental association between disturbed zinc metabolism and the low incidence of SCE in A46 cattle (Bosma et al. 1988).

9.4.4 Teratogenicity

Excess zinc is teratogenic to frog and fish embryos, possibly by inhibition of DNA synthesis (Dawson et al. 1988; Fort et al. 1989). Zinc at 150 mg/kg in rat diets was associated with inhibited fetal implantation, but this needs confirmation (Elinder 1986). No conclusive evidence now exists demonstrating that excessive zinc produces any teratogenic effect in mammals (NAS 1979; Dawson et al. 1988; Leonard and Gerber 1989). Excess zinc may protect against some teratogens, such as calcium EDTA (Leonard and Gerber 1989). Also, teratogenic effects of cadmium salts in golden hamsters was reduced by simultaneous administration of zinc salts (NAS 1979).

Zinc deficiency is clearly teratogenic in mammals (Dawson et al. 1988; Leonard and Gerber 1989). Severe maternal zinc deficiency is known to be teratogenic in rats. Fetal malformations — especially calcification defects — due to maternal zinc deficiency affect almost every tissue (Ferreira et al. 1989). Skeletal malformations are most common, possibly due to a reduction in cellular proliferation and in activity of bone alkaline phosphatase (Leonard and Gerber 1989). Human zinc deficiency may act teratogenically, either directly or indirectly via other toxic agents (Jameson 1980). Zinc deficiency may exacerbate effects of several teratogenic agents, such as thalidomide; there is also the possibility that zinc deficiency may increase the incidence of spina bifida and anencephaly, but this needs verification (Leonard and Gerber 1989). Diabetes during pregnancy can amplify the effects of a mild maternal zinc deficiency. In one study, diabetic and nondiabetic rat strains were fed a low-zinc diet (4.5 mg Zn/kg diet), an adequate-zinc diet (24.5 mg/kg) or a high-zinc diet (500 mg/kg) throughout gestation. Fetuses from diabetic dams were smaller, weighed less, and had less calcified skeletons and more malformations than did fetuses from control dams. In controls, maternal dietary zinc had a minor effect on fetal malformation frequency. In diabetic strains, however, the low-zinc diet had a strong teratogenic effect (Uriu-Hare et al. 1989).

9.5 CONCENTRATIONS IN FIELD COLLECTIONS

9.5.1 General

Total zinc concentrations in nonbiological samples seldom exceed 40 µg/L in water, 200 mg/kg in soils and sediments, or 0.5 µg/m³ in air. Environments heavily contaminated by anthropogenic activities may contain up to 99 mg Zn/L in water, 118 g/kg in sediments, 5 g/kg in soil, and 0.84 µg/m³ in the atmosphere. Zinc measurements in field collections of plants and animals (Table 9.4) show several trends: (1) zinc is present in all tissues of all organisms measured; (2) concentrations are elevated in organisms near anthropogenic point sources of zinc contamination; (3) concentrations are normally grossly elevated (>4 g/kg FW soft parts) in some species of bivalve molluscs and barnacles; (4) zinc-specific sites of accumulation include the frond in algae; kidney in molluscs; hepatopancreas in crustaceans; jaws in polychaete annelids; viscera, gonad, and brain in fishes; liver, kidney, and bone in birds; and serum, pancreas, feces, liver, kidney, and bone in mammals; (5) interspecies variations in zinc content are considerable, even among species closely related taxonomically; (6) intraspecies differences in zinc content vary with age, size, sex,

season, and other modifiers; and (7) many species regulate zinc within a threshold range of concentrations. Additional information on background concentrations of zinc is given in Vallee (1959), NAS (1979), Young et al. (1980), and Eisler (1980, 1981, 1993).

9.5.2 Nonbiological

Zinc concentrations in freshwater, seawater, groundwater, sewage sludge, sediments, and soils are listed in [Table 9.3](#). These data are considered reliable, although clean-laboratory techniques suggest that dissolved Zn concentrations in nonpolluted rivers may be 10 to 100 times lower than previously reported (Shiller and Boyle 1985).

Zinc concentrations in water seldom exceed 40 µg/L except near mining, electroplating, and similar activities, where concentrations between 260 and 954 µg/L have frequently been recorded. Drinking water usually contains <10 µg Zn/L, although concentrations >2 mg/L may occur after passage through galvanized pipes (Goyer 1986). Zinc-contaminated streams within the Platt River Basin sometimes contain up to 99 mg Zn/L, and in Arkansas up to 79 mg/L (Mirenda 1986). Zinc concentrations in water downstream of placer mining activities in Alaska sometimes exceed the concentrations found to be toxic to Arctic grayling, *Thymallus arcticus* (Buhl and Hamilton 1990). The disappearance of stone loach (*Noemacheilus barbatulus*) in the U.K. from streams receiving industrial wastes was attributed directly to zinc concentrations in the stream rising from 1 mg/L to a lethal 5 mg/L (Solbe and Flook 1975).

Concentrations of zinc in sediments and soils usually do not exceed 200 mg/kg, but can range between 3 and 118 g/kg as a result of human activities ([Table 9.3](#)). Atmospheric zinc levels were almost always <1 µg/m³, although they tended to be higher over industrialized areas (Goyer 1986). Average zinc concentrations, in µg/m³ atmosphere, were <0.001 at the South Pole, 0.01 to 0.02 in rural areas of the United States, <0.01 to 0.84 in U.S. cities, and 0.06 to 0.35 at various locations in the United Kingdom (Elinder 1986).

Table 9.3 Zinc Concentrations in Representative Nonbiological Materials (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Material	Concentration ^a (mg/kg or mg/L)	Reference ^b
EARTH'S CRUST	40 DW	11
FRESHWATER		
Canada		
Normal	<0.04 FW	1
Acidic mine tailings wastes, Sudbury, Ontario	0.9 FW, Max. 3.3 FW	2
United States		
Alaska		
Contaminated streams	0.029–0.882 FW	3
Downstream of placer mining activities	0.125 (0.075–0.165) FW	3
Nationwide	0.0005–0.010 FW	4
Worldwide, rivers	0.021 FW	2, 5
Groundwater, near Lake Erie	Max. 0.954 FW	1
SEAWATER		
Australia (polluted)	0.134 FW	6
Canada	0.01–0.04 FW	1
Irish Sea		
Coastal	0.007 FW	6
Near shore	0.003 FW	6
Offshore	0.003 FW	6

Table 9.3 (continued) Zinc Concentrations in Representative Nonbiological Materials
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Material	Concentration ^a (mg/kg or mg/L)	Reference ^b
Open Ocean		
Deep water	0.0006 FW	6
Surface	0.000002–0.0001 FW	4
United Kingdom		
Clyde estuary	0.006 FW	7
“Heavily polluted”	0.026 FW	6
“Polluted”	0.007–0.012 FW	6
Severn estuary	0.022 FW	7
United States, San Diego		
Coastal	0.0005 FW	6
Harbor	0.0026 FW	6
Western Mediterranean		
Coastal	0.0015–0.002 FW	6
Estuary	Max. 0.010 FW	6
Near Shore	0.0036 FW	6
SEDIMENTS		
Australia	35 DW; Max. 280	8
Canada		
Lakes	55–160 DW	1
Marine	64–180 DW	1
Streams and Rivers	50–138 DW	1
Mediterranean	5–20 DW	8
Sweden and Norway	Usually <130 DW; Max. 118,000	8
United Kingdom	70–245 DW; Max. 825 DW	8
United States		
Corpus Christi, Texas		
Bay	10–229 DW	9
Harbor	229–11,000 DW	9
New York Bight		
Uncontaminated site	18 DW	9
Sewage dump site	252 (54–416) DW	9
Northeast	15–20 DW; Max. 1500 DW	8
Puget Sound	65 DW; Max. 185 DW	8
Rhode Island, near electroplaters		
Narragansett Bay	110 (53–168) DW	9
Providence River	490 DW	9
Southern California Bight	55–75 DW; Max. 2800	8
SEWAGE SLUDGE		
United Kingdom, Glasgow	1125 DW	7
United States		
Average	1409 DW	10
Missouri	1200 (170–13,000) DW	10
SOILS		
United States	54 (<25–2000) DW	10
Uncontaminated	10–300 DW	11
Near smelters	5000 DW	11

^a Concentrations are shown as means, range (in parentheses) and maximum (Max.).

^b **1**, Spear 1981; **2**, Mann et al. 1989; **3**, Buhl and Hamilton 1990; **4**, USEPA 1987; **5**, Mann and Fyfe 1988; **6**, Sprague 1986; **7**, Nugegoda and Rainbow 1988b; **8**, Young et al. 1980; **9**, Eisler et al. 1977; **10**, Beyer 1990; **11**, Elinder 1986.

9.5.3 Terrestrial Plants and Invertebrates

Zinc concentrations in forest plants vary considerably. In oaks (*Quercus* spp.), for example, some species are accumulators, whereas others may be termed discriminators. For individual species, zinc concentrations tend to follow the pattern of roots > foliage > branch > trunk (Van Hook et al. 1980). Small lateral roots accumulate Zn to much greater levels than other vegetation components and are probably most sensitive to changes in zinc inputs. Half-time persistence of zinc in forest ecosystems varies from about 3 years in organic matter components to >200 years for large soil pools (Van Hook et al. 1980).

Terrestrial plants growing beneath corroded galvanized fencing have been poisoned by zinc (Jones and Burgess 1984). Vegetables are relatively low in zinc, but growing plants can accumulate zinc applied to soils (Goyer 1986). High soil level of zinc is the primary cause of vegetation damage near zinc smelters (Buchauer 1971; Leonard and Gerber 1989). Elevated zinc concentrations in soils near zinc smelters inhibit seedling root elongation and probably prevent establishment of invader species in denuded areas (Buchauer 1971). Lichen species richness and abundance were reduced by about 90% in lichen communities near a Pennsylvania zinc smelter; elevated zinc concentrations were the probable cause of the impoverished lichen flora (Nash 1975). Soils and vegetation surrounding zinc smelters in Palmerton, Pennsylvania, were grossly contaminated with zinc, cadmium, and lead. Zinc was primarily responsible for the destruction of trees and subsequent erosion of the soil, reductions in moss and lichen flora, reductions in litter arthropod populations, and reductions in species diversity of soil fungi and bacteria; zinc residues were elevated in slugs and millipedes (Sileo and Beyer 1985; Beyer 1988). Soil litter invertebrates were rare or absent 2 km downwind of the smelter. Invertebrates collected up to 10 km upwind of the smelters had significantly elevated zinc concentrations when compared to soil litter invertebrates from more distant sites (Beyer et al. 1985).

The maximum zinc concentration in earthworms collected from a contaminated site was 1600 mg/kg DW whole animal; for uncontaminated sites it was 650 mg/kg (Beyer and Cromartie 1987). Whole-body zinc concentrations in earthworms (*Dendrodrilus rubidus*, *Lumbricus rubellus*) tended to reflect zinc concentrations in soil, although zinc accumulations in both species seem to be physiologically regulated when soil zinc values exceeded 1000 mg/kg DW (Morgan and Morgan 1988).

Whole-body zinc content of terrestrial isopods seems to reflect soil zinc levels and may be a useful indicator of soil contamination (Hopkin et al. 1989). *Porcellio scaber*, a terrestrial isopod known as a woodlouse, is recommended as a biological indicator of zinc contamination because of the positive correlation between zinc content in soil or leaf litter and woodlouse hepatopancreas. Zinc content in *Porcellio*, litter, and soil near a zinc smelter, in mg/kg DW, was >1000 in whole isopod, >9000 in hepatopancreas, >10,000 in litter, and >50,000 in soil (Hopkin et al. 1986).

Interspecies variability in zinc content of terrestrial invertebrates is large and governed by numerous modifiers. For example, whole-body zinc content in closely related species of terrestrial gastropods collected from a single contaminated site ranged between 600 and 1200 mg/kg DW (Greville and Morgan 1989). Zinc was highest in grey field slugs (*Deroferas reticulatum*) in late spring, lowest in summer, and positively correlated with tissue cadmium concentrations. Starvation for 16 days had no effect on body zinc concentrations (Greville and Morgan 1989a). Zinc tends to concentrate in mechanical structures of various invertebrates, such as mandibular teeth. High concentrations of zinc are reported in jaws of polychaete worms, the cutting edge of the mandibles of herbivorous insects, mandibles of various species of beetles, copepod mandibles, chaetognath teeth and spines, mandibular teeth of ants, and fangs of spiders (Schofield and Lefevre 1989). Honeybees (*Apis mellifera*) collected near a lead smelting complex at East Helena, Montana, had depressed whole-body zinc concentrations despite increased ambient air Zn values. However, whole-body burdens of arsenic, cadmium, copper, and lead were significantly elevated, and this may have influenced zinc kinetics (Bromenshenk et al. 1988). Also, pollen was usually the most indicative source of zinc and other heavy metals in bees (Veleminsky et al. 1990).

9.5.4 Aquatic Organisms

Concentrations of zinc in tissues of aquatic organisms are usually far in excess of that required for normal metabolism. Much of the excess zinc is bound to macromolecules or present as insoluble metal inclusions in tissues (Eisler 1981, 1984, 1993; USEPA 1987). Diet is the most significant source of zinc for aquatic organisms and is substantially more important than uptake from seawater (Eisler 1981, 1984). In general, zinc concentrations in sediments and tissues of aquatic organisms are elevated in the vicinity of smelters and other point sources of zinc, and decrease with increasing distance (Ward et al. 1986; [Table 9.4](#)).

Freshwater algae in Canadian mine tailing environments heavily concentrate zinc and other metals and may retard metal dispersion through the water column (Mann and Fyfe 1988). Zinc levels in field collections of marine algae and macrophytes are usually at least several orders of magnitude higher than zinc concentrations in the surrounding seawater (Eisler 1981). In general, concentrations in marine aquatic flora were high when seawater zinc concentrations were elevated, although the relationship was not linear. Marine flora, especially red and brown algae, are among the most effective marine zinc accumulators. Increasing accumulations of Zn in marine algae were associated with decreasing light intensity, decreasing pH, increasing temperature, decreasing levels of DDT, and increasing oxygen. Ionic zinc was accumulated more rapidly than other forms (Eisler 1981). Many species of marine algae had zinc concentrations >1 g/kg DW (Eisler 1980). These grossly elevated levels were usually associated with nearby industrial or domestic outfalls containing substantial amounts of zinc (Eisler 1981). In eelgrass, *Zostera marina*, zinc concentrations increased with age of the leaf (Brix and Lyngby 1982).

In the Fal estuary, England, long-term metal pollution over the past 120 years has resulted in zinc sediment levels between 679 and 1780 mg/kg DW, producing benthic communities that favor zinc-tolerant organisms, such as oysters and nereid polychaetes, and a general impoverishment of mussels, cockles, other polychaetes, and gastropods (Bryan et al. 1987).

Zinc in molluscs is usually associated with high-molecular-weight proteins, with diet (as opposed to ambient water zinc concentrations), with elevated sediment zinc burdens, and with particulate matter resulting from dredging and storm perturbations (Eisler 1981). Zinc levels in molluscs were highest in animals collected near anthropogenic point sources of zinc. Excess zinc accumulations do not seem to affect normal molluscan life processes, and zinc is frequently accumulated far in excess of the organism's immediate needs (Eisler 1981). American oysters (*Crassostrea virginica*), for example, may naturally contain up to 4 g Zn/kg FW soft parts. This is comparable to accumulations observed in oysters exposed to 0.2 mg Zn/L for 20 weeks (NAS 1979). In general, zinc concentrations in American oysters were highest in summer and lowest in winter and spring (Jiann and Presley 1997). Zinc tends to accumulate in molluscan digestive gland and stomach as excretory granules, and in kidney as concretions (Eisler 1981; Sprague 1986; Sullivan et al. 1988). Kidney is the preferred storage site in mussels and scallops, and digestive gland in oysters (Sprague 1986). In oysters, granules may contain up to 60% of the total body zinc, explaining, in part, how some shellfish can exist with such high body burdens (Sprague 1986).

Zinc in molluscan tissues is usually elevated under conditions of increasing water temperature and pH, and decreasing salinity (Eisler 1981); however, zinc accumulation kinetics in molluscs vary considerably among species (Chu et al. 1990). Variations in zinc content of clam tissues were associated with seasonal changes in tissue weights (Cain and Luoma 1986). Gastropods nearest a ferro-nickel smelter had elevated zinc concentrations in hepatopancreas when compared to those collected at more distant sites; however, there were no consistent seasonal variations (Nicolaidu and Nott 1990). Fluctuations in zinc content of mussels (*Mytilus edulis*) related to size or season of collection were sufficient to conceal low chronic or short-term pollution (Amiard et al. 1986). Diet (the primary route of zinc accumulation in most molluscs) had no significant effect on whole-body zinc content of certain predatory marine gastropods. Whole-body zinc concentration of gastropod oyster drills (*Ocenebra erinacea*) ranged between 1451 and 2169 mg/kg DW, and remained

unchanged after feeding for 6 weeks on Pacific oysters (*Crassostrea gigas*) containing 1577 mg Zn/kg DW or mussels (*Mytilus edulis*) containing 63 mg Zn/kg DW (Amiard-Triquet et al. 1988).

High zinc concentrations in crustaceans are usually associated with industrial contamination. In the case of barnacles (*Balanus* spp.), high (>3.3 g/kg DW soft parts) levels are attributed to inorganic granules that contain up to 38% zinc and which accumulate in tissue surrounding the midgut (Eisler 1980, 1981). The granules consist of phosphorus, zinc, potassium, sulfur, and chlorine, in that order (Thomas and Ritz 1986). These insoluble, membrane-limited, spheres form in response to high zinc levels in the ambient seawater within 12 days of exposure, and concentrate in specialized cells around the gut: the stratum peritestinale (Walker et al. 1975; Sprague 1986; Thomas and Ritz 1986). Zinc granules in barnacles represent a detoxification mechanism for surplus zinc (Thomas and Ritz 1986). Older barnacles have greater whole-body zinc accumulations than younger stages, and accumulations change seasonally (Anil and Wagh 1988). Zinc concentrations in marine crustacean tissues are usually <75 mg/kg FW or <100 mg/kg DW; exceptions include hepatopancreas, molts, eggs, fecal pellets, and barnacles (Table 9.4). In crustaceans, zinc is slightly elevated in hepatopancreas, but most tissues are only 2 to 3 times higher than muscle (Sprague 1986). For marine crustaceans, the highest concentration recorded in muscle was 57 mg Zn/kg FW in king crab, *Paralithodes camtschaticus* (NAS 1979), and was associated with two metal-binding proteins of molecular weight 11,500 and 27,000 (Eisler 1981). In crustacean tissues, zinc levels were higher in summer, at lower salinities, and in young animals (Eisler 1981), although young amphipods had higher zinc residues than older stages (Rainbow 1989). Seasonal accumulations of whole-body zinc in the shrimp (*Palaemon serratus*) during spring and summer and loss in winter seem to reflect water zinc concentrations in the range 0.0 to 9.0 µg/L (Alliot and Frenet-Piron 1990). Zinc is present in crustacean serum at concentrations >1000 times higher than ambient seawater; in serum, it serves primarily as a cofactor of carbonic anhydrase — the principal enzyme involved in calcification. Serum zinc concentrations in crustaceans seem to be independent of season, water temperature, or salinity (Sprague 1986).

Molting results in a 33 to 50% loss of total zinc in marine crustaceans; molts, together with fecal pellets, constitute an important vehicle of zinc transfer in marine ecosystems (Eisler 1981). The freshwater opossum shrimp (*Mysis relicta*) can transport zinc from sediments into the water column, and the reverse, during their migratory cycle. *Mysis relicta* and other benthic invertebrates play an important role in determining the concentration of zinc and other metals in lake sediments (Van Duyn-Henderson and Lasenby 1986). Unlike decapod crustaceans, marine amphipods do not regulate body zinc concentrations; amphipod body burdens of zinc may reflect sediment total zinc levels and suggest that certain groups may be suitable bioindicators (Rainbow et al. 1989). Molting had no effect on body zinc concentration in four species of adult marine amphipods (Weeks and Moore 1991), and this forces a reexamination of the role of cast exuviae in zinc transport.

In annelids, zinc content was highest in nonselective deposit feeders, omnivores, and carnivores, and from animals collected from sediments with elevated zinc levels (Eisler 1981). Freshwater tubificid worms have the potential to increase zinc concentrations in the water column, particularly during short episodes of high burrowing activity (Krantzberg and Stokes 1985). A high zinc content appears to be a structural characteristic of jaws of marine nereid worms (Table 9.4). In the marine polychaete worm *Nereis diversicolor*, zinc is localized in the gut wall, epidermis, nephridia, and blood vessels; most of the body zinc is present in wandering amoebocytic cells of excretory organs. Zinc in *Nereis* may be present as insoluble granules in membrane-bound vesicles. Excretion is via exocytosis with the aid of amoebocytes (Fernandez and Jones 1989). Unlike the insoluble zinc phosphate granules of molluscs and crustaceans, zinc granules in *Nereis* were very soluble and retained only by sulfide precipitation (Pirie et al. 1985).

Marine vertebrates, including fishes and elasmobranchs, have low zinc concentrations in tissues (i.e., 6 to 400 mg/kg DW) when compared to marine plants and invertebrates (Eisler 1980, 1981, 1984). Highest concentrations in muscle of marine fishes (20.1 to 25.0 mg/kg FW) were recorded in northern anchovy (*Engraulis mordax*) and Atlantic menhaden (*Brevoortia tyrannus*; NAS 1979).

The highest zinc concentrations measured in whole freshwater fishes in the conterminous United States in 1978/79 were in common carp (*Cyprinus carpio*) from Utah; concentrations in carp from Utah ranged between 70 and 168 mg Zn/kg FW vs. an average of 63 mg Zn/kg FW for this species collected elsewhere (Lowe et al. 1985). Zinc concentrations in fishes tend to be higher near urban areas (Peterson et al. 1989); highest in eggs, viscera, and liver (Eisler and LaRoche 1972; Eisler 1981); lowest in muscle (Eisler 1981); positively correlated with metallothionein concentrations (Overnell et al. 1987); lower in all tissues with increasing age and growth (Eisler and LaRoche 1972; Eisler 1981, 1984; Grady et al. 1989); and relatively unaffected by water salinity, temperature, or copper concentrations (Eisler and LaRoche 1972; Eisler 1981). Zinc residue data from marine fishes that were dead on collection are of limited worth because dead fish accumulate zinc from seawater at a substantially higher rate than living teleosts (Eisler 1981).

Zinc concentrations in fishes and other aquatic vertebrates are modified by diet, age of the organism, reproductive state, and other variables. In fish, diet is the major route of zinc uptake and juveniles accumulate zinc from the medium more rapidly than embryos or larvae (Cutshall et al. 1977; Eisler 1981). Because the diet of many teleost carnivores changes dramatically with age, and because upper trophic level vertebrates are frequently used as indicators of water quality, it seems that more research is needed on zinc burdens in prey organisms (Eisler 1984). A reduction in serum zinc during egg formation in a flatfish (*Pleuronectes platessa*) may represent a transfer of zinc to eggs (Overnell et al. 1987). High (>35 mg/kg FW) zinc concentrations in eggs of Atlantic salmon (*Salmo salar*) are sometimes associated with increasing mortality, although low (14 mg/kg FW) concentrations seem to have no adverse effect on survival (Craik and Harvey 1988). Zinc concentrations in Atlantic salmon milt ranged from 0.5 to 5.5 mg Zn/kg and was linearly proportional to spermatozoan abundance (Poston and Ketola 1989). In lakes containing 1150 mg Zn/kg sediment and 209 to 253 µg Zn/L water column, white sucker (*Catostomus commersoni*) females did not grow after sexual maturity and had increased incidences of spawning failure. Alterations in growth and reproduction were related, in part, to nutritional deficiencies as a result of chronic effects of elevated sediment zinc on the food base of the sucker. That is, invertebrate fauna were absent in the uppermost 7 m (Munkittrick and Dixon 1988). Eggs of the white sucker incubated at a metals-contaminated site (400 µg Zn/L) produced larvae with a decreased tolerance to copper and with elevated zinc body burdens when compared to a noncontaminated (2.7 µg Zn/L) site; larval size and fertilization rate were the same at both sites (Munkittrick and Dixon 1989).

9.5.5 Birds

Zinc residues were elevated in birds collected near zinc smelters (Beyer 1988). In general, the highest concentrations of zinc in birds are in liver and kidney, and the lowest in muscle (Eisler 1981, 1984). In the giant Canada goose (*Branta canadensis maxima*), red muscle contains more zinc than does white muscle, and slow contracting muscle more than fast muscle (Rosser and George 1986). In nestling kittiwakes (*Rissa tridactyla*), zinc concentrations increased in liver and feathers throughout chick growth (Wenzel et al. 1996). Zinc concentrations in marine birds normally range between 12 mg/kg FW in eggs and 88 mg/kg FW in liver. The highest concentration of zinc recorded in a marine bird was 541 mg/kg DW in the liver of a booby (*Sula* sp.) that died from polychlorinated biphenyl poisoning. Elevated zinc levels in these birds may have been a manifestation of toxicant-induced stress (i.e., breakdown in osmoregulatory processes), as is the case for other taxonomic groups (Eisler 1981). Seabirds with high zinc concentrations in liver and kidney tend to have high cadmium levels in these tissues (Muirhead and Furness 1988). In flamingos, zinc in liver was positively correlated with copper levels in liver and kidney, and with metallothionein levels in kidney (Cosson 1989). In egrets, zinc was positively correlated with metallothionein protein levels in liver (Cosson 1989). In blue-winged teal (*Anas discors*), zinc concentrations were higher in liver than muscle, higher in males than females, and higher in autumn than in the spring (Warren et al. 1990). Zinc concentrations in liver of black-crowned night heron (*Nycticorax nycticorax*)

were usually higher in younger birds, although weight and sex had no direct effect on zinc content (Custer and Mulhern 1983). Zinc concentrations in tissues and feathers of California condors (*Gymnogyps californianus*) found dead from a variety of causes (Table 9.4) were similar to those found in turkey vultures (*Cathartes aura*), common ravens (*Corvus corax*), and ospreys (*Pandion haliaetus*) and are considered normal (Wiemeyer et al. 1988). The highest concentration recorded in condor liver (250 mg/kg FW) approaches those in livers of mallards (*Anas platyrhynchos*) that died from high dietary loadings of zinc (Wiemeyer et al. 1988). Zinc concentrations in liver of osprey were similar between age groups and sexes (Wiemeyer et al. 1987). With the onset of egg production in turkeys (*Meleagris gallopavo*), serum zinc in hens increased from 1.6 to 6.9 mg/L and remained significantly elevated throughout egg laying; during this same period, liver zinc concentration declined from 75 to 39 mg/kg DW, although total liver zinc increased because of an increase in liver weight (Richards 1989).

Zinc concentrations in the sediments of the Rhine River increased about sixfold between 1900 and 1950, and have remained stable since then. However, migratory waterfowl from this collection locale do not have elevated zinc concentrations in their primary feathers (Goede 1985). Zinc content in feathers of the hoopoe (*Upupa epops*) increased from 200 mg/kg DW at age 7 days to 1000 mg/kg DW at age 35 days (Kaur 1989). Hoopoe populations are declining in India, and this is said to be associated with increasing zinc concentrations in feathers (Kaur 1989). Feathers of the greater flamingo (*Phoenicopterus ruber*) have been proposed as indicators of atmospheric zinc contamination: outer barbs of the black primary feathers — exposed to air pollution — contained 53% more zinc, on average, than did inner barbs (Cosson et al. 1988). More research seems needed on the use of feathers as indicators of Zn contamination.

Zinc concentrations in seminal plasma of domestic chickens (*Gallus* sp.) are about 100 times lower than those for humans and most other mammals, except sheep. Concentrations of zinc in fowl seminal plasma after *in vitro* storage of spermatozoa for 24 h at 4°C were near the threshold values toxic to spermatozoa (Blesbois and Mauger 1989), suggesting that poultry spermatozoa normally function near their lower lethal zinc threshold.

9.5.6 Mammals

White-tailed deer (*Odocoileus virginianus*) collected near a zinc smelter had elevated tissue zinc concentrations when compared to those from more distant sites. Deer with zinc concentrations of 150 mg/kg FW (750 mg/kg DW) in the renal cortex of the kidney had swollen joints, lameness, and joint lesions similar to those seen in zinc-poisoned horses from the same area (Sileo and Beyer 1985). Zinc was elevated in kidney cortex of red deer (*Cervus elephas*), and older deer tended to have higher concentrations (up to 184 mg/kg DW) than did younger deer (as low as 20 mg/kg FW); in the case of older deer, zinc was associated with the metallothionein fraction (Holterman et al. 1984). Zinc residues were usually elevated in rodents near smelters (Beyer et al. 1985). Rodents from metals-contaminated forests had zinc loadings in tissues similar to those from control locations, although lead and cadmium were significantly elevated in the contaminated zone (Sawicka-Kapusta et al. 1987). Elevated zinc concentrations in mine tailings reportedly do not represent a notable contamination hazard to the invading mammalian fauna, although zinc concentrations in invertebrates (especially earthworms) and vegetation were elevated (Andrews et al. 1989; Table 9.4).

Otters (*Lutra lutra*) were found only on a single unpolluted tributary of a river system contaminated by zinc mine drainage waste, suggesting that a contaminated food supply may be responsible for avoiding otherwise suitable habitat (Mason and Macdonald 1988).

Marine mammals collected near heavily urbanized or industrialized areas or near zinc pollution point sources usually had elevated zinc concentrations when compared to individuals of the same species and of similar age from relatively pristine environments (Eisler 1984). Zinc concentrations in tissues of the ringed seal (*Phoca hispida*) were essentially the same in animals near a lead-zinc mine and in those of a distant reference site, although lead and selenium burdens were elevated in the vicinity

of the mine (Wagemann 1989). Concentrations of zinc in tissues of Steller sea lion (*Eumetopias jubata*) were highest in liver and pancreas, followed by kidney, muscle, heart, spleen, and lung; this rank order is comparable to that in human tissues (Hamanaka et al. 1982). There is considerable variation among species in tissue zinc concentrations; threefold differences are not uncommon for the same tissue in different species of marine mammals (Muir et al. 1988). In bottlenose dolphins (*Tursiops truncatus*), zinc concentrations were higher in juveniles than in adults (Beck et al. 1997). Marine mammals contained the lowest zinc concentrations (2 to 505 mg/kg DW, elevated in liver) of all groups of marine organisms examined. Because zinc is usually available in sufficient quantity in the marine environment and is usually accumulated in excess of the organism's immediate needs, it remains unclear why zinc is comparatively depressed in tissues of marine mammals (Eisler 1981).

Zinc toxicosis in horses near a zinc smelter was characterized by lameness, swollen joints, and unkempt appearance, particularly in foals. Zinc concentrations in afflicted foals were elevated in pancreas, liver, kidney, and serum when compared to foals at more distant sites (Gunson et al. 1982). Foals born near the smelter had joint swellings that were attributable to generalized osteochondrosis; lesions were similar to those induced experimentally in animals fed high-zinc diets, and may have been the result of a zinc-induced abnormal copper metabolism (Gunson et al. 1982). Concentrations of zinc in tissues of horses from farms near the Palmerton smelter were extremely high, in some cases approaching lethal thresholds; zinc poisoning was a cause of debility and death of foals (Sileo and Beyer 1985). Grazing mares managed with standard husbandry had significant monthly variations in plasma zinc due, in part, to dietary factors such as nutritional supplementation and to seasonal variations in the quality of grazing pasture (Auer et al. 1988). Peak plasma zinc levels in horses are positively related to age (in weanlings age 22 to 52 weeks) and to summer diets (Cymbaluk and Christison 1989).

Dairy cattle near a lead and zinc ore processing facility did not have elevated blood or hair zinc levels, although daily zinc intake was 5.6 mg/kg body weight vs. 1.2 mg/kg BW daily for a control area (Milhaud and Mehannaoui 1988). In cattle, proximity to zinc refineries did not result in significant elevation of liver or kidney zinc concentrations (Spierenburg et al. 1988). However, cows living within 6 km of a power plant in Czechoslovakia had elevated zinc loadings in hair and poor reproduction when compared to a herd 26 km distant (Pisa and Cibulka 1989). In adult bovines, zinc reserves are usually small and located primarily in the skeleton and muscle, although appreciable hepatic accumulations can occur in the fetus. At 270 days of gestation, for example, 30% of fetal zinc in cattle is present in liver; fetal zinc concentration is about 4 times higher than that in maternal liver (Gooneratne and Christensen 1989). Liver concentrations >120 mg Zn/kg DW in cattle are frequently associated with elevated dietary zinc loadings (Binnerts 1989). Concentrations of zinc in milk of cows and goats varied significantly between breeds, with zinc level in diet, and declined markedly after parturition (Park and Chukwu 1989).

A normal 70 kg human male contains 1.5 to 2.0 grams of zinc, or about 21 to 29 mg Zn/kg BW; normal zinc uptake is 12 to 15 mg daily, equivalent to 0.17 to 0.21 mg/kg BW (Prasad 1979). Foods rich in zinc are seafoods, meats, grains, dairy products, nuts, and legumes (Goyer 1986). About 90% of the total body zinc is in the musculoskeletal system (Rosser and George 1986). Highest zinc concentrations of 100 to 200 mg/kg occur in prostate, eye, brain, hair, bone, and reproductive organs; intermediate concentrations of 40 to 50 mg/kg occur in liver, kidney, and muscle (NAS 1979; Casey and Hambidge 1980). In blood, about 80% of the total zinc is in red cells, where it is associated with carbonic anhydrase. The mean plasma zinc level is about 0.9 mg/L; about half is in a freely exchangeable form loosely bound to albumin. Most of the remainder is tightly bound to macroglobulins and amino acids, especially histidine and cysteine (Casey and Hambidge 1980; Goyer 1986). The greatest zinc concentration in the human body is in the prostate and may be related to the elevated levels of acid phosphatase, a zinc-containing enzyme, in that organ (Goyer 1986). The prostate gland contributes zinc to spermatozoa in dogs — a necessary process for canine fertility and fecundity; in rats, however, the prostate does not contribute to zinc in spermatozoa, and its function is not essential for rat reproduction (Saito et al. 1967).

Table 9.4 Zinc Concentrations in Field Collections of Representative Plants and Animals (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
AQUATIC PLANTS		
<i>Euglena</i> sp.		
From acidic mine tailings waste discharges (0.9 mg Zn/L, Max. 3.3 mg/L)	143 DW; Max. 410 DW	1
Aquatic moss, <i>Fontinalis squamosa</i>		
Contaminated river, Wales, 1985	Max. 2810 DW	2
Uncontaminated site	<400 DW	2
Marine plants		
Phytoplankton	38 DW	3
Seaweeds	90 DW	3
Eelgrass, <i>Zostera marina</i>		
Leaf	Max. 195 DW	4
Rhizome	Max. 70 DW	4
Root	Max. 155 DW	4
Stem	Max. 85 DW	4
TERRESTRIAL PLANTS AND INVERTEBRATES		
Honey bee, <i>Apis mellifera</i> , Czechoslovakia, 1986–1987		
Drones	77–89 DW	5
Honey	0.6–4.5 DW	5
Pollen in combs	39–55 DW	5
Wax	11–249 DW	5
Workers, whole		
Foragers, spring	116–204 DW	5
Dead overwintering	8–13 DW	5
Young	83–160 DW	5
Grey field slug, <i>Deroceras reticulatum</i> , near lead-zinc mine		
Digestive gland	3968 DW	6
Foot/head	308 DW	6
Gonads	118 DW	6
Intestine	380 DW	6
Whole	800 DW	7
Earthworms, northeastern United States, whole		
From uncontaminated soils (23–200 mg Zn/kg DW), 6 species	120–650 DW	8
From mining sites (100–2500 mg Zn/kg DW), 5 species	200–950 DW	8
From industrial sites (24–320 mg Zn/kg DW soil), 6 species	320–1600 DW	8
Near galvanized towers (28–270 mg Zn/kg DW soil), 1 species	340–690 DW	8
Earthworms, whole, gut empty		
<i>Dendrodrilus rubidus</i>	(308–1683) DW	9
<i>Lumbricus rubellus</i>	(394–3873) DW	9
Gastropods, whole, near abandoned mine, soil contained 1377 mg Zn/kg DW		
<i>Arion ater</i>	900 DW	7
<i>Arion hortensis</i>	600 DW	7
<i>Arion subfuscus</i>	1200 DW	7
<i>Deroceras caruanae</i>	1000 DW	7
Lichen, <i>Lasallia papulosa</i>		
Near zinc smelter	2560 DW	10

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Control population	214 DW	10
Isopod, <i>Oniscus asellus</i> , whole		
From soil containing various concentrations of zinc, (mg Zn/kg soil DW)		
<0.3	Max. 150 DW	11
1–10	Max. 350 DW	11
>50	Max. >500 DW	11
Plants, terrestrial	Average 100 DW	114
Woodlouse, <i>Porcellio scaber</i>		
Near metal smelter of maximum soil Zn of 24,900 mg/kg DW, and soil litter of 4150 mg/kg DW		
Hepatopancreas	Max. 13,500 DW	12
Whole	Max. 1500 DW	12
From soil containing various concentrations of Zn (mg Zn/kg soil DW), whole organism		
<0.3	Max. 350 DW	11
1–10	Max. 550 DW	11
>50	Max. >1000 DW	11
		13
PROTOZOANS, MARINE	63–279 DW	
COELENTERATES		
Soft coral, <i>Alcyonium alcyonium</i> , whole	9.6 FW	14
Plumose anemone, <i>Metridium senile</i> , whole	18 FW	14
Various species, whole		
Uncontaminated areas	50 DW	3
Noncontaminated areas	<80 FW; <120 DW	13
Contaminated areas	Max. 603 DW	13
MOLLUSCS, AQUATIC		
Abalones, soft parts	55 (38–100) DW	17
Bivalves		
Kidney granules	10,000–43,320 DW	15
Soft parts	91–660 DW	16
Cephalopods		
Soft parts	81–150 DW; Max. 580 DW	16, 17
Whole	250 DW	3
Chitons, soft parts	290–700 DW	17
Clams, soft parts	81–115 DW; Max. 510 DW	17
Sydney rock oyster, <i>Crassostrea commercialis</i> , soft parts, Southeast Asia	800 (64–1920) DW	18
American oyster, <i>Crassostrea virginica</i> , soft parts		
Chesapeake Bay	3975 (60–12,800) DW	18
Gulf of Mexico	2150 (485–10,000) DW	18
Galveston Bay, Texas; 1992–93	2082 (602–4819) DW	123
South Carolina	2410 (280–6305) DW	18
United States	1018–1641 (204–4000) FW	19
Zebra mussel, <i>Dreissena polymorpha</i> ; soft parts; The Netherlands; 1994; Rhine-Meuse Basin vs. reference location	29–46 FW vs. 15 FW	133
Drills, soft parts	536–3470 DW	17
Gastropods, soft parts	84–763 DW	16

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Limpets, soft parts		
18 species	112 (14–760) DW	17
7 species	196 (86–430) DW	17
Clam, <i>Macoma balthica</i> , adults, San Francisco Bay, soft parts	200–600 DW	20
Mussels, soft parts	109–267 DW; Max. 7700 DW	17
Common mussel, <i>Mytilus edulis</i>		
Soft parts, weight 0.43 g DW		
Visceral mass	34–100 DW	21
Gills and palps	47–94 DW	21
Remainder	46–110 DW	21
Soft parts, weight 0.22 g DW		
Visceral mass	28–112 DW	21
Gills and palps	38–158 DW	21
Remainder	40–130 DW	21
Kidney, Newfoundland		
October 1984	144 (50–427) DW	22
April 1985	828 (94–3410) DW	22
Oyster drill, <i>Ocenebra erinacea</i> , soft parts	1451–2169 DW	23
European flat oyster, <i>Ostrea edulis</i> , soft parts		
Contaminated site	10,560 (4700–12,640) DW	24
Clean site	98 DW	24
Oysters		
Soft parts	1960–7270 DW; Max. 49,000 DW	17
Soft parts	100–271 FW	19
Scallop, <i>Pecten</i> sp.		
Kidney	32,000 DW	17
Kidney granules	120,000 DW	17
Soft parts	200 DW	17
Scallops, soft parts	105–212 DW; Max. 462 DW	17
Green-lipped mussel, <i>Perna viridis</i> , Hong Kong		
Soft parts, 1986–1987	56–134 DW	25
Soft parts, 1986		
March	63–150 DW	26
May	77–94 DW	26
Clam, <i>Pitar morrhuanus</i> , soft parts, near electroplating plant, Rhode Island, 1973	Max. 276 DW	27
Rock oyster, <i>Saccostrea cucullata</i> , soft parts, Hong Kong, 1986		
March	2082–3275 DW	26
May	2210–2863 DW	26
Whelks, soft parts	198 (13–650) DW	17

CRUSTACEANS

Amphipods, marine whole, western British coastal
waters

<i>Orchestia gammarellus</i>	104–392 DW	28
<i>Orchestia mediterranea</i>	120–506 DW	28
<i>Talitrus saltator</i>	178–306 DW	28
<i>Talorchestia deshayesii</i>	199–208 DW	28
Amphipods, <i>Themisto</i> spp., whole	76 (72–81) DW	29
Barnacle, <i>Balanus amphitrite</i> , soft parts	Max. 1937 DW	30
Barnacle, <i>Balanus balanoides</i> , soft parts	1028–3438 FW	31

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Crustaceans, marine		
Northeast Atlantic ocean, July 1985, whole		
Decapods	35–57 DW	32
Euphausiids	44–96 DW	32
Mysids	24–44 DW	32
Soft parts		
Amphipods	73–109 DW	16
Barnacles	690–27,837 DW	16
Barnacles	1050–5140 DW; Max. 113,000 DW	17
Copepods	60–170 DW	16
Copepods	164–177 DW; Max. 1300 DW	17
Crabs	68–102 DW; Max. 340 DW	17
Euphausiids	53–83 DW	16
Isopods	94 DW	16
Shrimps	14–69 DW; Max. 150 DW	17
Various species		
Blood	0.2–87 FW	19
Excretory organs	Max. 29 FW	19
External eggs	24–107 FW	19
Gills	8–69 FW	19
Hepatopancreas	34–169 FW	19
Muscle		
Leg	15–66 FW	19
Abdominal	10–24 FW	19
Shell	5–17 FW	19
Stomach fluid	1–92 FW	19
Ovary	26–82 FW	19
Vas deferens	13–30 FW	19
Urine	Max. 2.2 FW	19
Whole	18–54 FW	19
Hermit crab, <i>Eupagurus bernhardus</i> , whole	282 FW	19
Euphausid, <i>Euphausia superba</i> , whole	68 (42–75) DW	29
Euphausid, <i>Meganyctiphanes norvegica</i> , whole		
Firth of Clyde	43 (27–62) DW	29
Northeast Atlantic Ocean	102 (40–281) DW	29
Euphausiids, whole	13 FW	33
American lobster, <i>Homarus americanus</i>		
Gill	102–126 DW	34
Green gland	114–148 DW	34
Hepatopancreas	70–135 DW	34
Muscle		
Pincer	100–127 DW	34
Tail	80 DW	34
Crayfish, <i>Orconectes virilis</i> , collected 12–150 km distant from metal smelter		
Hepatopancreas		
12 km	190 DW	35
30 km	166 DW	35
150 km	92 DW	35
Digestive tract		
12 km	154 DW	35
30 km	100 DW	35
150 km	111 DW	35

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Muscle		
12 km	93 DW	35
30 km	97 DW	35
150 km	80 DW	35
Grass shrimp, <i>Palaemonetes pugio</i>		
From sediments containing 627 mg Zn/kg DW		
Exoskeleton	58 FW	36
Muscle	55 FW	36
From sediments containing 8 mg Zn/kg DW		
Exoskeleton	18 FW	36
Muscle	30 FW	36
Prawn, <i>Pandalus montagui</i>		
Cuticle	57 DW	37
Eye	70 DW	37
Gill	106 DW	37
Hepatopancreas	30 DW	37
Muscle	57 DW	37
Whole	58 DW	37
Pink shrimp, <i>Penaeus brasiliensis</i> , adults, whole	(47–75) DW; (181–290) FW	38
INSECTS, MARINE, WHOLE	110–197 DW	13
CHAETOGNATHS, WHOLE	76–90 DW	13
ANNELIDS, AQUATIC		
Annelids, marine		
Jaws		
Total	5000–24,000 DW	13
Basal section	1790 DW	13
Distal section	34,950 DW	13
Whole body	22–1564 DW	13
Lugworm, <i>Arenicola marina</i> , whole	1.8 FW	14
Freshwater leech, <i>Erpobdella octoculata</i> , adults, whole body	Upstream (18 µg Zn/L) from zinc-polluted mine waste discharge, whole body content of 1439–1559 DW; reproduction normal. Downstream (180 µg Zn/L), concentration after 19-month exposure was 1932–2432 DW; reproduction impaired	116
Sandworm, <i>Nereis diversicolor</i>		
Head	(843–995) DW	39
Parapodia	(216–413) DW	39
Trunk	(158–218) DW	39
ECHINODERMS		
Various species, whole	Usually 100 DW or lower, frequently >100 DW; Max. 245 FW, 1500 DW	3, 13
TUNICATES, WHOLE	200 DW; Max. 64 FW, 370 DW	3, 13
FISH		
Catostomids, 3 species, Missouri, blood		
Site contaminated with mine tailings	10.9–13.4 FW, 94–119 DW	40
Uncontaminated site	8.7–11.2 FW, 76–86 DW	40

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
White sucker, <i>Catostomus commersoni</i>		
From metals-contaminated lake (400 µg Zn/L)		
Eggs	83–158 DW	41
Larvae	511 DW	41
Ovaries		
Prespawning	114 DW	41
Postspawning	290 DW	41
Testes, postspawning	89 DW	41
From control lake (2.7 µg Zn/L)		
Eggs	69–108 DW	41
Larvae	163 DW	41
Ovaries		
Prespawning	84 DW	41
Postspawning	317 DW	41
Testes, postspawning	163 DW	41
New Brunswick, whole	92–93 DW	42
Nova Scotia, whole	98–122 DW	42
African sharptooth catfish, <i>Clarias gariepinus</i> , age 4–8 years, South Africa, 1988–1989, lake sediments contained 1104 mg Zn/kg DW (595–2189)		
Brain	335 DW	43
Fat	50 DW	43
Gill	177 DW	43
Gonad	126 DW	43
Heart	196 DW	43
Intestine	143 DW	43
Kidney	143 DW	43
Liver	143 DW	43
Muscle	59 DW	43
Spleen	163 DW	43
Vertebrae	75 DW	43
Baltic herring, <i>Clupea harengus</i> , liver	23 FW	14
Freshwater fishes, various species		
Great Lakes		
Whole, less intestines, 4 species	12–20 FW	19
Liver, 10 species	11–48 FW	19
Greece, 1987–1988, muscle, 11 species	7 (3–37) FW	44
United States, nationwide, whole		
1978–1979	25 (8–168) FW	45
1980–1981	24 (9–109) FW	45
1984		
Geometric mean	21.7 FW	121
85th percentile	34.2 FW	121
Maximum	118.4 FW	121
From metals-contaminated (636 µg dissolved Zn/L) Lake, Indiana, whole		
Bowfin, <i>Amia calva</i>	93 DW	46
White sucker, <i>Catostomus commersoni</i>	102 DW; Max. 152 DW	46
Brown bullhead, <i>Ictalurus nebulosus</i>	127 DW; Max. 139 DW	46
Warmouth, <i>Lepomis gulosus</i>	140 DW; Max. 166 DW	46
Orangespot sunfish, <i>Lepomis humilis</i>	248 DW	46
Redear sunfish, <i>Lepomis microlophus</i>	477 DW; Max. 820 DW	46
Largemouth bass, <i>Micropterus salmoides</i>	119 DW; Max. 207 DW	46
Golden shiner, <i>Notemigonus crysoleucas</i>	160 DW; Max. 171 DW	46
Yellow perch, <i>Perca flavescens</i>	160 DW; Max. 171 DW	46
Black crappie, <i>Pomoxis nigromaculatus</i>	123 DW	46

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
From metals-contaminated stream, Missouri, muscle, 5 species	3.1–24 FW	47, 115
Shortfin mako, <i>Isurus oxyrinchus</i> , vertebrae	36 (5–127) DW	48
Marine fishes, various species		
Muscle		
54 species	0–5 FW	19
32 species	5.1–10 FW	19
7 species	10.1–15 FW	19
4 species	15.1–20 FW	19
2 species	20.1–25 FW	19
Whole	80 DW	3
Red Sea, 1980–1982		
Triggerfish, <i>Balistoides viridiscens</i>		
Muscle	66 DW	49
Liver	154 (81–227) DW	49
Ovaries	291 (287–792) DW	49
Surgeonfish, <i>Ctenochaetus strigosus</i> , muscle	29 (11–43) DW	49
Halfbeak, <i>Hemiramphus marginatus</i> , muscle	32 DW	49
Labrids, 3 species, muscle	33 (19–51) DW	49
Lethrinids, <i>Lethrinus</i> spp.		
Muscle	33 (13–112) DW	49
Liver	95 (43–146) DW	49
Ovaries	146 (72–259) DW	49
Testes	152 (141–164) DW	49
Snapper, <i>Lutjanus fulviflamma</i> , muscle	48 (25–70) DW	49
Parrotfish, <i>Scarys gyttatus</i>		
Liver	17 DW	49
Muscle	62 DW	49
Serranids, 4 species		
Muscle	51 (8–112) DW	49
Liver	130 (78–183) DW	49
Rabbitfish, <i>Siganus oramin</i>		
Muscle	55 (18–195) DW	49
Liver	179 (68–611) DW	49
Sparids, 2 species, muscle	56 (34–76) DW	49
Goatfish, <i>Upeneus tragula</i> , muscle	51 (37–68) DW	49
Pacific hake, <i>Merluccius productus</i>		
Muscle	4 (3–6) FW	33
Whole	12 FW	33
Catfish, <i>Mystus gulio</i> , juveniles, whole, India		
From contaminated estuary (100–120 µg Zn/L, 120–145 mg Zn/kg sediment DW)	160–180 DW	50
From uncontaminated estuary (10 µg Zn/L, 30 mg Zn/kg sediment)	15 DW	50
Yellow perch, <i>Perca flavescens</i> , whole		
New Brunswick	81–103 DW	42
Nova Scotia	68–85 DW	42
Blue shark, <i>Prionace glauca</i> , vertebrae	95 (32–210) DW	48
Atlantic salmon, <i>Salmo salar</i>		
Eggs		
Hatchery	20–35 FW	51
Native	19–28 FW	51
Liver, juveniles		
Hatchery	29–41 FW	51
Native	34 FW	51
Muscle	13 DW	52

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Ovaries	166 DW	52
Spines	79–219 DW	52
Stomach contents	78 DW	52
Brook trout, <i>Salvelinus fontinalis</i> , whole		
New Brunswick	87–158 DW	42
Nova Scotia	90–110 DW	42
Atlantic mackerel, <i>Scomber scombrus</i> , liver	31 FW	14
King mackerel, <i>Scomberomorus cavalla</i> , otolith		
Age <1 year	16 DW; Max. 50 DW	53
Age 2 years	11 DW	53
Age 10 years	8 DW	53
Lesser spotted dogfish, <i>Scyliorhinus caniculus</i> , liver	8.7 FW	14
Monkfish, <i>Squatina squatina</i> , liver	8 FW	14
REPTILES		
American alligator, <i>Alligator mississippiensis</i> , eggs (less shell), Florida, 1984	4.9–9.2 FW	54
Leatherback turtle, <i>Dermochelys coriacea</i> ; Mexico; 1992–93; eggshells from eggs incubated in sand containing 58.9 mg Zn/kg DW	11.9 DW; Max. 60.0 DW	124
BIRDS		
Blue-winged teal, <i>Anas discors</i> , Texas, 1983		
Muscle		
Males	13.8 FW	55
Females	11.3 FW	55
Liver		
Autumn	41.4 FW	55
Spring	33.7 FW	55
Mallard, <i>Anas platyrhynchos</i> , liver	54 FW	56
Canvasback, <i>Aythya valisineria</i> , Chesapeake Bay, liver	41 FW	56
Nicobar pigeon, <i>Caloenas nicobarica</i> , zinc-poisoned		
Kidney	2107 DW	57
Liver	3575 DW	57
Ovary	654 DW	57
Cory's shearwater, <i>Calonectris diomedea</i> ; Azores, Portugal; 1992–93; fledglings age 12 weeks		
Kidney	111 (40–194) DW	128
Liver	199 (39–389) DW	128
Turkey vulture, <i>Cathartes aura</i> , California, 1980–81		
Liver	21–44 FW	58
Kidney	16–24 FW	58
Feather	81–110 DW	58
Willet, <i>Catoptrophorus semipalmatus</i> ; 1994; San Diego Bay; sediments vs. stomach contents		
Naval Air Station	22 DW vs. 79 DW	134
Tijuana Slough National Wildlife Refuge	57 DW vs. 170 DW	134
Common raven, <i>Corvus corax</i> , California, 1980–1981		
Liver	14–45 FW	58
Kidney	17–33 FW	58
Feather	110–160 DW	58

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Trumpeter swan, <i>Cygnus buccinator</i> , USA, 7 western states, 1976–87, found dead		
Liver, kidney, femur	96 (61–160) FW	118
Blood	5.2 (3.7–8.8) FW	118
Dutch Wadden Sea		
Knots, 3 species, recently-formed primary feathers		
Juveniles	100–400 DW	59
Adults	Max. 977 DW	59
Geese, 3 species, feather vane	93–164 DW; Max. 330 DW	59
Little egret, <i>Egretta garzetta</i> , France, found dead		
Bone	100 DW	60
Feather	80 DW	60
Gizzard	140 DW	60
Kidney	70 DW	60
Liver	120 DW	60
Lung	50 DW	60
Muscle	70 DW	60
Stomach	65 DW	60
Chicken, <i>Gallus</i> sp.		
Egg yolk	64 DW	61
Kidney	70 DW	61
Liver	69 DW	61
Liver	32 (25–56) FW	62
Pancreas	88 DW	61
Seminal plasma		
Age 30 weeks	9.8 FW	63
Age 60 weeks	9.8–25 FW	63
California condor, <i>Gymnogyps californianus</i> ,		
Dead on collection, 1980–1986		
Nestlings (death from handling shock)		
Liver	22 FW	64
Kidney	17 FW	64
Juveniles (died of cyanide poisoning)		
Liver	33 FW	64
Feather	99–100 DW	64
Subadults (death from lead poisoning)		
Liver	30 FW	64
Kidney	33 FW	64
Feather	85 DW	64
Adults (death from lead poisoning)		
Liver	27–250 FW	64
California, 1980–81, feather	(46–130) DW	58
Kern County, California, 1976		
Liver	49 FW	65
Kidney	16 FW	65
White-tailed eagle, <i>Haliaeetus albicilla</i>		
Blood, clotted	7.5 FW	66
Brain	20 FW	66
Feather	88 DW	66
Femur	284 (175–390) DW	66
Heart	28 (21–39) FW	66
Intestine	50 (27–76) FW	66
Kidney	43 (35–60) FW	66
Liver	68 (38–100) FW	66
Lung	14 (11–17) FW	66

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Muscle	55 (42–80) FW	66
Stomach	25 (20–30) FW	66
Bald eagle, <i>Haliaeetus leucocephalus</i> , egg, 1968		
Wisconsin	30–56 DW; 4–8 FW	67
Maine	32–52 DW; 4–7 FW	67
Florida	36–65 DW; 5–8 FW	67
Glaucous gull, <i>Larus hyperboreus</i>		
Liver	32 (26–47) FW	68
Kidney	46 (37–57) FW	68
Turkey, <i>Meleagris gallopavo</i>		
Laying hens		
Serum	6.9 FW	117
Liver	75 DW	117
Nonlaying hens		
Serum	1.6 FW	117
Liver	39 DW	117
Red-breasted merganser, <i>Mergus serrator</i> , egg, Lake Michigan, 1978	15 (12–20) FW	69
Norway; October–March 1992–95; passerines; liver; adults vs. juveniles		
Greenfinch, <i>Carduelis chloris</i>	67 DW vs. 56 DW	132
Great tit, <i>Parus major</i>	72 DW vs. 69 DW	132
Willow tit, <i>Parus montanus</i>	70 DW vs. 68 DW	132
Marsh tit, <i>Parus palustris</i>	74 DW vs. 68 DW	132
Bullfinch, <i>Pyrrhula</i>	79 DW vs. 66 DW	132
Norway; as above; industrial area vs. subalpine forest		
Tits	68.8 DW vs. 66.8 DW	132
Finches	77.2 DW vs. 65.1 DW	132
Black-crowned night-heron, <i>Nycticorax nycticorax</i> , liver, pre fledglings, 1979		
Massachusetts	602 (482–784) DW	70
North Carolina	649 (479–857) DW	70
Rhode Island	503 (246–885) DW	70
Osprey, <i>Pandion haliaetus</i>		
Eastern United States, 1975–1982, liver		
Iowa	98 FW	71
Maryland	19–34 FW	71
Massachusetts	89 FW	71
New Jersey	63–120 FW	71
North Carolina	69 FW	71
South Carolina	73 FW	71
Wisconsin	59 FW	71
Virginia	27–150 FW	71
Eastern United States, 1964–1973, liver		
Florida	(27–36) FW	56
Maryland	(18–93) FW	56
New Jersey	22 FW	56
Ohio	60–80 FW	56
All ospreys, liver		
Immature	67 FW	56
Adults	38 FW	56
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg contents		
South Carolina, 1971–72	6.4 (5.5–8.0) FW	119
Florida, 1969–70	6.4 (4.3–8.3) FW	119

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Liver		
Found dead		
South Carolina, 1973	26 FW	119
Florida, 1972–73	41–50 FW	119
Georgia, 1972	33 FW	119
Shot		
Florida, 1970	32–55 FW	119
South Carolina, 1973	31–38 FW	119
Greater flamingo, <i>Phoenicopterus ruber</i>		
Bone	123 (103–145) DW	60, 72
Feather		
Inner barbs	66 (38–105) DW	60, 72
Outer barbs	101 (45–190) DW	60, 72
Kidney	115 (90–167) DW	60, 72
Liver	758 (525–963) DW	60, 72, 73
Lung	43 (33–56) DW	60, 72
Muscle	53 (38–78) DW	60, 72
Kittiwake, <i>Rissa tridactyla</i> ; nestlings; Germany; 1992–94; age 1 day vs. age 21–40 days		
Brain	69 DW vs. 66 DW	122
Feather	79 DW vs. 116 DW	122
Kidney	104 DW vs. 120 DW	122
Liver	66 DW vs. 111 DW	122
Seabirds		
Albatrosses, 3 species		
Liver	(29–86) FW	68
Kidney	(31–65) FW	68
Fulmars, 2 species		
Liver	36–95 FW	68
Kidney	32–96 FW	68
Penguins, 4 species		
Liver	(27–73) FW	68
Kidney	(25–71) FW	68
Petrels, 7 species		
Liver	(28–81) FW	68
Kidney	(15–78) FW	68
Seabirds		
Liver, 11 species	Means 108–186 DW	135
3 species		
Brain, lung, heart, gonad, muscle, skin, gall bladder, uropygial gland, stomach, feather, trachea, esophagus	<100 DW	135
Intestine, liver, spleen, kidney, bone, eyeball	101–200 DW	135
Pancreas	208 DW	135
Shearwaters, 2 species		
Liver	(28–54) FW	68
Kidney	(27–88) FW	68
Skuas, 3 species		
Liver	(21–51) FW	68
Kidney	(22–53) FW	68
South Atlantic Ocean, adults, 15 species		
Kidney	28–63 (15–88) FW	74
Liver	22–67 (18–86) FW	74
Spain, infertile eggs, 1985–1986		
Golden eagle, <i>Aquila chrysaetos</i>	8.4 (5.5–11.9) FW	75
Buzzard, <i>Buteo buteo</i>	14 FW	75

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
White stork, <i>Ciconia ciconia</i>	9.8 (6.2–19.2) FW	75
Peregrine, <i>Falco peregrinus</i>	11.8 (8.8–16.7) FW	75
Booted eagle, <i>Hieraetus pennatus</i>	9.4 (7.7–13.0) FW	75
Black kite <i>Milvus migrans</i>	12.6 (6.4–29.4) FW	75
Common blackbird, <i>Turdus merula</i> , from metals-contaminated area (1750 mg Zn/kg DW soil), feathers of various age (days), feathers washed or unwashed before analysis		
4 days, unwashed	100 DW	76
400 days, unwashed	546 DW	76
26 days, washed	90 DW	76
150 days, washed	100 DW	76
400 days, washed	162 DW	76
Hoopoe, <i>Upupa epops</i> nestling feathers, age in days		
7	200 DW	77
21	600 DW	77
35	1000 DW	77
Waterbirds; lower Laguna Madre, Texas; 1993–94; 4 species; egg contents	9.2–13.4 (7.2–21.0) FW	129
MAMMALS		
Antelopes, zoo animals, 7 species, blood serum	4.6–9.4 (1.9–12.9) FW	78
Cattle, cow, <i>Bos</i> spp.		
Brain, fetus	50–86 DW	79
Feces		
Normal	220 DW	57
Zinc-poisoned	8740 DW	57
Food items		
Cereal grains, normal	20–30 DW	80
Grasses, normal	25–60 DW	80
Turnips, beets, chicory roots, potatoes	67–390 DW	80
Hair		
Distance from Czechoslovakian power plant		
6 km	167 (114–199) FW	81
26 km	32 (21–43) FW	81
Heart, fetus	78–160 DW	79
Kidney		
Adult	92–133 DW	79
Age 2+ years	16 (13–17) FW	82
Fetus	83–251 DW	79
Normal	18 (11–56) FW; 80 DW	57, 82
Zinc-poisoned	670 DW	57
Liver		
Adult	116–150 DW	79
Age 2+ years	40 (27–49) FW	82
Fetus	548–703 DW	79
Normal	135 DW	57
Zinc-poisoned	2000 DW	57
Milk, days postpartum		
0	21 FW	83
1	12 FW	83
30	6 FW	83
150	4 FW	83
Muscle, Age 2+ years	49 (28–80) FW	82

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Dog, <i>Canis familiaris</i>		
Serum		
Normal	1.7 (0.6–2.0) FW	84
Zinc-poisoned	29 FW	84
Seminal plasma	1750 DW	85
Spermatozoa		
Ejaculated	1040 DW	85
Nonejaculated	150–180 DW	85
Goat, <i>Capra</i> sp., milk, days postpartum		
0	17–25 FW	83
1	8–15 FW	83
90	5–6 FW	83
150	3–5 FW	83
Red deer, <i>Cervus elephas</i> , Germany		
Kidney	131 DW	86
Kidney cortex	33 (20–184) FW	87
Liver	111 DW	86
Bank vole, <i>Clethrionomys glareolus</i>		
Diet		
Spring	56–70 DW	88
July–December	37–43 DW	88
Bone	145–199 DW	88
Heart	69–74 DW	88
Kidney	79–91 DW	88
Liver	78–103 DW	88
Muscle	44–51 DW	88
Testes		
December–September	126–163 DW	88
October–November	ND	88
Hooded seal, <i>Cystophora cristata</i> , liver	57 FW	89
Indian elephant, <i>Elephas maximus</i> , serum		
Young, age <15 years	2.0 FW	90
Adult females	2.8 FW	90
Big brown bat, <i>Eptesicus fuscus</i> , captive colony, guano	340 DW	91
Horse, <i>Equus caballus</i>		
Near zinc smelter vs. control location		
Kidney	150 DW vs. 17 DW	92
Liver	402 DW vs. 23 DW	92
Pancreas	788 DW vs. 7 DW	92
Serum	2.65 FW vs. 0.8–1.2 FW	92
Kidney cortex	41 FW	87
Plasma, mares, Australia		
All	0.5–1.2 FW	93
Thoroughbreds	0.47 FW	94
Farm horses		
Pregnant	0.52 FW	94
Lactating	0.44 FW	94
Steller sea lion, <i>Eumetopias jubata</i>		
Brain	(33–51) DW	95
Heart	(94–101) DW	95
Kidney	(99–202) DW	95
Liver	(102–247) DW	95
Lung	(42–69) DW	95
Muscle	(90–140) DW	95

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Pancreas	(78–262) DW	95
Spleen	(56–117) DW	95
Atlantic pilot whale, <i>Globicephala melaena</i>		
Newfoundland, Canada, stranded, 1980–1982		
Blubber	1.5 (0.6–3.0) DW	96
Kidney	99 (58–139) DW	96
Liver	234 (68–716) DW	96
Muscle	62 (38–80) DW	96
Gorilla, <i>Gorilla gorilla</i> , captives, plasma	2.4 (0.9–7.3) FW	97
Gray seal, <i>Halichoerus grypus</i>		
Blubber	5 FW	14
Kidney	37 FW	14
Liver	84 FW	14
Muscle	43 FW	14
Human, <i>Homo sapiens</i>		
Diet		
Protein-rich foods (meat, seafood)	10–50 FW	113
Grains	10–100 FW	113
Vegetables, fruits	<5 FW	113
Erythrocytes	10.1–13.4 FW	98
Hair	>105 FW	98
Milk	3 FW	113
Plasma	0.7–1.6 FW	97, 98
Prostate	100 FW	113
Semen	100–350 FW	19
Skin	20–1000 DW	19
White-beaked dolphin, <i>Lagenorhynchus albirostris</i> , Newfoundland, Canada, ice-entrapped, 1980–1982, 2–6 years old		
Kidney	85 (68–112) DW	96
Liver	100 (43–136) DW	96
Muscle	53 (36–89) DW	96
European hare, <i>Lepus europaeus</i> ; Finland; 1980–82 vs. 1992–93		
Industrial area		
Kidney	36 FW vs. 29 FW	130
Liver	47 FW vs. 37 FW	130
Muscle	23 FW vs. 24 FW	130
Northern Finland (rural area)		
Kidney	31 FW vs. 29 FW	130
Liver	39 FW vs. 43 FW	130
Muscle	24 FW vs. 34 FW	130
Rhesus monkey, <i>Macaca mulatta</i> , plasma	0.66–0.98 FW	99
Marine mammals		
Pinnipeds, 9 species		
Liver	(27–97) FW; (123–406) DW	68
Kidney	(11–78) FW; (146–353) DW	68
Muscle	(14–49) FW	68
Cetaceans, 9 species		
Liver	(18–109) FW	68
Kidney	(4–86) FW	68
Muscle	(7–51) FW	68
Sirenians		
Liver	(58–1101) FW	68

**Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)**

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Kidney	(14–54) FW	68
Muscle	(8–28) FW	68
Southeastern bat, <i>Myotis austroriparius</i> , Florida, 1981–1983, liver		
Near battery salvage plant	31 (27–35) FW	91
Noncontaminated site	28 (26–30) FW	91
Gray bat, <i>Myotis grisescens</i> , Florida, 1981–1983, guano		
Near battery salvage plant	640 DW	91
Distant sites	390–530 DW	91
Mule deer, <i>Odocoileus hemionus</i> , Montana		
Kidney	97 FW	86
Liver	113 FW	86
White-tailed deer, <i>Odocoileus virginianus</i>		
Illinois, liver	70 DW	86
Pennsylvania		
Various distances from zinc smelter		
<8 km		
Feces	577 (185–1797) DW	86
Kidney	310 (211–454) DW	86
Liver	167 (137–205) DW	86
10–20 km		
Feces	574 (1384) DW	86
Kidney	274 (212–355) DW	86
Liver	167 (137–205) DW	86
>100 km		
Feces	185 (77–445) DW	86
Kidney	145 (103–205) DW	86
Liver	132 (95–182) DW	86
Sheep, <i>Ovis</i> sp., kidney	22 (14–38) FW	62
Ringed seal, <i>Phoca hispida</i>		
Liver	176 (121–576) DW	100
Kidney	209 (104–441) DW	100
Muscle	79 (52–135) DW	100
Deer mouse, <i>Peromyscus maniculatus</i> ; Vancouver Island, British Columbia; near abandoned copper mine vs. reference site		
Soil	81 DW vs. 80 DW	131
Bone	190 DW vs. 180 DW	131
Kidney	16 DW vs. 16 DW	131
Liver	100 DW vs. 80 DW	131
Stomach contents	150 DW vs. 68 DW	131
Baikal seal, <i>Phoca sibirica</i> ; Lake Baikal; 1992		
Kidney	34 (16–61) FW	125
Liver	42 (24–100) FW	125
Muscle	20 (9–40) FW	125
Harbour porpoise <i>Phocoena phocoena</i>		
Blubber	4 FW	14
Liver	37 FW	14
Muscle	22 FW	14
Dall's porpoise, <i>Phocoenoides dalli</i>		
Adults		
Bone, skin	270–296 FW	101
Heart, liver, pancreas, kidney, whole body	25–51 FW	101
Brain, lung, testes	11–20 FW	101
Blubber, blood, muscle	4–9 FW	101

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
 (Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Fetus		
Liver	82 FW	101
Other tissues	<6 FW	101
Rat, <i>Rattus</i> sp.		
Spermatozoa		
Ejaculated	890 DW	85
Nonejaculated	860 DW	85
Striped dolphin, <i>Stenella coeruleoalba</i>		
Blubber	16 FW	14
Muscle	11 FW	14
Pig, <i>Sus</i> spp., adults		
Kidney	22 (16–33) FW	62, 82
Liver	74 (28–160) FW	82
Muscle	24 (8–53) FW	82
Bottlenose dolphin, <i>Tursiops truncatus</i>		
Blubber	20 FW	14
Muscle	11 FW	14
South Carolina; found stranded; liver	57 (9–271) FW	127
Florida; found stranded; 1990–94		
Kidney	114 (86–176) DW	126
Liver	263 (80–722) DW	126
Muscle	110 (60–185) DW	126
Polar bear, <i>Ursus maritimus</i>		
Kidney	33 (20–49) FW	120
Liver	58–63 (33–100) FW	68, 120

INTEGRATED STUDIES

Electrical transmission towers (corroded, galvanized), Ontario, Canada		
Soils		
Near towers	11,480 DW	102
1 km	10,431 DW	102
2 km	10,869 DW	102
5 km	362 DW	102
10 km	160 DW	102
25–50 km	54–70 DW	102
Plants, 5 species, roots and shoots		
Near towers	Max. 1535 DW	102
1–5 km	Max. 297 DW	102
12–25 km	Max. 55 DW	102
Estuary, Calcasieu River, Louisiana		
Invertebrates		
Periphyton, whole	264 (49–1300) DW	103
Zooplankton, whole	330 (31–3550) DW	103
Ctenophores, whole	(31–64) DW	103
Hooked mussel, <i>Brachidontes exustus</i> , soft parts	61 (39–86) DW	103
American oyster, <i>Crassostrea virginica</i> , soft parts	3300 (1000–7794) DW	103
Blue crab, <i>Callinectes sapidus</i> , muscle	112 (106–213) DW	103
Brown shrimp, <i>Penaeus aztecus</i> , whole	(46–61) DW	103
White shrimp, <i>Penaeus setiferus</i> , whole	(44–62) DW	103
Fish, muscle		
Gulf menhaden, <i>Brevoortia patronus</i>	115 DW	103
Gizzard shad, <i>Dorosoma cepedianum</i>	25 DW	103
Threadfin shad, <i>Dorosoma petenense</i>	29 DW	103

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Blue catfish, <i>Ictalurus furcatus</i>	35 (16–61) DW	103
Spot, <i>Leiostomus xanthurus</i>	22 (17–31) DW	103
Spotted gar, <i>Lepisosteus oculatus</i>	(22–239) DW	103
Atlantic croaker, <i>Micropogonias undulatus</i>	31 (15–95) DW	103
White mullet, <i>Mugil curema</i>	36 DW	103
Southern flounder, <i>Paralichthys lethostigma</i>	24 DW	103
Flotation mill (Pb/Zn), Greenland		
Near outfall		
Suspended particulates	11,600 (1058–25,700) FW	104
Sediments	Max. 6799 FW	104
Water	0.035 FW	104
Mussel, <i>Mytilus edulis</i> , soft parts	502 (340–813) FW	104
Seaweed, <i>Fucus disticus</i>	300 FW	104
Control site		
Suspended particulates	123 FW	104
Sediments	129 FW	104
Water	0.0002 FW	104
Mussel	100 FW	104
Seaweed	8 FW	104
Freshwater lake, India		
Water	0.2 FW	105
Sediment	540 FW	105
Phytoplankton	11–15 FW	105
Zooplankton	60 FW	105
Fish, whole	10 FW	105
Grassland ecosystem		
On a revegetated mine tailings dam		
Soil (1–8 cm depth)	1915–2160 DW	106
Vegetation		
Live	157–201 DW	106
Dead	303–646 DW	106
Invertebrates, whole		
Herbivores	355–746 DW	106
Carnivores	403–515 DW	106
Detritivores	769–1275 DW	106
Field vole, <i>Microtus agrestis</i>		
Bony tissues	183–226 DW	106
Soft tissues	160–281 DW	106
Common shrew, <i>Sorex araneus</i>		
Bony tissues	438–547 DW	106
Soft tissues	160–281 DW	106
Control grassland ecosystem		
Soil (1–8 cm depth)	52–62 DW	106
Vegetation		
Live	23–41 DW	106
Dead	24–56 DW	106
Invertebrates, whole		
Herbivores	133–299 DW	106
Carnivores	277–372 DW	106
Detritivores	248–1095 DW	106
Field vole		
Bony tissues	178–249 DW	106
Soft tissues	53–121 DW	106
Common shrew		
Bony tissues	347–420 DW	106
Soft tissues	145–204 DW	106

Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Lead smelter, South Australia, marine outfall, whole organisms		
Samples collected 2.5–5.2 km from source		
Sediments	1270 DW; Max. 16,700 DW	107
Seagrasses, 5 species	823 DW; Max. 3540 DW	107
Crustaceans, 5 species	148 DW; Max. 767 DW	107
Tunicate, <i>Polycarpa peduculata</i>	153 DW; Max. 345 DW	107
Bivalve molluscs, 5 species	4880 DW; Max. 20,300 DW	107
Carnivorous fishes, 8 species	163 DW; Max. 440 DW	107
Omnivorous fishes, 3 species	222 DW; Max. 619 DW	107
Herbivorous fish, six-lined trumpeter, <i>Siphamia cephalotes</i>	310 DW; Max. 480 DW	107
Samples collected 18–18.8 km from outfall		
Sediments	21 DW	107
Seagrasses	72 DW	107
Crustaceans	68 DW	107
Tunicate	98 DW	107
Bivalve molluscs	2590 DW	107
Carnivorous fishes	78 DW	107
Omnivorous fishes	105 DW	107
Herbivorous fish	97 DW	107
Metals-contaminated forest vs. control location, Poland		
Yellow-necked field mouse, <i>Apodemus flavicollis</i>		
Liver	119 DW vs. 109 DW	108
Kidney	220 DW vs. 87 DW	108
Hair	179 DW vs. 122 DW	108
Carcass	109 DW vs. 98 DW	108
Bank vole, <i>Clethrionomys glareolus</i>		
Liver	120 DW vs. 116 DW	108
Kidney	156 DW vs. 143 DW	108
Hair	243 DW vs. 169 DW	108
Carcass	148 DW vs. 153 DW	108
Old-field community, Ohio, treated with sewage sludge for 10 consecutive years		
Treated area		
Sludge	866 DW	109
Soil	107 DW	109
Perennial plant, <i>Rubus frondosus</i>	41 DW	109
Giant foxtail, <i>Setaria faberii</i>	97 DW	109
Earthworm, <i>Lumbricus rubellus</i>	615 DW	109
Bluegrass, <i>Poa</i> spp.	85 DW	109
Japanese brome, <i>Bromus japonicum</i>	80 DW	109
Control area		
Perennial plant	14 DW	109
Bluegrass	35 DW	109
Japanese brome	35 DW	109
Zinc smelter, Palmerton, Pennsylvania		
Site 2 km downwind of smelter		
Soil	24,000 DW	110
Foliage, 8 species	660 DW	110
Acorns and berries, 4 species	59 DW	110
Fungi, 4 species	320 DW	110
Moths, 6 species	250–480 DW	110
Beetle, <i>Dendroides</i> sp.	1450 DW	110
Caterpillar, <i>Porthetria dispar</i>	280 DW	110

**Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)**

Taxonomic Group, Organism, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Birds, 10 species, carcasses	140 (93–210) DW	110
White-footed mouse, <i>Peromyscus leucopus</i> , carcass	192 DW	110
Short-tailed shrew, <i>Blarina brevicauda</i> , carcass	377 DW	110
Site 10 km upwind of smelter		
Soil	960 DW	110
Foliage	118 DW	110
Acorns and berries	27 DW	110
Fungi	120 DW	110
Moths, 9 species	140–340 DW	110
Beetles, 2 species	470 DW	110
Caterpillar, <i>P. dispar</i>	170 DW	110
Birds, 10 species, carcasses	120 (78–170) DW	110
White-footed mouse, carcass	145 DW	110
Short-tailed shrew	201 DW	110
Zinc smelter, Peru, South America, 1980–1984		
Soil, km from smelter		
1	575 DW	111
13	183 DW	111
27	154 DW	111
33	52 DW	111
35–55	16–29 DW	111
Domestic sheep, <i>Ovis aries</i> , liver, km from smelter		
13	305 DW	111
29	165 DW	111
>100	77 DW	111
Zinc smelters, various		
Soils	Max. 80,000 DW	112
Trees, foliage	Max. 4500 DW	112

^a Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

^b 1, Mann et al. 1989; 2, Mason and Macdonald 1988; 3, Young et al. 1980; 4, Brix and Lyngby 1982; 5, Veleminsky et al. 1990; 6, Greville and Morgan 1989a; 7, Greville and Morgan 1989; 8, Beyer and Cromartie 1987; 9, Morgan and Morgan 1988; 10, Nash 1975; 11, Hopkin et al. 1989; 12, Hopkin et al. 1986; 13, Eisler 1981; 14, Morris et al. 1989; 15, Sullivan et al. 1988; 16, White and Rainbow 1985; 17, Sprague 1986; 18, Presley et al. 1990; 19, NAS 1979; 20, Cain and Luoma 1986; 21, Amiard et al. 1986; 22, Lobel 1986; 23, Amiard-Triquet et al. 1988; 24, Bryan et al. 1987; 25, Chan 1988a; 26, Chu et al. 1990; 27, Eisler et al. 1978; 28, Weeks and Moore 1991; 29, Rainbow 1989; 30, Anil and Wagh 1988; 31, Walker et al. 1975; 32, Ridout et al. 1989; 33, Cutshall et al. 1977; 34, Waiwood et al. 1987; 35, Bagatto and Alikhan 1987; 36, Khan et al. 1989; 37, Nugegoda and Rainbow 1988b; 38, Shrestha and Morales 1987; 39, Fernandez and Jones 1989; 40, Schmitt et al. 1984; 41, Munkittrick and Dixon 1989; 42, Peterson et al. 1989; 43, Bezuidenhout et al. 1990; 44, Lazos et al. 1989; 45, Lowe et al. 1985; 46, Murphy et al. 1978; 47, Schmitt and Finger 1987; 48, Vas et al. 1990; 49, Hanna 1989; 50, Joseph 1989; 51, Craik and Harvey 1988; 52, Poston and Ketola 1989; 53, Grady et al. 1989; 54, Heinz et al. 1991; 55, Warren et al. 1990; 56, Wiemeyer et al. 1980; 57, Zee et al. 1985; 58, Wiemeyer et al. 1986; 59, Goede 1985; 60, Cosson et al. 1988; 61, Williams et al. 1989; 62, Ellen et al. 1989; 63, Blesbois and Mauger 1989; 64, Wiemeyer et al. 1988; 65, Wiemeyer et al. 1983; 66, Falandysz et al. 1988; 67, Krantz et al. 1970; 68, Thompson 1990; 69, Haseltine et al. 1981; 70, Custer and Mulhern 1983; 71, Wiemeyer et al. 1987; 72, Cosson et al. 1988a; 73, Cosson 1989; 74, Muirhead and Furness 1988; 75, Hernandez et al. 1988; 76, Weyers et al. 1988; 77, Kaur 1989; 78, Vahala et al. 1989; 79, Gooneratne and Christensen 1989; 80, Binnerts 1989; 81, Pisa and Cibulka 1989; 82, Jorhem et al. 1989; 83, Park and Chukwa 1989; 84, Latimer et al. 1989; 85, Saito et al. 1967; 86, Sileo and Beyer 1985; 87, Holterman et al. 1984; 88, Włostowski et al. 1988; 89, Nielsen and Dietz 1990; 90, Sreekumar and Nirmalan 1989; 91, Clark et al. 1986; 92, Gunson et al. 1982; 93, Auer et al. 1988b; 94, Auer et al. 1988a; 95, Hamanaka et al. 1982; 96, Muir et al. 1988; 97, McGuire et al. 1989; 98, Casey and Hambidge 1980; 99, Keen et al. 1989; 100, Wagemann 1989; 101, Fujise et al. 1988; 102, Jones and Burgess 1984; 103, Ramelow et al. 1989; 104, Loring and Asmund 1989; 105, Prahalad and Seenayya 1989; 106, Andrews et al. 1989; 107, Ward et al. 1986; 108, Sawicka-Kapusta et al. 1987; 109, Levine et al. 1989; 110, Beyer et al. 1985; 111, Reif et al. 1989; 112, Buchauer 1971; 113, Elinder 1986;

**Table 9.4 (continued) Zinc Concentrations in Field Collections of Representative Plants and Animals
(Concentrations are in mg Zn/kg fresh weight [FW], or dry weight [DW].)**

114, Vymazal 1986; 115, Dwyer et al. 1988; 116, Willis 1985a; 117, Richards 1989; 118, Blus et al. 1989; 119, Blus et al. 1977; 120, Norheim et al. 1992; 121, Schmitt and Brumbaugh 1990; 122, Wenzel et al. 1996; 123, Jiann and Presley 1997; 124, Vazquez et al. 1997; 125, Watanabe et al. 1996; 126, Wood and Van Vleet 1996; 127, Beck et al. 1997; 128, Stewart et al. 1997; 129, Mora 1996; 130, Venalainen et al. 1996; 131, Laurinolli and Bendell-Young 1996; 132, Hogstad 1996; 133, Hendricks et al. 1998; 134, Hui and Beyer 1998; 135, Kim et al. 1998.

9.6 ZINC DEFICIENCY EFFECTS

9.6.1 General

Zinc is important in the metabolism of proteins and nucleic acids and is essential for the synthesis of DNA and RNA. Zinc deficiency has been reported in humans and a wide variety of plants and animals — with severe effects on all stages of reproduction, growth, and tissue proliferation in the young. In early gestation, zinc deficiency may cause severe congenital abnormalities. Later in gestation, deficiency can cause growth inhibition and brain growth impairment, leading to altered behavioral development after birth. Feeding a low-zinc diet to lactating dams produces signs of zinc deficiency in suckling pups. In humans, zinc deficiency is associated with delayed sexual maturation in adolescent males; poor growth in young children; impaired growth of hair, skin, and bone; disrupted Vitamin A metabolism; and abnormal taste acuity, hormone metabolism, and immune function.

9.6.2 Terrestrial Plants

Zinc deficiencies in citrus groves in California, pecan trees in Texas, and various crops in Australia, have resulted in large crop losses (Vallee 1959). Applications of zinc salts were effective under acidic soil conditions, but neutral or alkaline soils rendered zinc salts insoluble and zinc therapy ineffective. Sprays of zinc salts applied to leaves, or injections into tree trunks overcame the problems of soil solubility and have generally been successful (Vallee 1959). Zinc is usually bound strongly in plants, particularly in grains, markedly decreasing its availability to animal consumers. Binding is attributed mainly to high content of phytate, and also to high levels of fiber, hemicelluloses, and amino acid-carbohydrate complexes (Casey and Hambidge 1980). Whole-grain cereals and legumes are considered rich sources of zinc (Casey and Hambidge 1980).

9.6.3 Aquatic Organisms

Nutritional zinc deficiency is rare in aquatic organisms (Spear 1981), although reports are available of experimentally induced zinc deficiency in algae, sponges, daphnids, echinoderms, fish, and amphibians.

Experimental zinc deficiency in euglenoids (*Euglena gracilis*) was associated with arrested growth and abnormal cell differentiation and development, leading to extensive teratological abnormalities. Zinc-deprived *Euglena* survived for extended periods through decreased metabolism (Falchuk et al. 1985; Falchuk 1988). Marine algae stopped growing when ambient zinc concentrations fell below 0.7 µg/L; also, zinc-deficient cultures of freshwater algae were unable to metabolize silicon (Vymazal 1986).

A freshwater sponge (*Ephydatia fluviatilis*) grew normally at a concentration of 0.65 µg Zn/L, but growth was reduced at lower concentrations tested (Francis and Harrison 1988). Daphnids (*Daphnia pulex*, *Daphnia magna*) reared for six brood cycles in zinc-free water showed reduced survival, inhibited reproduction, and cuticle damage (Keating and Caffrey 1989). Zinc is important

in pH regulation of sperm of marine invertebrates. Zinc reduction in semen to <6.5 µg/L adversely affected sperm pH and motility in sea urchins (*Strongylocentrotus purpuratus*, *Lytechinus pictus*), horseshoe crab (*Limulus polyphemus*), and starfish (Clapper et al. 1985a, 1985b).

Rainbow trout (*Oncorhynchus mykiss*) fry fed diets containing 1 to 4 mg Zn/kg ration have poor growth, increased mortality, cataracts, and fin erosion; supplementing the diet to 15 to 30 mg Zn/kg alleviates these signs (Spry et al. 1988). Spry et al. (1988) also fed rainbow trout fry diets containing 1, 90, or 590 mg Zn/kg ration and simultaneously exposed them to a range of waterborne zinc concentrations of 7, 39, 148, or 529 µg Zn/L. After 16 weeks, the 7 µg Zn/L plus 1 mg/kg diet group showed clear signs of deficiency, including a significantly reduced plasma zinc concentration (which was evident as early as the first week of exposure), reduced growth (with no growth after week 12), decreased hematocrit, and reduced plasma protein and whole-body zinc concentration. Elevating waterborne zinc to 39 or 148 µg Zn/L partially corrected the deficiency, but did not restore plasma or whole-body zinc to levels seen initially or in fish raised for 16 weeks on a zinc-adequate diet of 90 mg Zn/kg ration. There were no toxic effects at any other dietary–waterborne zinc mixture. It was concluded that zinc uptake from water was independent of uptake from diet, since at any dietary zinc level an increase in the waterborne zinc resulted in an increase in whole-body zinc. In freshwater, where waterborne concentrations of <10 µg Zn/L are most commonly encountered, waterborne zinc contributions to whole-body zinc loadings are likely to be insignificant. In cases where dietary zinc was adequate (i.e., 90 mg Zn/kg ration), the contribution of waterborne zinc was significant in the case of rainbow trout (Spry et al. 1988). In marine teleosts, diet is the major zinc source when seawater contained <15 µg Zn/L; at higher ambient concentrations of 600 µg Zn/L, waterborne zinc contributed up to 50% of the total body zinc burden (as quoted in Spry et al. 1988).

Experimentally produced zinc deficiency in toad (*Bufo arenarum*) embryos resulted in adults with abnormal ovarian development, altered meiotic and ovulation processes, and embryos with a high incidence of congenital malformations (Herkovits et al. 1989).

9.6.4 Birds

Zinc deficiency in chickens, turkeys, and Japanese quail is characterized by low survival, reduced growth rate and food intake, poor feathering, shortening and thickening of the long bones of legs and wings, reduced egg production and hatchability, skeletal deformities in embryos, an uncoordinated gait, reduced bone alkaline phosphatase activity, and increased susceptibility to infection (Blamberg et al. 1960; NAS 1979; Prasad 1979; Apgar 1985; O'Dell et al. 1989; Stahl et al. 1989a).

Laying hens (*Gallus* sp.) had low egg hatchability on diets that contained 6 mg Zn/kg, and produced chicks that were weak and poorly feathered; these chicks usually died within a few days on 8 to 9 mg Zn/kg diets (Blamberg et al. 1960). Zinc-deficient chicks (13 to 16 mg Zn/kg DW diet for 4 weeks) had pathological defects in epiphyseal cartilage; no interference with calcification was noted in controls fed diets containing 93 to 96 mg Zn/kg feed (Westmoreland and Hoekstra 1969). Pullets fed diets containing 28 mg Zn/kg for 4 months, then 4 mg Zn/kg ration for 4.5 months produced few hatchable eggs after 4 months. Prevalent malformations included faulty trunk and limb development, missing vertebrae, missing limbs and toes, abnormal brain morphology, small eyes, and skeletal malformations (Blamberg et al. 1960). Most zinc deficiency effects were reversed by increasing dietary zinc concentrations to 96 to 120 mg/kg (Blamberg et al. 1960).

Japanese quail fed an excess of zinc (25 to 30 mg Zn/kg diet) during their first week of life were protected during a subsequent period of zinc deprivation (1 mg Zn/kg diet for 1 week). Birds that received an initial intake of zinc in excess of requirements grew significantly better than those receiving a minimal amount of zinc. Japanese quail may store excess zinc in bones; this zinc store may become available during a subsequent period of zinc deprivation, especially during a period of rapid bone growth (Harland et al. 1975), but this requires verification.

Egg production constitutes a major loss of zinc and other trace metals by the laying hen. Vitellogenin mediates the transfer of zinc from liver to the maturing oocyte, ultimately resulting in deposition into yolk of the newly formed egg (Richards 1989). More research seems needed on the role of zinc in avian reproduction.

9.6.5 Mammals

Compared with zinc toxicity, zinc deficiency is a much more frequent risk to mammals (Leonard and Gerber 1989). Zinc is required in all stages of the cell cycle, and deficiency adversely affects metabolism of DNA, RNA, proteins, and activity of carbonic anhydrase, lactic dehydrogenase,mannosidase, and other enzymes (NAS 1979; Prasad 1979, 1980; Apgar and Everett 1988). In zinc deficiency, the activity of various zinc-dependent enzymes is reduced in testes, bone, esophagus, and kidney of rats, and alkaline phosphatase activity is reduced in bone and plasma from zinc-deficient rats, pigs, and cows (Prasad 1979; Vergnes et al. 1990). Deficiency leads to loss of appetite and taste, skin disturbances, slow wound healing, impaired brain development, deficient immune system, and disrupted water metabolism (Binnerts 1989). Zinc deficiency adversely affects testicular function in humans and animals and seems to be essential for spermatogenesis and testosterone metabolism (Prasad 1980). Zinc deficiency in young men with very low zinc intakes resulted in testicular lesions and reduced accessory gland weights, due primarily to reduced food intake and growth (Apgar 1985). Zinc deficiency during pregnancy has produced low birth weight, malformations, and poor survival in rat, lamb, and pig; the role of zinc in human reproductive problems is still unclear (Apgar 1985). Zinc-deficient diets for ruminants and small laboratory animals usually contain <1 mg Zn/kg ration, although rats show deficiency at <12 mg Zn/kg ration (Elinder 1986). Zinc deficiency has been documented in humans, small laboratory animals, domestic livestock, mink, and monkeys. Signs of severe zinc deficiency in mammals include decreased food intake, growth cessation, fetal malformations, testicular atrophy, swelling of feet, excessive salivation, dermal lesions, parakeratosis of the esophagus, impaired reproduction, hair loss, unkempt appearance, stiffness, abnormal gait, skin and organ histopathology, and hypersensitivity to touch (NAS 1979; Jameson 1980; Gupta et al. 1988; Elinder 1986; O'Dell et al. 1989). Selected examples of zinc deficiency in various species follow.

Zinc deficiency in humans is rare and is usually associated with severe malabsorption, parenteral alimentation lacking zinc, or geophagia (Sternlieb 1988). Symptoms of zinc deficiency depend, in part, on age, acuteness of onset, duration and severity of the zinc depletion, and the circumstances in which deficiency occurs. Many of the features of zinc deficiency observed in humans are similar to those seen in zinc-deficient animals (Casey and Hambidge 1980). Simple nutritional deficiency due to marginal zinc intake may be common, even in the United States (Casey and Hambidge 1980). Factors contributing to zinc deficiency include inadequate dietary intake (protein-calorie malnutrition), decreased availability (high fiber/phytate diets), decreased absorption, excessive losses (increased sweating, burns), increased requirements (rapid growth, pregnancy, lactation), as well as old age, alcoholism, and possible genetic defects (Casey and Hambidge 1980). Zinc deficiency may also occur as a result of liver or kidney disease, gastrointestinal disorders, skin disorders, parasitic infections, diabetes, and genetic disorders such as sickle cell disease (Prasad 1979). Clinical disorders aggravated by zinc deficiency include ulcerative colitis, chronic renal disease, and hemolytic anemia (Goyer 1986). In the 40 years since human zinc deficiency was demonstrated, it has been observed in a wide variety of geographic areas and economic circumstances. Severe zinc deficiency occurs in some areas of the Middle East and North Africa, and is frequently associated with the consumption of unrefined cereals as a major part of the diet (Casey and Hambidge 1980). Chronic zinc deficiency in humans is associated with dwarfism, infantile testes, delayed sexual maturity, birth defects, poor appetite, mental lethargy, immunodeficiency, skin disorders, night blindness, impotence, spleen and liver enlargement, defective mobilization of Vitamin A, delayed wound healing, impaired taste acuity, abnormal glucose tolerance, impaired

secretion of luteinizing hormone, and iron and folate deficiency (Prasad 1979, 1980; Casey and Hambidge 1980; Elinder 1986; Goyer 1986; Sternlieb 1988; Mackay-Sim and Dreosti 1989). A deficiency of zinc in the growing age period results in growth retardation; a severe zinc deficiency may be fatal if untreated (Prasad 1980). Zinc-deficient humans excrete <100 µg Zn daily in urine compared to a normal >300 µg Zn daily (Goyer 1986). Zinc deficiency may exacerbate impaired copper nutrition; interactions with cadmium and lead may modify the toxicity of these metals (Goyer 1986).

Acrodermatitis enteropathica is a disease characterized by skin eruptions, gastrointestinal disorders, and low serum zinc levels. One causative factor is poor intestinal absorption of zinc; a complete cure was accomplished by oral administration of 135 mg Zn daily as 600 mg of zinc sulfate (Elinder 1986). Using radiozinc-65, it was shown that afflicted individuals had a greater turnover of plasma zinc, a smaller pool of exchangeable zinc, and a reduced excretion of zinc in stool and urine (Prasad 1979). Zinc deficiency in humans is usually treated by oral administration of 1 mg Zn/kg BW daily (Casey and Hambidge 1980). However, zinc-deficient humans given daily intravenous injections of 23 mg of zinc experienced profuse sweating, blurred vision, and hypothermia (Saxena et al. 1989b).

An endemic zinc deficiency syndrome among young men has been reported from Iran and Egypt, and is characterized by retarded growth, infantile testes, delayed sexual maturation, mental lethargy, anemia, reduced concentration of zinc in plasma and red cells, enlarged liver and spleen, and hyperpigmentation; oral supplementation of 30 mg Zn daily had a prompt beneficial effect (Prasad 1979; Elinder 1986).

A zinc deficiency syndrome during human pregnancy includes increased maternal morbidity, abnormal taste sensations, prolonged gestation, inefficient labor, atonic bleeding, and increased risks to the fetus (Jameson 1980). Pregnant women with initially low and subsequently decreasing serum zinc levels had a high frequency of complications at delivery, including congenital malformations in infants (Jameson 1980). Multiple severe skeletal abnormalities and organ malformations in human fetuses have been attributed to zinc deficiency (Casey and Hambidge 1980). In newborns, zinc deficiency is manifested by growth retardation, dermatitis, hair loss, impaired healing, susceptibility to infections, and neuropsychologic abnormalities (Casey and Hambidge 1980; Goyer 1986).

Hereditary zinc deficiency occurs in certain strains of cattle (*Bos* spp.) and affects the skin and mucous membranes of the gastrointestinal tract. The disease — also known as Lethal Trait A46 — is caused by failure of a single autosomal recessive gene regulating zinc absorption from the intestine. Affected animals will die within a few months from secondary bacterial infections unless treated daily with high oral doses of zinc compounds (Bosma et al. 1988). Certain imported breeds of cattle in the western Sudan with low zinc serum levels (i.e., <0.6 mg/L) showed signs of zinc deficiency, including stunted growth, weakness, skin lesions, and loss of hair pigment (Damir et al. 1988). Cows fed a low (25 mg/kg ration) but adequate zinc diet had liver zinc concentrations below the expected 125 mg Zn/kg DW; increasing the total zinc dietary loading to 45 or 50 mg/kg DW is recommended for counteracting reduced zinc absorption in diets with soybean products (Binnerts 1989). Cows and calves fed low-zinc diets of 25 mg Zn/kg ration showed a decrease in plasma zinc from 1.02 mg/L at start to 0.66 mg/L at day 90; cows fed 65 mg Zn/kg diet had a significantly elevated (1.5 mg Zn/L) plasma zinc level and increased blood urea and plasma proteins (Ramachandra and Prasad 1989). Biomarkers used to identify zinc deficiency in bovines include zinc concentrations in plasma, unsaturated zinc-binding capacity, ratio of copper to zinc in plasma, and zinc concentrations in other blood factors; indirect biomarkers include enzyme activities, red cell uptake, and metallothionein content in plasma and liver (Binnerts 1989).

Domestic goats (*Capra* sp.) fed a zinc-deficient diet (15 mg Zn/kg) developed skin histopathology and alopecia (hair loss) after 177 days; zinc-deficient diets lacking Vitamin A hastened the process, with signs evident between 46 and 68 days (Chhabra and Arora 1989). No signs were evident in goats fed Vitamin A-adequate diets containing 80 mg Zn/kg ration (Chhabra and Arora 1989).

Guinea pigs (*Cavia* spp.) fed a zinc-deficient diet (1.25 mg Zn/kg FW) for 60 days, had significant reductions in zinc concentration of serum (0.5 mg/L), kidney (10 mg/kg FW), testes (9.5 mg/kg FW), and liver (9.4 mg/kg FW). Guinea pigs fed 1.25 mg Zn/kg FW diet for 45 days followed by a zinc-replete diet of 100 mg/kg FW for 15 days had normal concentrations of zinc (mg/kg FW) in serum (1.6 to 2.0), kidney (18 to 20), testes (19 to 27), and liver (15 to 17; Gupta et al. 1988). Zinc-deficient guinea pigs (<3 mg Zn/kg diet, 1 mg Zn/L drinking water) exposed from day 30 of gestation to term on day 68, when compared to zinc-adequate animals (<3 mg Zn/kg diet, 15 mg Zn/L) produced young of low birth weight, with severe skin lesions, sensitive to handling, slow in recovering balance when turned on their side, and a peculiar stance; fetal Zn concentrations were depressed 15 to 33% in liver and placenta (Apgar and Everett 1988). Disrupted immunocompetence responses and disordered protein metabolism were found in guinea pigs fed a zinc-deficient diet of 1.25 mg/kg FW ration for 45 days; marked, though incomplete, restoration occurred when this group was switched to 100 mg Zn/kg ration for 15 days (Verma et al. 1988). Neuromuscular pathology was evident in weanling guinea pigs fed a zinc-deficient diet (<1 mg Zn/kg) for 4 weeks, as judged by abnormal posture, skin lesions, and disrupted vocalizations; signs became severe after 5 to 6 weeks, but a single intraperitoneal injection of 1.3 mg Zn/kg BW (as ZnSO₄) caused remission within 7 days (O'Dell et al. 1989). Acute experimental allergic encephalomyelitis (EAE) was induced in guinea pigs maintained on low (6 mg/kg), normal (20 mg/kg), and high (200 mg/kg) levels of zinc in the diet. Acute EAE is usually a fatal disease of the central nervous system (CNS) induced by inoculation with protein found in myelin of the CNS. Those on the zinc-deficient diet exhibited the expected signs of zinc deficiency, but unlike other groups did not develop neurological signs of acute EAE (Scelsi et al. 1989). EAE suppression observed in the Zn-deficient guinea pigs is ascribed to the influence of zinc deficiency of the T-cell function. A model of autoimmune CNS disease, such as EAE, that requires a prominent T-lymphocyte sensitization, can be altered or suppressed when the immunoregulatory mechanisms are impaired by Zn deficiency (Scelsi et al. 1989).

Rhesus monkeys (*Macaca mulatta*) fed a marginally deficient zinc diet (4 mg Zn/kg diet) between age 5.5 and 30 months had lower plasma Zn levels, delayed onset of accelerated weight gain and linear growth, and no loss of subcutaneous fat — typical of early adolescence — when compared to those fed diets containing 100 mg Zn/kg (Golub et al. 1988). Marginal dietary zinc deprivation also depressed immune function in rhesus monkeys by about 30%, and impaired both learning and reversal of a visual discrimination task by 33 to 66% (Golub et al. 1988). When pregnant rhesus monkeys are fed a diet marginally deficient in zinc (4 mg/kg), perturbations in the mothers' immune system can occur. Their infants have reduced immune responsiveness despite the absence of marked differences in plasma or soft tissue zinc concentrations from control (100 mg Zn/kg diet) infants (Keen et al. 1989). Infant rhesus monkeys from zinc-deprived (4 mg Zn/kg ration) pregnant dams and subsequently fed the same low-zinc diet showed delayed skeletal maturation during their first year. The condition was most severe at age 6 months but began to return to normal despite continuation of the marginally deficient zinc diet (Leek et al. 1988).

Mice (*Mus* sp.) fed a zinc-deficient diet of 0.7 mg Zn/kg ration for 40 days, when compared to mice fed a zinc-adequate diet of 36.5 mg Zn/kg, had a reduced growth rate, impaired phagocytic function, increased susceptibility to lead poisoning, and reduced zinc content in blood (0.7 mg/L vs. 1.0–1.1) and liver (12 mg Zn/kg FW vs. 17–19; Tone et al. 1988). Zinc deficiency during early development affects neural tube development through arrested cell growth (Mackay-Sim and Dreosti 1989). Zinc deficiency in mice may disrupt olfactory function through interference with zinc-containing neurones in higher olfactory centers. Adult mice fed a zinc-deficient diet of 5 mg Zn/kg ration for 42 days, when compared to mice given 100 mg Zn/kg diet, could not distinguish odors, although olfactory epithelia seemed normal (Mackay-Sim and Dreosti 1989).

Mink (*Mustela vison*) kits fed a zinc-deficient diet of 4.1 mg Zn/kg FW ration for 4 days retained 0.49 mg Zn/kit and lost weight. Kits fed a zinc-adequate diet (35 to 45 mg Zn/kg FW, 100 to 150 mg/kg DW) retained 2.5 mg Zn/kit, and those fed 83 mg Zn/kg FW diet retained 7.8 mg Zn/kit.

Low-dose kits ate less than other groups. Urine was the most important excretory route in the zinc-deficient group, compared to feces in higher-dose groups (Mejborn 1989).

Domestic sheep (*Ovis aries*) fed a low-zinc diet (2.2 mg Zn/kg DW diet) for 50 days, when compared to those fed a zinc-adequate diet (33 mg Zn/kg DW diet), excreted less zinc (<4 mg daily vs. 23 to 25), consumed less food (409 g daily vs. 898), and had lower plasma zinc concentrations (0.18 mg/L vs. 0.53 to 0.58); a reduction in plasma alkaline phosphatase activity and an increase in plasma zinc binding capacity were also noted (Khandaker and Telfer 1990). Sensitive indicators of zinc deficiency in lambs include significant reductions in plasma alkaline phosphatase activity and plasma zinc concentrations; signs were clearly evident in lambs fed 10.8 mg Zn/kg DW diet for 50 to 180 days (Vergnes et al. 1990). A normal diet for lambs contains 124 to 130 mg Zn/kg DW ration vs. 33 for adults (Vergnes et al. 1990). One recommended treatment for zinc-deficient sheep is ruminal insertion of zinc-containing boluses every 40 days; bolus zinc release is about 107 mg daily (Khandaker and Telfer 1990).

Zinc-deficient pregnant laboratory white rats (*Rattus sp.*) have reduced litter size, a high frequency of fetal deformities, low birth weight, and a prolonged parturition; dams are inactive and behavior toward young seems indifferent (Harland et al. 1975). Fetal skeletal defects are prominent in rats fed zinc-deficient diets of 10 mg/kg ration during a 21-day gestation period. About 91% of zinc-deficient fetuses had multiple skeletal malformations vs. none in controls fed 76 mg Zn/kg diet (Ferreira et al. 1989). Zinc-deficient (1.5 mg Zn/kg diet) pregnant rats also had increased iron levels in liver, kidney, and spleen, depleted liver glycogen, and reduced levels of zinc in pancreas and duodenum (Mamba et al. 1989). Zinc deficiency causes testicular atrophy and hypogonadism in rats; the effects include spermatic arrest, histopathology of seminiferous tubules and interstitial cells, reduced serum testicular testosterone levels, and reduced testicular zinc concentrations (Hafiez et al. 1990). Zinc is required in Leydig cells for normal testosterone activity. Calcitonin inhibits transmembrane influx of zinc in the isolated rat Leydig cell, but these effects usually take >2 days and are critical only in states of borderline zinc deficiency (Chausmer et al. 1989). Zinc deficiency during pubertal development of rats depresses the activity of dipeptidyl carboxypeptidase in the testes and epididymis; this enzyme is required for maturation and development of sperm cells, and reduced activity may cause suppression of sexual maturity (Reeves 1990). Laboratory white rats fed zinc-deficient diets for 20 days show an aversion to the zinc-deficient diet. They readily consumed a familiar zinc-adequate diet for 15 days, but the previously deficient animals continued to avoid zinc-deficient diets when given a choice (Cannon et al. 1988). Zinc deficiency in rats (<1 mg Zn/kg diet for 26 days) significantly reduced blood pressure, and this correlated positively with serum angiotensin converting enzyme activity; increasing the dietary intake of calcium had no effect on these responses (Reeves and O'Dell 1988). During zinc deficiency, zinc is mobilized from bone in immature animals and may be available for metabolic processes including growth (Calhoun et al. 1978). Diabetic rats are at risk of developing zinc deficiency, owing to zinc's role in modulating immune system dysfunction in diabetes mellitus (Morradian et al. 1988). Cadmium toxicity is related to the zinc status of the body. Zinc-deficient rats (<1 mg Zn/kg diet) and zinc-adequate rats (40 mg/kg) were both challenged with cadmium. The zinc-deficient group had accelerated zinc loss from kidney; enlarged liver, kidney, spleen, and lungs; and increased distribution of cadmium in tissues (Sato and Nagai 1989). Other signs noted in zinc-deficient laboratory white rats include the following: decreased food intake and loss of body weight (Vallee 1959; Cannon et al. 1988; Dib et al. 1989; Reeves and O'Dell 1988; Ferreira et al. 1989; Mamba et al. 1989; Mansour et al. 1989; Sato and Nagai 1989), reduction in serum zinc (Calhoun et al. 1978; Reeves and O'Dell 1988), altered cholesterol metabolism (Sammon and Roberts 1988), increased serum magnesium (Reeves and O'Dell 1988), low bone (femur) zinc concentrations (Calhoun et al. 1978), degeneration of olfactory epithelium (Mackay-Sim and Dreosti 1989), reduction in serum total proteins (Mansour et al. 1989), decreases in activity of glutamate, glycine, methionine, arginine, lysine, and proline (Bettger 1989), and increased dental caries (Goldberg et al. 1990).

Zinc deficiency in domestic pig (*Sus* spp.) is associated with a condition known as porcine parakeratosis, characterized by dermatitis, diarrhea, vomiting, anorexia, severe weight loss, and eventually death. The condition is exacerbated by high calcium levels (Vallee 1959).

9.7 LETHAL AND SUBLETHAL EFFECTS

9.7.1 General

Significant adverse effects on growth, reproduction, and survival are documented for sensitive marine and freshwater species of aquatic plants, invertebrates, and vertebrates at nominal water concentrations between 10 and 25 µg Zn/L. Sensitive terrestrial plants died when soil zinc concentrations were >100 mg/kg, and showed decreased photosynthesis when total plant contained >178 mg Zn/kg DW. Representative soil invertebrates showed reduced growth at 300 to 1000 mg Zn/kg diet, and reduced survival at 470 to 6400 mg Zn/kg soil. Domestic poultry and avian wildlife had reduced growth at >2000 mg Zn/kg diet, and reduced survival at >3000 mg Zn/kg diet or at a single oral dose >742 mg Zn/kg BW; younger stages (i.e., chicks, ducklings) were least resistant. Sensitive species of livestock and small laboratory animals were adversely affected at >0.8 mg Zn/m³ air, 90 to 300 mg Zn/kg diet, >90 mg Zn/kg BW daily, >300 mg Zn/L drinking water, and >350 mg Zn/kg BW single oral dose.

9.7.2 Terrestrial Plants and Invertebrates

Sensitive terrestrial plants die when soil zinc levels exceed 100 mg/kg or when plant zinc content exceeds 178 mg/kg DW (Table 9.5). The phytotoxic zinc level for barley (*Hordeum vulgare*) is not known, but zinc content of barley leaf rarely exceeds 100 mg/kg DW (Chang et al. 1983). Uptake of zinc from soils by plants depends on soil type; for example, uptake is lower in coarse loamy soils than in fine loamy soils (Chang et al. 1983). Zinc uptake by barley leaf is greater with increasing rate of sludge application, but the relation is not proportional (Table 9.5).

Among terrestrial invertebrates, adverse effects on earthworm survival were documented at 470 to 662 mg/kg soil; slugs had reduced food consumption at 300 mg Zn/kg diet and reduced growth at 1000 mg Zn/kg diet; and woodlouse had impaired reproduction at 1600 mg Zn/kg soil, and reduced survival at 5000 mg Zn/kg diet or 6400 mg Zn/kg soil (Table 9.5). Woodlouse (*Porcellio scaber*) fed diets containing sublethal concentrations of zinc for 22 weeks at air temperatures of 12, 16, 20, or 24°C had decreased growth and increased accumulations at high dietary loadings and low temperatures; however, the interaction between temperature and zinc toxicity is not attributed to increased accumulations, but to a physiological interaction with energy metabolism (Donker et al. 1998).

High zinc concentrations in soils are responsible for reductions in populations of soil invertebrates near brass mills and zinc smelters (Beyer 1990). Soils in the vicinity of zinc smelters contained up to 35 g Zn/kg and had decreased populations of arthropods; experimentally, 20 grams of total zinc per kg of soil could account for the decreased survival (Beyer et al. 1984). Zinc concentrations exceeding 1600 mg/kg soil litter are associated with reduced natural populations of decomposer organisms in contaminated forest soil litter, and this has been verified experimentally (Beyer and Anderson 1985). Poisoning decomposer organisms, such as the woodlouse, may disrupt nutrient cycling and reduce the number of invertebrates available as wildlife food (Beyer and Anderson 1985). The woodlouse contains higher concentrations of zinc than other terrestrial invertebrates: up to 152 mg Zn/kg DW whole organism (Hopkin and Martin 1985). It is speculated that the large zinc stores in *P. scaber* repels predators that find zinc distasteful (Hopkin and Martin 1985).

Table 9.5 Effects of Zinc on Representative Terrestrial Plants and Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
PLANTS		
Fir, <i>Abies pindrow</i> , wooden stakes coated with 10% zinc oxide	Protects wood against termite damage for 5 years, compared to 4 years for copper sulfate, 2 years for calcium carbonate, and <6 months for untreated wood	1
Red maple, <i>Acer rubrum</i> , 100 mg Zn/kg culture medium	Lethal to seedlings	2
Lichen, <i>Cladonia uncialis</i> , whole plant zinc content	Depressed photosynthesis when whole lichen burden is >178 mg Zn/kg DW; decreased respiration at >3550 mg Zn/kg DW	3
Barley, <i>Hordeum vulgare</i> , leaf, from soil treated with sludge for 3 years		
No sludge	21–25 mg/kg DW	4
80 kg Zn/ha per year	26–47 mg/kg DW	4
160 kg Zn/ha per year	29–56 mg/kg DW	4
320 kg Zn/ha per year	41–57 mg/kg DW	4
Lichen, <i>Lasallia papulosa</i> , whole plant zinc content	Significant depression in photosynthesis at >308 mg Zn/kg DW and in respiration at >3300 mg Zn/kg DW	3
Oak, <i>Quercus rubra</i> , culture medium contained 100 mg Zn/kg	Lethal to seedlings	2
Corn, <i>Zea mays</i> , grown on sludge amended loam plots; soil contains a maximum of 460 mg Zn/kg DW	Leaf contains a maximum of 293 mg Zn/kg DW vs. 60 for controls; grain contains a maximum of 65 mg Zn/kg DW vs. 32 for controls	5
INVERTEBRATES		
Earthworm, <i>Aporrectodea tuberculata</i> ; concentrations of zinc in soil, in mg/kg DW, ranged from 28 to 470 vs. concentrations in whole worms (less gut contents), in mg/kg DW	At soil Zn concentration of 28 mg/kg DW (control), worms contained 320 mg Zn/kg DW. At soil Zn levels of 97, 110, 190, and 320 mg/kg DW, whole worms contained 810, 1300, 1100 and 650 mg Zn/kg DW, respectively. No worms were found at soil Zn levels of 470 mg/kg DW	6
Slug, <i>Arion ater</i> , fed diets containing 10, 25, 50, 100, 300 or 1000 mg Zn/kg ration for 27 days	No deaths in any group. Significantly reduced food consumption in 300 and 1000 mg/kg diets. All groups weighed less than controls at day 27, but growth was statistically impaired only in the 1000 mg/kg group	7
Slug, <i>Arion ater</i> , fed diets containing up to 1000 mg/kg feed for 30 days	No adverse effects except for glycogen depression at 1000 mg/kg diet	8, 9
Spider, <i>Dysdera crocata</i> , fed woodlice, <i>Porcellio scaber</i> at rate of 1 every 3 days for 36 days		
Woodlice from uncontaminated site (87 mg Zn/kg DW whole organism)	Whole spider contains 182 mg Zn/kg DW	10
Woodlice from contaminated site (152 mg Zn/kg DW whole organism)	Whole spider contains 118 mg Zn/kg DW vs. 116 mg Zn/kg DW in starved spiders	10
Earthworm, <i>Eisenia fetida</i>		
10–12 µg Zn/cm ² applied to epidermis	LC50 (48 h)	11
662 mg Zn/kg artificial soil (95% confidence interval: 574–674)	LC50 (2 weeks)	11
Springtail, <i>Folsomia candida</i>		
Soil		
1.5–34 mg pore water zinc/kg DW vs. 28–113 mg pore water zinc/kg DW	10% reduction in growth, survival, and reproduction vs. 50% reduction	14
6–34 mg water soluble zinc/kg DW vs. 36–97 mg water soluble zinc/kg DW	10% vs. 50% inhibition of growth, survival, and reproduction	14
Body residues; 59–149 mg Zn/kg DW whole springtail vs. 198–479 mg Zn/kg DW	10% vs. 50% effect level on growth, survival, and reproduction	14

Table 9.5 (continued) Effects of Zinc on Representative Terrestrial Plants and Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
Woodlouse, <i>Porcellio scaber</i> , fed soil litter containing up to 12,800 mg Zn/kg for 64 weeks	Soil litter containing 1600 mg Zn/kg or more had adverse effects on reproduction; adult survival was reduced at 6400 mg Zn/kg litter and higher	12
<i>P. scaber</i> , fed diets containing up to 20,000 mg Zn/kg feed for 8 weeks	Decreased survival at 5000 mg/kg and higher	13

^a 1, Roomi et al. 1990; 2, Buchauer 1971; 3, Nash 1975; 4, Chang et al. 1983; 5, Hinesly et al. 1977; 6, Beyer et al. 1987; 7, Marigomez et al. 1986; 8, Recio et al. 1988a; 9, Recio et al. 1988b; 10, Hopkin and Martin 1985; 11, Neuhauser et al. 1985; 12, Beyer and Anderson 1985; 13, Beyer et al. 1984; 14, Smit and Van Gestel 1998.

Slugs (*Arion ater*) are resistant to high dietary zinc intakes (1000 mg/kg feed) for 30 days, although zinc accumulations occur in excretory and calcium cells of the digestive gland (Recio et al. 1988a, 1988b). Histochemical detection of zinc in digestive gland of *Arion* is an indication of high levels of zinc in the environment (Recio et al. 1988a). Zinc elimination in *Arion* occurs directly from lipofuscin material of excretory cells and from spherules of calcium cells; excretion of lipofuscin material via feces is the major excretory route (Recio et al. 1988b).

Zinc normally aids wound healing in terrestrial invertebrates. Wounding of the optic tentacle, foot tissue, and partial shell removal in *Helix aspersa*, a terrestrial gastropod, resulted in deposition of zinc in the wound area after 2 to 5 days. Increased zinc in *Helix* wound areas may be necessary to promote protein synthesis, collagen formation, and mitotic cell division (Ireland 1986).

9.7.3 Aquatic Organisms

Significant adverse effects of zinc on growth, survival, and reproduction occur in representative sensitive species of aquatic plants, protozoans, sponges, molluscs, crustaceans, echinoderms, fishes, and amphibians at nominal water concentrations between 10 and 25 µg Zn/L (Table 9.6). Latent effects of zinc intoxication after brief exposures are poorly documented. One study showed that sensitive species of freshwater crustaceans exposed to zinc concentrations as low as 150 µg/L for as little as 30 minutes had delayed effects that included increasing immobility for up to 172 hours after exposure (Brent and Herricks 1998).

Acute LC50 (96 h) values for freshwater invertebrates ranged between 32 and 40,930 µg Zn/L; for fish, this range was 66 to 40,900 µg/L (USEPA 1987). For marine invertebrates, the LC50 (96 h) range was 195 µg/L for embryos of the hard-shelled clam (*Mercenaria mercenaria*) to >320 mg/L for adults of the Baltic clam (*Macoma balthica*). For marine teleosts LC50 (96 h) values ranged between 191 µg/L for larvae of the cabezon (*Scorpaenichthys marmoratus*) to 38 mg/L for juvenile spot, *Leiostomus xanthurus* (USEPA 1987). Many factors are known to modify the biocidal properties of zinc in aquatic environments. In general, zinc was more toxic to embryos and juveniles than to adults or to starved animals, at elevated temperatures, in the presence of cadmium and mercury, in the absence of chelating agents, at reduced salinities, under conditions of marked oscillations in ambient zinc concentrations, at decreased water hardness and alkalinity, and at low dissolved oxygen concentrations (Skidmore 1964; Weatherley et al. 1980; Spear 1981; USEPA 1987; Paulauskis and Winner 1988; Table 9.6).

Bioconcentration factors (BCF) for zinc accumulation from the medium varied widely between and within species of aquatic organisms. For representative freshwater organisms BCF values ranged from 107 to 1130 for insects, and 51 to 432 for fish (USEPA 1980). In marine environments the most effective zinc accumulators included red and brown algae, ostreid and crassostreid oysters, and scallops. The ranges of BCF values for representative marine groups were 370 to 64,000 for algae, 85 to 1,500,000 for crustaceans, 15 to 500 for echinoderms, up to 4,000,000 in scallop kidney, and 1900 to 6900 for fishes (Eisler 1980). Significant zinc accumulations were reported

after death in algae and fish, suggesting that residue data from these and other organisms found dead on collection are of limited worth (Eisler 1980). Maximum net daily accumulation rates recorded for various whole marine organisms, in mg Zn/kg FW, were 1.3 for the alga *Ascophyllum nodosum*, 7.7 for mussel *Mytilus edulis*, 19.8 for oyster *Crassostrea virginica*, 32 for the killifish *Fundulus heteroclitus*, 32 for softshell clam *Mya arenaria*, and 223 for sandworm *Nereis diversicolor*; in general, accumulation rates and total accumulations were higher at elevated water temperatures, and at higher ambient zinc water concentrations (Eisler 1980).

Algae and Macrophytes

Blue-green algae are among the most zinc-resistant aquatic plants (Vymazal 1986). Algae are classified by Vymazal (1986) as very resistant (>10 mg Zn/L), resistant (2 to 10 mg/L), moderately resistant (0.5 to 2 mg/L), having low resistance (0.1 to 0.5 mg/L; *Navicula*, *Synedra*), and having very low resistance (<0.1 mg Zn/L; *Diatoma*, *Tabellaria*, *Microspora*, *Ulothrix*).

The most sensitive aquatic plant was *Schroederella schroederi*, a diatom; 19 µg Zn/L was sufficient to inhibit growth 50% in 48 h (USEPA 1987). Freshwater aquatic plants are usually absent from areas containing >2.0 mg Zn/L; in the hard waters of artificial streams containing 170 mg CaCO₃/L, a water concentration of 1.1 mg Zn/L caused a 50% decrease in the number of algal species (Spear 1981). Most freshwater diatom populations decreased in the range of 175 to 380 µg Zn/L; this sensitivity may be useful as an indicator of zinc contamination (Spear 1981). Zinc and cadmium are strongly synergistic in their toxic action to plants. Any level of cadmium >10 µg/L should be suspected of producing a significant increase in the toxicity of available zinc to freshwater plants (Whitton 1980).

In heavily-contaminated zinc environments (i.e., 130 to 6500 µg Zn/L), zinc-tolerant species are dominant (Spear 1981). Highly tolerant strains of algae require 1.5 to 1.65 mg Zn/L for normal growth; at least three species of some tolerant strains can live in water containing 3 g Zn/L (Vymazal 1986). Highly tolerant mutant strains of *Anacystis nidulans* required 1.5 to 16.5 mg Zn/L. In France, at least 17 species of freshwater algae seemed to be flourishing at 42.5 mg Zn/L and pH 4.2 (Vymazal 1986). Zinc-tolerant strains of aquatic algae tolerate high zinc concentrations with little bioconcentration. A zinc-tolerant strain of *Euglena gracilis*, for example, tolerates >700 mg Zn/L, but contains <500 mg Zn/kg DW whole organism vs. 50 mg Zn/L and 5000 mg/kg DW for nontolerant strains (Fukami et al. 1988a). Another zinc-tolerant strain of *Euglena* had normal growth at 300 mg Zn/L and residues of about 7000 mg Zn/kg DW vs. population decline of nontolerant strains at 300 mg Zn/L (Fukami et al. 1988).

Algae are effective accumulators of zinc. Three species of marine algae had a mean bioconcentration factor (BCF) of 1530 in 12 days, 4680 in 34 days, and 16,600 in 140 days (USEPA 1980). Bioconcentration factors for zinc and various species of algae are quite variable and usually range between 76 and 163,750 (Vymazal 1986; USEPA 1987). Many species of aquatic plants contain 150 mg Zn/kg DW, and higher. In one case, algae (*Mougeotia* spp.) from northern England in Zn-contaminated waters contained a spectacular 219 g Zn/kg DW (Vymazal 1986); it is likely that most of the Zn in *Mougeotia* was not biologically incorporated. Algal accumulations of zinc are modified significantly by physicochemical variables. Zinc concentrations in algae were higher under conditions of decreasing light intensity, water pH, DDT levels, copper, cadmium, phosphate, suspended sediments, organic chelators and other complexing agents, calcium, and magnesium, and under conditions of increasing water temperature, dissolved oxygen, duration of exposure, and ambient zinc concentrations (Eisler 1980; Whitton 1980; Vymazal 1986).

Unlike algae, submerged aquatic macrophytes play a minor role in cycling zinc (Lyngby et al. 1982). Rooted aquatic macrophytes may participate in heavy-metal cycling in the aquatic environment either as a source or as a sink, but studies with eelgrass (*Zostera marina*) show that zinc exchange between the sediment and the water is insignificant (Lyngby et al. 1982).

Table 9.6 Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
PLANTS			
Alga, <i>Amphidinium carteri</i>	400	Growth inhibition	1
Aquatic plants, various	30->200,000	Adverse effects	2
Brown alga, <i>Ascophyllum nodosum</i>	100	No effect on growth in 10 days	2
<i>A. nodosum</i>	250	Decreased growth in 10 days	2
Coccolithophorid, <i>Cricospaera carterae</i>	77	Growth reduced 50% in 4 days	2
Freshwater algae, 11 species	140–800	Growth inhibition	3
Freshwater algae, most species	>1000	Growth inhibition	1
Brown macroalgae, <i>Fucus serratus</i>	9.5	BCF of 10,770 in 140 days	2
<i>F. serratus</i>	8.8	Altered lipid metabolism	2
Marine macroalgae, <i>Fucus vesiculosus</i>	3500	No adverse effects	2
<i>F. vesiculosus</i>	7000	Growth retardation	2
Dinoflagellate, <i>Glenodinium halli</i>	20	Chlorophyll reduced 65% in 2 days	2
Dinoflagellate, <i>Gymnodinium splendens</i>	110–392	Chlorophyll reduced about 65% in 2 days in temperature range 16–30°C	2
<i>G. splendens</i>	100	Growth inhibition in 38 days	3
Alga, <i>Isochrysis galbana</i>	74	Chlorophyll reduced 65% in 48 h at 16 ppt salinity, 20°C	2
<i>I. galbana</i>	430	Chlorophyll reduced 65% in 48 h at 16°C, 16 ppt salinity	2
Kelp, <i>Laminaria digitata</i>	100	Growth inhibition in 24 days	1
Brown macroalga, <i>Laminaria hyperborea</i>	250	Reduced growth of sporophytes in 8–10 days	2
Marine algae, 4 species	50–500	Decrease in cell numbers	1
Marine algae, 5 species	100	Growth inhibited in 48 h	2
Marine macroalgae, 4 species	100	No adverse effects	2
Marine macroalgae, 4 species	1400	Growth reduction	2
Diatom, <i>Nitzschia closterium</i>	271–300	50% growth inhibition in 4 days	2
Diatom, <i>Nitzschia longissima</i>	100	Growth stimulated during exposure for 1–5 days	2
Dinoflagellate, <i>Procentrum micans</i>	319	50% growth inhibition in 4 days	2
Diatom, <i>Phaeodactylum tricornutum</i>	250	BCF of 1800 in 3 days	2
<i>P. tricornutum</i>	4800	6.7% increase in growth during 12-day exposure	2
Phytoplankton	15	Primary productivity reduced in 14 days	2
Marine alga, <i>Rhizosolenia</i> sp.	15–25	Photosynthesis reduction	3
Alga, <i>Scenedesmus quadricauda</i>	2	Adverse effects	4
<i>S. quadricauda</i>	64	Growth inhibition in 14 days	2
<i>S. quadricauda</i>	300	Lethal	4

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Diatom, <i>Schroederella schroederi</i>	19	Growth inhibited 50% in 48–96 h	2
Freshwater alga, <i>Selenastrum capricornutum</i>	30	Some growth inhibition in 7 days	1
<i>S. capricornutum</i>	40–68	95% growth inhibition in 14 days	1
<i>S. capricornutum</i>	100	100% growth inhibition in 7 days	1
Diatom, <i>Skeletonema costatum</i>	19.6	Adverse effects	4
<i>S. costatum</i>	50–100	Growth reduced 20–23% in 10–15 days	2
<i>S. costatum</i>	200	Growth stimulated in 1–5 days	2
<i>S. costatum</i>	265	Metabolic disruption in 3 days	2
Diatom, <i>Thalassiosira pseudonana</i>	65	Adverse effects	4
<i>T. pseudonana</i>	500	Growth reduced 41% in 11–15 days	2
<i>T. pseudonana</i>	823	Growth reduced 50% in 72 h	2
Green macroalga, <i>Ulva lactuca</i>	65	BCF of 255 in 6 days	2
PROTISTS			
Protozoan, <i>Cristigera</i> sp.	50–125	Growth reduced in 5 h exposure	1, 2
Bacterium, <i>Escherichia coli</i>	650–1400	Growth inhibition	3
Microorganisms, various	650–1100	Growth inhibition, usually	3
Paramecium, <i>Paramecium multimicronucleatum</i>	560–10,000	LC50 (3 h)	3
Bacterium, <i>Pseudomonas</i> sp.	1000–10,000	Growth inhibition	3
Protozoan, <i>Vorticella convallaria</i>	50	LC50 (48 h)	3
PORIFERA			
Freshwater sponge, <i>Ephydatia fluviatilis</i>			
Adults	6.5	No effect on growth; no tolerance developed with long-term exposure	5
Adults	26	After exposure for 10 days, tissue deterioration and death during 3-week postexposure period	5
ROTIFERS			
Rotifer, <i>Philodena acutiformis</i>			
Adults	500	LC50 (48 h), 25°C	2
Adults	1550	LC50 (48 h), 5°C	2
MOLLUSCS			
Freshwater snail, <i>Ancylus fluviatilis</i>			
Juvenile	80	LC50 (100 days), shell length <2 mm	6
Adult	100	No adverse effect on reproduction in 100 days	6
Juvenile	130	LC50 (100 days), shell length >3 mm	6
Adult	180	Reproduction reduced in 100 days	6

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Bay scallop, <i>Argopecten irradians</i>			
Larvae	50	Growth rate reduced 22% in 9 days	7
Larvae	109	Growth reduced 50% in 9 days	7
Larvae	120	LC50 (9 days), increased shell deformities	7
Larvae	150–200	All dead at metamorphosis	7
Juvenile	2250	LC50 (96 h)	8
Freshwater snail, <i>Biomphalaria glabrata</i>	500	By day 33 of exposure embryo survival was reduced 50% and adult growth and reproduction inhibited	9
Asiatic clam, <i>Corbicula fluminea</i>	<20	Residues were 169 mg/kg DW soft parts after feeding on periphyton containing 393–1327 mg/kg DW for 30 days	11
<i>C. fluminea</i>	25	Normal growth during exposure for 30 days	10
<i>C. fluminea</i>	34	Residues were 433 mg/kg DW soft parts in 30 days after feeding on periphyton containing 956–4369 mg Zn/kg DW; growth reduced; cellulase enzyme activity reduced	11
<i>C. fluminea</i>	50–500	Growth inhibited between days 20 and 30 of exposure	10
<i>C. fluminea</i>	218	BCF of 126 in 28 days	2
<i>C. fluminea</i>	1000	After exposure for 30 days, about 30% dead. Survivors had osmoregulatory impairment and residues, in mg Zn/kg DW soft parts, of 2000 vs. 200 in controls. Depuration complete by day 17 post-exposure, and growth rate returns to normal	10
Pacific oyster, <i>Crassostrea gigas</i>			
Larvae	10–20	Reduced larval settlement in 20 days	2
Larvae	30–35	Reduced larval settlement in 6 days	2
Larvae	50	Normal growth and development in 5 days	12
Larvae	70	Abnormal shell development in 48 h	1
Larvae	75	No deaths in 48 h	1
Larvae	80–95	Growth reduced 50% in 4 days	2
Larvae	119–310	LC50 (48 h)	1, 3
Larvae	125	Substrate attachment inhibited in 5 days	1, 2
Larvae	200	No growth in 5 days	12
Embryo	233	LC50 (96 h)	2
Larvae	250	Increasing incidence of abnormal development and mortality	12
Sperm	444	Fertilization success reduced 50% in 60 min	2
Larvae	500	All dead in 48 h	1
American oyster, <i>Crassostrea virginica</i>			
Adult	100	Whole body concentration of 2560–2708 mg Zn/kg FW soft parts after 20-week exposure vs. 1036–1708 for controls	14
Adult	200	After exposure for 20 weeks, residues were 3185–3813 mg Zn/kg FW soft parts	14

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Embryo	230	LC50 (96 h)	2
Larvae	340	LC50 (48 h)	13
Red abalone, <i>Haliotis rufescens</i>			
Larvae	19	No adverse affects after 9-day exposure	13
Larvae	41	Normal development during 48-h exposure	13
Larvae	50	50% abnormal development during exposure for 9 days	13
Larvae	68	50% abnormal development in 48 h exposure	13
Marine gastropod, <i>Littorina littorea</i>			
Adult	0.2 (controls)	Zinc concentrations in all tissues were <185 mg/kg DW, except kidney which was 372 mg/kg DW	15
Adult	10	After exposure for 42 days tissue Zn residues, in mg/kg DW, were: head/foot 120, gills 255, whole soft parts 605, viscera 1322, stomach 1918, and kidney 2153	15
Freshwater pond snail, <i>Lymnaea luteola</i>			
Adult	1680	LC50 (96h)	85
Hard shell clam, <i>Mercenaria mercenaria</i>			
Larvae	50	5% dead in 12 days	1
Larvae	166	50% dead or abnormal in 48 h	1
Embryo	195	LC50 (96 h)	2
Larvae	195–341	LC50 (10–12 days)	1
Larvae	279	All dead in 48 h	1
Softshell clam, <i>Mya arenaria</i>			
Adult	10	Soft parts contained 9.5 mg Zn/kg FW after 16 weeks at 0–10°C, and 11 mg/kg after 2 weeks at 16–22°C	14
Adult	200	BCF of 85–135 in 50 days	2
Adult	500	Soft parts contained 31–48 mg Zn/kg FW after exposure for 6–16 weeks at 0–10°C, and 59–82 mg/kg after 1–2 week exposure at 16–22°C	14
Adult	900	No deaths in 7 days at 22°C	16
Adult	1550	LC50 (7 days) at 22°C	16
Adult	25,000	All dead after 70-day exposure at 0–10°C; at exposure temperature of 16–22°C, all dead by day 14	17
Common mussel, <i>Mytilus edulis</i>			
Adult	25	Maximum kidney zinc residue after 18 days was 14.1 g/kg DW vs. 4.9 g/kg in controls	18
Adult	60	Shell growth rate reduced 50% in 2–6 day exposure	2
Embryo	96–314	Development inhibited 50% in 72 h	2
Adult	100	No accumulations in tissues after 4-day exposure	19

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Adult	230–860	In 7-h exposure, pumping rate decreased with increasing Zn, and was completely stopped at >470 µg/L; recovery on return to background levels	20
Adult	1000	After exposure for 24 h, zinc concentration in soft parts rose from 150 mg/kg DW to 252 mg/kg DW and remained elevated for at least 6 weeks postexposure	21
Larvae	1752	LC50 (48 h)	13
Adult	1800	Reduced byssal thread production	2
Adult	5000	LC50 (7 days)	2
Adult	5000	LC 100 (16 days)	19
Adult	20,800	LC50 (24 h exposure plus 6 weeks post-exposure); none dead during exposure	22
Sperm	65,400	Respiration inhibited 50% in 20 min	23
Mud snail, <i>Nassarius obsoletus</i>			
Adult	200	Decreased oxygen consumption in 72 h	1
Egg	650	Abnormal veliger development	24
Adult	5000	No deaths in 168 h	25
Green-lipped mussel, <i>Perna viridis</i>			
Adult	<178–362	Maintains constant body concentration over 21-day exposure period	26
Adult	>362	Accumulation in tissue	26
Adult	6090	LC50 (96 h)	26
Freshwater snail, <i>Physa heterostropha</i> , juvenile	241	LC50 (96 h)	2
Surf clam, <i>Spisula solidissima</i> , juvenile	2950	LC50 (96 h)	8
BRYOZOANS			
Bryozoan, <i>Bugula neritina</i> , larvae	200	LC50 (5 h)	3
Bryozoan, <i>Watersipora cucullata</i> , larvae	650	LC50 (5 h)	3
CRUSTACEANS AND ARACHNOIDS			
Copepod, <i>Acartia tonsa</i>	290	50% immobilized in 48 h	1
<i>A. tonsa</i>	294	LC50 (96 h)	2
Amphipod, <i>Allorchestes compressa</i>	580–2000	LC50 (96 h)	3, 27
Brine shrimp, <i>Artemia</i> sp.	14–1360	Egg hatching significantly reduced in dose-dependent manner; no effect on survival of prenauplii larvae	28
Cladoceran, <i>Ceriodaphnia reticulata</i>	51	LC50 (96 h)	2
Hermit crab, <i>Clibanarius olivaceus</i>			
Larvae	1–90	Molting delayed in dose-dependent manner	29
Larvae	100	LC50 (96 h)	29
Larvae	125	LC 100 (96 h)	29
Daphnia, <i>Daphnia galeata mendotae</i>	15	BCF of 9400 in 2 weeks	2

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
<i>D. g. mendotae</i>	30	BCF of 5833 in 2 weeks	2
<i>D. g. mendotae</i>	60	BCF of 6333 in 2 weeks	2
Daphnid, <i>Daphnia magna</i>	5–14	LC50 (72 h) at 30°C	2
<i>D. magna</i>	25	No effect in soft water (50 mg CaCO ₃ /L) in 50 days	30
<i>D. magna</i>	42–52	MATC ^b ; water contains 104–211 mg CaCO ₃ /L	1, 2
<i>D. magna</i>	68–655	LC50 (96 h)	31
<i>D. magna</i>	70	Reproduction reduced 16% in 21 days	2
<i>D. magna</i>	100	LC50 (48 h), starved	84
<i>D. magna</i>	250	Nonlethal in 6 weeks when sediments present in test container. Final sediment value of 13,400 mg/kg DW vs. 600 in controls. Organisms had whole body residues of 450 mg/kg DW	32
<i>D. magna</i>	280	LC50 (48 h), fed	3
<i>D. magna</i>	560	LC50 (24 h) at 25°C	84
<i>D. magna</i>	560	50% immobilized in 48 h	33
<i>D. magna</i>	2300	LC50 (24 h) at 5°C	3
Daphnid, <i>Daphnia pulex</i>	253	LC50 (96 h)	2
<i>D. pulex</i>	280	LC50 (48 h)	1
<i>D. pulex</i>	500	LC50 (24 h) at 25°C	3
<i>D. pulex</i>	1550	LC50 (24 h) at 5°C	3
Copepod, <i>Eudiaptomus padanus</i>	500	LC50 (48 h)	31
Amphipod, <i>Gammarus duebeni</i>			
Natural population	>100	Survival reduced in 7 days	34
Natural population	1000	All dead in 7 days at 10 ppt salinity, 84% dead at 30 ppt	34
Zinc-tolerant population	1000	50% dead in 14 days at 10 ppt salinity, 33% dead at 30 ppt	34
American lobster, <i>Homarus americanus</i>			
Larvae	130	LC50 (17 days)	3
Larvae	381	LC50 (96 h)	2
Adult	13,000	LC50 (11 days)	3
Horseshoe crab, <i>Limulus polyphemus</i>			
Embryos	<100	LC50 (72 h), Sandy Hook Bay, NJ	86
Larvae	100,000	Normal survival and molting	86
Embryos	715,000	LC50 (72 h), Delaware Bay, Delaware	86
Mysid, <i>Mysidopsis bahia</i>	120–231	MATC ^b	1, 2
<i>M. bahia</i>	499	LC50 (96 h)	2, 13
Crayfish, <i>Orconectes virilis</i>	130,000	No deaths in 10 days	35
Hermit crab, <i>Pagurus longicarpus</i>			
Adult	200	LC50 (168 h)	25
Adult	400	LC50 (96 h)	1, 2
Prawn, <i>Palaemon elegans</i>	562	LC 67 (21 days)	36
Shrimp, <i>Pandalus montagui</i>	65	BCF of 3.7 in 14 days	2
Mysid, <i>Praunus flexuosus</i>	2000	LC50 (192 h), 5°C, 4.5 ppt salinity	37

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Mudcrab, <i>Rithropanopeus</i> <i>harrissii</i> , larvae	50	Delayed development in 16-day exposure	1
Copepod, <i>Tisbe holothuriae</i>			
Life cycle	7	No effect on population size after exposure for 4 generations	38
Life cycle	10	Some deaths in fourth generation	38
Life cycle	70	All dead by end of first generation	38
Copepodid	421	LC50 (48 h)	39
Adults	620–700	LC50 (48 h)	38, 40
Females with egg sacs	713	LC50 (48 h)	39
Copepod, <i>Tropocyclops prasinus mexicanus</i> , Quebec lakes, uncontaminated	52–264	LC50 (48 h) in soft water	41
<i>T. p. mexicanus</i> Quebec lakes, contaminated	2934	LC50 (48 h) in hard water lake; metal preexposure protective effect hypothesized	41
AQUATIC INSECTS			
Mayfly, <i>Epeorus latifolium</i>			
Larvae	30	Gradual decrease in growth rate in 4-week exposure; some deaths prior to emergence	42
Larvae	100–300	Growth inhibited after 2 weeks; all dead before emergence	42
Midge, <i>Tanytarsus dissimilis</i> , embryo through third instar	37	LC50 (10 days)	1,2
ANNELIDS			
Polychaete worm, <i>Capitella capitata</i>			
Larvae	50–100	Abnormal development during 16-day exposure	2
Adult	1250	LC50 (28 days)	2
Adult	10,700	LC50 (48 h)	13
Leech, <i>Erpobdella octoculata</i>			
Juveniles	60	LC50 (70 days)	43
Adults	100	LC50 (70 days)	43
Adults	180	High frequency of abnormal eggs produced in 60-day exposure	43
Adults	320	Inhibited reproduction in 60-day exposure	43
Juveniles	390	LC50 (40 days)	43
Juveniles	2100	LC50 (96 h)	43
Adults	4800	LC50 (40 days)	43
Adults	8800	LC50 (96 h)	43
Polychaete, <i>Neanthes arenaceodentata</i> , juveniles	900	LC50 (28 days)	3
Sandworm, <i>Nereis diversicolor</i>			
Adults	1500	No deaths in 168 h	25
Adults	2600	LC50 (168 h)	25

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Adults	10,000	Whole body zinc concentration, in mg/kg DW, in survivors after exposure for 34 days was 2500 vs. 180 in controls	14
Adults	10,000	After 96 h exposure at 6°C, zinc residues (mg/kg DW) were 1031 in head vs. 843 for controls, 366 vs. 158 in trunk, and 455 vs. 275 in parapodia; uptake higher at 12° and 20°C	44
Adults	20,000	No deaths in 96 h	44
Adults	40,000	LC50 (47 h) for nontolerant strains; LC50 (70 h) for zinc-tolerant strains	45
Worm, <i>Spirorbis lamellora</i> , larvae	350	LC50 (3 h)	3
ECHINODERMS			
Sea urchin, <i>Anthocidarius crassispina</i>			
Egg	65	No effect on fertilization membrane formation or development in eggs transferred 1 min after insemination	46
Egg	326	Irreversible inhibition of fertilization membrane formation in eggs transferred 10 sec. after insemination	46
Starfish, <i>Asterias rubens</i>			
Adult females	240	Increased steroid metabolism in pyloric caeca after 21 days	47
Adults	1000	No deaths in 168 h	25
Adults	2300	LC50 (168 h)	25
Sand dollar, <i>Dendraster excentricus</i> , sperm	28	Fertilization success reduced 50% in 60 min	2
Echinoderms, 3 species, embryos	60–200	Embryonic development inhibited	48
Red sea urchin, <i>Strongylocentrotus franciscanus</i> , sperm	313	Fertilization success reduced 50% in 60 min	2
Purple sea urchin, <i>Strongylocentrotus purpuratus</i> , embryos	23	Development inhibited 50% in 5 days	2
Embryos; field populations vs. laboratory-raised populations	97 vs. 107	50% inhibition of larval development in 96 h	87
FISH			
Longfin dace, <i>Agosia chrysogaster</i> , larvae	228	LC50 (96 h)	2
Murrel, <i>Channa punctatus</i> , fingerlings, 31-day exposure	12,000	Growth rate reduced by day 19; liver RNA and proteins decreased by day 20; muscle RNA and proteins reduced by day 30	49, 50
Texas cichlid, <i>Cichlasoma cyanoguttatum</i> , adults, exposure for 4 weeks	40 (control), 65, or 90	Residues in mg Zn/kg FW, were 0.8, 28, and 34 in muscle; 6, 56, and 25 for viscera; 6, 59, and 98 for gills; and 12, 66, and 92 for bone	51

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Air-breathing catfish, <i>Clarias lazera</i> , juveniles	26,000–52,000	LC50 (96 h) at 25.1°C (26,000) through 9.3°C (52,000); at 38,000 µg/L and 18.5°C, 50% died and survivors had BCF values of 544 in gill, 425 in liver, and 250 in muscle	52
Baltic herring, <i>Clupea harengus</i> , eggs exposed from fertilization through hatching	500, 2000, 6000, or 12,000	Histopathology of epidermis and kidney in larvae at 6000 µg/L and higher; no measurable effects at 2000 µg/L and lower	53, 54
Atlantic herring, <i>Clupea harengus harengus</i> , embryos and larvae	50	Significant increase in incidence of jaw and branchial abnormalities	2
Freshwater fishes, 4 species, adults	4600–17,300	LC50 (5 days)	55
Mummichog, <i>Fundulus heteroclitus</i>			
Adults	810	Bioconcentration factor (BCF) of 16 in whole fish after 56 days	2
Adults	10,000	Zinc concentration, in mg/kg DW scale, rose from 229 at start to 746 after 45 days and to 1608 after 94 days	56
Adults	10,000	Zinc content in scale, in mg/kg DW, after 45 days exposure and 21 to 49 days in uncontaminated water fell from 746 to 422–498	56
Adults	43,000	No deaths in 8 days; no significant increase in tissue Zn levels	57
Adults	52,000–66,000	LC50 (8 days)	25, 57
Adults	71,000–153,000	LC50 (48 h)	58
Mosquitofish, <i>Gambusia affinis</i> , adults, muscle	18,000	After 24 h, Zn increased from 82 to 134 µg/kg FW; significant increases in glycogen, total lipids, phospholipids, and cholesterol; decreases in RNA and proteins	59
Flagfish, <i>Jordanella floridae</i>			
Life cycle	26–51	MATC ^b	2
Larvae	85	LC80 (30 days)	3
Adults	139	BCF of 417 in whole fish in 100 days	2
Cypriniform freshwater fish, <i>Labeo rohita</i>			
Juveniles and adults	20,000	No deaths in 96 h	60
Juveniles	65,000	LC50 (96 h); liver glycogen reduced; BCF of 22 in whole fish	60
Adults	77,000	LC50 (96 h); survivors had disrupted respiration and decreased liver glycogen	60
Spangled perch, <i>Leiopotherapon unicolor</i> , adults, exposed for 2 h	5000, 10,000, or 20,000	Temporary decrease in ventilation rate at 5 mg/L; significant increase in ventilation rate at 10 and 20 mg/L; bradycardia at 20 mg/L	61
Spot, <i>Leiostomus xanthurus</i>	38,000	LC50 (96 h)	62
Bluegill, <i>Lepomis macrochirus</i>			
Adults	76–235	Reproduction inhibition	3
Adults	100	Hyperactivity	3

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Fry	235	Lethal in 3 days	1, 2
Adults, exposed for 7 days, then placed in a lethal NaCl salinity (1.46%) for 60 h	2350	Exposed fish all dead in 60 h vs. 8 h for controls; plasma chloride declined in Zn-exposed fish, suggesting that Zn reduces permeability of gills to chloride influx	63
Adults	5400	LC50 (96 h) at 20 mg CaCO ₃ /L	3
Adults	40,900	LC50 (96 h) at 360 mg CaCO ₃ /L	3
Marine fishes, most species	>1000	LC50 (96 h)	1
Tidewater silverside, <i>Menidia peninsulae</i>	5600	LC50 (96 h)	62
Striped bass, <i>Morone saxatilis</i>			
Larvae	100–119	LC50 (96 h)	1, 2
Fry	430–1180	LC50 (96 h)	1, 2
Adults	6700	LC50 (96 h)	1
Stone loach, <i>Noemacheilus barbatulus</i> , adults	1900–2000	LC50 (25 days)	3, 55
<i>N. barbatulus</i>	3500	LC50 (96 h)	55
Loach, <i>Noemacheilus</i> sp.	25,000	LC50 (96 h)	64
Cutthroat trout, <i>Oncorhynchus clarki</i>	61–600	LC50 (96 h)	1, 65
<i>O. clarki</i>	360	None dead in 14 days	66
<i>O. clarki</i>	670	LC50 (14 days)	3, 66
Coho salmon, <i>Oncorhynchus kisutch</i>			
Water hardness <50 mg CaCO ₃ /L	280	LC50 (96 h)	3
Juveniles	500–10,700	Decreased white blood cell count in 24 h	3
0.5–0.9 g body weight	820–1810	LC50 (96 h)	67
Rainbow trout, <i>Oncorhynchus mykiss</i>			
Immatures	5.6	Avoidance, 10 to 20 min tests	1, 2
Larvae and alevins	10	LC54 (28 days)	3
Immatures	47	94% avoidance, 40-min tests	2
Early life stages	70–140	LC50 (25 days)	3
Juveniles	81	Hyperglycemia in 24 h	3
Fry	90–93	LC50 (96 h)	1, 2
Life cycle	140–547	MATC ^b	1, 2
Weight 0.6 grams	169	LC50 (96 h)	67
Juveniles	210–1120	Increased blood glucose in 7–63 days	3
Parr	240–830	LC50 (96 h) at 30 mg CaCO ₃ /L	1
Juveniles	310	LC 20 (14 days)	66
Immatures	352	Hyperglycemia in 9 days	2
Larvae and alevins	400–2800	LC50 (120 h)	3
Juveniles	410	LC50 (14 days)	66
Juveniles	430	LC59 (96 h) at 26 mg CaCO ₃ /L	3
Juveniles	520	LC50 (96 h) at 47 mg CaCO ₃ /L	3
Fry	689	LC50 (96 h)	2
Juveniles	690	Increased respiration in 24 h	3
Immatures	1030	LC50 (96 h) value for group acclimatized to 80 µg Zn/L for 28 days (vs. 469 µg Zn/L for controls)	68
Adults	1120	Reduced growth in 85 days	3

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Parr	1190–4520	LC50 (96 h) at 350 mg CaCO ₃ /L	1
Juveniles	2960	LC50 (96 h) at 179 mg CaCO ₃ /L	3
Parr	4700	LC50 (96 h) at 500 mg CaCO ₃ /L	1
Juveniles	4800–7200	LC50 (96 h) at 333–504 mg CaCO ₃ /L	3
Fry	10,000	16% dead in 90 h vs. none dead in group pretreated with 5 mg Zn/L for 96 h	69
Fry	15,000	79% dead in 90 h vs. 20% dead in group pretreated with 5 mg Zn/L for 96 h	69
Sockeye salmon, <i>Oncorhynchus nerka</i>			
Embryo through smolt	242	No measurable effects in 18-month exposure	1
Immatures	447	LC50 (115 h)	1
Immatures	750	LC50 (96 h)	3
Chinook salmon, <i>Oncorhynchus tshawytscha</i>			
Swim up	97	LC50 (96 h)	1
Chronic exposure	270–510	MATC ^b	1, 2
Smolts	446	LC50 (96 h)	2
Minnow, <i>Phoxinus phoxinus</i>			
Yearlings	50–130	Reduced growth during exposure for 150 days; no deaths	70
Larvae	60	Decreased swimming ability after exposure for 108 days	3
Larvae	80	LC37 (40 days)	3
Adults	130	Reduced growth during 150-day exposure; some deaths	70
Juveniles	160	Decreased swimming ability after 109 days	3
Adults	200	Decreased swimming ability after 100 days	3
Adults	200	Reduced growth during 30-day exposure; some deaths	70
Adults	250	LC50 (150 days)	3
Fathead minnow, <i>Pimephales promelas</i>			
Life cycle	78–145	MATC ^b	1, 2
Juveniles	125	Reduced growth in 7 days	2
Larvae	152–294	LC84 (8 weeks)	3
Adults	180	65 to 83% reduction in fecundity in 10-month exposure	1, 2
Adults	480	Reduced growth in 30 days	3
Embryo/larvae	500–1400	50% developmental malformations in 96 h	71
Larvae	600	LC50 (96 h)	3
Adults	600	Preexposure for 14 days increased resistance 28% over controls in 96-h zinc toxicity assays	72
Adults	800	LC50 (30 days)	3
Adults	870	LC50 (96 h) at 20 mg CaCO ₃ /L	3
Adults	1800	Exposure for 7 days decreased tolerance 63% in 96-h Zn toxicity assays; tolerance decreased 74% after exposure for 14 days	72

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Adults	2800	LC 15 (10 months), no eggs deposited	73
Embryo/larvae	3600	LC50 (6 days)	71
Adults	4700–6100	LC50 (96 h) at 50 mg CaCO ₃ /L	3
Adults	6400–10,900	LC50 (96 h) at 100 mg CaCO ₃ /L	3
Adults	7100	LC50 (96 h) at 166 mg CaCO ₃ /L	3
Adults	8200–21,000	LC50 (96 h) at 200 mg CaCO ₃ /L	3
Adults	33,400	LC50 (96 h) at 360 mg CaCO ₃ /L	3
Guppy, <i>Poecilia reticulata</i>			
Age 5 days	125	After 134 days, whole body Zn content of 0.6 mg/kg DW vs. 0.3 in controls; growth reduced	74
Adults	173	Whole body BCF of 466–965 in 30 days	2
Age 5 days	250	Delayed sexual maturation after 134 days	74
Age 5 days	500	Reproduction inhibited	74
Age 5 days	1350–1500	LC50 (96 h)	74
Adult males	4400–5700	LC50 (96 h)	74
Adult females	5600–7300	LC50 (96 h)	74
Atlantic salmon, <i>Salmo salar</i>			
Parr	50	50% avoidance in 4 h	2
Parr	100	Avoidance within 20 min	3
Immatures	100–500	LC50 (21 days)	1
Water hardness, in mg CaCO ₃ /L			
14	420	LC50 (96 h)	1
20	600	LC50 (96 h)	1
Brown trout, <i>Salmo trutta</i>			
Yolk-sac fry	4.9	40% with noncalcified vertebrae center; all dead in 18 days at pH 4.5 and soft water	75
Yolk-sac fry	9.8–19.6	60% to 75% dead in 20–30 days; 6% to 21% with abnormal vertebrae in pH 4.5 and soft water	75
Yearlings	<140	LC50 (96 h) at pH 8, 10 mg CaCO ₃ /L	76
Adults	570	LC 17 (14 days)	66
Adults	640	LC50 (14 days)	66
Yearlings	3200	LC50 (96 h) at pH 5, 204 mg CaCO ₃ /L	76
Brook trout, <i>Salvelinus fontinalis</i>			
Chronic exposure	534–1360	MATC ^b	1, 2
Adults	630	LC 17 (14 days)	66
Adults	960	LC50 (14 days)	3, 66
Cabezon, <i>Scorpaenichthys marmoratus</i> , larvae	192	LC50 (96 h)	2
Dogfish, <i>Scyliorhinus</i> sp., exposure for 25 days	15,000	No significant accumulations in kidney and muscle, but elevated levels (as judged by BCF values) in gill filament (1.6), spleen (1.7), pancreas (2.7), and liver (5.2)	77, 78
Arctic grayling, <i>Thymallus arcticus</i>			
Body weight 0.2–1.8 g	112–168	LC50 (96 h)	67
Fry	315	LC50 (96 h)	67
Alevins	1580–2920	LC50 (96 h)	67

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (ppb)	Effects	Reference ^a
Tilapia, <i>Tilapia sparrmanii</i> , adults, exposure for 72 h	98,000	Decreased oxygen consumption, mucus precipitation on gills, histopathology of gill epithelium	79
Bolti, <i>Tilapia zilli</i>			
Adults	13,000	LC50 (96 h) at 25°C	52
Adults	21,000	LC50 (96 h) at 21°C; residues in survivors were 38,000 mg/kg DW vs. 70 in controls for gill; 23,000 vs. 50 for liver; and 2000 vs. 10 for muscle, blood, serum, and liver chemistry	52, 80
Adults	27,000	LC50 (96 h) at 15.3°C	52
Adults	33,000	LC50 (96 h) at 9.3°C	52
AMPHIBIANS			
Marbled salamander, <i>Ambystoma opacum</i> , embryos	2380	50% dead or deformed in 8 days	2
Narrow-mouthed toad, <i>Gastrophryne carolinensis</i> , embryos	10	50% dead or deformed in 7 days	2
Leapfrog, <i>Rana dalmatina</i> , larvae, exposed during formation of gonadal structures	9000	Toxic effect on larval gonad, especially on germ cells of ovarian structure	81
Columbia spotted frog, <i>Rana luteiventris</i> ; tadpoles	28,400	LC50 (96 h)	88
Newt, <i>Triturus cristatus</i> , adults, held in tank with a zinc-plated base	200 to 3000 over a 7-day period	Zinc-poisoned newts were lethargic, ate poorly, and had skin darkening prior to death. Zinc residues were elevated in kidney, brain, liver, and intestine, when compared to controls. The hippocampus region of the brain of poisoned newts contained zinc-rich cells	82
South African clawed frog, <i>Xenopus laevis</i>			
Embryos	>1500	At 96 h, some midgut malformations and pericardial edema	83
Embryos	2700	50% malformations in 96 h	83
Embryos	3600	50% developmental malformations in 6 days	71
Embryos	>4000	Severe edema of the pericardium and eye, gut miscoiling, head and mouth malformations. At high sublethal concentrations, severe skeletal kinking, microphthalmia, and microencephaly	83
Tadpoles, pretreated with 5 mg Zn/L for 96 h	15,000–20,000	At 15 mg/L, none died in pretreated group vs. 45% dead in controls at 90 h; at 20 mg/L, 15% died in pretreated group vs. 50% in untreated controls	69
Embryos	34,500	LC50 (96 h)	71, 83

^a 1, USEPA 1980; 2, USEPA 1987; 3, Spear 1981; 4, Vymazal 1986; 5, Francis and Harrison 1988; 6, Willis 1988; 7, Yantian 1989; 8, Nelson et al. 1988; 9, Munzinger and Guarducci 1988; 10, Belanger et al. 1986; 11, Farris et al. 1989; 12, Brereton et al. 1973; 13, Hunt and Anderson 1989; 14, Eisler 1980; 15, Mason 1988; 16, Eisler 1977a; 17, Eisler 1977b; 18, Lobel and Marshall 1988; 19, Amiard-Triquet et al. 1986; 20, Redpath

Table 9.6 (continued) Effects of Zinc on Representative Aquatic Plants and Animals (Concentrations are in micrograms of zinc per liter of medium.)

and Davenport 1988; **21**, Hietanen et al. 1988a; **22**, Hietanen et al. 1988; **23**, Akberali et al. 1985; **24**, Conra 1988; **25**, Eisler and Hennekey 1977; **26**, Chan 1988a; **27**, Ahsanullah et al. 1988; **28**, Bagshaw et al. 1986; **29**, Ajmalkhan et al. 1986; **30**, Paulauskis and Winner 1988; **31**, Attar and Maly 1982; **32**, Memmert 1987; **33**, Khangarot and Ray 1989; **34**, Johnson and Jones 1989; **35**, Mirenda 1986; **36**, Nugegoda and Rainbow 1989c; **37**, McLusky and Hagerman 1987; **38**, Verriopoulos and Hardouvelis 1988; **39**, Verriopoulos and Moraitou-Apostolopoulou 1989; **40**, Verriopoulos and Dimas 1988; **41**, Lalande and Pinel-Alloul 1986; **42**, Hatakeyama 1989; **43**, Willis 1989; **44**, Fernandez and Jones 1989; **45**, Grant et al. 1989; **46**, Nakamura et al. 1989; **47**, Voogi et al. 1987; **48**, Eisler 1981; **49**, Shukla and Pandey 1986a; **50**, Shukla and Pandey 1986b; **51**, Villegas-Navarro and Villarreal-Trevino 1989; **52**, Hilmy et al. 1987; **53**, Somasundaram 1985; **54**, Somasundaram et al. 1985; **55**, Solbe and Flook 1975; **56**, Sauer and Watabe 1989a; **57**, Eisler 1967; **58**, Burton and Fisher 1990; **59**, Taneja et al. 1988; **60**, Bengeri and Patil 1986; **61**, Gehrke 1988; **62**, Mayer 1987; **63**, Heath 1987; **64**, Pundir 1989; **65**, Mayer and Ellersieck 1986; **66**, Nehring and Goettl 1974; **67**, Buhl and Hamilton 1990; **68**, Anadu et al. 1989; **69**, Woodall et al. 1988; **70**, Bengtsson 1974; **71**, Dawson et al. 1988; **72**, Hobson and Birge 1989; **73**, Brungs 1969; **74**, Pierson 1981; **75**, Sayer et al. 1989; **76**, Everall et al. 1989a; **77**, Flos et al. 1979; **78**, Crespo et al. 1979; **79**, Grobler et al. 1989; **80**, Hilmy et al. 1987a; **81**, Gipouloux et al. 1986; **82**, Taban et al. 1982; **83**, Fort et al. 1989; **84**, NAS 1979; **85**, Khangarot and Ray 1988; **86**, Botton et al. 1998; **87**, Phillips et al. 1998; **88**, Lefcort et al. 1998.

^b MATC = Maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Molluscs

Zinc was most toxic to representative molluscs at elevated temperatures (Eisler 1977a; Sprague 1986; Khangarot and Ray 1987), in comparatively soft water or, in the case of marine molluscs, low salinity (Sprague 1986; Khangarot and Ray 1987), at earlier developmental stages (Munzinger and Guarducci 1988), at low dissolved oxygen concentrations (Khangarot and Ray 1987), and with increasing exposure to high zinc concentrations (Amiard-Triquet et al. 1986).

High zinc accumulations in molluscs are usually linked to high levels of calcium in tissues, low ambient concentrations of iron or cobalt, exposure to organochlorine or organophosphorus insecticides, low salinity, elevated temperatures, increased particulate loadings in medium, increasing length of exposure to higher doses of zinc, increasing age of the organism, and, especially, proximity to heavily carbonized and industrialized areas (Eisler 1980). Radiozinc-65 was rapidly accumulated in southern quahog (*Mercenaria campechiensis*) over a 10-day period; accumulation in kidney was linear over time and was enhanced at elevated phosphate loadings in the medium (Miller et al. 1985). Large variations in daily zinc accumulation rates by marine bivalve molluscs are typical. For example, softshell clams (*Mya arenaria*) immersed in 500 µg Zn/L at 16 to 22°C had daily accumulation rates, in mg/kg FW soft parts, of 2 on the first day of exposure, 7.7 between days 1 and 7, and 3.3 between days 7 and 14. At a lower temperature regimen of 0 to 10°C, immersion in 500 µg/L produced daily accumulation rates of 9.9 mg/kg FW soft parts for the first 42 days, but clams lost zinc at a rate of 0.24 mg/kg daily between days 42 and 112 (Eisler 1981). At 2500 µg/L and 16 to 22°C, daily accumulation rates in surviving *Mya* were 32.0 mg Zn/kg FW soft parts on the first day of exposure, and 11.7 between days 1 and 7. Changes in accumulation rates of zinc by *Mya* reflect, at least partially, complex interactions between water temperature, ambient zinc concentrations, duration and season of exposure, and physiological saturation and detoxification mechanisms (Eisler 1977a, 1977b).

The half-time persistence (T_b 1/2) of zinc in whole molluscs is extremely variable, and reported to range from 4 days in the common mussel (*Mytilus edulis*) to 650 days in the duck mussel (*Anodonta nuttalliana*); intermediate values were 23 to 40 days in limpet (*Littorina irrorata*), 76 days in the California mussel (*Mytilus californianus*), and 300 days in the Pacific oyster (NAS 1979). Zinc persistence in selected organs also shows considerable variability and may be significantly different from T_b 1/2 values seen in whole animal. For example, the T_b 1/2 of zinc in

Mytilus edulis kidney was estimated at 2 to 3 months (Lobel and Marshall 1988) vs. 4 days for whole animal (NAS 1979).

Mytilus edulis has been used extensively as a model for molluscan zinc kinetics. Results of selected studies follow. In mussels, zinc is taken up by the digestive gland, gills, and mantle and rapidly transported via hemolymph to kidney where it is stored in insoluble granules (Lobel and Marshall 1988). There is a high degree of variability in soft tissues of *M. edulis* due entirely to an unusually high degree of variability in kidney zinc of 97 to 7864 mg/kg DW (Lobel 1987). This variability in kidney zinc content is due largely to a low-molecular-weight zinc complex (MW 700 to 1300), that showed a high degree of variability and a positive correlation with kidney zinc concentration (Lobel and Marshall 1988). However, at low ambient concentrations of 50 µg Zn/L, the most sensitive bioindicators of zinc exposure were gills and labial palps (Amiard-Triquet et al. 1986). Food composition had little effect on tissue distribution of radiozinc-65 in mussels as judged by 5-day feeding studies of radiolabeled diatoms (*Thalassiosira pseudonana*), green alga (*Dunaliella tertiolecta*), glass beads, and egg albumin particles (Fisher and Teyssie 1986). Soft part BCF values ranged between 12 and 35 times and was probably due to a rapid desorption of radiozinc from the food particles into the acidic gut, followed by binding to specific ligands or molecules. The Tb 1/2 in mussel soft parts ranged from 42 to 80 days for all food items — including glass beads — and about 20 days in shell (Fisher and Teyssie 1986; Wang et al. 1996). Zinc concentrations in mussels are proportionately related to zinc loadings in the water column and the assimilation efficiency from ingested particles, which in *Mytilus edulis* ranges from 32 to 41% (Wang et al. 1996). Elevated temperatures in the range 10 to 25°C were associated with increased uptake rates of zinc from seawater by mussels (Watkins and Simkiss 1988). If the temperature is oscillated through this range over a 6-hour period, there is a further enhancement of zinc uptake. This effect parallels decreases in zinc content of cytosol fractions and increases in granular fractions (Watkins and Simkiss 1988). Mussels were more sensitive to zinc than were other bivalve molluscs tested. The pumping rate of mussels completely stopped for up to 7 h on exposure to 470 to 860 µg Zn/L; however, other bivalves tested showed only a 50% reduction in filtration rates in the range 750 to 2000 µg Zn/L (Redpath and Davenport 1988). *Mytilus edulis* accumulates zinc under natural conditions, but under some conditions does not depurate (Luten et al. 1986). This conclusion was based on results of a study wherein mussels were transferred from a pristine environment in the Netherlands to a polluted estuary for 70 days, then back again for 77 days. At the start, zinc concentration was 106 mg/kg DW soft parts. By day 70, it had risen to 265 mg/kg DW, at a linear daily uptake of 0.47 mg/kg, but mussels contained 248 mg/kg DW on day 147, indicating that elimination was negligible (Luten et al. 1986). In another study, zinc depressed sperm motility through respiratory inhibition at 6.5 mg/L, a concentration much higher than those normally found environmentally (Earnshaw et al. 1986). In mussel spermatozoa, zinc caused reductions of bound calcium and phosphorus in both acrosomes and mitochondria, suggesting increased permeability of organelle membranes to both elements (Earnshaw et al. 1986).

Arthropods

Arthropods were the most zinc-sensitive group of invertebrates tested (Table 9.6). Toxicity was usually greatest to marine crustaceans (Eisler 1981), to larvae (Eisler 1980), at elevated temperatures (Spear 1981; Sprague 1986; McLusky and Hagerman 1987), during extended exposures (USEPA 1980, 1987), in soft water (Winner and Gauss 1986; Paulauskis and Winner 1988), under conditions of starvation (NAS 1979; Verriopoulos and Moraitou-Apostolopoulou 1989), at salinity extremes above and below the isosmotic point (McLusky and Hagerman 1987), in summer (Eisler 1980), at low concentrations of humic acid (Winner and Gauss 1986; Paulauskis and Winner 1988), in proximity to anthropogenic discharges (Eisler 1980), and at low sediment particulate loadings (Memmert 1987). Acquired zinc tolerance is reported in amphipods collected from zinc-contaminated

sewage wastes (Johnson and Jones 1989) and in fiddler crabs (*Uca* spp.) from a metals-contaminated area. *Uca* from zinc-contaminated areas were more resistant to zinc than were crabs from pristine areas, as judged by increased survival and lower tissue zinc concentrations (Devi 1987; Devi and Rao 1989, 1989a). More research seems warranted on acquired zinc tolerance.

Adverse effects of zinc insult to crustaceans include gill histopathology in prawns, *Macrobrachium hendersdyanum* (Patel and Kaliwal 1989); increased tissue total proteins, decreased glycogen, and decreased acid phosphatase activity in crabs, *Portunus pelagicus* (Hilmy et al. 1988); retardation of limb regeneration of fiddler crab, *Uca pugilator* (Weis 1980); and elevated tissue residues in American lobster, *Homarus americanus* (Waiwood et al. 1987). For example, tissue zinc residues in *Homarus americanus* exposed for 4 days to 25 mg Zn/L were especially high in gill (2570 mg Zn/kg DW vs. 126 at start), hepatopancreas (734 vs. 135), and green gland (1032 vs. 148). After 7 days in uncontaminated media, tissue zinc residues remained elevated in gill (675 mg Zn/kg DW), hepatopancreas (603), green gland (286), and other tissues (Waiwood et al. 1987). Zinc concentrations in crustacean soft tissues usually range between 50 and 208 mg/kg DW, and exceed soft tissue zinc enzymatic requirements by factors of 1.4 to 6.0 (Depledge 1989).

Half-time persistence of zinc in the prawn (*Palaemon elegans*) is about 17 days (Nugegoda and Rainbow 1988b), and between 30 and 270 days for five other crustacean species (NAS 1979). Differences in half-time persistence are linked to differences in excretion rates of ionic zinc and complexed zinc. In general, ionic zinc in crustaceans is excreted first, then complexed zinc; surface-adsorbed zinc is turned over faster than internally adsorbed zinc; molting accounts for 33 to 50% loss of the total body burden in crabs (Eisler 1981).

Crustaceans can accumulate zinc from both water and food (USEPA 1987). In uncontaminated waters, the diet is probably the major source of zinc. Absorption from the stomach is efficient and occurs, in part, via the hepatopancreas. When a large pulse of zinc reaches the blood from the stomach, some is excreted, but much is resorbed and stored in the hepatopancreas in a relatively nonlabile form. Ultimately, stored zinc is also excreted, although removal via the gut is unimportant (Bryan et al. 1986). Zinc absorption occurs initially at the gill surface, followed by transport on a saturable carrier in the cell wall, and is most efficient at low dissolved ambient zinc concentrations. Urinary excretion is an important body removal pathway, especially at high dissolved ambient concentrations when it can account for 70 to 80% of total zinc excretion (Bryan et al. 1986).

Barnacles (*Elminius modestus*) usually accumulate zinc to high body concentrations with no significant excretion. Barnacle detoxification mechanisms of the stored zinc includes production of metabolically inert zinc phosphate granules (Rainbow and White 1989). However, *Elminius modestus* transplanted from an area of high ambient zinc (101 µg/L) to a low ambient zinc (4 µg/L) environment lost zinc slowly (0.3% body burden daily) over an 11-week period. Whole-body zinc burdens declined from 1554 mg/kg DW to 125 mg/kg DW, or about 4.1 mg/kg DW daily (Thomas and Ritz 1986). In the case of *Balanus balanoides*, another barnacle, high BCF values were attributed to inorganic granules that contained up to 38% zinc and accumulated in tissues surrounding the midgut (Eisler 1980).

Crustaceans — and other groups — can regulate body concentration of zinc against fluctuations in intake, although the ways in which regulation is achieved vary among species (Bryan et al. 1986). Regulation of whole body zinc to a constant level is reported for many crustaceans, including intertidal prawns (*Palaemon* spp.), sublittoral prawns (*Pandalus montagui*), green crab (*Carcinus maenus*), lobster (*Homarus gammarus*), amphipods (*Gammarus duebeni*), isopods (*Asellus communis*), and crayfish (*Austropotamobius pallipes*) (Devineau and Amiard-Triquet 1985; Bryan et al. 1986; Lewis and McIntosh 1986; Nugegoda and Rainbow 1988b; Johnson and Jones 1989; Rainbow and White 1989). The body zinc concentration at which zinc is regulated in crustaceans usually increases with temperature, salinity, molting frequency, bioavailability of the uncomplexed free metal ions, and chelators in the medium (Nugegoda and Rainbow 1987, 1988a, 1989a, 1989b). Lobsters (*Homarus gammarus*) are able to equilibrate over a 30-day period with seawater containing

between 2 and 505 µg/L. In response to a 100-fold rise in seawater concentrations (from 5 to 500 µg/L), zinc levels in whole body, blood, hepatopancreas, excretory organs, and gills approximately doubled but changed little in muscle. Shell zinc concentrations increased about 12 times, largely through adsorption (Bryan et al. 1986). Regulation of zinc in lobster blood is achieved by balancing uptake through the gills against urinary excretion and loss over the body surface including the gills (Bryan et al. 1986). The sublittoral prawn, *Pandalus montagui*, can regulate total body zinc concentration to a constant level (75 mg/kg DW) in dissolved zinc concentrations up to 22 µg/L, beyond which there is net accumulation of body zinc. This threshold of zinc regulation breakdown is lower than that in *Palaemon elegans* (93 µg Zn/L) and *Palaemonetes varians* (190 µg Zn/L) under the same physicochemical conditions (Nugegoda and Rainbow 1987; 1988a, 1988b, 1989a, 1989b, 1989c; Rainbow and White 1989). The authors conclude that regulation of body zinc concentration is most efficient in decapods adapted to the fluctuating environments of littoral habitats, possibly as a result of changes in permeability of uptake surfaces in combination with improved zinc excretion systems.

Freshwater crayfish (*Orconectes virilis*) are among the more resistant crustaceans (LC50 value of 84 mg Zn/L in two weeks), and can easily tolerate the recommended water-quality criteria of 50 to 180 µg/L; nevertheless, some streams in Arkansas and Colorado contain 79 to 99 mg Zn/L (Mirenda 1986). *Orconectes virilis* exposed to very high sublethal ambient zinc concentrations of 63 mg/L for 2 weeks show whole-body BCF values of only 2; a similar pattern was observed at other concentrations tested. In all cases, zinc tended to concentrate in gill and hepatopancreas at the expense of muscle, carapace, and intestine (Mirenda 1986). In freshwater crayfish (*Procambarus acutus*), the major uptake route was the ambient medium when compared to diet, although retention time was greater for dietary zinc (Giesy et al. 1980). When dietary zinc was the only zinc source, crayfish rapidly reached a steady state; when water was the only zinc source, crayfish did not reach a steady state (Giesy et al. 1980). Freshwater mysidaceans and their particulate wastes may play an important role in zinc cycling. The freshwater opossum shrimp (*Mysis relicta*) feeding on sediments ingested two to four times more zinc than did mysids feeding on zooplankton. However, sediment-feeding mysids excreted three to five times more zinc than did zooplankton consumers; zinc concentrations in fecal pellets of sediment feeders were up to 24 times higher than in food (Van Duyn-Henderson and Lasenby 1986). In the freshwater crayfish, *Austropotamobius pallipes*, fecal excretion is a major zinc removal pathway; a similar case is made for green crab (*Carcinus maenus*; Bryan et al. 1986). Marine copepods (*Anomalocera*, *Acartia*, *Temora*) excreted 52% of the ingested zinc in fecal pellets that subsequently leached all zinc to seawater within 24 h (Fisher et al. 1991).

Freshwater insects, including many species of mayflies, damselflies, stoneflies, and caddisflies, are relatively tolerant to zinc, with LC50 values usually >1.33 mg/L — although some species were adversely affected at concentrations between 30 and 37 µg Zn/L (USEPA 1987; Table 9.6). Mayfly (*Epeorus latifolium*) larvae were adversely affected at ambient water concentrations of 30 µg Zn/L, but could tolerate dietary loadings of 600 mg Zn/kg DW ration without measurable effects on growth or emergence (Hatakeyama 1989). Chironomid insect populations were reduced or missing immediately downstream from coal mine drainage containing 5 to 10 mg Zn/L. Populations further downstream recovered numerically, but diversity was reduced when compared to upstream communities (Wilson 1988).

Annelids

Populations of freshwater oligochaetes and leeches were reduced in numbers of individuals and numbers of taxa in mine tailing effluents containing 146 to 213 µg Zn/L or sediments containing >20 g Zn/kg DW (Willis 1985b). Leeches (*Erpobdella octoculata*) experienced a reduction in density and reproductive capacity in streams containing 25 to 310 µg Zn/L from mine wastes and did not avoid these harmful concentrations (Willis 1989).

The highest rate of net zinc absorption reported for any group of invertebrates was 2230 mg Zn/kg BW daily in sandworms (*Nereis diversicolor*) from sediments with low zinc levels during exposure for 34 days in 250 mg Zn/L. At 10 mg Zn/L, the rate decreased to 55 mg Zn/kg BW daily (Eisler 1981). Zinc uptake in *Nereis* increased with increasing sediment zinc levels, at lower salinities (Eisler 1980) and elevated temperatures (Fernandez and Jones 1987, 1989). Zinc had no significant effect on burrowing behavior of *Nereis*, even at acutely lethal concentrations (Fernandez and Jones 1987). Sandworms from zinc-contaminated sediments were more resistant to waterborne zinc insult by 10 to 100 times than those from clean sediments (USEPA 1987). Tolerance to zinc in sandworms may be a result of acclimatization or genetic adaptation. In either event, the degree of metal tolerance decreases rapidly as the level of zinc contamination declines, suggesting that some zinc-tolerant worms may be competitively inferior to normal individuals in clean environments (Grant et al. 1989). More research on zinc-tolerant populations seems merited.

Unlike other major groups of marine benthic organisms, the polychaete *Neanthes arenaceodentata* has a limited capacity to regulate zinc (Mason et al. 1988). Uptake in *Neanthes* occurs from the free ionic pool of zinc, whereas EDTA and EDTA-zinc complexes are largely excluded. Zinc accumulates linearly over time (350 h), and the rate decreases with increasing temperature in the range 4 to 21°C. Mason et al. (1988) conclude that uptake and accumulation of zinc is passive in *Neanthes* and does not require metabolic energy. Zinc transfer across the plasma membrane is by way of diffusion. Within the cell, zinc binds to a variety of existing ligands which maintain an inwardly directed diffusion gradient, preventing zinc efflux. Accumulation rate is determined by the number and binding characteristics of the available ligands and their accessibility to zinc. After 50 h of exposure, worms selectively accumulate zinc over cadmium from the medium by a process requiring metabolic energy, and this is attributed to a change in the turnover rate and to the size and nature of the pool of zinc-binding ligands (Mason et al. 1988).

Echinoderms

In echinoderms, zinc concentrations are usually higher in detrital feeders than in carnivores, higher in surface feeders than in sediment feeders, and higher in specimens collected inshore than those collected offshore in deeper waters (Eisler 1980). Sea cucumbers, *Stichopus tremulus*, accumulate radiozinc-65 from seawater by a factor of 1400; however, radiozinc accumulation data should be viewed with caution because addition of stable zinc can reduce zinc-65 accumulations in echinoderm viscera up to tenfold (Eisler 1981). Zinc inhibits the formation of the fertilization membrane in sea urchin eggs, possibly by interfering with cortical granule-derived proteases and proteins (Nakamura et al. 1989).

Fish

Several trends are evident from Table 9.6: (1) freshwater fishes are more sensitive to zinc than marine species; (2) embryos and larvae are the most sensitive developmental stages; (3) lethal and sublethal effects occur in the range 50 to 235 µg Zn/L for most species, and 4.9 to 9.8 µg Zn/L for brown trout (*Salmo trutta*); and (4) behavioral modifications, such as avoidance, occur at concentrations as low as 5.6 µg Zn/L.

Signs of zinc poisoning in fish included hyperactivity followed by sluggishness. Prior to death, fish swam at the surface, were lethargic and uncoordinated, showed hemorrhaging at the gills and base of the fins, shed scales, and had extensive body and gill mucus (Bengeri and Patil 1986). Zinc is most toxic to yearlings of brown trout in soft water at pH 4 to 6 and pH 8 to 9; toxicity at alkaline pH is attributed to the formation of $ZnOH^+$, $Zn(OH)_2$, and $ZnCO_3$ in both hard and soft water — suggesting increased entrapment of metal precipitates within mucous and epithelial layers of the gill (Everall et al. 1989). Acute zinc poisoning in fish is generally attributed to blockade of gas exchange across the gills, causing hypoxia at the tissue level. Tissue hypoxia in fish is a major

physiological change before death once the gas exchange process at the gills is no longer sufficient to meet its oxygen requirements (Burton et al. 1972; NAS 1979; Everall et al. 1989b; Grobler et al. 1989). Cardiorespiratory responses to zinc in the spangled perch (*Leiopotherapon unicolor*) are similar to those induced by hypoxia; zinc-poisoned perch had damaged gill epithelia, resulting in impaired gas exchange and lowered oxygen tension in arterial blood (Gehrke 1988). Acute exposures to high lethal concentrations of zinc also caused histopathology of epithelia lining the oral cavity (Eisler and Gardner 1973).

Many factors modify the lethal properties of zinc in fish. Zinc is more toxic under conditions of comparatively low dissolved oxygen concentrations, high sodium concentrations, decreased loadings of organic complexing agents (Spear 1981), and low pH (NAS 1979). In guppies (*Poecilia reticulata*), females were more resistant than males to acute zinc insult; adults of both sexes were more resistant than were 5-day-old fry (Pierson 1981). Dominant bluegills (*Lepomis macrochirus*) survived exposure to 32 mg Zn/L longer than did submissive fish (NAS 1979). Water temperature is also an important modifier, and it is generally agreed that zinc is more toxic at elevated temperatures (NAS 1979; Spear 1981; Hilmy et al. 1987), provided that acclimatization temperature is considered. For example, cold-acclimatized (3°C) Atlantic salmon (*Salmo salar*) survived longer than warm-acclimatized (19°C) salmon when exposed to lethal concentrations of zinc at their respective acclimatization temperatures. However, at test temperatures lower than their prior acclimatization temperatures, salmon were less tolerant of zinc (Hodson and Sprague 1975). Fish surviving high sublethal concentrations of zinc had significant alterations in blood and serum chemistry, liver enzyme activity (Hilmy et al. 1987a), and muscle glycogen, total lipids, phospholipids, cholesterol, RNA, and proteins (Taneja et al. 1988).

Reproductive impairment seems to be one of the more sensitive indicators of zinc stress in freshwater teleosts, with effects evident in the range 50 to 340 µg Zn/L (Spear 1981). In some cases, reproduction was almost totally inhibited at zinc concentrations that had no effect on survival, growth, or maturation of these same fish (Brungs 1969). Zinc-induced developmental abnormalities were documented in marine teleosts, but concentrations tested were grossly elevated. Eggs of the Baltic herring (*Clupea harengus*), for example, exposed to >6 mg Zn/L have an altered rate of development and produce deformed larvae with cellular disruptions in the brain, muscle, and epidermis (Somasundaram 1985; Somasundaram et al. 1985).

Avoidance tests with fathead minnows (*Pimephales promelas*) show that almost all fatheads, except males with established territories, will avoid 284 µg Zn/L when given a choice; however, avoidance thresholds were 6.4 times higher for established males (Korver and Sprague 1989).

Limited tolerance to zinc was observed in freshwater fishes preexposed to sublethal levels of zinc (Spear 1981; Heath 1987; Woodall et al. 1988; Anadu et al. 1989; Hobson and Birge 1989). In one case, rainbow trout acclimatized to 50 µg Zn/L for 21 days were up to five times more tolerant to subsequent zinc exposures than were nonacclimatized trout. This was not evident at 100 µg Zn/L; also, acclimatization to zinc produced tolerances to copper and cadmium in trout (Anadu et al. 1989). The mechanisms to account for this phenomenon are unknown, but several theories are proposed: increased metallothionein synthesis (Woodall et al. 1988), although this is disputed by Hobson and Birge (1989); high mortality during preexposure may have caused the selection of more zinc-tolerant individuals (Spear 1981); and tolerance may be limited to strains capable of increased zinc excretion, although no evidence now exists linking genetic mechanisms to zinc resistance (Spear 1981).

The half-time persistence (T_b 1/2) of zinc in whole mosquitofish (*Gambusia affinis*) was estimated at 215 days (Newman and Mitz 1988). The half-time persistence of zinc in whole marine fishes ranged from 35 to 75 days in mummichog (*Fundulus heteroclitus*) to 295 to 313 days in a flatfish (*Pleuronectes platessa*); T_b 1/2 in mummichog was shortest at 30°C, longest at 10°C, and intermediate at 20°C (NAS 1979).

Fish can accumulate zinc from both the surrounding medium and from their diet (USEPA 1987). The freshwater zebra danio (*Brachydanio rerio*) accumulated zinc from the medium, but there was

no additional zinc enrichment from a *Daphnia* diet (Memmert 1987). In marine fishes, however, diet was considered to be the major route of zinc intake, and significantly more important than water zinc levels (Eisler 1980).

In freshwater fishes, bioconcentration factors for whole individuals range between 51 and 500 times (USEPA 1987), but are strongly influenced by dose, duration of exposure, water chemistry, and other variables. In mosquitofish, uptake rate from water and zinc elimination rate decreased with increasing age of the fish (Newman and Mitz 1988). In three-spined stickleback (*Gasterosteus aculeatus*), uptake was greater in hard water than in soft water and higher in larger fish, suggesting a surface adsorption mechanism (Matthiessen and Brafield 1977). In brown trout, however, uptake was lower and excretion greater in hardwater of 220 mg CaCO₃/L than in soft water of 9 mg CaCO₃/L, thereby reducing tissue burdens (Everall et al. 1989b). Starved rainbow trout accumulated zinc more rapidly than did fed fish, due to an increased contribution of waterborne zinc to total body zinc levels (Handy and Eddy 1990). Rapidly growing chinook salmon (*Oncorhynchus tshawytscha*) fingerlings removed radiozinc-65 from the medium and retained nearly all of it for 63 days after transfer to uncontaminated media. Most of the zinc-65 was translocated to vertebral column, head, and visceral mass (Joyner and Eisler 1961). The outer surface of the bone seems to be an ion exchange medium capable of taking up large quantities of metal ions whether natural or foreign to the system. Metals thus exchanged from serum proteins may be prevented from undergoing further exchange by the overlaying action of growing bone (Joyner and Eisler 1961). Channel catfish (*Ictalurus punctatus*) fingerlings fed diets containing up to 200 mg Zn/kg FW ration for 12 weeks had elevated bone zinc levels (359 mg/kg DW vs. 254 in controls) and reduced hematocrit, but survival and feed conversion efficiency was the same as in controls (Gatlin et al. 1989). Plasma zinc levels in four species of freshwater fishes consuming diets containing 100 to 200 mg Zn/kg ration ranged between 9.3 and 15.1 mg Zn/L FW; in rainbow trout, zinc tended to concentrate in the erythrocyte membrane (Bettger et al. 1987).

In marine fishes, zinc residues were usually higher in dead fish than in live or moribund animals, higher in smaller fish, higher in liver and viscera, and higher with decreasing water cadmium levels (Eisler 1980). Uptake from the medium by adult mummichogs was inversely related to zinc concentration in the water (USEPA 1987). In mummichogs, zinc accumulates in scales during exposure to 10 mg Zn/L, significantly elevating the zinc:calcium ratio; ratios remained elevated for at least 4 months after transfer to low zinc media, and this phenomenon might have application for environmental monitoring (Sauer and Watabe 1989a). Scale osteoblasts of zinc-exposed mummichogs showed an increase in the number of lysosome-like structures contained by cytoplasm, and suggests that osteoblast lysosomes are involved in zinc accumulation in fish scales via enzymatic degradation of metallothioneins or other metal-binding proteins (Sauer and Watabe 1989). Dietary zinc is not well assimilated in marine flatfish. Turbot (*Scophthalmus maximus*) fed diets containing 100 (control) or 1000 mg Zn/kg DW for 200 days were not different in renal and hepatic metallothionein levels, or in zinc concentrations in liver, kidney, muscle, skin, or bone; a similar case is made for other marine flatfish (Overnell et al. 1988). However, turbot injected intraperitoneally (2 mg Zn/kg BW) had an 18-fold increase in liver metallothionein content, and a threefold increase in liver zinc, confirming the ability of this species to synthesize metallothionein rapidly to a high concentration (Overnell et al. 1988).

Amphibians

Amphibian embryos are more sensitive to zinc than older stages; developmental abnormalities were evident in most species at concentrations >1.5 mg Zn/L (Table 9.6). Embryos of the narrow-mouthed toad (*Gastrophryne carolinensis*) seem to be especially sensitive, with adverse effects reported at 10 µg Zn/L (USEPA 1987), but this requires verification. Amphibians, along with other taxonomic groups, were rare or absent in the vicinity of zinc smelters when compared to more distant sites (Beyer et al. 1985).

In tests with isolated skin of frogs (*Rana* spp.), Zn^{2+} stimulates sodium transport and inhibits chloride-related tissue conductance; however, skin of toads (*Bufo* spp.) is relatively insensitive to zinc (Nagel et al. 1988). In early stages of embryonic development, Zn^{2+} stimulates multiplication of germ cells, but long-term treatment with $ZnSO_4$ has a toxic effect upon the larval gonad and especially on the germ cells of the ovarian structure that is developed in frog larvae (Gipouloux et al. 1986).

9.7.4 Birds

Ducks (*Anas* spp.) had reduced survival when fed diets containing 2500 to 3000 mg Zn/kg ration or when force-fed zinc metal shot equivalent to 742 mg Zn/kg BW (Table 9.7). Domestic chickens (*Gallus* sp.) were more resistant: 8000 mg Zn/kg ration was fatal to chicks, although higher doses were routinely fed to laying hens to induce molting; 2000 to 3000 mg Zn/kg ration inhibited chick growth; 178 mg Zn/kg feed caused immunosuppression in chicks; and dietary concentrations as low as 100 mg Zn/kg caused pancreas histopathology in chicks under conditions of selenium deficiency (Table 9.7). Excessive zinc (2000 mg/kg diet for 21 days) fed to chicks (*Gallus* sp.) caused zinc accumulations in tissues, reduced tissue turnover of zinc, reduced liver turnover of iron, and reduced copper content in liver and pancreas, and of iron in tibia (Stahl et al. 1989b). However, hens were less sensitive and when fed diets containing 2000 mg Zn/kg for 44 weeks produced chicks that had no apparent alteration in tissue zinc, copper, or iron metabolism (Stahl et al. 1990).

Zinc-poisoned mallards (*Anas platyrhynchos*) force fed zinc shot pellets developed ataxia, paresis, and total loss of muscular control in their legs, including the ability to swim (Wobeser 1981). The muscular weakness associated with zinc intoxication would probably make ducks highly susceptible to predation and argues against the use of zinc shot as a substitute for lead shot (Grandy et al. 1968). Mallards fed 3000 mg Zn/kg DW ration for 60 days had diarrhea after 15 days, leg paralysis in 20 days, high mortality after 30 days, and zinc residues at day 60 that were 14 times higher in pancreas than in controls, 7 times higher in liver, 15 times higher in kidney, and 2 to 4 times higher in adrenals, muscle, testes, and ovary (Gasaway and Buss 1972).

In Australia, almost all aviary birds are held in cages made of galvanized wire mesh, resulting in sporadic cases of “new wire disease” caused by the ingestion of galvanized metal used in cage construction. In one case, peach-faced lovebirds (*Agapornis roseicollis*) died within 5 weeks of being placed in a newly erected wire cage; dead birds had elevated liver zinc concentrations of 75 to 156 mg/kg DW vs. normal values of 21 to 33 mg/kg DW (Reece et al. 1986). Zinc poisoning in a captive Nicobar pigeon (*Caloenas nicobarica*) was attributed to plated zinc metal fragments found in the gizzard — presumably ingested from the galvanized cage bars. In addition to elevated tissue zinc concentrations, this pigeon had a swollen liver and kidneys, and extensive kidney histopathology (Zee et al. 1985). A zinc-poisoned blue and gold macaw (*Ara ararauna*) showed weakness, ataxia, extreme thirst, diarrhea, cyanosis, and a plasma zinc concentration of 15.5 mg/L after ingesting galvanized hardware cloth that was 24% zinc by weight and 0.2% lead. The bird was treated with 35 mg/kg BW calcium versenate intramuscularly (im) and 30 mg thiamine hydrochloride kg BW/im; recovery following chelation therapy took 2 months, at which time plasma zinc was 0.6 to 0.8 mg/L vs. 1.3 to 2.0 mg/L for normal birds (Morris et al. 1986). New galvanized wire used in aviary construction should weather for 1 to 2 months, then be scrubbed with a mild acidic solution, such as vinegar, and rinsed; flakes of galvanized metal — which contain up to 2.4 g Zn/kg — should be removed before birds are put in cages (Reece et al. 1986). Zinc toxicosis was diagnosed in a gray-headed chachalaca (*Ortalis cinereiceps*) after it ingested a copper-plated zinc penny; necropsy showed pancreas histopathology and severe gizzard erosion; liver contained 1910 mg Zn/kg FW (Droual et al. 1991).

Zinc phosphide — a rodenticide — is relatively toxic when compared to elemental zinc or zinc oxide; most of the biocidal action is attributed to the phosphide fraction. Acute oral LD₅₀s for zinc

Table 9.7 Effects of Zinc on Representative Birds

Species, Dose, and Other Variables	Effects (reference)
Mallard, <i>Anas platyrhynchos</i>	
Fed diets containing 3000 mg Zn/kg feed, and higher, for 30 days	At 3000 mg/kg ration, ducks had leg paralysis and decreased food consumption; at >3000 mg/kg diet, many deaths occurred (NAS 1979).
Age 7 weeks. Fed diets containing 3000, 6000, 9000 or 12,000 mg Zn/kg dry weight (DW) diet for 60 days; zinc in form of zinc carbonate	Food intake reduced for all groups; the 9000 and 12,000 mg/kg groups had almost zero intake. High mortality after 30 days in all groups; only 17% of 3000 mg/kg group alive at day 60. Zinc residues, in mg/kg fresh weight (FW) at time of death or at day 60 for the 3000 mg/kg group were: 1252 in pancreas vs. 89 for controls; 401 vs. 54 in liver; 88 vs. 45 in adrenals; 413 vs. 27 in kidney; 32 v. 14 in muscle; 78 vs. 17 in testes; and 71 vs. 31 in ovary (Gasaway and Buss 1972).
Age one year. Single oral dose of five Number 6 zinc shot in gelatin capsules, equivalent to 0.40 g Zn or 495 mg Zn/kg body weight (BW)	All shot retained in gizzard after 14 days; no adverse effects after 28 days. Residues at 28 days, in mg/kg DW, were 217 in liver, 79 in kidney, and 126 in feather (French et al. 1987).
Drakes, 18 months old, force-fed eight Number 6 zinc shot pellets	By day 30 posttreatment, 20% had died. The mean weight loss was 33% in dead birds and 22% in survivors. About 83% of survivors developed signs of zinc poisoning (Grandy et al. 1968).
Age one year. Single oral dose of ten Number 6 zinc shot in gelatin capsules, equivalent to 0.80 g Zn or 990 mg Zn/kg BW	Two to 4 shot voided in first 48 h, but no further loss for 28 days. Residues, in mg Zn/kg DW, at 28 days were 211 in liver vs. 171 for control birds, 72 vs. 61 in kidney, and 143 vs. 128 in feather (French et al. 1987).
Pekin duck, <i>Anas platyrhynchos</i>	
3-day-old male white ducklings fed diet containing 2500 mg Zn/kg, as $\text{ZnSO}_4 \cdot \text{H}_2\text{O}$, for 56 days	Progressive ultrastructural degeneration of pancreatic acinar cells evident as early as day 5 (Kazacos and Van Vleet 1989).
Japanese quail, <i>Coturnix coturnix japonica</i>	
Intratesticular injection of 3% zinc chloride equivalent to 1 mg Zn/kg testes or 0.02 mg/kg BW	Testicular teratomas produced during a period of testicular growth stimulated by increased photoperiod (Guthrie 1971).
Hens fed diet containing 15,000 mg Zn/kg ration, as zinc oxide, for 7 days	Significant reduction in body weight, egg production approached zero at day 3, eggshell breaking strength reduced, molting induced (Hussein et al. 1988).
<i>Coturnix, Coturnix japonica</i>	
14-day-old quail fed diets containing various concentrations of zinc, as zinc phosphide (a rodenticide) for 5 days followed by 3 days of untreated fed.	At 600 mg Zn/kg ration, 7% died and all had reduced food intake. At 990 mg Zn/kg diet, 53% died; at 1634 mg/kg, 93% died (Hill and Camardese 1986).
Domestic chicken, <i>Gallus sp.</i>	
Developing embryos, 1-day-old, with 0.76 mg Zn/yolk at start, supplemented with 0.2, 0.4, or 0.6 mg zinc	Hepatic metallothionein levels increased by factors of 3.9 (0.2 mg), 4.7 (0.4 mg) and 7.1 (0.6 mg) (Fleet and McCormick 1988).
Femurs from 9-day-old chick embryos cultivated for 6 days at 3.26 mg Zn/L As above, 6.5 mg Zn/L	Inhibited calcium accumulations in bone and increased alkaline phosphatase activity of medium (Kaji et al. 1988). Decrease in calcified tissues (Kaji et al. 1988).
Domestic breeding hens fed diets containing 28, 38, 48, 68, 94, or 178 mg Zn/kg ration for up to 9 months	Progeny growth after 3 weeks was not affected by maternal zinc feeding levels. A minimum of 38 mg Zn/kg diet was considered necessary for minimal feather fraying and maximal immune response in chicks. Diets containing 178 mg Zn/kg may be excessive and cause immunosuppression of young progeny without affecting growth (Stahl et al. 1989a).

Table 9.7 (continued) Effects of Zinc on Representative Birds

Species, Dose, and Other Variables	Effects (reference)
Fed 28 (control), 48, 228, or 2028 mg Zn/kg diets for 12 or 44 weeks. Hens were 56-weeks old at start of short-term study and 24-weeks old at start of long-term study	Zinc treatments had no effect on overall egg production, feed conversion, feed consumption, hatchability, or progeny growth to age 3 weeks. Zinc was elevated in eggs from hens fed the 2000 mg/kg diet, but chick performance and tissue zinc content were unaffected by maternal zinc nutritional status (Stahl et al. 1990)
Chicks fed diets containing 37 (control), 100, or 2000 mg Zn/kg feed for 21 days	No accumulations in 100 mg/kg group; zinc excretion rate about twice that of controls. No deaths in 2000 mg/kg group, but growth rate was decreased, anemia evident, tissue copper and iron decreased, and tissue zinc increased (Stahl et al. 1989b).
Day-old chicks fed selenium-deficient diets plus 100 mg Zn/kg FW, as zinc oxide, purified ration for 9 days	Elevated zinc concentrations in pancreas, and pancreas histopathology (Lu and Combs 1988a).
Hens fed diets containing 218, 257, 1762, or 1861 mg Zn/kg diet for up to 40 weeks	Eggs from hens fed 218 or 257 mg Zn/kg diet containing a maximum of 14 mg/kg FW, equivalent to about 25% more zinc than eggs produced by control hens. Eggs from the two higher-dose diets had a maximum of 19 mg/kg FW or 57–90% more zinc than eggs produced by hens fed a control diet of 26–28 mg Zn/kg (Stahl et al. 1988).
9-day-old chicks fed purified diet containing 500 mg Zn/kg ration for 2 weeks	Plasma alpha-tocopherol reduced 64%; plasma and pancreas zinc concentrations elevated (Lu and Combs 1988b).
Day-old chicks fed selenium-adequate diet plus 2000 mg Zn/kg FW, as zinc oxide, nonpurified ration for 9 days	Negligible effects on pancreas zinc concentration and on pancreas exocrine function (Lu and Combs 1988a).
9-day-old chicks fed nonpurified diet containing 2000 mg Zn/kg ration for 30 days	No effect on plasma alpha-tocopherol or plasma and pancreas zinc content (Lu and Combs 1988b).
Chicks fed diets containing 2000 or 3000 mg Zn/kg ration for 30 days	Slight reduction in growth at 2000 mg/kg; significant growth reduction at 3000 mg/kg (NAS 1979).
Day-old chicks fed diets containing up to 4000 mg Zn/kg ration for 4 weeks	No effect on growth, survival, or feed conversion. Zinc accumulated in tissue metallothioneins, especially in liver and kidney; levels normal after 5 days on zinc-deficient diet (Oh et al. 1979).
Day-old chicks fed diets containing 4000, 8000 or 16,000 mg Zn/kg for 5 weeks	All dead at 16,000 mg/kg diet. The 8000 mg/kg group had 80% mortality; survivors had significantly reduced growth and feed conversion. At 4000 mg/kg, no significant effect on growth or survival; zinc concentrations elevated in kidney, liver, intestinal mucosa, and pancreas — but values normal after 10 days on basal diet (Oh et al. 1979).
Age 71 weeks, laying hens. Fed diet containing 10,000 mg Zn/kg feed for 2 days, then 5000 mg/kg diet for 4 days	Hens started to molt and ceased laying. Feed intake decreased about 90%. Zinc concentrations in pancreas increased 7-fold, in liver 6-fold, kidney 3-fold, and were elevated in shell gland and yolk. High Zn levels in kidney reflect high Zn excretion rates; high pancreatic Zn (410 mg Zn/kg FW) may suppress the release of insulin by calmodulin inhibition, and could account for the rapid cessation of lay (Verheyen et al. 1990).
White leghorns and brown layers were fed diets containing 10,000, 20,000, or 30,000 mg Zn/kg feed, as zinc oxide, for up to 3 weeks to induce molting	Cessation of egg laying in all treatments. On resumption of egg production, zinc levels in albumin or eggshell were not affected by the treatment or strain; Zn levels in yolk increased and depended on feed intake rather than dose. No increase in zinc content in eggs laid after egg production resumed, regardless of dose or duration of zinc treatment (Decuyper et al. 1988).
White leghorn laying pullets and hens fed diet containing 20,000 mg Zn/kg feed for 5 days	Reduced body weight on day 5, and significantly lowered egg production for 4 weeks. Eggs collected 14–28 days after the 5-day study period had reduced fertility and hatchability. Normal growth, egg production, fertility, and hatchability during weeks 4–12 posttreatment (Palafox and Ho-A 1980).
Laying hens fed diet containing 20,000 mg Zn/kg, as zinc oxide, for 4 days followed by 18 days on basal (35 mg Zn/kg) diet	At day 4, liver zinc concentrations increased 10-fold, kidney 3-fold, egg yolk 3-fold, and pancreas 25-fold; liver and kidney values returned to normal by day 22, but pancreas concentration (1673 mg/kg DW) remained elevated when compared to controls (88 mg/kg DW). At day 10, reduced weight of ovary and oviduct (Williams et al. 1989).
Turkey, <i>Meleagris gallopavo</i>	
Zinc concentration of sperm storage medium increased from 25 to 90 mg/L	Fertilizing ability of stored sperm significantly reduced (Blesbois and Mauger 1989).

phosphide ranged between 16 and 47 mg/kg BW for ring-necked pheasant (*Phasianus colchicus*), golden eagle (*Aquila chrysaetos*), mallard, and horned lark (*Eremophila alpestris*; Hudson et al. 1984). Signs of zinc phosphide poisoning include excessive drinking, regurgitation, muscular incoordination, appetite loss, sluggishness, rapid breathing, and eyelid droop. Signs appeared as soon as 15 min after dosing, and death usually occurred between 2 and 21 h; remission took up to 1 month (Hudson et al. 1984).

Large amounts of zinc are crucial for new feather growth. Zinc deficiency during this period results in stunted, frayed, easily broken feathers. Studies with the giant Canada goose (*Branta canadensis maxima*) show that zinc was released from the pectoralis muscle during molt-induced atrophy and used for growth of feathers and leg muscles during this period (Rosser and George 1986). High dietary levels of zinc are frequently fed to poultry to force molting and reduce egg deposition (Decuyper et al. 1988; Hussein et al. 1988). Extremely high dietary levels of 20 g Zn/kg ration have been used as a commercial management technique to force the molting of laying hens and the subsequent improvement of long-term egg production that molting produces (Lu and Combs 1988a). Laying hens (*Gallus* sp.) given high zinc diets increased their zinc uptakes five- to 40-fold in a dose-dependent pattern despite the decreased food intake associated with high zinc dietary levels. Zinc preferentially accumulated in chicken kidney, liver, pancreas, and gizzard; significant increases in egg zinc occurred at dietary levels of 10 and 20 g Zn/kg (Verheyen et al. 1990). Unlike adults, high dietary levels of zinc adversely affected pancreatic exocrine function in the chick. Effects were exacerbated under conditions of selenium deficiency and feeding of purified diets (Lu and Combs 1988a). Impaired enteric absorption and transport of Vitamin E as a consequence of zinc-induced pancreatic insufficiency is a major cause of reduced tissue concentrations of alpha-tocopherol produced in chicks by excess dietary zinc; these effects were magnified by diets low in corn, soybean meals, and other materials known to chelate zinc, and thus reduce its biological availability (Lu and Combs 1988b). Excess dietary zinc causes pancreatic damage in the chick, including reduced activities of major digestive enzymes, elevated plasma amylase activities, reduced digestibility of starch, and reduced Vitamin A activity. These changes were associated directly with elevated tissue zinc concentrations, especially in the pancreas (Lu et al. 1990).

Zinc sulfate-treated homing pigeons had impaired navigational ability when released approximately 60 km from their roosts. Homing pigeons made anosmic by treating their olfactory mucosa with zinc sulfate solution had significantly poorer homing behavior than did unmanipulated or treated control pigeons, as judged by homeward initial orientation and homing performance (Benvenuti and Gagliardo 1996).

9.7.5 Mammals

Livestock and small laboratory animals are comparatively resistant to zinc, as judged by their tolerance for extended periods to dietary loadings >100 times the minimum recommended daily zinc requirement (Table 9.8). Nevertheless, excessive zinc intake through inhalation or oral exposure can have dramatic effects on survival, metabolism, and well being. Sensitive species of mammals were affected at 90 to 300 mg Zn/kg diet, >300 mg Zn/L drinking water, >90 mg/kg BW daily, >350 mg Zn/kg BW as a single oral dose, and >0.8 mg Zn/m³ air (Table 9.8).

Zinc is relatively nontoxic in mammals. A wide margin of safety exists between normal intakes and those producing deleterious effects. In most cases, dietary levels up to 100 times the daily requirement for extended periods show no discernible effects (NAS 1979; Wentink et al. 1985; Goyer 1986; Leonard and Gerber 1989). The possibility of oral zinc intoxication in adult humans is unusually low, as judged by the low (40%) bioavailability of zinc from the gastrointestinal tract and the high tolerances to zinc reported in domestic livestock and small laboratory animals (Llobet et al. 1988). Humans ingesting up to 12 g of elemental zinc over a 2-day period, equivalent to 33 mg/kg BW for a 60 kg adult, show no evidence of hematologic, hepatic, or renal toxicity (Goyer 1986).

Excessive zinc intake adversely affects survival of all mammals tested (including humans) and produces a wide variety of neurological, hematological, immunological, hepatic, renal, cardiovascular, developmental, and genotoxic effects (USPHS 1989). The most sensitive species of mammals tested showed adverse effects at dietary levels of 80 to 90 mg Zn/kg in humans, 300 mg Zn/kg ration in domestic cats, and 500 mg Zn/kg feed in rats; drinking water concentrations of 300 mg/L in domestic mice, and 800 mg Zn/L in laboratory white rats; daily whole-body intakes >90 mg Zn/kg in horses; acute oral LD₅₀ doses of 350 to 800 mg Zn/kg BW in rats; intraperitoneal injections of 13 mg Zn/kg BW in mice; and 0.8 mg Zn/m³ air in guinea pigs ([Table 9.8](#)).

Metal fume fever is commonly encountered among industrial workers exposed to zinc fumes and is characterized by pulmonary irritation, fever, chills, and gastroenteritis (Saxena et al. 1989b). Attacks begin 4 to 8 h after exposure, and recovery is in 24 to 48 h. The pathogenesis of metal fume fever is unknown but may be associated with endogenous pyrogens released by cell lysis (Goyer 1986). Rabbits, rats, and cats exposed to zinc oxide fumes for 3.5 hours at concentrations of 110 to 600 mg/m³ reacted with a transient fall in body temperature followed by leucocytosis; heavily-exposed animals had signs of bronchopneumonia (Elinder 1986). The atmospheric threshold limit value (TLV) for zinc is 5 mg/m³; however, results of studies with guinea pigs suggest that the TLV value for zinc oxide should be lowered (Lam et al. 1985; [Table 9.8](#)).

Excessive zinc uptake is associated with lameness, unthrifty appearance, and osteochondrosis in foals and pigs, nephrosis in ferrets, and pancreatic fibrosis in sheep (Gunson et al. 1982). Zinc-poisoned mammals are usually characterized by a decreased growth rate, subcutaneous hematomas, ulcerative gastritis, hemorrhagic enteritis, lesions of major limb joints, renal lesions, elevated serum and tissue zinc concentrations, acute diarrhea, copper deficiency, impaired reproduction, and decreased activity of cardiac and hepatic cytochrome oxidase (Saxena et al. 1989b). In severe cases histopathological changes in liver and especially pancreas are evident, as are degenerative changes in kidney and gastrointestinal tract, followed by life-threatening hemolytic anemia (Straube et al. 1980; Allen et al. 1983; Robinette 1990). The pancreas is key in the diagnosis of zinc toxicity and in estimating the period of exposure; in sheep, it takes about four weeks of continued ingestion of toxic amounts of zinc before the pancreas is affected (Allen et al. 1983). More research is needed on the role of the pancreas in zinc toxicokinetics.

Zinc is important to the normal functioning of the central nervous system (CNS). At low concentrations, zinc protects mammalian brain neurons by blocking N-methyl-D-aspartate receptor-mediated toxicity. At high concentrations, zinc is a potent, rapidly acting neurotoxicant in the mammalian brain, as judged by zinc-induced neuronal injury of *in vitro* mature cortical cell cultures (Choi et al. 1988). Increased brain levels of zinc are associated with Pick's disease in certain strains of rodents with inherited epileptic seizures. Intravenous injection of zinc in rats with genetically inherited epilepsy produces seizures; a similar response occurs with intracranial injection of zinc in rabbits with inherited audiogenic seizures (Choi et al. 1988).

Zinc fed to adult male rats at 500 mg/kg diet for 3 weeks or longer negatively impacts the testes and other male accessory organs; effects are a direct result of zinc cytotoxicity from transfer across the blood-testes barrier (Saxena et al. 1989a). Elevated dietary zinc also depresses bone calcium levels and increases fecal calcium loss in rats (Greger 1989). Increases in serum zinc levels of rats after acute zinc overload is due mainly to increases in the zinc bound to the albumin fraction, and secondarily to that bound to the globulin fraction (Castellano et al. 1988). Albumin may play a new physiological role by fitting its binding capacity to serum zinc levels, essentially binding all excess zinc that arrives in the blood (Castellano et al. 1988).

Zinc toxicosis has been observed in humans and livestock after ingestion of acidic foods or drink prepared and stored in galvanized containers (Latimer et al. 1989). Symptoms appear within 24 hours and include nausea, vomiting, diarrhea and abdominal cramps. The emetic dose for zinc in humans was estimated at 225 to 450 mg (3.2 to 6.4 mg Zn/kg BW), equivalent to 1 to 2 g of zinc sulfate (Elinder 1986). Zinc poisoning in dogs is well documented as a result of ingestion of galvanized metal objects, calamine lotion, skin and sunblock preparations containing zinc oxide, staples, nails,

fertilizers, some paints, products containing zinc undecylenate, metallic hardware items with a high zinc content, nuts found on certain types of animal transport cages, and pennies (Latimer et al. 1989; Robinette 1990). The propensity of some individuals to throw pennies (U.S. coinage) into animal cages while visiting zoos and animal parks should be considered a potential source of zinc poisoning in captive animals. Pennies minted prior to 1982 contain 95% copper and 5% zinc; however, copper-clad pennies minted after 1981 contain 97.6% zinc and 2.4% copper (Ogden et al. 1988).

Humans given zinc supplements should be aware of possible complications (Fosmire 1990). Low intakes of 100 to 300 mg of zinc daily in excess of the recommended dietary allowance of 15 mg Zn daily may produce induced copper deficiency, impaired immune function, and disrupted blood lipid profiles. Patients treated with zinc supplements (150 mg daily) to control sickle cell anemia and nonresponsive celiac disease developed a severe copper deficiency in 13 to 23 months; normal copper status was restored by cessation of zinc supplements and increased dietary copper (Fosmire 1990).

Due to false positives, zinc may confound interpretation of the paralytic shellfish poisoning (PSP) mouse bioassay, one of the routine tests used to measure shellfish safety for human consumption. For example, mice injected intraperitoneally with extracts of healthy oyster tissues showed extreme weakness, a drop in body temperature, cyanosis, and some deaths (McCulloch et al. 1989). The threshold for a toxic PSP response corresponds to a drained tissue zinc level >900 mg/kg FW, and this overlaps the zinc concentration range of 230 to 1650 mg/kg FW (1900 to 9400 mg/kg DW) recorded in healthy oyster soft tissues (McCulloch et al. 1989).

Table 9.8 Effects of Zinc on Representative Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
Cows, cattle, <i>Bos spp.</i>		
Dairy cows fed control diet (310 mg Zn/kg DW feed) or control diet supplemented with 1000 or 2000 mg Zn/kg DW ration (as $\text{ZnSO}_4 \cdot \text{H}_2\text{O}$)	The 1000 mg/kg supplement had no adverse effects on milk production, feed intake, body weight, general health, or reproduction; there was a moderate increase in Zn content of plasma and milk. Cows fed the 2000 mg Zn/kg diet, however, had decreased milk yield and feed intake after several weeks; calf weights were lower; adverse effects reversed when excess zinc was removed from diet.	1
Calves fed diets containing 600 mg Zn/kg for 21 days	Appeared normal, although zinc levels were elevated in pancreas, liver, and kidney.	2
Lactating dairy cows fed diets containing 700 or 1000 mg Zn/kg feed for 6 weeks	No change in general health or milk production; no increase in milk zinc content.	2
Lactating cows fed diets containing up to 1386 mg Zn/kg feed for 5 weeks	No significant change in food intake, weight gain, milk production or in zinc concentrations in plasma (1.15–1.3 mg/kg FW) or milk (3.7–4.3 mg/kg FW).	3
Calves and young female cattle fed roughage harvested in vicinity of a factory galvanizing steel tubes, and containing 3000–7300 mg Zn/kg DW roughage	Signs of chronic zinc poisoning evident after 12–14 months. Signs included reduced appetite, emaciation, submandibular edema, diarrhea, moderate anemia, elevated serum zinc (4.3–6.0 mg/L vs. normal 1.8–2.1), liver Zn (420–1600 mg/kg DW vs. normal 72–248), kidney Zn (910–1680 mg/kg DW vs. normal 40–114), and low serum calcium and magnesium.	4
Dog, <i>Canis familiaris</i>		
Fed diets containing up to 1000 mg Zn/kg ration for up to 1 year	No measurable signs of damage.	2
Pomeranian, 2.2 kg, 4-months old, ingested four copper-clad zinc pennies	Hemolytic anemia, vomiting, salivation, serum zinc dropped from 29 mg/L to 4.4 mg/L 15 days after coins were surgically removed (normal dog serum Zn values range between 0.6 and 2.0 mg/L).	5

Table 9.8 (continued) Effects of Zinc on Representative Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
Zinc-poisoned oral route, (lethal) dose unspecified	Tissue zinc concentrations (in mg/L or mg/kg FW) were 32 in serum, 16–32 in plasma, 20–25 in urine, 369 in liver, and 295 in kidney. Normal values were 0.7–1.1 in serum, 0.6–1.0 in plasma, 1.3–2.0 in urine, 17–32 in liver, and 9–23 in kidney.	6
Died from ingestion of 34 copper-clad zinc pennies	Elevated zinc levels in serum, liver, and kidney; jaundice, anoxemia, anemia, vomiting, dark red urine.	7
Guinea pig, <i>Cavia</i> sp.		
Inhalation of 0.8 mg Zn/m ³ for 1 h	Difficulty in breathing.	8
Inhalation of 4 mg Zn/m ³ , 3 h daily for 6 days	Temporary lung damage.	8
Inhalation of 5 mg Zn/m ³ , as ultrafine zinc oxide, 3 h daily for 6 days	Decrease in lung capacity, alveolar volume, and diffusing capacity for carbon monoxide; values remained depressed for at least 72 h after last exposure. Persistent inflammation of proximal portion of alveolar ducts and adjacent alveoli.	9, 10
Horse, <i>Equus caballus</i>		
Weanling foals, age 3 months, fed diets containing 7.7 mg copper/kg plus 29, 250, 1000, or 2000 mg Zn/kg ration for 15 weeks. At start, serum zinc level was 0.6 mg/L and serum copper level 1.4 mg/L	Foals fed 29 or 250 mg Zn/kg diets had normal serum copper and zinc concentrations. Those fed 1000 or 2000 mg Zn/kg diet became hypocupremic in 5 to 6 weeks and developed lameness owing to cartilaginous disease similar to osteochondritis dessicans. Foals fed high zinc diets became lame when serum copper fell to 0.3 mg/L for >1 week; at end of study arthritic foals had <0.2 mg copper/L serum. Serum zinc concentrations rose to >2 mg/L within 2 weeks at 1000 or 2000 mg Zn/kg diet; liver zinc was <333 mg/kg DW at diets of <250 mg Zn/kg, 2728–3511 mg/kg DW at 1000 mg Zn/kg diet, and 4364–4524 mg/kg DW at the highest dietary loading of 2000 mg Zn/kg in 15 weeks	2
Adults, vicinity of lead-zinc smelter, ingesting >90 mg Zn/kg BW daily	Decreased growth, lameness, bone deformities, death.	2
Cat, <i>Felis domesticus</i>		
Fed diet containing 300 mg Zn/kg ration for 16 weeks	Weight loss and pancreas histopathology.	2
Fed diets containing >600 mg Zn/kg ration	Diets rejected.	2
Fed diet containing 9000 mg Zn/kg ration for 3–53 weeks	Pancreas histopathology.	8
Human, <i>Homo sapiens</i>		
Dietary route		
80 mg/kg ration for 6 weeks	Digestive problems.	8
90 mg Zn/kg ration for 5 weeks	Decreased serum cholesterol levels.	8
153 mg Zn/kg ration for 6 weeks	Altered immune system.	8
<150 mg Zn daily	No effect on male plasma cholesterol; females have decreased cholesterol.	12
>160 mg Zn daily	Increased plasma cholesterol level in both sexes; increased risk of heart disease in males.	12
Inhalation route		
600 mg Zn/m ³ for 10 min	Metal fume fever; i.e., difficulty in breathing, flu-like symptoms.	8

Table 9.8 (continued) Effects of Zinc on Representative Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
Oral route		
15-year-old girl who consumed 220 mg of zinc sulfate twice daily "for some time"	Acute gastrointestinal bleeding ulcers.	13
Boy who consumed 12 g of elemental zinc	Headache and lethargy.	13
Single oral dose of 45 grams of zinc as ZnSO_4 (normal is 15–20 mg daily)	Death, preceded by dehydration, electrolyte imbalance, abdominal pain, nausea, vomiting, dizziness, muscular incoordination, and acute renal failure.	14
Celebes ape, <i>Macaca nigra</i>; male; age 16 years; zoo animal; serum		
Routine examination showed stomach containing 4 zinc-clad US pennies	8.0 mg/L FW	24
36 h after unaided passage of last penny	6.15 mg/L FW	24
6 months after above	1.3 mg/L FW	24
Control animal	2.3 mg/L FW	24
Domestic mouse, <i>Mus sp.</i>		
Dietary route		
68, 682, or 6820 mg Zn/kg ration for 13 weeks (fed as 300, 3000, or 30,000 mg $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ /kg ration)	No observed effects at 682 mg/kg diet (and lower), equivalent to 104–109 mg Zn/kg BW daily. At 6820 mg Zn/kg ration, however, adverse effects were documented on survival, growth, food and water intake, and blood chemistry; lesions noted in pancreas, stomach, intestine, spleen, and kidney.	15
500 mg/kg for 3 months	Anemia.	8
30,000 mg/kg ration for 13 weeks	Some deaths, liver and kidney histopathology.	8
Drinking water		
300 mg/L for 5–14 months	Pancreas histopathology.	8
Intraperitoneal injection		
4 injections over 9-day period totalling 13 mg Zn/kg BW	Toxic. Severe weight loss, some deaths.	23
European ferret, <i>Mustela putorius furo</i>		
Fed basal diet (27 mg Zn/kg feed) or basal diet plus 500, 1500, or 3000 mg Zn/kg ration for up to 197 days; four animals per group	Ferrets fed 500 mg/kg all survived with no significant histopathology; zinc concentrations, in mg/kg DW, were 148 in liver vs. 115 in controls, and 383 in kidney vs. 180 in controls. At 1500 mg/kg, all 4 ferrets were <i>in extremis</i> or dead by day 21. At death, liver zinc was 859 mg/kg DW and kidney zinc 1000 mg/kg DW; ferrets had 40–50% loss in body weight; food intake had decreased 80%; and erythrocyte number, hemoglobin, and hematocrit had significantly decreased. Ferrets fed the 3000 mg/kg diet died between days 9 and 13, lost up to 40% of initial body weight, and food intake decreased 77%; postmortem examination showed blood in intestine, orange-colored liver, and kidney histopathology. Elevated zinc content in liver of 1273 mg/kg DW and in kidney of 1138 mg/kg DW.	8, 16, 17
Rabbit, <i>Oryctolagus sp.</i>		
Single oral dose of 65 mg Zn/kg BW, as ZnSO_4	Half-time persistence of 713 min.	8

Table 9.8 (continued) Effects of Zinc on Representative Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference^a
Intravenous injection of 0.325 mg Zn/kg BW, as ZnSO ₄	Half-time persistence of 268 min.	8
Intraperitoneal injection of 3.4 mg Zn daily	Associated with lowered plasma cholesterol levels.	12
<i>Domestic sheep, Ovis aries</i>		
Domestic ewe, age 5 years, found moribund, suspected zinc poisoning	Elevated zinc levels (mg/kg DW) in liver of 650 vs. 144 in controls, and in kidney 760 vs. 84 in controls; muscle residues same as controls, i.e., 154 vs. 158; generalized jaundice; liver degeneration and blockage of bile ducts.	18
Found dead, zinc-poisoned naturally	Zinc concentrations, in mg/kg DW, were 463 in liver (vs. 165 in controls), 274 in kidney (vs. 150 in controls), and 752 in pancreas (vs. 88 in controls).	19
Zinc-poisoned experimentally, oral route	Zinc concentrations, in mg/kg DW, were 1125–1671 in liver, 2130–2442 in kidney, 1440–1932 in pancreas, and 4900 in feces (vs. 158 in controls).	19
Lambs fed diets containing 1000 mg Zn/kg	Food intake reduced; approaching toxic level.	2,7
<i>Laboratory white rat, Rattus sp.</i>		
Dietary route		
Adult males given 500 mg Zn/kg ration, as ZnSO ₄ , for 6 weeks	After 3 weeks, spermatogenesis was arrested at the primary spermatocyte stage. After 4 weeks, food consumption declined, forelimb lameness, and swelling in cervical lymph nodes. At 6 weeks, testes showed enlarged lumen and abnormal germinal epithelium.	20
682 mg Zn/kg ration, as ZnSO ₄ · 7H ₂ O, for 13 weeks	No observable effect level, equivalent to 53–55 mg Zn/kg BW daily.	15
2000 mg Zn/kg ration, chronic exposure	“Tolerated.”	2
4000–5000 Zn/kg ration for 18 days	Fetotoxic dose, poor reproduction.	8, 2
5000–10,000 mg Zn/kg ration	Reduced growth, anemia, poor reproduction, disrupted liver catalase and cytochrome oxidase activity, copper deficiency.	14
6820 mg Zn/kg ration for 13 weeks	Retarded growth, low food intake, abnormal blood chemistry, regressive changes in pancreas.	15
Drinking water route		
Doses equivalent to zero, 160, 320, and 640 mg Zn/kg BW daily for 3 months	No significant effect of any dose on organ weight, hematocrit, hemoglobin, glucose, and enzyme activity. Effects noted only at 640 mg Zn/kg BW daily: some deaths, less drinking water ingested, decreased volume of urine, significant increase in urea and decrease in creatinine. Tissue residues, in mg Zn/kg FW, were significantly elevated over controls in high dose group at 3 months: 60 vs. 20 in liver, 38 vs. 16 in kidney, 330 vs. 92 in bone, 21 vs. 3 in blood, 36 vs. 16 in spleen. Residues were the same as controls in brain (9), lung (13), and muscle. Liver alterations.	21
800 mg Zn/L for 30 days		8
Intragastric administration		
180 g adults given single dose of 500 mg, equivalent to 2777 mg/kg BW	Serum zinc reached a maximum of 3.5 mg Zn/L after 60 min, and returned to normal (1.6 mg/L) within 24 h.	22
165 g adults given 500 mg daily for up to 30 days, equivalent to 3030 mg Zn/kg BW daily	Serum zinc, in mg/L, after 7, 14, or 30 days was 1.9, 2.2, and 2.1, respectively; 10 days after last dose, serum zinc was normal.	22

Table 9.8 (continued) Effects of Zinc on Representative Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
Single oral dose 350–800 mg Zn/kg BW	Acute oral LD50.	2, 21
Domestic pig, <i>Sus spp.</i>		
Weanlings fed diet containing 1000 mg Zn/kg feed for 30 days	Decreased growth rate and food intake, arthritis, lameness, and inflammation of the gastrointestinal tract.	13

^a 1, Miller et al. 1989; 2, NAS 1979; 3, Gaynor et al. 1988; 4, Wentink et al. 1985; 5, Latimer et al. 1989; 6, Robinette 1990; 7, Ogden et al. 1988; 8, USPHS 1989; 9, Lam et al. 1985; 10, Goyer 1986; 11, Bridges 1990; 12, Sammon and Roberts 1988; 13, Elinder 1986; 14, Prasad 1979; 15, Maita et al. 1981; 16, Straube et al. 1980; 17, Reece et al. 1986; 18, Schlosberg 1976; 19, Allen et al. 1983; 20, Saxena et al. 1989b; 21, Llobet et al. 1988a; 22, Castellano et al. 1988; 23, Kreppel et al. 1988; 24, Murray et al. 1997.

9.8 RECOMMENDATIONS

For growing agricultural crops: (1) sewage sludge may be applied to soils provided that total zinc content does not exceed 150 to 560 kg per surface hectare ([Table 9.9](#)); (2) a maximum permissible extractable soil zinc concentration of 23 mg/kg DW is recommended, according to Soviet agronomists (Beyer 1990); and (3) seedlings of oak (*Quercus spp.*) and red maple (*Acer rubrum*) will eventually die in culture medium containing >100 mg Zn/kg (Buchauer 1971), although total zinc concentrations for global crop production routinely exceed 100 mg/kg DW soil ([Table 9.9](#)). Research is needed in standardized methodology for measuring bioavailable (i.e., extractable) soil zinc and on its relation to other soil measurements, such as total zinc and depth of cultivation, in the case of surface application.

Data are limited on zinc hazards to terrestrial invertebrates; however, sensitive species are adversely affected at dietary concentrations >300 mg Zn/kg, or at soil concentrations >400 mg/kg ([Table 9.9](#)).

Water-quality criteria protection of aquatic life should include both total recoverable zinc and acid-soluble zinc (USEPA 1980, 1987). For example, if total recoverable zinc is substantially above the proposed criteria and acid-soluble zinc is below the limit, there is cause for concern (USEPA 1987). To protect approximately 95% of freshwater animal genera, the U.S. Environmental Protection Agency recommends water concentrations that average <47 µg total recoverable zinc per liter, not to exceed 180 µg/L at any time in soft water (i.e., <50 mg CaCO₃/L), or a mean concentration of 59 µg acid soluble zinc per liter, not to exceed 65 µg/L at any time in soft water ([Table 9.9](#)). These criteria are unsatisfactory because lower ambient zinc concentrations between 5 and 51 µg/L clearly have significant negative effects on growth, survival, and reproduction of important species of freshwater fishes, amphibians, insects, sponges, and crustaceans ([Table 9.9](#)). Some downward modification seems necessary in the current proposed zinc criteria for freshwater aquatic life protection.

To protect important species of marine animals, the U.S. Environmental Protection Agency recommends that total recoverable zinc in seawater should average <58 µg/L and never exceed 170 µg/L; for acid-soluble zinc, these values are <86 and 95 µg/L ([Table 9.9](#)). As was the case for freshwater biota, there is a growing body of evidence ([Table 9.9](#)) demonstrating that many species of marine plants, crustaceans, molluscs, echinoderms, and fish are adversely affected at ambient zinc concentrations between 9 and 50 µg/L, or significantly below the current proposed criteria for marine life protection.

Zinc deficiency effects have been produced experimentally in freshwater sponges at <0.65 µg Zn/L (Francis and Harrison 1988), in rainbow trout fed diets containing <15 mg Zn/kg FW (Spry et al. 1988), in certain species of marine algae at <0.7 µg Zn/L (Vymazal 1986), and in certain species of marine invertebrates at <6.5 µg Zn/L (Clapper et al. 1985a, 1985b) or <34 mg Zn/kg DW whole organism (White and Rainbow 1985). Zinc deficiency in natural aquatic ecosystems has not yet been credibly documented.

In aquatic environments, Spear (1981) spotlights three research needs: (1) development of analytical procedures for measurement of individual dissolved zinc species, notably the aquo ion and zinc chloride, and for nondissolved species that occur in natural waters; (2) separation of natural from anthropogenic influences of sediment-water interactions on flux rates, with emphasis on anoxic conditions, the role of microorganisms, and the stability of organozinc complexes; and (3) establishment of toxicity thresholds for aquatic organisms based on bioaccumulation and survival to determine the critical dose and the critical dose rate, with emphasis on aquatic communities inhabiting locales where zinc is deposited in sediments. These research needs are still valid.

Bird diets, in mg Zn/kg DW feed, should contain 25 to 38 to prevent zinc deficiency effects, 93 to 120 for adequate to optimal growth, <178 to prevent marginal sublethal effects, and <2000 to prevent the death of chicks and ducklings (Table 9.9). Extremely high dietary levels of 20 g Zn/kg ration are fed routinely to laying hens by poultry managers to force molting and to improve long-term egg production (Lu and Combs 1988a); in these cases zinc preferentially accumulates in kidney, liver, pancreas, and eggs (Verheyen et al. 1990). Much additional work now seems warranted on the role of zinc in avian nutrition, and on the significance of tissue concentrations as an indicator of zinc stress.

The normal daily intake for all human age groups ranges between 8 and 14 mg (Casey and Hambidge 1980), but pregnant women require an additional 350 to 375 mg of zinc during the course of their pregnancy (Jameson 1980). Zinc used therapeutically in humans at >160 mg daily may have deleterious effects on copper status (Sammon and Roberts 1988). Lower levels — close to the recommended daily allowance of 15 mg — are reported to interfere with iron metabolism and with high-density lipoprotein cholesterol concentrations (Fosmire 1990), but this requires verification. The proposed air quality criterion for human health protection is 5 mg Zn/m³, although this is demonstrably harmful to guinea pigs (Table 9.9). It is not yet known if guinea pigs are more sensitive than man to atmospheric zinc, or if some downward modification is needed in the current zinc air quality criterion for protection of human health, and presumably wildlife.

Single oral doses >350 mg Zn/kg BW were fatal to rats, although doses of 320 mg/kg BW were tolerated (Table 9.9), suggesting a rapid breakdown in ability to regulate zinc in a relatively narrow critical threshold range. More research seems needed on zinc regulation of massive doses.

Data are scarce in mammals that link zinc concentrations in tissues with environmental zinc perturbations. In harbor porpoises, impaired homeostasis reportedly occurs when zinc exceeds 100 mg/kg FW liver; however, livers of many species of marine mammals routinely exceed this value (Wood and Van Vleet 1996). Elevated zinc concentrations, in mg Zn/kg DW tissue, were >120 in cattle liver, >180 in sheep kidney, and >250 in sheep liver (Table 9.9), but their significance is unclear. No international regulations or guidelines applicable to zinc are available (USPHS 1989). No U.S. Food and Drug Administration “action level” or other maximum acceptable concentration exists for zinc, and therefore no Final Residue Value can be calculated (USEPA 1987). This seems to be a high priority research need.

Eating seafoods that contain high concentrations of zinc does not seem to present a threat to human health. However, oysters from Tasmania allegedly caused nausea and vomiting in some people who ate them; these oysters contained about 20 grams of zinc per kg soft parts FW, or about 500 times more than the Australian food regulation of 40 mg/kg FW (Eisler 1981).

In mammals, large differences are evident between and within species in resistance to zinc poisoning and in sensitivity to zinc nutritional needs (Table 9.9). Adverse effects of excess dietary

zinc occurred in sensitive species at 80 (human) and 300 (cat) mg Zn/kg DW; other species tested were significantly more resistant. Daily intake rates considered harmful over long periods ranged from about 2.3 mg/kg BW in man to >90 mg/kg BW in horses. Dietary loadings that optimally prevented zinc deficiency, in mg Zn/kg DW diet, were 30 for bank voles, 33 for adult sheep (124 to 130 for lambs), 37 for mice, 45 to 60 for cattle, 76 for rat, 80 for goat, 100 for monkey, and 150 for mink; recommended daily intake rates in mg/kg BW, ranged from about 0.2 in man to 110 to 140 in cattle (Table 9.9). More research is needed on the interaction effects of zinc with proteins, calcium, chloride, and other trace elements, and on the long-term consequences of nutrient interactions using animals of various age and nutrient status (Greger 1989).

Table 9.9 Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
CROP PLANTS		
<i>Sewage sludge applied to agricultural soils</i>		
Europe, acceptable	150–<300 kg/ha at pH 6.0–7.0	1
Florida		
Maximum permissible	205 kg/ha	1
Unacceptable	>10,000 mg/kg dry weight (DW)	1
Oregon ^b , Wisconsin ^b , acceptable	250–<1000 kg/ha	1
Vermont ^b , acceptable	280–<1120 kg/ha	1
Maryland ^b , Massachusetts ^b , acceptable	280–<560 kg/hg	1
Minnesota ^b , Missouri ^b , acceptable	280–<1120 kg/ha	1
Illinois, maximum	560 kg/ha	1
<i>Soils</i>		
Soviet Union		
Maximum permissible	23 mg/kg DW, extractable by ammonium acetate buffer at pH 4.8	1
Alberta, Canada		
For growing livestock forage	<100 mg/kg DW	1
Quebec, Canada		
Background	200 mg/kg DW	1
Marginal	500 mg/kg DW	1
Unacceptable	>3000 mg/kg DW	1
Netherlands		
Background	200 mg/kg DW	1
Marginal	500 mg/kg DW	1
Unacceptable	>3000 mg/kg DW	1
Ontario, Canada, acceptable	<220 mg/kg DW	1
Germany, acceptable	<300 mg/kg DW	2
New Jersey, goal	<350 mg/kg DW	1
New York, acceptable		
Agricultural soils	168–<250 kg/ha DW	1
Forest soils	<560 kg/ha DW	1
TERRESTRIAL INVERTEBRATES		
<i>Earthworms</i>		
Soil		
High accumulations, but otherwise safe	97 mg/kg DW	3
Adverse effects	>400 mg/kg DW	3
<i>Slugs</i>		
Diet, adverse effects	>300 mg/kg DW	4

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
FRESHWATER AQUATIC LIFE		
Water		
Total recoverable zinc		
50 mg CaCO ₃ /L	47 µg/L, 24 h average; not to exceed 180 µg/L at any time	5
100 mg CaCO ₃ /L	47 µg/L, 24 h average; not to exceed 320 µg/L at any time	5
200 mg CaCO ₃ /L	47 µg/L, 24 h average; not to exceed 570 µg/L at any time	5
Acid-soluble zinc ^c	4-day average concentration not to exceed the numerical value $e^{((0.8473 \ln \text{hardness})+0.7614)}$ more than once every 3 years on average; 1-h concentration not to exceed $e^{((0.8473 \ln \text{hardness})+0.8604)}$ more than once every 3 years on average. See below for examples.	6
50 mg CaCO ₃ /L	4-day average not to exceed 59 µg/L; 1-h average not to exceed 65 µg/L	6
100 mg CaCO ₃ /L	4-day average not to exceed 110 µg/L; 1-h average not to exceed 120 µg/L	6
200 mg CaCO ₃ /L	4-day average not to exceed 190 µg/L; 1-h average not to exceed 210 µg/L	6
Adverse effects, most sensitive species		
Brown trout, <i>Salmo trutta</i> , embryos and fry	4.9–19.6 µg/L	7
Daphnid, <i>Daphnia magna</i>	5–14 µg/L	6
Rainbow trout, <i>Oncorhynchus mykiss</i>	5.6–10 µg/L	5, 6, 8
Narrow-mouthed toad, <i>Gastrothryne carolinensis</i> , embryos	10 µg/L	6
Daphnid, <i>Daphnia galeata mendotae</i>	15–30 µg/L	6
Freshwater sponge, <i>Ephydatia fluviatilis</i>	26 µg/L	9
Mayfly, <i>Epeorus latifolium</i>	30 µg/L	10
Midge, <i>Tanytarsus dissimilis</i>	37 µg/L	5, 6
Atlantic salmon, <i>Salmo salar</i>	50 µg/L	6
Cladoceran, <i>Ceriodaphnia reticulata</i>	51 µg/L	6
Flagfish, <i>Jordanella floridae</i>	51 µg/L	6
Diet		
Channel catfish, <i>Ictalurus punctatus</i>		
Minimum	20 mg/kg DW	11
Recommended ^d	150–200 mg/kg DW	11
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Minimum	10–30 mg/kg DW; 15–30 mg/kg fresh weight (FW)	12, 13
Adequate	90 mg/kg FW	13
Sediments		
Great Lakes		
Safe	<90 mg/kg DW	1
Marginal	90–200 mg/kg DW	1
Unacceptable	>200 mg/kg DW	1
Wisconsin and Ontario, for Great Lakes sediments dredged from harbors and for disposal in water	<100 mg/kg DW	1
MARINE AQUATIC LIFE		
Seawater		
Total recoverable zinc	58 µg/L, 24-h average; not to exceed 170 µg/L at any time	5

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
Acid-soluble zinc ^c	4-day average concentration does not exceed 86 µg/L more than once every 3 years on average; 1-h average concentration does not exceed 95 µg/L more than once every 3 years on average	6
No adverse effects, most species		
Algae	<1400 µg/L	14
Molluscs	<54 µg/L	15
Crustaceans	<230 µg/L	15
Adverse effects, most sensitive species		
Brown algae, <i>Fucus serratus</i>	8.8–9.5 µg/L	6
Copepod, <i>Tisbe holothuriae</i>	10 µg/L	16
Pacific oyster, <i>Crassostrea gigas</i> , larvae	10–20 µg/L	6
Alga, <i>Rhizosolenia</i> spp.	15–25 µg/L	8
Diatom, <i>Schroederella schroederi</i>	19 µg/L	6
Diatom, <i>Skeletonema costatum</i>	19.6 µg/L	17
Dinoflagellate, <i>Glenodinium halli</i>	20 µg/L	6
Purple sea urchin, <i>Strongylocentrotus purpuratus</i> , embryos	23 µg/L	6
Sand dollar, <i>Dendraster excentricus</i>	28 µg/L	6
Atlantic herring, <i>Clupea harengus</i> , embryos	50 µg/L	6
Mud crab, <i>Rithopanopeus harrissii</i> , larvae	50 µg/L	5
Diet		
Fish, adequate	90 mg/kg FW	13
Tissue residues		
Minimum theoretical requirement for whole molluscs and crustaceans	34.5 mg/kg DW	18
BIRDS		
<i>Mallard, Anas platyrhynchos</i>		
Zinc-poisoned		
Diet	2500–3000 mg/kg DW ration	19, 20, 21
Single oral dose	0.64 mg; 517–742 mg/kg body weight (BW)	22
<i>Birds, various</i>		
Tissue concentrations		
Normal		
Liver	21–33 mg/kg DW	23
Plasma	1.3–2.0 µg/L	24
Zinc-poisoned		
Liver	75–156 mg/kg DW	23
Plasma	15.5 mg/L	24
<i>Japanese quail, Coturnix japonica</i>		
Safe level	25–30 mg/kg DW diet	25
<i>Chicken, Gallus sp.</i>		
Recommended daily intake	>31 mg	26
Diet		
Adverse effects, zinc deficiency	<38 mg/kg DW ration	27, 28, 29
Adequate	93–120 mg/kg DW ration	28, 29
Excessive	>178 mg/kg DW ration	27
Toxic	>2000 mg/kg DW ration	20, 30, 31

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
MAMMALS		
Cattle, <i>Bos spp.</i>		
Diet		
Soluble zinc, recommended level		
Calves	>8 mg/kg DW	20
Adults		
Beef cattle	10–30 mg/kg DW	20
Dairy cattle	40 mg/kg DW	20
Total zinc		
Marginal	25 mg/kg DW	32
Recommended	45–60 mg/kg DW	32, 33
Maximum tolerated		
Calves	500 mg/kg DW	35
Adults	1000 mg/kg DW	34, 35
Toxic	>900–2000 mg/kg DW	34, 35
Tissue residues		
Liver		
Zinc-deficient	<10 mg/kg DW	32
Suboptimal	10–30 mg/kg DW	32
Optimal	30–120 mg/kg DW	32
Excessive	>120 mg/kg DW	32
Lethal	>500 mg/kg DW	34
Plasma		
Zinc-deficient	<0.66 mg/L	33
Normal	1.02 mg/L	33
Elevated	1.5 mg/L	33
Serum		
Zinc-deficient	<0.6 mg/L	36
Recommended daily intake		
Calves		
5-months old	3 grams (25–35 mg/kg BW)	34
14–18 months old	16 grams (50–80 mg/kg BW)	34
Cows	55 grams (110–140 mg/kg BW)	34
Dog, <i>Canis familiaris</i>		
Tissue concentrations, normal vs. zinc-poisoned		
Serum	0.7–1.1 vs. 33 mg/L	37
Plasma	0.6–1.0 vs. 16–32 mg/L	37
Urine	1.3–2.0 vs. 20–25 mg/L	37
Liver	17–32 vs. 369 mg/kg FW	37
Kidney	9–23 vs. 295 mg/kg FW	37
Guinea pig, <i>Cavia spp.</i>		
Air		
Adverse effects	0.8–4.0 Zn/m ³	38
Diet		
Deficient	3 mg/kg DW plus 1 mg/L drinking water	39
Adequate	3 mg/kg DW plus 15 mg/L drinking water	40
Normal	20 mg/kg DW	41
Adequate	100 mg/kg FW	39
High	200 mg/kg DW	41
Tissue concentrations, zinc deficient vs. normal		
Serum	0.5 vs. 1.6–2.0 mg/L	39

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
Liver	9.4 vs. 15–17 mg/kg FW	39
Testes	9.5 vs. 19–27 mg/kg FW	39
Kidney	10 vs. 18–20 mg/kg FW	39
<i>Domestic goat, Capra sp.</i>		
Diet		
Soluble zinc, recommended		
Adults	>4 mg/kg DW	20
Kids	>7 mg/kg DW	20
Total zinc		
Deficient	<15 mg/kg DW	42
Recommended	80 mg/kg DW	42
<i>Bank vole, Clethrionomys glareolus</i>		
Diet, recommended	30 mg/kg DW	43
<i>Horse, Equus caballus</i>		
Diet		
No adverse effects	250 mg/kg DW	44
Adverse effects	1000 mg/kg DW	44
Daily intake		
Adverse effects	>90 mg/kg BW	20
<i>Domestic cat, Felis domesticus</i>, diet, adverse effects		
	300 mg/kg DW	20
<i>Humans, Homo sapiens</i>		
Air		
Safe levels		
Zinc chloride, fumes	<1 mg/m ³	20, 38
Zinc oxide, fumes	<5 mg/m ³	28, 38, 45, 46
Zinc and zinc oxides	5–10 mg/m ³	47
Zinc oxide, total dust	10 mg/m ³	38
Zinc oxide, fume and dust, ceiling limit	15 mg/m ³	38
Adverse effects		
Zinc oxides	600 mg/m ³ for 10 min	38
Daily intake		
Recommended dietary intake, assuming availability of 20%		
Children		
To age 1 year	3–6 mg	48
1–10 years	8–10 mg	48
No age specified	10 mg	2, 20
Males		
Age 11–17	14–15 mg	48
Age 18+	11–15 mg	48
No age specified	15 mg	2, 20, 26, 47, 49, 50
Females		
Age 10–13	13–15 mg	48
Age 14+	11–15 mg	48
No age specified	12 mg	
Pregnant	15–20 mg	48
Lactating	25–27 mg	47, 48

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
Maximum safe total, adults		
Not zinc deficient	0.3–1.0 mg/kg BW	2
Zinc deficient	1 mg Zn/kg BW, oral administration	48
Adverse effects level	>160 mg (>2.3 mg/kg BW)	51
Diet		
Seafoods, safe level, Australia	<40 mg/kg fresh weight (FW)	14
Adverse effects		
Gastrointestinal disorders	>80 mg/kg DW diet for 6 weeks	38
Severe copper deficiency	150 mg Zn daily for 13–23 months	49
Vomiting	Single dose of 225–450 mg Zn or 1–2 grams of ZnSO ₄	49
Drinking water		
Safe level	5 mg/L	2, 20, 38
Adverse effects		
Acute GI distress	>280 mg/L	20
Intravenous injection		
Adverse effects	23 mg/kg BW daily	52
Soils		
Canada, nonhazardous to human health		
Ontario		
Residential, parkland, commercial, industrial	<800 mg/kg DW	1
Alberta		
Noncrop uses	<700 mg/kg DW	1
Tissue residues		
Serum		
Normal	0.5–1.29 mg/L	38
No toxic effects	1.92 mg/L	38
Plasma		
Zinc-deficient	0.4–0.6 mg/L	45
Normal	0.7–1.1 mg/L	48
GI disturbances	1.51 mg/L	38
Rhesus monkey, <i>Macaca mulatta</i>		
Diet		
Deficient	4 mg/kg DW	52
Adequate	100 mg/kg DW	53
Mouse, <i>Mus</i> spp.		
Diet		
Zinc-deficient	<5 mg/kg DW	54
Zinc-adequate	36.5 mg/kg DW	54
Tolerated	100 mg/kg DW	54
Tolerated	682 mg/kg DW for 13 weeks (107 mg/kg BW)	55
Harmful	500 mg/kg DW for 3 months	38
Harmful	6820 mg/kg DW	55
Fatal	30,000 mg/kg DW for 13 weeks	38
Drinking water		
Adverse effects	300 mg/L	38
Tissue residues		
Blood		
Deficient	0.7 mg/L	56
Normal	1.0–1.1 mg/L	56
Liver		
Deficient	12 mg/kg FW	56
Normal	17–19 mg/kg FW	56

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
<i>European ferret, Mustela putorius furo</i>		
Diet		
Tolerated	500 mg/kg DW	57
Fatal	1500 mg/kg DW	38
<i>Mink, Mustela vison</i>		
Diet		
Zinc-deficient	4.1 mg/kg FW	58
Adequate	35–45 mg/kg FW; 100–150 mg/kg DW	58
<i>Domestic sheep, Ovis aries</i>		
Diet		
Soluble zinc, adequate		
Adults	>4 mg/kg DW	20
Lambs	>7 mg/kg DW	20
Total zinc		
Adults, adequate	33 mg/kg DW	59, 60
Lambs		
Adequate	124–130 mg/kg DW	59
Harmful	>1000 mg/kg DW	20, 61, 62
Recommended daily intake	>18 mg	26
Tissue residues		
Feces		
Normal	158 mg/kg DW	61
Zinc-poisoned	4900 mg/kg DW	61
Kidney		
Normal	84–150 mg/kg DW	61, 63
Elevated	>180 mg/kg DW	61
Zinc-poisoned	274–760 mg/kg DW	61, 63
Liver		
Normal	144–165 mg/kg DW	61, 63
Elevated	>250 mg/kg DW	61
Zinc-poisoned	463–650 mg/kg DW	61, 63
Pancreas		
Normal	88 mg/kg DW	61
Zinc-poisoned	752 mg/kg DW	61
<i>Harbor porpoise, Phocoena phocoena; liver</i>		
Normal homeostatic range	20–100 mg/kg FW	66
Impaired regulating mechanism	<20 or >100 mg/kg FW	66
<i>Laboratory white rat, Rattus sp.</i>		
Diet		
Soluble zinc		
Recommended	15 mg/kg DW	20
Total zinc		
Zinc-deficient	<12 mg/kg DW	47
Adequate	76 mg/kg DW	64
Adverse effects	>500 mg/kg DW	52
Fetotoxic	>4000 mg/kg DW	20, 38
Daily intake		
Tolerated	320 mg/kg BW	65
Harmful	640 mg/kg BW	65
Single oral dose		
Harmful	>350 mg/kg BW	20, 65

Table 9.9 (continued) Proposed Zinc Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Zinc Concentration	Reference ^a
<i>Domestic pig, Sus spp.</i>		
Diet		
Soluble zinc, safe levels		
Normal	14–20 mg/kg DW	20
Cassava-rice-bran	>40 mg/kg DW	20
Soy base	50 mg/kg DW	20
Total zinc		
Harmful	1000 mg/kg DW	47
Recommended daily intake	>20 mg	26

^a 1, Beyer, 1990; 2, Leonard and Gerber 1989; 3, Beyer et al. 1987; 4, Marigomez et al. 1986; 5, USEPA 1980; 6, USEPA 1987; 7, Sayer et al. 1989; 8, Spear 1981; 9, Francis and Harrison 1988; 10, Hatakeyama 1989; 11, Gatlin et al. 1989; 12, Bettger et al. 1987; 13, Spry et al. 1988; 14, Eisler 1981; 15, Sprague 1986; 16, Verriopoulos and Hardouvelis 1988; 17, Vymazal 1986; 18, White and Rainbow 1985; 19, Kazacos and Van Vleet 1989; 20, NAS 1979; 21, Gasaway and Buss 1972; 22, Grandy et al. 1968; 23, Reece et al. 1986; 24, Morris et al. 1986; 25, Harland et al. 1975; 26, Ellen et al. 1989; 27, Stahl et al. 1989a; 28, Blamberg et al. 1960; 29, Westmoreland and Hoekstra 1969; 30, Stahl et al. 1990; 31, Oh et al. 1979; 32, Binnerts 1989; 33, Ramachandra and Prasad 1989; 34, Wentink et al. 1985; 35, Miller et al. 1989; 36, Damir et al. 1988; 37, Robinette 1990; 38, USPHS 1989; 39, Gupta et al. 1988; 40, Apgar and Everett 1988; 41, Scelsi et al. 1989; 42, Chhabra and Arora 1989; 43, Włostowski et al. 1988; 44, Bridges 1990; 45, Goyer 1986; 46, Lam et al. 1985; 47, Elinder 1986; 48, Casey and Hambridge 1980; 49, Fosmire 1990; 50, Sternlieb 1988; 51, Sammon and Roberts 1988; 52, Saxena et al. 1989b; 53, Golub et al. 1988; 54, Mackay-Sim and Dreosti 1989; 55, Maita et al. 1981; 56, Tone et al. 1988; 57, Straube et al. 1980; 58, Mejbom 1989; 59, Vergnes et al. 1990; 60, Khandaker and Telfer 1990; 61, Allen et al. 1983; 62, Ogden et al. 1988; 63, Schlosberg 1976; 64, Ferreira et al. 1989; 65, Llobet et al. 1988a; 66, Wood and Van Vleet 1996.

^b Higher values permissible for soils with higher cation exchange capacity (Beyer 1990).

^c Zinc that passes through a 0.45 µm membrane filter after acidification to pH 1.5–2.0 with nitric acid (USEPA 1987).

^d Higher concentrations recommended to compensate for reduced bioavailability caused by excess calcium and phytate in diet (Gatlin et al. 1989).

9.9 SUMMARY

Ecological and toxicological aspects of zinc (Zn) in the environment are reviewed, with emphasis on natural resources. Subtopics include: sources and uses; chemical and biochemical properties; carcinogenicity, mutagenicity, and teratogenicity; background concentrations in biological and nonbiological compartments; zinc deficiency effects; toxic and sublethal effects to terrestrial plants and invertebrates, aquatic organisms, birds, and mammals; and recommendations for protection of sensitive resources.

World production of zinc is estimated at 7.1 million tons; the United States produces about 4% of the total and consumes 14%. Zinc is used primarily in the production of brass, noncorrosive alloys, and white pigments; in galvanizing iron and steel products; in agriculture as a fungicide, and as a protective agent against soil zinc deficiency; and therapeutically in human medicine. Major sources of anthropogenic zinc in the environment include electroplaters, smelting and ore processors, mine drainage, domestic and industrial sewage, combustion of solid wastes and fossil fuels, road surface runoff, corrosion of zinc alloys and galvanized surfaces, and erosion of agricultural soils.

Zinc has its primary effect on zinc-dependent enzymes that regulate RNA and DNA. The pancreas is a primary target organ in birds and mammals, followed by bone; in fish, gill epithelium is a primary target site. Dietary zinc absorption is highly variable in animals; in general, it increases with low body weight and low zinc status, and decreases with excess calcium or phytate and by deficiency of pyridoxine or tryptophan. Low molecular weight proteins called metallothioneins

play an important role in zinc homeostasis and in protection against zinc poisoning; zinc is a potent inducer of metallothioneins. Zinc interacts with many chemicals to produce altered patterns of accumulation, metabolism, and toxicity. Some interactions are beneficial to the organism, while others are not, depending on the organism, its nutritional status, and other variables. Knowledge of these interactions is essential to understanding zinc toxicokinetics.

In natural waters, dissolved zinc speciates into the toxic aquo ion $[Zn(H_2O)_6]^{2+}$, other dissolved chemical species, and various inorganic and organic complexes; zinc complexes are readily transported. Aquo ions and other toxic species are most harmful to aquatic life under conditions of low pH, low alkalinity, low dissolved oxygen, and elevated temperatures. Most of the zinc introduced into aquatic environments is eventually partitioned into the sediments. Zinc bioavailability from sediments is enhanced under conditions of high dissolved oxygen, low salinity, low pH, and high levels of inorganic oxides and humic substances.

Zinc and its compounds induce testicular sarcomas in birds and rodents when injected directly into the testes; however, zinc is not carcinogenic by any other route. Growth of animal tumors is stimulated by zinc, and retarded by zinc deficiency. Under some conditions excess zinc can suppress carcinoma growth, although the mechanisms are imperfectly understood. Organozinc compounds are effective mutagens when presented to susceptible cell populations in an appropriate form; the evidence for mutagenic potential of inorganic zinc compounds is incomplete. Zinc deficiency can lead to chromosomal aberrations, but excess zinc was not mutagenic in the majority of tests. Excess zinc is teratogenic to frog and fish embryos, but conclusive evidence of teratogenicity in higher vertebrates is lacking. In mammals, excess zinc may protect against some teratogens. Zinc deficiency may exacerbate the teratogenic effects of known teratogens, especially in diabetic animals.

Background concentrations of zinc seldom exceed 40 $\mu\text{g/L}$ in water, 200 mg/kg in soils and sediments, or 0.5 $\mu\text{g/m}^3$ in air. Environments heavily contaminated by anthropogenic activities may contain up to 99 mg Zn/L in water, 118 g/kg in sediments, 5 g/kg in soil, and 0.84 $\mu\text{g/m}^3$ in air. Zinc concentrations in field collections of plants and animals are extremely variable and difficult to interpret. Most authorities agree on six points: (1) elevated concentrations (i.e., >2 g Zn/kg fresh weight = FW) are normally encountered in some species of oysters, scallops, barnacles, red and brown algae, and terrestrial arthropods; (2) concentrations, in mg Zn/kg dry weight (DW) tissue, are usually <700 in fish, <210 in birds, and <210 in mammals; (3) concentrations are higher in animals and plants collected near zinc-contaminated sites than in the same species collected from more distant sites; (4) zinc content in tissue is not proportionate to that of the organism's immediate surroundings; (5) for individual species, zinc concentration varies with age, sex, season, tissue or organ, and other variables; and (6) many species contain zinc loadings far in excess of immediate needs, suggesting active zinc regulation.

The balance between excess and insufficient zinc is important. Zinc deficiency occurs in many species of plants and animals, with severe adverse effects on all stages of growth, development, reproduction, and survival. In humans, zinc deficiency is associated with delayed sexual maturation in adolescent males; poor growth in children; impaired growth of hair, skin, and bones; disrupted Vitamin A metabolism; and abnormal taste acuity, hormone metabolism, and immune function. Severe zinc deficiency effects in mammals are usually prevented by diets containing >30 mg Zn/kg DW ration. Zinc deficiency effects are reported in aquatic organisms at nominal concentrations between 0.65 and 6.5 $\mu\text{g Zn/L}$ of medium, and in piscine diets at <15 mg Zn/kg FW ration. Avian diets should contain >25 mg Zn/kg DW ration for prevention of zinc deficiency effects, and <178 mg Zn/kg DW for prevention of marginal sublethal effects.

Sensitive terrestrial plants die when soil zinc levels exceed 100 mg/kg (oak and maple seedlings), and photosynthesis is inhibited in lichens at >178 mg Zn/kg DW whole plant. Sensitive terrestrial invertebrates have reduced survival when soil levels exceed 470 mg Zn/kg (earthworms), reduced growth at >300 mg Zn/kg diet (slugs), and inhibited reproduction at >1600 mg Zn/kg soil (woodlouse). The most sensitive aquatic species were adversely affected at nominal water concentrations between 10 and 25 $\mu\text{g Zn/L}$, including representative species of plants, protozoans, sponges,

molluscs, crustaceans, echinoderms, fishes, and amphibians. Acute LC50 (96 h) values ranged between 32 and 40,930 µg/L for freshwater invertebrates, 66 and 40,900 µg/L for freshwater teleosts, 195 and >320,000 µg/L for marine invertebrates, and 191 and 38,000 µg/L for marine teleosts. Acute toxicity values were markedly affected by the age and nutrient status of the organism, by changes in the physicochemical regimen, and by interactions with other chemicals, especially copper salts. Pancreatic degeneration occurred in ducks fed diets containing 2500 mg Zn/kg ration. Ducks died when fed diets containing 3000 mg Zn/kg feed, or when given single oral doses >742 mg Zn/kg body weight (BW). Domestic poultry are routinely fed extremely high dietary levels of 20 g Zn/kg ration as a commercial management technique to force the molting of laying hens and the subsequent improvement of long term egg production that molting produces. However, poultry chicks died at 8 g Zn/kg diet, had reduced growth at 2 to 3 g Zn/kg diet, and experienced pancreas histopathology when fed selenium-deficient but zinc-adequate (100 mg Zn/kg) diets. Mammals are comparatively resistant to zinc, as judged by their tolerance for extended periods to diets containing >100 times the minimum daily zinc requirement. But excessive zinc through inhalation or orally will negatively impact mammalian survival, metabolism, and well-being. The most sensitive species of mammals were adversely affected at dietary concentrations of 90 to 300 mg Zn/kg, drinking water concentrations >300 mg Zn/L, daily intakes >90 mg Zn/kg BW, single oral doses >350 mg Zn/kg BW, and air concentrations >0.8 mg Zn/m³. Humans are comparatively sensitive to excess zinc. Adverse effects occur in man at >80 mg Zn/kg diet, or at daily intakes >2.3 mg/kg BW.

Proposed criteria for protection of aquatic life include mean zinc concentrations of <47 to <59 µg/L in freshwater, and <58 to <86 µg Zn/L in seawater. Results of recent studies, however, show significant adverse effects to a growing number of freshwater organisms in the range of 5 to 51 µg Zn/L, and to saltwater biota between 9 and 50 µg Zn/L, suggesting that some downward modification in the proposed criteria is necessary.

Although tissue residues are not yet reliable indicators of zinc contamination, zinc poisoning usually occurs in birds when liver or kidney contains >2.1 g Zn/kg DW, and in mammals when concentrations, in mg Zn/kg DW, exceed 274 in kidney, 465 in liver, or 752 in pancreas. The proposed air quality criterion for human health protection is <5 mg Zn/m³, but guinea pigs were more sensitive with adverse effects evident at >0.8 to 4.0 mg/m³.

Current research needs include the development of protocols to: (1) separate, quantitate, and verify the different chemical species of zinc; (2) identify natural from anthropogenic sources of zinc; (3) establish toxicity thresholds based on accumulation; (4) evaluate the significance of tissue concentrations in target organs as indicators of zinc stress; and (5) measure the long term consequences of zinc interactions with other nutrients using animals of various age and nutrient status.

9.10 LITERATURE CITED

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CHAPTER 10

Acrolein

10.1 INTRODUCTION

Acrolein ($\text{CH}_2=\text{CHCHO}$) is an aldehyde that was first isolated in 1843 from the dry distillation of fats and glycerol (Beauchamp et al. 1985). It is now known that acrolein is ubiquitous in the environment; it is often present in trace amounts in foods and as a component of smog, fuel combustion products such as wood smoke, exhaust emissions from internal combustion engines, and cigarette smoke (Smith 1962; U.S. Environmental Protection Agency [USEPA] 1980; Beauchamp et al. 1985). Atmospheric concentrations of acrolein over urban areas are between 2 and 7 $\mu\text{g/L}$. Cigarette smoke, however, contains about 10,000 μg of acrolein/L (Beauchamp et al. 1985). Acrolein is classified as a hazardous chemical because of its reactivity and flammability (USEPA 1980). At low, sublethal concentrations, acrolein is widely known for its acrid pungent odor and strong irritating effects on mucous membranes of the eyes and upper respiratory tract, its toxicity to cilia in all organisms, and its interference with nucleic acid synthesis in bacteria (Marano and Puiseux-Dao 1982; Beauchamp et al. 1985). In bulk, acrolein during storage or transfer is potentially hazardous if it becomes overheated or contaminated with water. For example, in 1982, 17,000 residents of Toft, Louisiana, were evacuated when two large tanks of acrolein began to burn (Bowmer and Smith 1984).

Acrolein enters the aquatic environment from its use as an aquatic herbicide, from industrial discharges, and as a by-product of the chlorination of organic compounds in wastewater and drinking water treatment (USEPA 1980). Dilute solutions of acrolein kill undesirable plant life in irrigation streams and ditches (National Research Council [NRC] 1977) and have been used routinely in about 4000 km of irrigation canals in southeastern Australia to control submerged weeds, including *Potamogeton tricarinatus*, *Elodea canadensis*, and *Vallisneria gigantia* (Bowmer and Smith 1984). Acrolein has also been used for many years in channel maintenance in the United States (especially in the western states), Canada, Egypt, Argentina, Mexico, and Turkey (Bowmer and Smith 1984). Unlike most other aquatic herbicides, acrolein rapidly dissipates from the water by volatilization and degradation without leaving phytotoxic residues (Bowmer and Smith 1984; Parent et al. 1992; Joyce 1993). However, acrolein provides only temporary control of submerged weeds and also kills fish and other aquatic life at recommended treatment concentrations (Bowmer and Smith 1984). In one Montana stream, acrolein killed all fish in a 4-km stretch after application to control submerged weeds; some fish deaths were recorded as far as 6.4 km downstream (Fritz-Sheridan 1982). Useful reviews on ecological and toxicological aspects of acrolein are presented by Smith (1962), USEPA (1980), Beauchamp et al. (1985), Agency for Toxic Substances and Disease Registry [ATSDR] (1990), and Eisler (1994).

10.2 SOURCES AND USES

10.2.1 General

Acrolein enters the environment as a result of normal metabolic processes; incomplete combustion of coal, wood, plastics, tobacco, and oil fuels; and industrial emissions. Acrolein has been detected in smog, foods, and water. It is used extensively in chemical manufacture, for control of fouling organisms, and as an herbicide to control submerged weeds in irrigation canals.

10.2.2 Sources

Acrolein is ubiquitous in the environment as a result of natural and anthropogenic sources. Sources of atmospheric acrolein include smog; incomplete combustion of coal, wood, gasoline, plastics, and fats; tobacco smoke; and industrial emissions. The total amount of acrolein released into the atmosphere is unknown. In 1978, production losses of acrolein by emission from the four main U.S. plant locations were estimated at 34,682 kg; however, the gaseous emission streams are now either burned on emergence from the exhaust stack or sent to a furnace to destroy residual material (Beauchamp et al. 1985). Acrolein is found in photochemical smog and contributes to the smog's irritant capacity to the eye and respiratory pathways (Beauchamp et al. 1985; Leikauf et al. 1989). Recorded maximum acrolein concentrations in smog ranged from 12 to 14 µg/L (0.025 to 0.032 mg/m³) in Los Angeles between 1961 and 1963, and were 13 µg/L in Hudson County, New Jersey (USEPA 1980). For humans, exposure to atmospheric acrolein is greatest in the vicinity of incompletely combusted organic materials such as coal, wood, and petrol; highest acrolein concentrations are reported near forest fires and urban area fires (Beauchamp et al. 1985; Srivastava et al. 1992). The burning of southern pine (*Pinus* sp.), for example, generates 22 to 121 mg of acrolein/kg of wood burned (USEPA 1980). Acrolein is also in the smoke of burning plastic materials. Air samples from more than 200 fires in Boston, Massachusetts, contained greater than 3000 µg acrolein/L (greater than 6.8 mg/m³) in more than 10% of all samples; greater than 3000 µg acrolein/L air is an immediately hazardous concentration for human life and health (Beauchamp et al. 1985). Cigarette smoke in some enclosed areas may account for as much as 12,400 µg of acrolein/L air (Feron et al. 1978; Astry and Jakab 1983; Beauchamp et al. 1985; Leikauf et al. 1989; Cohen et al. 1992). In the case of an enclosed room of 30 m³ capacity, smoking five cigarettes raises the air concentration to about 50 µg acrolein/L and 30 cigarettes to 380 µg/L (USEPA 1980).

Acrolein is also generated when animal or vegetable fats are subjected to high temperatures (Feron et al. 1978; USEPA 1980). Acrolein was detected aboard submarines in trace concentrations as a degradation product during the heating of lubrication oils and edible fats (Lyon et al. 1970). Large amounts of acrolein are generated from exhausts of internal combustion engines (Astry and Jakab 1983; Heck et al. 1986; Ballantyne et al. 1989). Acrolein concentrations of 10,000 µg/L (23 mg/m³) have been measured in non-diesel automobile exhausts, 2900 µg/L in diesel engine emissions, and 2600 to 9600 µg/L in other internal combustion engines (USEPA 1980). Acrolein concentrations in air from several U.S. urban areas ranged from a maximum of 10 µg/L in 1960 to 1.8 to 3.4 µg/L in 1968; air in Tokyo during this period had an average acrolein concentration of 7.2 µg/L (Beauchamp et al. 1985). Urban acrolein pollution is derived mainly from automobile exhaust and incomplete burning of refuse (Beauchamp et al. 1985). Acrolein is formed during normal metabolic degradation of spermine and spermidine, glycerol, allyl formate, allyl alcohol, and cyclophosphamide (USEPA 1980; Marano and Puiseux-Dao 1982; Leach et al. 1987). Acrolein was also found in spores from the wheat stem fungus (*Puccinia graminis*) of infected wheat (*Triticum aestivum*); and acrolein was the major chemical factor that normally induced infection structure formation in *Puccinia* (Macko et al. 1978).

Acrolein has been detected in effluent water streams from industrial and municipal sources. Municipal effluents from Dayton, Ohio, for example, contained between 20 and 200 µg acrolein/L in 6 of 11 analyzed samples (USEPA 1980; Beauchamp et al. 1985). Acrolein is also a component of many foods, and processing may increase the acrolein content (USEPA 1980). Acrolein has been identified in raw turkey, potatoes, onions, coffee grounds, raw cocoa beans, alcoholic beverages, hops (USEPA 1980), white bread, sugarcane molasses, souring salted pork, and cooked bluefin tuna (*Thunnus thynnus*) (Beauchamp et al. 1985).

Occupational exposure to acrolein can occur during its production and isolation as a chemical intermediate or during the manufacture of acrylic acid, acrylic acid esters, and methionine (Beauchamp et al. 1985). Other sources of acrolein in the workplace include emissions from rubber vulcanization plants, welding of metals treated with anticorrosion primers, and pitch-cooking plants; skin contact during herbicidal applications for aquatic weed control; and its use as a slimicide in paper and paperboard manufacture. Acute acrolein poisoning from occupational exposure is improbable. However, the risks of poisoning are significant in certain industries, including welding of fat and oil cauldrons, smelting work and foundry operations, printing plants, linoleum and oil cloth factories, manufacture of insulators, tin plating of sheet iron, and processing of linseed oil (Beauchamp et al. 1985).

10.2.3 Uses

Since its discovery in 1843, acrolein has been known to polymerize readily in the presence of many chemicals, and since 1947 it has been used safely in a wide variety of commercial applications (Albin 1962; Fischer 1962). Acrolein is presently produced by the catalytic oxidation of propylene for the manufacture of methionine, glutaraldehyde, 1,2,6-hexane thiol, and other chemicals. The largest quantity of acrolein produced by this process is converted directly to acrylic acid and acrylic acid esters (Beauchamp et al. 1985). In 1975, global production of acrolein was 59,000 metric tons; in 1980, this value was 102,000 tons — including 47,600 tons produced by the United States (USEPA 1980). In 1983, about 250,000 tons (about 550 million pounds) of acrolein were produced, and 92% was converted to acrylic acid, 5% to methionine, and 3% was used as an aquatic herbicide (Beauchamp et al. 1985; Heck et al. 1986). Acrolein copolymers are used in photography, in textile treatment, in the paper industry, as builders in laundry and dishwasher detergents, and as coatings for aluminum and steel panels (USEPA 1980). Acrolein is used to scavenge sulfides from oilfield floodwater systems (Kissel et al. 1981), to crosslink protein collagen in the leather tanning industry, and to fixate tissue of histological samples (USEPA 1980). The use of acrolein as a military poison gas has been advocated because of its lacrimatory and blistering properties. During World War I, the French used acrolein under the name of Papite in hand grenades because of its irritating effect on the respiratory airways and the ocular mucosa (Beauchamp et al. 1985).

Acrolein has been used since 1960 to control submerged aquatic weeds in irrigation systems in the United States, Australia, and other countries where open channels distribute water for crop production (Hill 1960; Bartley and Hattrup 1975; Bowmer and Higgins 1976; USEPA 1980; Reinert and Rodgers 1987). Acrolein — as Magnacide H herbicide — is applied directly into agricultural irrigation systems at 1 to 15 mg/L. Water in treated canals is required by the Magnacide H label to be held for 6 days before discharge into receiving waters (Nordone et al. 1998). Acrolein is preferable to sodium arsenite for herbicidal control of submerged weeds because arsenicals are persistent (up to 1 year) and the high arsenic concentrations that are attained in water may be hazardous to humans and livestock (Hill 1960). Acrolein is extremely effective in killing submerged weeds that are difficult to control with other herbicides (Hill 1960). Acrolein has also been used as an herbicide in ponds, drains, and other bodies of water (Donohue et al. 1966). In Australia, the concentration of acrolein in irrigation canals to control various species of *Elodea*, *Potamogeton*,

and *Vallisneria* is usually less than 15,000 µg/L (Bowmer and Higgins 1976). In general, acrolein has a low order of toxicity to terrestrial plants (Donohue et al. 1966). Most field and garden crops can tolerate water with as much as 15,000 µg acrolein/L without serious adverse effects (Bartley and Hattrup 1975). Acrolein, as discussed later, has comparatively low persistence and low accumulation in aquatic ecosystems. One disadvantage to its use as an herbicide is its pungent, irritating odor (Hill 1960). At recommended treatment concentrations, however, acrolein kills fish and other aquatic organisms; therefore, acrolein should be used only in aquatic systems where these resources are considered expendable (Reinert and Rodgers 1987).

Acrolein has been used to control bacteria, fungi, algae, and molluscs in cooling water systems: 1500 µg/L killed as much as 95% of the target species in a once-through treatment (Donohue et al. 1966). Acrolein has been applied directly to the marine environment to control the growth and settlement of mussels (*Mytilus edulis*) and other fouling organisms in cooling water systems of coastal steam electric station power plants (USEPA 1980; Rijstenbil and van Galen 1981). Mussels in marine cooling water systems are controlled with 600 µg acrolein/L for 8 h daily for 3 days or with 700 µg/L for 3 h daily for 2 weeks (Rijstenbil and van Galen 1981). Acrolein prevents growth of microorganisms in liquid fuels such as jet fuels, in feed lines of subsurface wastewater injectors, and in water conduits of paper manufacturing plants (USEPA 1980; Beauchamp et al. 1985).

10.3 ENVIRONMENTAL CHEMISTRY

10.3.1 General

Acrolein, the simplest member of the class of unsaturated aldehydes, has a pungent, irritating odor. It is volatile, flammable, and explosive and requires elaborate and specific conditions for storage and use. The half-time persistence of acrolein in freshwater is usually less than 50 h; in seawater, it is less than 20 h; and in the atmosphere, less than 3 h. Biochemical and toxic effects of acrolein are caused by its rapid and essentially irreversible reaction with sulphydryl compounds to form a stable thiol ether; however, many compounds can mitigate or block its toxicity. Acrolein is eventually metabolized to acrylic acid and glyceraldehyde; glycidaldehyde — an intermediate metabolite with mutagenic and carcinogenic properties — has been produced *in vitro* but not *in vivo*.

10.3.2 Chemical Properties

Acrolein is soluble in water and in many organic solvents, including ethanol, acetone, and ether (Table 10.1) (Beauchamp et al. 1985). Acrolein is a highly reactive molecule with two reactive centers: one at the carbon–carbon double bond and the other at the aldehydic group. Typical reactions involving acrolein are shown in detailed figures in Beauchamp et al. (1985). Acrolein is extremely volatile, flammable, and explosive (Table 10.1) (Reinert and Rodgers 1987), especially in sunlight or in the presence of alkali or strong acid (Albin 1962; USEPA 1980). A potential hazard in handling acrolein is its rapid exothermic polymerization caused by the use of insufficient hydroquinone inhibitor or lack of strict control of pH (Beauchamp et al. 1985). Commercial acrolein should be maintained at pH 6.0 and contain less than 3% water and 0.1 to 0.25% hydroquinone as a polymerization inhibitor. A typical commercial sample contains about 97% acrolein, 0.5% other carbonyls, and 2.5% water. The addition of hydroquinone (0.1 to 0.25%) prevents the vinyl polymerization of acrolein, and controlling the pH between 5 and 6 by acetic acid increases stability of commercial acrolein by preventing aldol condensation. Elaborate and specific conditions are now prescribed for the storage of acrolein and include vents and safety valves, construction materials, fire control, spills, and waste disposal (Beauchamp et al. 1985). Commercial acrolein is stored and shipped under a blanket of oxygen-free inert gas (Albin 1962).

Table 10.1 Chemical and Other Properties of Acrolein

Variable	Data
Chemical name	2-Propenal
Alternate names	Acraldehyde Acraldehyde Acrolein Acryladehyde Acrylaldehyde Acrylic aldehyde Allyl aldehyde Aqualin Aquilin, Magnacide H Propenal
CAS Number	107-02-8
Structural formula	$\text{CH}_2 = \text{CHCHO}$
Molecular weight	56.06
Specific gravity	0.8427–0.8442
Physical state	Colorless or yellow liquid at 25°C
Odor	Pungent, irritating
Boiling point	52.5–53.5°C
Melting point	–86.95°C
Solubility	
Water	206–208 g/L
Organic solvents	Miscible
Log K_{ow}	0.01
Vapor pressure	215–220 mmHg at 20°C
Explosive limits of vapor and air	
Upper limit	31% acrolein
Lower limit	2.8% acrolein

Data from Hill 1960; Anderson and Hood 1962; Folmar 1977; USEPA 1980; Hudson et al. 1984; Beauchamp et al. 1985; Mayer 1987; Reinert and Rodgers 1987; Ballantyne et al. 1989; Sine 1991; Agency for Toxic Substances and Disease Registry [ATSDR] 1990; and National Institute for Safety and Health [NIOSH] 1990.

Spectrophotometric determination with 4-hexylresorcinol and a fluorometric method with *m*-aminophenol are the most commonly used procedures for the determination of acrolein. However, gas chromatography and high-performance liquid chromatography procedures are also used (USEPA 1980; Kissel et al. 1981; Nishikawa and Hayakawa 1986). Acrolein concentrations in rainwater between 4 and 200 µg/L can be measured rapidly (less than 80 min) without interference from related compounds; the method involves acrolein bromination and analysis by gas chromatography with electron capture detection (Nishikawa and Hayakawa 1986). Kissel et al. (1981) emphasize that water samples from potential acrolein treatment systems require the use of water from that system in preparing blanks, controls, and standards and that acrolein measurements should be made at the anticipated use concentrations.

10.3.3 Persistence

Degradation and evaporation seem to be the major pathways for acrolein loss in water; smaller amounts are lost through absorption and uptake by aquatic organisms and sediments (USEPA 1980; Reinert and Rodgers 1987). The half-time persistence of acrolein in freshwater is 38 h at pH 8.6 and 50 h at pH 6.6; degradation is more rapid when initial acrolein concentrations are less than 3000 µg/L (Bowmer and Higgins 1976). Nordone et al. (1998) show a half-time persistence of 2.9 to 11.3 h at initial nominal concentrations of 20 µg/L, and 27.1 to 27.8 h at 101 µg/L. At pH 5, acrolein reacts by reversible hydrolysis to produce an equilibrium mixture with 92% beta-hydroxy-

propionaldehyde and 8% acrolein. In alkali, the primary reaction is consistent with a polycondensation reaction (USEPA 1980). In natural waters, acrolein degradation proceeds to carboxylic acid via a microbial pathway (USEPA 1980); beta-hydroxypropionaldehyde is readily biotransformed in about 17.4 days (Reinert and Rodgers 1987). Microbial degradation plays a major role in the transformation of acrolein in aquatic systems (Nordone et al. 1998).

Acrolein is applied to irrigation canals to control submerged aquatic weeds at greatly different time-concentration treatments. Regardless of time-concentration regimens — which vary from 100 µg/L for 48 h in the United States to 15,000 µg/L for several hours in Australia — the daily decay rate constants are remarkably similar, ranging from 0.14 to 0.21, and are probably affected by variations in weed density (O'Loughlin and Bowmer 1975; Parent et al. 1992). In one case, acrolein applied to the Columbia River at an average initial concentration of 125 µg/L degraded to 25 µg/L after 48 h in samples greater than 65 km from the application point — a loss of 80% (USEPA 1980). High initial concentrations (50,000 to 160,000 µg/L) of acrolein in natural waters degraded 57 to 80% in 192 h, suggesting that high concentrations can alter the rate of hydrolysis (Kissel et al. 1981). In seawater, the half-time persistence of acrolein was less than 20 h (Rijstenbil and van Galen 1981). In photochemical smog, acrolein is comparatively unstable and not likely to persist; the dominant removal mechanism involves hydroxide attack on acrolein, and the atmospheric half-life persistence is 2 to 3 h under these conditions (Beauchamp et al. 1985).

10.3.4 Metabolism

Biochemical and toxic effects of acrolein are probably caused by its reaction with critical protein and nonprotein sulfhydryl groups (USEPA 1980; Beauchamp et al. 1985; Heck et al. 1986). The reaction of acrolein with sulfhydryl compounds is rapid and essentially irreversible, resulting in the formation of a stable thiol ether (Beauchamp et al. 1985; Heck et al. 1986). Metabolism of acrolein is believed to result in the formation of acrylic acid and glyceraldehyde (Figure 10.1). The postulated metabolites of acrolein can be oxidized to carbon dioxide (Beauchamp et al. 1985). Acrylic acid does not seem to represent a significant toxic hazard when compared to the parent acrolein because at low airborne concentrations of less than 1000 µg acrolein/L, the quantity of acrylic acid produced by metabolism is negligible. Thus, metabolism to acrylic acid after inhalation should be regarded as a detoxification pathway. Conjugation of acrylic acid with glutathione represents another elimination and detoxification pathway (Beauchamp et al. 1985). *In vitro* studies of acrolein metabolism in mammals suggest that acrolein exposures might result in exposure to glycidaldehyde, an intermediate in acrolein metabolism (Figure 10.1). The major toxic effects of acrolein exposure — including irritation, ciliastasis, and hypersensitivity — are probably due either

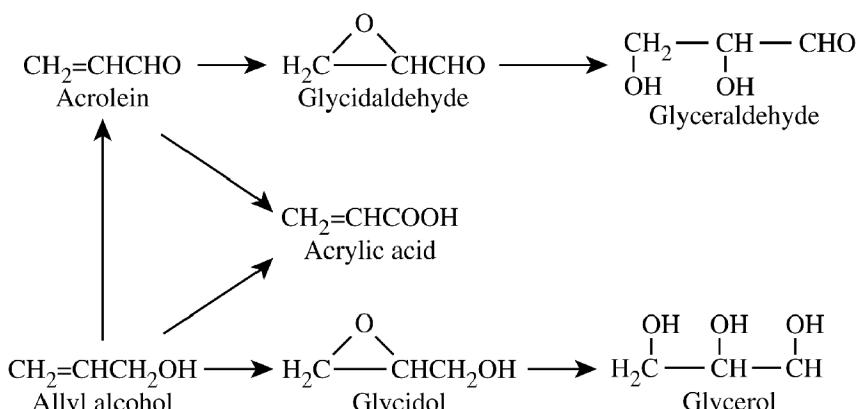


Figure 10.1 Proposed scheme for *in vitro* mammalian metabolism of acrolein and allyl alcohol, a precursor of acrolein. (Adapted from Beauchamp et al. 1985; ATSDR 1990; Eisler 1994.)

to the parent acrolein or to the reaction of glyceraldehyde with cell proteins. Glyceraldehyde is a potent mutagen and carcinogen; however, no evidence is available showing that acrolein can produce glyceraldehyde *in vivo* (Beauchamp et al. 1985). Acrolein is more toxic when inhaled than when taken orally (USEPA 1980). Inhalation of acrolein decreased the concentrations of protein and nonprotein sulphydryl groups in nasal mucosal tissue (Heck et al. 1986). Acrolein is highly reactive toward thiol groups and rapidly conjugates with glutathione and cysteine (USEPA 1980). When glutathione is depleted, acrolein potentiates the nasal toxicity of formaldehyde to rats (Heck et al. 1986).

Acrolein is a metabolite of allyl alcohol and cyclophosphamide, and these compounds should be considered in acrolein metabolism schemes (Beauchamp et al. 1985; Cohen et al. 1992). Allyl alcohol in the presence of NADPH and liver or lung microsomes degrades to acrolein, acrylic acid, and glycidol (Figure 10.1).

When added to water as an aquatic herbicide, acrolein undergoes rapid decomposition, especially in sunlight. At the same time, it reacts rapidly with amines, alcohols, and mercaptans of aquatic plants, destroying cell structure and killing the plants (Parent et al. 1992). Mammals drinking acrolein-contaminated water rapidly convert acrolein to saturated alcohol compounds because of the low pH in the upper portion of their GI tracts; the primary breakdown product is beta-propionaldehyde (USEPA 1980).

Many compounds, including glutathione, 2-mercaptoethanol, beta-dimethylcysteamine, penicillamide, gamma-mercaptopropionylglycine, and *N*-acetylcysteine, mitigate or block the toxic effects of acrolein (USEPA 1980; Beauchamp et al. 1985; Heck et al. 1986). In frogs (*Rana japonica*), sulphydryl compounds reduce the effects of acrolein on excitation-contraction uncoupling in skeletal muscle (Fujino et al. 1985). In mice, cysteine reduced the cytotoxic effects of acrolein on tumor cells; in rabbits, cysteine mitigated acrolein-induced alveolar macrophage calcium-dependent ATP-ase, phagocytosis, and adhesiveness (USEPA 1980). In male rats, cysteine and ascorbic acid antagonized the acute lethal effects of orally administered acrolein, and 2-mercaptoethanol antagonized the inhibitory effect of acrolein on liver DNA-polymerase (USEPA 1980).

10.4 LETHAL AND SUBLETHAL EFFECTS

10.4.1 General

Acrolein degrades quickly in soils and in plant tissues, regardless of mode of administration. Most terrestrial crop plants easily tolerate 25,000 µg acrolein/L of irrigation water, and some can tolerate 70,000 to 80,000 µg/L without adverse effects. Terrestrial plants were adversely affected at atmospheric concentrations of 500 µg acrolein/L air, but this concentration exceeds the recommended value of 110 µg/L (0.25 mg/m³) air for protection of human health in occupational settings.

Adult fruitflies (*Drosophila* sp.) were comparatively resistant to acrolein and had lowered survival when reared in culture media with greater than 3,700,000 µg acrolein/L. At recommended concentrations for control of nuisance submerged aquatic weeds (frequently 100 to 1000 µg/L, and often greater than 9600 µg/L), acrolein was lethal or harmful to almost all aquatic vertebrates and invertebrates tested in short-term exposures. The most sensitive groups of tested aquatic organisms in short-term assays were frog tadpoles (dead at 7 µg/L) and representative species of fish (reduced survival at 14 to 62 µg/L) and crustaceans (death or immobilization at 34 to 80 µg/L). Adverse effects of acrolein on birds were observed at acute oral doses of 9100 µg/kg BW (reduced survival), concentrations greater than 51 µg/kg egg for egg injection (abnormal development and reduced survival), and at greater than 50,000 µg/L air (respiratory tract histopathology). In mammals, acrolein is a strong cytotoxic and ciliostatic agent that is irritating to mucous membranes of dermal, ocular, gastrointestinal, and respiratory systems, and is systemically toxic by all routes of exposure. Adverse effects of acrolein are documented in sensitive species of mammals under the following

regimens: 50 µg/L air for 1 min (increased blood pressure and heart rate); 300 µg/L air for 10 min (ocular and nasal irritation); 500 to 1000 µg/L air (repelled by odor); 660 µg/L air for 24 days (reduced survival); 8000 to 11,000 µg/L air for 4 to 6 h, or 875,000 µg/L air for 1 min (death); dietary concentrations equivalent to 500 µg/kg BW for 102 weeks (decreased survival); 850 to 6000 µg/kg BW by way of intravenous injection (liver necrosis, embryo resorption); and single oral doses between 4000 and 28,000 µg/kg BW (death).

Acrolein was mutagenic to certain microorganisms and to the fruitfly; mutagenicity may be due, in part, to glyceraldehyde, an acrolein metabolite. Injected into the amniotic fluid, acrolein is teratogenic to rats. Teratogenicity may be due to acrylic acid, an acrolein metabolite. There is limited evidence that acrolein acts as a weak carcinogen and tumor promoter. Acrolein interacts with other chemicals, sometimes synergistically, additively, or antagonistically. Also, some chemicals normally contain acrolein as an impurity or yield acrolein as a metabolite.

10.4.2 Terrestrial Plants and Invertebrates

Most crop plants easily tolerate irrigation water with 25,000 µg of acrolein/L and many tolerate 70,000 to 80,000 µg/L without adverse effects — including corn (*Zea mays*), cotton (*Gossypium hirsutum*), milo (*Sorghum* spp.), squash (*Cucurbita* spp.), castor bean (*Ricinus communis*), tomato (*Lycopersicon esculentum*), alfalfa (*Medicago sativa*), and sugarcane (*Saccharum officinarum*) (Ferguson et al. 1961). Acrolein degrades quickly in soils and plant tissues, regardless of mode of administration (Ferguson et al. 1961). Atmospheric concentrations of 500 µg acrolein/L and higher were harmful to certain plants (Beauchamp et al. 1985). Leaves of the pinto bean (*Phaseolus* spp.) and morning glory (*Ipomoea* spp.) developed brown foliar lesions after exposure to 500 µg/L air for 4 to 7 h; damage was more severe if the plants were moist during exposure. Leaves of the radish (*Raphanus* spp.) developed lesions after exposure to 1500 µg acrolein/L air for 6 to 7 h. However, leaves of the geranium (*Geranium* spp.) and the tomato showed no adverse effects after exposure to 1500 µg/L air for 7 h (Beauchamp et al. 1985).

Acrolein inhibits DNA, RNA, and protein synthesis in the bacterium *Escherichia coli*, and this inhibition probably accounts for its cytotoxic and inhibitory effects on *E. coli* cell division (USEPA 1980; Beauchamp et al. 1985). Acrolein is demonstrably mutagenic to microorganisms and to larvae of the fruitfly (*Drosophila melanogaster*). Acrolein-induced mutagenicity — including point mutations, sister chromatid exchanges, and chromosome breakages — has been observed in selected strains of bacteria (*E. coli*, *Salmonella typhimurium*), yeast (*Saccharomyces cerevisiae*), fruitfly larvae, and cultured Chinese hamster ovary cells (USEPA 1980; Beauchamp et al. 1985; Sierra et al. 1991; Cohen et al. 1992). Acrolein's mutagenicity may be due to the metabolite glyceraldehyde. Glyceraldehyde was mutagenic to bacteria and yeast under controlled conditions (Beauchamp et al. 1985; Sierra et al. 1991). Studies with *D. melanogaster* show that acrolein is mutagenic in the sex-linked recessive lethal test when injected but not when fed (Sierra et al. 1991). Acrolein caused 2.2% sex-linked mutations in *D. melanogaster* — the highest percentage recorded among several tested aldehydes (USEPA 1980). In studies by Comendador (1984), early embryonic stages of fruitflies were most sensitive to the mutagenic properties of acrolein, and sensitivity decreased with increasing development to the point that adults showed negligible mutagenic responses. Adult fruitflies were generally resistant to acrolein; mortality was 25% when the culture medium contained 3,700,000 µg of acrolein/L, 50% at 8,600,000 µg/L, and 75% at 22,100,000 µg/L (Comendador 1984).

10.4.3 Aquatic Organisms

Adverse effects of acrolein on sensitive groups of aquatic organisms are documented (Table 10.2) at concentrations (in µg acrolein/L medium) as low as 7 for frog tadpoles (death), 14 to 62 for fish (death), 34 to 80 for crustaceans (death, immobilization), 50 for oysters (reduction

in shell growth rate), 100 to 200 for freshwater algae (DNA and RNA reduction, photosynthesis inhibition), 151 for gastropods (death), >151 for insects (death), 500 to 2000 for macrophytes (leaf cell deterioration, death), 1250 for trematodes (death of miracidia in 20 min), and 62,000 for bacteria (growth reduction). Aquatic vertebrates were more sensitive than invertebrates (Holcombe et al. 1987), and younger fish were more sensitive than older fish (Burdick et al. 1964). Aquatic insects do not avoid acrolein at concentrations that repel fish (Folmar 1978). Freshwater fishes and macroinvertebrates, when exposed under static conditions to sublethal concentrations of ¹⁴C-labeled acrolein, metabolize acrolein so rapidly that neither acrolein nor its major oxidative and reductive metabolites (acrylic acid, allyl alcohol) were detected in edible tissues within 24 h after dosing (Nordone et al. 1998).

As an herbicide, acrolein is most effective in controlling dense accumulations of submerged weeds in habitats where waterflow is rapid and uniform, such as irrigation canals and rapidly flowing streams (Ferguson et al. 1961). Acrolein is lethal to various genera of submerged plants (*Hydrodictyon*, *Spirogyra*, *Potamogeton*, *Zannichellia*, *Cladophora*, *Ceratophyllum*, *Elodea*, *Chara*, *Najas*) at 1500 to 7500 µg/L (Ferguson et al. 1961; Beauchamp et al. 1985), but some floating plants (*Pistia*, *Eichhornia*, *Jussiaea*) are more resistant to acrolein than submerged plants and require concentrations that are at least double those necessary for submerged forms (Ferguson et al. 1961). Also, acrolein has little effect on emergent aquatic macrophytes and should not be used to control emergents (Ferguson et al. 1961). Acrolein is the only herbicide now used in Australia for control of submerged aquatic weeds in larger irrigation canals (Bowmer et al. 1979); effective plant control was obtained at 9.6 to 28.8 mg/L for 3 h (Bowmer and Smith 1984). In the United States, the U.S. Bureau of Reclamation controls aquatic algae and weeds at lower concentrations (0.1 mg/L) and longer exposures (48 h; Folmar 1980). In the Columbia River Basin in the state of Washington, acrolein is used to control submerged aquatic macrophytes at concentrations of 0.1 mg/L for 48 h or 1.0 mg/L for 4 to 8 h with applications every 3 to 5 weeks (Bartley and Hattrup 1975). Vegetation destruction by acrolein is maximal 1 week after application, and green filamentous algae are usually the first plants to return after 1 month (Ferguson et al. 1961). Biomass and species diversity were altered in acrolein-treated phytoplankton populations in Egyptian irrigation canals 1 year after treatment (Kobbia 1982). Although acrolein is a powerful cytotoxic agent, its inhibitory effects at sublethal concentrations on plant mitosis, nucleic acid synthesis, and protein synthesis are considered completely reversible (Marano and Puiseux-Dao 1982).

Acrolein in concentrations sufficient to control nuisance submerged aquatic weeds may also kill snails, crayfish, shrimp, fish, and toads (Ferguson et al. 1961). In one case, acrolein was used to control *Potamogeton* and *Chara* in an Ohio farm pond during June 1960 (Hill 1960). Acrolein was applied at 16,100 µg/L to a 0.1-ha portion of the 0.7-ha pond. Within 1 h of application, many dead amphibian tadpoles and small bluegills (*Lepomis macrochirus*) were recovered. In 24 h, *Chara* had turned white and *Potamogeton* brown; both plant species seemed dead; fish were swimming in the treated area. In 72 to 96 h, several large dead walleyes (*Stizostedium vitreum vitreum*) were found. One week posttreatment, all algae and weeds in the treated area were dead; weeds were present in the untreated areas. The treated section remained weed-free for 4 to 6 weeks. After 8 weeks, the treated area was heavily infested with *Chara*. Hill (1960) concluded that tadpoles, walleyes, and small bluegills were more susceptible to acrolein toxicity than larger bluegills and bass (*Micropterus* spp.) in the pond. Acrolein is also effective in controlling trematodes that cause schistosomiasis wherein snails are the intermediate host, especially in irrigation systems. For example, native species of snails (*Lymnaea*, *Helisoma*), along with *Potamogeton* weeds, were destroyed within 12 km in the main irrigation canal of Kern County, California, after a single application of acrolein (Ferguson et al. 1961).

Acrolein was the most toxic of 15 herbicides tested for toxicity to fish (USEPA 1980). Responses by rainbow trout (*Oncorhynchus mykiss*) surviving 77 µg acrolein/L, a concentration that killed 50% in about 21 h, were characteristic of respiratory irritants (McKim et al. 1987). These responses included a steady increase in cough rate; decreases in ventilation rate, oxygen utilization, and heart

rate; increases in hematocrit; and decreases in total arterial oxygen, carbon dioxide, and pH (McKim et al. 1987). In studies by Bartley and Hattrup (1975), no-observable-effect concentrations of acrolein for rainbow trout were 240 µg/L for exposures of 4.8 h, and 48 µg/L for exposures of 48 h; these values are below the concentrations that control aquatic weeds. In the same study, rainbow trout that survived exposure to high sublethal concentrations for 48 h were unable to recover completely after acrolein treatments ended. Trout and other teleosts are poorly adapted to detoxify acrolein and other xenobiotic aldehydes (Parker et al. 1990). The low metabolic capacity of fish liver aldehyde dehydrogenase for aldehydes, in general, suggests that these compounds may be hazardous to fish populations (Parker et al. 1990). Applications of acrolein to waters where fish may be taken for human consumption should be made with caution; rainbow trout surviving exposure to acrolein in reservoirs or connecting canals frequently presented odor and taste problems to human consumers (Folmar 1980).

In addition to weeds, acrolein is used to control fouling organisms in cooling water systems. Effective control was established in a once-through cooling system of a steel mill with continuous application of 200 µg acrolein/L (Donohue et al. 1966). Acrolein controlled bacteria in condenser pipes of a power-plant cooling system, but only at extremely high concentrations of 125,000 µg/L for 120 h or 500,000 µg/L for 2 h (Starzecka 1975). Acrolein reduced settlement of young mussels (*Mytilus* sp.) in cooling seawater systems of power plants (Rijstebil and van Galen 1981). In recirculating cooling water systems, algae and bacteria can be controlled at 500 µg/L for 5 months or at 5000 µg/L for 1 week (Table 10.2).

Table 10.2 Acrolein Effects on Representative Aquatic Organisms

Taxonomic Group, Organism, Concentration, and Other Variables	Effect	Reference ^a
BACTERIA, ALGAE, AND MACROPHYTES		
Freshwater algae, <i>Anabaena</i> sp.; 690 µg/L; 24-h exposure	50% reduction in photosynthesis at 25°C	1
Aquatic bacteria: 3 species 62,000 µg/L; 48-h exposure	Some growth reduction, but recovery by 120 h	2
125,000 µg/L; 120-h exposure	LC100	2
500,000 µg/L; 2-h exposure	LC100	2
Freshwater alga, <i>Cladophora glomerata</i> 100 µg/L	Onset of photosynthesis inhibition at 30°C	1
760 µg/L; 24-h exposure	50% reduction in photosynthesis at 30°C	1
1000 µg/L; 24-h exposure	50% reduction in photosynthesis at 25°C	1
Alga, <i>Dunaliella bioculata</i> 100 µg/L; 48-h exposure	DNA concentration reduced 28%	3
200 µg/L; 48-h exposure	DNA concentration reduced 36% and RNA 28%	3
400 µg/L; 48-h exposure	DNA reduced 93%, RNA 68%, and proteins 74%	3
1000 µg/L; 48-h exposure	No development in 48 h	3
8000 µg/L; 3-h exposure	Ultrastructural anomalies and cytoplasmic inclusions	4
Elodea, <i>Elodea canadensis</i> Sublethal (actual exposure concentration and duration unknown)	Growth stimulation (from reduced competition by aufwuchs, bacteria, and epiphytic algae)	5
500 µg/L; 24-h exposure	Leaf cell deterioration	6, 7
2800 µg/L; 3-h exposure in irrigation canal	80% reduction in density; recovery began in 17 days	5
15,000 µg/L; 2–6-h exposure in Australian canals	Effective control for up to 21 km in flowing-water irrigation canals	8
18,000 µg/L; 2–12-h exposure in smaller channels and up to 72 h in major canals; New South Wales	Effective control	5
22,000 µg/L; 3-h exposure in irrigation canal	94% reduction in biomass after 14 days	5

Table 10.2 (continued) Acrolein Effects on Representative Aquatic Organisms

Taxonomic Group, Organism, Concentration, and Other Variables	Effect	Reference ^a
Filamentous algae, unidentified 500 µg/L; 5-month exposure; petroleum-refinery recirculating cooling-water system	Effective control	9
1000 µg/L; 20-h exposure in Arizona irrigation canal	Effective control for 2 weeks	10
3500 µg/L; 2-week exposure in petroleum refinery cooling water	Lethal	9
5000 µg/L; 1-week exposure in petroleum refinery cooling water	Lethal	9
Freshwater alga, <i>Enteromorpha intestinalis</i> 1800 µg/L; 24-h exposure	50% reduction in photosynthesis at 25°C	1
2500 µg/L for 24 h	50% reduction in photosynthesis at 20°C	1
>5000 µg/L for 24 h	50% reduction in photosynthesis at 15°C	1
Freshwater plants: 6 species of submerged plants, 2 species of floating plants, 4 groups of phytoplankton; irrigation drains, Egypt; 15,000–25,000 µg/L for 45 min, repeated 4 times	Effective control of all plants within 2–7 days; phytoplankton recovery over a 1-year period was most rapid for the Cyanophyceae, followed by the Bacilliarophyceae, Chlorophyceae, and Euglenophyceae, and resulting in altered biodiversity when compared to a control canal	11
Submerged macrophytes, 3 species (<i>Najas</i> sp., <i>Ceratophyllum</i> sp., and <i>Ipomea</i> sp.); 25,000 µg/L	All dead 1 week after application	6
Floating pondweed, <i>Potamogeton carinatus</i> 2000 µg/L for 12 h	LC50	12
10,000–15,000 µg/L for >1 h (actual exposure time unknown)	LC50	12
15,000 µg/L for 1.7 h	LC50	12
22,000–26,000 µg/L for >1 h (actual exposure time unknown)	LC80	12
Pondweed, <i>Potamogeton crispus</i> ; 20,000 µg/L for 5 h	All dead in 8 days	6
Pondweed, <i>Potamogeton tricarinatus</i> ; 4000 µg/L; 1-h exposure in irrigation canal	Minimum effective concentration	5
Submerged macrophyte, <i>Vallisneria gigantea</i> ; 26,000 µg/L for 1 h in irrigation canal	Minimum effective concentration	5
Ribbonweed, <i>Vallisneria spiralis</i> 1600 (95% confidence interval [CI] of 1300–2000) µg/L	50% reduction in biomass	12
3700 (95% CI of 3200–4600) µg/L for 1 h	80% reduction in biomass	12
INVERTEBRATES		
Snail, <i>Aplexa hypnorum</i> ; 151 µg/L for 96 h	Less than 50% mortality	13
Snail, <i>Australorbis glabratus</i> 1250 µg/L for 24 h	All adults and 90% of embryos survived	7
2500 µg/L for 24 h	35% of adults and 40% of embryos died	7
10,000 µg/L for 24 h	98% of adults and 100% of embryos died	6, 7
Barnacle, <i>Balanus ebarneus</i> ; 1600–2100 µg/L for 48 h	LC50	6
American oyster, <i>Crassostrea virginica</i> ; 50–55 µg/L for 96 h	50% reduction in shell growth rate	6, 14, 15
Daphnid, <i>Daphnia magna</i> 17–34 µg/L	MATC ^b	6, 16, 24
51 (95% CI of 43–62) µg/L for 48 h	50% immobilized	13
57–80 µg/L for 48 h	LC50	6

Table 10.2 (continued) Acrolein Effects on Representative Aquatic Organisms

Taxonomic Group, Organism, Concentration, and Other Variables	Effect	Reference ^a
Clam, <i>Elliptio complanata</i> ; 101 µg/L for 7 days	Acrolein not detected in tissues; glyceric acid and unidentified carbohydrates were the major metabolites	25
Mayfly, <i>Ephemerella walkeri</i> ; 100 µg/L for 1 h	No avoidance of acrolein by nymphs	17
Freshwater snails, 3 species (<i>Physa</i> , <i>Biomphalaria</i> , <i>Bulinus</i>); 25,000 µg/L for 3.5–4 h	All dead	14
Common mussel, <i>Mytilus edulis</i>		
200–1000 µg/L; exposed for as much as 8 h daily for 3 days	Valves closed immediately after start of exposure to acrolein, regardless of concentration or duration; effect in 45% of mussels at 200 µg/L, 80% at 400 µg/L, and 90% at 600 µg/L	8
600 µg/L; single 8-h exposure followed by 48-h of uncontaminated seawater	70% of the mussels (1–2.5 mm shell length) in the cooling water systems of power plants became detached in 3 days vs. 13% of controls	18
600 µg/L; 8-h exposure daily for 3 days	97% of mussels became detached	18
600 µg/L; 29-h continuous exposure	100% detachment	18
Northern crayfish, <i>Orconectes virilis</i> ; 101 µg/L for 7 days	Acrolein not detected in tissues; glycerol and lactic acid were the major metabolites	25
Brown shrimp, <i>Penaeus aztecus</i>		
100 µg/L for 48 h	LC50	14
100 µg/L for 48 h	50% loss in equilibrium	6, 15
Trematode, <i>Schistosoma mansoni</i>		
1250 µg/L for 20 min	Killed all miracidia	7
2500 µg/L	Killed all miracidia in 10 min, and all cercariae in 18 min	7
Midge, <i>Tanytarsus dissimilis</i> ; 151 µg/L for 48 h	Less than 50% mortality	13
VERTEBRATES		
Bowfin, <i>Amia calva</i> ; 62 µg/L for 24 h	LC50, fry	14
Goldfish, <i>Carassius auratus</i>		
80 µg/L for 24 h	LC50	6
1000–2000 µg/L for 3 h	Fatal	14
White sucker, <i>Catostomus commersoni</i> ; 14 (95% CI of 8–25) µg/L for 96 h	LC50	13
Longnose killifish, <i>Fundulus similis</i> ; 240 µg/L for 48 h	LC50	6, 15
Western mosquitofish, <i>Gambusia affinis</i>		
61 µg/L for 48 h	LC50	6, 14
149 µg/L for 24 h	LC50	14
Channel catfish, <i>Ictalurus punctatus</i> ; 20 µg/L for 7 days	Acrolein not detected in tissues; glycidol was the main metabolite	25
Bluegill, <i>Lepomis macrochirus</i>		
13 µg/L for 28 days	Whole fish, bioconcentration factor of 344	6
20 µg/L for 7 days, juveniles	Acrolein not detected in tissues; major metabolites were 1,3-propanediol and glyceric acid	25
33 (95% CI of 27–40) µg/L for 96 h	LC50	13
79 µg/L for 24 h	LC50	6, 19
90–100 µg/L for 96 h	LC50	6, 14
Largemouth bass, <i>Micropterus salmoides</i>		
160 µg/L for 96 h	LC50	6, 14
183 µg/L for 24 h	LC50	14
Rainbow trout, <i>Oncorhynchus mykiss</i>		
8 µg/L for 48 h	None dead	20
16 (95% CI of 14–19) µg/L for 96 h	LC50	13

Table 10.2 (continued) Acrolein Effects on Representative Aquatic Organisms

Taxonomic Group, Organism, Concentration, and Other Variables	Effect	Reference ^a
20, 50, or 100 µg/L; exposure for 4 h; trout collected 1, 4, and 7 days postexposure; cooked fillets evaluated for odor and taste by human panel	Unacceptable organoleptic qualities were recorded for fillets 1 and 4 days ($P = 0.05$) after treatment with 100 µg/L; some unacceptable qualities were detected 1 and 4 days after treatment with 50 µg/L, and at 7 days after treatment with 100 µg/L	17
29 (95% CI of 22–37) µg/L for 96 h	LC50	21
48 µg/L for 48 h	LC32	6, 20
65 µg/L for 24 h	LC50, fingerlings	6
77 µg/L for 20.5 h	LC50	21
90 µg/L for 4.8 h	No deaths	20
96 µg/L for 48 h	All dead	20
100 µg/L for 1 h	Avoidance by fry	6, 14, 23
150 µg/L	Lethal	22
240 µg/L for 4.8 h	LC10	20
410 µg/L for 4.8 h	LC70	20
>500 µg/L for 4.8 h	All dead	20
Chinook salmon, <i>Oncorhynchus tshawytscha</i> ; 80 µg/L for 24 h	LC50	6, 19
Fathead minnow, <i>Pimephales promelas</i>		
11.4–41.7 µg/L	MATC ^b	6, 16, 24
14 (95% CI of 8–25) µg/L for 96 h	LC50	13
84 µg/L for 6 days	LC50	6
115 µg/L for 48 h	LC50	6, 14
150 µg/L for 24 h	LC50	14
Harlequin fish, <i>Rasbora heteromorpha</i> ; 130 µg/L for 48 h	LC50	14
Brown trout, <i>Salmo trutta</i>		
46 µg/L for 24 h	LC50	6, 14, 19
1500 µg/L for 76–138 min	All dead	19
6000 µg/L for 28–61 min	All dead	19
16,000 µg/L for 15–39 min	All dead	19
South African clawed frog, <i>Xenopus laevis</i> , tadpoles; 7 (95% CI of 6–8) µg/L for 96 h	LC50	13

^a 1, Fritz-Sheridan 1982; 2, Starzecka 1975; 3, Marano and Puiseux-Dao 1982; 4, Baron-Marano and Izard 1968; 5, Bowmer and Smith 1984; 6, USEPA 1980; 7, Ferguson et al. 1961; 8, Bowmer et al. 1979; 9, Donohue et al. 1966; 10, Corbus 1982; 11, Kobbia 1982; 12, Bowmer and Sainty 1977; 13, Holcombe et al. 1987; 14, Folmar 1977; 15, Mayer 1987; 16, Beauchamp et al. 1985; 17, Folmar 1978; 18, Rijstenbil and van Galen 1981; 19, Burdick et al. 1964; 20, Bartley and Hattrup 1975; 21, McKim et al. 1987; 22, Kissel et al. 1981; 23, Folmar 1976; 24, Macek et al. 1976; 25, Nordone et al. 1998.

^b Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

10.4.4 Birds

Acrolein was lethal to birds at single oral doses of 9100 µg/kg BW (Table 10.3). Observed signs of acrolein poisoning in subadult mallards (*Anas platyrhynchos*) after oral administration included regurgitation, a reluctance to leave the swimming area, slow responses, muscular incoordination, heavy-footed walking, phonation, wing tremors, running and falling, weakness, and withdrawal (Hudson et al. 1984). Treatment concentrations as low as 3300 µg/kg BW have produced signs of acrolein poisoning. These signs appeared as soon as 10 min after administration and persisted for as long as 36 days. At lethal oral concentrations, deaths occurred as soon as 32 min posttreatment and continued for several days (Hudson et al. 1984). Acrolein was lethal to developing

Table 10.3 Acrolein Effects on Birds

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
MALLARD, <i>Anas platyrhynchos</i> Oral route; 9100 µg/kg body weight (BW), 95% confidence interval [CI] of 6300–13,100 µg/kg BW	LD50, age 3–5 months	1
DOMESTIC CHICKEN, <i>Gallus</i> sp. Inhalation route; adults subjected to 50,000 or 200,000 µg acrolein/L (113 or 454 mg/m ³) air via an endotracheal cannula for up to 27 days	Decreases in trachea complement of ciliated and goblet cells; inhibited mucus transport activity in trachea; lymphocytic inflammatory lesions in the tracheal mucosa; changes were more pronounced at the higher dose and with increasing exposures	2
Air sac injection route; embryos 2–3 days old; examined at day 13 >127 µg/kg fresh weight (FW) whole egg 182 µg/kg FW whole egg 1818 µg/kg FW whole egg	Dose-dependent decrease in survival LD50 LD80	3 3 3
Air sac injection route; embryos 3 days old 1 µg/kg FW whole egg 10 µg/kg FW whole egg 1000 µg/kg FW whole egg	20% developmental abnormalities vs. 5% in controls No malformations Lethal	4 4 4
Inner shell injection of membrane on heart route; embryos 72–76 h old; examined on day 14 of incubation 25 µg/kg FW whole egg 51 µg/kg FW whole egg 82 µg/kg FW whole egg 102 µg/kg FW whole egg 203 µg/kg FW whole egg	No deaths or malformations 50% dead or malformed LD50 71% dead, 6% malformed 97% dead, 3% malformed	5 5 5 5 5
Yolk-sac injection route; embryos 3 days old, examined at day 14 51 µg/kg FW whole egg 1018 µg/kg FW whole egg	LD50 LD90; no evidence of increased teratogenicity over controls	6 6

^a 1, Hudson et al. 1984; 2, Denine et al. 1971; 3, Chhibber and Gilani 1986; 4, Beauchamp et al. 1985; 5, Korhonen et al. 1983; 6, Kankaanpaa et al. 1979.

avian embryos when whole eggs were injected with 51 to 182 µg/kg FW. In descending order, embryos were most sensitive when acrolein was administered by way of the yolk sac (51 µg/kg), by inner shell (82 µg/kg), and by air sac (182 µg/kg) (Table 10.3). Acrolein is 50 times more toxic to embryos of the domestic chicken (*Gallus* sp.) than acrylonitrile, and 100 times more toxic than acrylamide (Kankaanpaa et al. 1979). Acrolein inhibits mucus transport in the trachea of the domestic chicken (Denine et al. 1971), probably through ciliostatic action (USEPA 1980). Adverse effects of acrolein were observed on chicken respiratory-tract physiology and pathology at greater than 50,000 µg/L air (Table 10.3).

Malformations of the eye, coelom, neck, back, wings, and legs were observed in surviving acrolein-treated chicken embryos (Korhonen et al. 1983) after whole eggs were injected with greater than 51 µg acrolein/kg FW (Table 10.3). In other studies, acrolein showed no clear evidence of teratogenicity in chicken embryos, although there is a dose-dependent embryotoxic effect (Beauchamp et al. 1985; Chhibber and Gilani 1986). Acrolein-treated chicken embryos had a higher frequency of abnormal limbs, abnormal neck, and everted viscera than the controls, but the frequency was not dose related. The overall incidence of abnormal embryos when treated at age 48 h was 24%, but only 4% in controls. In embryos given acrolein at age 72 h, these values were 26%, and 12% in controls (Chhibber and Gilani 1986).

10.4.5 Mammals

Acrolein is a strong cytotoxic and ciliostatic agent; its irritating effects on mucous membranes and its acute inhalation toxicity in mammals are well documented (Feron and Kruysse 1977; Feron et al. 1978; USEPA 1980; Astry and Jakab 1983; Beauchamp et al. 1985; Leach et al. 1987; Leikauf et al. 1989). A characteristic of acrolein is its pungent, offensive, and acrid smell, which is highly irritating to ocular and upper respiratory-tract mucosae (Beauchamp et al. 1985). Acrolein is toxic by all routes of exposure, and many of its toxic and biochemical effects are produced by interfering with critical sulphydryl groups (Srivastava et al. 1992). In isolated rat liver fractions, acrolein is a potent inhibitor of the high-affinity aldehyde dehydrogenase isozymes in mitochondrial and cytosolic fractions (Mitchell and Petersen 1988). Acrolein impairs DNA replication *in vitro* and inhibits certain mitochondrial functions (Feron et al. 1978). Studies with isolated rat liver-membrane proteins revealed that acrolein inhibits plasma membrane enzymes and alters the membrane protein profile; this may be due to acrolein-induced polymerization of plasma-membrane proteins (Srivastava et al. 1992).

Measurable adverse effects of acrolein have been documented in representative species of mammals, but the severity of the effects is contingent on the mode of administration, concentration, dose, and duration of exposure (Table 10.4). Single oral doses of 4000 µg/kg BW were lethal to guinea pigs, and 28,000 µg/kg BW to mice; diets containing the equivalent of 500 µg/kg BW and more decreased survival in rats after 102 weeks (Table 10.4). Concentrations of 60,000 µg acrolein/L in drinking water had no measurable adverse effects on cows (*Bos* sp.) after 24 h. Rats initially rejected drinking water containing 200,000 µg/L, but eventually tolerated this concentration (Table 10.4). Dermal toxicity seems low; rabbits that were immersed up to their necks in water containing 20,000 µg acrolein/L for 60 min showed no adverse effects (Table 10.4). No dermal sensitization occurred in healthy female guinea pigs (*Cavia* spp.) after repeated skin exposures to acrolein (Susten and Breitenstein 1990). In undiluted liquid or pungent vapor form, however, acrolein produces intense irritation of the eye and mucous membranes of the respiratory tract, and direct contact with the liquid can produce skin or eye necrosis (Beauchamp et al. 1985). A single intravenous injection of 850 µg acrolein/kg BW produced liver necrosis in rats; 6000 µg/kg BW caused increased embryo resorption in mice (Table 10.4). Rats receiving near-lethal doses of acrolein by subcutaneous injection had liver and kidney damage and lung pathology (USEPA 1980). Although subcutaneous injections revealed LD₅₀ values between 164,000 and 1,022,000 µg/kg BW in rabbits, these results are questionable because acrolein may be sequestered at the injection site and delay delivery to the systemic circulation (Beauchamp et al. 1985). A single intraperitoneal injection of 1000 µg/kg BW caused peritonitis in rats and 7000 µg/kg BW was lethal to mice; daily injections of 1000 µg/kg BW were eventually lethal to rats (Table 10.4). Sublethal intraperitoneal injections of acrolein induced ascites, increased hematocrit, and prolonged sleeping times (Beauchamp et al. 1985). Acquired tolerance to acrolein in mice given repeated intraperitoneal injections suggests that an increased metabolism can partially explain the acquired tolerance (Warholm et al. 1984).

The largest number of studies of the toxicity of acrolein in animals was conducted by way of inhalation, probably because acrolein has an appreciable vapor pressure under ambient conditions and inhalation is the principal exposure for humans (Beauchamp et al. 1985). Because of their intolerance to sharp and offensive odor and to intense irritation of conjunctiva and upper respiratory tract, humans have not suffered serious intoxication from acrolein. The strong lacrimation effect of acrolein is usually a warning to occupational workers. Physiological perception of acrolein by humans begins at about 500 to 1000 µg/L air with eye and nasal irritation. The irritating effects compel afflicted individuals to immediately leave the polluted area (Beauchamp et al. 1985). Laboratory animals died from inhalation of 8000 to 11,000 µg/L after 4 to 6 h, mice from 875,000 µg/L after 1 min, and rats from 660 µg/L for 24 days (Table 10.4). Animals dying from

acute and subacute exposure to acrolein vapor had lung injury with hemorrhagic areas and edema (Albin 1962). Repeated exposures of hamsters, rats, and rabbits to high sublethal concentrations of acrolein caused ocular and nasal irritation, growth depression, and respiratory tract histopathology in all species (Feron and Kruysse 1977) (Table 10.4). However, repeated exposures to low, tolerated concentrations of acrolein did not produce toxicological effects (Albin 1962), suggesting that acrolein effects are not cumulative and that minimal damage is quickly repaired.

Inhaled acrolein (in μg acrolein/L air) had sublethal effects at 10 to 50 for 1 min on rats (increased blood pressure and heart rate); at 10 for 5 weeks on mice (reduction in pulmonary compliance); at 140 to 150 for 2 min on humans (eye irritation in 30%); at 300 to 500 on humans (odor threshold); at 300 for 10 min on humans (acute irritation); at 400 for 13 weeks on rats (nasal histopathology); at 400 to 600 for 1 to 3 min on dogs (accumulations in upper respiratory tract); and at 1000 for 90 days on dogs, monkeys, and guinea pigs (ocular and nasal discharges) (Table 10.4). Sublethal effects of inhaled acrolein in representative small laboratory mammals were greatest on the upper respiratory tract and bronchial airways and included edema, ciliastasis, inflammation, degenerative loss of epithelia, altered ventilatory function, and bronchoconstriction (Feron and Kruysse 1977; Feron et al. 1978; USEPA 1980; Astry and Jakab 1983; Beauchamp et al. 1985; Barkin et al. 1986; Leach et al. 1987; Leikauf et al. 1989) (Table 10.4). Typical signs of toxicity from inhaled acrolein in small mammals include ocular and nasal irritation; growth depression; shortness of breath; lesions in the urinary tract, respiratory tract, trachea, and nasal passages; laryngeal edema; reduced resistance to bacterial infection; enlarged liver and heart; elevated blood pressure and heart rate; altered enzyme activities; and protein synthesis inhibition (USEPA 1980; Beauchamp et al. 1985; Leach et al. 1987) (Table 10.4). Signs of inhaled acrolein toxicity varied significantly with dose and species. For example, acrolein toxicity in rats at environmental concentrations was confined to local pathologic nasal changes, including metaplastic, hyperplastic, and dysplastic changes in the mucous, respiratory, and olfactory epithelium of the nasal cavity (Leach et al. 1987). Some inhaled toxicants, including acrolein, can prolong bacterial viability in the lung and thus enhance severeness of the disease. Mice convalescing from viral pneumonia became severely deficient in antibacterial defenses when exposed to acrolein (Astry and Jakab 1983). But acrolein-treated mice subjected to 100 $\mu\text{g}/\text{L}$ air (five consecutive daily 3-h exposures) were not significantly sensitive to pulmonary bacteria *Klebsiella pneumoniae* or *Streptococcus zooepidemicus* (Aranyi et al. 1986).

Acrolein may be a carcinogen, a cocarcinogen, or a tumor initiator. As an aldehyde with strong affinity for sulphydryl groups, acrolein is theoretically expected to remove free tissue thiols — compounds that protect bronchial epithelia against attack by carcinogens (Feron and Kruysse 1977; Feron et al. 1978). However, no carcinogenicity from inhalation of acrolein has been reported (Lijinsky and Reuber 1987). Nor was acrolein an evident cofactor in studies of respiratory-tract carcinogenesis with hamsters (*Cricetus* spp.) exposed to benzo[*a*]pyrene or diethylnitrosamine (Feron and Kruysse 1977). Moreover, long-term studies with rodents given acrolein by gavage did not increase incidences of neoplastic or nonneoplastic lesions (Parent et al. 1992). Other studies, however, suggest that acrolein is carcinogenic. Compounds closely related to acrolein are carcinogenic to rodents and humans and include acrylonitrile (vinyl cyanide) and vinyl acetate (Lijinsky 1988). Glycidaldehyde — an acrolein intermediate metabolite — is classified as an animal carcinogen by The International Agency for Research on Cancer; however, no convincing data are available on the carcinogenic potential of acrylic acid and other acrolein metabolites (Beauchamp et al. 1985). Acrolein can account, at least partially, for the initiating activity of cyclophosphamide carcinogenesis (Cohen et al. 1992). Cyclophosphamide and its analogs are a group of chemotherapeutic and immunosuppressive drugs. Toxic side effects of this drug group are attributed to its metabolites, especially acrolein (Cohen et al. 1992). Acrolein is a suspected carcinogen because of its 2,3-epoxy metabolite and its weak mutagenic activity in the *Salmonella* screen (Leach et al.

1987). Acrolein may be a weak carcinogen, as judged by the increased frequency of adrenal adenomas in female rats after exposure for 2 years to drinking water with 625,000 µg acrolein/L (Lijinsky and Reuber 1987). Acrolein has cancer-initiating activity in the rat urinary bladder, but studies with *N*-[4-(5-nitro-2-furyl)-2-thiazoyl] formamide precluded evaluation of acrolein as promoting a complete carcinogenic activity from low rodent survival (Cohen et al. 1992). Additional studies are needed to evaluate the carcinogenic potential of acrolein.

After intraamniotic injection, acrolein is teratogenic to rats *in vivo* but not *in vitro*. When administered intraamniotically to the whole embryo culture system of the rat on day 13 of gestation, acrolein caused edema, hydrocephaly, open eyes, cleft palate, abnormal umbilical cord, and defects of the limbs and face (Slott and Hales 1986). Beauchamp et al. (1985) suggest that acrolein-associated teratogenicity is caused by acrylic acid, an acrolein metabolite. Acrylic acid injected into amniotic fluid of rats on day 13 of gestation produced a dose-dependent increase in the percent of fetuses with skeletal and other abnormalities (Beauchamp et al. 1985).

Acrolein can react synergistically, additively, or antagonistically with other chemicals (Beauchamp et al. 1985). Rat embryos were protected by glutathione against acrolein-induced mortality, growth retardation, and developmental abnormalities — provided that glutathione was concurrently present with acrolein. When rat embryos were cultured in the presence of acrolein for 2 h prior to glutathione exposure, there was no protection against acrolein-induced embryolethality, teratogenicity, and growth retardation (Slott and Hales 1987). Acrolein effects — including altered liver enzyme activity in rats — were reduced by pretreatment of animals with chemicals that inhibited protein synthesis (NRC 1977). Exposure to acrolein is sometimes accompanied by exposure to formaldehyde and other short-chain saturated aliphatic aldehydes, which in combination cause allergic contact dermatitis (Susten and Breitenstein 1990). A 40-mL puff of cigarette smoke contains 8.2 µg acrolein and 4.1 µg formaldehyde; irritation, ciliastasis, and pathologic changes of the respiratory tract from both compounds have been widely studied (Egle and Hudgins 1974). The toxicities of acrolein and formaldehyde appear similar; both exert their principal effects in the nasal passages (Leach et al. 1987). Acrolein in combination with formaldehyde was synergistic in reducing respiratory rate in mice; however, mixtures of sulfur dioxide and acrolein were antagonistic (Beauchamp et al. 1985). Formaldehyde pretreatment (15,000 µg/L, 6 h daily for 9 days) of rats protects against respiratory rate depression by acrolein. Rats pretreated with formaldehyde had a 50% respiratory-rate depression at 29,600 µg acrolein/L vs. 6000 µg/L from acrolein alone (Babiuk et al. 1985), suggesting cross tolerance. Effects of interaction of acrolein with other toxicants are not comparable between rodents and humans. In rodents, the presence of irritant gases in smoke — such as acrolein — may delay the effects of other toxicants. In humans, however, the inhalation of acrolein and other irritant gases may cause a hypoxic effect that can enhance the effects of hypoxia-producing gases (Kaplan 1987).

Some chemicals normally contain acrolein as a metabolite or impurity. For example, allylamine toxicity to the rat cardiovascular system is believed to involve metabolism of allylamine to the highly reactive acrolein (Toraason et al. 1989). Certain mercapturic acids can be used as biological markers of exposure for chemicals that are metabolized to acrolein and excreted as mercapturic acid in the urine (Sanduja et al. 1989). In one case, rats given 13,000 µg acrolein/kg BW by gavage excreted 79% of the acrolein and 3-hydroxypropylmercapturic acid (3-OHPrMCA) in urine within 24 h. These data suggest that 3-OHPrMCA can be used as a marker of exposure to allylic and other compounds that lead to the formation of acrolein (Sanduja et al. 1989). The common industrial chemical MDP (2-methoxy-3,4-dihydro-2H-pyran) is frequently contaminated with acrolein during its synthesis; MDP causes severe irritancy and death of rats from accumulation of acrolein vapor (Ballantyne et al. 1989). Sparging acrolein-contaminated MDP with nitrogen gas before atmospheric release significantly reduced or abolished lethal toxicity to rats (Ballantyne et al. 1989).

Table 10.4 Acrolein Effects on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference^a
COW, <i>Bos</i> spp.		
Drinking water route; lactating dairy cows given 60,000 µg acrolein/L for 24 h	No change in feed or water intake or milk production; acrolein residues in milk <500 µg/L	1
DOG, <i>Canis familiaris</i>		
Inhalation route		
220, 1000, or 1800 µg/L air (0.5, 2.3, or 4.1 mg/m ³); continuous exposure for 90 days	Low concentration group appeared normal and gained weight. At 1000 µg/L, ocular and nasal discharges. At the high concentration, severe irritation evident plus nonspecific inflammation of brain, heart, lung, liver, and kidney; no deaths	2
400–600 µg/L air for 1–3 min	81–84% of acrolein retained; accumulations greater in upper respiratory tract than lower respiratory tract	3, 4
700 or 3700 µg/L air (1.6 or 8.4 mg/m ³); exposure for 8 h daily, 5 days weekly for 6 weeks	Low concentration group appeared normal and gained weight; high concentration group visibly affected with weight loss, excessive salivation, ocular discharges, labored breathing, and histopathology of lung, liver, and kidney; blood and serum chemistry normal	2
150,000 µg/L air (340 mg/m ³) for 30 min	LC50	3, 5, 6
GUINEA PIG, <i>Cavia</i> spp.		
Inhalation route		
200, 1000, or 1800 µg/L continuously for 90 days	The low concentration group appeared normal; at 1000 µg/L, pulmonary inflammation and liver necrosis; at high concentration, all had nonspecific inflammation of brain, heart, lung, liver, and kidney	2
400–1000 µg/L for 2 h	Decreased respiratory rate; effects reversed after exposure stopped	6, 7
400–1000 µg/L for as long as 12 h	Concentration-related increases in respiratory resistance, together with prolonged and deepened respiratory cycles	3
700 or 3700 µg/L; 8 h daily, 5 days weekly for 6 weeks	Low concentration group seemed normal. At high concentration, histopathology of lung, liver, and kidney	2
10,500 µg/L for 6 h	LC50	6
20,000 µg/L for 10 min	Bronchoconstriction	6
CAT, <i>Felis domesticus</i>		
Inhalation route		
650,000 µg/L air for 2.25 h	Died within 18 h	6
870,000 µg/L air for 2.5 h	Died during exposure	6
HUMAN, <i>Homo sapiens</i>		
Inhalation route		
20 µg/L air	Threshold for affecting electrocortical activity	6
30–40 µg/L air	Odor threshold for the most acrolein-sensitive people	6
90–300 µg/L air	Increasing concentration and increasing exposure caused increasing eye blinking, irritation, and decreasing respiratory frequency	8
140–150 µg/L air for 2 min	Eye irritation in 30% of subjects	6
250 µg/L air for 5 min	Moderate irritation of sensory organs	3, 5
300 µg/L air for 10 min	Considerable acute irritation	8
300–500 µg/L air	Odor threshold for most people	3, 6

Table 10.4 (continued) Acrolein Effects on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
1000 µg/L air for 1 min	Slight nasal irritation	3, 5
1000 µg/L for 5 min	Moderate nasal irritation; intolerable eye irritation	3, 5
1800 µg/L air for 1 min	Slight eye irritation	3
5500 µg/L air for 20 sec	Painful eye and nasal irritation	3, 5
21,800 µg/L air for 1 sec	Intolerable	3, 5
SYRIAN GOLDEN HAMSTER, <i>Mesocricetus auratus</i>		
Gavage route; 1000 µg/animal, equivalent to about 4000 µg/kg BW	Fatal within a few hours	11, 12
Inhalation route		
400 or 1400 µg/L air; exposure for 6 h daily, 5 days weekly for 13 weeks	No adverse effects at low concentration; nasal histopathology at high concentration	9
4000 µg/L air (9.2 mg/m ³); 7 h daily, 5 days weekly for 52 weeks	No effect on survival; no indication of cancer. Abnormal behavior, growth retardation, increased lung weight, decreased liver weight, nasal histopathology	10
6000 µg/L air (13.8 mg/m ³) for 4 h	Cytotoxic to airway cells	3
25,400 µg/L air for 4 h	LC50	6, 10
MOUSE, <i>Mus</i> sp.		
Drinking water route; 24,000 µg/L for 18 months	Death	29
Inhalation route		
10 µg/L air continuously for 5 weeks	Some reduction in pulmonary compliance	4
1000–2000 µg/L (2.3–4.6 mg/m ³) air for 24 h	Decreased pulmonary ability to kill bacteria <i>Staphylococcus aureus</i> and <i>Proteus mirabilis</i>	3
1700 µg/L air for 10 min	50% reduction in respiratory rate	6, 14
3000 or 6000 µg/L air for 8 h	Concentration-dependent impairment of pulmonary antibacterial responses	15
6000–15,000 µg/L air; 6 h daily, 5 days weekly for 6 weeks	Decreased body weight (6%) in all test groups, but not concentration related	3
66,000 µg/L for 6 h	LC50, 24 h postexposure	6
175,000 µg/L air for 10 min	LC50	3, 5, 6
875,000 µg/L air for 1 min	LC50	3, 5, 6
Intraperitoneal injection route		
4000 µg/kg BW; single injection	Plasma total lactic dehydrogenase activity (LDH) increased 5 times, with peak after 10 h	16
4000 µg/kg BW; multiple daily or weekly injections	Progressively less pronounced effect on LDH activity	16
7000 µg/kg BW; single injection	LD50	16
12,000 µg/kg BW; preceded by daily injections of 4000 µg/kg BW for 5 days	50% mortality	16
Oral route; 28,000 µg/kg BW	Acute oral LD50	3–6
RABBIT, <i>Oryctolagus</i> sp.		
Dermal route; immersed up to necks for 60 min in water with 20,000 µg/L	No adverse effects	1
Drinking water route		
9000 µg/L for 13 days	Miscarriages	29
36,000 µg/L for 13 days	Stomach ulcers	29
Inhalation route		
400 or 1400 µg/L; 6 h daily, 5 days weekly for 13 weeks	No adverse effects at low concentration; some signs of distress at 1400 µg/L	9
600 µg/L; 4 h daily for 30 days	No ocular effects	2
1700–2400 µg/L for 10 min; with or without 1000 µg ozone/L	Acrolein alone had no effect on respiratory rate. Ozone–acrolein mixtures produced a marked decrease in respiratory rate	6

Table 10.4 (continued) Acrolein Effects on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference^a
4900 µg/L air; 6 h daily, 5 days weekly for 13 weeks	Ocular and nasal irritation, growth depression, respiratory tract histopathology	10
6500–10,500 µg/L; exposure duration unknown	Emphysema, tracheobronchitis, some deaths	2
10,500 µg/L air for 6 h	LC50	6
Intravenous injection route; 3000, 4500, or 6000 µg acrolein/kg BW on day 9 of gestation; killed on day 28 of gestation	Embryo resorption was significantly higher in 6000 µg/kg group vs. controls, but was the same as controls in lower concentration groups	6
Percutaneous injection route		
164,000 µg/kg BW	LD50 for 20% acrolein in mineral spirits	3, 5
238,000 µg/kg BW	LD50 for 10% acrolein in mineral spirits	3, 5
335,000 µg/kg BW	LD50 for 20% acrolein in water	3, 5
562,000 µg/kg BW	LD50 for undiluted acrolein	3, 5
1,022,000 µg/kg BW	LD50 for 10% acrolein in water	3, 5
DOMESTIC SHEEP, <i>Ovis aries</i>		
Inhalation route via cervical trachea; ewes, 3–4 years old; exposed to smoke containing high (but unknown) concentrations of acrolein for 20 min; killed 1–22 days after exposure	Within 24 h of exposure, there was total sloughing of cervical tracheal epithelium and a 35% reduction in tracheal basal cells; trachea was normal 18–22 days after exposure	13
BABOON, <i>Papio anubis</i>		
Inhalation route; juveniles exposed to air concentrations of 12,000–2,780,000 µg acrolein/L (272–63,100 mg/m ³) for 5 min, then tested for learned avoidance/escape response	Avoidance/escape response enhanced in all animals at all concentrations tested. The group exposed to 1,025,000 µg/L air died with respiratory complications within 24 h postexposure. The group exposed to the highest concentration of 2,780,000 µg/L for 5 min died within 90 min postexposure with severe respiratory complications	17
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Dermal route; exposure duration and dose unknown	Skin burns; severe ocular effects	18
Drinking water route		
5000, 13,000, 32,000, 80,000, or 200,000 µg/L for 12 weeks	Water consumption in the 200,000 µg/L group was reduced by about 33% for the first 3 weeks; by week 12, all groups appeared normal and had apparently adapted to the odor and taste of acrolein	4
80,000 µg/L for 3 days	Some deaths	29
100,000 or 250,000 µg/L for 124 weeks	No increase in tumors over controls; no decrease in survival	11
100,000, 250,000, or 625,000 µg/L for 120 weeks	No significant decrease in survival when compared to controls. The 100,000 µg/L group had a 30% frequency of liver neoplasms and a 5% frequency of adrenal cortex neoplasms; however, no neoplasms were found in the 250,000 µg/L group. The 625,000 µg/L group had a 10% frequency of liver neoplasms vs. 25% in controls	12
200,000 µg/L for 90 days	No adverse effects	1
600,000, 1,200,000 or 1,800,000 µg/L for 60 days	Rats in the two high-concentration groups refused to drink and all died, apparently from dehydration. In the low-concentration group 20% died, but survivors were not dehydrated and had no tissue pathology	4

Table 10.4 (continued) Acrolein Effects on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
625,000 µg/L for 100 weeks	No decrease in survival; 20% of females developed adrenal cortical adenomas and 10% had neoplastic nodules in the adrenal cortex vs. 0% in controls	6
625,000 µg/L for 104 weeks	No decrease in survival. Increased frequency of adrenal cortex adenomas in females: 25% vs. 1.3% in controls	11
Inhalation route		
10 or 50 µg/L air for 1 min	Increased blood pressure and heart rate	19
10, 500, 1000, or 2400 µg/L air for 3 h	At 500 µg/L and higher, effects on respiratory mucosa included depletion of nonprotein sulfhydryl (NPSH) concentration and slight decrease in protein sulfhydryl (PSH) concentration. Effects on olfactory mucosa showed no changes in PSH at all test concentrations, but significant depletion of NPSH in the two high-concentration groups	20
100, 1000, or 3000 µg/L air; exposed 6 h daily, 5 days weekly for 3 weeks	No adverse effects in the two low-concentration groups. The high-concentration group had depressed spleen weight and body weight and extensive nasal histopathology	14
150, 510, or 1520 µg/L air; continuous exposure for 61 days	At low concentration, no respiratory tract lesions or deaths. At 510 µg/L, bronchial epithelium abnormalities but all survived. At high concentration, reduced survival; bronchopneumonia and bronchial abnormalities in survivors	6
220 or 660 µg/L air; exposed continuously for 60 days	No deaths at 220 µg/L; 70% died within 24 days at 660 µg/L	2
220, 1000, or 1800 µg/L air; exposed continuously for 90 days	The low concentration group appeared normal and gained weight. At 1000 µg/L, liver necrosis and pulmonary hemorrhage. At 1800 µg/L, all had nonspecific inflammation of brain, heart, lung, liver, and kidney	2
400 µg/L air; exposed 6 h daily, 5 days weekly for 13 weeks	Nasal histopathology	9
400, 1400, or 4000 µg/L air; exposed 6 h daily, 5 days weekly for 62 days	Some bronchial histopathology at 1400 µg/L; some deaths among males at 4000 µg/L	6
520 µg/L (1.2 mg/m ³); continuous exposure for 30 days	Decreased growth, altered liver enzyme activity	3
550 µg/L air; continuous exposure for up to 77 days	Upper respiratory irritation, reduced resistance to infection by <i>Salmonella</i> , and increased pulmonary macrophages; all effects disappeared by day 63	6
700 or 3700 µg/L air; exposed 8 h daily, 5 days weekly for 6 weeks	No adverse effects noted at low concentration. At 3700 µg/L, histopathology of lung, liver, and kidney	2
2000 µg/L air for 40 h	Increased hepatic alkaline phosphatase activity; increased liver and adrenal weight	3
2500–5000 µg/L air for 1 min	Cardioinhibitory effect that was reversed within 10 s after inhalation of acrolein ceased	19
4900 µg/L air; exposed 6 h daily, 5 days weekly for 13 weeks	50% mortality during first 4 weeks with no deaths thereafter. Survivors had depressed growth and respiratory tract histopathology	9
6000–8888 µg/L air; exposed 6 h daily, 5 days weekly for 3 weeks	Most died within 5 exposure days	14
8000–8300 µg/L air for 4 h	LC50 within 14 days; death due to lung injury	5, 6, 21
26,000 µg/L air for 1 h	LC50	21
43,500–304,000 µg/L air for 30 min	Respiratory distress; nasal and ocular irritation; some deaths in 4–5 days; pulmonary edema; bronchial degeneration; excess blood in heart, liver, and kidney	2, 6

Table 10.4 (continued) Acrolein Effects on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
131,000 µg/L air for 30 min	50% dead in 3 weeks	6
283,000 µg/L air; daily 10-min exposures for 6 months	No deaths; some bronchial pathology	6
326,000 µg/L air; daily 10-min exposures for 6 months	50% dead; tracheobronchial pathology	6
435,000 µg/L air; daily 10-min exposures for 6 months	All dead; severe histopathology of respiratory tract	6
5,000,000–10,000,000 µg/L air for 5 min	Rats on a motor-driven exercise wheel were incapacitated within 5–7 min and died shortly thereafter	17
Intraamniotic injection route. Embryos given 0.1, 1, 10, or 100 µg of acrolein on day 13 of gestation; examined on day 20 of gestation	98–100% dead at 10 and 100 µg; 85% of live fetuses receiving 1 µg were malformed (edema, hydrocephaly, cleft palate, defects of limbs and tail); no teratogenic effects at 0.1 µg	6
Intraperitoneal injection route		
1000 µg/kg BW, single injection	Peritonitis	22
1000 µg/kg BW daily for at least 5 days	Lethal	22
2000 µg/kg BW twice a week for 6 weeks followed by uracil as 3% of the diet for 20 weeks, then control diet for 6 weeks	Acrolein followed by uracil produced a 60% incidence of papilloma in urinary bladder in treated group (acrolein plus uracil) vs. 27% in water controls (uracil only). No tumors in either group	22
2500 µg/kg BW daily	All dead after second dose	3
3360 µg/kg BW; single injection; tissues analyzed after 24 h	Most (89%) of the acrolein recovered was in the acid-soluble fraction of the liver, 3% in the liver lipids, and minor amounts (0.4–1.7%) in liver proteins and RNA and DNA fractions	3
Intravenous injection route		
50–500 µg/kg BW to spontaneously hypersensitive rats	At 50–200 µg/kg BW, blood pressure increased; at 300–500 µg/kg BW, blood pressure decreased	23
250–1000 µg/kg BW	Increased blood pressure within 5 s which peaked at 20–30 s and lasted about 1 min	19
850 or 1700 µg/kg BW	Liver necrosis	3
10,000 µg/kg BW	Cardioinhibitory effects	19
<i>In vitro</i> studies		
Cultured embryos		
4500 µg/L serum medium	Growth retardation; 50% malformation frequency among survivors	24, 25
6700 µg/L serum medium	Mortality of 64%; all surviving embryos malformed	24, 25
7800–9000 µg/L serum medium	All dead	24, 25
160 µg/L serum-free medium	50% frequency of malformations in brain, facial area, and heart	25
300–1100 µg/L serum-free medium	50–100% lethal	25
Cultured myocytes and fibroblasts from neonatal heart		
600 µg/L culture medium for 4 h	Myocyte ATP levels reduced	26
2800 µg/L culture medium for 4 h	Irreversible cell lysis and ciliastasis	26
Isolated liver fractions		
1700 µg/L medium	Mitochondrial aldehyde dehydrogenase (ALDH) activity inhibited 91%; cytosolic ALDH activity inhibited 33%	27
2700 µg/L medium; 5 s preincubation in aldehyde substrate	Inhibition of mitochondrial and cytosolic ALDH	27
Oral route		
Daily gavage of 50, 500, or 2500 µg/kg BW for 102 weeks	Dose-related mortality in males during first year and in females during entire study; significant lethality in the 500 and 2500 µg/kg groups. No increased incidence of microscopic neoplastic or nonneoplastic lesions in treated rats; decreased creatinine phosphokinase levels in treated rats	28

Table 10.4 (continued) Acrolein Effects on Selected Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
Two treatments of 4000–10,000 µg/kg BW (estimated), 2–3 days apart; total dose of 8000–20,000 µg/kg BW	All died shortly after the second dose	12
5000 µg/kg BW daily for 9 days via stomach intubation	No deaths	3
10,000 µg/kg BW, single stomach intubation	Fatal	3
25,000 µg/kg BW, single gastric dose	Lethal within 48 h	22
42,000–46,000 µg/kg BW, single dose	LD50 within 14 days	3–6, 18, 22
SQUIRREL MONKEY, <i>Saimiri sciurea</i>		
Inhalation route		
220, 1000, or 1800 µg/L air; continuous exposure for 90 days	Low-concentration group appeared normal and gained weight; 1000 µg/L monkeys were visibly affected with ocular and nasal discharges. No deaths at 1800 µg/L, but excessive salivation, ocular discharges, and hyperplasia of trachea	2
700 or 3700 µg/L air; 8 h daily, 5 days weekly for 6 weeks	Low-concentration group appeared normal. High-dose group had weight loss; histopathology of lung, liver, and kidney; 22% mortality (2 of 9 died on days 6 and 9 of exposure), excessive salivation, and frequent blinking	2

^a 1, Ferguson et al. 1961; 2, Lyon et al. 1970; 3, USEPA 1980; 4, NRC 1977; 5, Albin 1962; 6, Beauchamp et al. 1985; 7, Leikauf et al. 1989; 8, Weber-Tschopp et al. 1977; 9, Feron et al. 1978; 10, Feron and Kruysse 1977; 11, Lijinsky and Reuber 1987; 12, Lijinsky 1988; 13, Barrow et al. 1992; 14, Leach et al. 1987; 15, Astry and Jakab 1983; 16, Warholm et al. 1984; 17, Kaplan 1987; 18, Sine 1991; 19, Egle and Hudgins 1974; 20, Heck et al. 1986; 21, Ballantyne et al. 1989; 22, Cohen et al. 1992; 23, Green and Egle 1983; 24, Slott and Hales 1987; 25, Slott and Hales 1986; 26, Toraason et al. 1989; 27, Mitchell and Petersen 1988; 28, Parent et al. 1992; 29, ATSDR 1990.

10.5 RECOMMENDATIONS

Agricultural crops can usually tolerate as much as 15,000 µg acrolein/L of irrigation water; however, aquatic invertebrates and fish die in acute exposures to 55 to 68 µg/L or in chronic exposures to greater than 21 µg/L (Table 10.5). Those who use acrolein to control submerged aquatic macrophytes are strongly advised that acrolein treatment at recommended application concentrations also eliminates nontarget fish and aquatic invertebrates. No acrolein criteria are now available or promulgated by regulatory agencies for the protection of avian and terrestrial wildlife; this seems to be a high-priority research need. Beauchamp et al. (1985) recommend additional research in several areas: long-term effects of acrolein inhalation on carcinogenicity and respiratory histology with rodent models; biochemical mechanisms of acrolein toxicity; genotoxic potential with chromosome breakage and exchange systems; acute and chronic toxicity from interaction effects of acrolein with other gases; and fate of accumulated acrolein in animals.

The human threshold concentration of acrolein in the United States for an 8-h workday/40-h workweek is 110 µg/L (0.25 mg/m³) air; the short-term exposure limit is 350 µg/L (0.8 mg/m³) air and is predicated on continuous exposure of workers for short intervals (Table 10.5) (Beauchamp et al. 1985). Humans can tolerate a total daily intake of 47.8 µg acrolein, equivalent to 0.68 µg/kg BW by a 70-kg individual (Table 10.5).

For handling acrolein, gloves, vapor-proof goggles or a full face mask, and other protective clothing are mandatory (Albin 1962; Beauchamp et al. 1985; NIOSH 1990). Acrolein spills should be neutralized with 10% sodium bisulfite solutions (Albin 1962). Air packs or fresh-air breathing masks, safety showers, and eye baths should be available wherever acrolein is handled (Beauchamp

et al. 1985). Purging confined areas with nitrogen is recommended prior to entering a suspected acrolein-contaminated enclosure. The eyes are particularly susceptible to liquid acrolein and, if exposed, should receive prompt treatment, although severe residual injury is probable regardless of treatment. Dilute solutions of acrolein may also cause residual eye injury. Acrolein represents a serious fire hazard because of its high flammability and potential for vapors to form explosive mixtures with air. Flame-proof electrical equipment and proper grounding are required to prevent acrolein ignition. Individuals exposed to acrolein by inhalation should be removed from the area and given oxygen; subsequent treatment by physicians of pulmonary inflammation with corticosteroids and hydroxocobalamin is recommended even if there are no symptoms (Beauchamp et al. 1985) because adverse effects from acrolein exposure may not become apparent until 4 to 24 h after exposure (Albin 1962). Oxygen therapy should be continued and analgesics given for relief of other symptoms as necessary (Beauchamp et al. 1985). There are many synthetic and natural sources of acrolein; however, special precautions are recommended when acrolein occurs as a contaminant in the synthesis of widely used chemicals such as 2-methoxy-3,4-dihydro-2H-pyran (Ballantyne et al. 1989).

Table 10.5 Proposed Acrolein Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
AGRICULTURAL CROPS		
Irrigation water, tolerated level	<15,000 µg/L	1
AQUATIC LIFE		
<i>Freshwater organisms</i>		
Sensitive species, tolerated level		
Acute exposures	<68 µg/L	2
Chronic exposures	<21 µg/L	2
Rainbow trout, safe level	20 µg/L for <48 h or 200 µg/L for <4.8 h	3
Marine organisms; acute exposures, tolerated level	<55 µg/L	2
LABORATORY WHITE RAT		
<i>Air</i>		
Maximum daily average	<13 µg/L (<0.03 mg/m ³)	7
Maximum daily	<44 µg/L (<0.1 mg/m ³)	7
HUMAN HEALTH		
<i>Air</i>		
Maximum allowable emission concentration in populated areas of former Soviet Union	132 µg/L (0.3 mg/m ³)	4
No observable effect level	<22 µg/L (<0.05 mg/m ³)	4
90-day confined space (i.e., submarines) guideline	22 µg/L (0.05 mg/m ³)	5
Odor threshold	<44 µg/L (<0.1 mg/m ³)	4
Maximum acceptable concentration in room air of former Soviet Union	44 µg/L (0.1 mg/m ³)	2, 4
Irritation threshold	44–88 µg/L (0.1–0.2 mg/m ³)	4
Occupational exposure standard (8 h daily, 40 h work week) in United States; not to exceed in most European countries, Australia, and Japan	100–110 µg/L (0.25 mg/m ³)	2, 4–6, 8
Occupational exposure standard in Hungary and former Soviet Union	308 µg/L (0.7 mg/m ³)	4
Maximum 15-min exposure limit in U.S. workplace	300–352 µg/L (0.8 mg/m ³)	4, 8
Ceiling standard for occupational exposure in the former Czechoslovakia	440 µg/L (1.0 mg/m ³)	4

Table 10.5 (continued) Proposed Acrolein Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
Acceptable ambient air concentrations		
New York	0.83 µg/m ³ for 1 year	9
Florida	2.5 µg/m ³ for 8 hr	9
North Dakota	8.0 µg/m ³ for 1 hr	9
North Carolina	80 µg/m ³ for 15 min	9
Diet		
Water plus consumption of contaminated aquatic organisms from that water body	<320 µg/L medium	2
Consumption of contaminated aquatic organisms alone	<780 µg/L medium	2
Food packaging materials; food starch	<0.6%	2
Total daily intake	<47.8 µg = <0.68 µg/kg body weight daily for a 70-kg person	2

^a 1, Ferguson et al. 1961; 2, USEPA 1980; 3, Bartley and Hattrup 1975; 4, Beauchamp et al. 1985; 5, Lyon et al. 1970; 6, Leach et al. 1987; 7, NRC 1977; 8, NIOSH 1990; 9, ATSDR 1990.

10.6 SUMMARY

Acrolein ($\text{CH}_2 = \text{CHCHO}$) is the simplest member of the class of unsaturated aldehydes and enters the environment from incomplete combustion of fossil fuels, industrial discharges, herbicides, chemical control agents of fouling organisms, and normal metabolic processes of animals. Acrolein is volatile, flammable, and explosive. Biochemical and toxic effects of acrolein are caused by its reaction with sulfhydryl compounds to form a stable thiol ether. Acrolein metabolites under certain conditions are reportedly mutagenic, teratogenic, or carcinogenic. Acrolein degrades quickly in soils and in plant tissues. In water, the half-time persistence is usually less than 50 h and in the atmosphere, less than 3 h. In treated irrigation canals, acrolein probably eliminates or seriously depletes all populations of aquatic fauna in treated areas. Recommended herbicidal concentrations of acrolein for the control of submerged aquatic weeds usually exceed 1000 µg/L; however, short-term tests with various species show that frog tadpoles die at 7 µg/L, representative fish are killed at 14 to 62 µg/L, and sensitive crustaceans are immobilized or die at 34 to 80 µg/L. Terrestrial plants and insects are comparatively resistant to acrolein: terrestrial plants tolerated 500 µg acrolein/L air and 25,000 µg/L in irrigation water, and adult fruitflies (*Drosophila melanogaster*), 3,700,000 µg acrolein/L culture medium. Birds are adversely affected by concentrations greater than 51 µg acrolein/kg whole egg by injection of eggs, greater than 9100 µg/kg body weight (BW) by single oral doses, and greater than 50,000 µg/L (greater than 113 mg/m³) by air concentrations. Mammals were affected by 50 µg acrolein/L air for 1 min, and 4000 to 28,000 µg/kg BW by single oral doses, or when fed diets equivalent to 500 µg/kg BW for 102 weeks. Proposed acrolein criteria for the protection of various resources include less than 15,000 µg/L in irrigation water of agricultural crops, less than 68 µg/L for aquatic fauna in acute exposures and less than 21 µg/L in chronic exposures, and less than 44 µg/L (less than 0.1 mg/m³) in air for rats. No acrolein criteria are presently available for the protection of avian and terrestrial wildlife. Acrolein criteria for the protection of human health include less than 320 µg/L in drinking water, less than 110 µg/L in air (less than 0.25 mg/m³), and less than 0.68 µg/kg BW daily intake from all sources. More research is needed on acrolein and its metabolites.

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CHAPTER 11

Atrazine

11.1 INTRODUCTION

Atrazine (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine) is the most heavily used agricultural pesticide in North America (DeNoyelles et al. 1982; Stratton 1984; Hamilton et al. 1987; Eisler 1989) and is registered for use in controlling weeds in numerous crops, including corn (*Zea mays*), sorghum (*Sorghum vulgare*), sugarcane (*Saccharum officinarum*), soybeans (*Glycine max*), wheat (*Triticum aestivum*), pineapple (*Ananas comusus*), and various range grasses (Reed 1982; Grobler et al. 1989; Neskovic et al. 1993). Atrazine was first released for experiment station evaluations in 1957 and became commercially available in 1958 (Hull 1967; Jones et al. 1982). In 1976, 41 million kg (90 million pounds) were applied to 25 million ha (62 million acres) on farms in the United States, principally for weed control in corn, wheat, and sorghum crops. This volume represented 16% of all herbicides and 9% of all pesticides applied in the United States during that year (DeNoyelles et al. 1982; Hamala and Kollig 1985). By 1980, domestic usage had increased to 50 million kg (Reed 1982). In Canada, atrazine was the most widely used of 77 pesticides surveyed (Frank and Sirons 1979). Agricultural use of atrazine has also been reported in South Africa, Australia, New Zealand, Venezuela, and in most European countries (Reed 1982; Neskovic et al. 1993). Current global use of atrazine is estimated at 70 to 90 million kg annually, although Germany banned atrazine in 1991 (Steinberg et al. 1995). Resistance to atrazine has developed in various strains of weeds typically present in crop fields — sometimes in less than two generations (Bettini et al. 1987; McNally et al. 1987) — suggesting that future agricultural use of atrazine may be limited.

Atrazine has been detected in lakes and streams at levels ranging from 0.1 to 30.3 µg/L; concentrations peak during spring, which coincides with the recommended time for agricultural application (Hamilton et al. 1987; Richards and Baker 1999). In runoff waters directly adjacent to treated fields, atrazine concentrations of 27 to 69 µg/L have been reported and may reach 1000 µg/L (DeNoyelles et al. 1982). Some of these concentrations are demonstrably phytotoxic to sensitive species of aquatic flora (DeNoyelles et al. 1982; Herman et al. 1986; Hamilton et al. 1987). Although atrazine runoff from Maryland cornfields was suggested as a possible factor in the decline of submerged aquatic vegetation in Chesapeake Bay, which provides food and habitat for large populations of waterfowl, striped bass (*Morone saxatilis*), American oysters (*Crassostrea virginica*), and blue crabs (*Callinectes sapidus*), it was probably not a major contributor to this decline (Forney 1980; Menzer and Nelson 1986).

11.2 ENVIRONMENTAL CHEMISTRY

Atrazine is a white crystalline substance that is sold under a variety of trade names for use primarily as a selective herbicide to control broadleaf and grassy weeds in corn and sorghum

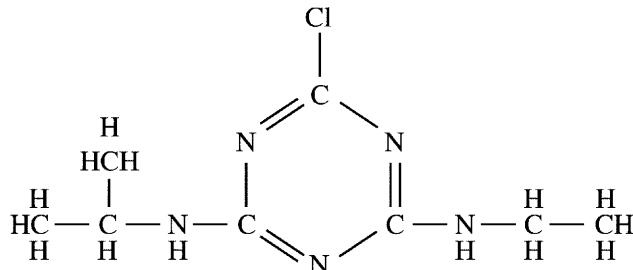


Figure 11.1 Structural formula of atrazine.

(Table 11.1; Figure 11.1). It is slightly soluble in water (33 mg/L at 27°C), but comparatively soluble (360 to 183,000 mg/L) in many organic solvents. Atrazine is usually applied in a water spray at concentrations of 2.2 to 4.5 kg/ha before weeds emerge. Stored atrazine is stable for several years, but degradation begins immediately after application (Table 11.1). The chemical is available as a technical material at 99.9% active ingredient and as a manufacturing-use product containing 80% atrazine for formulation of wettable powders, pellets, granules, flowable concentrates, emulsifiable concentrates, or tablets (U.S. Environmental Protection Agency [USEPA] 1983).

There are three major atrazine degradation pathways: hydrolysis at carbon atom 2, in which the chlorine is replaced with a hydroxyl group; N-dealkylation at carbon atom 4 (loss of the ethylpropyl group) or 6 (loss of the isopropyl group); and splitting of the triazine ring (Knuesli et al. 1969; Reed 1982). The dominant phase I metabolic reaction in plants is a cytochrome P450-mediated N-dealkylation, while the primary phase II reaction is the glutathione S-transferase (GST)-catalyzed conjugation with glutathione (Egaas et al. 1993). The presence of GST isoenzymes that metabolize atrazine has been demonstrated in at least 10 species: in the liver of rainbow trout (*Oncorhynchus mykiss*), starry flounder (*Pleuronectes stellatus*) English sole (*Pleuronectes vetulus*), rat (*Rattus norvegicus*), mouse (*Mus musculus*), the leaves of common groundsel (*Senecio vulgaris*), and soft tissues of the cabbage moth (*Mamestra brassica*) and the Hebrew character moth (*Orthosia gothica*) (Egaas et al. 1993).

The major atrazine metabolite in both soil and aquatic systems is hydroxyatrazine. In soils, it accounts for 5 to 25% of the atrazine originally applied after several months compared to 2 to 10% for all dealkylated products combined, including deethylated atrazine and deisopropylated atrazine (Stratton 1984; Schiavon 1988a, 1988b). Atrazine can be converted to nonphytotoxic hydroxyatrazine by chemical hydrolysis, which does not require a biological system (Dao 1977; Wolf and Jackson 1982). Bacterial degradation, however, proceeds primarily by N-dealkylation (Giardi et al. 1985). In animals, N-dealkylation is a generally valid biochemical degradation mechanism (Knuesli et al. 1969). In rats, rabbits, and chickens, most atrazine is excreted within 72 hours; 19 urinary metabolites — including hydroxylated, N-dealkylated, oxidized, and conjugated metabolites — were found (Reed 1982). There is general agreement that atrazine degradation products are substantially less toxic than the parent compound and not normally present in the environment at levels inhibitory to algae, bacteria, plants, or animals (DeNoyelles et al. 1982; Reed 1982; Stratton 1984).

Residues of atrazine rapidly disappeared from a simulated Northern Prairie freshwater wetland microcosm during the first 4 days, primarily by way of adsorption onto organic sediments (Huckins et al. 1986). This is consistent with the findings of others who report 50% loss (T_b 1/2) from wetlands in about 10 days (Alvord and Kadlec 1996) and freshwater in 3.2 days (Moorhead and Kosinski 1986), 82% loss in 5 days, and 88 to 95% loss in 55 to 56 days (Lay et al. 1984; Runes and Jenkins 1999), although one report presents evidence of a 300-day half-life for atrazine (Yoo and Solomon 1981), and another for months to years in the water column of certain Great Lakes (Schottler and Eisenreich 1994). In estuarine waters and sediments, atrazine is inactivated by adsorption and metabolism; half-time persistence in waters has been estimated to range between

Table 11.1 Chemical and Other Properties of Atrazine

Variable	Data
Chemical name	2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine
Alternate names	CAS 1912-24-9, ENT 28244, G-30027, Aatrex, Aatrex 4L, Aatrex 4LC, Aatrex Nine-0, Aatrex 80W, Atranex, ATratol, Atratol 8P, Atratol 80W, Atrazine 4L, Atrazine 80W, Atred, Bicep 4.5L, Co-Op, Co-Op Atra-pril, Cristatrina, Crisazine, Farmco atrazine, Gasparim, Gesaprim, Gesaprim 500 FW, Griffex, Primatal A, Shell atrazine herbicide, Vectal, Vectal SC
Primary uses	Selective herbicide for control of most annual broadleaf and grassy weeds in corn, sugarcane, sorghum, macadamia orchards, rangeland, pineapple, and turf grass sod. Nonselective herbicide for weed control on railroads, storage yards, along highways, and industrial sites. Sometimes used as selective weedicide in conifer reforestation, Christmas tree plantations, and grass seed fields
Major producer	Ciba-Geigy Corporation
Application methods	Usually as water spray or in liquid fertilizers applied preemergence, but also may be applied preplant or postemergence. Rates of 2–4 pounds/acre (2.24–4.48 kg/ha) are effective for most situations; higher rates are used for nonselective weed control, and on high organic soils
Compatibility with other pesticides	Compatible with most other pesticides and fertilizers when used at recommended rates. Sold in formulation with Lasso®, Ramrod®, and Bicep®
Stability	Very stable over several years of shelf life, under normal illumination and extreme temperatures. Stable in neutral, slightly acid, or basic media. Sublimes at high temperatures and when heated, especially at high temperatures in acid or basic media, hydrolyzes to hydroxyatrazine (2-hydroxy-4-ethylamino-6-isopropylamino-S-triazine), which has no herbicidal activity
Empirical formula	$C_8H_{14}ClN_5$
Molecular weight	215.7
Melting point	173°C to 175°C
Vapor pressure	5.7×10^{-8} mm mercury at 10°C, 3.0×10^{-7} at 20°C, 1.4×10^{-6} at 30°C, and 2.3×10^{-5} at 50°C
Henry's Law constant	6.13×10^{-8} to 2.45×10^{-7} atm-m³/mole
Physical state	The technical material is a white, crystalline, noncombustible, noncorrosive substance
Purity	No impurities or contaminants that resulted from the manufacturing process were detected
Solubility	
Water	22 mg/L at 0°C, 32 mg/L at 25°C, 320 mg/L at 85°C
N-Pentane	360 mg/L at 27°C
Petroleum ether	12,000 mg/L at 27°C
Methanol	18,000 mg/L at 27°C
Ethyl acetate	28,000 mg/L at 27°C
Chloroform	52,000 mg/L at 27°C
Dimethyl sulfoxide	183,000 mg/L at 27°C
Log K_{ow}	2.71

Data from Anonymous 1963; Hull 1967; Knuesli et al. 1969; Gunther and Gunther 1970; Reed 1982; Beste 1983; Hudson et al. 1984; Huber and Hock 1986; Huckins et al. 1986; USEPA 1987; Grobler et al. 1989; Du Preez and van Vuren 1993.

3 and 30 days, being shorter at elevated salinities. For sediments, this range was 15 to 35 days (Jones et al. 1982; Stevenson et al. 1982; Glotfelty et al. 1984; Isensee 1987). The comparatively rapid degradation of atrazine to hydroxyatrazine in estuarine sediments and water column indicates a low probability for atrazine accumulation in the estuary, and a relatively reduced rate of residual phytotoxicity in the estuary for the parent compound (Jones et al. 1982).

Atrazine is leached into the soil by rain or irrigation water. The extent of leaching is limited by the low water solubility of atrazine and by its adsorption onto certain soil constituents (Anonymous 1963). Runoff loss in soils ranges from 1.2 to 18% of the total quantity of atrazine applied, but usually is less than 3% (Wolf and Jackson 1982). Surface runoff of atrazine from adjacent conventional tillage and no-tillage corn watersheds in Maryland was measured after single annual applications of 2.2 kg/ha for 4 years (Glenn and Angle 1987). Most of the atrazine in surface runoff was lost during the first rain after application. In 1979, the year of greatest precipitation, 1.6% of the atrazine applied moved from the conventional tillage compared to 1.1% from the no-tillage

watershed, suggesting that no-tillage should be encouraged as an environmentally sound practice (Glenn and Angle 1987). Lateral and downward movement of atrazine was measured in cornfield soils to a depth of 30 cm when applied at 1.7 kg/ha to relatively moist soils; in lower elevation soils, atrazine accumulated by way of runoff and infiltration (Wu 1980). Downward movement of atrazine through the top 30 cm of cornfield soils indicates that carryover of atrazine to the next growing season is possible; between 5 and 13% of atrazine was available 1 year after application (Wu 1980; Wu and Fox 1980). Atrazine is not usually found below the upper 30 cm of soil in detectable quantities, even after years of continuous use; accordingly, groundwater contamination by atrazine is not expected at recommended application rates (Anonymous 1963; Hammons 1977; Wolf and Jackson 1982; Beste 1983).

Atrazine persistence in soils is extremely variable. Reported T_b 1/2 values ranged from 20 to 100 days in some soils to 330 to 385 days in others (Jones et al. 1982). Intermediate values were reported by Forney (1980), Stevenson et al. (1982), and Stratton (1984). Atrazine activity and persistence in soils is governed by many physical, chemical, and biological factors. In general, atrazine loss was more rapid under some conditions than others. It was more rapid from moist soils than from dry soils during periods of high temperatures than during periods of low temperatures, from high organic and high clay content soils than from sandy mineral soils, during summer than in winter, from soils with high microbial densities than from those with low densities, from soils of acidic pH than from those of neutral or alkaline pH, during storm runoff events than during normal flows, at shallow soil depths than at deeper depths, and under conditions of increased ultraviolet irradiation (Anonymous 1963; McCormick and Hiltbold 1966; Hull 1967; Gunther and Gunther 1970; Dao 1977; Hammons 1977; Frank and Siron 1979; Forney 1980; Stevenson et al. 1982; Wolf and Jackson 1982; Beste 1983; USEPA 1987). Microbial action, usually by way of N-dealkylation and hydrolysis to hydroxyatrazine, probably accounts for the major breakdown of atrazine in the soil, although nonbiological degradation pathways of volatilization, hydroxylation, dealkylation, and photodecomposition are also important (Hull 1967; Gunther and Gunther 1970; Reed 1982; Menzer and Nelson 1986). The photolytic transformation rate of atrazine is enhanced at higher atrazine concentrations and in the presence of dissolved organic carbon (DOC) and DOC mimics (Hapeman et al. 1998).

11.3 CONCENTRATIONS IN FIELD COLLECTIONS

Although annual use of atrazine in the United States is about 35 million kg (Alvord and Kadlec 1996; Carder and Hoagland 1998), atrazine concentrations in human foods are negligible. Monitoring of domestic and imported foods in the human diet by the U.S. Food and Drug Administration between 1978 and 1982 showed that only 3 of 4500 samples analyzed had detectable atrazine residues. Two samples in 1980 contained 0.01 and 0.08 mg atrazine/kg and one in 1978, following a known contamination incident, contained 47 mg/kg (Reed 1982).

Atrazine was present in 100% of 490 samples analyzed in Lakes Michigan, Huron, Erie, and Ontario in 1990 to 1992. Concentrations were highest in Lake Erie at 0.11 µg/L (Schottler and Eisenreich 1994). Atrazine concentrations in river waters of Ohio show strong seasonality (1995 to 1998), with the period of higher concentrations lasting 6 to 12 weeks, beginning with the first storm runoff following application, usually in May (Richards and Baker 1999). The use of atrazine in the U.S. Great Lakes Basin is estimated at 2.7 million kg annually, and more than 600,000 kg atrazine have entered the Great Lakes (Schottler and Eisenreich 1994). Atrazine and its metabolites have been observed in freshwater streams contiguous to agricultural lands; 0.1 to 3% of the atrazine applied to the fields was lost to the aquatic environment (Jones et al. 1982). Atrazine concentrations as high as 691 µg/L were reported in agricultural streams during storm runoff events (Carder and Hoagland 1998). In some cases, atrazine concentrations in runoff waters from treated cornfields can exceed 740 µg/L (Table 11.2). Elevated levels were associated with high initial treatment rates, major storms shortly after application, conventional tillage practices (vs. no tillage), and increased

flow rates, increased suspended solids, and increased dissolved nitrates and nitrites. Concentrations in runoff water usually declined rapidly within a few days (Forney 1980; Setzler 1980; Stevenson et al. 1982). In 1991, maximum atrazine concentrations in the Des Plaines River, Illinois, after spring rains, briefly exceeded the federal proposed drinking water criterion of 3 µg/L (Alvord and Kadlec 1996). Groundwater contamination by way of atrazine treatment of cornfields has been unexpectedly reported in parts of Colorado, Iowa, and Nebraska. Contamination was most pronounced in areas of highly permeable soils that overlie groundwater at shallow depths (Wilson et al. 1987).

The total amount of atrazine reaching the Wye River, Maryland, estuary depended on the quantity applied in the watershed and the timing of runoff. In years of significant runoff, 2 to 3% of the atrazine moved to the estuary within 2 weeks after application and effectively ceased after 6 weeks (Glotfelty et al. 1984). In Chesapeake Bay waters, a leakage rate of 1% of atrazine from agricultural soils resulted in aqueous concentrations averaging 17 µg/L—concentrations potentially harmful to a variety of estuarine plants (Jones et al. 1982). The maximum recorded atrazine concentration in runoff water entering Chesapeake Bay was 480 µg/L (Forney 1980). However, these concentrations seldom persisted for significant intervals and only rarely approached those producing long-term effects on submerged aquatic vegetation (Glotfelty et al. 1984).

Atmospheric transport of atrazine-contaminated aerosol particulates, dusts, and soils may contribute significantly to atrazine burdens of terrestrial and aquatic ecosystems. The annual atmospheric input of atrazine in rainfall to the Rhode River, Maryland, as one example, was estimated at 1016 mg/surface ha in 1977, and 97 mg/ha in 1978 (Wu 1981). A similar situation exists with fog water. When fog forms, exposed plant surfaces become saturated with liquid for the duration of the fog (Glotfelty et al. 1987).

Table 11.2 Atrazine Concentrations in Selected Watersheds

Locale and Other Variables	Concentration ^a (g/L or g/kg)	Reference ^b
ATRAZINE-TREATED CORNFIELDS		
Iowa, shortly after application		
Runoff water	4900	1
Sediments	7350	1
Kansas, 1974		
Runoff water		
May	1074	1
June	739	1
Soil from drainage canal	50	1
Water from drainage canal		
Summer	100	1
Winter	10	1
Ontario, Canada (1.7 kg/ha)		
Clay-dominated soils	Max. 25	2
Loam-dominated soils	Max. 14	2
Sand-dominated soils	Max. 4	2
STREAMWATER, QUEBEC		
Atrazine	(0.01–26.9)	3
Metabolites	(<0.01–1.3)	3
NORTH AMERICA		
Natural waters	0.1–69.4	11, 13
Tail-water pits receiving runoff from corn and sorghum fields treated with atrazine	Max. 1000	11
Surface water; golf course ponds; North Carolina; 1995	Max. 0.14	15

Table 11.2 (continued) Atrazine Concentrations in Selected Watersheds

Locale and Other Variables	Concentration^a (g/L or g/kg)	Reference ^b
Mississippi River; 1990–1994; south of Memphis, TN		
River water	0.42	17
Fish muscle	Max. 58	17
NORTHERN OHIO STREAMS		
Sandusky River Basin, 1980	(1.0–45.7)	4
Others, 1980	(0.1–23.2)	4
Maumee and Sandusky Rivers, 1995–1998		
Mean	0.4	16
90th percentile	4–7	16
SOUTH AFRICA		
Surface waters after atrazine treatment of agricultural lands	Max. 82.3	11, 12
STREAMS ENTERING GREAT LAKES FROM CANADA		
To Lake Erie	4.0	2
To Lake Huron	1.4	2
To Lake Ontario	1.1	2
SUSQUEHANNA DRAINAGE BASIN		
Pennsylvania, 1980		
May	Max. 67.8	2
Other months	(1.1–2.5)	2
DRINKING WATER		
Colorado	Usually <1.8; Max. 2.3	5
Tiffin, Ohio, 1980		
May 30	16.4	4
June 16	7.2	4
June 26	5.3	4
July 1	3.3	4
U.S. reservoirs	Max. 88.4	13
FOG WATER, BELTSVILLE, MARYLAND	(0.27–0.82)	6
CHESAPEAKE BAY WATERSHED		
Runoff water	Max. 480.0	1
Chesapeake Bay, 1980		
April	Max. 0.3	2
June	Max. 1.1	2
July	Max. 0.4	2
Chesapeake Bay tributaries		
Horn Point		
May–July, 1980	(0.1–18.3)	7
May, 1981	(0.7–46.0)	7
Choptank, estuary		
May–July, 1980	(0.0–0.8)	7
May, 1981 (runoff event)	(0.2–9.3)	7
Wye River, Maryland	Usually <3.0 at peak loadings; Max. ~15.0	8
Rhode River, Maryland 1977–78		
Water column, depth ~0.3 m	0.04 (0.003–0.19)	9
Microsurface layer	0.13 (0.01–3.3)	9

Table 11.2 (continued) Atrazine Concentrations in Selected Watersheds

Locale and Other Variables	Concentration^a (g/L or g/kg)	Reference ^b
Rainwater, May	Max. 2.2	10
GERMANY		
Groundwater	>0.5	13
Surface water	Often up to 1.5	14
Rainwater	Max. 3.5	13

^a Concentrations are shown as mean, range (in parenthesis), and maximum (Max.).

^b 1, Forney 1980; 2, Stevenson et al. 1982; 3, Frank and Siron 1979; 4, Setzler 1980; 5, Wilson et al. 1987; 6, Glotfelter et al. 1987; 7, Kemp et al. 1985; 8, Glotfelter et al. 1984; 9, Lu et al. 1980; 10, Wu 1981; 11, Du Preez and van Vuren 1992; 12, Grobler et al. 1989; 13, Fischer-Scherl et al. 1991; 14, Steinberg et al. 1995; 15, Ryals et al. 1998; 16, Richards and Baker 1999; 17, Hartley et al. 1999.

11.4 EFFECTS

11.4.1 General

In terrestrial ecosystems, atrazine effectively inhibits photosynthesis in target weeds and can also affect certain sensitive crop plants. Atrazine metabolites are not as phytotoxic as the parent compound. Degradation is usually rapid, although atrazine can persist in soils for more than one growing season. Soil fauna may be adversely affected shortly after initial atrazine application at recommended levels, but long-term population effects on this group are considered negligible.

Sensitive species of aquatic flora experience temporary adverse effects at concentrations as low as 1.0 to 5.0 µg/L. However, most authorities agree that potentially harmful levels (i.e., >10 µg/L for long periods) have not been documented and are probably unrealistic under current application protocols and degradation rates. The observed declines in submerged aquatic vegetation in the Chesapeake Bay are not now directly attributable to atrazine use. Atrazine indirectly affects aquatic fauna at concentrations of 20 µg/L and higher by reducing the food supply of herbivores and, to some extent, their macrophyte habitat. Direct adverse effects on growth and survival of aquatic fauna were evident in the range of 94 to 500 µg/L. Bioaccumulation of atrazine is limited and food chain biomagnification is negligible in aquatic ecosystems.

Birds show a low probability for atrazine uptake and accumulation. Known acute oral LD50 and dietary LD50 values are high: >2000 mg/kg body weight and 5000 mg/kg diet. Indirect ecosystem effects of atrazine on insect- and seed-eating birds are not known and seem to merit study. Data are lacking for mammalian wildlife, but tests with domestic livestock and small laboratory animals strongly indicate that this group is comparatively resistant to atrazine. Acute oral LD50 values are >1750 mg/kg body weight, and no adverse effects are evident at dietary levels of 25 mg/kg food (about 1.25 mg/kg body weight) and sometimes 100 mg/kg food over extended periods.

11.4.2 Terrestrial Plants and Invertebrates

Atrazine enters plants primarily by way of the roots and secondarily by way of the foliage, passively translocated in the xylem with the transpiration stream, and accumulates in the apical meristems and leaves (Hull 1967; Forney 1980; Reed 1982; Wolf and Jackson 1982). The main phytotoxic effect is the inhibition of photosynthesis by blocking the electron transport during Hill reaction of photosystem II. This blockage leads to inhibitory effects on the synthesis of carbohydrate, a reduction in the carbon pool, and a buildup of carbon dioxide within the leaf, which subsequently causes closure of the stomates, thus inhibiting transpiration (Stevenson et al. 1982; Jachetta et al. 1986; Shabana 1987).

Atrazine is readily metabolized by tolerant plants to hydroxyatrazine and amino acid conjugates. The hydroxyatrazine can be further degraded by dealkylation of the side chains and by hydrolysis of resulting amino groups on the ring and some carbon dioxide production (Hull 1967; Reed 1982; Beste 1983). Resistant plant species degrade atrazine before it interferes with photosynthesis. Corn, for example, has an enzyme (2,4-dihydroxy-7-methoxy-1,4-[2H]-benzoxazin-3-[4H]-one) that degrades atrazine to nonphytotoxic hydroxyatrazine (Wu 1980; Stevenson et al. 1982). In sensitive plants, such as oats, cucumber, and alfalfa, which are unable to detoxify atrazine, the compound accumulates, causing chlorosis and death (Anonymous 1963; Hull 1967). Corn and sorghum excrete about 50% of accumulated atrazine and metabolize the rest to insoluble residues that are indigestible to sheep (*Ovis aries*) and rats (*Rattus* sp.). These results strongly suggest that the final disposition of atrazine metabolites does not occur in either plants or animals, but ultimately through microbial breakdown (Bakke et al. 1972b).

Long-term applications of atrazine for weed control in corn result in degradation products, mainly hydroxylated analogues, that may persist in soil for at least 12 months after the final herbicide application, and may enter food crops planted in atrazine-treated soil in the years after cessation of long-term treatment (Frank and Siron 1979; Kulshrestha et al. 1982). In one example, atrazine was applied to a corn field for 20 consecutive years at rates of 1.4 to 2.2 kg/ha (Khan and Saidak 1981). Soils collected 12 months after the last application contained atrazine (55 µg/kg dry weight), hydroxyatrazine (296 µg/kg), and various mono-dealkylated hydroxy analogues (deethylatrazine at 14 µg/kg, deethylhydroxyatrazine at 17 µg/kg, and desopropylhydroxyatrazine at 23 µg/kg). Oat (*Avena sativa*) seedlings grown in this field contained hydroxyatrazine (64 to 73 µg/kg fresh weight) and desopropylhydroxyatrazine (84 to 116 µg/kg). Similar results were obtained with timothy, *Phleum pratense* (Khan and Saidak 1981). In areas with a relatively long growing season, a double cropping of soybeans (*Glycine max*) — planted after corn is harvested for silage or grain — is gaining acceptance. Under conditions of warm weather, relatively high rainfall, and sandy soils, soybeans can be safely planted after corn (14 to 20 weeks after atrazine application) when rates of atrazine normally recommended for annual weed control (1.12 to 4.48 kg/ha) are used (Brecke et al. 1981).

Seed germination of sensitive species of plants was reduced by 50% at soil atrazine concentrations between 0.02 and 0.11 mg/kg (Table 11.3). Mustard (*Brassica juncea*) was especially sensitive and died shortly after germination. Soil atrazine residues of this magnitude were typical of those remaining at the beginning of a new growing season following corn in sandy loam under tropical conditions (Kulshrestha et al. 1982). Reduction in seed germination was also noted at soil atrazine concentrations of 0.25 to 0.46 mg/kg for the lentil *Lens esculenta*, the pea *Pisum sativum*, and the grain *Cicer arietinum* (Kulshrestha et al. 1982). Many species of mature range grasses are tolerant of atrazine but are susceptible as seedlings; seedlings of the most sensitive three species of eight tested were adversely affected in soils containing 1.1 mg atrazine/kg (Bahler et al. 1984) (Table 11.3).

Soil fungi and bacteria accumulated atrazine from their physicochemical environment by factors of 87 to 132 (Wolf and Jackson 1982), probably through passive adsorption mechanisms. Atrazine stimulated the growth of at least two common species of fungal saprophytes known to produce antibiotics: *Epicoccum nigrum* and *Trichoderma viride* (Richardson 1970). *Trichoderma*, for example, grew rapidly at all treatments tested (up to 80 mg/kg soil) and showed optimal growth 3 to 10 days postinoculation (Rodriguez-Kabana et al. 1968). Atrazine suppressed the growth of various species of soil fungi, including *Rhizoctonia solani*, *Sclerotium rolfsii*, and *Fusarium* spp., and stimulated the growth of other species known to be antagonistic to *Fusarium*. This selectivity is likely to induce a shift in the fungal population of atrazine-treated soil that would be either harmful or beneficial to subsequent crops, depending on whether saprophytic or pathogenic fungi attained dominance (Richardson 1970).

At 2.5 mg atrazine/kg soil, equivalent to 2 kg/ha in the top 10 cm, field and laboratory studies demonstrated that mortality in arthropod collembolids (*Onchiurus apuanicus*) was 47% in 60 days; however, fecundity was not affected at dose levels up to 5.0 mg/kg soil. It was concluded that

atrazine applications at recommended treatment levels had negligible long-term population effects on sensitive species of soil fauna (Mola et al. 1987). At 5 or 8 kg atrazine/ha, all species of soil fauna tested, except some species of nematodes, were adversely affected (Popovici et al. 1977). One month postapplication, population reductions of 65 to 91% were recorded in protozoa, mites, various insect groups, and collembolids at 5 kg/ha; after 4 months, populations were still depressed by 55 to 78% (Popovici et al. 1977). At 9 kg atrazine/ha, soil faunal populations of beetles, collembolids, and earthworms remained depressed for at least 14 months after initial treatment (Mola et al. 1987). Final instar larvae of the cabbage moth (*Mamestra brassica*) fed synthetic diets for 48 h containing 500 or 5000 mg atrazine/kg rations had significant changes in xenobiotic metabolizing activities of soft tissues and midgut, especially in aldrin epoxidase substrates; growth was retarded in the high-dose group (Egaas et al. 1993).

Table 11.3 Atrazine Effects on Selected Species of Terrestrial Plants

Species, Dose, and Other Variables	Effect and Reference
Soil alga, <i>Chlorella vulgaris</i>	
0.1 and 0.5 mg/L soil water	Chlorophyll production stimulated (Torres and O'Flaherty 1976)
1.0 mg/L and higher	Chlorophyll production inhibited; more-than-additive toxicity observed in combination with simazine and malathion (Torres and O'Flaherty 1976)
Mustard, <i>Brassica juncea</i>	
20 mg/kg dry weight soil	Seed germination reduced 50%; death shortly thereafter (Kulshrestha et al. 1982)
Cyanobacteria, 4 species, isolated from rice-cultivated soils in Egypt	
50 mg/L soil water for 7 days	Suppressed pigment biosynthesis in <i>Aulosira fertissima</i> and <i>Tolyphothrix tenuis</i> , reduced growth in <i>Anabaena oryzae</i> and <i>Nostoc muscorum</i> , and reduced carbohydrate content in <i>Nostoc</i> and <i>Tolyphothrix</i> (Shabana 1987)
100–500 mg/L soil water for 7 days	All variables affected in all species (Shabana 1987)
Barley, <i>Hordeum vulgare</i>	
50 mg/kg dry weight soil	Seed germination reduced 50% (Kulshrestha et al. 1982)
Oat, <i>Avena sativa</i>	
70 mg/kg dry weight soil	Seed germination reduced 50% (Kulshrestha et al. 1982)
Wheat, <i>Triticum aestivum</i>	
110 mg/kg dry weight soil	Seed germination reduced 50% (Kulshrestha et al. 1982)
0.6 kg/ha	Effectively controls weeds in wet sandy soils; some damage to crop possible in dry clay soils (Amor et al. 1987)
Range grasses, four species, seedlings	
1.1 mg/kg soil	Survival reduced, and growth reduced in surviving seedlings (Bahler et al. 1984)
Weed, <i>Chenopodium album</i> , seedlings from French garden never treated with chemicals	
0.5 kg/ha	Survival 12%; progeny of these survivors were resistant to 1 kg/ha treatment (Bettini et al. 1987)
1.0 kg/ha	Fatal to 100% (Bettini et al. 1987)
Corn, <i>Zea mays</i>	
1.25 kg/ha	No effect on growth or yield (Malan et al. 1987)
5.0 kg/ha	Severe phytotoxicity 25–30 days after planting; growth inhibition during early development. Recovery, with no negative effect on final yield (Malan et al. 1987)
Soybean, <i>Glycine max</i> , planted after corn, <i>Zea mays</i>	
2.24 kg/ha	No effect on yield when planted at least 8 weeks after atrazine application (Brecke et al. 1981)
4.48 kg/ha	At least 10-week interval required after atrazine application for successful germination (Brecke et al. 1981)

11.4.3 Aquatic Plants

Since the mid-1960s, seagrasses and freshwater submersed vascular plants have declined in many aquatic systems, especially in Chesapeake Bay (Forney and Davis 1981; Stevenson et al. 1982; Kemp et al. 1983; Cunningham et al. 1984). These plants provide food and habitat to diverse and abundant animal populations. In Chesapeake Bay, this decline has been associated with an overall decline in the abundance of fish and wildlife, and has been interpreted as an indication of serious disturbance in the ecological balance of the estuary. More than 10 native species of submersed aquatic plants in Chesapeake Bay have decreased in abundance. In the upper estuary, this decline was preceded by an invasion of Eurasian watermilfoil (*Myriophyllum spicatum*), which eventually also died back (Kemp et al. 1983). Runoff of herbicides, including atrazine, from treated agricultural lands has been suggested as a possible factor involved in the disappearance of Chesapeake Bay submersed vegetation. During the past 20 years, the most widely used herbicide in the Chesapeake Bay watershed — and in the surrounding coastal plain — has been atrazine. Since its introduction into the region in the early 1960s, atrazine use has grown to about 200,000 kg annually in Maryland coastal communities alone (Kemp et al. 1983). Potentially phytotoxic concentrations of atrazine would be expected in estuaries with the following characteristics (which seem to apply in most of upper Chesapeake Bay): immediately adjacent to cornfields in the watershed; rains occur shortly after atrazine application; clay soils in fields producing more rapid runoff; soils with circumneutral pH and relatively low organic content; and large estuarine areas of low salinity and poor mixing (Stevenson et al. 1982).

Most authorities agree that atrazine could induce some loss in aquatic vegetation but was not likely to have been involved in the overall decline of submersed plants in Chesapeake Bay (Forney 1980; Plumley and Davis 1980; Forney and Davis 1981; Kemp et al. 1983, 1985; Jones et al. 1986), and that nutrient enrichment and increased turbidity probably played major roles (Kemp et al. 1983, 1985). In the open waters of Chesapeake Bay, atrazine concentrations have rarely exceeded 1 µg/L. In major tributaries, such as the Choptank and Rappahanock Rivers, concentrations of 5 µg/L can occur after a major spring runoff. These runoffs sometimes generate transient, 2- to 6-hour concentrations up to about 40 µg/L in secondary tributaries (Kemp et al. 1983). In some small coves on the Chesapeake Bay, submersed plants may be exposed periodically to atrazine concentrations of 5 to 50 µg/L for brief periods during runoffs; however, dilution, adsorption, and degradation tend to reduce concentrations in the water phase to <5 µg/L within 6 to 24 h (Jones et al. 1986). Since atrazine degrades rapidly in estuarine conditions (half-time persistence [T_b 1/2] of 1 to 6 weeks), concentrations of atrazine on suspended and deposited estuarine sediments were seldom >5 µg/kg, suggesting little potential for accumulation (Kemp et al. 1983). The photosynthesis of redheadgrass (*Potamogeton perfoliatus*) was significantly inhibited by atrazine concentrations of 10 to 50 µg/L; however, it returned to normal levels within 1 h after atrazine was removed (Jones et al. 1986). Recovery of redheadgrass within several weeks has also been documented after exposure to 130 µg/L for 4 weeks (Cunningham et al. 1984). In Chesapeake Bay, potential long-term exposure of submersed aquatic plants to concentrations of atrazine in excess of 10 µg/L is doubtful. Therefore, any observed reductions in photosynthesis by these plants under such conditions would be minor and reversible (Jones et al. 1986).

Some authorities, however, suggest that the effects of atrazine on aquatic plants may be substantial. For example, atrazine concentrations between 1 and 5 µg/L adversely affect phytoplankton growth and succession; this, in turn, can adversely affect higher levels of the food chain, beginning with the zooplankton (DeNoyelles et al. 1982). Also, exposure to environmentally realistic concentrations of 3.2 to 12 µg atrazine/L for about 7 weeks was demonstrably harmful to wild celery (*Vallisneria americana*), a submersed vascular plant in Chesapeake Bay (Correll and Wu 1982). At highest concentrations of 13 to 1104 µg/L for 3 to 6 weeks, growth of representative submersed macrophytes in Chesapeake Bay was significantly depressed, and longer exposures were fatal to most species (Forney 1980). Atrazine concentrations of 100 µg/L reportedly cause permanent changes in algal community structure after exposure for 14 days, including decreased density

and diversity, altered species composition, and reduced growth (Hamala and Kollig 1985). It seems that additional research is needed on the role of atrazine and on its interactions with other agricultural chemicals in regard to observed declines in submerged plants. It is emphasized that degradation products of atrazine did not play a role in the disappearance of the submerged vascular plants from the Chesapeake Bay. For example, 500 µg/L of deethylated atrazine was needed to produce 20 to 40% photosynthetic inhibition in four major species of submerged macrophytes in 2 hours, but only 95 µg/L of the parent atrazine caused 50% inhibition in a similar period (Jones and Winchell 1984).

Many studies have been conducted on the effects of atrazine on various species of aquatic flora under controlled conditions (Table 11.4). At concentrations of 1 to 5 µg/L and exposure periods of 5 minutes to 7 weeks, documented adverse effects in sensitive species included inhibition of photosynthesis, growth, and oxygen evolution (Table 11.4). Higher concentrations were associated with altered species composition, reduced carbon uptake, reduced reproduction, high accumulations of atrazine, decreased chlorophyll *a* production, ultrastructural changes on chloroplasts, and death (Table 11.4). Phytotoxic effects were significantly increased at elevated levels of incident illumination, elevated water temperatures, decreased water pH, decreased dissolved oxygen concentrations, decreased nutrient content, and at increasing atrazine concentrations in the water column (Forney and Davis 1981; Karlander et al. 1983; Jones and Estes 1984; Malanchuk and Kollig 1985; Mayasich et al. 1986). Phytotoxicity was not significantly influenced by atrazine concentrations in the sediments or hydrosoils, or by the salinity of the medium (Forney 1980; Forney and Davis 1981; Jones and Estes 1984; Huckins et al. 1986). There are marked differences in sensitivity to atrazine among estuarine marsh plant species (Lytle and Lytle 1998). Atrazine, at typical concentrations occurring in areas draining agricultural fields, should pose no significant adverse effects to *Spartina alterniflora*. In contrast, *Juncus roemerianus* at 250 µg atrazine/L or greater will likely die or decline (Lytle and Lytle 1998).

Atrazine was 4 to 10 times more effective than its degradation products in producing growth reduction, photosynthesis inhibition, and acetylene-reducing ability in two species of green algae (*Chlorella pyrenoidosa* and *Scenedesmus quadricauda*) and three species of cyanobacteria (*Anabaena* spp.) (Stratton 1984). Atrazine reduced growth 50% at 0.03 to 5.0 mg/L and inhibited photosynthesis 50% at 0.1 to 0.5 mg/L. Comparable values for deethylated atrazine were 1.0 to 8.5 mg/L for growth reduction and 0.7 to 4.8 mg/L for photosynthesis inhibition. For deisopropylated atrazine, these values were 2.5 to >10 mg/L for growth reduction and 3.6 to 9.3 mg/L for photosynthesis inhibition; hydroxyatrazine and diaminoatrazine were nontoxic to most cultures tested (Stratton 1984). Smooth cordgrass (*Spartina alterniflora*), the major emergent species in North American salt marshes, is only slightly affected by relatively high levels of atrazine, due possibly to its ability to metabolize this compound (Davis et al. 1979; Forney and Davis 1981; Stevenson et al. 1982). Studies with radiolabeled atrazine and *Spartina* roots were conducted during 2-day exposures, followed by 28 days in atrazine-free solution (Pillai et al. 1977; Weete et al. 1980). After 2 days, 90% of the atrazine had translocated to the shoots. Atrazine was readily metabolized to chloroform-soluble substances, then to water-soluble substances, and finally to insoluble substances. Atrazine in the chloroform-soluble fraction decreased from 85 to 24% by day 28; the aqueous fraction contained 15% at the start and 60% at day 28. The basis of *Spartina* resistance is due primarily to its ability to convert atrazine to N-dealkylation products, such as 2-chloro-4-amino-6-isopropylamino-s-triazine. However, at least 14 water-soluble metabolites were isolated; about half contained the fully alkylated triazine rings, and most of the others had the 4-amino-6-isopropylamino derivative. Acid hydrolysates of the metabolites contained small amounts of amino acids, suggesting that a conjugation pathway, in addition to N-dealkylation, may be operative in *Spartina*.

Freshwater species of algae are among the most sensitive of all aquatic species tested (Tang et al. 1998). The ability of freshwater algal cells to accumulate atrazine was significantly correlated with cell volume and surface area, and accumulations were higher in the more sensitive species. Uptake of radiolabeled atrazine by four species of freshwater green algae and four species of diatoms was rapid: about 90% of the total uptake occurred within the first hour of exposure during

exposure for 24 h; maximum levels were reached 3 to 6 h after initial exposure; and accumulations were higher in algae than in diatoms (Tang et al. 1998). A green alga (*Chlorella kessleri*) showed numerous adverse effects when subjected to sublethal concentrations of atrazine over a 72-h period, including dose-dependent growth inhibition, protein synthesis decrease, photosynthesis reduction, and stimulation of fatty acid synthesis (El-Sheekh et al. 1994).

Estuarine fungi contribute substantially to plant detritus due to their abundance and potential for degradation. Fungi are known to accumulate soluble atrazine from seawater through sorption, and release up to 2.2% as hydroxyatrazine and other atrazine metabolites; another 4.6% is more tightly associated and less available to the external environment. The combined processes result in atrazine accumulation, and may contribute to its transport and redistribution through the estuary (Schocken and Speedie 1982, 1984).

11.4.4 Aquatic Animals

A marine copepod (*Acartia tonsa*) was the most sensitive aquatic animal tested against direct effects of atrazine, having a 96-h LC50 of 94 µg/L (Table 11.5). Atrazine was most toxic to estuarine crustaceans at low salinities; however, it was most toxic to estuarine fishes at high salinities (Hall et al. 1994). Adverse effect levels to selected species of aquatic invertebrates and fishes ranged from 120 µg/L to 500 µg/L, based on lifetime exposure studies (Table 11.5). The most sensitive criterion measured during long-term chronic exposure varied among species. Among freshwater invertebrates, for example, the most useful criterion was survival for *Gammarus*, the number of young produced for *Daphnia*, and developmental retardation for *Chironomus* (Macek et al. 1976).

Ambient concentrations as low as 20 µg atrazine/L have been associated with adverse effects on freshwater aquatic fauna, including benthic insects (Dewey 1986) and teleosts (Kettle et al. 1987), although effects were considered indirect. For example, the abundance of emerging chironomids (*Labrundinia pilosella*) and other aquatic insects declined at 20 µg atrazine/L (Dewey 1986). Richness of benthic insect species and total emergence declined significantly with atrazine addition. The effects were primarily indirect, presumably by way of reduction in food supply of nonpredatory insects, and to some extent their macrophyte habitat. Dietary habits and reproductive success were negatively affected in three species of fish after exposure for 136 days in ponds containing 20 µg atrazine/L (Kettle et al. 1987). About 70% of the original concentration applied was present in water at the end of the study. The reproduction of channel catfish (*Ictalurus punctatus*) and gizzard shad (*Dorosoma cepedianum*) failed, and that of bluegills, as measured by number of young per pond, was reduced more than 95%. Also, the number of prey items in the stomachs of bluegills was significantly higher in control ponds (25.6) than in a treated pond (3.8), and the number of taxa represented was significantly greater. Macrophyte communities in treated ponds were reduced more than 60% in 2 months. The authors concluded that the effects of atrazine on bluegills were probably indirect, and that the reduction of macrophytes that had provided habitat for food items led to impoverished diets and more cannibalism by adult bluegills (Kettle et al. 1987).

Bioaccumulation of atrazine from freshwater is limited, and food chain biomagnification is negligible (Cossarini-Dunier et al. 1988; Du Preez and van Vuren 1992). Rainbow trout fed diets containing 100 mg atrazine/kg of ration for 84 days had no significant accumulations in tissues, although some accumulation occurred (maximum of 0.9 mg/kg lipid weight in liver) at 1000 mg/kg ration (Cossarini-Dunier et al. 1988). In a farm pond treated once with 300 µg atrazine/L, residues at 120 days posttreatment ranged between 204 and 286 µg/kg in mud and water, and from not detectable in bullfrog (*Rana catesbeiana*) tadpoles to 290 µg/kg (all fresh weights) in whole bluegills; values were intermediate in zooplankton and clams. No residues were detectable in biological components at 1 year posttreatment, when residues were <21 µg/kg in water and mud (Klaasen and Kadoum 1979). In a laboratory stream treated four times with 25 µg atrazine/L for 30 days, followed by depuration for 60 days, maximum accumulation factors ranged from about 4 in annelids to 480 in mayfly nymphs; however, residue concentrations declined to posttreatment

Table 11.4 Atrazine Effects on Selected Species of Aquatic Plants

Species, Dose, and Other Variables	Effect and Reference
PHYTOPLANKTON COMMUNITIES IN EXPERIMENTAL MICROCOOSMS	
0.5–5.0 µg/L, 39 weeks	No measurable adverse effects (Brockway et al. 1984)
1.0–5.0 µg/L, several days	Reduced photosynthesis in sensitive species (DeNoyelles et al. 1982)
>17.9 µg/L, 21 days	Decreased oxygen production, decreased content of calcium and magnesium (Pratt et al. 1988)
12 µg/L, 4 weeks	Biovolume of benthic algal communities was reduced at both dose levels when compared to controls (Carder and Hoagland 1998)
20 µg/L, 20 days	Altered species composition (DeNoyelles and Kettle 1985)
20 µg/L, 136 days	Reduced growth, altered succession; atrazine-resistant species now dominant (DeNoyelles et al. 1982)
50 µg/L, 12 days	Oxygen production decreased 20–30% (Brockway et al. 1984)
100 µg/L, 14 days	Algal densities and biomass reduced, diversity decreased, and species composition altered. Within 16 days after removal of atrazine stress, net productivity was indistinguishable from controls, but community structure remained altered at day 21 (Hamala and Kollig 1985)
100 µg/L, 20 days	Carbon uptake reduced >40% (DeNoyelles and Kettle 1985)
500 µg/L, 53 days	Immediate decline in primary productivity and community metabolism; no recovery (Stay et al. 1985)
5000 µg/L, 12 days	Death (Brockway et al. 1984)
ALGA, <i>Cyclotella meneghiniana</i>	
1.0 µg/L, 5 min	Some inhibition in oxygen evolution (Millie and Hersh 1987)
99–243 µg/L, 5 min	Oxygen evolution reduced 50% (Millie and Hersh 1987)
500 µg/L, 5 min	Oxygen evolution 100% inhibited (Millie and Hersh 1987)
WILD CELERY, <i>Vallisneria americana</i>	
1.3 µg/L, 47 days	No measurable effect (Correll and Wu 1982)
3.2 µg/L, 49 days	Some reduction in leaf area (Correll and Wu 1982)
12 µg/L, 47 days	LC50; reduced reproduction and leaf area in survivors (Correll and Wu 1982)
75 µg/L, 12–28 days	Inhibited photosynthesis (Correll and Wu 1982)
100 µg/L, 6 weeks	Growth inhibited 29% (Forney and Davis 1981)
120 µg/L, 30 days	LC100 (Correll and Wu 1982)
163 µg/L, 21–42 days	Growth inhibition of 50% (Forney 1980)
320 µg/L, 6 weeks	Growth inhibited 36% (Forney and Davis 1981)
ELODEA, <i>Elodea canadensis</i>	
3.2 µg/L, 3–4 weeks	Growth inhibited 1% (Stevenson et al. 1982)
13 µg/L, 21–42 days	Growth inhibited 50% (Forney 1980)
32 µg/L, 3–4 weeks	Growth inhibited 15–39% (Forney and Davis 1981)
100 µg/L, 3–4 weeks	Growth inhibited 53% (Forney and Davis 1981)
REDHEADGRASS, <i>Potamogeton perfoliatus</i>	
4 µg/L, 4 weeks	Photosynthesis reduced 10% (Kemp et al. 1985)
10 µg/L, 3 weeks	Growth inhibited 15% (Forney and Davis 1981)
50 µg/L, 2 h	Equilibrium reached within 15 min, maximum residues of 3.5 mg/kg dry weight (Jones et al. 1986)
55 µg/L, 4 weeks	Photosynthesis reduced 50% (Kemp et al. 1985; Larsen et al. 1986)
80 µg/L, 2 h	Photosynthesis inhibited 50% (Jones et al. 1986)
100 µg/L, 2 h	Photosynthesis inhibition and residues of about 9.0 mg/kg dry weight; recovery rapid in atrazine-free medium but some photosynthetic depression for up to 77 h (Jones et al. 1986)
100 µg/L, 4 weeks	Photosynthesis inhibition; water levels of 87 µg atrazine/L at 4 weeks; recovery in 2–3 weeks in atrazine-free medium (Kemp et al. 1985)

Table 11.4 (continued) Atrazine Effects on Selected Species of Aquatic Plants

Species, Dose, and Other Variables	Effect and Reference
130 µg/L, 4 weeks	Decreased oxygen production immediately on exposure; significant recovery within 2 weeks despite constant atrazine concentrations (Cunningham et al. 1984)
320 µg/L, 3 weeks	Growth inhibited 45–54% (Forney and Davis 1981)
450–650 µg/L, 2 h	Photosynthesis inhibited 87%; residues of about 5 mg/kg dry weight (Jones et al. 1986)
474 µg/L, 21–42 days	Growth reduced 50% (Forney 1980)
1200 µg/L, 4 weeks	Pronounced phytotoxic effects; no recovery (Cunningham et al. 1984)
EURASIAN WATERMILFOIL, <i>Myriophyllum spicatum</i>	
5 µg/L, 4 weeks	Enhanced oxygen production (Kemp et al. 1985)
11 µg/L, 4 weeks	Photosynthesis reduced 1% (Kemp et al. 1985)
50 µg/L, 4 weeks	Oxygen production depressed (Kemp et al. 1985)
117 µg/L, 4 weeks	Photosynthesis reduced 50% (Kemp et al. 1985; Larsen et al. 1986)
320 µg/L, 4 weeks	Growth inhibited 22% (Forney and Davis 1981)
1000 µg/L, 4 weeks	Growth inhibited 62% (Forney and Davis 1981)
1000 µg/L, 4 weeks	Residues <1 µg/kg (Kemp et al. 1985)
1104 µg/L, 21–42 days	Growth inhibited 50% (Forney 1980)
COMMON CORDGRASS, <i>Spartina alterniflora</i>	
10 µg/L, 3–4 weeks	Biomass reduction of 6% (Stevenson et al. 1982)
Exposed for 35 days to 30, 250, or 3000 µg atrazine/L	The high concentration significantly enhanced peroxidase activity but did not affect growth or chlorophyll production (Lytle and Lytle 1998)
100 µg/L, 3–4 weeks	Biomass reduction of 34% (Stevenson et al. 1982)
1000 µg/L, 3–4 weeks	Biomass reduction of 46% (Stevenson et al. 1982)
SHOAL GRASS, <i>Halodule wrightii</i>	
10, 40, or 120 µg/L for 22 days	Enhanced growth when compared to controls (Mitchell 1985)
420 µg/L for 22 days	Above-ground biomass reduced 26% (Mitchell 1985)
1490 µg/L for 22 days	Above-ground biomass reduced 45% compared to controls (Mitchell 1985)
MARINE ALGA, <i>Nannachloris oculata</i>	
15 µg/L, 7 days	Growth reduction (Mayasich et al. 1987)
50 µg/L, 72 h	Some growth inhibition; inhibition greatest under conditions of elevated temperature and illumination (Karlander et al. 1983)
ALGA AND MACROPHYTES (various species)	
20 µg/L, 6 weeks	Bioconcentration factors up to 32 (Huckins et al. 1986)
21–132 µg/L, 14 days	50% reduction in growth rate of 4 species of freshwater macrophytes (Fairchild et al. 1998)
SUBMERGED AQUATIC MACROPHYTES	
4 species: <i>Potamogeton</i> sp., <i>Ruppia</i> sp., <i>Myriophyllum</i> sp., <i>Zannichellia</i> sp.	
20 µg/L, 2 h	Photosynthesis inhibition of about 1% (Jones and Winchell 1984)
95 µg/L, 2 h	Photosynthesis inhibition 50%; atrazine significantly more effective than deethylated atrazine, deisopropylated atrazine, and hydroxyatrazine, in that order, in effecting inhibition (Jones and Winchell 1984)
ALGAE (various species)	
22 µg/L, 7 days	No effect on photosynthesis rate, chlorophyll content, or cell numbers (Plumley and Davis 1980)
37–308 µg/L, 24 h	Carbon uptake reduced 50% (Larsen et al. 1986)

Table 11.4 (continued) Atrazine Effects on Selected Species of Aquatic Plants

Species, Dose, and Other Variables	Effect and Reference
60–100 µg/L, 72 h	Growth inhibited 50% in 7 species (Mayer 1987)
60–460 µg/L, 1 h	Oxygen evolution inhibited 50% in 18 species (Hollister and Walsh 1973)
77–102 µg/L, 24 h	Photosynthesis reduction of 50% (Larsen et al. 1986)
90–176 µg/L, 96 h	50% inhibition in chlorophyll fluorescence for 5 species of freshwater algae (Fairchild et al. 1998)
80–907 µg/L, 3 weeks	Growth inhibited 50% (Larsen et al. 1986)
100 µg/L, 2 h	Growth inhibited 50% in 3 species (Mayer 1987)
100 µg/L, 3 days	Reduced productivity; complete recovery by day 7 (Moorehead and Kosinski 1986)
100–300 µg/L, 10 days	Growth inhibited 50% in 4 species (Mayer 1987)
100–460 µg/L, 72 h	Growth inhibited 50% in 8 species (Mayer 1987)
220 µg/L, 7 days	Reduced photosynthesis; no effect on chlorophyll production and cell division rate in 3 estuarine species (Plumley and Davis 1980)
ESTUARINE MARSH PLANT, <i>Juncus roemerianus</i>	
Exposed for 35 days to 30, 250, or 3000 µg atrazine/L	A dose-dependent response was evident in increased lipid peroxidation products, and inhibited chlorophyll production (Lytle and Lytle 1998)
ALGAE, <i>Chlorella</i> spp.	
54 µg/L, 10 days	Growth reduction of 30% (Gonzalez-Murua et al. 1985)
200 µg/L, 48 h	Photosynthesis reduced 30%, but no effect on growth (Lay et al. 1984)
250 µg/L, 7 days	Growth reduction; 90% of atrazine passively accumulated within 1 h (Veber et al. 1981)
SUBMERSED VASCULAR PLANT, <i>Zannichellia palustris</i>	
75 µg/L, 21–42 days	Photosynthesis inhibition (Correll and Wu 1982)
SUBMERSED VASCULAR PLANT, <i>Potamogeton pectinatus</i>	
75 µg/L, 21–42 days	Photosynthesis stimulation (Correll and Wu 1982)
650 µg/L, 21–42 days	Photosynthesis inhibition (Correll and Wu 1982)
SUBMERSED VASCULAR PLANT, <i>Zostera marina</i>	
75 µg/L, 21–42 days	Photosynthesis stimulation (Correll and Wu 1982)
650 µg/L, 21–42 days	Photosynthesis inhibition (Correll and Wu 1982)
PERIPHYTON COMMUNITIES IN FRESHWATER ENCLOSURES	
80–1560 µg/L, 10 months	Declines in net production, cell numbers, biomass, number of taxa, and chlorophyll activity; larger algal species (<i>Mougeotia</i> , <i>Oedogonium</i> , <i>Tolyphothrix</i> , <i>Epithemia</i>) were the most sensitive. At higher concentrations, population shifted from a chlorophyte-dominated to a diatom-dominated community (Hamilton et al. 1987)
100 µg/L, 2 treatments, 6 weeks apart	After initial application, all blue-green algae disappeared and organic matter significantly decreased. Within 3 weeks of second treatment, a 36–67% reduction in organic matter, chlorophyll, algal biomass, and rate of carbon assimilation was measured. Some species of green algae decreased in abundance, but others increased (Herman et al. 1986)
DUCKWEED, <i>Lemna</i> sp.	
92 µg/L, 96 h	50% reduction in frond count (Fairchild et al. 1998)
250 µg/L, 15 days	Ultrastructural changes on chloroplasts of mesophyll cells; no effect on chlorophyll and lipid distribution (Beaumont et al. 1980; Grenier et al. 1987)

levels within a few days after depuration began. Maximum atrazine concentrations recorded, in mg/kg whole organism fresh weight, were 0.2 in the clam *Strophitus rugosus*, 0.4 in the snail *Physa* sp., 0.9 in crayfish *Orconectes* sp., 2.4 in the mottled sculpin *Cottus bairdi*, 3.0 in the amphipod *Gammarus pseudolimnaeus*, and 3.4 in mayflies *Baetis* sp. (Lynch et al. 1982). In studies with the freshwater snail *Ancylus fluviatilis* and fry of the whitefish *Coregonas fera*, atrazine was rapidly accumulated from the medium by both species and saturation was reached within 12 to 24 h; bioconcentration factors were 4 to 5 at ambient water concentrations of 50 to 250 µg atrazine/L (Gunkel and Streit 1980; Gunkel 1981). Elimination of atrazine was rapid: 8 to 62 min for *C. fera*, and 18 min for *A. fluviatilis*. No accumulation of atrazine was recorded in molluscs, leeches, cladocerans, or fish when contamination was by way of the diet (Gunkel and Streit 1980; Gunkel 1981). Atrazine accumulations in *Daphnia pulicaria* were significantly correlated with whole-body protein content at low (8°C) water temperatures, and with fat content at elevated (20°C) water temperatures (Heisig-Gunkel and Gunkel 1982).

Atrazine is rapidly degraded in boxcrabs (*Sesarma cinereum*) feeding on smooth cordgrass (*Spartina alterniflora*) grown in radiolabeled atrazine solution. After 10 days, only 1.2% of the total radioactivity in the crab was unchanged atrazine, compared to 24% in the food source. The accumulation of water-soluble atrazine metabolites (86% of total radioactivity) in *Sesarma* suggested that glutathione conjugation, or a comparable pathway, was responsible for the almost complete degradation and detoxification of atrazine in crabs (Davis et al. 1979; Pillai et al. 1979). Atrazine does not appear to be a serious threat to crabs in Chesapeake Bay, where water concentrations of 2.5 µg/L have been recorded, although it could have an indirect effect on crabs by decreasing the algae population, which composes a portion of their diet (Plumley et al. 1980).

Table 11.5 Lethal and Sublethal Effects of Atrazine on Selected Species of Aquatic Animals
(Concentrations listed are in micrograms of atrazine per liter of medium.)

Ecosystem, Organism, and Other Variables	Concentration (g/L)	Effect	Reference ^a
FRESHWATER INVERTEBRATES			
Freshwater shrimp, <i>Paratya australiensis</i>	10–50	MATC ^b	15
Midge, <i>Chironomus riparius</i>			
Adults	20	Whole-body residue of 160 µg/kg in 6 weeks	1
Larvae	20	Whole-body residue of 569 µg/kg in 6 weeks	1
Cladoceran, <i>Daphnia magna</i>	20	After 6 weeks, whole-body residue of 300 µg/kg	1
<i>D. magna</i>	200	Exposure for six generations. Number of young per female in 21 days did not differ from controls in generations 1, 2, and 3, but significant reduction measured in generations 4, 5, and 6	2
<i>D. magna</i>	6900	LC50 (48 h)	3
Scud, <i>Gammarus fasciatus</i>	60–140	MATC ^b	3
<i>G. fasciatus</i>	>2400	Some deaths in 48 h	3
<i>G. fasciatus</i>	5700	LC50 (48 h)	3
Midge, <i>Chironomus tentans</i>	110–230	MATC ^b	3
<i>C. tentans</i>	500	Some deaths in 48 h	3
<i>C. tentans</i>	720	LC50 (48 h)	3
Leeches, 2 species (<i>Glossiphonia complanata</i> , <i>Helobdella stagnalis</i>)	<1000	Adverse effects on growth, food intake, and egg production	11
Leeches, 2 spp.	6300–9900	LC50 (28 days)	11
Leeches, 2 spp.	16,000	No deaths in 96 h	11

Table 11.5 (continued) Lethal and Sublethal Effects of Atrazine on Selected Species of Aquatic Animals
 (Concentrations listed are in micrograms of atrazine per liter of medium.)

Ecosystem, Organism, and Other Variables	Concentration (g/L)	Effect	Reference ^a
FRESHWATER VERTEBRATES			
Goldfish, <i>Carassius auratus</i>	0.5, 5, or 50	After 24 h, accelerated swimming performance at 0.5 µg/L; reduced grouping behavior and increased surfacing activity at 5.0 and 50 µg/L	27
<i>C. auratus</i>	100, 1000 or 10,000	After 10 min, all concentrations had a significant increase in burst swimming reactions	27
Rainbow trout, <i>Oncorhynchus mykiss</i>	5–40	Lowest observed effective concentrations for producing adverse effects on gills and kidneys (5 µg/L), liver and heart (10 µg/L), enzyme activities and other tissues (20–40 µg/L)	24
<i>O. mykiss</i>	5–80	Juveniles exposed for 28 days had alterations of renal corpuscles and renal tubules at 5, 10, 20, or 40 µg/L exposures; necrosis of endothelial cells and renal hematopoietic tissue were prominent at 80 µg/L	17
<i>O. mykiss</i>	10	After 14 days, no adverse effects on survival, growth, or liver xenobiotic metabolizing activities	16
<i>O. mykiss</i>	50	Plasma protein decreased after 10 days	15
<i>O. mykiss</i>	340	No deaths; decreased growth; increased plasma glucose	15
<i>O. mykiss</i>	1400–2800	After 96 h, reduced motility, balance disturbances, darkening of the body surface; kidney histopathology	17
<i>O. mykiss</i>	2000	Predicted no adverse effect on survival after 30 days for fingerlings	26
<i>O. mykiss</i>	4500–24,000	LC50 (96 h)	4, 6, 26
Cricket frog, <i>Acris crepitans</i>	30–600	Tadpoles exposed through metamorphosis had normal growth and normal time to reach metamorphosis	18
Wood frog, <i>Rana sylvatica</i>	30–600	Tadpoles exposed through metamorphosis developed normally	18
Brook trout, <i>Salvelinus fontinalis</i>	60–120	MATC ^b	3
<i>S. fontinalis</i>	450	Reduced incubation time of developing embryos	3
<i>S. fontinalis</i>	740	After 44 weeks, concentration in muscle <0.2 mg/kg fresh weight	3
<i>S. fontinalis</i>	6300 (4100–9700)	LC50 (8 days)	3
Freshwater fishes, various species	60–2130	No deaths in 96 h	25
	8800–76,000	LC50 (96 h) range	25
Bluegill, <i>Lepomis macrochirus</i>	90–500	MATC ^b	3, 13
<i>L. macrochirus</i>	94	After 78 weeks, concentration in muscle <0.2 mg/kg fresh weight	3
<i>L. macrochirus</i>	500	At 28 days, fish were lethargic, ate poorly, and swam erratically	3
<i>L. macrochirus</i>	6700	LC50 (7 days)	3
<i>L. macrochirus</i>	8000–42,000	LC50 (96 h)	3–6
<i>L. macrochirus</i>	46,000	LC50 (24 h)	6
Fathead minnow, <i>Pimephales promelas</i>	210	After 43 weeks, concentration in eviscerated carcass was <1.7 mg/kg fresh weight	3
<i>P. promelas</i>	210–520	MATC ^b	3, 13
<i>P. promelas</i> fry	520	LC25 (96 hours)	3
<i>P. promelas</i>	15,000 (11,000–20,000)	LC50 (8 days)	3

Table 11.5 (continued) Lethal and Sublethal Effects of Atrazine on Selected Species of Aquatic Animals
 (Concentrations listed are in micrograms of atrazine per liter of medium.)

Ecosystem, Organism, and Other Variables	Concentration (g/L)	Effect	Reference ^a
Zebrafish, <i>Brachydanio rerio</i>	Exposed for 5 weeks to 5, 25, 125, 625, or 3125 µg/L under conditions of light and dark habitat preferences	After 1 week, all atrazine-treated fish significantly avoided light habitats when compared to controls; this became more pronounced after 5 weeks of exposure	25
<i>B. rerio</i>	300–1300	MATC ^b	14
<i>B. rerio</i>	1300	LC50 (96 h), embryos	14
<i>B. rerio</i>	37,000	LC50 (96 h), adults	14
Banded tilapia, <i>Tilapia sparrmanii</i>	310–6700	Sublethal effects after 72 h include decreased activity, color changes, "coughing," and maximum blood atrazine concentrations of about 3 mg/L	20
<i>T. sparrmanii</i>	320–6700	Maximum bioconcentration factors after 72 h ranged between 5.1 for muscle (7.7 mg/kg FW) and 20.0 for ovaries (50.6 mg/kg FW)	21
<i>T. sparrmanii</i>	8100	No deaths in 72 h. Oxygen consumption decreased in first 3 h of exposure	22
Northern leopard frog, <i>Rana pipiens</i>	650	Predicted no adverse effect on survival for late-stage larvae after 30 days	26
<i>R. pipiens</i>	5100	As above for early-stage larvae	26
<i>R. pipiens</i>	14,500	LC50 (96 h) for late-stage larvae	26
<i>R. pipiens</i>	47,600	LC50 (96 h) for early-stage larvae	26
American toad, <i>Bufo americanus</i>	690	Predicted no effect on survival of late-stage larvae after exposure for 30 days	26
<i>B. americanus</i>	1900	As above for early-stage larvae	26
<i>B. americanus</i>	10,700	LC50 (96 h) for late-stage larvae	26
<i>B. americanus</i>	26,500	LC50 (96 h) for early-stage larvae	26
Mozambique tilapia, <i>Tilapia mossambicus</i>	1100	No deaths in 90 days. Increased growth and body water content; disrupted serum electrolytes	23
<i>T. mossambicus</i>	8800	LC50 (96 h)	23
Common carp, <i>Cyprinus carpio</i>	1500–6000	After 14 days, gill and liver histopathology and disrupted alkaline phosphatase activity in serum, heart, liver, and kidneys	19
<i>C. carpio</i>	18,800	LC50 (96 h), juveniles weighing 4.3 g	19
Channel catfish, <i>Ictalurus punctatus</i> , fingerlings	4300	Predicted no adverse effect on survival after exposure for 30 days	26
<i>I. punctatus</i>	23,800	LC50 (96 h)	26

MARINE INVERTEBRATES

Mysid shrimp, <i>Mysidopsis bahia</i>	80–190	MATC ^b	7
<i>M. bahia</i>	1000 (650–3100)	LC50 (96 h)	7
Copepod, <i>Acartia tonsa</i>	94 (52–167)	LC50 (96 h)	7
Copepod, <i>Eurytemora affinis</i>	500	LC50 (96 h) at 0.5% salinity	12
<i>E. affinis</i>	2600	LC50 (96 h) at 1.5% salinity	12
<i>E. affinis</i>	13,200	LC50 (96 h) at 2.5% salinity	12
Brown shrimp, <i>Penaeus aztecus</i>	1000	50% immobilized in 48 h	8
American oyster, <i>Crassostrea virginica</i>	1000	No effect on survival or growth	9
<i>C. virginica</i>	>1000	Growth reduced 50% in 96 h	8
<i>C. virginica</i>	>30,000	No effect on development in 48 h	7
"Shrimp"	1000	LC30 (96 h)	9

Table 11.5 (continued) Lethal and Sublethal Effects of Atrazine on Selected Species of Aquatic Animals
 (Concentrations listed are in micrograms of atrazine per liter of medium.)

Ecosystem, Organism, and Other Variables	Concentration (g/L)	Effect	Reference ^a
Pink shrimp, <i>Penaeus duorarum</i>	6900	LC50 (96 h)	7
Grass shrimp, <i>Palaemonetes pugio</i>	9000	LC50 (96 h)	7
Fiddler crab, <i>Uca pugilator</i>	>29,000	LC50 (96 h)	7
Fiddler crab, <i>Uca pugnax</i>	100,000	Interfered with escape response when exposed in August; negligible effects in November; young males most sensitive	10
<i>U. pugnax</i>	1–10 × 10 ⁶	Reduced survival after 10 weeks	10
Mud crab, <i>Neopanope texana</i>	750,000	No deaths in 96 h	9
<i>N. texana</i>	1 × 10 ⁶	LC50 (96 h)	9
MARINE FISHES			
Sheepshead minnow, <i>Cyprinodon variegatus</i>	1900–3400	MATC ^b	7
<i>C. variegatus</i>	2000–2300	LC50 (96 h) at 1.5–2.5% salinity	12
<i>C. variegatus</i>	16,200	LC50 (96 h) at 0.5% salinity	12
Spot, <i>Leiostomus xanthurus</i>	8500	LC50 (96 h)	7

^a 1, Huckins et al. 1986; 2, Kaushik et al. 1985; 3, Macek et al. 1976; 4, Beste 1983; 5, Klaasen and Kadoum 1979; 6, Mayer and Ellersiek 1986; 7, Ward and Ballantine 1985; 8, Mayer 1987; 9, Stevenson et al. 1982; 10, Plumley et al. 1980; 11, Streit and Peter 1978; 12, Hall et al. 1994; 13, DuPreez and van Vuren 1992; 14, Gorge and Nagel 1990; 15, Davies et al. 1994; 16, Egaas et al. 1993; 17, Fischer-Scherl et al. 1991; 18, Gucciardo and Farrar 1996; 19, Neskovic et al. 1993; 20, Grobler-van Heerden et al. 1991; 21, Du Preez and van Vuren 1992; 22, Grobler et al. 1989; 23, Prasad and Reddy 1994; 24, Bruggemann et al. 1995; 25, Steinberg et al. 1995; 26, Howe et al. 1998; 27, Saglio and Trijasse 1998.

^b Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

11.4.5 Birds

Atrazine is not acutely lethal to birds at realistic environmental levels; that is, oral LD50 values were >2000 mg/kg BW and dietary LC50 values were >5000 mg/kg ration (Table 11.6). Also, the probability is low for chronic effects of atrazine on wetland aquatic organisms and for biomagnification of toxic residues through waterfowl food chains (Huckins et al. 1986). However, indirect effects of atrazine on insect- and seed-eating birds have not been investigated, and this may be critical to the survival of certain species during nesting and brood-rearing. Studies are needed on the potential indirect ecosystem effects of atrazine, with special reference to seed-eating birds.

Domestic chickens (*Gallus* sp.) rapidly metabolized atrazine by way of partial N-dealkylation accompanied by hydrolysis. Dealkylation occurred mainly at the ethylamino group, resulting in intermediate degradation products (Foster and Khan 1976; Khan and Foster 1976). *In vitro* studies with bird liver homogenates also demonstrated active transformation of atrazine and its metabolites. Chicken liver homogenates released nonextractable atrazine residues that had accumulated in corn plants, present mainly as 2-chloro-mono-N-dealkylated compounds, and subsequently metabolized them to 2-hydroxy analogues (Khan and Akhtar 1983). Liver homogenates in the goose (*Anser* sp.) contained enzyme systems that metabolized atrazine by partial N-dealkylation and hydrolysis. Hydrolysis predominated and resulted in the formation of hydroxyatrazine, which does not undergo further degradation by dealkylation. But partly N-dealkylated metabolites, such as deethylatrazine and deisopropylatrazine, were further hydrolyzed to the corresponding hydroxy analogues (Foster et al. 1980).

Table 11.6 Atrazine Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effect and Reference
CHICKEN, <i>Gallus</i> sp.	
Laying hens were fed diets containing 100 mg/kg for 7 days	No visible adverse physiological effects or signs of toxicity. No effect on egg production or growth. No residues of atrazine or its metabolites detected in eggs. In excreta, however, atrazine and atrazine metabolites were detected after 24 h on treated diet and remained measurable until day 11, or after 4 days on an untreated diet (Foster and Khan 1976; Reed 1982)
Adults fed diets containing 100 mg/kg for 7 days, followed by uncontaminated diet for 7 days. Residues of atrazine and its metabolites were determined in selected tissues	Residues, in mg/kg FW, were as follows: atrazine, 38.8 in abdominal fat and 0.04 in muscle; hydroxyatrazine, 16.2 in liver, 4.3 in kidney 2.5 in oviduct, 0.7 in abdominal fat, and 0.5 in gizzard; and deethylhydroxyatrazine, 15.5 in liver, 2.3 in kidney, 0.8 to 1.8 in muscle, and 0.3 in gizzard (Khan and Foster 1976)
RING-NECKED PHEASANT, <i>Phasianus colchicus</i>	
Males, age 3 months, given 2000 mg/kg body weight (BW), administered orally	Survivors showed weakness, hyperexcitability, ataxia, and tremors; remission by day 5 posttreatment (Hudson et al. 1984)
MALLARD, <i>Anas platyrhynchos</i>	
Females, age 6 months, given 2000 mg/kg BW, administered orally	Survivors showed weakness, tremors, ataxia, and weight loss. Signs of poisoning appeared within 1 h posttreatment and persisted up to 11 days (Tucker and Crabtree 1970; Hudson et al. 1984)
19,650 mg/kg diet for 8 days	LD50 (Beste 1983)
COTURNIX, <i>Coturnix japonica</i>	
Chicks, age 7 days, given diets containing 5000 mg/kg for 5 days plus 3 days on untreated feed	One of 14 birds tested died on day 3 of feeding; no other adverse effects reported (Hill and Camardese 1986)
NORTHERN BOBWHITE, <i>Colinus virginianus</i>	
5760 mg/kg diet for 8 days	LD50 (Beste 1983)

11.4.6 Mammals

Data are lacking for atrazine's effects on mammalian wildlife, although there is a growing body of evidence on domestic and small laboratory mammals. Available data demonstrate that mammals are comparatively resistant to atrazine, and that the compound is not carcinogenic, mutagenic, or teratogenic (Reed 1982) (Table 11.7). However, there is a reported increase in the incidence of mammary gland tumors in rats given dietary equivalents of a lifetime dose of 70 mg atrazine/kg BW (Egaas et al. 1993). There have been no established cases of skin irritation resulting from experimental or commercial applications of atrazine, and no documented cases of poisoning in man (Anonymous 1963; Hull 1967). No observable ill effects were detected in cattle, dogs, horses, or rats fed diets that included 25 mg atrazine/kg food over extended periods (Beste 1983). Most members of the triazine class of herbicides, including atrazine, have low acute oral toxicities — usually >1000 mg/kg body weight (Murphy 1986) (Table 11.7). But at dosages bordering on lethality, rats showed muscular weakness, hypoactivity, drooped eyelids, labored breathing, prostration (Beste 1983), altered liver morphology and renal function (Santa Maria et al. 1986, 1987), and embryotoxicity (Peters and Cook 1973). There seems to be a causal link between tumor formation and triazine-mediated hormonal balance, suggesting the existence of a threshold value below which contact with atrazine will have no effect on tumor formation (Egaas et al. 1993).

Biomarkers of atrazine exposure is a developing field (Lu et al. 1998) that merits additional research. For example, concentrations of atrazine in saliva of rats was significantly correlated with rat free atrazine plasma concentrations. About 26% of the atrazine in rats is bound to plasma proteins (and is unavailable for transport from blood to saliva) and is independent of plasma levels of atrazine. Salivary concentrations of atrazine reflect total plasma free atrazine concentration — in the 50 to 250 µg/L range — which may be of toxicological significance (Lu et al. 1998).

Animals feeding on atrazine-treated crops are at limited toxicological risk. Crop plants metabolize atrazine to hydroxyatrazine, dealkylated analogues, and cysteine- and glutathione-conjugates of atrazine; mature plants contain little unchanged atrazine. Bound atrazine residues in plants are of limited bioavailability to animals (Bakke et al. 1972a; Khan and Akhtar 1983; Khan et al. 1985). Metabolic degradation of atrazine in mammals is usually rapid and extensive; unchanged atrazine was recovered only from the feces (Anonymous 1963). Liver enzyme systems in pigs, rats, and sheep metabolize atrazine by partial N-dealkylation and hydrolysis (Bakke et al. 1972a; Dauterman and Muecke 1974; Foster et al. 1980). However, atrazine is reportedly converted *in vivo* to N-nitrosoatrazine in mice, *Mus* sp. (Krull et al. 1980). Since N-nitrosoatrazine is carcinogenic and mutagenic to laboratory animals (Krull et al. 1980), more research is recommended on the extent of nitrosation of atrazine in the environment.

Table 11.7 Lethal and Sublethal Effects of Atrazine on Selected Species of Mammals

Organism, Dose, and Other Variables	Effect and Reference
CATTLE, COW, <i>Bos</i> spp.	
30 mg atrazine/kg diet for 21 days	Tissue residues <0.1 mg/kg fresh weight (Reed 1982)
100 mg atrazine/kg diet for 21 days	No detectable atrazine (<0.04 mg/kg) or hydroxyatrazine (<0.05 mg/kg) found in milk (Reed 1982)
DOMESTIC SHEEP, <i>Ovis aries</i>	
30 mg atrazine/kg diet for 28 days	Tissue residues <0.1 mg/kg fresh weight (Reed 1982)
100 mg atrazine/kg diet for 28 days	No adverse effects (Reed 1982)
MICE, <i>Mus</i> spp.	
46.4 mg/kg body weight (BW) given daily on days 6 through 14 of pregnancy	No effect on reproduction (Peters and Cook 1973)
82 mg/kg diet for 18 months	Negative oncogenicity results (Reed 1982)
1750–3900 mg/kg BW	Acute oral LD50 value (Anonymous 1963; Hull 1967; Reed 1982)
DOG, <i>Canis familiaris</i>	
150 mg/kg diet for 2 years, equivalent to 3.75 mg/kg BW daily	No observable effect level (Reed 1982)
1500 mg/kg diet for 2 years	No oncogenic effects; decreased body weight, reduced hemoglobin and hematocrit (Reed 1982)
LABORATORY WHITE RAT, <i>Rattus</i> spp.	
Inhalation exposure to a dust aerosol of Atrazine 80W (80% wettable powder) for 1 h to concentrations between 1.8 and 4.9 mg/L atmosphere	No deaths, or signs of toxicological or pharmacological effects (Hull 1967)
100 mg/kg diet for 2 years, equivalent to 5 mg/kg BW daily	No gross microscopic signs of toxicity (Anonymous 1963; Reed 1982; Beste 1983)
100 mg/kg diet for 3 generations, equivalent to 5 mg/kg BW daily	No teratogenic or reproductive effects (Reed 1982)
Daily oral administration on days 6–15 of gestation, in mg/kg BW	
10	No adverse maternal or fetal effects (Infurna et al. 1988)
70	Increased salivation; initial reduction in feed consumption (Infurna et al. 1988)

Table 11.7 (continued) Lethal and Sublethal Effects of Atrazine on Selected Species of Mammals

Organism, Dose, and Other Variables	Effect and Reference
700	Mortality 78% before necropsy; increased incidences of salivation, ptosis, bloody ulva, swollen abdomen, and fetal skeletal malformations (Infurna et al. 1988)
100, 200, 400, or 600 mg/kg BW daily, given orally for 14 days	All dose levels increased elimination of sodium, potassium, chloride, and urine protein; interference with creatinine clearance at 200 mg/kg BW and higher (Santa Maria et al. 1986)
100, 200, 400, or 600 mg/kg BW daily, given orally for 14 days	At 100 mg/kg, significant increases in serum lipids, serum alkaline phosphatase, and serum alanine aminotransferase; no liver histopathology. At 200 mg/kg, a significant reduction in body weight. At 400 mg/kg, liver enlargement and loss in body weight. A dose-dependent decrease in growth and in serum glucose and a dose-related increase in total serum lipids were recorded. At 600 mg/kg, liver histopathology (Santa Maria et al. 1987)
100, 300, or 900 mg/kg diet for 3 weeks	Except for lymphopenia, which was observed at all dose levels, no other effects were measured in the 100 and 300 mg/kg groups. At 900 mg/kg, significant decreases occurred in body weight, food intake, blood lymphocytes, and thymus weight, and significant increases occurred in thyroid weight, mesenteric lymph nodes, and histopathology (Vos et al. 1983)
200 mg/kg BW injected subcutaneously on days 3, 6, and 9 of gestation	No effect on number of pups per litter or on weight at weaning (Peters and Cook 1973)
800, 1000, or 2000 mg/kg BW injected subcutaneously on days 3, 6, and 9 of gestation	At 2000 mg/kg BW, most pups born dead; at 800 and 1000 mg/kg BW, litter size reduced 50–100% (Peters and Cook 1973)
1000 mg atrazine/kg diet from first day of pregnancy throughout gestation	No effect on number of pups per litter or on weight on weaning (Peters and Cook 1973)
1000 mg/kg diet for 2 years, equivalent to 50 mg/kg BW daily	No signs of oncogenicity, but reduced food intake and lower body weight (Reed 1982)
1800–5100 mg/kg BW	Acute oral LD50 (Anonymous 1963; Hull 1967; Reed 1982; Beste 1983)
WHITE RABBIT, <i>Oryctolagus cuniculus</i>	
Daily oral administration on gestational days 7 through 19, in mg/kg BW	
1	No adverse maternal or fetal affects (Infurna et al. 1988)
5	Moderate reductions in food consumption and body weight gain (Infurna et al. 1988)
75	Increased abortion rate; no death of does. Weight loss, reductions in feed consumption and fetal and embryotoxic effects, including reduced fetal weight and increased incidence in skeletal variations (Infurna et al. 1988)
9300	Acute dermal LD50 (Beste 1983)

11.5 RECOMMENDATIONS

Labels on products containing atrazine are required to contain information on acceptable uses and potential hazards to groundwater and to fish and wildlife (USEPA 1983). At present, atrazine is approved for use as an herbicide to control broadleaf and grassy weeds on corn, sorghum, sugarcane, pineapple, macadamia nuts, rangeland, turf grass sod, conifer reforestation areas, Christmas tree plantations, grass seed fields, noncrop land, guava, grass in orchards, millet, perennial ryegrass, and wheat. Because atrazine is expected to leach into groundwater, it was recommended (USEPA 1983) that labels of atrazine products bear the following statement: “Atrazine leaches readily and accepted label rates have been found to result in contamination of water supplies by way of groundwater. Therefore, users are advised to avoid use of atrazine in well-drained soils, particularly in areas having high groundwater tables.” Cautionary statements on potential hazards to living resources is another labeling requirement: “This pesticide is toxic to aquatic invertebrates.

Do not apply to water or wetlands. Runoff and drift from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes. Do not discharge into lakes, streams, ponds, or public water supplies unless in accordance with an [approved USEPA] permit." (USEPA 1983)

Permissible tolerances for atrazine range from 0.02 mg/kg in meat, milk, and eggs, to 15 mg/kg in orchard grass forage, fodder, and hay (Reed 1982; USEPA 1983). However, the 15 mg/kg tolerance in forage is considered high, and a new upper limit of 4 mg/kg is proposed. This limit would be expressed in terms of atrazine and three major metabolites (Reed 1982; USEPA 1983):

2-Amino-4-chloro-6-isopropylamino-1,3,5-triazine
2-Amino-4-chloro-6-ethylamino-1,3,5-triazine
2-Chloro-4,6-diamino-1,3,5-triazine

The maximum recommended safe level of atrazine to algal diatoms is 10 µg/L (Karlander et al. 1983), although temporary inhibition of chlorophyll production in sensitive algal species has been reported in the range of 1 to 5 µg/L (Torres and O'Flaherty 1976). Proposed atrazine concentrations for aquatic life protection range from about 1 to 11 µg/L: 1 to 2 µg/L for protection of estuarine productivity (Stevenson et al. 1982; Ward and Ballantine 1985); 1 to 7 µg/L for no adverse effect levels to most species of submerged aquatic vegetation (Glotfelty et al. 1984); less than 5 µg/L to prevent gill and kidney histopathology in rainbow trout and disrupted swimming behavior in zebrafish (Steinberg et al. 1995) and goldfish (Saglio and Trijasse 1998); 5 to 10 µg/L for minor reductions in photosynthesis in sensitive species of aquatic macrophytes (Glotfelty et al. 1984); 9 µg/L for sensitive aquatic invertebrates, as judged by an uncertainty factor of 10 applied to a 96-hour LC₅₀ (Ward and Ballantine 1985); and 11 µg/L for salt marsh algae, based on the least effect level of 110 µg/L, and an uncertainty factor of 10 (Plumley and Davis 1980). Atrazine concentrations >11 µg/L sometimes occur during periods of runoff and non-flushing (Stevenson et al. 1982), but rarely persist at levels necessary to markedly inhibit photosynthesis in aquatic plants (i.e., 60 to 70 µg/L) (Glotfelty et al. 1984). At 80 µg/L, rainbow trout show kidney necrosis of endothelial cells after exposure for 28 days (Fischer-Scherl et al. 1991), and this suggests that atrazine criteria that protect sensitive plants will also protect aquatic vertebrates.

In laboratory animals, atrazine is only slightly toxic on an acute basis. No carcinogenic, mutagenic, or reproductive effects have been seen at low doses, and reduced food intake and body weight were the primary adverse effects seen at high doses in chronic studies with rats and dogs (Reed 1982). However, data are lacking on indirect ecosystem effects of atrazine application on terrestrial wildlife — especially on insectivores and granivores. Studies should be initiated in this subject area.

No allowable daily intake of atrazine in the human diet has been established, although 0.0375 mg/kg body weight daily has been proposed — equivalent to 2.25 mg daily for a 60-kg adult, or 1.5 mg/kg diet based on 1.5 kg food daily (Reed 1982). In humans, the theoretical maximum residue contribution (TRMC) — a worst-case estimate of dietary exposure — is 0.77 mg daily, assuming 1.5 kg of food eaten daily; this is equivalent to 0.51 mg/kg diet, or 0.013 mg/kg body weight daily for a 60-kg person (USEPA 1983). Another TRMC calculation is based on 0.233 mg daily per 1.5 kg diet, equivalent to 0.156 mg/kg diet, or 0.0039 mg/kg body weight daily for a 60-kg person (Reed 1982). Both TRMC estimates are substantially below the proposed limit of 0.0375 mg/kg body weight daily. Lifetime exposure to drinking water concentrations of 2.3 µg atrazine/L poses negligible risk to human health, as judged by the no adverse effect level of 7.5 µg/L when 1% of the allowable daily intake is obtained from this source (USEPA 1987; Wilson et al. 1987). Higher allowable concentrations are proposed over short periods: 123 µg/L for adults and 35 µg/L for children over a 10-day period (USEPA 1987). The proposed drinking water criterion to protect human health in western Europe is <0.1 µg/L (Fischer-Scherl et al. 1991). In the United States, it should not exceed 3.0 µg atrazine/L drinking water (Alvord and Kadlec 1996; Carder and Hoagland 1998), although Ryals et al. (1998) recommend less than 3.6 µg atrazine/L.

Additional data are needed on toxicity, environmental fate, and chemistry of atrazine in order to maintain existing registrations or to permit new registrations (USEPA 1983). Specifically, data are needed on mobility and degradation rates of atrazine and its metabolites in soils; accumulation studies in rotational crops, fish, and aquatic invertebrates; and chronic testing with representative flora and fauna on survival, reproduction, carcinogenesis, teratogenesis, and mutagenesis (USEPA 1983). Animal metabolism studies are required if tolerances for residues in animal products are expressed in terms of atrazine and its metabolites (USEPA 1983). Finally, more research on aquatic species is merited on synergistic and additive effects of atrazine in combination with other agricultural chemicals at realistic environmental levels of 1 to 50 µg/L, and on the toxic effects of dealkylated atrazine metabolites (Stevenson et al. 1982).

11.6 SUMMARY

The herbicide atrazine (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine) is the most heavily used agricultural pesticide in North America. In the United States alone, more than 50 million kg (110 million pounds) are applied annually to more than 25 million ha (62 million acres), primarily to control weeds in corn and sorghum. Residues have been detected at phytotoxic concentrations in groundwater, lakes, and streams as a result of runoff from treated fields. Atrazine degrades rapidly, usually by way of hydrolysis, nitrogen dealkylation, and splitting of the triazine ring to less toxic compounds not normally inhibitory to plants and animals. The half-time persistence of atrazine in soils is usually about 4 days, but may range up to 385 days in dry, sandy, alkaline soils, under conditions of low temperature and low microbial densities. Half-time persistence is about 3 days in freshwater, 30 days in marine waters, 35 days in marine sediments, and less than 72 h in vertebrate animals.

Sensitive species of aquatic plants experience temporary, but reversible, adverse effects at concentrations in the range of 1 to 5 µg atrazine/L. However, potentially harmful phytotoxic concentrations of atrazine (i.e., >10 µg/L for extended periods) have not been documented in the environment and are probably unrealistic under current application and degradation rates. Aquatic fauna are indirectly affected at atrazine concentrations of 20 µg/L and higher, partly through reduction of the food supply of herbivores, and partly through loss of macrophyte habitat. Direct adverse effects to aquatic invertebrates and fishes were measured at 94 µg/L and higher. Bioaccumulation of atrazine is limited, and food chain biomagnification is negligible in aquatic ecosystems. Birds are comparatively resistant to atrazine, having a low probability for uptake and retention. Known acute oral LD₅₀ values for birds are >2000 mg/kg body weight, and dietary LD₅₀ values are >5000 mg/kg ration. However, indirect ecosystem effects of atrazine on seed- and insect-eating birds are unknown, and should be investigated. Data are lacking for atrazine toxicity to mammalian wildlife, but tests with domestic livestock and small laboratory animals indicate that this group is also comparatively resistant. Acute oral LD₅₀ values for mammals are >1750 mg/kg body weight. No adverse effects were measured at chronic dietary levels of 25 mg/kg (about 1.25 mg/kg body weight) and, for some species, 100 mg/kg diet.

Proposed criteria for aquatic life protection include <5 µg atrazine/L for sensitive species of aquatic flora and fauna, and <11 µg/L for most species of aquatic plants and animals. No criteria have been promulgated for human or animal health protection, although it has been suggested that <3.0 µg/L in drinking water, and <0.0375 mg atrazine/kg body weight (<2.25 mg daily for a 60-kg adult, <1.5 mg/kg diet based on consumption of 1.5 kg food daily) would pose negligible risk to human health. Additional data are needed on toxicity, environmental fate, and chemistry of atrazine and its metabolites in order to maintain existing registrations or to permit new registrations. In particular, more research is needed on possible synergistic or additive effects of atrazine with other agricultural chemicals in aquatic environments.

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CHAPTER 12

Carbofuran

12.1 INTRODUCTION

Carbofuran is a broad-spectrum systemic insecticide, acaricide, and nematicide that is widely used in forestry and in agricultural crop production of corn, alfalfa, peanuts, rice, sugarcane, tobacco, potatoes, strawberries, onions, mixed vegetables, mustard, carrots, sunflowers, turnips, and many other crops (Anonymous 1971; Dorrough 1973; Palmer and Schlinke 1973; Kuhr and Dorrough 1976; U.S. Environmental Protection Agency [USEPA] 1976; Finlayson et al. 1979; Flickinger et al. 1980; Hayes and Laws 1991; Trotter et al. 1991; Ballantyne and Marrs 1992). Carbofuran, together with other carbamate compounds, organophosphorus insecticides, and pyrethroids, are the major substitutes for the more persistent pesticides such as DDT, chlordane, and heptachlor. In 1974, domestic carbofuran use was slightly over 3.2 million kg (7 million pounds) active ingredients, most of which was applied to control corn pests (USEPA 1976). By 1989, annual use was about 4.5 million kg, mostly in granular formulations (USEPA 1989a). As a group, the carbamates, including carbofuran, have controlled insects effectively; their residual life in the environment is relatively short. Excretion from the animal body is comparatively rapid and almost quantitative, and the terminal residues produced are polar and formed by chemical processes normally considered as steps in metabolic detoxication.

Flowable and granular formulations of carbofuran have histories of heavy wildlife losses associated with recommended rates of application as well as misuse (Flickinger et al. 1986). At recommended application rates, which ranged from 0.28 to 10.9 kg active ingredients/ha (0.25 to 9.7 lb/acre), and in a variety of formulations, carbofuran was responsible for sporadic kills of fish, wildlife, beneficial insects, and terrestrial and aquatic invertebrates (Eisler 1985; USEPA 1989a; Trotter et al. 1991; Mineau 1993). In California between 1984 and 1988, carbofuran residues up to 640 mg/kg fresh weight (FW) were measured in gizzard and crop content of dead birds found near rice fields treated with granular carbofuran; secondary intoxication was noted in raptors that fed on carbofuran-poisoned ducks (Littrell 1988). A decline of 80% in populations of striped bass (*Morone saxatilis*) in California was attributed, in part, to carbofuran and other contaminants in agricultural drainwater associated with rice culture (Bailey et al. 1994). Carbofuran was implicated in the deaths of egrets and herons found dead in San Joaquin County, California, in 1991 near an area treated a few days earlier to control grape phylloxera. Brain cholinesterase activity in birds was inhibited, and food items (crayfish) in crop contained 0.6 mg carbofuran/kg FW (Hunt et al. 1995). Aerial spraying of carbofuran to control grasshoppers killed California gulls (*Larus californicus*). In a carbofuran-sprayed field, gulls were found convulsing with their gullets packed with grasshoppers containing 4 to 7 mg carbofuran/kg (Leighton et al. 1987). Among birds that only occasionally consume domestic crops, carbofuran applied to vegetables reportedly killed about 1400 ducks, largely green-winged teal (*Anas carolinensis*), pintail (*A. acuta*), and American widgeon (*A. americana*) in British Columbia between 1973 and 1975 (Flickinger et al. 1980). Carbofuran

applied to alfalfa killed 2450 American widgeons at one California location in 1974 (Stickel 1975), 500 Canada geese (*Branta canadensis*) in southern Oklahoma in 1976, 1000 widgeons in Kansas in 1976, and more than 1063 widgeons in California in 1976/1977 (Flickinger et al. 1980). Secondary poisoning of red-shouldered hawks (*Buteo lineatus*) was reported after the application of carbofuran to Maryland cornfields (Balcomb 1983). Carbofuran-contaminated sand (7 g carbofuran and metabolites/kg dry weight sand) is associated with the death of Pacific Island seabirds, crabs, and insects which come into contact with the sand (David et al. 1999). Secondary poisoning was also documented in northern harriers (*Circus cyaneus*) feeding on a dead eastern cottontail rabbit (*Sylvilagus floridanus*) (Mineau 1993). Aerial application to flooded rice fields in various portions of Texas between 1970 and 1975 at the rate of 0.56 kg/ha resulted in deaths of three species of sandpipers (*Erolia* spp.) and red-winged blackbirds (*Agelaius phoeniceus*), as well as frogs, crayfish, leeches, earthworms, and four species of fish. However, no carbofuran residues were detectable among survivors 2 to 11 days postexposure (Flickinger et al. 1980). Carbofuran was responsible for the deaths of American crows (*Corvus brachyrhynchos*), a red-tailed hawk (*Buteo jamaicensis*), and European starlings (*Sturnus vulgaris*) in a Pennsylvania cornfield in 1986; an intentional poisoning of starlings by a farmer is the most probable explanation of the high carbofuran residues (67 to 425 mg/kg) found in stomach contents (Stone and Gradoni 1986). Application of granular carbofuran to Virginia cornfields in 1991 was accompanied by deaths from anticholinesterase poisoning of mammals, birds, and reptiles. Carbofuran residues were found in the upper gastrointestinal tract of 81% of the birds examined (Stinson et al. 1994). Many die-offs of adult waterfowl wintering in the southern United States have been attributed to carbofuran use (Martin and Forsyth 1993). Granular formulations of carbofuran were especially toxic to birds, and their sale and use was prohibited after September 1, 1994, except for some minor uses (USEPA 1989a, 1991).

12.2 CHEMICAL PROPERTIES AND PERSISTENCE

Carbofuran (2,3-dihydro-2,2-dimethyl-1,7-benzofuranyl methylcarbamate) is also known as Furadan, Bay 70142, Brifur, Crisfuran, Cristofuran, CAS 1563-66-2, Curaterr, D-1221, ENT-27164, FMC 10242, Niagara NIA-10242, OMS 864, Pillarfuran, and Yaltox (Leuck et al. 1968; Johnson and Finley 1980; Hayes and Laws 1991). Carbofuran has a molecular weight of 221.25 and a melting point of 150 to 152°C. It is comparatively stable under neutral or acidic conditions, but degrades rapidly in alkaline media (Anonymous 1971; Trotter et al. 1991). This white, crystalline solid of empirical formula $C_{12}H_{15}NO_3$ (Figure 12.1) is soluble at concentrations up to 700 mg/L in water, but at <30 mg/L in various organic solvents. It degrades at >130°C and supports combustion if ignited (FMC 1979). The compound is available as a wettable powder, a granular formulation, and in solution as a flowable formulation (Anonymous 1971; USEPA 1976; Trotter et al. 1991).

Pharmacologically, carbofuran inhibits cholinesterase, resulting in stimulation of the central, parasympathetic, and somatic motor systems. Sensitive biochemical tests have been developed to measure cholinesterase inhibition in avian and mammalian brain and plasma samples and are useful in the forensic assessment of carbamate exposure in human and wildlife pesticide incidents (Ballantyne and Marrs; Hunt and Hooper 1993). Acute toxic clinical effects resulting from carbofuran exposure in animals and humans appear to be completely reversible and have been successfully treated with atropine sulfate. However, treatment should occur as soon as possible after exposure because acute carbofuran toxicosis can be fatal; younger age groups of various species are more susceptible than adults (Finlayson et al. 1979). Carbofuran labels indicate that application is forbidden to streams, lakes, or ponds. In addition, manufacturers have stated that carbofuran is poisonous if swallowed, inhaled, or absorbed through the skin. Users are cautioned not to breathe carbofuran dust, fumes, or spray mist; and treated areas should be avoided for at least 2 days (Anonymous 1971). Three points are emphasized at this juncture. First, some carbofuran degradation

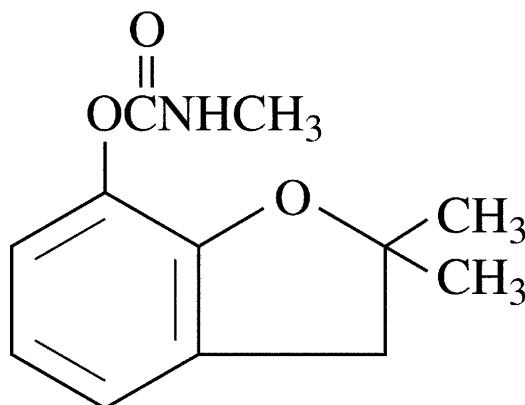


Figure 12.1 Structural formula for carbofuran (2,3-dihydro-2,2-dimethyl-1,7-benzofuranyl methylcarbamate).

products have not been identified. Second, toxicologic, mutagenic, carcinogenic, and teratogenic properties of most carbofuran degradation products have not been satisfactorily evaluated. And third, numerous physical, chemical, and biological vectors modify carbofuran degradation processes, as well as biological uptake, retention, and translocation. Each of these points is developed in greater detail later.

Carbofuran is metabolized by hydroxylation and hydrolysis in plants, insects, and mammals (Metcalf et al. 1968). The primary transformation product in most plants appears to be 3-hydroxy-carbofuran. However, levels of 3-hydroxycarbofuran and other degradation products in plants are influenced by numerous factors, including plant age, soil type, pesticide formulation, application method and rate, and weather conditions, as shown later. Oxidation of unconjugated 3-hydroxy-carbofuran yields 3-ketocarbofuran, which is, in turn, rapidly hydrolyzed to the much less toxic 3-ketocarbofuran phenol. Accordingly, 3-ketocarbofuran is not likely to be detected as a terminal residue in plants above trace levels. Residue analyses indicated that carbofuran and 3-hydroxycarbofuran are the compounds that occur most often in plant tissues after treatment (Finlayson et al. 1979). In measurements of carbofuran and its degradation products in corn at 117 and 149 days after carbofuran application (Table 12.1), the decrease of 62% in the total carbamate residues detected between silage and harvest was attributed to cessation of root uptake, volatilization from

Table 12.1 Carbofuran and Its Degradation Products (mg/kg dry weight) in Corn (*Zea mays*) at Silage Stage (117 days) and at Harvest (149 days) Following Application of Carbofuran (10%) Granules at 5.41 kg/ha

Plant Stage and Part	Carbamates			
	Carbofuran	3-Ketocarbofuran	3-Hydroxycarbofuran	Total Carbamates
SILAGE				
Leaves	0.43	0.40	4.67	5.50
Stalks	0.24	0.00	0.04	0.28
Cobs	0.04	<0.02	<0.02	0.05
Kernels	0.00	<0.01	0.00	<0.01
HARVEST				
Leaves	0.21	0.34	1.51	2.06
Stalks	0.03	0.00	0.05	0.08
Cobs	0.06	0.00	0.00	0.06
Kernels	<0.01	<0.01	0.00	<0.01

Modified from Turner, B.C. and J.H. Caro. 1973. Uptake and distribution of carbofuran and its metabolites in field-grown corn plants. *Jour. Environ. Qual.* 2:245-247.

drying plant surfaces, and further degradation to phenolic compounds. No losses of carbofuran or 3-hydroxycarbofuran were detected in fortified corn silage after storage at -18°C for 1 year (Finlayson et al. 1979).

Granular carbofuran is believed to persist for at least several months in the Fraser Delta of British Columbia under conditions of high humidity and low pH, and to kill waterfowl and cause secondary poisoning of raptors. During the winter of 1990 in British Columbia, bald eagles (*Haliaeetus leucocephalus*) and red-tailed hawks (*Buteo jamaicensis*) found dead or moribund had evidence of anticholinesterase exposure and crop contents that contained as much as 200 mg carbofuran/kg (Elliott et al. 1996). Bald eagles, red-tailed hawks, and coyotes (*Canis latrans*) found dead in a field in Kansas in December 1992 were poisoned by flowable carbofuran placed on sheep (*Ovis aries*) carcasses in October 1992 to kill coyotes. Flowable carbofuran can cause direct and secondary deaths of wildlife under some circumstances for at least 60 days. In this case, cold, dry weather and snow cover contributed to carbofuran preservation on the carcass (Allen et al. 1996).

Carbofuran residues of 10.8 to 13.3 mg/kg in vegetation usually declined by 50% in 24 h (Forsythe and Westcott 1994). Variation in content of carbofuran and its degradation products was evident among crop species (Finlayson et al. 1979). Strawberries (*Fragaria vesca*), for example, contained higher residues of phenol than either carbamate or hydroxy products. Carbofuran can persist in Mugho pine needles for at least 2 years at insecticidally active concentrations. This unequal distribution of carbofuran in different parts of a plant has also been observed for tobacco (*Nicotiana tabacum*), in which more of the compound was in large leaves than in the tops of plants, suggesting that carbofuran moved in the plant fluids to the point of greatest transpiration in the leaves (Finlayson 1979).

Carbofuran in animals may also be hydrolyzed to produce carbofuran-7-phenol. Hydrolysis of the 3-hydroxyderivative leads to formation of 3-hydrocarbofuran-7-phenol. Other degradation products include *N*-hydroxymethyl carbofuran and, as in plants, 3-hydroxy- and 3-ketoderivatives. All of these compounds may become conjugated and excreted by animals in urine and, presumably, bile (Metcalf et al. 1968; Finlayson et al. 1979). At least 10 metabolites of carbofuran are known at present; their interrelations are shown in detail by Menzie (1978).

Carbofuran accumulates in surface waters because of its relatively high water solubility and its relatively low adsorption on soils and sediments. It is stable in acid waters but is subject to increasing chemical hydrolysis as the water becomes more alkaline (Trotter et al. 1991). In water, the carbofuran degradation rate is strongly influenced by pH. The time to 50% degradation of carbofuran in water was 3.2 years at pH 4.5; 13.3 years at pH 5.0 and 6.0; 1.9 months at pH 7.0; 1 week at pH 8.0 (Chapman and Cole 1982); and only 5 h at pH 9.5 (Trotter et al. 1991). The rate of carbofuran loss is also influenced by sunlight, trace impurities, and temperature, but not as dramatically as by pH (Seiber et al. 1978; Trotter et al. 1991). Carbofuran is highly mobile and has the potential to leach into groundwater where it could persist under conditions of low temperature and low pH (USEPA 1989a, 1989b).

Persistence of carbofuran in soils is a function of many factors, including pesticide formulation, rate and method of application, soil type, pH, rainfall, temperature, moisture content, and microbial populations (Ahmad et al. 1979; Deuel et al. 1979; Finlayson et al. 1979; Fuhremann and Lichtenstein 1980; Gorder et al. 1982). Results of several studies indicate that loss from soil samples also takes place at low temperatures when air drying is used. This loss may present a problem to chemists who are unable to conduct analyses immediately after samples are collected (Finlayson et al. 1979). Soil pH is one of the more extensively documented variables affecting degradation; it may become increasingly important as acidic precipitation (acid rain) increases. Carbofuran decomposes rapidly at pH levels >7.0, but becomes increasingly stable as pH decreases. The hydrolysis half-life is about 16 years at a soil pH of 5.5; the half-lives are about 35, 6, and 0.25 days at pH levels of 7.0, 8.0, and 9.0, respectively (Finlayson et al. 1979). Similar results were reported by Getzin (1973), Caro et al. (1976), Seiber et al. (1978), and, in Table 12.2, by Chapman and Cole

Table 12.2 Effect of pH, Soil Type, and Application Rate on Carbofuran Degradation in Soils

Soil Type	pH	Initial Application Rate of Carbofuran (mg/kg)	Carbofuran Remaining after 3 Weeks (%)
ALUMINA SOILS			
Acid	5.4–6.1	1	76
Acid	5.4–6.1	20	82
Neutral	6.9–7.1	1	85
Neutral	6.9–7.1	20	79
Basic	8.3–8.5	1	55
Basic	8.3–8.5	20	72
NATURAL SOILS			
Mineral	8.0	1	95
Mineral	8.0	20	92
Mineral	6.8	1	100
Mineral	6.8	20	100
Organic	6.1	1	58
Organic	6.1	20	73
Organic	5.2	1	47
Organic	5.2	20	73
Sandy	6.6	1	8 ^a
Sandy	8.0	1	28 ^a

^a Carbofuran remaining after 8 weeks (rather than 3 weeks as indicated in boxheading).

Adapted from Chapman, R.A. and C.M. Cole. 1982. Observations on the influence of water and soil pH on the persistence of pesticides. *Jour. Environ. Sci. Health* B17:487-504.

(1982). Temperature and moisture content of soils were both positively related to degradation of carbofuran to 3-hydroxycarbofuran, 3-ketocarbofuran, carbofuran phenol, and 3-ketocarbofuran phenol. In general, an increase in temperature from 15 to 27°C had a greater influence on degradation than did an increase from 27 to 35°C, although 27 to 35°C was the range in which maximum degradation rates were observed (Ou et al. 1982). Similar results were recorded by Caro et al. (1976), Seiber et al. (1978), and Gorder et al. (1982).

The role of soil bacteria in carbofuran degradation is unclear. Most investigators agree that carbofuran is hydrolyzed to its phenol, which is immediately bound to soil constituents and then metabolized by microorganisms, either slowly (Getzin 1973; Siddaramapa et al. 1978) or rapidly, especially when associated with a *Pseudomonas* sp. isolate (Felsot et al. 1981). Others believe that carbofuran is degraded primarily by chemical hydrolysis, in which bacterial processes assume a negligible role (Venkatswarlu and Sethunathan 1978; Finlayson et al. 1979). Evidence exists demonstrating that

- Soil microbial populations increased by up to 3 times following application of carbofuran (Mathur et al. 1976, 1980)
- Prior treatment with carbofuran produced rapid degradation attributed to acclimatized soil bacteria (Felsot et al. 1981)
- Estuarine bacteria are comparatively resistant to carbofuran (Brown et al. 1975)
- Sterilized soils did not show evidence of carbofuran degradation (Felsot et al. 1981)
- Degradation to carbofuran phenol was most rapid under anaerobic conditions (Venkatswarlu and Sethunathan 1978).

It appears that additional research is required on bacterial degradation of carbofuran, with special emphasis on acid-resistant strains.

12.3 LETHAL EFFECTS

12.3.1 General

In acute toxicity tests with aquatic organisms, LC50 (96 h) values — with only one exception — exceeded 130 µg/L. The exception was the larva of a marine crab with an LC50 (96 h) value of 2.5 µg/L. In tests of longer duration with fish, safe concentrations were estimated to range between 15 and 23 µg/L. Among the most sensitive species of birds tested, the acute oral LD50 was 238 µg/kg body weight (BW), the dietary carbofuran LD50 value was 190 mg/kg ration, dermal LD50 values exceeded 100 mg/kg BW, and the LC100 value in drinking water was 2 mg/L. Mammals were comparatively resistant, having LD50 acute oral toxicities >2 mg/kg BW, a dietary LD38 of 100 mg/kg ration after 8 months, and dermal LD50 values >120 mg/kg BW. However, only 2 µg/L as an aerosol killed 50% of rhesus monkeys in 6 hours, and 40 µg/L killed all pheasants within 5 min. Bees and earthworms were relatively sensitive to carbofuran, but test conditions were sufficiently different to preclude a strict comparison with vertebrate species. Among photosynthetic species, concentrations of 200 mg/L carbofuran partly inhibited germination of rice seeds, but not other species tested, after exposure for 24 hours. Effects of carbofuran on plants are considered negligible when contrasted to faunal damage effects.

12.3.2 Aquatic Organisms

Among freshwater organisms, LC50 values for carbofuran ranged from 130 to 14,000 µg/L in tests of 72 to 96 h. Fish were the most sensitive and worms the most resistant ([Table 12.3](#)). A relatively narrow toxic range for carbofuran in the climbing perch (*Anabas testudineus*) was indicated by the LC0 (120 h) value of 560 µg/L and the LC100 (24 h) value of 1560 µg/L (Bakthavasalam and Reddy 1981). It is noteworthy that carbofuran was not as toxic to aquatic biota as were various cyclodiene chlorinated hydrocarbon insecticides, almost all of which were subsequently withdrawn from commercial use and replaced by carbofuran and other carbamates, and organophosphorus and other compounds.

In flow-through toxicity tests with the marine sheepshead minnow (*Cyprinodon variegatus*), LC50 values had stabilized by day 60 of exposure with no significant mortality afterwards. However, the LC50 value was 386 µg/L at 96 h, or 7.8 times greater than that (49 µg/L) at 131 days ([Table 12.3](#)). At concentrations up to 49 µg/L, carbofuran did not significantly affect the growth of parent fish nor the number of eggs produced. But mortality of fry from fish exposed to 23 and 49 µg/L was measurably greater than that of controls (Parrish et al. 1977). On the basis of these and other observations that indicate that growth of surviving fry in all concentrations was not affected and that carbofuran was degraded rapidly in seawater and in sheepshead minnows, it was concluded that the MATC (maximum allowable toxicant concentration) for carbofuran and sheepshead minnow lies between 15 and 23 µg/L (Parrish et al. 1977). This observation is similar to that of Caldwell (1977), who demonstrated that adult Dungeness crabs (*Cancer magister*) showed no deleterious effects on growth, survival, or reproduction during exposure to 25 µg/L of carbofuran for 69 days. Larvae of Dungeness crabs were substantially more sensitive than adults in 96-h tests ([Table 12.3](#)). In addition, Caldwell (1977) indicated that 1.5 µg/L of carbofuran inhibited swimming ability in zoeal stages of Dungeness crabs, and 1.0 µg/L inhibited molting and prevented metamorphosis to more advanced larval stages. These observations require verification because mortality in control groups was high, a typical problem in bioassays with larvae of marine invertebrates.

Table 12.3 Acute Toxicities of Carbofuran to Aquatic Organisms
 (Concentrations shown are in micrograms of carbofuran per liter of medium [g/L] fatal to 50% of test organisms in the designated time period.)

Type of Water and Species Tested	Time (h)	LC50 (g/L)	Reference ^a
FRESHWATER			
Fish, 8 species	96	88–1990	13
Yellow perch, <i>Perca flavescens</i>	96	147	1
Green sunfish, <i>Lepomis cyanellus</i>	72	160	2
Lake trout, <i>Salvelinus namaycush</i>	96	164	1
Bluegill, <i>Lepomis macrochirus</i>	96	240	1
Channel catfish, <i>Ictalurus punctatus</i>	96	248	1
Static test, tapwater	96	1420	3
Partial media replacement	96	510	3
Rice paddy water ^b			
With history	96	130	3
With no prior history	96	370	3
African catfish, <i>Mystus vittatus</i>	96	310	4
Rainbow trout, <i>Oncorhynchus mykiss</i>	96	380	1
Crayfish, <i>Procambarus acutus</i>	96	500	5
Mosquitofish, <i>Gambusia affinis</i>	72	520	6
Coho salmon, <i>Oncorhynchus kisutch</i>	96	530	1
Indian carp, <i>Saccobranchus fossilis</i>	96	547	7
Brown trout, <i>Salmo trutta</i>	96	560	1
Fathead minnow, <i>Pimephales promelas</i>	96	872	1
Goldfish, <i>Carassius auratus</i>	96	7900	12, 14
Annelid worm, <i>Limnodrilus hoffmeisterei</i>	96	11,000	8
Annelid worm, <i>Tubifex tubifex</i>	96	14,000	8
MARINE			
Dungeness crab, <i>Cancer magister</i>			
Larva	96	2.5	9
Adult	96	190	9
Sheepshead minnow, <i>Cyprinodon variegatus</i>	96	386	10
<i>C. variegatus</i>	3144	49	10
Bivalve molluscs			
Cockle, <i>Clinocardium nuttali</i>	96	3750	11
Clam, <i>Macoma nasuta</i>	96	17,000	11
Mussel, <i>Mytilus edulis</i>	96	22,000	11
Clam, <i>Rangia cuneata</i>	96	125,000	11

^a 1, Johnson and Finley 1980; 2, Brungs et al. 1978; 3, Brown et al. 1979; 4, Verma et al. 1980; 5, Cheah et al. 1980; 6, Davey et al. 1976; 7, Verma et al. 1982a; 8, Dad et al. 1982; 9, Caldwell 1977; 10, Parrish et al. 1977; 11, Zakour 1980; 12, Anton et al. 1993a; 13, Mayer and Ellersiek 1986; 14, Sanchez and Ariz 1997.

^b Rice paddy water from rice paddies with and without a history of pesticide application, as shown.

12.3.3 Birds and Mammals

Acute oral toxicities of carbofuran to birds ranged from 238 µg/kg body weight (BW) for fulvous whistling-ducks (*Dendrocygna bicolor*) to 38,900 µg/kg BW for domestic chickens (Table 12.4). The fulvous whistling-duck has been listed as endangered since 1972 by the Texas Organization for Endangered Species (Flickinger et al. 1980). Concentrations of 1 mg/L of carbofuran

in the drinking water of the ducks caused symptoms of intoxication in 7 days, and 2 mg/L was lethal in the same period (Tucker and Crabtree 1970). Acute symptoms of carbofuran poisoning in birds, which may persist for up to 7 days, include a loss in muscular coordination, wings crossed high over the back, head nodding, vocal sounds, salivation, tears, diarrhea, immobility with wings spread, labored breathing, eye pupil constriction, arching of back, and arching of neck over back. Death may occur within 5 min after ingestion (Tucker and Crabtree 1970). Birds given a fatal oral dose of carbofuran showed a depression in brain cholinesterase activity of 83 to 91% within 8 h of dosing (Wiemeyer and Sparling 1991). Among mallards (*Anas platyrhynchos*), sensitivity to carbofuran was greater in ducklings than in older birds (Table 12.4). This relation appears to hold true for other birds for which data are available.

Acute oral toxicities of carbofuran to various species of mammals ranged from 2000 µg/kg BW in mice to 34,500 µg/kg BW in rats (Table 12.4). Mammals were generally more resistant than birds to acute biocidal properties of carbofuran.

**Table 12.4 Acute Oral Toxicities of Carbofuran to Birds and Mammals
(Concentrations shown are in micrograms carbofuran
administered per kilogram body weight [g/kg] in a single dose
fatal to 50% within 14 days.)**

TAXONOMIC GROUP AND SPECIES TESTED	LD50 (g/kg BW)	REFERENCE ^a
BIRDS		
Fulvous whistling-duck, <i>Dendrocygna bicolor</i>	238	1
Mallard, <i>Anas platyrhynchos</i>		
Age 36 h	280–480	2
Age 1.5 days	400	11
Age 7 days	530–740	2, 11
Age 30 days	410–640	2, 11
Age 3–4 months	320–500	1
Age 6 months	330–520	2, 11
Red-winged blackbird, <i>Agelaius phoeniceus</i>	422	3, 11
Red-billed quelea, <i>Quelea quelea</i>	422–562	3, 11
American kestrel, <i>Falco sparverius</i>	600 (500–1000)	8
House finch, <i>Carpodacus mexicanus</i>	750	3
Japanese quail, <i>Coturnix japonica</i>	1300–2100	4, 9
House sparrow, <i>Passer domesticus</i>	1330	3, 11
Common grackle, <i>Quiscalus quiscula</i>	1300–3160	3
Rock dove, <i>Columba livia</i>	1330	3
Brown-headed cowbird, <i>Molothrus ater</i>	1330	3
Eastern screech-owl, <i>Otus asio</i>	1900 (1400–2700)	8
Ring-necked pheasant, <i>Phasianus colchicus</i>	2380–7220	1, 9, 11
Northern bobwhite, <i>Colinus virginianus</i>	3640–10,000	1, 8
European starling, <i>Sturnus vulgaris</i>	5620	3
Domestic chicken, <i>Gallus gallus</i>	25,000–38,900	5
MAMMALS		
Mouse, <i>Mus musculus</i>	2000	4, 10
Cat, <i>Felis domesticus</i>	2500–3500	5
Rat, <i>Rattus</i> sp.	3800–34,500	5, 10, 11
Old-field mouse, <i>Peromyscus polionotus</i>	4000	6
Beagle dog, <i>Canis familiaris</i>	7500–19,000	5, 10
Sheep, <i>Ovis aries</i>	8000	7
Guinea pig, <i>Cavia cobaya</i>	9200	5

^a 1, Tucker and Crabtree 1970; 2, Hudson et al. 1972; 3, Schafer et al. 1983; 4, Sherman and Ross 1969; 5, Finlayson et al. 1979; 6, Wolfe and Esher 1980; 7, Palmer et al. 1973; 8, Wiemeyer and Sparling 1991; 9, Mineau 1993; 10, Hayes and Laws 1991; 11, Hill 1992.

The ingestion of carbofuran by mallard ducklings walking through carbofuran-sprayed vegetation appears to be the critical mode of intake, with dermal absorption being minimal (Martin and Forsyth 1993). In one case, deaths were observed among mallard ducklings exposed to vegetation sprayed with 132 or 264 g carbofuran/ha; mortality was associated with depression of brain acetylcholinesterase activity by more than 53%. Treated ducklings seemed to spend a larger proportion of time than controls hidden in emergent vegetation, but this was not statistically significant at the 0.05 level (Martin and Forsyth 1993). Mallard ducklings force-fed carbofuran for 10 days at 0.85 mg/kg BW daily (but not at 0.45 mg/kg BW daily) had survival of 31% and delayed fledging in survivors (Martin et al. 1991a). Carbofuran administered to birds in the diet for 5 days, plus 3 days postexposure on an untreated diet, produced 50% kill values of 140 to 1459 mg carbofuran/kg ration. Younger birds were more sensitive than older ones (Table 12.5). Food consumption in groups of Japanese quail (*Coturnix japonica*) with high carbofuran-induced mortality was markedly depressed during the first 3 days of treatment (Hill and Camardese 1982). Red-winged blackbirds, the most sensitive bird species tested in food repellency tests, consumed a normal ration of food contaminated with carbofuran (Schafer et al. 1983). As a result, carbofuran has a high potential for causing acute poisoning episodes in birds (Schafer et al. 1983).

Secondary poisoning of avian raptors with carbofuran has been documented (Balcomb 1983; USEPA 1989a; Mineau 1993). Consider the case of a female red-shouldered hawk in adult plumage weighing 683 g, found in a cornfield near Beltsville, Maryland, in May 1981. The field had been treated the previous day with Furadan 10 granules (10% carbofuran), applied at 1.12 kg/ha active ingredients. The bird was entirely paralyzed except for some head and neck movement, salivating a brown fluid, and respiring in rapid pants. These signs are consistent with those observed in birds dosed in the laboratory with carbofuran. Stomach contents contained remains of a northern short-tailed shrew (*Blarina brevicauda*) and a common grackle (*Quiscalus quiscula*). A total of 96.6 µg carbofuran was extracted from the gastrointestinal tract and stomach contents and tissues. Judging by the body weight of the hawk and an LD₅₀ range of 0.26 to 5.6 mg/kg BW in various nondonesticated birds (Table 12.4), this amount of carbofuran would constitute between 2.5 and 59% of the known LD₅₀ values. However, carbofuran in birds is readily absorbed from the gut and widely transported in the body. Accordingly, the amount of toxicant extracted from the digestive tract was probably only a portion of that ingested by the hawk. In the same cornfield, at the same time, a smaller adult red-shouldered hawk (possibly the female's mate) was found that showed similar, but less severe, signs. Within 24 h, it appeared to have recovered completely and was released. As judged by carbofuran residues in small mammals and birds at this site, the residues present in the digestive tract of the female hawk, and the nature of the toxic symptoms observed, the two red-shouldered hawks were probably poisoned by carbofuran acquired from small vertebrate prey or scavenged from the treated areas (Balcomb 1983).

Field application of carbofuran granules to corn, at planting, in Maryland during 1980 was presumed to be responsible for deaths of songbirds (order Passeriformes) and white-footed mice (*Peromyscus leucopus*). All organisms contained high levels of carbofuran in the gastrointestinal tract and liver, suggesting extensive feeding in treated fields (Balcomb et al. 1984a). A similar situation occurred in Perry, Florida, after treatment of pine seed orchards (Overgaard et al. 1983). Laboratory studies with house sparrows (*Passer domesticus*) and red-winged blackbirds demonstrated that ingestion of a single carbofuran granule is fatal to either species (Balcomb et al. 1984a, 1984b; Mineau 1993). In groups of old-field mice (*Peromyscus polionotus*) fed diets containing 100 mg carbofuran/kg ration for 8 months, mortality was 38%. However, growth, development, and behavior were normal among survivors from this group and their offspring (Wolfe and Esher 1980). In a preliminary study with rats and old-field mice fed 100 mg carbofuran/kg ration, parents lost weight (but none died), and the survival of young was reduced (Wolfe and Esher 1980) (Table 12.5).

Table 12.5 Toxicity of Dietary Carbofuran to Birds and Mammals

Organism	Dose ^a	Exposure Interval (days exposure/ postexposure)	Mortality (%)	Reference ^b
Mallard, <i>Anas platyrhynchos</i>	190	5/3	50	1
Ring-necked pheasant, <i>Phasianus colchicus</i>	573	5/3	50	1
Japanese quail, <i>Coturnix japonica</i>				
Age 1 day	140–471	5/3	50	2
Age 7 days	436–1103	5/3	50	2
Age 14 days	586–1004	5/3	50	2
Age 21 days	779–1459	5/3	50	2
Old-field mouse, <i>Peromyscus polionotus</i>	500	4/0	100	3
Old-field mouse	250	4/0	20	3
Old-field mouse	100	240/0	38	3

^a Concentration of carbofuran in diet, in mg/kg (ppm) fresh weight ration.^b 1, Hill et al. 1975; 2, Hill and Camardese 1983; 3, Wolfe and Esher 1980.

Aerosol toxicity of carbofuran to warm-blooded animals ranged from about 2 µg/kg for rhesus monkeys to 110 µg/kg for rats (Table 12.6). These values substantially exceed the established Threshold Limit Value (TLV) of 0.05 µg/kg (50.0 µg/m³) for protection of human health (Draper et al. 1981). The TLV is a time-weighted concentration for a 40-h work week that nearly all workers can withstand without adverse effects, including eye and skin irritations and other minor irritations. Inhalation doses to humans were estimated during and immediately after aerial spraying of Furadan 4-Flowable at the rate of 446 g active ingredients carbofuran/ha, a concentration that generally controls most pests. During aerial sprayings at this level, the concentration of carbofuran in ambient air did not exceed 0.0033 µg/L at any location (Draper et al. 1981), suggesting that most birds and wildlife are afforded a high degree of protection during aerial spraying at recommended dosages. Studies with rats subjected to 1.2 µg/L of carbofuran aerosols for 50 to 70 min showed a substantial (55%) decrease in red blood cell cholinesterase 10 min posttreatment and a return to normal levels in 2 h (Ferguson et al. 1982). After 8 h, a maximum of 55% of the carbofuran was excreted by respiration (38%) or in the urine (12%) or feces (5%); the remainder was located primarily in the liver and gastrointestinal tract. Plasma half-lives in rats for carbofuran (36 min) and 3-hydroxycarbofuran (62 min) were similar to those previously determined after oral and intravenous exposures (Ferguson et al. 1982).

Table 12.6 Acute Aerosol Inhalation Toxicity of Carbofuran to Warm-Blooded Animals

Organism	Exposure Time (min)	Concentration (g/L = ppb)	Effect	Ref. ^a
Rhesus monkey, <i>Macaca</i> sp.	360	2	LC50	1
Guinea pig, <i>Cavia</i> sp.	240	10–70	LC50	1
Rat, <i>Rattus</i> sp.	50–70	26	LC50	2
Pheasant, <i>Phasianus</i> sp.	5 ^b	40	LC100	1
Guinea pig	Unknown	43–53	LC50	3
Dog, <i>Canis</i> sp.	60	50	LC50	1
Pheasant	5 ^c	80	LC100	1
Rat	60	90–100	LC50	1
Human, <i>Homo sapiens</i>	2400 ^d	0.05	^d	4

^a 1, Tucker and Crabtree 1970; 2, Hudson et al. 1972; 3, Schafer et al. 1983; 4, Sherman and Ross 1969; 5, Finlayson et al. 1979; 6, Wolfe and Esher 1980; 7, Palmer et al. 1973.^b Air delivery rate of 8 L/min.^c Air delivery rate of 10 L/min.^d Exposure = 40-hour work week; threshold limit value.

Carbofuran is not considered a chronic health hazard to humans because all existing evidence demonstrates that carbofuran is neither carcinogenic, mutagenic, or teratogenic. The database is considered acceptable and complete (USEPA 1989a). Dermal toxicity of carbofuran to birds and mammals is comparatively low. The LD50 dermal values ranged from about 1000 mg/kg BW in cattle (Palmer et al. 1981) down to 100 mg/kg BW in birds (i.e., house sparrows and queleas) (Schafer et al. 1983). Rats and rabbits were intermediate in sensitivity at 120 and 885 mg/kg BW, respectively (Draper et al. 1981). Birds contaminated by carbofuran spray could possibly ingest significant amounts while preening (Finlayson et al. 1979), but such ingestion has not been demonstrated. For humans, the maximum potential dermal exposure based on exposed face, hands, forearms, back and front of the neck, and "V" of the chest is 3.1 mg (Draper et al. 1981) or 0.04 mg/kg BW for a person weighing 70 kg. This relationship suggests that human populations would be at greater risk than wildlife populations under recommended carbofuran spray application protocols.

12.3.4 Terrestrial Invertebrates

At recommended field application rates of granular carbofuran formulations, some losses of earthworms, springtails, and other soil-inhabiting organisms should be expected. Spray and dust formulations adversely affect honeybees and other airborne crop pollinators (Finlayson et al. 1979). Bees are extremely susceptible to carbofuran. In one study with honeybees (*Apis* spp.) subjected to high levels of carbofuran, some young adults in the contaminated hive were unable to emerge from their cells, and those that did emerge remained weak and unfed. Eventually, the hive became vulnerable to invasion by the greater wax moth (*Galleria melonella*), an insect that subsequently destroyed the entire hive (Keener and Pless 1974). The LD50 dose for honeybees was estimated at 0.16 µg/bee. If 1.12 kg carbofuran/ha were uniformly distributed at a height of 10 m, flying bees could encounter a lethal dose in only 2 seconds (Atkins et al. 1976).

Studies with susceptible and selectively bred carbofuran-resistant houseflies (*Musca domestica*) indicated that LD50 values for susceptible and resistant strains were 0.1 and 1.3 µg/insect, respectively (Dorough 1973). Resistant flies contained up to 34% more cholinesterase than susceptible strains and could excrete carbofuran almost twice as fast (Dorough 1973). Carbofuran resistance among pestiferous insects is not yet widely known or adequately documented.

Among earthworms, the characteristic symptoms of carbofuran poisoning were rigidity, immobility, lesions, and segmental swelling, as well as cholinesterase inhibition (Stenerson et al. 1973). Worms maintained in soils to which commercial applications of carbofuran had been applied developed two types of lesions within 72 h: multisegmental swelling that often ulcerated, causing death of the worm, and a discrete nodular mass protruding from the surface of the worm (Sileo and Gilman 1975). The LC50 values were 0.5 mg/kg soil at 5 h for *Lumbricus herculeus* (Lebrun et al. 1981), but 2.4 and 13.0 mg/kg soil at 5 days for *Lumbricus terrestris* and *Eisenia foetida*, respectively. The differences in sensitivity were attributed to a greater excretion rate of carbofuran by *Eisenia* (Gilman and Vardanis 1974). However, mortality of *Eisenia* was 50% after 14 days in soils containing 3.1 mg carbofuran/kg DW (Anton et al. 1993b). When applications of carbofuran to soils was 9.1 kg/ha, 50% of the *Lumbricus* died in 72 h (Ruppel and Laughlin 1977). At lower application rates of 2 kg/ha, populations of two species of Australian earthworms were reduced; juvenile stages were most severely affected (Martin 1980). The loss of earthworms could result in reduced food for many wildlife species.

Field application of granular carbofuran can result in contamination of earthworms under rainy conditions (Dietrich et al. 1995). Earthworms contaminated with carbofuran may cause secondary poisoning in birds of prey, including buzzards (*Buteo buteo*), red kites (*Milvus milvus*), and black kites (*Milvus migrans*). In one case, buzzards found dead in fodder and sugar beet fields treated with granular carbofuran were poisoned by consuming dead and dying earthworms, mostly *Lumbricus*.

terrestris, from these fields. Remains of earthworms — which contained as much as 3.2 mg carbofuran/kg FW — were detected in all buzzard crop contents (Dietrich et al. 1995). A similar case is documented for American robins (*Turdus migratorius*) (Mineau 1993). Finlayson et al. (1979) have suggested that the woodcock (*Philohela minor*), a species that consumes up to 50% of its body weight (about 125 g food) daily from earthworms, may be at special risk for carbofuran poisoning. If each worm contained 1.3 mg carbofuran/kg BW, a woodcock would then ingest 0.16 mg carbofuran or the equivalent of 0.65 mg/kg BW (Finlayson et al. 1979), an oral dose lethal to many bird species. To date, secondary poisoning of woodcocks has not been verified under controlled conditions.

12.3.5 Plants

Carbofuran was more toxic to blue-green alga (*Nostoc muscorum*) at pH 5 to 6 than at pH 7.5 to 10. Toxicity was lessened under conditions of reduced illumination and low population density (Kar and Singh 1978). All effects were observed at comparatively high carbofuran concentrations of 25 to 100 mg/kg. Seeds of okra (*Abelmoschus esculentus*) treated with carbofuran, at 1, 3, or 5% active ingredient carbofuran by weight of seed, germinated normally after 90 days of storage (Gaikwad and Pawar 1979). After 6 months of storage, however, germination was measurably reduced at all carbofuran treatments. Okra plants developed normally except for a reduction in plumule length, but this effect was also observed among okra seeds tested with a wide variety of agricultural chemicals.

The effect of carbofuran on the germination of seeds of cotton (*Gossypium hirsutum*), rice, and groundnut (*Arachis hypogea*) were investigated by Arunchalam and Lakshmanan (1979). In rice seeds exposed for 24 h to 100 or 200 mg/L carbofuran, germination decreased 8 and 23%, respectively. Seeds of the other two species were not affected at these exposure rates. Treated rice seedlings that germinated grew 2 to 3 times faster than controls, especially in the roots and leaves. No reasons were offered to account for these differences in rice plants. Carbofuran residues in seeds of the three test species exposed for 24 h to 100 ppm carbofuran ranged from 17.5 to 28.1 mg/kg. At 200 mg/kg carbofuran, these values ranged from 24.0 to 30.4 mg/kg. At 72 h posttreatment, residues had declined markedly to 0.1 to 4.7 mg/kg in the groups treated with 100 mg/L carbofuran, and 2.3 to 3.8 mg/kg in the groups treated with 200 mg/L. Observed growth promotion effects in certain plants by carbofuran and some of its metabolites may be due to effects on plant oxidase systems, rather than on insecticidal or nematocidal properties of the compound. However, the source of the effects has not been demonstrated conclusively (Finlayson et al. 1979).

12.4 SUBLETHAL EFFECTS

12.4.1 General

Most investigators agree that carbofuran degrades or is biotransformed rapidly, with negligible accumulations in biota. Numerous studies have demonstrated that carbofuran, at high sublethal concentrations, was capable of disrupting enzyme and lipid metabolism but that effects were reversible with no observable permanent damage. Three major data gaps appear still to exist. First, latent biochemical and physiological effects that appear at substantial intervals posttreatment have not been explained. Second, interaction of carbofuran with other environmental compounds, especially other agricultural chemicals, are largely unknown, and the effects may cause more than additive damage. Third, and most important, data are scarce or lacking on chronic toxicity, teratogenicity, mutagenicity, and carcinogenicity of the degradation products of carbofuran, especially degradation products that may also form nitroso compounds. (Nitrosated carbofuran metabolites, for example, are demonstrably mutagenic.)

12.4.2 Aquatic Organisms

Aquatic plants are comparatively resistant to carbofuran. Green alga (*Selenastrum capricornutum*) and several species of submergent macrophytes tolerated 1.0 mg carbofuran/L for 30 days without any measurable adverse effect (Johnson 1986). Elevated concentrations of 10.0 mg carbofuran/L did not affect growth or survival of duckweed (*Lemna minor*) or tubers of sago pondweed (*Potamogeton pectinatus*) (Trotter et al. 1991). Growth inhibition (50%) of algae (*Chlorella pyrenoidosa*) occurred in 96 h at 205 mg carbofuran/L, with no growth observed at 562 mg/L (Anton et al. 1993a). A similar case is documented for *Chlorella emersonii* (Sanchez and Ariz 1997). However, first instar daphnids (*Daphnia magna*) and fourth instar midge (*Chironomus raparius*) were effectively immobilized within 48 h at only 48 to 64 µg carbofuran/L (Johnson 1986). And larvae of the Japanese medaka (*Oryzias latipes*) exposed to 88 to 110 µg/L for 4 days had impaired swimming performance immediately after exposure, which remained impaired after 10 days in uncontaminated water (Heath et al. 1993).

Carbofuran reportedly disrupts enzyme and lipid metabolism in fishes and may not degrade as rapidly under field conditions as suggested by laboratory studies. However, most investigators argue that carbofuran, under current application rates, does not accumulate to a significant extent in aquatic systems and rapidly degrades under field and model microcosm study conditions. In studies with the African catfish (*Mystus vittatus*) exposed to 31 or 62 µg/L of carbofuran for 30 days, serum transaminases were significantly elevated (Verma et al. 1981a). In comparison with catfish exposed to concentrations of 21 µg/L or less during the same period, there were also significant depressions in alkaline phosphatase activity in the liver; acid phosphatase activity in the liver, kidneys, and gills; and glucose-6-phosphatase in the liver and kidneys (Verma et al. 1981b). In climbing perch, mean lipid levels in muscle and liver were elevated after exposure to an LC0 (120 h) dose of 560 µg/L carbofuran for 120 h. A similar pattern was observed following exposure to an LC100 (24 h) concentration of 1560 µg/L for 6 h (Bakthavathsalam and Reddy 1981). Carbofuran-induced alterations have also been documented in serum chemistry of the African catfish during immersion in 21 µg/L for 30 days (Verma et al. 1982b); in brain acetylcholinesterase activity of climbing perch and milkfish (*Channa punctatus*) 30 days after exposure to high sublethal levels for 48 h (Jash and Bhattacharya 1983); and in blood and tissue enzyme and ammonia levels in the air-breathing catfish (*Clarias batrachus*) 1 month after exposure for 30 days to 500 µg/L carbofuran (Mukhopadhyay et al. 1982). In field studies with *Trichogaster pectoralis*, a fish extensively cultured in flooded Malaysian rice paddies, Gill (1980) found that the degradation of carbofuran in the liver was slower than that reported for laboratory animals and suggested that caution be exercised in the extrapolation of rates of carbofuran oxidative hydroxylation activity from laboratory organisms to fishes cultured in rice fields. In fish, neurotoxic effects of carbofuran were localized to the brain regions that regulate motor activity and behavior. For example, adult snakeheads (*Channa punctatus*) exposed to 600 µg carbofuran/L for 15 days had a reduction in the level of neurotransmitters in the cerebral cortex of the brain (Gopal and Ram 1995). Histopathology of the liver and thyroid are reported in snakeheads after exposure for 6 months to extremely high sublethal (4.5 mg/L) concentrations of carbofuran (Ram 1988; Ram and Singh 1988).

Negligible accumulations of carbofuran were observed in egg masses of the caddisfly (*Triaenodus tardus*) during immersion for 120 h in water containing 8 µg/L of carbofuran; the low uptake was apparently related to the low partition coefficient of carbofuran (Bellick and Fels 1981). Rapid equilibrium and low accumulation was also reported for the sheepshead minnow (*Cyprinodon variegatus*). In a 28-day flow-through study, maximum tissue concentrations were measured between days 3 and 10 when upper concentration factors of 5 to 20 were recorded (Parrish et al. 1977). Field applications of carbofuran in farm ponds in Arkansas and Kansas were associated with low mortality in fish (Davey et al. 1976) or negligible effects on fish and plankton (Klaasen and Kadoum 1979). Kansas farm ponds subjected to 25 µg carbofuran/L contained 10.6 µg/L in surface waters 1 day later, but nondetectable residues thereafter; residues were <0.4 µg/kg at 1 day

in mud, zooplankton, and fish (Klaasen and Kadoum 1979). Farm ponds treated with 50 µg/L of carbofuran after 3 days contained 15 µg/L carbofuran in surface water and 26 to 46 µg/kg in mud, but nondetectable residues in biota; no measurable residues were found in any sample after 25 days (Klaasen and Kadoum 1979). When atrazine at 300 µg/L was applied in combination with 50 µg/L carbofuran, carbofuran was detectable in surface water at 23 days posttreatment at 1.5 µg/L, but not in the soil, biota, or any other compartment (Klaasen and Kadoum 1979).

Koeppe and Lichtenstein (1982), in a well-designed agromicrocosm study, evaluated the influence of percolating water on soils containing 3.6 mg/L of ¹⁴C-radiolabeled carbofuran. After 3 weeks, 49% of the carbofuran had been removed with percolating water from soils, and 37% was later recovered from soils and corn. In nonpercolated soils, 80% of the carbofuran was still associated with soils and corn. The aquatic components, including water, lake mud, plants (*Elodea*), and fish (the guppy *Poecilia*), contained 25% of the soil-applied carbofuran, although 49% had been initially added to the aquariums by way of percolated water. This loss of 24% was attributed partly to the degradation of carbofuran to CO₂. About 75% of all the radiocarbon was in lake mud, most of it unextractable. Carbofuran was the major compound recovered from control and percolated soils, accounting for 39% and 15%, respectively; 3-ketocarbofuran and 3-hydroxycarbofuran were identified as the major metabolites. The addition of captafol, a fungicide, to carbofuran-treated soils resulted in a more rapid disappearance of the insecticide from terrestrial soils and reduced uptake by corn. The addition of EPTC, an herbicide, had no measurable effect on terrestrial components, but EPTC and captafol both caused increased recoveries of ¹⁴C-labeled carbofuran residues from lake bottom mud. In another study, radiolabeled carbofuran was applied at 1.12 kg/ha to a model ecosystem containing seedling sorghum plants (*Sorghum halopense*), saltmarsh caterpillar larvae (*Estigmene acrea*), the alga *Oedogonium cardiacum*, freshwater clams (*Corbicula manilensis*), crabs (*Uca minax*), a cladoceran (*Daphnia* sp.), mosquito larvae, unidentified species of frogs and snails, and the freshwater macrophyte *Elodea canadensis* (Yu et al. 1979). Carbofuran was rapidly, but not completely, degraded in water to carbofuranphenol, 3-ketocarbofuran, 3-hydroxycarbofuranphenol, N-hydroxy-methylcarbofuran, 3-hydroxycarbofuran, and several unknown compounds. Carbofuran was highly toxic to crabs, clams, and *Daphnia* immediately after application to the model ecosystem, but all animals, except one crab, survived restocking 20 days later.

The freshwater bivalve molluscs *Glebula rotundata* and *Rangia cuneata* absorbed waterborne carbofuran but did not appear to concentrate it (Zakour 1980). Both species of clams were very tolerant, although symptoms of poisoning, such as shell gaping, foot extension, and incoordination, were evident when carbofuran exposures were high (75 mg/L). *Glebula* converted injected radiolabeled carbofuran to a variety of free metabolites, primarily hydrolysis products, and also polar carbofuran metabolites that were not degraded by conditions known to hydrolyze glycosidic conjugates. These polar metabolites may contain some type of amino acid moiety. The rate of carbofuran metabolism by *Glebula* was slower than that reported for most other animals, but was more rapid than that of plants and microorganisms (Table 12.7). Bacterial metabolism of carbofuran was negligible in both *in vivo* and *in vitro* studies with bivalve molluscs (Zakour 1980).

Table 12.7 Rates of Carbofuran Metabolism by Various Organisms

Organism	Parent Carbofuran Converted (%)	Time (d = day; h = hour)
Rat, <i>Rattus</i> sp.	100	24 h
Chicken, <i>Gallus</i> sp.	100	24 h
Saltmarsh caterpillar, <i>Estigmene</i> sp.	100	7 h
Intact cotton plant, <i>Gossypium</i> sp.	100	5 d
Alfalfa, roots, <i>Medicago</i> sp.	95	30 d
Land snail, <i>Helix aspersa</i>	90	1 h
Bean plants, <i>Phaseolus</i> sp.	68	3 d
House fly, <i>Musca</i> sp.	58	1 h

Table 12.7 (continued) Rates of Carbofuran Metabolism by Various

Organism	Parent Carbofuran Converted (%)	Time (d = day; h = hour)
Bivalve, <i>Glebula rotundata</i>	54–62	24–48 h
Tobacco, leaves, <i>Nicotiana</i> sp.	50	4 d
Microorganisms, unidentified	40–70	7–56 d
Cotton, leaves	20	2 d
Mugho pine, needles, <i>Pinus</i> sp.	17	14 d

Modified from Zakour, H.R. 1980. Toxicity, Uptake and Metabolism of the N-methyl-carbamate Pesticide Carbofuran by the Freshwater Bivalve Mollusc *Glebula rotundata* (Lamarck). Ph.D. Thesis, Rice University, Houston. 148 pp.

12.4.3 Birds

Short-term studies demonstrate that juvenile ring-necked pheasants (*Phasianus colchicus*) given a 3.6 mg carbofuran/kg grain diet (equivalent to 132 g/ha) for 5 days, followed by 3 days on a clean diet, had normal survival, growth, and brain acetylcholinesterase activity (Somers et al. 1991). Similarly, adult and nestling passerines were able to tolerate the dietary exposure resulting from ingestion of grasshoppers sprayed at the rate of 134 g/ha (Forsythe et al. 1994). Mallard ducklings, fed for up to 300 m through vegetation plots sprayed with 132 or 164 g carbofuran/ha, had normal growth and survival, but brain cholinesterase activity inhibition was directly related to spray rate and exposure distance (Martin et al. 1991b). Growth and cholinesterase activity levels in mallard ducklings were reduced at 0.25 mg carbofuran/kg BW daily (but not 0.15 mg/kg BW daily) for 10 days (Martin et al. 1991a).

Birds may encounter carbofuran through respiratory, dermal, and oral routes. Depending on the dietary requirements of particular species, ingestion of contaminated vegetables and poisoned invertebrates may be important exposure routes (Finlayson et al. 1979). Carbofuran may prove harmful alone or in combination with other substances. For example, male Japanese quail fed 0.5 mg carbofuran/kg ration for 18 weeks exhibited a 79% inhibition of plasma cholinesterase activity (Dieter and Ludke 1978). The reduction was slightly greater (84%) when carbofuran was fed in combination with 0.05 mg morsodren/kg ration, a methylmercury compound, although morsodren had no measurable effect on cholinesterase activity when fed alone at that dosage. Since many species of fish-eating birds frequently contain 0.05 mg/kg BW of mercury in various tissues, interaction effects of mercury with carbofuran and other cholinesterase-inhibiting compounds may produce synergistic, deleterious effects (Dieter and Ludke 1978).

Low oral dosages or high dietary levels of carbofuran produced no permanent damage in northern bobwhites. A single oral dose of 2 mg carbofuran/kg BW did not affect brain cholinesterase levels at 48 h, or growth, metabolic efficiency, or metabolized energy at 8 days (Solomon and Robel 1980). The activities of bobwhites fed 131 mg carbofuran/kg ration for 14 days were reduced, but this effect was temporary and recovery was complete within 14 days on a carbofuran-free diet. The temporarily reduced activity was attributed to the rapid metabolic breakdown of carbofuran (Robel et al. 1983). Among laying white leghorn hens, 80% of a single oral dose of 2.7 mg carbofuran/kg BW was eliminated in feces within 10 days (Hicks et al. 1970). All eggs contained detectable carbofuran; an egg with the highest concentration of 0.13 mg/kg developed on day 4. Residues in liver and kidney were about 2.6 mg/kg at 6 h but declined to 0.2 mg/kg in 24 h. Muscle and fat contained about 0.3 mg/kg at 6 h, and <0.1 mg/kg at 24 h. Hicks et al. (1970) indicated that hydroxylation of carbofuran and hydrolysis of the carbamate ester were the predominant pathways in the metabolism of carbofuran by laying hens. Similar results were obtained at single oral doses of 2.7 or 0.3 mg carbofuran/kg BW.

12.4.4 Mammals

Granular carbofuran applications at 7.9 to 11.2 kg/ha on conventionally tilled or no-till fields in Maryland and Pennsylvania in 1986 had no adverse effects on resident white-footed mice (*Peromyscus leucopus*). Exposed mice had normal blood chemistry, liver function, growth, migration, and populations (Albers et al. 1990). Among larger mammals, carbofuran is associated with a variety of stress symptoms, including increased salivation, muscle tremors, prostration, labored breathing, loss of appetite, and (in rare cases) death. These signs were observed in 1- to 2-week-old calves given single doses of carbofuran at 0.25 to 5.0 mg/kg BW orally or 0.05 to 0.1% dermally, in cattle yearlings at 1.0 to 5.0 mg/kg orally or 0.1% dermally, and in sheep at 2.5 to 5.0 mg/kg orally. All survivors had completely recovered at 5 days posttreatment (Palmer and Schlinke 1973). Ewes given 0.3 mg carbofuran/kg BW orally three times weekly for 43 days had elevated serum thyroxine levels (Rawlings et al. 1998), suggesting additional research on the use of metabolic hormones as biomarkers of carbofuran exposure.

Lactating cows fed corn silage containing 1.4 to 3.9 mg carbofuran/kg ration for 8 weeks, or about 74 mg carbofuran daily, showed no decrease in blood cholinesterase. Furthermore, no carbofuran residues were detected in the milk (Leuck et al. 1968). Other studies with lactating cows dosed orally with carbofuran (Dorough and Ivie 1968; Ivie and Dorough 1968) showed almost complete excretion in 10 days, mostly through urine (94%), feces (0.7%) and milk (0.2%). Carbofuran metabolites in urine, feces, and excreted milk included the 3-hydroxy-, 3-keto-, and 3-hydroxy-N-hydroxymethyl derivatives, both conjugated and free, and unknown constituents, perhaps carbon dioxide formed by carbofuran hydrolysis.

In investigations of the effects of carbofuran or its metabolites on mice and rats, pregnant mice receiving 0.01 or 0.5 mg dietary carbofuran/kg daily throughout gestation gave birth to viable, overtly normal offspring at term (Barnett et al. 1980). Significant elevation of serum immunoglobins was measured in 101-day-old male offspring of female parents receiving 0.5 mg/kg dietary carbofuran. This effect was not observed at day 400 or 800. In female offspring from the group receiving 0.01 mg/kg carbofuran, serum immunoglobins were significantly depressed at day 101, but not thereafter (Barnett et al. 1980). Disturbances in immunoglobulin contents may decrease immunocompetence and, thus, indirectly contribute to morbidity and premature mortality. In rats fed comparatively high dietary levels of 30 mg carbofuran/kg ration for 90 days, with mean daily intake of 1.97 mg carbofuran/kg BW, growth was significantly reduced and ventral prostate gland metabolism of RNA, DNA, and protein was altered (Shain et al. 1977). Prenatal exposure of mice to 0.01 mg carbofuran/kg BW daily, administered orally during gestation, resulted in persistent postnatal endocrine dysfunction in adults, specifically, the impairment of hepatic metabolism and elevation of plasma corticosterone (Crammer et al. 1978). Unexpectedly, however, at a higher dose of 0.05 mg/kg, there were no significant differences from controls, and the endocrine function of tested mice was normal. In female rats given a single dose of 0.05 mg carbofuran per kg body weight orally on the 18th day of gestation, acetylcholinesterase (AChE) activity decreased significantly in maternal and fetal blood and in the maternal liver within 1 hour (Cambon et al. 1979). At higher dosages of 0.25 and 2.5 mg/kg, AChE was also depressed in the fetal liver and in the maternal and fetal brains; the effects were not measurable 24 hours postadministration.

Carbamate pesticides can easily be converted to *N*-nitroso derivatives in the presence of sodium nitrite under acidic conditions. The *N*-nitroso form of carbofuran could possibly be formed in the human stomach (Nelson et al. 1981). Since carbofuran is used routinely on a variety of crops and nitrite is a common component of the human diet and present in human saliva, nitrosation of carbamates under conditions simulating those in the human stomach is possible. Lijinsky and Schmal (1978) tested nitrosocarbofuran and five other nitrosated carbamate pesticides for carcinogenicity in rats. Nitrosocarbofuran, at 16.5 mg/kg BW administered orally once weekly for 23 weeks, was the most toxic compound tested and caused the death of several animals by liver damage early in the experiment. Among survivors, nitrosocarbofuran was the most carcinogenic,

as judged by the numbers of carcinomas and tumors that developed. Nitrosation rates of carbofuran in the environment are not now adequately documented but conceivably could represent an environmental risk to wildlife. Surprisingly, nitrosocarbofuran was among the least mutagenic compounds tested in rats. No obvious explanation is available for the differences in carcinogenic and mutagenic properties (Lijinsky and Schmal 1978). It is noteworthy that data on chronic toxicity, teratogenicity, mutagenicity, and carcinogenicity of degradation products of carbofuran, especially carbofuran-7-phenol, and 3-hydroxycarbofuran-7-phenol are either scarce or lacking (Finlayson et al. 1979). A similar case is made for nitrosocarbofuran and other degradation products of carbofuran, which may also form nitroso compounds. Nelson et al. (1981) indicated that nitrosated 3-hydroxycarbofuran and 3-ketocarbofuran produced mutagenic responses in bacterial strains of *Salmonella* and chromosome aberrations in ovary cells of Chinese hamsters. Nitrosocarbofuran and 3-hydroxynitrosocarbofuran also induced large numbers of sister chromatid exchanges in the same cells. Furthermore, nitroso derivatives of carbofuran were considerably more active than nitroso forms of other carbamate pesticides in producing mutagenicity in *S. typhimurium* (Nelson et al. 1981). On the other hand, technical formulations of the parent carbofuran were neither genotoxic nor mutagenic to bacteria, yeast, or corn (Gentile et al. 1982).

12.4.5 Terrestrial Invertebrates

In decomposing the dead organic matter in a deciduous forest ecosystem, the detritus food chain may account for more than half the energy flowing through the ecosystem. Carbofuran can significantly disturb decomposition rates of litter communities, with profound consequences for nutrient recycling and incorporation of organic matter into the soils. For example, application of 0.29 kg/ha of carbofuran to a red maple (*Acer rubrum*) litter community near Ottawa, Canada, reduced daily decomposition rates by about 40%. All of the groups of macrodecomposers present, including Collembola, Acarina, Lepidoptera, Coleoptera, Diplopoda, and Annelida, have been shown to be susceptible to carbofuran and may have been affected by the treatment (Weary and Merriam 1978).

12.5 RECOMMENDATIONS

In Canada, for regulatory purposes, the tolerance level for carbofuran in animal tissues or food, feed, and fiber crops is based on the total carbamate content of the sample, as indicated by total carbofuran, 3-hydroxycarbofuran, 3-ketocarbofuran, and their conjugates (Finlayson et al. 1979), presumably carbofuran phenol, 3-ketocarbofuran phenol, and 3-hydroxycarbofuran phenol. In the United States, the tolerance level is based on carbofuran and four metabolites: 3-hydroxycarbofuran, carbofuran phenol, 3-hydroxycarbofuran phenol, and 3-ketocarbofuran phenol (USEPA 1976). Carbofuran levels considered safe range from 0.05 mg/kg (including 0.02 mg/kg carbofuran metabolites) in meat, fat, and meat by-products, to 40.0 mg/kg (including 20.0 mg/kg carbofuran metabolites) in alfalfa hay; intermediate values are 0.1 mg/L in milk, 0.2 mg/kg in corn grain, and 25.0 mg/kg in corn fodder and forage (USEPA 1976). The acceptable daily intake for protection of human health should not exceed 0.01 mg carbofuran/kg BW (Hayes and Laws 1991). No recommended carbofuran level is currently being promulgated by any regulatory agency for the protection of sensitive species of aquatic biota and wildlife.

On the basis of evidence presented herein, this author conservatively estimates that, in terms of total carbofuran in water, damage is possible to aquatic invertebrates at $>2.5 \mu\text{g/L}$ and to teleosts at $>15 \mu\text{g/L}$. These levels could be attained during a heavy rainfall shortly after carbofuran treatment of adjacent fields. Among sensitive species of warm-blooded animals, dietary concentrations as low as 10 $\mu\text{g/kg}$ ration have demonstrable effects, which were measurable only after extended periods postingestion. For comparison, this level is about 1/5 that allowed in meat by-products for

human consumption. Current maximum permissible aerosol levels of 0.05 µg/L (50 µg/m³) appear sufficient to protect wildlife with the proviso that concentrations not exceed 2.0 µg/L at any time.

Sporadic kills of migratory birds were associated with carbofuran formulations containing 3% active ingredients (a.i.). For example, migratory sandpipers died after eating Furadan 3 G granules (3% a.i.) applied to rice crops in Texas (Flickinger et al. 1980). The granules probably were ingested while the sandpipers were probing and skimming the surface of wet soil for insects and crustaceans. Other species of migratory waterfowl may have mistaken the small size and density of Furadan granules for seed, particularly in areas where concentrations of granules were abundant after misuse and careless applications. It appears that granular carbofuran formulations need to be developed that contain less than 3% a.i. in order to protect waterfowl, yet still maintain their effectiveness against target organisms. Nevertheless, the sale and use of granular formulations of carbofuran have been prohibited in the United States since September 1, 1994, except for five minor uses: bananas in Hawaii, spinach grown for seed, pine tree progeny tests, cucurbits (cucumbers, squash, pumpkins, cantaloupes, and watermelons), and dry-harvested cranberries (USEPA 1991). Total sales of granular carbofuran for these five uses is limited to 2500 pounds (1136 kg) annually. All other uses of granular carbofuran were to be deleted from the label, and remaining stocks were to be used before August 31, 1995 (USEPA 1991).

In rice field pest control, carbofuran should be applied before the fields are flooded and delayed to avoid peak bird migration. Research also appears warranted on the effects on fish and wildlife of the numerous carbofuran formulations used, especially liquid spray formulations (flowables), and on applications to crops other than rice, such as corn, alfalfa, and hay. Additional long-term research is urgently needed on potential impacts of degradation products of carbofuran on sensitive species of aquatic organisms and wildlife, with special attention to nitrosated carbofuran metabolites. Such data are now scarce or lacking. Research is also needed on chemical and biological interactions of carbofuran with other agricultural chemicals applied to the same locations, which are imperfectly understood. Finally, researchers must elucidate the significance of metabolic upset recorded in various species of laboratory mammals at considerable periods after carbofuran insult.

The American Ornithologists' Union passed a resolution in 1990 calling for the cancellation and immediate suspension of all carbofuran granular products — which has since been implemented — and urging the United States to also ban the liquid formulations (as quoted in Mineau 1993). Carbofuran flowable formulations are considered hazardous to the burrowing owl (*Athene cunicularia*), and nests have been abandoned following exposure. In Canada, all carbofuran formulations are prohibited within 250 m of owl burrows (Mineau 1993). In the United States, carbofuran prohibitions to protect endangered species of mammals and birds in fragile ecological areas are under consideration (USEPA 1989a, 1989b, 1991).

12.6 SUMMARY

Carbofuran (2,3-dihydro-2,2-dimethyl-1,7-benzofuranyl methylcarbamate) and other carbamate compounds, together with organophosphorus compounds, have virtually replaced the more persistent and hazardous organochlorine systemic pesticides used in agriculture. In general, carbofuran effectively controls insects through an anticholinesterase mode of action. Compared with chlorinated hydrocarbon insecticides, it has a relatively short residual life in the environment, degrades rapidly, and is almost completely excreted by nontarget organisms. Carbofuran degradation is complex and demonstrably modified by numerous biological and physicochemical factors. Little is known of the biological properties of the degradation products, especially nitrosated metabolites, in relation to chronic toxicity, teratogenicity, mutagenicity, or carcinogenicity.

At currently recommended application rates and in present formulations, carbofuran has caused sporadic, and sometimes extensive, field kills of fish, wildlife, and invertebrates. In short-term laboratory tests, significant death rates were observed at concentrations of about 200 µg carbofuran/L

(in water) for sensitive species of aquatic biota, 238 µg/kg BW (acute oral), and 190,000 µg/kg ration (dietary) for birds, and 2000 µg/kg BW (acute oral) and 100,000 µg/kg ration (dietary) for mammals. Among representative indicator species, harmful and sometimes life-threatening effects of carbofuran have been recorded for fish at nominal water concentrations of >15 µg/L and for aquatic invertebrates at >2.5 µg/L. For birds and mammals, harmful effects were observed at 10 to 50 µg/kg in the diet and 1000 µg/L in drinking water. For comparison, the "safe" level of carbofuran in meat products for human consumption is 50 µg/kg. Current maximum permissible aerosol levels of 0.05 µg/L (50.0 µg/m³) carbofuran appear sufficient to protect wildlife; however, evidence suggests that aerosol concentrations should never exceed 2 µg/L. Plants are significantly more resistant to carbofuran than are invertebrates and higher organisms. Carbofuran hazards to migratory waterfowl have been reduced by effectively prohibiting granular formulations. In rice culture, carbofuran should be applied before the fields are flooded and after the peak of bird migration. More research is merited on the biotic effects of various formulations of carbofuran, especially flowable formulations, and on applications to crops other than rice, such as corn, alfalfa, and hay.

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CHAPTER 13

Chlordane

13.1 INTRODUCTION

Technical chlordane is a mixture of chlorinated hydrocarbons that has been used as an insecticide since its introduction in 1947. Chlordane was the first cyclodiene insecticide to be used in agriculture and was the second most important organochlorine insecticide in the United States in 1976/1977, behind toxaphene, with an estimated annual production of 9 million kg (Nomeir and Hajjar 1987). Chlordane is a leading insecticide in controlling termites, with about 1.2 million homes in the United States alone treated annually for this purpose (Nomeir and Hajjar 1987).

Chlordane has been detected in human milk in Canada, Japan, Mexico, Spain, Hawaii, and Mississippi (World Health Organization [WHO] 1984; Ohno et al. 1986). Chlordane compounds have been detected in oysters from the South Atlantic Ocean and Gulf of Mexico, in fish from the Great Lakes and major river basins of the United States, in the blubber of cetaceans from the coastal waters of North America, and in the Antarctic atmosphere (Kawano et al. 1988; Gooch et al. 1990). In fact, all available evidence suggests that chlordane is ubiquitous in the environment. Air and water transport of technical chlordane has resulted in the detection of chlordane and its metabolites in rainwater, drinking water, air, surface waters, soils, sediments, plankton, earthworms, fish, shellfish, birds and their eggs, aquatic invertebrates, cats, dogs, livestock, and humans (Zitko 1978; U.S. Environmental Protection Agency [USEPA] 1980; Sudershan and Khan 1980; Kerkhoff and Boer 1982; Wickstrom et al. 1983; Johnson et al. 1986; Nomeir and Hajjar 1987; Suzuki et al. 1988). Despite its widespread use, persistence, and tendency to accumulate in fat, there was no firm evidence of direct lethal or sublethal effects on terrestrial vertebrate wildlife until Blus et al. (1983) recorded several chlordane-related mortalities. A North Dakota marsh treated with chlordane had decreased reproductive success and some deaths of young of several bird species, but this was attributed to depletion of invertebrate prey and not to acute poisoning (Hanson 1952). Chlordane was implicated as the principal toxicant in 30 pesticide poisoning cases of hawks, owls, herons, and other birds in New York between 1982 and 1986 (Stone and Okoniewski 1988). In New York, Maryland, and New Jersey between 1986 and 1990, chlordane was implicated in the poisoning of opossum (*Didelphis virginiana*), red fox (*Vulpes vulpes*), striped skunk (*Mephitis mephites*), big brown bat (*Eptesicus fuscus*), eleven species of songbirds, and nine species of raptors (Okoniewski and Novesky 1993).

The U.S. Environmental Protection Agency (USEPA) considers chlordane as a probable human carcinogen (defined as inadequate evidence from human studies and sufficient evidence from animal studies), as judged by chlordane-induced cancer of the liver in domestic mice (Arruda et al. 1987). In 1978, the USEPA restricted chlordane use to subterranean termite control, nonfood plants, and root dip. Limited agricultural use was permitted until 1980. In 1987, the USEPA registered chlordane again, limiting its sale and use to licensed applicators for subterranean termite control (Arruda et al. 1987). However, it seems that significant home and garden use exists, especially for control of

termites and undesirable lawn insects (Wood et al. 1986). On April 14, 1988, the USEPA moved to cancel the registrations of termiticide products containing chlordane and to forbid the sale or commercial use of those products (U.S. Public Health Service [USPHS] 1994). Reviews on ecological and toxicological aspects of chlordane in the environment are available; particularly useful are those by Ingle (1965), Menzie (1974), the National Research Council of Canada [NRCC] (1975), the International Agency for Research on Cancer [IARC] (1979), the USEPA (1980, 1988), WHO (1984), Klaassen et al. (1986), Nomeir and Hajjar (1987), Eisler (1990), and USPHS (1994).

13.2 CHEMICAL AND BIOCHEMICAL PROPERTIES

Technical chlordane (64 to 67% chlorine) is produced by the condensation of cyclopentadiene and hexachlorocyclopentadiene to yield chlordene (Figure 13.1). Addition of chlorine across the 2-3 olefinic bond of chlordene forms *cis*-chlordane and *trans*-chlordane; substitution of chlorine into position 1 of chlordene forms heptachlor; and further addition of chlorine across the 2-3 olefinic bond forms *cis*-nonachlor and *trans*-nonachlor (Ribick and Zajicek 1983). Technical chlordane includes about 45 components. Its approximate composition is 19% *cis*-chlordane ($C_{10}H_6Cl_8$), 24% *trans*-chlordane ($C_{10}H_6Cl_8$), 21.5 to 25% chlordene isomers ($C_{10}H_6Cl_6$), 7 to 10% heptachlor ($C_{10}H_5Cl_7$), 7 to 10% *cis*- and *trans*-nonachlor ($C_{10}H_5Cl_9$), 2% Diels–Alder adduct of cyclopentadiene and pentachlorocyclopentadiene, 1% hexachlorocyclopentadiene, 1% octachlorocyclopentene, and 15.5% miscellaneous constituents (NRCC 1975; IARC 1979; USEPA 1980; WHO 1984; Gooch et al. 1990). Oxychlordane and heptachlor epoxide are toxicologically significant degradation products (Figure 13.1; Perttila et al. 1986; Gooch et al. 1990).

Chlordane produced before 1951 contained a significant quantity of hexachlorocyclopentadiene — a toxic irritant to warm-blooded animals. Chlordane produced since 1951 contains little or none of this compound (Ingle 1965). A high-purity chlordane formulation containing about 74% *cis*-chlordane and 24% *trans*-chlordane is also available (Nomeir and Hajjar 1987).

Chemical analysis of technical chlordane is difficult because of frequent variations in both the number and relative composition of components in weathered chlordane (Ribick and Zajicek 1983). Other difficulties are encountered from analytical interferences from various organochlorine compounds. Furthermore, the exact structure has not been determined for a number of compounds in technical chlordane, and the majority of compounds have not been isolated or synthesized for use as comparative standards (Ribick and Zajicek 1983).

Cis-chlordane (CAS number 5103-71-9) and *trans*-chlordane (CAS number 5103-74-2) are characterized by the following properties: molecular weight 409.76; chemical formula of $C_{10}H_6Cl_8$; viscous, amber-colored liquid; boiling point between 104 and 105°C for *trans*-chlordane, and between 106 and 107°C for *cis*-chlordane; density of 1.59 to 1.63 g/mL at 25°C; soluble in most organic solvents, but only sparingly soluble in water (9 µg/L at 25°C); vapor pressure of 0.00001 mmHg at 25°C; and a log K_{ow} (octanol/water partition coefficient) of 5.16 (Ingle 1965; NRCC 1975; IARC 1979; USEPA 1980, 1988; WHO 1984). Pesticides containing chlordane or technical chlordane have been sold under a variety of names including 1068, Aspon, Belt, CD-68, Chloridan, Chlordan, Chlorindan, Chlor-kil, Chlorodane, Chlortox, Cortilan-neu, Corodane, Dichloro-chlordene, Dichlorodene, Dowchlor, ENT 9932, HCS 3260, Kypclor, M 140, M 410, Niram, Niram 5% granular bait, Octachlor, Octa-klor, Octaterr, Ortho-klor, Synklor, Tat Chlor 4, Topiclor 20, Toxicchlor, and Velsicol 1068 (IARC 1979; Johnson and Finley 1980; Hudson et al. 1984; WHO 1984; Hill and Camardese 1986; Mayer 1987; USEPA 1988).

Technical chlordane is stable under ultraviolet (UV) light, although some components, such as chlordene, heptachlor, *cis*-chlordane, and *trans*-chlordane, will form photoisomers under high-intensity UV light in the presence of sensitizers, such as ketones (NRCC 1975; Menzie 1978). Several compounds were measured in alfalfa grown on soils treated with chlordane, including 1,2-

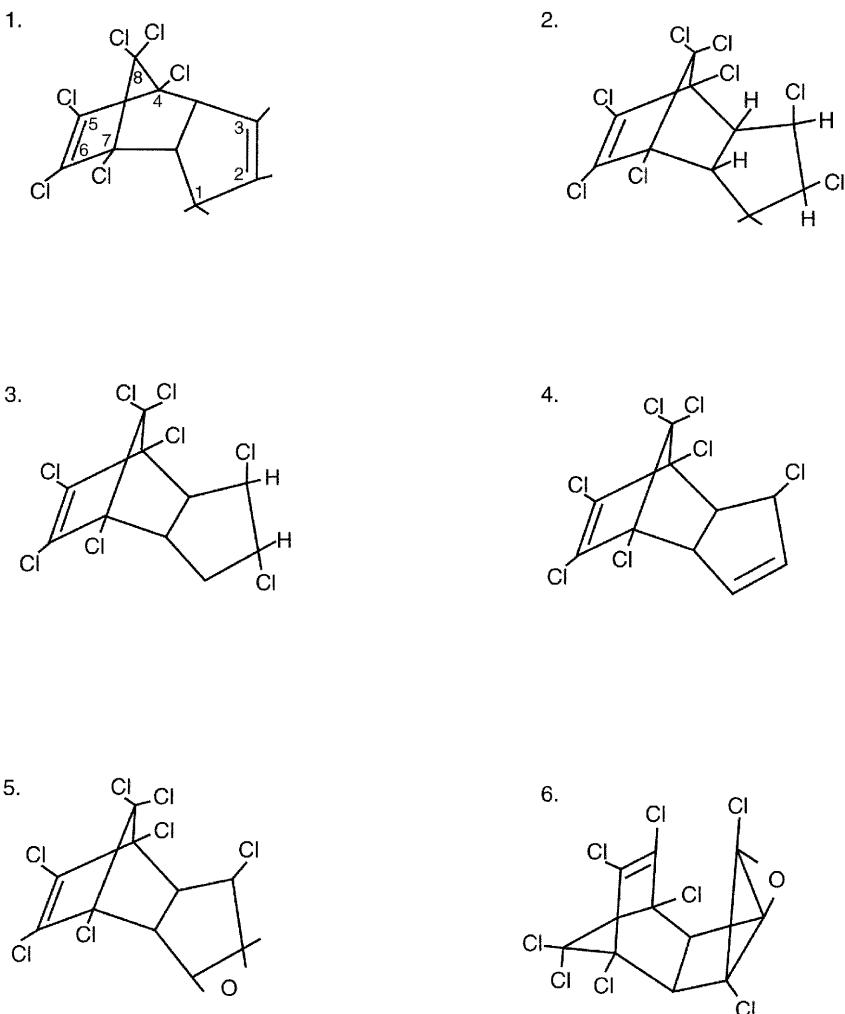


Figure 13.1 Chemical structure of chlordane-related compounds: **1**, chlordene (4,5,6,7,8,8-hexachloro-3a,4,7,7a-tetrahydro-4, 7-methanoindene); **2**, *cis*-chlordane, also known as *alpha*-chlordane (1-exo, 2-exo, 4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene); **3**, *trans*-chlordane, also known as *gamma*-chlordane (1-exo, 2-*endo*, 4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene); **4**, heptachlor (1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene) — technical heptachlor contains about 15% *cis*-chlordane and 2.5% *trans*-chlordane; **5**, heptachlor epoxide (1,4,5,6,7,8,8-heptachloro-2,3-epoxy-3a,4,7,7a-tetrahydro-4,7-methanoindene); and **6**, oxychlordane, also known as octachlor epoxide (1-exo, 2-*endo*, 4,5,6,7,8,8-octachloro,2,3-exo-epoxy-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene).

dichlorochlordanes, oxychlordanes, and photo-*cis*-chlordanes, as well as the parent chlordane compounds (WHO 1984). The half-life ($T_{1/2}$) of *cis*-chlordanes in water is comparatively short, between 1.1 and 17.5 h (Feroz and Khan 1979a). In soils, technical chlordane has a half-life ranging from 0.5 to 1.0 years for some samples, and 4 to 10 years for other samples. The lower $T_{1/2}$ values refer to the initial rapid disappearance of chlordane from the soil; if studies continue over several years, the remaining chlordane is relatively persistent, with a $T_{1/2}$ of 5 to 7 years (NRCC 1975). Measurable residues of chlordanes in soils were present more than 14 years after application (USEPA 1988). Chlordanes persist in soils because of its low solubility in water, relatively low vapor pressure, and high tendency to adsorb to soil particles. Accordingly, soil-bound chlordanes

are not likely to become serious contaminants of the lower soil strata or deep-water sources (WHO 1984). Transport into the hydrosphere from contaminated soils will occur through erosion of soil particles or sediments, not by desorption and dissolution (Klaassen et al. 1986).

Chlordane is a nerve stimulant. At low chronic doses, it produces hyperexcitability and lack of coordination in animals, and at high acute doses causes tremors and convulsions (Ingle 1965; Klaassen et al. 1986). Chlordane induces hepatic microsomal drug-metabolizing enzymes, resulting in enhanced biotransformation at low doses, although high doses may result in liver hypertrophy (Klaassen et al. 1986). The physiological target sites are in nerve and muscle membranes, presumably on proteins and phospholipids. The ultimate effect is axonic with membrane disruption, resulting in spastic muscle twitching and death (Greenhalgh 1986).

Chlordane is readily absorbed by warm-blooded animals through skin, diet, and inhalation. It is quickly distributed in the body and tends to concentrate in liver and fat (WHO 1984). Up to 75% of a single oral dose of chlordane administered to rats and mice was absorbed in the gut, and up to 76% of an aerosol dose was absorbed in the respiratory tract (Nomeir and Hajjar 1987). Rabbits absorbed 33% in the gut following oral administration (USEPA 1988). Chlordane residues in mammals were usually not measurable 4 to 8 weeks after cessation of exposure (Ingle 1965). Chlordane persistence in human serum and whole body was estimated at 88 days and 21 days, respectively; this compares to a Tb 1/2 of about 23 days in rats fed chlordane for 56 days (USEPA 1980).

Excretion kinetics of chlordane are complex, and different isomers exit through different pathways (USEPA 1980, 1988). In rats, chlordane elimination was almost complete 7 days after receiving single oral doses up to 1 mg/kg body weight (BW); 24 hours after treatment, 70% of the *cis*-chlordane and 60% of the *trans*-chlordane had been excreted (WHO 1984). In rodents, chlordane and its metabolites were usually excreted in feces, regardless of the administration route; the *cis*-isomer was excreted slightly faster than the *trans*-isomer, although identical metabolites seemed to be formed (Menzie 1969, 1980; USEPA 1980; WHO 1984; Nomeir and Hajjar 1987). In rabbits, however, up to 47% of the administered dose was voided in the urine, and *cis*- and *trans*-chlordane were excreted at the same rate (Nomeir and Hajjar 1987).

Microorganisms such as *Nocardiopsis* sp., an actinomycete, can metabolize *cis*- and *trans*-chlordane to at least eight solvent-soluble substances, including dichlorochlordanone, oxychlordanone, heptachlor, heptachlor *endo*-epoxide, chlordene chlorhydrin, and 3-hydroxy-*trans*-chlordane (Beaman and Matsumura 1981). Based on studies of chlordane metabolism in animals, four metabolic pathways are proposed (Feroz and Khan 1979a; WHO 1984; Nomeir and Hajjar 1987; USEPA 1988):

1. Hydroxylation to form 3-hydroxychlordanone, which on dehydration forms 1,2-dichlorochlordanone, with subsequent epoxidation to oxychlordanone (*trans*-chlordane is converted to oxychlordanone 7 times faster than is *cis*-chlordane)
2. Dehydrochlorination to form heptachlor, from which heptachlor epoxide and other hydroxylation products may be formed
3. Dechlorination to monochlorodihydrochlordanone
4. The replacement of chlorine by hydroxyl groups resulting in the formation of hydroxy metabolites, which are excreted or further transformed by conjugation with glucuronic acid

Metabolism of chlordanes and nonachlors to oxychlordanone is orders of magnitude greater in fish-eating and carnivorous birds than in marine mammals (Kawano et al. 1988). The reasons for this are unclear and merit further research.

Trans-nonachlor, a major component of technical chlordane, was frequently found as the major chlordane residue in humans, whereas oxychlordanone was the major component in rats fed technical chlordane (Nomeir and Hajjar 1987). *Trans*-nonachlor is converted efficiently by rat liver microsomes to *trans*-chlordane, but this ability is lacking in humans, resulting in the accumulation of *trans*-nonachlor in humans (Nomeir and Hajjar 1987).

Although technical chlordane is a mixture of compounds, two metabolites — heptachlor epoxide and oxychlordane — can kill birds when administered through the diet (Blus et al. 1983). These two metabolites originate from biological and physical breakdown of chlordanes in the environment, or from metabolism after ingestion. Heptachlor can result from breakdown of *cis*- and *trans*-chlordane, eventually oxidizing to heptachlor epoxide; oxychlordane can result from the breakdown of heptachlor, *cis*-chlordane, *trans*-chlordane, or *trans*-nonachlor (Blus et al. 1983). Heptachlor epoxide has been identified in soil, crops, and aquatic biota, but its presence is usually associated with the use of heptachlor, not technical chlordane — which also contains some heptachlor (NRCC 1975). Various components in technical chlordane may inhibit the formation of heptachlor epoxide or accelerate the decomposition of the epoxide, but the actual mechanisms are unclear (NRCC 1975).

In mammals, oxychlordane ($C_{10}H_4Cl_8O$) is a metabolite of *cis*- and *trans*-chlordanes and *trans*-nonachlor (Miyazaki et al. 1980), and has proven much more toxic and persistent than the parent chemicals (WHO 1984; Kawano et al. 1988). Oxychlordane has been measured in the fat of rats, dogs, and pigs fed either isomer, and in milk and cheese from cows fed alfalfa treated with technical chlordane (WHO 1984; Nomeir and Hajjar 1987; USEPA 1988). Oxychlordane was isolated and identified from adipose tissues of pigs fed diets for 90 days containing 300 mg/kg of *cis*-chlordane or *trans*-chlordane (Schwemmer et al. 1970). Sharply elevated oxychlordane levels were detected in milk from cows fed chlordane for 60 days. When chlordane was removed from their diet, oxychlordane residues in milk dropped rapidly during the week following termination and stabilized after 2 weeks (USEPA 1980). The Tb 1/2 for oxychlordane in beef cattle grazing in heptachlor-contaminated pastures for 4 weeks was about 92 days (Petterson et al. 1988). Rats and rabbits given chlordane orally or through the diet retained the highest levels in adipose tissue, followed by liver, kidney, brain, and muscle. Oxychlordane was the most persistent residue after chlordane was removed from the diet (WHO 1984; USEPA 1988).

13.3 USES

Chlordane was first produced commercially in the United States in 1947 and became available in five basic formulations, including 5% granules, oil solutions containing 2 to 200 g/L, and emulsifiable concentrates containing chlordane at 400 to 800 g/L (WHO 1984). Production of chlordane in the United States in 1971 was estimated at 11.3 million kg (Glooschenko and Lott 1977). By 1974, about 9.5 million kg of chlordane were used domestically to control commercial pests (35%); in homes, lawns, and gardens (30%); on corn (20%); turf (6%); potatoes (5%); tomatoes (2%); and other uses (IARC 1979). On March 6, 1978, the USEPA issued a cancellation proceeding on chlordane, allowing limited use on certain crops and pests until July 1, 1983, but no use thereafter except for underground termite control (IARC 1979; USEPA 1988). A similar situation exists in Japan, where the only permitted use of chlordane is for control of termites and powder post beetles (Miyazaki et al. 1980). Use in Japan is estimated at 500,000 kg per year (Yamagishi et al. 1981b).

In Canada, chlordane had been used in soils (usually at 0.45 to 4.5 kg/ha) against corn rootworms, strawberry root weevils, wireworms, white grubs, and subterranean cutworms infesting a wide range of crops (Glooschenko and Lott 1977). In the past, at least 75 different formulations containing chlordane as the active insecticidal ingredient had been registered for sale in Canada. The most widely sold formulation, accounting for about 60% of chlordane in soils, was the 25% granular type that was used extensively for corn rootworm control (NRCC 1975). Sales of chlordane in Canada increased about 10 times between 1969 and 1971 because of restrictions on DDT and other organochlorines; however, chlordane use was restricted in Canada in 1978 (Elliott et al. 1988).

13.4 CONCENTRATIONS IN FIELD COLLECTIONS

13.4.1 General

Chlordanes and their metabolites are ubiquitous in the environment at low concentrations, but at a high occurrence in samples analyzed. Atmospheric transport is considered to be the major route of global dissemination. Some chlordane isomers persist in soils for 3 to 15 years, although there seems to be little accumulation of chlordanes by crop plants grown in these soils. Lengthy persistence of various chlordane isomers, especially *cis*-chlordane and *trans*-nonachlor, has been reported in certain organisms, but this has varied greatly between species and tissues.

In living organisms, chlordane concentrations are usually highest in samples collected near areas where chlordane was applied to control termites or other pests, in predatory species, and in tissues with high lipid content. Food chain biomagnification is usually low, except in certain marine mammals. In some fishes, chlordane levels in muscle have been sufficient to endanger fish health ($>100 \mu\text{g/kg}$ fresh weight) or human fish consumers ($>300 \mu\text{g/kg}$ fresh weight).

13.4.2 Nonbiological Samples

Air and water transport of technical chlordane has resulted in the detection of chlordane and its metabolites in nonbiological samples worldwide (Table 13.1). Chlordane enters the atmosphere mainly through aerial applications of dust and spray formulations, soil erosion by wind, and volatilization from soil and water (WHO 1984). In aquatic systems, chlordane enters by way of surface runoff and rainfall; chlordane is rapidly adsorbed onto bottom sediments, where it persists (WHO 1984). Atmospheric transport of chlordanes is considered the major route of global dissemination (Pyysalo et al. 1981; Wickstrom et al. 1981). Levels of chlordane compounds in the marine atmosphere of the southern hemisphere are nearly the same as those of DDT and its metabolites; this strongly suggests that chlordane compounds are globally distributed and dispersed (Kawano et al. 1985). The yearly input of *cis*-chlordane to the Arctic Ocean from atmospheric sources is estimated at 3000 kg. If *cis*-chlordane constitutes 19% of technical chlordane, then more than 600,000 kg of technical chlordane have entered the Arctic Ocean since 1948 (Hoff and Chan 1986). Chlordane is frequently measured in the air of buildings where the compound has been used for insect control (WHO 1984). Chlordane has been found in household dust in the homes of farmers and pesticide formulators at exceedingly high mean levels: 5.8 to 23.1 mg/kg air-dried dust (WHO 1984).

Chlordane has been detected in both groundwater and surface water at low levels of 0.001 to 0.01 $\mu\text{g/L}$ (USEPA 1988). A high frequency of chlordane detection was noted in seawater samples collected from a Hawaiian marina: up to 90% of all samples contained *cis*-chlordane, and 68% contained *trans*-chlordane (IARC 1979). Because of chlordane's use as a soil-injected insecticide and its persistence, it has the potential to contaminate groundwater, particularly when it is applied near existing wells (USEPA 1988).

In soils, chlordane is comparatively immobile and persistent and has only a limited capacity for translocation into edible portions of food crops (NRCC 1975). Total chlordane content in cropland soils nationwide in 1971/72 averaged 0.05 to 0.06 mg/kg dry weight, and ranged between 0.01 and 7.9 mg/kg dry weight (Table 13.1). Maximum values, in excess of 3.0 mg/kg, were recorded in soils from Illinois (7.0), Ohio (5.0), Indiana (4.1), and Iowa (3.4) (Carey et al. 1978, 1979). The half-life of chlordane in soil when used at agricultural rates is about 1 year (IARC 1979), but residues may be measurable much longer, depending on soil type (NRCC 1975). For example, 10 years after application of 8.5 kg technical chlordane/ha, up to 20% of the active ingredients were still measurable; in another study, 15% of the active ingredients remained in turf soils after 15 years (WHO 1984). *Cis*- and *trans*-chlordanes were less persistent in mineral soils

than in organic mucky soils (WHO 1984). Chlordanes were usually detected in surface soils of basins receiving urban runoff water at a maximum concentration of 2.7 mg/kg. This decreased with soil depth to <0.03 mg/kg at depths below 24 cm (Nightingale 1987). Chlordane levels in soils near Air Force bases in the United States in 1975/76 were similar to those found in nonmilitary urban environments (Lang et al. 1979).

Chlordanes in sediments usually were highest in those sediments with the highest organic content, especially downstream from the center of anthropogenic activities (Smith et al. 1987). Sediments from a lake in which the overlying water column initially was treated to contain 10 µg technical chlordane/L contained measurable residues 2.8 years after application: total chlordanes — consisting of *cis*-chlordane, *trans*-chlordane, and *trans*-nonachlor — averaged 20 µg/kg and ranged up to 46 µg/kg (Albright et al. 1980). The yearly flux of chlordanes from sediments to the overlying water column has been estimated at 0.02 µg/m², based on measurements made in the Sargasso Sea and deep North Atlantic Ocean between 1978 and 1980 (Knap et al. 1986).

Table 13.1 Chlordane Concentrations in Selected Nonbiological Samples

Sample, Units of Measurement, Chlordane Isomer, and Other Variables	Concentration ^a	Reference ^b
AIR, in ng/m³		
Between Bermuda and Rhode Island, February–June 1973, total chlordanes	(<0.005–0.9)	1
United States, 16 states		
2477 of 2479 samples	ND	2
2 samples	84, 204	2
Southern Hemisphere, 1980–84, various locations, total chlordanes	(0.005–0.19)	3
Northern Hemisphere, 1973–78, Atlantic Ocean, total chlordanes	(0.009–0.084)	3
Pacific Ocean, 1979–81, total chlordanes	0.013	3
Canadian Arctic, summer 1984		
<i>cis</i> -Chlordane	0.0015	4
<i>trans</i> -Chlordane	(0.0005–0.002)	4
<i>cis</i> -Nonachlor	(ND–0.0004)	4
<i>trans</i> -Nonachlor	0.0012	4
FRESHWATER, in g/L		
Lake Baikal, Siberia; June 1991; dissolved vs. particulate		
<i>cis</i> -Chlordane	0.009–0.013 vs. 0.003	18
<i>trans</i> -Chlordane	0.014–0.017 vs. 0.002	18
Heptachlor	0.0059 vs. <0.001	18
<i>cis</i> -Nonachlor	0.0007 vs. ND	18
<i>trans</i> -Nonachlor	0.004–0.009 vs. 0.002	18
Total chlordanes	0.040 vs. 0.006	18
Nova Scotia		
<i>cis</i> -Chlordane	(ND–31.3)	1
<i>trans</i> -Chlordane	(ND–17.9)	1
Ontario, Canada		
<i>trans</i> -Chlordane	(<0.001–0.021)	1
Lower Mississippi River		
<i>trans</i> -Chlordane	(0.0004–0.0012)	1
Iraq, Tigris–Euphrates Delta, 1986		
<i>cis</i> -Chlordane	0.057, Max. 0.067	5
<i>trans</i> -Chlordane	0.015, Max. 0.021	5
Urban runoff		
Lake water, total chlordanes		
Start (treated)	10.0	7
Day 421 after treatment	(0.008–0.011)	7

Table 13.1 (continued) Chlordane Concentrations in Selected Nonbiological Samples

Sample, Units of Measurement, Chlordane Isomer, and Other Variables	Concentration ^a	Reference ^b
SEAWATER, in g/L		
Northern Pacific Ocean and Bering Sea, 1980–82		
<i>cis</i> -Chlordane	(0.004–0.005)	8
<i>trans</i> -Chlordane	(0.004–0.005)	8
<i>cis</i> -Nonachlor	<0.0002	8
<i>trans</i> -Nonachlor	(0.0013–0.0015)	8
Oxychlordane	<0.0002	8
Sargasso Sea		
<i>cis</i> -Chlordane	<0.001	8
<i>trans</i> -Chlordane	<0.001	8
Tokyo Bay, Japan, total chlordanes	0.002	8
SOILS, in mg/kg dry weight		
Everglades National Park, Florida, 1976, total chlordanes		
In National Park	Max. 0.005	9
Adjacent agricultural area	Max. 0.195	9
United States, total chlordanes		
Croplands		
1970	0.08 (0.01–13.3)	10
1971	0.06 (0.01–7.0)	11
1972	0.05 (0.01–7.9)	12
35 states	(0.01–13.3)	1
Urban areas		
8 cities	(0.02–20.5)	1
14 cities	(0.04–13.9)	1
Near U.S. military bases, 1975–76, upper 7.6 cm		
Residential areas		
1975	5.4 (ND–52.1)	13
1976	0.2 (ND–1.2)	13
Nonuse areas		
1975	0.09 (ND–1.8)	13
1976	0.2 (ND–3.4)	13
Golf course		
1975	0.7 (ND–4.6)	13
1976	0.6 (ND–3.1)	13
Turf soils, northeastern U.S., 1986–90		
Golf course turf, total chlordanes		
Greens	11.0 (0.03–40.0)	17
Fairways	1.1 (0.3–2.1)	17
Private residence lawns		
Oxychlordane	<0.1–0.18	17
Heptachlor	0.0–0.15	17
<i>cis</i> -Chlordane	0.14–2.6	17
<i>trans</i> -Chlordane	0.08–2.2	17
Total chlordanes	Max. 15.0	17
SEDIMENTS, in g/kg		
Total chlordanes		
Lake Superior, 1973	ND	14
Long Island, New York	Usually 20–200, Max. 580	15
New England	Max. 30	19
Streams tributary to San Francisco Bay	(4–8)	1
Upper Rockaway River, New Jersey	(<1–510)	16

Table 13.1 (continued) Chlordane Concentrations in Selected Nonbiological Samples

Sample, Units of Measurement, Chlordane Isomer, and Other Variables	Concentration ^a	Reference ^b
Hawaiian marina		
<i>cis</i> -Chlordane	3.0 (0.4–5.3)	1
<i>trans</i> -Chlordane	2.3 (1.3–5.1)	1
Bottom muds, Ontario, Canada		
<i>trans</i> -Chlordane	<0.1–3.1	1
Stream beds, drainage ditches, Nova Scotia		
<i>cis</i> -Chlordane	(0–664)	1
<i>trans</i> -Chlordane	(0–51)	1

^a Concentrations are shown as mean, extremes in parentheses, maximum (Max.), and nondetectable (ND).

^b 1, IARC 1979; 2, USEPA 1980; 3, Kawano et al. 1985; 4, Hoff and Chan 1986; 5, DouAbul et al. 1988; 6, Nightingale 1987; 7, Albright et al. 1980; 8, Kawano et al. 1988; 9, Requejo et al. 1979; 10, WHO 1984; 11, Carey et al. 1978; 12, Carey et al. 1979; 13, Lang et al. 1979; 14, Frank et al. 1980; 15, Wood et al. 1986; 16, Smith et al. 1987; 17, Okoniewski and Novecky 1993; 18, Kucklick et al. 1994; 19, Johnson et al. 1993.

13.4.3 Terrestrial Crops

Maximum total chlordane concentrations in corn (*Zea mays*) and sorghum (*Sorghum halepense*) samples collected nationwide in 1971, in µg/kg dry weight, were 480 in corn kernel, 1260 in cornstalk, and 420 in sorghum (Carey et al. 1978). These values were somewhat lower in 1972: 150 in kernels, 410 in stalks, and 150 in sorghum (Carey et al. 1979). Concentrations in various crops grown in soils treated with 15 kg technical chlordane/ha were always <260 µg/kg dry weight when clay content was 12%, and <150 µg/kg when clay content was 28% (WHO 1984).

13.4.4 Aquatic Invertebrates

Extremely high levels of chlordanes (e.g., 1746 to 7643 µg/kg FW) were measured in several species of South Florida corals collected in 1985 (Table 13.2). It has been speculated that the elevated levels were due to the illegal disposal of chlordanes off Key Largo, Florida, in 1982 (Glynn et al. 1989).

Maximum concentrations of chlordanes in American oysters (*Crassostrea virginica*) taken in the Gulf of Mexico in 1976 were near 0.1 µg/kg dry weight (Table 13.2). Chlordane concentrations were substantially lower than concentrations of other organochlorines measured in oysters, such as DDT (28 µg/kg) and polychlorinated biphenyls (90 µg/kg), suggesting a need for additional studies on interaction effects of chlordane residues with those of other environmental chemicals (Rosales et al. 1979).

Marine clams and worms tended to underrepresent chlordane concentrations in the ambient sediments. Concentration factors were less than 0.2 for clams and 0.6 for worms (Ray et al. 1983). Similarly, chlordane concentrations in clams from the Shatt al-Arab River in Iraq closely reflected chlordane concentrations in water particulates when compared to levels in water columns or in sediments (DouAbul et al. 1988).

13.4.5 Fishes

Health advisories have been issued near Lawrence, Kansas, based on chlordane levels in edible fish tissues. In fish from the Kansas River, Kansas, in 1986, chlordanes were detected more frequently and at higher levels than other contaminants measured (Arruda et al. 1987). More than 80% of the sites sampled in Kansas had detectable chlordanes in fish; at more than 50% of these sites, levels exceeded 0.1 mg/kg fresh weight — a guideline for the protection of predatory fish. At three urban sites in Kansas, concentrations of chlordanes in fish have approached or exceeded

the Food and Drug Administration action level of 0.3 mg chlordane/kg fresh weight for protection of human health. The most likely source of chlordane in fish from the Kansas River is urban and suburban use of chlordane as a termite control agent (Arruda et al. 1987). Other health advisories based on chlordane contamination have been issued. In 1985, people were warned not to eat shovelnose sturgeon (*Scaphirhynchus platorynchus*) from the Missouri and Mississippi Rivers. In 1987, advisories warned against sturgeon consumption in the Missouri River between Kansas City and St. Louis, and against bullhead catfishes, suckers, carps, sturgeons, and sturgeon eggs in the Mississippi River near St. Louis (Bush and Grace 1989). Chlordane residues in fish muscle decreased by 25 to 33% with baking, char broiling, and frying (Zabik et al. 1995).

In general, chlordane residues in fishes were elevated in the vicinity of sewage outfalls (Miskiewicz and Gibbs 1994), in older fishes (Borgmann and Whittle (1991), and near industrialized areas (McCain et al. 1996). Chlordane residues were detected in 36% of all fish samples collected in major domestic watersheds in 1976 (Veith et al. 1979). In the Great Lakes region in 1979, chlordane residues in fish tissues exceeded 100 µg/kg on a fresh weight basis in about 40% of the samples measured. Residues were highest in samples collected near Alton, Illinois, and Fairborn, Ohio (Kuehl et al. 1983). In 1987, chlordane was ubiquitous in catfish tissues throughout a 1968-km stretch of the Mississippi River and its tributaries, being highest in catfish from the Illinois River, Missouri River, Ohio River, and the Mississippi River near Chester, IL, Helena, AK, Arkansas City, AK, and at the confluence of the Old River, LA, and at Belle Chaise, LA (Leiker et al. 1991). Elevated concentrations of chlordanes in sediments, stomach contents, liver, and bile of winter flounder (*Pleuronectes americanus*) from 22 sites in the northeastern United States were significant risk factors for the development of several lesion types, including proliferative and necrotic lesions (Johnson et al. 1993).

The two most abundant components of technical chlordane found in fish tissues from Tokyo Bay, Japan, were *trans*-nonachlor and *cis*-chlordane (Yamagishi et al. 1981b) (Table 13.2). However, this may vary between locales. For example, *cis*-chlordane and *trans*-chlordane were the most abundant components in fish samples collected throughout Japan during the past 20 years, followed, in order, by *cis*-nonachlor, *trans*-nonachlor, and oxychlordane (Loganathan et al. 1989). Of the total chlordanes measured in muscle of northern pike (*Esox lucius*) from the Baltic Sea, 37% was *cis*-chlordane, 34% *trans*-chlordane, and 15% each *trans*-nonachlor and oxychlordane (Moilanen et al. 1982). For liver tissue of northern pike, 35% was oxychlordane, 28% *trans*-chlordane, 22% *cis*-chlordane, and 14% *trans*-nonachlor (Moilanen et al. 1982). In the United States, only chlordanes and nonachlors have been detected as significant residues in fish collected nationwide. The most abundant component was *cis*-chlordane, followed by *trans*-nonachlor, *trans*-chlordane, and *cis*-nonachlor (Ribick and Zajicek 1983). The two most abundant components were detected in about 93% of all fish samples collected in 1978 and 1979. Residues were usually highest in Hawaii, the Great Lakes, and the Corn Belt (Ribick and Zajicek 1983). Fish from the Manoa Stream in Hawaii had high residues because of heavy use of technical chlordane in pineapple culture and termite control (Ribick and Zajicek 1983). Nationwide monitoring of freshwater fishes showed that mean chlordane concentrations in whole fish did not change from 1980 to 1984, following a period of decline; however, *trans*-nonachlor replaced *cis*-chlordane as the most abundant component, suggesting a lower influx of chlordane to the aquatic environment from terminated use of chlordane in agriculture in the mid-1970s (Schmitt et al. 1990) (Table 13.2). Residues of *cis*-chlordane and *trans*-nonachlor — the most abundant and persistent of the chlordane components measured — were present at 85% and 89%, respectively, of the stations sampled in 1984 (Schmitt et al. 1990). Maximum chlordane levels in fish in 1984 occurred in the Great Lakes, Hawaii, watersheds of the Ohio, Missouri, and Mississippi Rivers, and in the Delaware and Raritan Rivers in the Northeast (Schmitt et al. 1990).

Atmospheric transport may be the main source of chlordane in Finland — a country that prohibits chlordane use — because chlordanes are distributed evenly in the Finnish environment (Pyysalo et al. 1983). No chlordane compounds were detected in rainbow trout (*Oncorhynchus*

mykiss) taken from lakes in eastern Finland, although measurable residues were detected in other fish species. This phenomenon is attributed to the superior ability of rainbow trout to metabolize chlordanes to oxychlordane (Pyysalo et al. 1981).

13.4.6 Amphibians and Reptiles

Chlordane residue data for amphibians and reptiles are extremely limited. Maximum concentrations of chlordane isomers did not exceed 70 µg/kg FW of oxychlordane in eggs of the American crocodile, *Crocodylus acutus*, or 250 µg/kg FW in carcass of the common garter snake, *Thamnophis sirtalis* (Table 13.2). However, California newts, *Taricha torosa*, taken near a lake treated with 10 µg/L technical chlordane had greatly elevated chlordane residues in liver and comparatively low concentrations in carcass, stomach, and stomach contents. After 14 days, livers contained about 34 mg/kg total chlordanes lipid weight — about 19% chlordanes, 9% nonachlors, and 6% chlorides (Albright et al. 1980). After 2.8 years, 98% of the total chlordanes was lost. *Trans*-nonachlor was the most persistent component in newt liver, accounting for up to 55% of the total chlordanes in specimens collected 2.8 years after application (Table 13.2) (Albright et al. 1980).

13.4.7 Birds

Technical chlordane components and their metabolites — especially oxychlordane — are comparatively elevated in tissues with high lipid content, in older birds, and in raptors (Table 13.2). The oxychlordane concentration of 5.2 mg/kg FW in the liver of one sharp-shinned hawk (*Accipiter striatus*) from the eastern United States was in the range (3 to 10 mg/kg FW liver) associated with acute toxicity of raptors (Wood et al. 1996) (Table 13.2). Other organochlorine compounds were frequently associated with chlordanes, sometimes at life-threatening concentrations. For example, eggs of peregrine falcons (*Falco peregrinus*) collected nationwide in 1986 to 1989 had DDT levels that ranged between 8.8 and 11.0 mg/kg FW, and total PCB concentrations as high as 14.0 mg/kg FW (Jarman et al. 1993).

Chlordane isomers occur frequently in birds collected nationwide. In 1976, for example, 41% of European starlings (*Sturnus vulgaris*) contained chlordane isomers. In 1979, 60% contained chlordane isomers (Cain and Bunck 1983). In 1982, oxychlordane was detected in 45% of all starlings analyzed, *trans*-nonachlor in 40%, *cis*-nonachlor in 9%, and *cis*- and *trans*-chlordanes in fewer than 2% (Bunck et al. 1987). Chlordane isomers were detected at frequencies exceeding 50% in wings of American black ducks (*Anas rubripes*) and mallards (*Anas platyrhynchos*) from the Atlantic Flyway in 1976/77 (White 1979), in eggs of 19 species of Alaskan seabirds in 1973 to 1976 (Ohlendorf et al. 1982), and in carcasses of ospreys (*Pandion haliaetus*) found dead in the eastern United States between 1975 and 1982 (Wiemeyer et al. 1987). Frequency of detection for chlordane isomers ranging between 14 and 40% has been reported in wings of black ducks and mallards from flyways other than the Atlantic Flyway (White 1979), in 19 species of passeriformes from the western United States in 1980 (DeWeese et al. 1976), and in seven species of Texas shorebirds in 1976/77 — although residues in shorebirds were below levels known to adversely affect reproduction or survival (White et al. 1980).

Carcasses of bald eagles (*Haliaeetus leucocephalus*) collected between 1978 and 1981 usually contained oxychlordane at 45 to 56% frequency, *trans*-nonachlor at 62 to 74%, *cis*-chlordanes at 38 to 45%, and *cis*-nonachlor at 38 to 47%. Frequency of occurrence in the brain was lower, ranging between 19 and 55% for individual isomers (Reichel et al. 1984). However, a positive correlation was established in bald eagles between concentration of chlordanes in brain on a fresh weight basis and in carcass on a lipid weight basis. This relation seems to extend to other avian species as well (Barbehenn and Reichel 1981). Bald eagles also contained appreciable quantities of other organochlorine compounds, and a few — for example, dieldrin — were sometimes present at concentrations

considered life-threatening (Reichel et al. 1984). A similar situation exists in other species of raptors (Ambrose et al. 1988).

Some chlordane isomers tend to persist in avian tissues for lengthy periods. In northern gannets (*Sula bassanoides*), the half-time persistence of *cis*-chlordane, *cis*-nonachlor, and oxychlordane was estimated at 11.2, 19.4, and 35.4 years, respectively (Elliott et al. 1988). Oxychlordane residues in the thick-billed murre (*Uria lomvia*) tend to be high because of rapid excretion through uropygial gland secretions of *cis*- and *trans*-chlordanes and nonachlors, and to biotransformation of these and other chlordane components to oxychlordane (Kawano et al. 1988). This observation is alarming because the metabolite oxychlordane has proven much more toxic and persistent than the parent chemicals (Kawano et al. 1988). Secondary poisonings of raptors after consumption of poisoned bait or prey that had accumulated a large quantity of chlordane were documented for the red-shouldered hawk (*Buteo lineatus*) and the great horned owl (*Bubo virginianus*); concentrations of oxychlordane and heptachlor epoxide found in brain and carcass of both species (Blus et al. 1983) were within the lethal range reported in experimental studies (Stickel et al. 1979).

Chlordane-induced mortality of the long-billed curlew (*Numenius americanus*) has been documented at least four times since 1978, despite restriction of technical chlordane use since 1980 to subterranean applications for termite control (Blus et al. 1985). Death of these curlews was probably due to over-winter accumulations of oxychlordane of 1.5 to 5.0 mg/kg brain FW and of heptachlor epoxide at 3.4 to 8.3 mg/kg — joint lethal ranges for oxychlordane and heptachlor epoxide in experimental birds — compared to 6 mg/kg brain for oxychlordane alone and 9 mg/kg for heptachlor epoxide alone (Blus et al. 1985). Additional research is needed on toxic interactions of chlordane components with each other and with other chemicals in the same environment.

13.4.8 Mammals

Chlordane levels in mammals were usually highest in lipids, in animals collected near areas of high chlordane use, and in aquatic mammals, especially marine species (Table 13.2). In mammals, lipid-soluble and persistent organochlorines are transferred from maternal lipid stores to pups during lactation. The milk of marine mammals is especially rich in lipids and can range up to 60%; about 98% of the chlordane pesticide residues in pups of marine mammals is accumulated from maternal milk (Jenssen et al. 1996). In the ringed seal (*Phoca hispida*), lactational transfer of chlordanes is estimated at 30% of the whole-body chlordane burden in the mature female (Nakata et al. 1998). Biomagnification of total chlordanes through the food chain was strongly evident in marine mammals; chlordanes were concentrated gradually from zooplankton, through squid and fish, to porpoises and dolphins (Kawano et al. 1986; Muir et al. 1988) (Table 13.2). Chlordane residues in marine mammals were positively related to lipid content and not to the age of the animal (Pertilla et al. 1986). Chlordanes and other organochlorine compounds in adipose tissues and milk of polar bears (*Ursus maritimus*) increased markedly on a lipid weight basis with increased fasting typical of hibernation. The possibility of chlordane-induced effects on the reproduction of polar bears exists and could be a factor in the slow decline of the western Hudson Bay, Canada, polar bears (Polischuk et al. 1995). Concentrations of chlordanes in adipose tissues of polar bears in their known range sampled between 1989 and 1993 ranged between 727 and 4632 µg/kg LW; adult males had 30% less chlordanes than females, and chlordane concentrations in both sexes were dominated by oxychlordane (46.8% of total chlordanes), nonachlors (19.9%), and heptachlor epoxide (7.7%) (Norstrom et al. 1998).

A high death rate over a 2-year period was evident in the little brown myotis (*Myotis lucifugus*) following application of chlordane. Young bats were most affected in the first year after application and adults in the second year (Kunz et al. 1977). Residues were greatly elevated in the brain and carcass of another bat, the gray myotis (*Myotis grisescens*) — an endangered species — found dead near areas of high chlordane use (Table 13.2). Animals reared in captivity for slaughter may

contain chlordane and other pesticides in tissues obtained most probably from forage, and possibly from drinking water. Some animals, such as bison (*Bison bison*), habitually roll in the dust and residual pesticides — including oxychlordane — adsorbed on soil particles may contribute to the residues (MacNeil et al. 1991). Chlordane levels in raccoons (*Procyon lotor*) from Mississippi declined between 1978 and 1988, with the decline attributed to decreased pesticide use of chlordane compounds (Ford and Hill 1990).

Chlordane levels in human blood were comparatively elevated among individuals living in residences treated with chlordane during the past 5 years, and in termite control operators. Oxy-chlordane levels were usually significantly higher than *trans*-nonachlor, except among those who consumed large quantities of fish (Wariishi et al. 1986; Wariishi and Nishiyama 1989).

Table 13.2 Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
AQUATIC INVERTEBRATES		
Bivalve molluscs, 3 species, Ebro River, Spain, 1980, soft parts, total chlordanes	(<1–21) DW	1
Corals, 10 species, Biscayne National Park, near Miami, Florida, July–September 1985, <i>cis</i> - and <i>trans</i> -chlordane		
Scleractinian corals		
<i>Colpophyllia amaranthus</i>	Max. 6 FW	84
<i>Colpophyllia natans</i>	Max. 62 FW	84
<i>Diploria clivosa</i>	Max. 32 FW	84
<i>Diploria strigosa</i>	Max. 6 FW	84
<i>Montastrea annularis</i>	Max. 1746 FW	84
<i>Porites asteroides</i>	Max. 2256 FW	84
<i>Siderastrea siderea</i>	Max. 145 FW	84
Octacorals		
<i>Briareum abestinum</i>	Max. 1180 FW	84
<i>Gorgia flabellum</i>	Max. 6626 FW	84
<i>Pseudopterogorgia acerosa</i>	Max. 7643 FW	84
Asiatic clam, <i>Corbicula fluminea</i> , Iraq, 1986, soft parts		
<i>cis</i> -Chlordane	6 FW; Max. 10 FW	2
<i>trans</i> -Chlordane	5 FW; Max. 9 FW	2
American oyster, <i>Crassostrea virginica</i> , Gulf of Mexico, Mexico, summer, 1976, soft parts, <i>cis</i> -chlordane	Max. 0.1 DW	3
Krill, <i>Euphausia superba</i> , Antarctic Ocean 1980–82, whole		
<i>cis</i> -Chlordane	0.58 LW	4
<i>trans</i> -Chlordane	0.51 LW	4
<i>cis</i> -Nonachlor	0.22 LW	4
<i>trans</i> -Nonachlor	0.8 LW	4
Oxychlordane	0.1 LW	4
Eight-armed squid, <i>Gonatopsis borealis</i> , North Pacific Ocean, 1980–82, whole		
<i>cis</i> -Chlordane	15 (11–18) LW	4
<i>trans</i> -Chlordane	8.1 (6.3–9.9) LW	4
<i>cis</i> -Nonachlor	2.4 (2.2–2.8) LW	4
<i>trans</i> -Nonachlor	18 (14–20) LW	4
Oxychlordane	1.2 (0.8–1.6) LW	4
Total chlordanes	44 (35–52) LW	5
American lobster, <i>Homarus americanus</i> , east coast of Canada, 1971–77, hepatopancreas		
<i>cis</i> - and <i>trans</i> -Chlordane	80–100 LW	6
<i>cis</i> -Nonachlor	30 LW	6
<i>trans</i> -Nonachlor	(380–440) LW	6

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Mysid shrimp, <i>Mysis relicta</i> , Lake Michigan, 1980–81, whole		
July		
<i>cis</i> -Chlordane	Max. 35 DW	7
<i>trans</i> -Chlordane	Max. 44 DW	7
October		
<i>cis</i> -Chlordane	ND	7
<i>trans</i> -Chlordane	(72–151) DW	7
Sandworm, <i>Neanthes virens</i> , Portland, Maine, 1980, whole, total chlordanes	Max. 5.4 FW	8
Oysters, Hawaii, soft parts		
<i>cis</i> -Chlordane	13 (1.6–58) FW	9
<i>trans</i> -Chlordane	8 (1.4–23) FW	9
Norway lobster, <i>Nephrops norvegicus</i> ; Scotland; 1991–92; muscle	0.05–23.0 FW	87
Amphipod, <i>Pontoporeia hoyi</i> , Lake Michigan, 1980–81, whole		
<i>cis</i> -Chlordane	Max. 68 DW	7
<i>trans</i> -Chlordane	Max. 184 DW	7
Crawfish, <i>Procambarus clarkii</i> , Louisiana, 1978–79, whole		
<i>cis</i> -Chlordane	Max. 20 FW	10
<i>trans</i> -Chlordane	Max. 26 FW	10
Short-necked clam, <i>Tapes philippinarum</i> , Tokyo Bay, Japan, 1978		
Muscle		
<i>cis</i> -Chlordane	5.1 FW	11
<i>trans</i> -Chlordane	2.3 FW	11
<i>cis</i> -Nonachlor	0.7 FW	11
<i>trans</i> -Nonachlor	1.3 FW	11
Oxychlordane	0.1 FW	11
Total chlordanes	9.5 FW	11
Viscera		
<i>cis</i> -Chlordane	19.0 FW	11
<i>trans</i> -Chlordane	11.0 FW	11
<i>cis</i> -Nonachlor	3.1 FW	11
<i>trans</i> -Nonachlor	7.9 FW	11
Oxychlordane	0.2 FW	11
Total chlordanes	40.6 FW	11
Soft parts		
<i>cis</i> -Chlordane	10.0 FW	11
<i>trans</i> -Chlordane	5.7 FW	11
<i>cis</i> -Nonachlor	3.7 FW	11
<i>trans</i> -Nonachlor	4.4 FW	11
Oxychlordane	0.3 FW	11
Total chlordanes	21.0 FW	11
Zooplankton, North Pacific Ocean, 1980–82, whole		
<i>cis</i> -Chlordane	19 (13–27) LW	4
<i>trans</i> -Chlordane	13 (7–20) LW	4
<i>cis</i> -Nonachlor	5 (3.2–8.7) LW	4
<i>trans</i> -Nonachlor	14 (12–15) LW	4
Oxychlordane	3 (2.3–3.8) LW	4
Total chlordanes	54 (40–72) LW	5

TERRESTRIAL INVERTEBRATES

Calliphorid fly larvae; from chlordane-poisoned dead birds; Rochester, NY; total chlordanes	700–1000 DW	106
Earthworms; from treated golf course turf; whole	200–2700	106

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Japanese beetle, <i>Popillia japonica</i> ; from chlordane-treated lawn; total chlordane-related compounds	Up to 15,600 FW (may be a chlordane-resistant strain)	106
June beetle, <i>Phyllophaga</i> sp.; found in stomach of chlordane-poisoned screech owl (<i>Otus asio</i>)	800 DW	106
FISH		
Goby, <i>Acanthogobius flavimanus</i> , Tokyo Bay, Japan, 1978, whole		
<i>cis</i> -Chlordane	6 FW; Max. 62 FW	11, 12
<i>trans</i> -Chlordane	9 FW; Max. 15 FW	11, 12
<i>cis</i> -Nonachlor	8 FW; Max. 21 FW	11, 12
<i>trans</i> -Nonachlor	18 FW; Max. 120 FW	11, 12
Oxychlordane	3 FW; Max. 25 FW	11, 12
White shark, <i>Carcharodon carcharias</i> , liver, east coast of Canada, 1971		
<i>cis</i> - and <i>trans</i> -Chlordanes	2600 LW	6
<i>cis</i> -Nonachlor	1700 LW	6
<i>trans</i> -Nonachlor	8500 LW	6
Baltic herring, <i>Clupea harengus</i> , Baltic Sea, 1978–82, whole, total chlordanes		
1978	(200–600) LW	13
1982	(400–800) LW	13
Atlantic herring, <i>Clupea harengus harengus</i> , oil, east coast of Canada, 1977		
<i>cis</i> - and <i>trans</i> -Chlordanes	(40–110) LW	6
<i>cis</i> -Nonachlor	Max. 30 LW	6
<i>trans</i> -Nonachlor	Max. 170 LW	6
Pelagic sculpin, <i>Comephorus dybowski</i> ; whole; Lake Baikal, Siberia; June 1991		
<i>trans</i> -Chlordane	(28–41) LW	107
<i>cis</i> -Chlordane	(62–100) LW	107
<i>trans</i> -Nonachlor	(68–110) LW	107
Heptachlor	<2 LW	107
<i>cis</i> -Nonachlor	(34–41) LW	107
Total chlordanes	240 LW	107
Omul (whitefish), <i>Coregonus autumnalis migratorius</i> ; whole; Lake Baikal, Siberia; June 1991		
Heptachlor	(<2–11) LW	107
<i>trans</i> -Chlordane	(13–35) LW	107
<i>cis</i> -Chlordane	(37–76) LW	107
<i>trans</i> -Nonachlor	(31–71) LW	107
<i>cis</i> -Nonachlor	(9–18) LW	107
Total chlordanes	140 LW	107
Lake whitefish, <i>Coregonus clupeaformis</i>		
Great Lakes, 1978, whole		
<i>cis</i> -Chlordane	(16–94) FW	14
<i>trans</i> -Chlordane	(21–87) FW	14
Total chlordanes	111 FW	14
Lake Superior, Siskiwit Lake, Isle Royale, 1983, whole		
Chlordanes	260 LW; Max. 330 LW	15
Nonachlors	450 LW; Max. 500 LW	15
Oxychlordane	16 LW; Max. 200 LW	15
Common carp, <i>Cyprinus carpio</i>		
Great Lakes, 1979, whole		
<i>cis</i> -Chlordane	Max. 390 FW	16
<i>trans</i> -Chlordane	Max. 360 FW	16

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
<i>cis</i> -Nonachlor	Max. 390 FW	16
<i>trans</i> -Nonachlor	Max. 300 FW	16
San Joaquin River, CA, 1981, whole, total chlordanes	Max. 273 FW; Max. 3578 LW	17
Shad, <i>Dorosoma</i> spp., Louisiana, 1978–79, whole body		
<i>cis</i> -Chlordane	Max. 76 FW	10
<i>trans</i> -Chlordane	Max. 82 FW	10
<i>cis</i> -Nonachlor	Max. 26 FW	10
<i>trans</i> -Nonachlor	Max. 12 FW	10
Northern pike, <i>Esox lucius</i> , Baltic Sea, 1971–82, total chlordanes		
Muscle		
1971	(100–1000) LW	13
1972	(100–1300) LW	13
1973	100 LW	13
1974	800 LW	13
1975	1900 LW	13
1978	(2600–3100) LW	13
1982	(2300–6300) LW	13
Liver		
1971	(100–400) LW	13
1972	(100–300) LW	13
1973	500 LW	13
1974	600 LW	13
1975	700 LW	13
1978	700 LW	13
1982	(1100–2100) LW	13
Fish; Australia; 1989; near sewage outfall, oxychlordane		
Sharks and rays, 6 species		
Liver	Max. 100 FW	96
Muscle	Max. 40 FW	96
Bony fishes, 14 species		
Liver	Max. 860 FW	96
Muscle	Max. 40 FW	96
Fish; Tampa Bay, FL; 1990–92; livers		
Hardhead catfish, <i>Arius felis</i>	14–55 DW	88
Gulf killifish, <i>Fundulus grandis</i>	25–410 DW	88
Longnose killifish, <i>Fundulus majalis</i>	40–560 DW	88
Red drum, <i>Sciaenops ocellatus</i>	170–1080 DW	88
Fish; New Jersey; 1986–91; skin-on muscle fillets; total chlordanes; Camden region vs. Delaware region		
Common carp, <i>Cyprinus carpio</i>		
1986–87	260 FW vs. 51 FW	93
1988–91	275 FW vs. No data	93
Brown bullhead, <i>Ictalurus nebulosus</i>		
1986–87	124 FW vs. 6 FW	93
1988–91	102 FW vs. 65 FW	93
Largemouth bass, <i>Micropterus salmoides</i>		
1986–87	21 FW vs. No data	93
1988–91	48 FW vs. 5 FW	93
Fish, 2 species, muscle, Belmont Lake, Long Island, NY, total chlordanes	380–5200 FW	18
Fish, 4 species, Chesapeake Bay, MD, 1976–80, total chlordanes		
Muscle	70–120 FW; Max. 310–700 FW	19
Gonad	(10–1900) FW	19

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Fish, various species, Maryland, Patuxent River, whole, maximum values, total chlordanes		
1978 vs. 1979	190 FW vs. 480 FW	86
1980 vs. 1981	90 FW vs. 81 FW	86
1982 vs. 1983	275 FW vs. 884 FW	86
1984 vs. 1988	487 FW vs. 90 FW	86
Fish, 4 species, eastern Finland, 1979–82		
Liver		
<i>cis</i> -Chlordane	(ND–76) FW	20
<i>trans</i> -Chlordane	(ND–277) FW	20
<i>trans</i> -Nonachlor	(ND–20) FW	20
Total chlordanes	Max. 320 FW; Max. 410 LW	21
Muscle		
<i>cis</i> -Chlordane	(ND–53) FW	20
<i>trans</i> -Chlordane	(ND–232) FW	20
<i>trans</i> -Nonachlor	(ND–20) FW	20
Total chlordanes	Max. 1770 LW	21
Fish, Great Lakes, 1990–91; skin-on fillets; raw; total chlordanes		
White bass, <i>Morone chrysops</i>	340–470 FW	90
Walleye, <i>Stizostedium vitreum vitreum</i>	22–34 FW	90
Fish, 11 species, Lake Texoma, Texas and Oklahoma, 1979, total chlordanes, whole fish	(ND–24) FW	22
Fish, Mississippi River, 1984–86, total chlordanes		
Shovelnose sturgeon, <i>Scaphirhynchus platorynchus</i>		
Muscle	325–2285 FW	75
Eggs	163–1926 FW	75
Common carp, muscle	55–556 FW	75
Channel catfish, <i>Ictalurus punctatus</i> , muscle	322–1389 FW	25
Fish, Mississippi River, 4 species of catfish, summer 1987, whole, total chlordanes	11–170 FW; 154–3121 LW	91
Fish, Mississippi River, 1988, total chlordanes, muscle		
Channel catfish	Max. 853 FW	75
Common carp	Max. 614 FW	75
Fresh water drum, <i>Aplodinotus grunniens</i>	Max. 19 FW	75
Flathead catfish, <i>Pylodictis olivaris</i>	Max. 272 FW	75
River carpsucker, <i>Carpoides carpio</i>	Max. 160 FW	75
Smallmouth buffalo, <i>Ictiobus bubalus</i>	Max. 200 FW	75
Sauger, <i>Stizostedion canadense</i>	Max. 19 FW	75
Paddlefish, <i>Polyodon spathula</i>	Max. 93 FW	75
Blue catfish, <i>Ictalurus furcatus</i>	Max. 895 FW	75
Bigmouth buffalo, <i>Ictiobus cyprinellus</i>	Max. 360 FW	75
White bass, <i>Morone chrysops</i>	Max. 436 FW	75
Fish, Missouri River, 1984–86, total chlordanes, 3 locations		
Shovelnose sturgeon		
Muscle	146–860 FW	75
Eggs	921–6735 FW	75
Channel catfish, muscle	205–777 FW	75
Common carp, muscle	118–548 FW	75
Fish, Missouri River, 1988, muscle		
Near Rockport, 6 species		
Total chlordanes	Max. 438 FW	75
Heptachlor epoxide	Max. 15 FW	75
Heptachlor	ND	75

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Oxychlordane	Max. 11 FW	75
<i>trans</i> -Chlordane	Max. 25 FW	75
<i>cis</i> -Chlordane	Max. 24 FW	75
<i>trans</i> -Nonachlor	Max. 51 FW	75
<i>cis</i> -Nonachlor	Max. 25 FW	75
Total chlordenes	Max. 4 FW	75
Above Kansas City, 2 species		
Total chlordanes	Max. 290 FW	75
Heptachlor epoxide	Max. 39 FW	75
Heptachlor	ND	75
Oxychlordane	Max. 48 FW	75
<i>trans</i> -Chlordane	Max. 20 FW	75
<i>cis</i> -Chlordane	Max. 25 FW	75
<i>trans</i> -Nonachlor	Max. 55 FW	75
<i>cis</i> -Nonachlor	Max. 14 FW	75
Total chlordenes	Max. 35 FW	75
Below Kansas City, 6 species		
Total chlordanes	95–2450 FW	75
Heptachlor epoxide	3–24 FW	75
Heptachlor	ND	75
Oxychlordane	ND–29 FW	75
<i>trans</i> -Chlordane	4–266 FW	75
<i>cis</i> -Chlordane	7–260 FW	75
<i>trans</i> -Nonachlor	9–167 FW	75
<i>cis</i> -Nonachlor	5–66 FW	75
Total chlordenes	4–144 FW	75
Fish, various species, whole		
Wabash River, Indiana		
<i>cis</i> -Chlordane	13 FW	16
<i>trans</i> -Chlordane	9 FW	16
<i>cis</i> -Nonachlor	5 FW	16
<i>trans</i> -Nonachlor	20 FW	16
Oxychlordane	<0.5 FW	16
Ashtabula River, Ohio,		
Total chlordanes	<0.5 FW	16
Great Lakes area, 1978		
<i>cis</i> - and <i>trans</i> -Chlordanes	Max. 2680 FW	23
<i>cis</i> - and <i>trans</i> -Nonachlors	Max. 3070 FW	23
Oxychlordane	Max. 167 FW	23
Fish, United States, nationwide, 1976–84, whole		
<i>cis</i> -Chlordane		
1976–77	60 FW; Max. 930 FW; 600 LW	24, 76
1978–79	70 FW; Max. 2530 FW; 700 LW	24, 76
1980–81	30 FW; Max. 360 FW; 300 LW	24, 76
1984	30 FW; Max. 660 FW	76
<i>trans</i> -Chlordane		
1976–77	20 FW; Max. 320 FW; 300 LW	24, 76
1978–79	20 FW; Max. 540 FW; 300 LW	24, 76
1980–81	20 FW; Max. 220 FW; 200 LW	24, 76
1984	20 FW; Max. 350 FW	76
<i>cis</i> -Nonachlor		
1976–77	10 FW; Max. 490 FW; 100 LW	24, 76
1978–79	30 FW; Max. 710 FW; 300 LW	24, 76
1980–81	20 FW; Max. 270 FW; 300 LW	24, 76
1984	20 FW; Max. 450 FW	76

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
<i>trans</i> -Nonachlor		
1976–77	30 FW; Max. 950 FW; 300 LW	24, 76
1978–79	50 FW; Max. 2710 FW; 600 LW	24, 76
1980–81	40 FW; Max. 770 FW; 500 LW	24, 76
1984	30 FW; Max. 1000 FW	76
Oxychlordane		
1978–79	10 FW; Max. 740 FW; 100 LW	24, 76
1980–81	10 FW; Max. 330 FW; 100 LW	24, 76
1984	10 FW; Max. 290 FW	76
Heptachlor epoxide		
1976–77	10 FW; Max. 780 FW	76
1978–79	20 FW; Max. 1170 FW	76
1980–81	10 FW; Max. 270 FW	76
1984	10 FW; Max. 290 FW	76
Fish, marine, Scotland, 1991–92, various locations, total chlordanes, liver vs. muscle		
Baltic herring, <i>Clupea harengus</i>	No data vs. <0.8–204.0 FW	87
Atlantic cod, <i>Gadus morhua</i>	31–126 FW vs. 0.05–1.5 FW	87
Dab, <i>Limanda limanda</i>	6–98 FW (Max. 475 LW) vs. 0.5 FW	87
Haddock, <i>Melanogrammus aeglefinus</i>	6–54 FW vs. <0.02–14.4 FW	87
Whiting, <i>Merlangius merlangus</i>	12–130 FW vs. 0.04–2.7 FW	87
Plaice, <i>Pleuronectes platessa</i>	0.1–12.0 FW vs. 0.08–0.5 FW	87
Atlantic cod, <i>Gadus morhua</i>		
East coast Canada, 1977, liver		
<i>cis</i> - and <i>trans</i> -Chlordanes	ND	6
<i>cis</i> -Nonachlor	70 LW	6
<i>trans</i> -Nonachlor	(60–1900) LW	6
Northern Baltic Sea, liver, <i>cis</i> - and <i>trans</i> -Chlordanes	Max. 50 LW	25
Baltic Sea, liver oil, 1971–80 vs. 1981–89		
Total chlordanes	280 (170–350) LW vs. 310 (190–420) LW	89
Heptachlor	3 LW vs. 2 LW	89
Heptachlor epoxide	11 LW vs. 18 LW	89
Shad, <i>Kynosurus punctatus</i> , Tokyo Bay, Japan, 1979, total chlordanes		
Muscle	Max. 41 FW	11
Viscera	Max. 95 FW	11
Sea bass, <i>Lateolabrax japonicus</i> , Tokyo Bay, Japan, 1979, total chlordanes		
Gill	11 FW	11
Muscle	5 FW	11
Brain	41 FW	11
Kidney	37 FW	11
Liver	81 FW	11
Abdominal fat	279 FW	11
Bluegill, <i>Lepomis macrochirus</i> , San Joaquin River, CA, whole fish, 1981, total chlordanes	Max. 14 FW; Max. 759 LW	17
Striped bass, <i>Morone saxatilis</i> , San Francisco Bay, CA, livers		
<i>cis</i> -Chlordane	Max. 9.4 FW	92
<i>trans</i> -Chlordane	Max. 6.1 FW	92
<i>cis</i> -Nonachlor	Max. 9.2 FW	92
<i>trans</i> -Nonachlor	Max. 18.0 FW	92
Total chlordanes	13–42 FW	92

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Fourhorn sculpin, <i>Myoxocephalus quadricornis</i> , Lake Michigan, 1980–81, whole		
<i>cis</i> -Chlordane	Max. 15 DW	7
<i>trans</i> -Chlordane	Max. 70 DW	7
Cutthroat trout, <i>Oncorhynchus clarki</i> , liver, from lake sprayed with 10 µg technical chlordane/L, total chlordanes		
Time, after application		
13.3 weeks	Max. 46,449 LW	26
39.8 weeks	Max. 3940 LW	26
1.15 years	Max. 870 LW	26
2.78 years	ND	26
Chum salmon, <i>Oncorhynchus keta</i> , North Pacific Ocean, 1980–81, whole		
<i>cis</i> -Chlordane	9 (8–11) LW	4
<i>trans</i> -Chlordane	5.2 (5.1–5.9) LW	4
<i>cis</i> -Nonachlor	2 (1.6–2.7) LW	4
<i>trans</i> -Nonachlor	17 (13–21) LW	4
Oxychlordane	2.5 (2.4–2.6) LW	4
Total chlordanes	36 LW	5
Sea lamprey, <i>Petromyzon marinus</i> , Great Lakes, 1978, whole		
<i>cis</i> -Chlordane	(9–202) FW	14
<i>trans</i> -Chlordane	(3–243) FW	14
Total chlordanes	88 FW	14
Winter flounder, <i>Pleuronectes americanus</i> ; NY, NJ, MA, RI; total chlordanes		
Liver	Max. 500 DW	108
Stomach contents	Max. 11,000 DW	108
Lizard goby, <i>Rhinogobius flumineus</i> , Nagarawa River, Japan, whole fish, total chlordanes		
1968–74	(ND–7.6) FW	85
1977–86	(13–40) FW	85
Atlantic salmon, <i>Salmo salar</i> , east coast of Canada, 1976, egg		
<i>cis</i> - and <i>trans</i> -Chlordanes	150 LW	6
<i>cis</i> -Nonachlor	60 LW	6
<i>trans</i> -Nonachlor	(130–210) LW	27
Lake trout, <i>Salvelinus namaycush</i> , Great Lakes, 1977–82, whole fish, oxychlordane		
Lake Michigan		
1977	250 FW	28
1978	180 FW	28
1979	240 FW	28
1980	160 FW	28
1981	60 FW	28
1982	70 FW	28
Lake Huron		
1978	40 FW	28
1979	60 FW	28
1980	60 FW	28
1981	60 FW	28
1982	60 FW	28
Lake Superior		
1977	120 FW	28
1978	40 FW	28

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
1979	140 FW	28
1980	30 FW	28
1981	60 FW	28
1982	40 FW	28
Great Lakes, 1979, whole		
<i>cis</i> -Chlordane	Max. 25 FW	18
<i>trans</i> -Chlordane	Max. 75 FW	18
<i>cis</i> -Nonachlor	Max. 160 FW	18
<i>trans</i> -Nonachlor	Max. 42 FW	18
Great Lakes, Lake Superior, Siskiwit Lake, Isle Royale, 1983, whole		
Chlordanes	420 LW; Max. 770 LW	15
Nonachlors	570 LW; Max. 1100 LW	15
Oxychlordane	73 LW; Max. 170 LW	15
Lake Michigan, 1983–85		
Belly muscle without skin		
<i>cis</i> -Chlordane	510 FW	94
<i>trans</i> -Chlordane	260 FW	94
Heptachlor epoxide	120 FW	94
<i>trans</i> -Nonachlor	740 FW	94
Oxychlordane	360 FW	94
Total chlordanes	1200–2000 FW	94
Dorsal muscle		
Total chlordanes	600 FW	94
Lake Ontario, 1977–88, <i>cis</i> - and <i>trans</i> -chlordane, whole fish	20–140 FW	95
Shovelnose sturgeon, Mississippi River, 1988		
Muscle		
Total chlordanes	Max. 1025 FW	75
Heptachlor epoxide	Max. 31 FW	75
Heptachlor	Max. 3 FW	75
Oxychlordane	Max. 42 FW	75
<i>trans</i> -Chlordane	Max. 75 FW	75
<i>cis</i> -Chlordane	Max. 90 FW	75
<i>trans</i> -Nonachlor	Max. 95 FW	75
<i>cis</i> -Nonachlor	Max. 65 FW	75
Eggs		
Total chlordanes	Max. 1484 FW	75
Heptachlor epoxide	Max. 51 FW	75
Heptachlor	Max. 5 FW	75
Oxychlordane	Max. 56 FW	75
<i>trans</i> -Chlordane	Max. 123 FW	75
<i>cis</i> -Chlordane	Max. 148 FW	75
<i>trans</i> -Nonachlor	Max. 146 FW	75
<i>cis</i> -Nonachlor	Max. 90 FW	75
Walleye pollack, <i>Theragra chalcogramma</i> , North Pacific Ocean, 1980–82, whole		
<i>cis</i> -Chlordane	44 (34–54) LW	4
<i>trans</i> -Chlordane	17 (16–20) LW	4
<i>cis</i> -Nonachlor	10 (6–12) LW	4
<i>trans</i> -Nonachlor	62 (47–92) LW	4
Oxychlordane	8 (5–11) LW	4
Total chlordanes	140 (110–190) LW	5

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Benthic fish, <i>Trematodus bernacchii</i> , Antarctic Ocean, 1980–82, whole		
<i>cis</i> -Chlordane	4 (2–8) LW	4
<i>trans</i> -Chlordane	1.7 (0.8–3.4) LW	4
<i>cis</i> -Nonachlor	3 (0.8–7) LW	4
<i>trans</i> -Nonachlor	11 (2–29) LW	4
Oxychlordane	1 (0.2–1.8) LW	4
AMPHIBIANS		
Frogs, <i>Rana</i> spp., Louisiana, 1978–79, chlordanes, muscle, whole body	ND	10
California newt, <i>Taricha torosa</i> , liver, from lake sprayed with 10 µg technical chlordane/L, total chlordanes		
Time, after application		
14 days	Max. 34,094 LW	26
9.3 months	Max. 10,094 LW	26
1.24 years	Max. 4882 LW	26
2.84 years	Max. 601 LW	26
REPTILES		
American crocodile, <i>Crocodylus acutus</i> , infertile eggs		
<i>cis</i> -Chlordane	Max. 10 FW	29
<i>cis</i> -Nonachlor	Max. 30 FW	29
<i>trans</i> -Nonachlor	Max. 40 FW	29
Oxychlordane	Max. 70 FW	29
Northern water snake, <i>Nerodia sipedon</i> , Lake Michigan, 1978, chlordanes, all tissues, stomach contents	ND	30
Common garter snake, <i>Thamnophis sirtalis</i> , Lake Michigan, 1978		
<i>trans</i> -Nonachlor		
Carcass	(100–250) FW	30
Stomach contents	ND	30
Other chlordane isomers	ND	30
BIRDS		
Sharp-shinned hawk, <i>Accipiter striatus</i> , eastern United States, 1991–93, maximum concentrations from several sites		
Heptachlor epoxide		
Blood	10 FW	97
Brain	<100 FW	97
Liver	60–1100 FW	97
<i>cis</i> -Nonachlor		
Brain	<100 FW	97
Liver	400–1600 FW	97
<i>trans</i> -Nonachlor		
Blood	<20 FW	97
Oxychlordane		
Blood	10–30 FW	97
Liver	10–5210 FW	97
Western grebe, <i>Aechmophorus occidentalis</i> ; Puget Sound, WA; 1985–86; carcass less feathers, bill, legs, and viscera; total chlordanes	10–240 FW	98

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Mallard, <i>Anas platyrhynchos</i> , wing, nationwide 1976–77		
Chlordane isomers		
Atlantic Flyway	(10–60) FW	31
Mississippi Flyway	(10–20) FW	31
Central Flyway	(10–20) FW	31
Pacific Flyway	(10–20) FW	31
1981–82		
<i>cis</i> -Chlordane	Max. 20 FW	32
<i>trans</i> -Nonachlor	Max. 50 FW	32
American black duck, <i>Anas rubripes</i>		
Atlantic Flyway, 1978, egg		
Maryland	50 FW	33
Massachusetts	80 FW	33
Maine	120 FW	33
New Hampshire	(130–160) FW	33
Atlantic Flyway, 1976–77, wing, chlordane isomers	10–50 FW	31
Great blue heron, <i>Ardea herodias</i> , northwestern United States, 1977–82		
Egg		
Oxychlordane	Max. 570 FW	78
Heptachlor epoxide	Max. 460 FW	78
<i>cis</i> -Chlordane	Max. 1360 FW	78
<i>cis</i> -Nonachlor	Max. 690 FW	78
<i>trans</i> -Nonachlor	Max. 2250 FW	78
Whole body, oxychlordane	Max. 470 FW	78
Brain, oxychlordane	Max. 230 FW	78
Canvasback, <i>Aythya valisineria</i>		
Egg, breeding areas, 1972–73		
<i>cis</i> -Chlordane	<1000 FW	34
<i>cis</i> -Nonachlor	ND	34
Oxychlordane	<1000 FW	34
Carcass, (less GI tract, skin, feet, beak), Chesapeake Bay, MD, winter		
<i>cis</i> -Chlordane		
1973	ND	35
1975	9000 FW	35
<i>trans</i> -Nonachlor		
1973	ND	35
1975	11,000 FW	35
Oxychlordane		
1973	ND	35
1975	5000 FW	35
Birds, 4 species, eastern and southern United States, 1972–74, egg, total chlordanes	<100 FW	36
Birds, New York State, 1982–86, found dead or debilitated, brain tissue, chlordane implicated as primary cause of distress		
Cooper's hawk, <i>Accipiter cooperii</i>		
Oxychlordane	Max. 5800 FW	79
Heptachlor epoxide	Max. 4300 FW	79
<i>trans</i> -Nonachlor	Max. 1300 FW	79
Sharp-shinned Hawk, <i>Accipiter striatus</i>		
Oxychlordane	Max. 4300 FW	79
Heptachlor epoxide	Max. 3500 FW	79
<i>trans</i> -Nonachlor	Max. 1000 FW	79

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Great blue heron		
Oxychlordane	Max. 2400 FW	79
Heptachlor epoxide	Max. 600 FW	79
Great horned owl, <i>Bubo virginianus</i>		
Oxychlordane	Max. 8700 FW	79
Heptachlor epoxide	Max. 7700 FW	79
trans-Nonachlor	Max. 2300 FW	79
Blue jay, <i>Cyanocitta cristata</i>		
Oxychlordane	Max. 5000 FW	79
Heptachlor epoxide	Max. 3700 FW	79
trans-Nonachlor	Max. 2000 FW	79
Eastern screech-owl, <i>Otus asio</i>		
Oxychlordane	Max. 2600 FW	79
Heptachlor epoxide	Max. 1800 FW	79
trans-Nonachlor	Max. 1800 FW	79
Common grackle, <i>Quiscalus quiscula</i>		
Oxychlordane	Max. 10,800 FW	79
Heptachlor epoxide	Max. 9100 FW	79
Eastern bluebird, <i>Sialia sialis</i>		
Oxychlordane	Max. 3000 FW	79
Heptachlor epoxide	Max. 2200 FW	79
European starling, <i>Sturnus vulgaris</i>		
Oxychlordane	Max. 7700 FW	79
Heptachlor epoxide	Max. 5000 FW	79
trans-Nonachlor	Max. 500 FW	79
American robin, <i>Turdus migratorius</i>		
Oxychlordane	Max. 1300 FW	79
Heptachlor epoxide	Max. 2700 FW	79
trans-Nonachlor	Max. 1900 FW	79
Cackling Canada geese, <i>Branta canadensis minima</i> , 1973–74, carcass, breeding areas, total chlordanes		
Uncontaminated sites	<1 FW	37
Contaminated (OR, CA)		
Immature male	<0.2 FW	37
Adult male	1.7 FW	37
Adult female	2.0 FW	37
Common goldeneye, <i>Bucephala clangula</i> , fat, oxychlordane		
On arrival at wintering grounds, New York		
Juveniles	40 (10–300) LW	38
Adults	220 (120–370) LW	38
Just prior to spring migration, adults	250 (190–320) LW	38
Dunlin, <i>Calidris alpina</i> , Washington State, 1980, whole, total chlordanes	Max. 60 FW	39
Prairie falcon, <i>Falco mexicanus</i> ; eggs, California, 1986–89		
trans-Nonachlor	(11–60) FW	99
cis-Nonachlor	4 (1–11) FW	99
Heptachlor epoxide	13 (10–18) FW	99
Oxychlordane	30 (18–50) FW	99
Total chlordanes	120 (79–180) FW	99
Peregrine, <i>Falco peregrinus</i>		
Alaska, 1979–84, egg		
trans-Nonachlor	Max. 290 FW	40
Oxychlordane	130 FW; Max. 960 FW	40

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
1986–89, eggs		
East coast, U.S.		
<i>trans</i> -Nonachlor	330 (130–810) FW	99
<i>cis</i> -Nonachlor	290 (100–800) FW	99
Heptachlor epoxide	230 (140–390) FW	99
Oxychlordane	530 (310–890) FW	99
Total chlordanes	1800 (940–3300) FW	99
Total chlordanes		
California	580 (240–1400) FW	99
Colorado	560 (490–640) FW	99
Atlantic puffin, <i>Fratercula arctica</i> , Norway 1982–83, Hornoy, oxychlordane plus <i>trans</i> -nonachlor		
Adults		
Uropygial gland	1429 (48–2815) LW	41
Liver	93 (262–1531) LW	41
Chicks		
Brain	833 (445–1289) LW	41
Chicken, <i>Gallus</i> sp.		
Contaminated through use of former chlordane container to hold cage disinfectants, Australia		
Egg	300 DW	42
Pullets, fat		
30-weeks-old	920 DW	42
80-weeks-old	670 DW	42
Nationwide, U.S., egg		
<i>cis</i> -Chlordane	1 FW	9
<i>trans</i> -Chlordane	2 FW	9
Bald eagle, <i>Haliaeetus leucocephalus</i>		
Addled eggs		
Maine, 1974–79 vs. 1980–84		
Heptachlor epoxide	40 FW vs. 20 FW	100
Oxychlordane	90 FW vs. 110 FW	100
<i>cis</i> -Chlordane	30 FW vs. 70 FW	100
<i>trans</i> -Nonachlor	210 FW vs. 230 FW	100
<i>cis</i> -Nonachlor	30 FW vs. 60 FW	100
Maryland, 1973–79 vs. 1980–84		
Heptachlor epoxide	60 FW vs. 50 FW	100
Oxychlordane	100 FW vs. 90 FW	100
<i>cis</i> -Chlordane	560 FW vs. 210 FW	100
<i>trans</i> -Nonachlor	1000 FW vs. 610 FW	100
<i>cis</i> -Nonachlor	220 FW vs. 160 FW	100
Virginia, 1976–79 vs. 1981–84		
Heptachlor epoxide	120 FW vs. 40 FW	100
Oxychlordane	240 FW vs. 80 FW	100
<i>cis</i> -Chlordane	920 FW vs. 220 FW	100
<i>trans</i> -Nonachlor	1400 FW vs. 480 FW	100
<i>cis</i> -Nonachlor	460 FW vs. 130 FW	100
Wisconsin, 1976–77 vs. 1982–83		
Heptachlor epoxide	80 FW vs. 30 FW	100
Oxychlordane	50 FW vs. 30 FW	100
<i>cis</i> -Chlordane	40 FW vs. 50 FW	100
<i>trans</i> -Nonachlor	310 FW vs. 140 FW	100
<i>cis</i> -Nonachlor	40 FW vs. 40 FW	100

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Egg, total chlordanes		
Maryland, Virginia, 1980–84	1100 FW	82, 100
Maine, 1980–84	500 FW	82, 100
Ohio, 1981–84	840 FW	82, 100
Oregon, 1980–83	220 FW	82, 100
Arizona, 1982–84	160 FW	82, 100
Wisconsin, 1980–83	330 FW	82, 100
Nationwide, found dead or moribund		
1971–74		
Brain		
<i>cis</i> -Chlordane + <i>trans</i> -Chlordane	270 FW	43
<i>cis</i> -Nonachlor	290 FW	43
Oxychlordane	150 FW	43
Carcass (less skin, beak, feet, GI tract, liver)		
<i>cis</i> -Chlordane + <i>trans</i> -Chlordane	27,000 LW	43
<i>cis</i> -Nonachlor	30,000 LW	43
Oxychlordane	15,000 LW	43
1975–77		
Brain		
<i>cis</i> -Chlordane	90–190 FW; Max. 6400 FW	44
<i>cis</i> -Nonachlor	130–170 FW; Max. 750 FW	44
<i>trans</i> -Nonachlor	200–330 FW; Max. 7400 FW	44
Oxychlordane	180–290 FW; Max. 2600 FW	44
Carcass (less skin, viscera)		
<i>cis</i> -Chlordane	220–320 FW; Max. 4500 FW	44
<i>cis</i> -Nonachlor	100–150 FW; Max. 1700 FW	44
<i>trans</i> -Nonachlor	280–380 FW; Max. 6000 FW	44
Oxychlordane	130–180 FW; Max. 2300 FW	44
1978–81		
Brain		
<i>cis</i> -Chlordane	90–190 FW; Max. 2300 FW	45
<i>cis</i> -Nonachlor	100–230 FW; Max. 1600 FW	45
<i>trans</i> -Nonachlor	180–410 FW; Max. 4100 FW	45
Oxychlordane	120–260 FW; Max. 2700 FW	45
Carcass (less skin, viscera)		
<i>cis</i> -Chlordane	120–290 FW; Max. 2200 FW	45
<i>cis</i> -Nonachlor	120–190 FW; Max. 1200 FW	45
<i>trans</i> -Nonachlor	230–370 FW; Max. 4100 FW	45
Oxychlordane	90–130 FW; Max. 1450 FW	45
Loggerhead shrike, <i>Lanius ludovicianus</i> ; eggs; Virginia, 1985–88 (percent frequency of detection)		
Oxychlordane (100%)	60 (20–100) FW	101
Heptachlor (13%)	10 FW	101
Heptachlor epoxide (63%)	20 (10–30) FW	101
<i>cis</i> -Nonachlor (50%)	10 FW	101
<i>trans</i> -Nonachlor (63%)	20 FW	101
<i>cis</i> -Chlordane (13%)	10 FW	101
<i>trans</i> -Chlordane (25%)	10 FW	101
Herring gull, <i>Larus argentatus</i>		
Egg, Canada, 1973		
<i>cis</i> - and <i>trans</i> -Chlordanes	220 LW	6
<i>cis</i> -Nonachlor	20 LW	6
<i>trans</i> -Nonachlor	520 LW	6
Egg, Maine, 1977		
<i>trans</i> -Nonachlor	50 (ND–500) FW	46

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Egg, Virginia, 1977		
<i>trans</i> -Nonachlor	40 (ND–440) FW	46
Oxychlordane	20 (ND–180) FW	46
Chicks, age 21 days		
Liver, oxychlordane	6 (2–13) FW	47
Muscle, oxychlordane	4–140 FW	47
Embryos		
Liver, oxychlordane	110 FW	47
Muscle, oxychlordane	61–140 FW	47
Glaucous-winged gull, <i>Larus glaucescens</i> , Alaska, 1973–76, egg		
<i>cis</i> -Chlordane	Max. 75 FW	48
<i>cis</i> -Nonachlor	Max. 26 FW	48
Oxychlordane	Max. 250 FW	48
Great black-backed gull, <i>Larus marinus</i> , egg, Maine, 1977		
<i>cis</i> -Chlordane	40 (ND–500) FW	46
Oxychlordane	220 (ND–430) FW	46
Red-breasted merganser, <i>Mergus serrator</i> , Lake Michigan, U.S., 1978, carcass		
<i>trans</i> -Nonachlor	Max. 480 FW	30
Long-billed curlew, <i>Numenius americanus</i> , Oregon, 1981–83, convulsions noted, brain		
<i>cis</i> -Chlordane	(110–300) FW	49
<i>trans</i> -Chlordane	(ND–50) FW	49
<i>cis</i> -Nonachlor	(ND–470) FW	49
<i>trans</i> -Nonachlor	(140–4100) FW	49
Oxychlordane	(2500–4400) FW	49
Heptachlor epoxide	(1000–4800) FW	49
Yellow-crowned night-heron, <i>Nycticorax violaceus</i> , Louisiana 1978–79, whole body, total chlordanes	ND	10
Osprey, <i>Pandion haliaetus</i>		
Eastern U.S., 1975–82, dead or moribund, carcass (less skin, feet, and beak)		
<i>cis</i> -Chlordane	Max. 680 FW	50
<i>cis</i> -Nonachlor	Max. 480 FW	50
<i>trans</i> -Nonachlor	Max. 280 FW	50
Oxychlordane	Max. 350 FW	50
Eagle Lake, California, 1973–84, egg		
<i>cis</i> -Chlordane	Max. 10 FW	51
<i>trans</i> -Nonachlor	Max. 6 FW	51
Oxychlordane	Max. 6 FW	51
Fourteen states, U.S., 1970–79, egg		
<i>cis</i> -Chlordane	Usually <100 FW; Max. 1100 FW	52
<i>cis</i> -Nonachlor	Usually <100 FW; Max. 400 FW	52
<i>trans</i> -Nonachlor	Usually <100 FW; Max. 500 FW	52
Oxychlordane	Usually <100 FW; Max. 400 FW	52
Passeriformes, 38 species, western U.S., 1980, carcass (less beak, feet, GI tract, feathers), oxychlordane	Usually <50 FW; Max. 290 FW	53
Brown pelican, <i>Pelecanus occidentalis</i> , South Carolina, 1974–75, egg		
Oxychlordane	Max. 530 FW	81
Heptachlor epoxide	Max. 500 FW	81
<i>cis</i> -Chlordane	Max. 960 FW	81
<i>trans</i> -Nonachlor	Max. 980 FW	81
<i>cis</i> -Nonachlor	Max. 630 FW	81

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Common cormorant, <i>Phalacrocorax carbo</i> ; Japan, 1993; liver; total chlordanes		
Lake Biwa		
Adults	54 (16–98) FW	102
Diet (fish)	35–130 FW	102
Tokyo, Shinobazu Pond		
Chick	120 (20–380) FW	102
Juvenile	320 (33–1100) FW	102
Adult	360 (120–900) FW	102
Diets (fish)	26–87 FW	102
Adelie penguin, <i>Pygoscelis adeliae</i> , Antarctic Ocean, 1980–82, subcutaneous fat		
cis-Chlordane	0.9 LW	4
trans-Chlordane	<0.05 LW	4
cis-Nonachlor	1.7 LW	4
trans-Nonachlor	15 LW	4
Oxychlordane	16 LW	4
Light-footed clapper rail, <i>Rallus longirostris</i> , eggs, California, 1986–89		
trans-Nonachlor	170 (120–250) FW	99
cis-Nonachlor	3 (2–6) FW	99
Heptachlor epoxide	9 (6–14) FW	99
Oxychlordane	240 (190–310) FW	99
Total chlordanes	610 (460–810) FW	99
Black skimmer, <i>Rynchops niger</i> , South Carolina, 1972–75		
Egg		
Oxychlordane	Max. 520 FW	80
trans-Nonachlor	Max. 520 FW	80
Adults, found dead		
Oxychlordane		
Brain	Max. 880 FW	80
Carcass	Max. 560 FW	80
cis-Chlordane		
Brain	Max. 540 FW	80
Carcass	Max. 150 FW	80
Shorebirds, 7 species, Corpus Christi, Texas, winter 1976–77, skinned carcasses, total chlordanes	Usually <1000 FW; Max. 1700 FW	54
Forster's tern, <i>Sterna forsteri</i> , egg, Lake Michigan, 1983		
cis-Chlordane	(<10–60) FW	77
trans-Chlordane	(<10–20) FW	77
trans-Nonachlor	(<10–170) FW	77
Oxychlordane + heptachlor epoxide	(10–230) FW	77
Heptachlor	(10–300) FW	77
Gull-billed tern, <i>Sterna nilotica</i> , South Carolina, 1972–75, egg		
Oxychlordane	Max. 290 FW	80
trans-Nonachlor	ND	80
European starling, <i>Sturnus vulgaris</i> ; whole (less beak, wing tip, feet, skin); nationwide		
1972: oxychlordane	Max. 100 FW	55
1979: total chlordanes	Max. 290 FW	56
1982:		
cis-Chlordane	Max. 30 FW	57
cis-Nonachlor	Max. 70 FW	57
trans-Nonachlor	Max. 40 FW	57
Oxychlordane	Max. 140 FW	57

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Northern gannet, <i>Sula bassanoides</i> ; eastern Canada; 1969–84; egg <i>cis</i> -Chlordane 1969 1970 1984	Max. 550 FW Max. 520 FW Max. 150 FW	58 58 58
<i>cis</i> -Nonachlor 1969 1970 1984	Max. 380 FW Max. 370 FW Max. 150 FW	58 58 58
Oxychlordane 1969 1970 1984	Max. 208 FW Max. 202 FW Max. <100 FW	58 58 58
Tree swallow, <i>Tachycineta bicolor</i> , Alberta, Canada, 1978–79, eggs and nestlings <i>cis</i> -Chlordane Oxychlordane	<30 FW <30 FW	59 59
Thick-billed murre, <i>Uria lomvia</i> ; northern Pacific Ocean; 1980–82; subcutaneous fat <i>cis</i> -Chlordane <i>trans</i> -Chlordane <i>cis</i> -Nonachlor <i>trans</i> -Nonachlor Oxychlordane Total chlordanes	3 (1.4–3.9) LW <0.05 LW 10 (3–15) LW 3 (1.7–4.5) LW 82 (63–130) LW 98 (63–150) LW	4 4 4 4 4 4
Waterbirds, 3 species; Galveston Bay, TX; 1980–82; total chlordanes Carcass (less skin, feet, bill, GI tract) Egg	Max. 1200 FW Max. 900 FW	60 60
MAMMALS		
Bats, 3 species, Maryland and West Virginia, 1973, near high chlordane use area, oxychlordane Carcass Guano	Max. 3000 FW Max. 100 FW	61 61
Cow, <i>Bos taurus</i> ; milk; total chlordanes Nationwide Illinois, 1971–73	20–60 FW 50 FW	9 62
Cattle, <i>Bos taurus</i> , grazing heptachlor-contaminated pastures for 4 weeks (some deaths), oxychlordane, subcutaneous fat End of grazing 48 days later	5700 FW 180 FW	63 63
Dog, <i>Canis familiaris</i> , Tokyo, 1979, adipose tissue <i>trans</i> -Nonachlor Oxychlordane Total chlordanes	17 FW 71 FW 88 FW	11 11 11
Beluga whale, <i>Delphinapterus leucas</i> ; St. Lawrence River estuary; 1993–94; blubber; animals dead on collection; females vs. males Oxychlordane <i>trans</i> -Chlordane <i>cis</i> -Chlordane	1500 (316–3800) LW vs. 1790 (1370–2450) LW 95 LW vs. 118 LW 186 (119–275) LW vs. 220 (167–276) LW	103 103 103

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
<i>trans</i> -Nonachlor	4140 (1130–8050) LW vs. 5200 (3520–7200) LW	103
<i>cis</i> -Nonachlor	811 LW vs. 953 LW	103
Heptachlor epoxide	343 LW vs. 462 LW	103
Cat, <i>Felis domesticus</i> ; Tokyo, 1979; adipose tissue		
<i>cis</i> -Nonachlor	60 FW	11
<i>trans</i> -Nonachlor	51 FW	11
Oxychlordane	50 FW	11
Total chlordanes	160 FW	11
Long-finned pilot whale, <i>Globicephala melaena</i> , Newfoundland, 1980, blubber, total chlordanes		
Males	1600 (1000–3200) FW	64
Females	700 (200–1900) FW	64
Grey seal, <i>Halichoerus grypus</i> , Gulf of Finland, 1976–82, blubber		
<i>cis</i> -Chlordane	50 FW	65
<i>trans</i> -Chlordane	130 FW	65
<i>trans</i> -Nonachlor	700 FW	65
Oxychlordane	210 FW	65
Total chlordanes	970 FW	65
Human, <i>Homo sapiens</i>		
Mother's milk		
Hawaii, 1979		
<i>trans</i> -Nonachlor	2.5 FW	66
Oxychlordane	1.9 FW	66
Arkansas and Mississippi; 1973–74; total chlordanes	5 FW; Max. 20 FW	62
Japan, 1979		
<i>cis</i> -Chlordane	0.1 FW	66
<i>trans</i> -Chlordane	0.2 FW	66
<i>cis</i> -Nonachlor	0.2 FW	66
<i>trans</i> -Nonachlor	0.8 FW	66
Oxychlordane	0.5 FW	66
Japan, 1983		
<i>cis</i> -Chlordane	0.1 FW; 3.1 LW	67
<i>trans</i> -Chlordane	0.04 FW; 1.2 LW	67
<i>cis</i> -Nonachlor	0.1 FW; 4.0 LW	67
<i>trans</i> -Nonachlor	0.5 FW; 15.7 LW	67
oxychlordane	0.4 FW; 11.5 LW	67
Finland, 1982		
<i>cis</i> -Chlordane	<0.05 FW; <1.0 LW	66
<i>trans</i> -Chlordane	<0.05 FW; <1.0 LW	66
<i>cis</i> -Nonachlor	0.08 FW; 2.0 LW	66
<i>trans</i> -Nonachlor	0.4 FW; 10.0 LW	66
Oxychlordane	0.2 FW; 5.0 LW	66
Blood, Tokushima City, Japan		
<i>cis</i> -Chlordane	0.05 FW, Max. 0.14 FW	68
<i>trans</i> -Chlordane	0.1 FW; Max. 0.22 FW	68
<i>cis</i> -Nonachlor	0.03 FW; Max. 0.08 FW	68
<i>trans</i> -Nonachlor	0.08 FW; Max. 0.29 FW	68
Oxychlordane	0.2 FW; Max. 0.75 FW	68
Total chlordanes	0.5 FW; Max. 1.1 FW	68
Fat, worldwide, oxychlordane	140 (30–400) FW	69
White-beaked dolphin, <i>Lagenorhynchus albirostris</i> ; Newfoundland, 1982; blubber; total chlordanes		
Males	12,700 (6300–25,000) FW	64
Females	8300 (3700–15,000) FW	64

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Weddell seal, <i>Leptonychotes weddelli</i> ; Antarctic Ocean; 1980–82; blubber		
<i>cis</i> -Chlordane	7 LW	4
<i>trans</i> -Chlordane	<0.05 LW	4
<i>cis</i> -Nonachlor	8 LW	4
<i>trans</i> -Nonachlor	41 LW	4
Oxychlordane	13 LW	4
River otter, <i>Lutra canadensis</i> , liver, Alberta, Canada, 1980–83		
<i>cis</i> -Chlordane	Max. 6 FW	70
Oxychlordane	Max. 13 FW	70
Mink, <i>Mustela vison</i> ; NWT, Canada; 1991–95; total chlordanes		
Liver	0.9–3.5 FW	111
Mink prey species; liver		
Snowshoe hare, <i>Lepus americanus</i>	1.1 FW	111
Northern red-backed vole, <i>Clethrionomys rutilus</i>	0.6–9.3 FW	111
Gray bat, <i>Myotis griseescens</i> ; Missouri; 1976–77; found dead		
Brain		
<i>cis</i> -Chlordane	Max. 1000 FW	71
<i>trans</i> -Nonachlor	Max. 2100 FW	71
Oxychlordane	Max. 2300 FW	71
Carcass		
<i>cis</i> -Chlordane	6300 (15,000–108,000) LW	71
<i>trans</i> -Nonachlor	159,000 (91,000–252,000) LW	71
Oxychlordane	68,000 (16,000–167,000) LW	71
Pacific walrus, <i>Odobenus rosmarus divergens</i> ; oxychlordane; blubber		
Alaska, 1981–84	20–60 FW	83
Soviet Union, 1984	100 FW	83
Ringed seal, <i>Phoca hispida</i> ; Kara Sea, Russian Arctic; 1995; blubber; males vs. females		
Total chlordanes	470 LW vs. 390 LW	112
Oxychlordane	230 LW vs. 190 LW	112
<i>trans</i> -Nonachlor	200 LW vs. 180 LW	112
Saimaa ringed seal, <i>Phoca hispida saimensis</i> ; Finland; 1977–81; total chlordanes		
Blubber	590 (110–1700) LW	72
Liver	200 (10–400) FW	72
Muscle	20 (10–30) FW	72
Baikal seal, <i>Phoca siberica</i> ; Lake Baikal, Siberia; June 1991; blubber		
<i>cis</i> -Chlordane	55–160 LW	107
<i>trans</i> -Chlordane	<10–17 LW	107
Heptachlor	<3 LW	107
<i>trans</i> -Nonachlor	1100–1500 LW	107
<i>cis</i> -Nonachlor	130–140 LW	107
Total chlordanes	1500 LW	107
Harbor seal, <i>Phoca vitulina</i>		
Netherlands, blubber		
<i>trans</i> -Nonachlor	2700 LW	73
Oxychlordane	3000 LW	73
Northern Ireland, 1988		
Blubber		
Heptachlor and heptachlor epoxide	130 (<5–460) FW	109
Alpha-, gamma-, and oxy-Chlordane	220 (10–720) FW	109

Table 13.2 (continued) Chlordane Concentrations in Field Collections of Selected Animals (Values shown are in micrograms per kg [parts per billion] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, Chlordane Isomer, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Liver vs. kidney, total chlordanes	Max. 38 FW vs. Max. 25 FW	109
Dall's porpoise, <i>Phocoenoides dalli</i> ; North Pacific Ocean; 1980–82; blubber		
<i>cis</i> -Chlordane	440 (360–550) LW	4
<i>trans</i> -Chlordane	63 (53–73) LW	4
<i>cis</i> -Nonachlor	270 (240–310) LW	4
<i>trans</i> -Nonachlor	1800 (1600–2000) LW	4
Oxychlordane	250 (160–340) LW	4
Total chlordanes	2800 (2700–3000) LW	5
Raccoon, <i>Procyon lotor</i>		
Louisiana, 1978–79; muscle		
<i>cis</i> -Chlordane	17 FW	10
<i>trans</i> -Chlordane	17 FW	10
Mississippi delta region; adipose tissue; 1978–79 vs. 1988		
Heptachlor epoxide	10 FW vs. 10 FW	105
<i>trans</i> -Nonachlor	60 (Max. 4200) FW vs. 10 (Max. 300) FW	105
Oxychlordane	40 (Max. 2200) FW vs. 10 (Max. 100) FW	105
Gray squirrel, <i>Sciurus carolinensis</i> , Jacksonville, FL, 1974, fat		
Nonachlors	Max. 110 LW	74
Oxychlordane	Max. 62 LW	74
Seals, 3 species; Baltic coast and west coast of Sweden; blubber		
Juveniles	430–3700 LW	104
Adult males		
Sweden	Max. 440 LW	104
Baltic	Max. 11,000 LW	104
Adult females, Baltic	Max. 54,000 LW	104
Polar bear, <i>Ursus maritimus</i> ; adipose tissue; adults; known range; 1989–93; total chlordanes	1952 (727–4632) LW	110

^a Concentrations are shown as means, extremes in parentheses, maximum (Max.), and nondetectable (ND).

^b 1, Risebrough et al. 1983; 2, DouAbul et al. 1988; 3, Rosales et al. 1979; 4, Kawano et al. 1988; 5, Kawano et al. 1986; 6, Zitko 1978; 7, Evans et al. 1982; 8, Ray et al. 1983; 9, IARC 1979; 10, Dowd et al. 1985; 11, Yamagishi et al. 1981; 12, Miyazaki et al. 1980; 13, Molilanen et al. 1982; 14, Kaiser 1982; 15, Swackhamer and Hites 1988; 16, Kuehl et al. 1980; 17, Saiki and Schmitt 1986; 18, Kuehl et al. 1983; 19, Eisenberg and Topping 1985; 20, Pyysalo et al. 1981; 21, Pyysalo et al. 1983; 22, Hunter et al. 1980; 23, Veith et al. 1981; 24, Schmitt et al. 1985; 25, Wickstrom et al. 1981; 26, Albright et al. 1980; 27, Zitko and Saunders 1979; 28, DeVault et al. 1986; 29, Hall et al. 1979; 30, Heinz et al. 1980; 31, White 1979; 32, Prouty and Bunck 1986; 33, Haseltine et al. 1980; 34, Stendell et al. 1977; 35, White et al. 1979; 36, Klaas et al. 1980; 37, Anderson et al. 1984; 38, Foley and Batcheller 1988; 39, Schick et al. 1987; 40, Ambrose et al. 1988; 41, Ingebrigtsen et al. 1984; 42, Reece et al. 1985; 43, Barbehenn and Reichel 1981; 44, Kaiser et al. 1980; 45, Reichel et al. 1984; 46, Szaro et al. 1979; 47, Peakall et al. 1986; 48, Ohlendorf et al. 1982; 49, Blus et al. 1985; 50, Wiemeyer et al. 1987; 51, Littrell 1986; 52, Wiemeyer et al. 1988; 53, De Weese et al. 1986; 54, White et al. 1980; 55, Nickerson and Barbehenn 1975; 56, Cain and Bunck 1983; 57, Bunck et al. 1987; 58, Elliott et al. 1988; 59, Shaw 1984; 60, King and Kryniotsky 1986; 61, Clark and Prouty 1976; 62, USEPA 1980; 63, Petterson et al. 1988; 64, Muir et al. 1988; 65, Pertilla et al. 1986; 66, Wickstrom et al. 1983; 67, Tojo et al. 1986; 68, Wariishi et al. 1986; 69, WHO 1984; 70, Somers et al. 1987; 71, Clark et al. 1980; 72, Helle et al. 1983; 73, Kerkhoff and Boer 1982; 74, Nalley et al. 1978; 75, Bush and Grace 1989; 76, Schmitt et al. 1990; 77, Kubiak et al. 1989; 78, Fitzner et al. 1988; 79, Stone and Okoniewski 1988; 80, Blus and Stafford 1980; 81, Blus et al. 1979; 82, S. Wiemeyer, Patuxent Wildlife Research Center, personal communication; 83, Taylor et al. 1989; 84, Glynn et al. 1989; 85, Loganathan et al. 1989; 86, Nair 1990; 87, Kelly and Campbell 1994; 88, McCain et al. 1996; 89, Kannan et al. 1992; 90, Zabik et al. 1995; 91, Leiker et al. 1991; 92, Pereira et al. 1994; 93, Kennish et al. 1997; 94, Gooch et al. 1990; 95, Borgmann and Whittle 1991; 96, Miskiewicz and Gibbs 1994; 97, Wood et al. 1996; 98, Henny et al. 1990; 99, Jarman et al. 1993; 100, Wiemeyer et al. 1993; 101, Blumton et al. 1990; 102, Guruge et al. 1997; 103, Muir et al. 1996; 104, Andersson and Wartanian 1992; 105, Ford and Hill 1990; 106, Okoniewski and Novesky 1993; 107, Kucklick et al. 1994; 108, Johnson et al. 1993; 109, Mitchell and Kennedy 1992; 110, Norstrom et al. 1998; 111, Poole et al. 1998; 112, Nakata et al. 1998.

13.5 LETHAL AND SUBLETHAL EFFECTS

13.5.1 General

Chlordane has been applied extensively to control pestiferous soil invertebrates, usually at rates between 0.6 and 2.24 kg/ha. Within this range, sensitive nontarget species, especially earthworms, were adversely affected. Nominal water concentrations between 0.2 and 3.0 µg/L were harmful to various species of fish and aquatic invertebrates. Effects included a reduction in survival, immobilization, impaired reproduction, histopathology, and elevated chlordane accumulations. *Cis*-chlordane, when compared to *trans*-chlordane, was more toxic, preferentially stored, and concentrated to a greater degree. In aquatic organisms, *cis*-chlordane photoisomers were frequently more toxic than the parent form. Oxychlordane was not a major metabolite in aquatic fauna. Sensitive bird species had reduced survival after consumption of diets as low as 1.5 mg chlordane/kg ration, or after a single oral dose as low as 14.1 mg/kg BW. Accumulations were documented in tissues following consumption of diets containing 0.1 to 0.3 mg chlordane/kg feed. Oxychlordane was the most persistent metabolite in avian brain tissue.

Concern for the continued widespread use of chlordane centers on its ability to cause liver cancer in domestic mice. Other adverse effects in mammals, such as elevated tissue residues and growth inhibition, were frequently associated with diets containing between 0.76 and 5.0 mg chlordane/kg feed. Metabolism of technical chlordane by mammals results primarily in oxychlordane, a metabolite that is about 20 times more toxic than the parent compound and the most persistent metabolite stored in adipose tissues. Chlordane interactions with other agricultural chemicals produced significant biological effects in warm-blooded organisms, indicating a need for additional research on this subject.

13.5.2 Terrestrial Invertebrates

Chlordane has been used extensively to control grubs, ants, snails, and other terrestrial invertebrates. Chlordane applied to wheat crops in India at 0.6 kg/ha and higher controlled infestation by two species of termites (*Odontotermes obesus*, *Microtermes obesi*) and increased grain yield; chlordane applications of 0.4 kg/ha and lower were ineffective (Khan and Singh 1985). Chlordane has been used to control the imported fire ant (*Solenopsis invicta*), although registration for this purpose by the USEPA has now been withdrawn (Williams and Lofgren 1983). Application of 4.5 g of chlordane per ant mound, applied as an emulsifiable concentrate, resulted in 83 to 94% control 4 to 5 weeks posttreatment (Williams and Lofgren 1983). Cricket (*Acheta pennsylvanicus*) nymphs died within 1 minute of contact with technical chlordane. Dead crickets showed cellular disruption of the caecal lining, the malpighian tubules, and the digestive tract (Greenhalgh 1986).

Chlordane, at 1.12 to 2.24 kg/ha, was lethal to fly and beetle larvae and also caused reductions in populations of various species of soil invertebrates (WHO 1984). Among nontarget soil species, earthworms were especially sensitive. Significant reductions in earthworm populations were recorded following application of 2.2 kg/ha. Metabolism was adversely affected in 2 weeks at 13 kg/ha, and remained depressed for at least 5 years; at 80 kg/ha, 46% died in 4 days (NRCC 1975). In soil, chlordane effects decreased with increasing soil temperature and organic content; the heptachlor component in technical chlordane had the greatest biological activity to soil fauna (NRCC 1975).

13.5.3 Aquatic Organisms

Signs of chlordane poisoning in fish included hyperexcitability, increased respiration rate, erratic swimming, loss of equilibrium, and convulsions; death frequently occurred within 12 h of exposure (NRCC 1975). Chlordane adversely affected sensitive species of fish and aquatic invertebrates at

nominal water concentrations between 0.2 and 3.0 µg/L (Table 13.3). Specifically, reduced survival was measured in shrimp and crabs at water concentrations of 0.2 to 2.0 µg/L, and in freshwater and marine fishes between 1.7 and 3.0 µg/L; immobilization, impaired reproduction, and histopathology were recorded in shrimp, fish, and planarians between 0.8 and 3.0 µg/L; and high accumulations were evident in fish, shrimp, and oysters between 0.2 and 4.2 µg/L. Growth stimulation and high residues were measured in resistant species of algae, such as *Scenedesmus quadricauda*, at media concentrations up to 100 µg chlordane/L. In sensitive algal species, however, growth was inhibited at water concentrations as low as 10 µg/L (Table 13.3).

Large intra- and inter-specific differences in sensitivity to chlordane were evident (Table 13.3). Some of this variability was attributed to variations in water temperature, salinity, and sediment loadings; some to the age, condition, and nutritional history of the test organism; and some to the chlordane formulation and isomer tested (NRCC 1975; USEPA 1980; Johnson and Finley 1980; McLeese and Metcalf 1980; Mayer and Ellersieck 1986; Rai and Mandal 1993). In general, granular chlordane formulations were most toxic; organisms at a young developmental stage and organisms with reduced lipid content were most sensitive; and adverse effects were most pronounced under conditions of elevated water temperatures, reduced salinities, decreased sediment loadings, and increased duration of exposure. Reduced bioavailability and lessened toxicity of chlordane to daphnids was associated with increasing concentrations (up to 200 mg/L) of suspended solids and their associated carbon content (Hall et al. 1986). Sediment loadings of 5.8 mg chlordane/kg were fatal to 50% of sandworms (*Nereis virens*) in 12 days (McLeese et al. 1982). Resistance or adaptation to chlordane has been reported in mosquitofish (*Gambusia affinis*) collected from ditches near treated cotton fields. These fish were up to 20 times more resistant than newly exposed fish (NRCC 1975).

Residues of *cis*-chlordane were preferentially stored and magnified over *trans*-chlordane by freshwater fish and invertebrates in ponds treated with technical chlordane at concentrations up to 1.14 µg/L. The *cis*-isomer, with an estimated Tb 1/2 of 46 days, persisted longer than did the *trans*-isomer (Johnson and Finley 1980). Tissue concentrations of 106,000 µg total chlordanes/kg, on a lipid weight basis, were associated with reduced survival of estuarine invertebrates (Zitko 1978). Moribund amphipods (*Hyalella azteca*), for example, contained 137,000 to 2,180,000 µg/kg lipid of various chlordanes, heptachlors, and chlordenes (Zitko 1978). In fish, chlordane concentrations of 300,000 to 4,000,000 µg/kg lipid weight in tissues were lethal (Zitko 1978).

Cis-chlordane was 8 times more toxic to bluegill (*Lepomis macrochirus*) than was *trans*-chlordane (Johnson and Finley 1980). *Cis*-chlordane was also more toxic to goldfish (*Carassius auratus*) than was *trans*-chlordane because of its comparatively rapid uptake from the medium and lengthy storage in body tissues, estimated at 99% after 25 days (Feroz and Khan 1979b). The elimination rate of *cis*-chlordane from a cichlid (*Cichlasoma* sp.) was estimated at 2.9% weekly over a 20-week period, with a Tb 1/2 of about 17 weeks. Metabolites accounted for 12.5% (dichlorochlordene, oxychlordane, chlordene chlorhydrin, dihydroxyheptachlor, dihydroxydihydrochlordene, plus four unidentified compounds) and unchanged *cis*-chlordane for 87.5% (Feroz and Khan 1979a). The assemblage of chlordane-related compounds present in lake trout (*Salvelinus namaycush*) from the Great Lakes is substantially different from technical chlordane, and is 3 to 5 times more toxic to mosquito larvae than the technical mixture. The increased toxicity is attributed to the presence of the stable metabolites oxychlordane and heptachlor epoxide (Gooch et al. 1990).

Photoisomers seem to be more toxic than the parent form. For example, *cis*-photochlordane was about twice as lethal to bluegills and goldfish as *cis*-chlordane (Sudershan and Khan 1980). Bluegills exposed to 5 µg/L of radiolabeled *cis*-photochlordane or *cis*-chlordane for 48 h accumulated *cis*-chlordane from the medium by a factor of 78, and *cis*-photochlordane by a factor of 140 (Sudershan and Khan 1980). During the next 6 weeks, 20% of the *cis*-chlordane was eliminated in a linear pattern, and about 50% was eliminated in 46 days. Elimination of *cis*-photochlordane followed a biphasic pattern and was most rapid during the first 3 weeks: 40% was eliminated in

the first 6 weeks, and 50% was eliminated in 15 weeks. Less than 7% of the radioactivity retained in *cis*-chlordane-treated bluegills was in the form of two conjugates, compared to 16% in the form of 14 metabolites for *cis*-photochlordane. No oxychlordane was found in bluegill tissues after treatment; this compound is one of the predominant metabolites found in chlordane-treated rodents and cockroaches. Thus, absence of epoxidation and presence of a mechanism of hydroxylation followed by conjugation seems to be the most active mode of chlordane metabolism in bluegill (Sudershan and Khan 1980).

Cis-photochlordane was about 10 times less toxic to *Daphnia pulex* than *cis*-chlordane (Podowski et al. 1979). This is in sharp contrast to the pattern shown in bluegill and goldfish (Sudershan and Khan 1980). Further, *cis*-photochlordane and *cis*-chlordane toxicity to mice and houseflies was about the same (Podowski et al. 1979), which demonstrates the difficulty in generalizing about the comparative toxicity of chlordane isomers.

Table 13.3 Chlordane Effects on Selected Aquatic Organisms (Compound tested was technical chlordane, unless indicated otherwise.)

Organism and Concentration in Medium (g/L)	Effect	Reference ^b
ALGAE		
Alga, <i>Chlamydomonas</i> sp.		
0.1–50	Stimulatory to growth	1
>100	Inhibitory to growth	1
Estuarine phytoplankton, mixed species		
5	No effect on growth in 5 days	2
10	Daily additions of 10 µg/L for 8 days reduced algal growth rate and carbon uptake; inhibition persisted for 2–48 h and did not affect community composition	2
Marine dinoflagellate, <i>Exuviaella baltica</i>		
50	Exposure for 7 days resulted in disintegration of many cells, reduced cell density, and reduced carbon fixation; particle size distribution altered, and this could affect availability of food for particle-feeding herbivores	3
Green alga, <i>Scenedesmus quadricauda</i>		
0.1–100	Stimulatory to respiration and growth; bioconcentration factor (BCF) ranged from 6000–15,000 in 24 h for all doses, and from 6700–103,000 in 5 days	1, 4
>1000	Growth inhibition	4
INVERTEBRATES		
Blue crab, <i>Callinectes sapidus</i>		
260	50% immobilization in 48 h	5
Dungeness crab, <i>Cancer magister</i>		
0.015	No effect on survival or molting	6
0.15	LC50 (37 days), molting inhibited	6
1.3	LC50 (96 h), zoeae	6
220	LC50 (96 h), adults	6
Chironomid, <i>Chironomus tentans</i>		
5.8	LC50 (48 h)	27
Sand shrimp, <i>Crangon septemspinosa</i>		
2	LC50 (96 h)	7
American oyster, <i>Crassostrea virginica</i>		
4.2	8% reduction in shell growth in 96 h, BCF of 2619 in soft parts	8
6.2–10	50% reduction in shell growth in 96 h, BCF of 3200–8300	5, 6, 8
100	BCF of 7300 after exposure for 10 days	9

Table 13.3 (continued) Chlordane Effects on Selected Aquatic Organisms (Compound tested was technical chlordane, unless indicated otherwise.)

Organism and Concentration in Medium (g/L)	Effect	Reference ^b
Daphnid, <i>Daphnia magna</i>		
12.1–21.6	Maximum acceptable toxicant concentration (MATC) ^a	6
28	50% immobilization in 96 h	10
97	LC50 (48 h) for chlorinated chlordane	11
152	LC50 (48 h) for chlorinated emulsifiable concentrate	11
270	LC50 (48 h)	12
813	LC50 (48 h) for dechlorinated chlordane	11
1174	LC50 (48 h) for dechlorinated emulsifiable concentrate	11
Daphnid, <i>Daphnia pulex</i>		
2.3	50% immobilization in 48 h for <i>trans</i> -nonachlor	13
24	LC50 (48 h)	14, 15
57	LC50 (96 h) for <i>cis</i> -chlordane	16
269	LC50 (96 h) for <i>trans</i> -chlordane	16
550	LC50 (96 h) for <i>cis</i> -photochlordane	16
930	LC50 (96 h) for oxychlordane	16
Planarian, <i>Dugesia dorotocephala</i>		
0.2	No deaths in 5 days	17
>1.0	Impaired reproduction after 10-day exposure	17
3.0	LC50 (10 days), many survivors with head lesions	17
7.0	LC50 (5 days)	17
10.0	LC100 (10 days)	17
Amphipod, <i>Gammarus fasciatus</i>		
40	LC50 (96 h), 95% confidence interval of 21–60 µg/L	14, 15
Amphipod, <i>Hyalella azteca</i>		
61	LC50 (48 h)	27
97	50% immobilization in 168 h	10
Freshwater bivalve mollusc, <i>Lamellidens marginalis</i> , exposed to 0.12 mg technical chlordane/L for up to 30 days		
2 days	Residues (in mg/kg FW) were 5.0 in gill, 3.6 in foot, 3.1 in muscle, and 2.2 in intestine	26
8 days	Residues, in mg/kg FW, ranged from 2.4 in gill to 1.1 in muscle	26
30 days	Residues, in mg/kg FW, were 1.0 in gill, 1.0 in foot, 0.4 in intestine, and 0.1 in muscle	26
Sandworm, <i>Nereis virens</i>		
220	LC50 (12 days), but no deaths in 96 h; at 96 h, signs of stress included everted proboscis, loss of equilibrium, emergence from sediments, and failure to burrow	18
Crayfish, <i>Orconectes nais</i>		
31.6	LC50 (35 days)	14
50	LC50 (96 h)	14
Korean shrimp, <i>Palaemon macrodactylus</i>		
11	LC50 (96 h)	15
Grass shrimp, <i>Palaemonetes pugio</i>		
4.2	LC15 (19 h), BCF about 1070	8
4.8	LC50 (96 h), BCF of 1900–2300	8
Brown shrimp, <i>Penaeus aztecus</i>		
2.4	50% immobilization in 48 h	5
Pink shrimp, <i>Penaeus duorarum</i>		
0.24	LC10 (96 h), whole-body BCF of 2960 in survivors	8
0.4	BCF of 4000–6000 in 96 h	8
4.4	LC50 (48 h)	8

Table 13.3 (continued) Chlordane Effects on Selected Aquatic Organisms (Compound tested was technical chlordane, unless indicated otherwise.)

Organism and Concentration in Medium (g/L)	Effect	Reference ^b
Stonefly, <i>Pteronarcys californica</i> 15	LC50 (96 h), 95% confidence interval of 9–24 µg/L	14, 15
Daphnid, <i>Simocephalus serrulatus</i> 20	LC50 (48 h)	14, 15
FISH		
Goldfish, <i>Carassius auratus</i> 13	LC50 (96 h) for <i>cis</i> -photochlordane	16
15	LC50 (96 h) for oxychlordane	16
26	Exposed for 24 h to <i>cis</i> -chlordane; whole-body BCF at 10 and 25 days after exposure were 2280 and 1820, respectively	19
27	LC50 (96 h) for <i>cis</i> -chlordane	16
82	LC50 (96 h)	6
440	LC50 (96 h) for <i>trans</i> -chlordane	16
Sheepshead minnow, <i>Cyprinodon variegatus</i> 0.5 and 0.8	MATC ^a	20
0.8	Reduced hatch during continuous exposure	20
1.7	Some deaths in second-generation fish during continuous exposure	20
2.8	Some deaths in adult fish during exposure for 189 days	20
3.3	No deaths in 28 days, whole-body BCF of 3333	8
7.1	Equilibrium loss in fry after exposure for 10 days	8
12.5–24.5	LC50 (96 h)	8, 20
15	LC25 (96 h), BCF up to 18,700 in survivors	8
36	No effect on fertilization success or embryo survival after adults exposed for 28 days	8
Common carp, <i>Cyprinus carpio</i> 3.0	LC50 (96 h)	6
Threespine stickleback, <i>Gasterosteus aculeatus</i> 90–160	LC50 (96 h)	6, 15
Indian catfish, <i>Heteropneustes fossilis</i> 150	No deaths in 96 h	21
247	Muscle glycogenolysis and hyperglycemia in 2–12 h	21
275	LC50 (96 h)	21
3500	LC100 (96 h)	21
Channel catfish, <i>Ictalurus punctatus</i> 7–46	LC50 (96 h)	14
Pinfish, <i>Lagodon rhomboides</i> 5.4	LC30 (94 h), whole-body BCF of 3070	8
6.4	LC50 (96 h), BCF up to 7500	8
Bluegill, <i>Lepomis macrochirus</i> 1.2 and 2.2	MATC ^a	10
9.2	LC50 (96 h) for oxychlordane	16
12	LC50 (48 and 96 h) for <i>cis</i> -photochlordane	16, 22
7.1–17	LC50 (96 h) for <i>cis</i> -chlordane	14, 16
19–85	LC50 (96 h)	6, 10, 14, 15
41	LC50 (96 h) for chlorinated technical chlordane	11
62	LC50 (96 h) for chlorinated emulsifiable concentrate	11
50.5–140	LC50 (96 h) for <i>trans</i> -chlordane	14, 16
582	LC50 (96 h) for dechlorinated technical chlordane	11
800	LC50 (96 h) for dechlorinated emulsifiable concentrate	11

Table 13.3 (continued) Chlordane Effects on Selected Aquatic Organisms (Compound tested was technical chlordane, unless indicated otherwise.)

Organism and Concentration in Medium (g/L)	Effect	Reference ^b
Largemouth bass, <i>Micropterus salmoides</i> 3.0	LC50 (96 h)	14
Striped bass, <i>Morone saxatilis</i> 11.8	LC50 (96 h)	6
Striped mullet, <i>Mugil cephalus</i> 3.2	LC50 (48 h)	5
Cutthroat trout, <i>Oncorhynchus clarki</i> 27	LC50 (96 h)	14
Coho salmon, <i>Oncorhynchus kisutch</i> 14–56	LC50 (96 h)	6, 14, 15
Rainbow trout, <i>Oncorhynchus mykiss</i> 8–47	LC50 (96 h)	6, 14, 15, 24
Chinook salmon, <i>Oncorhynchus tshawytscha</i> 57	LC50 (96 h)	15
Sea lamprey, <i>Petromyzon marinus</i> 1000	LC100 (14 h)	9
Fathead minnow, <i>Pimephales promelas</i> 21	LC50 (49 h)	27
25–115	LC50 (96 h)	10, 14, 15
Indian carp, <i>Saccobranchus fossilis</i> 420	LC50 (96 h)	23
Brown trout, <i>Salmo trutta</i> 11	LC50 (96 h)	14
Brook trout, <i>Salvelinus fontinalis</i> 0.32	Adverse effects during chronic exposure	10
22	No deaths in 96 h	25
30–47	LC50 (96 h)	6, 10, 25

^a MATC = Maximum Acceptable Toxicant Concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

^b 1, Gloschenko et al. 1979; 2, Biggs et al. 1978; 3, Magnani et al. 1978; 4, Gloschenko and Lott 1977; 5, Mayer 1987; 6, USEPA 1980; 7, McLeese and Metcalfe 1980; 8, Parrish et al. 1976; 9, NRCC 1975; 10, Cardwell et al. 1977; 11, Randall et al. 1979; 12, Hall et al. 1986; 13, Passino and Smith 1987; 14, Johnson and Finley 1980; 15, USEPA 1973; 16, Podowski et al. 1979; 17, Best et al. 1981; 18, McLeese et al. 1982; 19, Feroz and Khan 1979b; 20, Parrish et al. 1978; 21, Mishra and Srivastava 1984; 22, Sudershan and Khan 1980; 23, Verma et al. 1982; 24, Mayer and Ellersiek 1986; 25, Zitko 1979; 26, Agrawal 1986; 27, Moore et al. 1998.

13.5.4 Amphibians and Reptiles

Shortly after chlordane was applied to wooden huts in Australia for termite control, large numbers of dead skinks (*Morethia boulengeri*, *Lerista pectorittata*) and frogs (*Litoria caerulea*, *L. peronii*) were discovered, presumably killed by the chlordane (Henle 1988). Toad (*Bufo arenarium*) embryos survived 0.5 mg technical chlordane/L for 8 days, but died by day 20; all embryos held in 15 mg/L were dead by day 15 (Juarez and Guzman 1984). For tadpoles of the common toad (*Bufo bufo*), a 48-h LC50 of 2 mg/L was reported (WHO 1984).

13.5.5 Birds

Signs of chlordane intoxication in birds include sluggishness, drooped eyelids, fluffed feathers, low crouching on perch, reduced food intake, and weight loss. Later, afflicted animals rested on their breast, wings spread, quivering and panting rapidly, back arched, neck arched over the back, and sometimes convulsing (Stickel et al. 1983). Signs of intoxication appeared within 5 min, and

death usually occurred in the first 8 days of exposure. Remission took up to 4 weeks in some birds (Hudson et al. 1984).

The most sensitive avian species tested against technical chlordane were California quail (*Callipepla californica*), with an acute oral LD₅₀ of 14.1 mg/kg BW; the ring-necked pheasant (*Phasianus colchicus*), with an acute oral LD₅₀ of 24 to 72 mg/kg BW; and European starlings (*Sturnus vulgaris*) fed diets containing 1.5 mg/kg ration for 57 days or 6.25 mg/kg for 24 days (Table 13.4). Accumulations of various chlordane isomers and metabolites were evident in chickens (*Gallus* sp.) fed diets containing as little as 0.1 mg technical chlordane/kg feed for 6 weeks, or 0.3 mg/kg for 4 weeks (NRCC 1975). Vapor toxicity of chlordane is persistent. In one instance, a room used for housing pigeons was sprayed with a chlordane solution; walls and floors were then scrubbed and the room left unoccupied for 2 months. When pigeons were returned to the room, enough chlordane remained to be lethal to all birds (Ingle 1965). Similar cases were reported for mice, presumably after use of very concentrated chlordane solutions (Ingle 1965).

Reproductive impairment was reported in several species of waterfowl from a marsh treated with 1.12 kg technical chlordane/ha (Table 13.4). Studies by Lundholm (1988) with two species of ducks (*Anas* spp.) and the domestic chicken (*Gallus* sp.) demonstrated that various organochlorine compounds, including chlordane, interfered (in a dose-dependent manner) with reproduction by reducing the binding of progesterone to its cytoplasmic receptor in the shell gland mucosa of birds, especially ducks.

The lethal effect of technical chlordane in birds is attributed primarily to chlordane metabolites, especially oxychlordane and, to a lesser extent, heptachlor epoxide (Stickel et al. 1983). Oxychlordane was the most persistent chlordane component in avian brain tissues. The half-time persistence of oxychlordane in brain was 63 days, and 95% loss was estimated in 280 days. The Tb 1/2 for heptachlor epoxide was 29 days, and for *trans*-nonachlor it was 19 days (Stickel et al. 1979). Oxychlordane residues in brain tissue approaching 5 mg/kg FW were considered within the lethal hazard zone to birds (Stickel et al. 1979).

Technical heptachlor contains about 15% *cis*-chlordane and 2.5% *trans*-chlordane. Diets containing 50 mg technical heptachlor/kg fed to brown-headed cowbirds (*Molothrus ater*), red-winged blackbirds (*Agelaius phoeniceus*), common grackles (*Quiscalus quiscula*), and European starlings produced 50% mortality in 9 to 24 days. Birds that died contained 9.2 to 27 mg oxychlordane/kg FW brain, and survivors contained 2.7 to 7.8 mg/kg (Stickel et al. 1979). Red-winged blackbirds fed diets containing 10 mg technical chlordane/kg for 84 days, 50 mg/kg for 42 days, or 100 mg/kg for 21 days, all contained about 17% of the total diet fed as *cis*-chlordane, with whole-body residues in mg/kg FW of 1.8, 9.2, and 14.8, respectively; accumulations of *trans*-chlordane were negligible (Stickel et al. 1983).

Chlordane interactions with other agricultural chemicals are significant and merit additional research. In one study, male Japanese quail (*Coturnix japonica*) pretreated for 8 weeks with 10 mg chlordane/kg diet had increased resistance to parathion, but not to paraoxon, as judged by cholinesterase activity (Ludke 1977). In another study, northern bobwhites (*Colinus virginianus*) treated with 10 mg chlordane/kg diet for 10 weeks, followed by endrin stress, had greater accumulations of chlordane in the brain than did birds treated only with chlordane (Ludke 1976).

Table 13.4 Chlordane Effects on Selected Birds

Organism and Other Variables	Effect and Reference
RED-WINGED BLACKBIRD, <i>Agelaius phoeniceus</i>	
Fed diets containing 10 mg/kg for 84 days	Residue of 1.8 mg <i>cis</i> -chlordane/kg body weight (BW), fresh weight (FW) (Stickel et al. 1983)
Diet containing 50 mg/kg for 42 days	Whole-body <i>cis</i> -chlordane content of 9.2 mg/kg FW (Stickel et al. 1983)
Diet containing 100 mg/kg for 21 days	Whole-body <i>cis</i> -chlordane content of 14.8 mg/kg FW (Stickel et al. 1983)
As above, plus 3 or 7 days off dosage 200 mg/kg diet	Whole-body <i>cis</i> -chlordane content of 5.4 and 2.6 mg/kg, FW respectively (Stickel et al. 1983) LD ₅₀ within 9 days (Stickel et al. 1983)

Table 13.4 (continued) Chlordane Effects on Selected Birds

Organism and Other Variables	Effect and Reference
MALLARD, <i>Anas platyrhynchos</i>	
Single oral dose, age 4–5 months 1200 mg/kg BW	LD50 (Hudson et al. 1984)
858 mg/kg diet for 5 days followed by 3 days of clean diet, ducklings age 10 days	LD50 (Hill et al. 1975)
709 mg/kg diet	LD50 (NRCC 1975)
BIRDS, 4 species , from marsh treated with 1.12 kg chlordane/ha	No reproduction in blue-winged teal (<i>Anas discors</i>) and northern shovelers (<i>Anas clypeata</i>); reproduction inhibited by 60% in coots (<i>Fulica americana</i>) and red-winged blackbirds (<i>Agelaius</i> <i>phoeniceus</i>); disruption of food cycles in marsh was probable cause (NRCC 1975)
BIRDS, 4 species , fed diets containing 71% <i>cis</i> -chlordane and 23% <i>trans</i> - chlordane at 50–500 mg/kg diet	Oxychlordane concentrations in brain of dead birds ranged from 9.4–22.1 mg/kg FW in cowbirds (<i>Molothrus ater</i>), grackles (<i>Quiscalus</i> <i>quiscula</i>), and red-winged blackbirds; in European starlings (<i>Sturnus</i> <i>vulgaris</i>), oxychlordane ranged from 5.0–19.1 mg/kg FW in birds that died, and from 1.4–10.5 mg/kg FW in sacrificed birds (Stickel et al. 1983)
BIRDS, 3 species , fed diets containing 150 mg technical chlordane/kg	LD50 reached in 6–7 days for starlings, cowbirds, and red-winged blackbirds (Stickel et al. 1979)
CALIFORNIA QUAIL, <i>Callipepla</i> <i>californica</i>	
Single oral dose of 14.1 mg/kg BW	LD50 (Hudson et al. 1984)
NORTHERN BOBWHITE, <i>Colinus</i> <i>virginianus</i>	
10–120 mg/kg diet for 14 weeks	LD50 (NRCC 1975; WHO 1984)
250 mg/kg diet for 10 days, juveniles	LD50 (WHO 1984)
250 mg/kg diet for 100 days, adults	LD50 (WHO 1984)
JAPANESE QUAIL, <i>Coturnix japonica</i>	
25 mg/kg diet, 4 weeks	No effect on survival, weight gain, or activity (NRCC 1975)
200 mg/kg diet, 7 days	LD100 (NRCC 1975)
14-day-old chicks fed treated diets for 5 days, then untreated diets for 3 days	No effect on survival or food consumption (Hill and Camardese 1986)
203 mg/kg diet	LD50 (Hill and Camardese 1986)
308 mg/kg diet	LD73, reduced food consumption (Hill and Camardese 1986)
370 mg/kg diet	LD93, reduced food consumption (Hill and Camardese 1986)
500 mg/kg diet	
CHICKEN, <i>Gallus</i> sp.	
Fed diet containing 0.1 mg/kg for 6 weeks	Egg chlordane residue about 0.2 mg/kg FW, and fat residue about 0.33 mg/kg FW (NRCC 1975)
Adults fed diet containing 0.3 mg/kg for 4 weeks	No adverse effects on growth, hatchability, or chick growth (NRCC 1975)
Fed diet containing 10 mg/kg for 5 days	Egg chlordane residue about 4 mg/kg FW (NRCC 1975)
220–230 mg/kg BW	Acute oral LD50 (NRCC 1975)
RING-NECKED PHEASANT, <i>Phasianus colchicus</i>	
Single oral dose of 24–72 mg/kg BW	LD50 (Hudson et al. 1984)
50 mg/kg diet for 100 days, juveniles	LD50 (WHO 1984)
318 mg/kg diet	LD50 (NRCC 1975)
430 mg/kg diet for 5 days, then clean diet for 3 days, juveniles	LD50 (Hill et al. 1975)
EUROPEAN STARLING, <i>Sturnus</i> <i>vulgaris</i>	
Fed diet containing 1.5, 6.25, 25, or 100 mg chlordane/kg	Time for 50% mortality was 57 days for 1.5 mg/kg diet, 24 days for 6.25 mg/kg diet, 6.5 days for the 25 mg/kg diet, and 3.25 days for the 100 mg/kg diet (Stickel et al. 1979)
Fed diet containing 100 mg nonachlor/kg for 35 days	8% dead (Stickel et al. 1983)

Table 13.4 (continued) Chlordane Effects on Selected Birds

Organism and Other Variables	Effect and Reference
200 mg chlordane/kg diet	LD50 usually within 14 days (Stickel et al. 1983)
500 mg chlordane/kg diet	LD50 in 5 days (Stickel et al. 1983)
BARN OWL, <i>Tyto alba</i>, adults	
Fed diets containing 75 mg/kg until 50% died; survivors sacrificed and residues measured	Mortality reached 50% on day 40; maximum residues in brains of birds dying during exposure (or sacrificed), in mg/kg FW, were 6.5 (9.0) for <i>cis</i> -chlordane, 4.5 (9.0) for <i>trans</i> -nonachlor, 3.2 (9.0) for <i>trans</i> -chlordane, and 1.0 (2.0) for <i>cis</i> -nonachlor (Dr. O.H. Pattee, Patuxent Wildlife Research Center, personal communication)
Fed diets containing 150 mg/kg until 50% died; survivors sacrificed and residues measured	Mortality reached 50% on day 17; maximum residues in brains of owls dying during exposure (or sacrificed), in mg/kg FW, were 5.1 (1.8) for <i>cis</i> -chlordane, 3.6 (1.8) for <i>trans</i> -chlordane, 3.2 (2.1) for <i>trans</i> -nonachlor, and 0.9 (0.4) for <i>cis</i> -nonachlor (Dr. O.H. Pattee, Patuxent Wildlife Research Center, personal communication)

13.5.6 Mammals

Concern for the continued widespread use of chlordane is centered around its carcinogenicity in mice, *Mus* sp. (Ewing et al. 1985). Chlordane produced liver cancer in both sexes of two different strains of domestic mice (USEPA 1980; WHO 1984; Tojo et al. 1986) (Table 13.5). A dose-dependent incidence of hepatocellular carcinoma was evident in mice fed chlordane in their diets. Frequency of liver carcinomas was not significantly different from controls at dietary levels of 5 mg/kg and lower, but was greatly elevated (i.e., >70% frequency) at dietary levels of 50 mg/kg and higher (USEPA 1980). In contrast to mice, chlordane was not a hepatic carcinogen in rats at dietary levels up to 64 mg/kg ration (WHO 1984; USEPA 1988); however, dose-related increases in follicular cell thyroid neoplasms and malignant fibrous histiocytomas were recorded in chlordane-exposed rats (Ohno et al. 1986). In humans, no increased evidence of cancer was proven among employees in chlordane manufacturing facilities, although there is a statistically significant increase in death rate from cerebrovascular disease in that group (Klaassen et al. 1986).

Human toxicity data for chlordane is usually obtained after accidental exposure through spillage onto clothing or ingestion (Ingle 1965; NRCC 1975; USEPA 1980). In one case, a 15-month-old girl accidentally swallowed a mouthful of chlordane suspension and within 3 h displayed tremors and incoordination. Repeated seizures developed and she was treated with ethyl chloride, amobarbitol, and gastric lavage with magnesium sulfate; ataxia and excitability disappeared in about 3 weeks. At age 26 years, she was in excellent health and seemed not to have experienced latent effects from the childhood incident (WHO 1984). Other cases of accidental chlordane poisoning in children are documented, and all appear to have recovered completely after treatment (WHO 1984).

Symptoms of acute chlordane poisoning in humans include irritability, salivation, labored respiration, muscle tremors, brain wave abnormalities, incoordination, convulsions, deep depression, and sometimes death (IARC 1979; USEPA 1980, 1988). Signs of acute chlordane intoxication in other mammal species are similar to those in humans and may also include aplastic anemia and acute leukemia; cyanosis; pathology of gastrointestinal tract, liver, kidney, lung, and heart; pulmonary congestion; degenerative changes in the central nervous system; impaired uptake and utilization of glucose; interference with immunocompetence response; diarrhea; avoidance of food and water; enhanced estrone metabolism; increased production of hepatic mixed function oxidase enzymes; altered enzyme activity in brain and in kidney cortex; enlarged liver; hair loss; abdominal distension; hunched appearance; inhibited oxidative phosphorylation in liver mitochondria; and thyroid carcinoma (Saxena and Karel 1976; IARC 1979; Reuber and Ward 1979; WHO 1984; Barnett et al. 1985; Johnson et al. 1986, 1987; Klaassen et al. 1986; USEPA 1988; Suzaki et al. 1988).

Acute oral LD50 values for technical chlordane and sensitive mammals usually ranged between 25 and 50 mg/kg BW (Table 13.5). Chlordane-related compounds (i.e., *cis*-chlordane, *trans*-chlordane, heptachlor, heptachlor epoxide) stimulate superoxide (O_2^-) generation in guinea pig leukocytes,

alter membrane potential, and increase intracellular calcium concentration; toxicity of individual compounds seems to be related to superoxide generation (Suzuki et al. 1988). Metabolism of chlordane isomers results in oxychlordane, a metabolite that is about 20 times more toxic to rats than is the parent compound and is the most persistent metabolite stored in rat adipose tissue (Menzie 1978; USEPA 1980). Oxychlordane accounted for 53% in females and 63% in males of all chlordane isomers in fat of rats killed 24 h after a single oral dose of 1.0 mg/kg BW technical chlordane (Nomeir and Hajjar 1987). Acute oral LD₅₀ values in the rat, in mg/kg BW, were 19.1 for oxychlordane; 89 to 392 for *cis*-chlordane; 200 to 590 for technical chlordane; 327 for *trans*-chlordane; >4600 for chlordene, 3-chlordene, 1-hydroxychlordene, chlordene epoxide, 1-hydroxy, and 2,3-epoxy chlordene; and >10,000 for 2-chlorochlordanne ([Table 13.5](#)).

Chlordane adversely affects growth and fertility of laboratory animals (Talamantes and Jang 1977; IARC 1979; Klaassen et al. 1986; USEPA 1988) ([Table 13.5](#)). Neonatal exposure of mice to chlordane retards growth, as judged by lowered body weights during the first 12 weeks (Talamantes and Jang 1977). No fetotoxic or teratogenic effects were observed in rats born to dams fed chlordane in their diets for 2 years at levels up to 300 mg/kg diet. However, pups nursed by dams consuming chlordane at 150 or 300 mg/kg diet developed signs of toxicity (USEPA 1988). In uterine mucosa of the rabbit, chlordane isomers (as well as isomers of DDE and polychlorinated biphenyls) reduced the binding of progesterone to its cytoplasmic receptor in a dose-dependent manner, which suggests a pathway to account for chlordane-induced reproductive impairment (Lundholm 1988).

Chlordane tends to accumulate in adipose tissues and, to a lesser extent, in liver ([Table 13.5](#)). In general, animals given a single oral dose of chlordane eliminated 80 to 90% of the dose within 7 days, usually via the feces; the *cis*-isomer is eliminated more rapidly than the *trans*-isomer and results in preferential accumulations of *trans*-chlordane (Nomeir and Hajjar 1987). In rats, *trans*-chlordane is rapidly absorbed and distributed to liver and kidney at single oral dosages as low as 0.05 mg/kg BW (Ohno et al. 1986). Rabbits fed *trans*-chlordane for 10 weeks excreted 70% of accumulated chlordane during the following 2 weeks on a chlordane-free diet (Menzie 1974). Treatment with *trans*-chlordane resulted in a greater percentage of oxychlordane in fat than did treatment with *cis*-chlordane. When chlordane was removed from the diet of treated animals, levels in fat declined 60% at a relatively steady rate over 4 weeks, but then only slightly thereafter. Accumulations in liver, kidney, brain, and muscle were much lower than in fat, but excretion kinetics were similar (Nomeir and Hajjar 1987).

Results of chronic feeding studies show that dietary concentrations of chlordane between 0.76 and 5 mg/kg ration did not affect survival but did produce adverse effects on various species of laboratory animals and livestock ([Table 13.5](#)). Dietary concentrations of 0.76 mg/kg (equivalent to 0.09 mg/kg BW daily) were associated with enlarged livers in mice, 1.0 mg/kg produced elevated residues in cow's milk, 2.5 mg/kg resulted in liver pathology in rats, 3 mg/kg (equivalent to 0.075 mg/kg BW daily) produced high residues in fat of dogs, and 5 mg/kg caused liver pathology in mice ([Table 13.5](#)).

Negative results for mutagenicity of *cis*-chlordane and *trans*-chlordane were reported in various strains of bacteria and in hepatocyte cultures of small mammals. But technical chlordane proved mutagenic to selected strains of *Salmonella typhimurium* and induced gene conversions in certain strains of the yeast, *Saccharomyces cervisiae* (IARC 1979; USEPA 1980, 1988; WHO 1984).

Chlordane interacts with other chemicals to produce additive or more-than-additive toxicity. For example, chlordane increased hepatotoxic effects of carbon tetrachloride in the rat (USEPA 1980; WHO 1984), and in combination with dimethylnitrosamine acts more than additively in producing liver neoplasms in mice (Williams and Numoto 1984). Chlordane in combination with either endrin, methoxychlor, or aldrin is additive or more-than-additive in toxicity to mice (Klaassen et al. 1986). Protein deficiency doubles the acute toxicity of chlordane to rats (WHO 1984). In contrast, chlordane exerts a protective effect against several organophosphorus and carbamate insecticides (WHO 1984), protects mouse embryos against influenza virus infection, and mouse newborns against oxazolone delayed hypersensitivity response (Barnett et al. 1985). More research seems warranted on interactions of chlordane with other agricultural chemicals.

Table 13.5 Chlordane Effects on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
COW, <i>Bos bovis</i>	
Oral doses equivalent to 1, 10, or 100 mg/kg diet for 60 days, then no dose for 30 days	At 1 mg/kg diet equivalent, total chlordane in fat increased from 0.24 mg/kg at day 30 to 0.47 at day 60; 30 days later, residues remained elevated at 0.45 mg/kg. The same pattern was seen at higher dose levels but residues were higher at 1.2–1.5 mg/kg in the 10-mg/kg diet group, and 2.6–4.0 in the 100-mg/kg group (Nomeir and Hajjar 1987) Milk contained less than 50 µg/L (NRCC 1975)
Fed diets containing 10 mg/kg for 10 days	Milk contained less than 200 µg/L (NRCC 1975)
Fed diets containing 20 mg/kg for 150 days	
25–90 mg/kg body weight (BW)	Acute oral LD ₅₀ (WHO 1984)
DOG, <i>Canis familiaris</i>	
Fed diets containing 0.3, 3, 15, or 30 mg chlordane/kg food for 2 years	Liver abnormalities in 15- and 30-mg/kg groups; no adverse effects at lower doses on behavior, appearance, survival, weight gain, or blood chemistry. In the 3-mg/kg group, equivalent to 0.075 mg/kg BW daily, maximum residue in fat was 3.6 mg/kg (NRCC 1975; WHO 1984; USEPA 1988)
Daily oral dose ranging between 5 and 200 mg/kg BW	Dose-dependent mortality. All died between 25 days and 93 weeks (WHO 1984)
Single oral dose of 200–700 mg/kg BW	No deaths (WHO 1984)
GOAT, <i>Capra</i> sp.	
180 mg/kg BW	Acute oral LD ₅₀ (WHO 1984)
GUINEA PIG, <i>Cavia</i> spp.	
Males exposed daily for 90 days to 67 mg/kg BW through dermal painting	Mild degenerative changes in skin and testes (WHO 1984)
HAMSTER, <i>Cricetus</i> spp.	
1720 mg/kg BW	Acute oral LD ₅₀ (USEPA 1980; WHO 1984)
HUMANS, <i>Homo sapiens</i>	
100 µg/L	Reduced growth and altered cell morphology in human cell cultures (USEPA 1980)
25–50 mg/kg BW	Acute lethal oral dose (WHO 1984)
100 mg/kg BW	Fatal (IARC 1979)
Suicidal female swallowed 6 g chlordane, equivalent to 104 mg/kg BW	Death in 9 days (WHO 1984)
Contamination of water supply in Chattanooga, Tennessee, by up to 1.2 g chlordane/L	Gastrointestinal/neurological symptoms in 13 reported cases (WHO 1984)
MONKEY, <i>Macaca fascicularis</i>	
1 or 10 mg/kg BW of <i>trans</i> -chlordane given once weekly for 5 weeks by subcutaneous injection. Adipose tissue, blood, and skin lipids analyzed for up to 20 weeks after the last injection	<i>trans</i> -Chlordane and oxychlordane were detected in all tissues. In blood and adipose tissue, <i>trans</i> -chlordane decreased rapidly and oxychlordane increased gradually until a plateau was reached. Good correlations were determined for all chemicals between blood and adipose tissue, regardless of collection time and dose level, and between skin lipids and adipose tissue. At the high dose, <i>trans</i> -chlordane reached a maximum of 35 mg/kg FW in adipose tissue, but was not detectable after 20 weeks. The oxychlordane concentration in adipose tissue of the high-dose group was 25 mg/kg FW after the last injection, and 18 mg/kg FW after 20 weeks (Sasaki et al. 1992)

Table 13.5 (continued) Chlordane Effects on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
CYNOMOLGUS MONKEY, <i>Macaca</i> spp.	
Inhalation for 90 days of air containing 10 µg technical chlordane/L	No measurable effect (Khasawinah et al. 1989)
INDIAN DESERT GERBIL, <i>Meriones hurrianae</i>	
Males dosed intramuscularly at 2.5 mg/kg BW every 3 days for 45 days	Hyperproteinemia, hyperglycemia, and enhanced serum alkaline and acid phosphatase activities (WHO 1984)
Single intramuscular injection of 25, 50, or 75 mg/kg BW	Dose-dependent hyperglycemia, due to increased production of liver glucose, in blood of treated animals, reaching a maximum glucose level about 1 h post-injection, persisting for up to 3 days, and approaching control levels within 1 week (Saxena and Karel 1976)
MOUSE, <i>Mus</i> spp.	
On days 2, 3, and 4 of life, each received 0.075 or 0.15 mg of either <i>cis</i> -chlordane or <i>trans</i> -chlordane	Depressed growth and delayed development in eye and vaginal opening during first 12 weeks; all normal at necropsy after 15 weeks (Talamantes and Jang 1977)
Oral doses of 0.08 or 0.25 mg daily for 30 days, equivalent to 100 and 300 mg/kg BW	Dose-related reduction in size of seminiferous tubules and in percentage of damaged tubules. High-dose group experienced 24–58% reduction in spermatogenesis (and high death rate); low-dose group 11–21% reduction; and controls 0.5–6.1% reduction (Balash et al. 1987)
0.09 mg/kg BW daily for 2 years, equivalent to 0.76 mg/kg diet	Increased liver to BW ratios in both sexes. At higher dietary concentrations equivalent to 0.43 and 1.1 mg/kg BW daily, liver necrosis was observed in males (USEPA 1988)
Daily oral doses for 14 days of 0.1, 4, and 8 mg <i>trans</i> -chlordane/kg BW	Significant dose-related increase in liver weight and leukocytes; no effect on immunocompetence (Johnson et al. 1986)
Pregnant females treated with 0.16 or 8 mg/kg BW throughout gestation	Decreased immune competence in offspring of high-dose group challenged with oxazolone at age 101 days (WHO 1984)
Single oral dose of <i>cis</i> -chlordane of 1.0 mg/kg BW	Peak tissue concentrations reached (in µg/kg FW) were 1180 in liver, 880 in fat, 349 in kidney, 248 in lungs, 164 in muscle, 92 in testes, and 68 in brain. Peak concentration in blood of 113 µg/L reached in 8 h; 34% of total dose excreted in feces by 12 h after treatment. After 14 days, measurable residues detected in gonad, muscle, fat, and kidney (Ewing et al. 1985)
Offspring from parents given 1.0 or 2.5 mg/kg BW for 7 consecutive days	Impaired conditioned avoidance response behavior and hyperactivity (WHO 1984)
Fed diets containing 5, 25, or 50 mg technical chlordane/kg ration for 18 months	Dose-related incidence of hepatic nodular hyperplasias in the 25 and 50 mg/kg diets and an increased incidence of hepatomas in the male 5- and 25-mg/kg groups. Controls experienced a high incidence of premature deaths (Epstein 1976)
Females injected intraperitoneally with 25 mg/kg BW once weekly for 3 weeks	Fertility reduced by about 50% (USEPA 1988)
Fed diets containing 25 to 100 mg chlordane/kg food for six generations	At 100 mg/kg, decreased viability in first and second generations and no offspring in third generation. At 50 mg/kg, viability was reduced in fourth and fifth generations. No significant effects in the 25-mg/kg group, even after six generations (WHO 1984)
Males fed diets containing 29.9 or 56.2 mg technical chlordane/kg for 80 weeks	Frequency of liver tumors was 88% in high-dose group, 33% in low-dose group, and 19% in controls (USEPA 1980)
Females fed diets containing 30 or 64 mg technical chlordane/kg for 80 weeks	Frequency of liver tumors was 70% in high-dose group, 6% in low-dose group, and 4% in controls (USEPA 1980)
Males given single dose of 50 or 100 mg/kg BW, then mated with untreated females	No dominant lethal changes produced (USEPA 1980)
390–430 mg/kg BW	Acute oral LD ₅₀ (IARC 1979; USEPA 1980)

Table 13.5 (continued) Chlordane Effects on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
RABBIT, <i>Oryctolagus</i> sp.	
Oral doses of 1, 5, or 15 mg/kg BW daily on days 6–18 of gestation	Some miscarriages in 1 and 15 mg/kg groups; no changes in behavior, appearance, or body weight; no teratogenic effects observed (WHO 1984).
Dosed orally with 14.3 mg of radiolabeled <i>trans</i> -chlordane daily for 10 weeks and killed 2 weeks after the last dose	Residues were highest in abdominal and subcutaneous fat (235 mg/kg FW), followed by heart and spleen (75–91 mg/kg), then liver, brain, and blood (25–44 mg/kg) (Nomeir and Hajjar 1987)
20 mg/kg BW, single intravenous injection	LD74 (Ingle 1965)
Dermal exposure for 90 days equivalent to 20–40 mg/kg BW	LD50 (WHO 1984)
Dosed orally with <i>cis</i> -chlordane at 67 mg/kg BW, or <i>trans</i> -chlordane at 30 mg/kg BW every 4 days for a total of 4 doses, then killed 5 days after the last dose	Residues in the <i>trans</i> -chlordane group were higher (17–77 mg/kg) than in the <i>cis</i> -chlordane group (8–67 mg/kg), although <i>trans</i> -chlordane was given at a much lower dose. Fat and kidney usually contained the highest concentrations, and brain the lowest. Oxychlordane was found in all tissues at 0.1 mg/kg in brain, 11 mg/kg in fat, and 0.5–2 mg/kg in liver, muscle, and kidney (Nomeir and Hajjar 1987)
100–500 mg/kg BW	Acute oral LD50 (Ingle 1965; USEPA 1980)
780–1200 mg/kg BW	Acute dermal LD50; death preceded by skin irritation, tremors, and convulsions (WHO 1984)
SHEEP, <i>Ovis aries</i>	
Single oral dose of 500 mg/kg BW	Incoordination and partial blindness; full recovery in 5–6 days (WHO 1984)
Single oral dose of 1000 mg/kg BW	Severe respiratory and nervous signs in 16 h, and death in 48 h (WHO 1984)
BABOON, <i>Papio anubis</i>	
Fed diets containing chlordane, equivalent to 0.1–1.0 mg/kg BW daily, for 2 years	At 1.0 mg/kg BW, cytochrome P-450 activity was significantly increased, but no other significant effects were recorded on general health or on any major organ system (WHO 1984)
RAT, <i>Rattus</i> spp.	
Inhalation of air containing technical chlordane	
0.1 µg/L, 90 days	Adverse biological response (Khasawinah et al. 1989)
5.8 or 28.2 µg/L, 28 days	No measurable difference from controls at low dose; impaired liver function at high dose (Khasawinah et al. 1989)
154 µg/L, 5 days	Death (Khasawinah et al. 1989)
413 µg/L, 2 days	Death (Khasawinah et al. 1989)
Fed technical chlordane at dietary levels of 1, 5, or 25 mg/kg, equivalent to daily doses of 0.045, 0.229, and 1.175 mg/kg BW, respectively, for 130 weeks (2.5 years)	No significant effects on hematology, clinical chemistry, body weight, or survival rate. Dose-dependent hepatocellular necrosis (34% in high-dose group); liver adenomas in males and hepatocellular swelling in females from the high-dose group (USEPA 1988)
0.05 mg radiolabeled <i>trans</i> -chlordane/kg BW, single oral dose, residues measured over 96 h after exposure	Maximum residues (in mg/kg FW) and time post-administration were: liver, 0.1, 2 h; fat tissue, 0.09, 96 h; kidney, 0.07, 4 h; skin, 0.03, 8 h; brain, 0.01, 4 h; muscle, 0.008, 4 h; and blood 0.003, 4 h. Half-time persistence was 6.5–13 h for the rapidly decreasing phase, and 4.8–8.9 days for the slowly decreasing phase (Ohno et al. 1986)
Daily intraperitoneal injections of technical chlordane at 0.15, 1.75, or 25 mg/kg daily for 42 days	Dose-dependent alterations of brain potentials without behavioral signs of chronic toxicity (USEPA 1980)
Single oral dose of 0.2 mg/kg BW of <i>cis</i> -chlordane, <i>trans</i> -chlordane, or oxychlordane	Maximum residues in fat after 24 h, in mg/kg FW, were 0.3 for <i>cis</i> -chlordane, 0.7 for <i>trans</i> -chlordane, and 0.5 for oxychlordane (Nomeir and Hajjar 1987)
Single oral dose of 0.2 or 1.0 mg/kg BW technical chlordane	Maximum residues in fat at 24 h (in mg/kg FW) were 0.5 for the low-dose group, and 3.7 for the high-dose group (Nomeir and Hajjar 1987)

Table 13.5 (continued) Chlordane Effects on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
Fed diets containing 0.3, 3, 15, 30, or 60 mg technical chlordane/kg diet for 3 generations	Levels up to and including 30 mg/kg diet had no measurable effect on fertility, number of young produced, growth, or mortality rate; no gross or microscopic differences between the groups. At 60 mg/kg the second F ₃ generation litters had elevated mortality (11%) during the latter part of the nursing period; these animals also showed gross and microscopic pathology (NRCC 1975; WHO 1984)
Single oral dose of 1.0 mg <i>cis</i> -chlordane/kg BW	Peak tissue concentrations (in mg/kg FW) were noted within 4 h after treatment: liver, 1.9; fat, 1.2; kidney, 0.7; lung, 0.3; brain 0.2; testes, 0.1; muscle, 0.1; and blood, 0.08. After 12 h, 7% was excreted, and after 3 days, 83% was voided (Ewing et al. 1985)
Single oral dose of 1.0 mg/kg BW	About 50% excreted in feces after 1 day and >90% in 7 days; only 2–3% of the dose was detected in the urine (Nomeir and Hajjar 1987)
Fed oxychlordane in diets for 90 days at rate equivalent to 2.0 mg/kg BW daily	No gross pathology or histological lesions (NRCC 1975; WHO 1984)
Fed 2.5, 25, or 75 mg technical chlordane per kg of diet for 2 years	Severe toxic signs at 25 and 75 mg/kg; liver damage at 2.5 mg/kg diet (WHO 1984)
Long-term feeding studies at dietary concentrations between 5 and 320 mg technical chlordane/kg	Reduced survival and growth at dietary levels >150 mg/kg; liver enlargement and micropathology at >20 mg/kg; no effect on reproduction at 150 mg/kg diet; no adverse effects at 5 mg/kg diet (Ingle 1965)
Fed <i>cis</i> -chlordane at dietary levels of 0, 5, 15, 25, or 35 mg/kg	Increased mortality and growth retardation in 4–5 months at 35-mg/kg diet; growth normal in other groups; some liver damage in 25- and 35-mg/kg groups (WHO 1984)
Daily oral dose of 6.5–25 mg technical chlordane/kg BW, for 15 days	No tremors or convulsions; however, dose-related liver pathology was noted (WHO 1984)
Single oral dose of 10 mg radiolabeled <i>trans</i> -chlordane/kg BW	Maximum residues, in mg/kg FW and time after administration were: liver, 21, 4 h; kidney, 18, 4 h; adipose tissue, 11, 16 h; skin, 5, 8 h; brain, 3.4, 4 h; muscle 1.4, 4 h; and blood, 0.6, 4 h. Tb 1/2 of 5–12 h for the fast component, and 4.3–7.3 days for the slow component (Ohno et al. 1986)
Fed diets containing 15 or 25 mg/kg of <i>cis</i> -chlordane for 78 weeks	No adverse effects on liver at 15-mg/kg diet; some effects at 25-mg/kg (NRCC 1975)
Fed <i>trans</i> -chlordane at dietary levels of 15, 25, 35, or 75 mg/kg diet	Decreased survival, liver damage, and growth retardation of males in 8 months at 75-mg/kg diet; growth normal at other doses (WHO 1984)
19.1 mg oxychlordane/kg BW	Acute oral LD50 (WHO 1984)
20 mg technical chlordane/kg diet for 350 days	Residues (in mg/kg FW) were about 20 for adipose tissue, 0.8 for liver, and 0.2 for heart (NRCC 1975)
Daily oral doses of 25 mg/kg BW for 15 days	No toxic signs (USEPA 1980)
Fed diets containing 35 mg/kg <i>trans</i> -chlordane for 78 weeks	No adverse effects on liver (NRCC 1975)
Daily oral dose of 50 mg technical chlordane/kg BW for 15 days	2 of 5 rats died; toxic signs in survivors (WHO 1984)
83–392 mg/kg BW	Acute oral LD50 for <i>cis</i> -chlordane (USEPA 1980, 1988)
Fed diets containing 100 or 200 mg/kg ration of <i>cis</i> -chlordane or <i>trans</i> -chlordane for 11–15 days	Maximum residues, in mg/kg lipid, in females fed 100 mg/kg <i>cis</i> -chlordane were 23 for <i>cis</i> -chlordane and 100 for oxychlordane; for the 200 <i>cis</i> -chlordane group, levels were 48 for <i>cis</i> -chlordane and 182 for oxychlordane. Females fed 100 mg/kg <i>trans</i> -chlordane had 10 mg/kg lipid of <i>trans</i> -chlordane and 201 of oxychlordane; for the 200 mg/kg group, residues were 23 mg/kg lipid of <i>trans</i> -chlordane and 470 of oxychlordane; for all groups, residues in males were 6–21 times lower than in females (Nomeir and Hajjar 1987)
Fed diets averaging 121 and 241 mg/kg feed (females) and 203 and 407 mg technical chlordane/kg diet (males) for 80 weeks	Increased mortality, tremors, growth reduction; elevated incidence of thyroid neoplasms and malignancies in all treated animals, but no hepatocellular carcinomas (IARC 1979; USEPA 1988)
137 mg/kg BW	Acute oral LD50 for rats fed a low protein diet (USEPA 1980)
200–590 mg technical chlordane/kg BW	Acute oral LD50 (NRCC 1975; USEPA 1980; WHO 1984)

Table 13.5 (continued) Chlordane Effects on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
205 mg technical chlordane/kg BW	Acute dermal LD50 for females (WHO 1984)
Fed diets containing 300, 500, or 1000 mg technical chlordane/kg	75% dead at 300 mg/kg diet after 100 days; all dead in 70 days at 500 mg/kg, or in 10 days at 1000 mg/kg (WHO 1984)
311 mg/kg BW	Acute oral LD50 for rats fed a normal protein diet (USEPA 1980)
Fed diets containing 320 mg technical chlordane/kg from weaning	Reduced sexual activity, reduction in number of viable litters, increased rate of death of progeny prior to weaning (WHO 1984)
327 mg <i>trans</i> -chlordane/kg BW	Acute oral LD50 (USEPA 1980; WHO 1984)
335 mg/kg BW	Acute oral LD50 for males IARC 1979
343 mg/kg BW	Acute intraperitoneal (IP) LD50 for adults (USEPA 1980)
350 mg/kg BW	IP injection produced mild tremors and disorientation within a few minutes, and death within 1 h (USEPA 1980)
530–690 mg/kg BW	Acute dermal LD50 for females (USEPA 1980; WHO 1984)
539 mg/kg BW	Acute IP LD50 for newborns pretreated with 40 mg/kg BW phenobarbital (USEPA 1980)
840 mg/kg BW	Acute dermal LD50 for males (USEPA 1980)
1121 mg/kg BW	Acute IP LD50 for newborns (USEPA 1980)
Oral administration (in mg/kg BW) of 4600 chlordene, 4600 3-chlorochlordanne, 4600 1-hydroxychlordanne, 4600 chlordene epoxide, 4600 1-hydroxy, 2, 3-epoxy chlordanne, or 10,200 2-chlorochlordanne	Less than 50% dead (WHO 1984)
PIG, <i>Sus</i> spp.	
Fed diet containing 300 mg/kg of <i>cis</i> -chlordanne or <i>trans</i> -chlordanne for 60–90 days	Residues of total chlordanes in fat ranged from 9 mg/kg to 72 mg/kg; values were highest for <i>trans</i> -chlordanne and lowest for <i>cis</i> -chlordanne (NRCC 1975)

13.6 RECOMMENDATIONS

All use of chlordane was banned in Norway in 1967 (Ingebrigtsen et al. 1984). In August 1975, the USEPA issued its intent to suspend registrations and prohibit production of all pesticides containing heptachlor or chlordane, based on evidence of carcinogenicity (Glooschenko and Lott 1977). On July 1, 1983, chlordane use was prohibited in the United States for any purpose except to control underground termites. A similar situation exists in Japan (Ohno et al. 1986; Tojo et al. 1986).

The continued use of chlordane, coupled with its general persistence in the environment, suggests that extreme caution be taken in all stages of its manufacture, transport, storage, and application (Greenhalgh 1986). In particular, chlordane use near marine environments is not recommended because of chlordane's high toxicity to marine life (USEPA 1988). At elevated risk of chlordane toxicity in the human population are children, as a result of the milk they consume; fishermen and their families, because of high consumption of fish and shellfish; people living downwind from fields treated with chlordane; and individuals residing in houses treated with chlordane-containing pesticides (USEPA 1980).

The proposed criterion for marine life protection of 0.004 µg/L as a 24-h mean, not to exceed 0.09 µg/L at any time (Table 13.6), seems to offer a reasonable degree of protection. But the proposed freshwater criterion of 0.0043 µg/L, 24-h average, not to exceed 2.4 µg/L at any time (Table 13.6), overlaps the range of 0.2 to 3.0 µg/L shown earlier to be harmful to sensitive species of fish and aquatic invertebrates. Accordingly, the maximum permissible freshwater value should

be adjusted downward. "Safe" residues in tissues of aquatic biota require clarification, and probably additional research effort. Criteria on chlordane for protection of mammalian wildlife are missing, and those formulated for birds are incomplete and require data on no-observable-effect levels from lifetime exposures (Table 13.6). Until this information becomes available, it seems prudent to use criteria developed for human health protection as temporary guidelines for the protection of vertebrate wildlife. Specifically, daily intake should not exceed 0.001 mg total chlordane, including *cis*-chlordane, *trans*-chlordane, and oxychlordane/kg BW; and food items should not exceed 0.3 mg/kg FW (Table 13.6).

Table 13.6 Proposed Chlordane Criteria for Protection of Natural Resources and Human Health

Resource	Criterion or Effective Chlordane Concentration	Reference ^a
AQUATIC LIFE		
Water concentration, safe level		
Freshwater	<0.0043 µg/L, 24 h average; not to exceed 2.4 µg/L at any time	1
Saltwater	<0.004 µg/L, 24 h average; not to exceed 0.09 µg/L at any time	1
Tissue concentrations		
Fish		
Reduced survival	>300 mg/kg tissue, lipid weight (LW) basis	2
No observed adverse effect level (NOEL)	<0.1 mg/kg fresh weight (FW) tissue	3
Estuarine invertebrates, lethal	>106 mg/kg tissue LW	2
BIRDS		
Concentration in brain		
Joint lethal range	1.1–5.5 mg/kg FW for oxychlordane and 3.4–8.3 mg/kg FW for heptachlor epoxide	4, 12
Single lethal range	6 mg/kg FW for oxychlordane or 9 mg/kg FW for heptachlor epoxide	4, 12
Diet, acceptable range, but producing slight elevation in tissue concentrations	0.1–0.3 mg/kg diet	6
MAMMALS		
Dog, <i>Canis familiaris</i> , NOEL	<3 mg/kg diet, equivalent to <0.075 mg/kg body weight (BW) daily	5, 6
Rat, <i>Rattus</i> sp., NOEL	<5 mg/kg diet, equivalent to 0.25 mg/kg BW daily	5
Livestock water use, USA	<3 µg/L	7
HUMAN HEALTH		
Drinking water		
Worldwide	<0.3 µg/L	5, 15
Canada, United States	<3.0 µg/L	1, 7
Chronic, child, U.S.	<0.5 µg/L	7, 15
Maximum 1-day exposure, adult, U.S.	63.0 µg/L	7
Increased lifetime risk of cancer, 70-kg adult, 2 liters daily ^b		
10 ⁻⁴	2.7 µg/L	7
10 ⁻⁵	0.27 µg/L	7
10 ⁻⁶	0.027 µg/L	7
Acceptable daily intake ^c , 70-kg adult	<70 µg, equivalent to <0.001 mg/kg BW	1, 3, 5, 6, 8, 14, 15
Diet		
U.S. Food and Drug Administration "action level"	0.3 mg/kg FW	3, 8-10, 13
Australia	<0.05 mg/kg FW in meats, including oxychlordane	11

Table 13.6 (continued) Proposed Chlordane Criteria for Protection of Natural Resources and Human Health

Resource	Criterion or Effective Chlordane Concentration	Reference ^a
Worldwide	Usually <0.3 mg/kg FW, but residue tolerances vary between 0.02 and 0.5 mg/kg FW, based on the sum of <i>cis</i> -chlordane, <i>trans</i> -chlordane, and oxychlordane	5, 8
Air		
USSR	Maximum allowable concentration of 0.01 mg/m ³	5
Romania	<0.3 mg/m ³ , maximum allowed is 0.6 mg/m ³	5
Belgium, Finland, U.S., Japan, the Netherlands	<0.5 mg/m ³	1, 5, 7, 8, 15
15-min exposure limit, United States	<2 mg/m ³	1

^a 1, USEPA 1980; 2, Zitko 1978; 3, Arruda et al. 1987; 4, Blus et al. 1983; 5, WHO 1984; 6, NRCC 1975; 7, USEPA 1988; 8, IARC 1979; 9, Ingle 1965; 10, Wood et al. 1986; 11, Petterson et al. 1988; 12, Stickel et al. 1979; 13, Kennish and Ruppel 1997; 14, Rai and Mandal 1993; 15, USPHS 1994.

^b One excess cancer per million (10^{-6}) is associated with lifetime exposure to chlordane in drinking water at concentrations as low as 0.027 µg/L, the most conservative estimate. A lifetime health advisory computation was not possible because chlordane is a probable human carcinogen (USEPA 1988).

^c Consumed fish are considered to be the only source of chlordane; up to 98% of chlordane exposure results from aquatic organisms with high (up to 14,100X) bioconcentration potential (USEPA 1980). Urban residents should not consume more than 8 ounces (227 mg) of fish daily containing 0.03 mg total chlordanes/kg FW, and nonurban residents up to 1135 mg of fish daily containing 0.03 mg/kg FW (Arruda et al. 1987). The value of 0.001 mg/kg BW daily is based on the no-observed-effect level of 5 mg/kg in the diet of the rat, equivalent to 0.25 mg/kg BW, and 3 mg/kg in the diet of the dog, equivalent to 0.075 mg/kg BW (WHO 1984).

Additional research on chlordane is recommended in nine general areas:

1. Monitoring of background concentrations of oxychlordane in wildlife, since this metabolite is more toxic and persistent than the parent chemical (Kawano et al. 1988)
2. Interpretation of the biological significance of residue levels found in wildlife
3. Adoption of improved uniform methods of quantitation so that residue levels can be compared, and so that a time estimate of their environmental significance can be made (NRCC 1975; USEPA 1988)
4. Reexamination of aquatic toxicity data wherein concentrations tested exceeded the solubility of chlordane in water of 6 to 9 µg/L (WHO 1984)
5. Evaluation of interaction of chlordane with other agricultural chemicals, including heptachlor, to clearly delineate any additive, synergistic, or antagonistic effects (WHO 1984)
6. Reevaluation of the cancer risk of chlordane to experimental animals (WHO 1984)
7. Measurement of chronic exposures of fish and wildlife to realistic environmental levels (WHO 1984)
8. Measurement of effects of depleted soil fertility from chlordane-induced earthworm suppression on migratory birds and other wildlife (NRCC 1975; WHO 1984)
9. Continuance of epidemiological studies on workers who have been exposed to chlordane (WHO 1984).

13.7 SUMMARY

Technical chlordane is an organochlorine compound first introduced into the United States in 1947 in a variety of formulations for use as a broad-spectrum pesticide. By 1974, about 9.5 million kg of chlordane were being produced annually. Concern over the potential carcinogenicity of chlordane has led to sharply curtailed production. Since 1983, chlordane use in the United States has been prohibited, except for control of underground termites.

Technical chlordane consists of about 45 components, primarily *cis*-chlordane (19%), *trans*-chlordane (24%), heptachlor (10%), *cis*- and *trans*-nonachlor (7%), and various chlordane isomers (22%). Chemical analysis of technical chlordane is difficult because of analytical interferences from other organochlorine compounds, nonstandardization of analytical techniques, variations in the number and relative composition of components in weathered chlordane, and uncertainty of the structural formulas and other properties of several compounds present.

Past chlordane use, coupled with atmospheric transport as the major route of dissemination, produced global contamination of fish and wildlife resources and human populations. The chemical and its metabolites were frequently detected in all species examined, but usually at low concentrations. Residues in fish muscle sometimes exceeded the U.S. Food and Drug Administration action level of 0.3 mg/kg fresh weight recommended for human health protection. In general, chlordane in animals is highest near areas where the chemical has been applied to control termites; concentrations are highest in fat and liver, especially in predatory species.

The half-life of chlordane in water is comparatively short. *cis*-Chlordane, for example, usually persists less than 18 h in solution. In soils, however, some chlordane isomers persist for 3 to 14 years because of low solubility in water, high solubility in lipids, and relatively low vapor pressure. There seems to be little accumulation of chlordane in crops grown in contaminated soils.

Chlordane is readily absorbed by warm-blooded animals via skin, diet, and inhalation, and distributed throughout the body. In general, residues of chlordane and its metabolites are not measurable in tissues 4 to 8 weeks after exposure, although metabolism rates varied significantly between species. Food chain biomagnification is usually low, except in some marine mammals. In most mammals, the metabolite oxychlordane has proven much more toxic and persistent than the parent chemical.

Many species of aquatic organisms are adversely affected at concentrations in water between 0.2 and 3.0 µg/L technical chlordane. Sensitive bird species had reduced survival on diets containing 1.5 mg chlordane per kilogram ration, or after a single oral dose as low as 14.1 mg chlordane per kilogram body weight. Chlordane has produced liver cancer in laboratory strains of domestic mice, but carcinogenicity has not been established in other mammals.

Chlordane criteria for protection of marine life (0.004 µg/L, 24-h mean; not to exceed 0.09 µg/L) appear satisfactory. Proposed criteria for freshwater life protection (0.0043 µg/L, 24-h mean; not to exceed 2.4 µg/L), however, overlap the range of 0.2 to 3.0 µg/L shown to adversely affect certain fish and aquatic invertebrates, suggesting that some downward modification in the maximum permissible level is needed. Chlordane criteria for protection of birds and mammals are inadequate because the database is incomplete. Until these data become available, a reasonable substitute is the criteria proposed for human health protection — namely, daily intake not to exceed 0.001 mg chlordane per kilogram body weight, and diet not to exceed 0.3 mg chlordane per kilogram fresh weight.

Most authorities agree that more studies are needed in several areas:

- Monitoring of oxychlordane concentrations in wildlife
- Interpretation of the biological significance of residue levels found in wildlife
- Standardization of analytical extraction and other techniques for quantitation of chlordane and its metabolites
- Reexamination of aquatic toxicity data where test concentrations exceeded the solubility of chlordane in water (6 to 9 µg/L)
- Interaction effects with other agricultural chemicals
- Reevaluation of the cancer risk of chlordane on representative organisms at realistic environmental levels
- Effects of depleted soil fertility from chlordane-induced earthworm suppression
- Continuance of epidemiological studies on exposed workers.

13.8 LITERATURE CITED

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CHAPTER 14

Chlorpyrifos

14.1 INTRODUCTION

Chlorpyrifos (phosphorothioic acid *O,O*-diethyl *O*-(3,5,6-trichloro-2-pyridinyl) ester), also commonly known as Dursban and Lorsban, was first registered as a broad-spectrum insecticide in 1965, and subsequently used widely to control a variety of pests such as fire ants, turf and ornamental plant insects, cockroaches, mosquitoes, leatherjackets, termites, hornflies, lice, and fleas (U.S. Environmental Protection Agency [USEPA] 1986; Hughes et al. 1991; Clements et al. 1992; U.S. Public Health Service [USPHS] 1995; Ryals et al. 1998). In 1982, total agricultural use of chlorpyrifos was estimated at 2.2 to 3.2 million kg, and industrial uses ranged between 0.68 and 1.04 million kg (USEPA 1982). In 1984, about 0.15 million kg (0.33 million pounds) of chlorpyrifos were applied to about 600,000 ha (1.48 million acres) of wetlands in the United States for mosquito control (Odenkirchen 1987). More than 1.1 million kg chlorpyrifos were used in California in 1990 (Menconi and Paul 1994). Atmospheric transport of chlorpyrifos from California's Central Valley to the Sierra Nevada mountains in California was estimated at 27 kg annually in 1995 and 1996 (McConnell et al. 1998). Treatment programs in which chlorpyrifos concentrations suitable for mosquito control and other insect pests were used have been shown to be detrimental to nontarget species, including aquatic organisms, waterfowl, and terrestrial organisms from surrounding ecosystems (Linn 1968; Hurlbert et al. 1970, 1972; Atkins 1972; Streu and Cruz 1972; Nelson and Evans 1973; Butcher et al. 1977; Thirugnanam and Forgash 1977; Tagatz et al. 1982; Goodman et al. 1985a; McEwen et al. 1986; Mayer 1987; Odenkirchen 1987; Smith 1987; Odenkirchen and Eisler 1988). Domestic use of chlorpyrifos has resulted in the death of an 11-day-old infant (Center for Disease Control [CDC] 1980) and the poisoning of office workers (Hodgson et al. 1986). Prophylactic use of chlorpyrifos on farm animals has caused reproductive impairment of livestock (Everett 1982). Chlorpyrifos-resistant strains of insects have been detected; they include the German cockroach (*Blattella germanica*) in Florida and Nebraska (Milio et al. 1987) and the sawtoothed grain beetle (*Oryzaephilus surinamensis*) in Australia (Collins 1985).

14.2 ENVIRONMENTAL CHEMISTRY

Formulations of chlorpyrifos include emulsifiable concentrates, wettable powders, granules, pellets, microencapsulates, and impregnated materials. Suggested diluents for concentrates include water and petroleum distillates, such as kerosene and diesel oil. Carrier compounds include synthetic clays with alkyl/aryl sulfonates as wetting agents (Table 14.1). Little information is available to assess the influence of various use formulations on toxicity, dispersal, decomposition, and bioavailability. Chemical and other properties of chlorpyrifos are summarized in Table 14.2 and Figure 14.1.

Table 14.1 Selected Chlorpyrifos Formulations and Carriers

Compound ^a	Formulation	Carrier
Dursban 2E	Emulsifiable concentrate of 0.285 kg/L (2.4 lb/gal)	Solution in aromatic distillate with anionic/nonionic emulsifier blend and residual chlorinated solvent
Dursban M	Emulsifiable concentrate of 0.57 kg/L (4.8 lb/gal)	As above
Dursban 6	Solution of 0.855 kg/L (7.2 lb/gal)	Solution in an aromatic distillate
Dursban 2 1/2	Granular, 2.5%	Absorbed onto stabilized clay with release agents added
Lorsban 4C	Emulsifiable concentrate of 0.479 kg/L (4.0 lb/gal)	Solution in aromatic naphtha with emulsifiers
Lorsban 25W	Wettable powder, 25%	Dispersion on blended clays with alkyl/aryl sulfonates as wetting agents

^a Dursban and Lorsban are registered trademarks of the Dow Chemical Company.

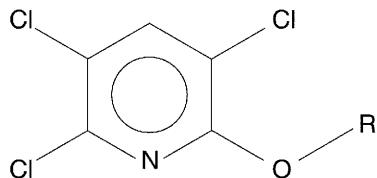
Modified from Marshall, W.F. and J.R. Roberts. 1978. *Ecotoxicology of Chlorpyrifos*. Natl. Res. Coun. Canada, Assoc. Comm. Sci. Crit. Environ. Qual., Publ. 16059, Ottawa, Ontario, Canada. 314 pp.

Table 14.2 Chemical and Other Properties of Chlorpyrifos

Variable	Datum
Chemical name	Phosphorothioic acid O,O-diethyl O-(3,5,6-trichloro-2-pyridinyl) ester
Alternate names	CAS 2921-88-2; Dursban; Lorsban; 27311; Trichlorpyrophos; Brodan; Pyrinex; Chlorpyriphos-ethyl
Primary uses	Insecticide, acaricide
Producers	Dow Chemical Company; India Medical Corp.; Makhteshim-Agan (Israel); Planters Products, Inc.
Empirical formula	C ₉ H ₁₁ Cl ₃ NO ₃ PS
Molecular weight	350.57
Physical state at 25°C	White granular crystalline solid
Melting point	41.5–43.5°C
Vapor pressure	
25°C	1.87 × 10 ⁻⁵ mmHg
35°C	8.87 × 10 ⁻⁵ mmHg
Heat of sublimation	26,800 cal/mol
Percent by weight	
Carbon	30.83
Hydrogen	3.16
Chlorine	30.34
Nitrogen	4.00
Oxygen	13.69
Phosphorus	8.83
Sulfur	9.15
Solubility	
Water, 23–25°C	0.4–2.0 mg/L
Isooctane, 23°C	790.0 g/kg
Methanol, 23°C	450.0 g/kg
Log K _{ow}	5.2
Soil organic carbon/water partition coefficient	13,600

Data from Brust 1966; Rigerink and Kenaga 1966; Kenaga 1971; Windholz 1976; Menconi and Paul 1994.

The degradation half-life time (T_b 1/2) of chlorpyrifos is 7.1 days in seawater (Schimmel et al. 1983), and 53 days in distilled water (Freed et al. 1979). Degradation is usually through hydrolysis to produce 3,5,6-trichloro-2-pyridinol and phosphorothioic acid (Brust 1966; Smith 1966, 1968; Marshall and Roberts 1978). Temperature, pH, radiation, and metal cations all significantly affect chlorpyrifos T_b 1/2 in water: half-life is decreased with increasing water pH, temperature, sunlight, and metal cation concentrations (Brust 1966; Mortland and Raman 1967; Smith 1968; Schaefer and Dupras 1969, 1970; Meikle and Youngson 1970; Menconi and Paul 1994).



Chemical	R
Chlorpyrifos	$\begin{array}{c} \text{S} \\ \parallel \\ -\text{P} \\ \backslash \quad / \\ \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array}$
Chlorpyrifos oxon	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{P} \\ \backslash \quad / \\ \text{OC}_2\text{H}_5 \quad \text{OC}_2\text{H}_5 \end{array}$
Methoxytrichloropyridine Trichloropyridinol	$\begin{array}{c} -\text{CH}_3 \\ \\ -\text{H} \end{array}$
O-ethyl trichloropyridyl phosphorothioate	$\begin{array}{c} \text{S} \\ \parallel \\ -\text{P} \\ \backslash \quad / \\ \text{OH} \quad \text{OC}_2\text{H}_5 \end{array}$

Figure 14.1 Structures of chlorpyrifos and some of its metabolites. (Modified from Barron, M.G., S.M. Plakas, and P.C. Wilga. 1991. Chlorpyrifos pharmacokinetics and metabolism following intravascular and dietary administration in channel catfish. *Toxicol. Appl. Pharmacol.* 108:474-482.)

In soil, Tb 1/2 values for chlorpyrifos range from less than 1 week to more than 24 weeks, depending on soil moisture, microbial activity, clay and organic content, and temperature. In 411 soils studied, increasing temperature resulted in decreased Tb 1/2 values (Miles et al. 1983). Degradation was more rapid in sandy loam than in organic muck soils, more rapid in moist than in dry soils, and more rapid in clay than in other soil types (Getzin 1981; Miles et al. 1983, 1984). The major routes of chlorpyrifos loss from soils are chemical hydrolysis in moist soils, clay-catalyzed hydrolysis in dry soils, and microbial degradation and volatilization (Marshall and Roberts 1978). Chlorpyrifos is poorly metabolized by soil bacteria and frequent treatments of agricultural soils may result in accumulation with occasional adverse effects (Gonzalez-Lopez et al. 1997). For example, at 2 to 10 kg/ha, chlorpyrifos significantly reduces the growth and dinitrogen fixation of heterotrophic nitrogen-fixers. The negative effects of chlorpyrifos on nitrogen-fixing bacteria are important because root colonization by microorganisms such as *Azospirillum*, *Azotobacter*, and *Rhizobium* is positive for plant growth (Gonzalez-Lopez et al. 1997).

The half-life of chlorpyrifos in sediments is comparatively long; it was 24 days in a sediment–water slurry (Schimmel et al. 1983). In a pond treated with chlorpyrifos, total water-borne residues decreased by a factor of more than 10, while total sediment residues rose by about 3 (Hurlbert et al. 1970). Similar results were noted in an artificial lake treated with chlorpyrifos: lake water concentrations peaked 1 day after treatment at 0.9 µg/L and plateaued near 0.2 µg/L after 3 weeks (Mulla et al. 1973).

Chlorpyrifos inhibits substrate-borne reception and emission of sex pheromone in *Trichogramma brassicae*, an entomophagous insect massively used as a biological control agent of corn borers, among survivors of an LC20 dose. Inhibition was probably due to nervous system effects and was not specific to pheromone communication (Delpuech et al. 1998).

Fish rapidly absorb, metabolize, and excrete chlorpyrifos from the diet (Barron et al. 1991). The mechanism of action of chlorpyrifos occurs via phosphorylation of the active site of acetyl-cholinesterase after initial formation of chlorpyrifos oxon by oxidative desulfurization. In studies with channel catfish (*Ictalurus punctatus*), the oral bioavailability of chlorpyrifos was 41%, substantially higher than in mammals. Catfish muscle contained less than 5% of the oral dose with an

elimination half-life (T_b 1/2) of 3.3 days. Chlorpyrifos residues in whole catfish were more than 95% chlorpyrifos, while bile and urine primarily contained metabolites. The dephosphorylated metabolite trichloropyridinol (TCP) was the major metabolite in the blood, while the glucuronide conjugate of TCP was the major metabolite in urine and bile. The toxic metabolite chlorpyrifos oxon was not detected in blood, tissues, or excreta. Extensive metabolism resulted in a low potential for chlorpyrifos to accumulate in catfish from dietary exposure. In both fish and mammals, TCP is a major biotransformation product (Barron et al. 1991). Channel catfish rapidly distribute water-borne chlorpyrifos into the blood and more slowly to peripheral tissues, with concentrations highest in fat and lowest in muscle (Barron et al. 1993). As was true with dietary chlorpyrifos, TCP was the major metabolite in blood, and the glucuronide conjugate of TCP was the major metabolite in urine and bile. Pharmacokinetics and metabolism of water-borne chlorpyrifos in channel catfish were similar to the disposition of chlorpyrifos in other vertebrates (Barron et al. 1993; USPHS 1995).

14.3 LABORATORY INVESTIGATIONS

14.3.1 Aquatic Organisms

During 96-h toxicity tests, several species of freshwater and marine invertebrates and fishes died at chlorpyrifos concentrations between 0.04 and 0.6 µg/L. LC₅₀ (96-h) values, in µg chlorpyrifos/L, for sensitive species tested were 0.04 for mysid shrimp, *Mysidopsis bahia*; 0.11 for amphipod, *Gammarus lacustris*; 0.38 for stonefly, *Pteronarcella badia*; and 0.6 for striped bass, *Morone saxatilis*; (Mayer and Ellersieck 1986) (Table 14.3). Toxicity was usually greater at elevated temperatures and at increasing pH levels (Johnson and Finley 1980). Aquatic invertebrates were usually more sensitive to chlorpyrifos than were vertebrates (Moore et al. 1998). Significant differences in genotype frequencies of the glucose phosphate isomerase (P_{gi}) locus were observed between chlorpyrifos-susceptible and chlorpyrifos-tolerant groups of mosquitofish, *Gambusia affinis* (Hughes et al. 1991). In general, arthropods were the most sensitive group assayed and molluscs the most tolerant (Borthwick and Walsh 1981) (Table 14.3). Adult newts (*Triturus vulgaris*) had normal survival and activity patterns during exposure to 96 µg chlorpyrifos/L for 96 h (van Wijngaarden et al. 1993). The bullfrog (*Rana catesbeiana*) also appears to be comparatively tolerant to chlorpyrifos, as judged by a single oral LD₅₀ value of >400 mg/kg body weight (Hudson et al. 1984).

Sublethal effects of chlorpyrifos exposure have been documented for many species of freshwater and marine fauna. They include inhibition of cholinesterase (ChE) activity levels in brain and hematopoietic organs, reduction in blood glucose levels, sluggishness, motor incoordination, delayed maturation and growth, renal histopathology, reproductive impairment, and reduced feed intake (Rongsriyam et al. 1968; Thirugnanam and Forgash 1977; Marshall and Roberts 1978; Tagatz et al. 1982; Jarvinen et al. 1983; USEPA 1985, 1986; Goodman et al. 1985b; Norberg and Mount 1985; Hansen et al. 1986; Jarvinen et al. 1988; Srivastava et al. 1990; Jimenez and Pocsido et al. 1994; Holladay et al. 1996). Reproductive impairment, for example, was observed in *Daphnia magna* at 0.08 µg chlorpyrifos/L (USEPA 1985). Reduction in setting rate was shown in oyster larvae after exposure to 0.1 µg/L for 8 days (Tagatz et al. 1982). Equilibrium loss was documented in 50% of brown shrimp (*Penaeus aztecus*) after exposure to 0.32 µg chlorpyrifos/L for 24 hours (Marshall and Roberts 1978). Growth of the California grunion (*Leuresthes tenuis*) was reduced 20% in an early life stage during immersion in 0.5 µg chlorpyrifos/L for 35 days and 26% in fry after exposure to 1.0 µg/L for 26 days (Goodman et al. 1985b). Nile tilapia (*Oreochromis niloticus*) exposed to 1 µg/L for 3 months had renal pathology and disrupted immune function (Holladay et al. 1996). Larvae of fathead minnows exposed to 2.1 µg/L for 30 days had increased deformities at day 30, as did larvae exposed to 122 µg/L for 5 h (Jarvinen et al. 1988). Guppies exposed to 3 µg/L for 2 weeks had 80 to 90% inhibition of acetylcholinesterase within 2 weeks; partial recovery occurred after

4 days in clean water, but cholinesterase levels were still 56% inhibited after 14 days (van der Wel and Welling 1989). In fathead minnows exposed to 120 µg chlorpyrifos/L for 200 days, ChE activity was significantly reduced, fecundity was reduced, maturation delayed, and, in second-generation fish, growth and maturation were reduced (Jarvinen et al. 1983). Chlorpyrifos was associated with deformities in fathead minnows. Additional data on sublethal effects of chlorpyrifos to aquatic biota are listed elsewhere (USEPA 1986; Odenkirchen and Eisler 1988; Menconi and Paul 1994).

Bioconcentration factors for tilapia (*Oreochromis aureus*) for individual tissues ranged from 85 in muscle to 939 in liver; gills (497) and bile (517) were intermediate (Herzberg 1987). Bioconcentration of chlorpyrifos from the medium varied substantially among five species of fishes, but generally paralleled ambient levels of chlorpyrifos (Table 14.4). Increases in bioconcentration factors (BCF) in chlorpyrifos-exposed teleosts may be associated with three variables: increased metabolic rate, as indicated by hyperventilation, hyperactivity, and decreased growth; increased bioavailability of chlorpyrifos as a result of solvent-induced supersaturation or increased food availability; and decreased depuration rates due to possible physiological dysfunction (Goodman et al. 1985a, 1985b; Hansen et al. 1986). At high BCFs, adverse effects on growth and survival were observed in sheepshead minnow (*Cyprinodon variegatus*) by Cripe et al. (1986) and in Gulf toadfish (*Opsanus beta*) by Hansen et al. (1986). Chlorpyrifos is excreted rapidly from fish; the estimated Tb 1/2 for many species is 8.7 h, and equilibration occurs with the surrounding medium in 24 to 72 h (Smith et al. 1966; Blau and Neely 1975; Marshall and Roberts 1978). Higher Tb 1/2 values of 13.4 to 69.3 h were recorded for various species of freshwater fishes (Welling and de Vries 1992; Deneer 1994; Tsuda et al., 1994), with slow excretion rates associated with high BCF values (Tsuda et al. 1994) and impaired metabolic breakdown (Welling and de Vries 1992). No detectable chlorpyrifos residues were found after 12 days in 10 species of estuarine invertebrates — including oligochaete annelids, molluscs, and crustaceans — after treatment with 0.046 kg chlorpyrifos/ha (Marganian and Wall 1972).

Table 14.3 Acute Toxicities of Chlorpyrifos to Selected Species of Aquatic Invertebrates and Fishes (Values are in micrograms of chlorpyrifos per liter of medium [g/L] fatal to 50% in 96 h.)

Organism and Other Variables	LC50 (g/L)	Reference ^a
INVERTEBRATES		
Mysid, <i>Mysisdopsis bahia</i>	0.04	1, 18
Amphipod, <i>Gammarus pulex</i>	0.07	15
Dragonfly (naiad), <i>Pseudagrion</i> spp.	0.10 ^b	2
Cladoceran, <i>Ceriodaphnia dubia</i>	0.10	18
Amphipod, <i>Hyalella azteca</i>	0.1 ^d	22
Amphipod, <i>Gammarus lacustris</i>	0.11	3
Cladoceran, <i>Daphnia pulex</i>	0.17 ^h	23
Cladoceran, <i>Daphnia longispina</i>	0.3	15
Chironomid, <i>Chironomus tentans</i>	0.3 ^d	22
Aquatic insects, 4 species	0.3–6.6	15
Stonefly, <i>Pteronarcella badia</i>	0.38	4
Cladoceran, <i>Simocephalus vetulus</i>	0.5	15
Stonefly, <i>Claassenia sabulosa</i>	0.57	4
Cladoceran, <i>Daphnia magna</i>	0.6 ^d	22
Cladoceran, <i>Daphnia magna</i>	1.0 ^c	5
Grass shrimp, <i>Palaemonetes pugio</i>	1.5 ^d	5
Crayfish, <i>Orconectes immunis</i>	6.0	6
Dragonfly (naiad), <i>Crocothemis erythryaea</i>	6.0 ^b	2
Stonefly, (larva), <i>Pteronarcys californica</i>	10.0	4
Red crayfish, <i>Procambarus clarkii</i>	41.0 ^e	7
Ram's horn snail, <i>Helisoma trivolvis</i>	>2000 ^f	8
Snail, <i>Lanistes carinatus</i>	2710 ^b	2

Table 14.3 (continued) Acute Toxicities of Chlorpyrifos to Selected Species of Aquatic Invertebrates and Fishes (Values are in micrograms of chlorpyrifos per liter of medium [g/L] fatal to 50% in 96 h.)

Organism and Other Variables	LC50 (g/L)	Reference ^a
FISH		
Striped bass, <i>Morone saxatilis</i>	0.6	10
Tidewater silverside, <i>Menidia peninsula</i>		
Flow-through test	0.7	11
Static test	3.0	11
California grunion, <i>Leuresthes tenuis</i>		
Flow-through test	1.1	11
Static test	3.1	11
Atlantic silverside, <i>Menidia menidia</i>		
Flow-through test	1.4	11
Static test	3.4	11
Bluegill, <i>Lepomis macrochirus</i>		
13°C	5.1	12
29°C	1.1	12
Longnose killifish, <i>Fundulus similis</i>	4.1	1
Inland silverside, <i>Menidia beryllina</i>	4.2	13
Ninespine stickleback, <i>Pungitius pungitius</i>	4.7	15
Striped mullet, <i>Mugil cephalus</i>	5.4	1
Threespine stickleback, <i>Gasterosteus aculeatus</i>	8.5	15
Rainbow trout, <i>Oncorhynchus mykiss</i>		
17.3°C	9.0	6
12.7°C	7.1	14
7.2°C	15.0	14
1.6°C	51.0	14
Cutthroat trout, <i>Salmo clarki</i>	18.0	12
Guppy, <i>Poecilia reticulata</i>	21.5 ^g	16
Lake trout, <i>Salvelinus namaycush</i>	98	12
Fathead minnow, <i>Pimephales promelas</i>	130–249	9, 18
Fathead minnow, <i>Pimephales promelas</i>	163 ^d	22
Sheepshead minnow, <i>Cyprinodon variegatus</i>	136	13
Nile tilapia, <i>Oreochromis niloticus</i>	115–190	19
Channel catfish, <i>Ictalurus punctatus</i>	280	12, 17
Mosquitofish, <i>Gambusia affinis</i>		
Susceptible population	340 ^b	2, 20
Resistant population	>1000	20
Tilapia, <i>Oreochromis aureus</i>	418	19
Gulf toadfish, <i>Opsanus beta</i>	520	13
European eel, <i>Anguilla anguilla</i>	540	21

^a 1, Shimmel et al. 1983; 2, Karim et al. 1985; 3, Sanders 1969; 4, Sanders and Cope 1968; 5, Marshall and Roberts 1978; 6, Phipps and Holcombe 1985; 7, Chang and Lange 1967; 8, Kenaga et al. 1965; 9, Jarvinen and Tanner 1982; 10, Korn and Earnest 1974; 11, Borthwick et al. 1985; 12, Johnson and Finley 1980; 13, Clark et al. 1985; 14, Macek et al. 1969; 15, van Wijngaarden et al. 1993; 16, van der Wel and Welling 1989; 17, Barron et al. 1991; 18, Menconi and Paul 1994; 19, Herzberg 1987; 20, Hughes et al. 1991; 21, Ferrando et al. 1991; 22, Moore et al. 1998; 23, van der Hoeven and Gerritsen 1997.

^b 24-h LC50.

^c 6.6-h LC50.

^d 48-h LC50.

^e 36-h LC50.

^f 72-h LC50.

^g 21-day LC50.

^h 10-day LC50

Table 14.4 Chlorpyrifos Bioconcentration Factor (BCF) of Selected Species of Fishes

Species	Exposure Duration (days)	Mean Concentration in Medium (g/L)	Approximate BCF ^a
Willow shiner, <i>Gnathopogon caerulescens</i>	1–14	0.08	810 ^b
Gulf toadfish, <i>Opsanus beta</i>	49	1.4	100
	49	3.7	260
	49	8.2	270
	49	9.7	480
	49	24.0	620
	49	46.0	650
California grunion, <i>Leuresthes tenuis</i>	35	0.14	1000
	35	0.30	700
	35	0.63	620
	26	0.13	<1
	26	0.28	58
	26	0.62	66
	26	1.3	450
Inland silverside, <i>Menidia beryllina</i>	28	0.08	<1
	28	0.18	105
	28	0.36	200
	28	0.75	130
	28	1.8	440
Atlantic silverside <i>Menidia menidia</i>	28	0.08–1.1	<1
Tidewater silverside, <i>Menidia peninsulae</i>	28	0.09	410
	28	0.19	400
	28	0.38	580
Guppy, <i>Poecilia reticulata</i>	2	10.0	407 ^c
	10	10.0	1618 ^d

^a Bioconcentration factor: concentration in whole organism (µg/kg fresh weight) divided by concentration in medium (µg/L).

^b Half-time persistence in shiners was 69.3 h (Tsuda et al. 1994).

^c BCF of 110 after 48 days, 30 after 120 days, and 2 after 504 days (Welling and de Vries 1992).

^d BCF of 210 after 120 days, 5 after 360 days, and 2 after 504 days (Welling and de Vries 1992).

Data from Goodman et al. 1985a, 1985b; Hansen et al. 1986; Welling and de Vries 1992; Tsuda et al. 1994.

14.3.2 Birds and Mammals

Signs of chlorpyrifos intoxication, as summarized by Hudson et al. (1984), include excessive blinking, hypoactivity, hyperexcitability, excessive drinking, muscular incoordination, rapid breathing, muscular weakness, tremors, piloerection (mammals) or fluffed feathers (birds), salivation, lacrimation, diarrhea, excessive urination, prostration, loss of righting reflex, spasms, tetany, coma, and convulsions. Death usually occurs between 1 h and 9 days after exposure. Chlorpyrifos oxon (*O,O*-diethyl-*O*-(3,5,6-trichloro-2-pyridyl) phosphate) is the active oxygen analog of chlorpyrifos and is probably responsible for most of the anticholinesterase mode of action of chlorpyrifos; the oxon is extensively and rapidly detoxified in mammalian liver via enzymatic hydrolysis by at least two microsomal esterases (Sultatos and Murphy 1983; USPHS 1995). Significant accumulations of chlorpyrifos were not detected in domestic turkeys (*Meleagris gallopavo*) and chickens. In birds kept in pens on soil treated with 4.5 to 9.0 kg active ingredients chlorpyrifos/ha, tissue residues were 0.16 mg/kg after 1 week; these decreased thereafter, although birds remained on the treated soil (Kenaga 1974).

LD50 values, based on a single oral dose, ranged from 5 to 157 mg chlorpyrifos/kg body weight (BW) in birds, and from 151 to 1000 in mammals. However, 7 of 14 avian species had reported LD50 values of <25.0 mg/kg BW (Table 14.5). As little as 2 mg/kg BW to nestling red-winged

blackbirds (*Agelaius phoeniceus*) was associated with reduced survival during the first 24-h post-exposure interval; however, nestling European starlings had normal survival when given a single oral dose of 2 mg/kg BW (Meyers et al. 1992). Many species of birds that survived chlorpyrifos poisoning showed gross pathological changes (Tucker and Crabtree 1970). Furthermore, the slope of the acute dose-response curve was low (Hudson et al. 1984). These findings suggest that decreasing dosage levels did not produce proportional decreases in response, and indicate a reduced safety margin for chlorpyrifos owing to mortalities that occur frequently at levels much lower than the calculated LD₅₀ values (Hudson et al. 1984).

Table 14.5 Chlorpyrifos Lethality to Selected Birds and Mammals via Single Oral Dose Route of Administration (Values are in mg chlorpyrifos/kg body weight lethal to 50% within 14 days.)

Organism and Other Variables	LD ₅₀ (mg/kg body weight)	Reference ^a
BIRDS		
European starling, <i>Sturnus vulgaris</i>	5	1, 8
Ring-necked pheasant, <i>Phasianus colchicus</i>		
Male	8.4	2
Female	17.7	3
Red-winged blackbird, <i>Agelaius phoeniceus</i>	13	1, 8
Common grackle, <i>Quiscalus quiscula</i>	13	1
House sparrow, <i>Passer domesticus</i>	10–21	1, 3
Mallard, <i>Anas platyrhynchos</i>		
Age 36 h	14.5	6
Age 7 days	29.4	6
Age 30 days	50.4	6
Age 6 months	83.3	6
Japanese quail, <i>Coturnix japonica</i>	15.9	2
Sandhill crane, <i>Grus canadensis</i>	25–50	3
Rock dove, <i>Columba livia</i>	26.9	2
Domestic chicken, <i>Gallus</i> sp.	32	9
Northern bobwhite, <i>Colinus virginianus</i>		
Technical grade	32	5
Lorsban 15G	108	5
Crow, <i>Corvus brachyrhynchos</i>	>32	1
Canada goose, <i>Branta canadensis</i>	40–80	4
Chukar, <i>Alectoris chukar</i>		
Male	61.1	3
Female	60.7	2
Ringed turtle dove, <i>Streptopelia risoria</i>	157	5
MAMMALS		
Albino rat, <i>Rattus norvegicus</i>	151	4
Guinea pig, <i>Cavia porcellus</i>	500	7
Domestic goat, <i>Capra hircus</i>	500–1000	4
White rabbit, <i>Oryctolagus cuniculus</i>	1000–2000	7

^a 1, Schafer 1972; 2, Tucker and Haegle 1971; 3, Tucker and Crabtree 1970; 4, Hudson et al. 1984; 5, Hill and Camardese 1984; 6, Hudson et al. 1972; 7, Smith 1987; 8, Meyers et al. 1992; 9, Clements et al. 1992.

Reduction in cholinesterase activity levels of various tissues (blood, brain) is one of the earliest signs of chlorpyrifos intoxication. Cholinesterase reductions have been demonstrated in turkeys fed diets containing 50 mg chlorpyrifos/kg (estimated daily dose of 0.7 mg/kg BW) for 20 days (Schlinke et al. 1969); in chickens fed diets of 25 mg/kg (estimated daily dose of 0.94 mg/kg BW) for 20 days (Schlinke 1970); in quail (*Coturnix coturnix*) given a single (sublethal) esophageal

intubation of 13 mg/kg BW (Solar-Rodriguez et al. 1998); and in mallard (*Anas platyrhynchos*) ducklings fed 75 mg chlorpyrifos/kg diet for 14 days (Herin et al. 1978). Brain cholinesterase activity in quail was normal after 11 days despite 81% inhibition 8 h postadministration (Solar-Rodriguez et al. 1998). Low temperatures (27.5°C vs. 35°C) potentiated dose-related cholinesterase depression in juvenile northern bobwhite (*Colinus virginianus*), suggesting a need for more research on cold stress interactions between acute oral chlorpyrifos exposure (Maguire and Williams 1987). In adult female rats, brain cholinesterase activity was inhibited by as much as 96% following subcutaneous injection of 280 mg/kg BW; all survived without extensive signs of toxicity, but weight loss was evident 2 to 7 days after treatment (Liu and Pope 1998).

Dietary concentrations of 30 to 100 mg chlorpyrifos/kg feed produce some deaths in birds, and 136 to about 500 mg/kg feed usually kills at least 50% (Table 14.6). In chickens fed diets of 100 mg chlorpyrifos/kg — equivalent to an estimated daily dose of 6.8 mg/kg BW — egg fertility was reduced by 15% and hatchability by 17% (Schom et al. 1973). Dietary levels lethal to mallard ducklings were 136 to 180 mg/kg feed, equivalent to 10 mg/kg BW fed daily for 5 days (Kenaga 1974). In adult mallards given diets containing 80 mg chlorpyrifos/kg for 60 to 84 days, body weight, food consumption, brain cholinesterase activity levels, and egg production were all reduced. Moreover, egg weight and eggshell thickness were reduced, the resultant ducklings weighed less than controls, and survival was comparatively poor at age 7 days. No effect on any variable was observed at diets of 8 mg/kg (Gile and Meyers 1986; Meyers and Gile 1986).

Table 14.6 Dietary Toxicity of Chlorpyrifos to Selected Species of Birds

Species and Age (days)	Duration of Dietary Exposure (days)	Minimum Lethal Concentration (mg/kg diet)	LD50 (mg/kg diet)	Reference ^a
Mallard, <i>Anas platyrhynchos</i>				
(1–5)	5	30	136	1
(5–7)	5	30–90	180	1
(10)	5 plus 3 untreated	—	940	2
Pekin duck, <i>Anas</i> sp.				
(5)	21	—	>1000	1
Northern bobwhite, <i>Colinus virginianus</i>				
(1–5)	5	50–100	505	1
Turkey, <i>Meleagris gallopavo</i>				
(84)	28	>100	>100	1
Japanese quail, <i>Coturnix japonica</i>				
(14)	5 plus 3 untreated	—	299	2
(14)	5 plus 3 untreated	—	492	3
Chicken, <i>Gallus</i> sp.				
(10–12)	14	<200	400	1
(28)	28	50–100	>100	1
(Adults)	365	—	>200	1
Ring-necked pheasant, <i>Phasianus colchicus</i>				
(10)	5 plus 3 untreated	—	553	2
Coturnix quail, <i>Coturnix risoria</i>				
(14–21)	5	—	299	1
(Adults)	28	300	500	1

^a 1, Kenaga, 1974; 2, Hill et al. 1975; 3, Hill and Camardese 1986.

Dermal application routes are also toxic. Some deaths were recorded in turkeys from dermal treatments of 15 to 20 mg chlorpyrifos/kg BW (Schlinke et al. 1969). Higher levels applied to feathers killed turkeys within 8 h (Marshall and Roberts 1978). Newborn piglets (*Sus* spp.) were especially more sensitive than those 30 to 36 h old to cutaneous applications of chlorpyrifos;

newborns showed clinical signs consistent with organophosphorus toxicosis after a 2.5% aerosol preparation (dosage unknown) was applied to the tail and umbilicus (Long et al. 1986). Accidental poisoning of cattle (*Bos* spp.) by chlorpyrifos through dermal application to control ticks resulted in some deaths. Among bulls that survived, sperm production was reduced 43% in seriously affected animals and 12% in those with no outward signs of poisoning (Everett 1982).

Chlorpyrifos is not mutagenic, as judged by mitotic recombination assays (Poole et al. 1976), and did not increase sister chromatid exchange above background in tests with chick (*Gallus* spp.) embryos and Chinese hamster (*Cricetus* spp.) ovary cells (Muscarella et al. 1984). Chlorpyrifos altered serum cortisol and decreased thyroxine concentrations in sheep given oral doses of 12.5 mg chlorpyrifos/kg BW twice weekly for 43 days (Rawlings et al. 1998), indicating a need for more research on the role of chlorpyrifos in hormone metabolism.

Chlorpyrifos-impregnated ear tags are under development to control horn flies (*Haematobia irritans*) in U.S. cattle (Byford et al. 1986). Cattle fitted with ear tags (0.96 g chlorpyrifos per tag/365 kg animal, or about 2.6 mg chlorpyrifos/kg BW) had slightly elevated tissue residues (0.13 mg/kg fat) after 12 weeks, but residues were well within acceptable tolerance levels of 2.0 mg chlorpyrifos/kg fresh weight cattle fat, meat, or meat by-products (Byford et al. 1986). In dogs (*Canis familiaris*), chlorpyrifos-impregnated collars provided effective control of adult fleas (*Ctenocephalides* spp.) for up to 11 months, with no significant adverse reactions regardless of canine coat length, size, or age (Higgins and Jarvis 1986).

14.4 FIELD INVESTIGATIONS

There have been many accidental spills of chlorpyrifos, but little quantitative assessment of its environmental effects. One exception is a spill in April 1985 in England (Boreham and Birch 1987). In that instance, a truck overturned, spilling 205 L chlorpyrifos into an adjacent stream that drained into the Roding River. A resulting sharp decrease in the number and type of macroinvertebrate benthic organisms in affected parts of the river, compared to unaffected areas, lasted 6 months. In addition, certain chlorpyrifos-resistant benthic organisms were unusually abundant.

Chlorpyrifos controls mosquito larvae at applied dosages between 0.028 and 0.056 kg/ha, equivalent to 9 to 18 µg chlorpyrifos/L in 152 mm (6 inches) of water (Marshall and Roberts 1977; Eaton et al. 1985). In 1984 alone, chlorpyrifos was used for this purpose on about 600,000 ha (Odenkirchen 1987). Surface waters of ponds on golf courses in North Carolina often contain 7.2 to 11.5 µg chlorpyrifos/L as a result of turf treatment with chlorpyrifos (Ryals et al. 1998). At this time, no obvious deleterious effects of chlorpyrifos have been recorded in mammals, amphibians, or reptiles under field conditions of current use (Table 14.7). For example, bullfrogs (*Rana catesbeiana*) from an Iowa pond that received runoff from a 16-ha cornfield treated with the label rate of Lorsban 15G, when compared to a reference pond, had the same level of plasma activity and reactivation for total cholinesterase, acetylcholinesterase, and butylcholinesterase (Richards et al. 1999). However, at recommended dosage application rates for control of mosquitoes and other pestiferous insects (usually 0.028 to 0.056 kg/ha), adverse effects have been documented on survival, reproduction, metabolism, and species diversity of a variety of fishes, terrestrial and aquatic invertebrates, freshwater flora, waterfowl, and horned larks (*Eremophila alpestris*), and on the marketability of various crops (Mulla et al. 1971, 1973; Hurlbert et al. 1972; Macek et al. 1972; Nelson and Evans 1973; Hoy and Shea 1981) (Table 14.7). For example, field populations of daphnids (*Daphnia pulex*) were reduced 50% by 0.38 µg chlorpyrifos/L after 2 days and by 0.25 µg/L in 7 days; similar values were found in laboratory populations of this species (van der Hoeven and Gerritsen 1997). It is emphasized that the effectiveness of chlorpyrifos under field conditions, like that of other organophosphorus pesticides, is significantly modified by numerous variables such as formulation, route of administration, pond substrate, dose, and water temperature (Macek et al. 1969; Bailey et al. 1970; Rawn et al. 1978; Odenkirchen 1987).

Table 14.7 Chlorpyrifos Effects on Selected Ecosystems

Ecosystem and Other Information	Application Rate and Other Variables	Effects and Reference
AQUATIC		
Lake	0.004 kg/ha, emulsifiable concentrate, oil diluent single application	After 24 h, aquatic insect populations reduced 14–40% and snails reduced 10% (Moore and Breeland 1967)
Freshwater ponds, (8 m × 17 m × 0.3 m deep)	Individual applications of 0.011, 0.056, 0.11, or 1.11 kg/ha; 4 applications at 2-week intervals	Initial population inhibition of mosquitofish (<i>Gambusia</i> sp.), but reproduction resumed except for 1.11 kg/ha group. Fish whole-body residues in 0.056 kg/ha group, in mg/kg body weight, were 2.8 at 4 h, 1.7 at 24 h, and 0.1 after 2 weeks. Insect and zooplankton populations reduced >92%; little recovery was evident after third treatment. The 0.056 kg/ha treatment regimen, at 4 h, resulted in residues of 10 µg/L in water, 375 µg/kg in vegetation, and nondetectable levels in mud; at 14 days, all residues were nondetectable (Hurlbert et al. 1970)
Freshwater ponds (8 m × 17 m × 0.3 m deep)	Individual applications of 0.011, 0.056, 0.11 and 1.11 kg/ha; 4 applications at 2-week intervals	High mortality (>42%) of mallard (<i>Anas platyrhynchos</i>) ducklings on all treated ponds, vs. none dead on control ponds (Hurlbert et al. 1970)
Freshwater lake	0.014 kg/ha (equivalent to about 1.2 µg/L), single application	Freshwater algae (<i>Ankistrodesmus</i> sp., <i>Tetraedron</i> sp.) reduced 30–90% 7 days posttreatment; reduced population growth evident 1 year postapplication (Brown et al. 1976)
Flooded rice field	Individual applications of 0.014–0.019 kg/ha, emulsifiable concentrate, oil diluent, 3 applications at 5-week intervals	Mortality after 72 h, 32% in caged bluegills (<i>Lepomis macrochirus</i>), 50 to 70% in mayfly nymphs (<i>Siphlonurus</i> sp.), and 32% in predatory diving beetles (Washino et al. 1972)
Artificial lake	0.02 kg/ha, granular formulation, single application	Chironomid larvae population remained >90% depressed for 5 months (Mulla et al. 1971)
Salt marsh	0.025 kg/ha, single application	No gross effects on wildlife (Ludwig et al. 1968)
Salt marsh	0.028 kg/ha (0.025 lbs/acre), single aerial application, mosquito larvicide granules	No observable effects on caged blue crabs (<i>Callinectes sapidus</i>), penaeid shrimp, or fishes; some fiddler crabs (<i>Uca</i> sp.) dead (USFWS 1968)
Salt marsh	Individual applications of 0.028 kg/ha, 4 applications at 2-week intervals	In killifish (<i>Fundulus heteroclitus</i>), convulsions, ChE depression, and deaths noted. ChE remained depressed for about 10 weeks after final application (Thirugnanam and Forgash 1977)
Shallow pond, mean depth 0.25 m, surface area 0.11 ha, high vegetation	Individual applications of 0.056 kg/ha technical grade, 2 applications at 34-day interval	After 63 days, 46–55% mortality in centrarchid populations, and 75% reduction in insect populations of caddisflies, mayflies, and midges (Macek et al. 1972)
Shallow ponds	0.056 kg/ha, emulsifiable concentrate, oil diluent single application	All caged green sunfish (<i>Lepomis cyanellus</i>) died (Linn 1968)
Woodland pools	Single application of 0.056 kg/ha, granular formulation	Increased algal growth on leaf litter observed months after treatment, attributed to reduction in grazing stress by mosquito larvae (Hagmann and Porteus 1972)
Woodland pools	0.056 kg/ha, granular formulation, single application	Isopod populations reduced 90–95% (Cooney and Pickard 1974)
Salt marsh, 202 ha (500 acres)	0.56 kg/ha (0.5 lb/acre), single application applied as aerial spray, to kill mosquito larvae	Killed significant numbers of fishes and crustaceans (USFWS 1968)
Salt marsh, 78 ha plot	0.56 kg/ha, emulsifiable concentrate, once, aerially	After 48 h, mortality was 35% in caged fish and 84% in caged shrimp; no other adverse effects were noted during the next 27 days (Wall and Marganian 1971)

Table 14.7 (continued) Chlorpyrifos Effects on Selected Ecosystems

Ecosystem and Other Information	Application Rate and Other Variables	Effects and Reference
Salt marsh estuary, Bay St. Louis, Mississippi, 408 ha site (1008 acres)	0.56 kg/ha (0.5 lb/ acre), granular, single aerial application, for mosquito control	After spraying, all caged fiddler crabs died, white shrimp (<i>Penaeus setiferus</i>) populations were reduced, and large numbers of blue crabs were found dead. No observable effects on terrestrial organisms, including insects. One month after spraying, shrimp and blue crab populations seemed normal, although fiddler crabs were absent (USFWS 1967)
Artificial streams, each 520 m long, 0.14 ha of surface area, with pools 30.5 m long × 3.6 m wide × 81 cm deep	Continuous treatment stream received 0.22 µg chlorpyrifos/L for days 1 to 41, and 1.0 µg/L from days 41–100. Intermittent treatment stream received dosage 14 times higher than continuous treatment stream, but dosage was confined to 24 h every 14 days. Chlorpyrifos administered as emulsifiable concentrate in petroleum derivative solvent	When compared to control stream, no effect on total abundance of benthic organisms. However, in both treated streams, species diversity decreased by equal amounts and was still decreasing at day 100. Adverse sublethal effects were noted in fathead minnow, <i>Pimephales promelas</i> (spinal deformities) and bluegills (cholinesterase inhibition, signs of organophosphorus poisoning) only in the pulse-dosed stream. In all streams, however, fish survived, grew, and reproduced equally well (Eaton et al. 1985)
Outdoor ponds, Minnesota, June	Single dose of 0.5, 5, or 20 µg/L; observed for 30 days	Larvae of fathead minnows had dose-dependent growth inhibition (controls grew 8.3% and high-dose group 3.1%) and seemed related to reductions in crustacean and rotifer populations in the treated enclosures. Chlorpyrifos in high-dose enclosure was <3 µg/L at 96 h and <0.16 µg/L at day 30 (Brazner and Kline 1990)
Temporary woodland pool	Average maximum water concentration of 1.6 µg chlorpyrifos/L	No obvious adverse effects on wildlife (i.e., 3 spp. of rodents, 1 sp. frog, 1 sp. turtle (Nelson and Evans 1973)
Freshwater ponds	Single dose of chlorpyrifos, equivalent to 4, 10, or 1000 µg/L	Increased algal bloom duration in treated ponds, possibly due to loss of grazing fauna (Butcher et al. 1977)
Freshwater pond	Single application of pelletized 10.6% chlorpyrifos to obtain theoretical water concentrations of 250 µg/L and higher	Species diversity of diatoms reduced >50% in 6 weeks, vs. 12% increase in controls (Nelson et al. 1976)
TERRESTRIAL		
Rice field area	0.029 kg/ha, single application	All honeybees (<i>Apis</i> sp.) within 0.4 km downwind of spray area were dead; 95% were dead at 0.8 km and 89% at 1.2 km (Atkins 1972)
Savannah region of Senegal; 1989	0.27 and 0.39 kg/ha to control desert locust (<i>Schistocerca gregaria</i>) and Senegalese grasshopper (<i>Oedaleus senegalensis</i>)	Total bird numbers on treated plots decreased. Some of the decrease (2–3%) was due to death, but most represented movements of birds in reaction to a reduction in their arthropod food. Brain cholinesterase levels in several avian species were depressed 1 week posttreatment (Mullie and Keith 1993)
New Mexico ranchlands	Dust formulations of 0.48 and 1.97 kg/ha, to control wildlife flea populations	No observable deleterious effects in rodents and rabbits 3–4 weeks posttreatment (Miller et al. 1970)
Wheat fields	0.56 and 1.0 kg/ha, to control pale western cutworm (<i>Agrotis orthogonia</i>)	Horned larks (<i>Eremophila alpestris</i>) had brain cholinesterase activity levels depressed 22% at 3 days posttreatment, and 8% at 16 days. No sick or dead birds found; however, no systematic searches were made for the small lark carcasses, nor were specific observations for toxic signs conducted (McEwen et al. 1986)

Table 14.7 (continued) Chlorpyrifos Effects on Selected Ecosystems

Ecosystem and Other Information	Application Rate and Other Variables	Effects and Reference
Perennial rye (<i>Lolium perenne</i>) grasslands in United Kingdom infested with 3–6 million leatherjackets (<i>Tipula</i> spp.)/ha	0.72 kg active ingredients per hectare; single application; posttreatment effects on earthworms, birds, and mammals measured up to 14 days after spraying	Almost all leatherjackets were dead 14 days after spraying; maximum chlorpyrifos residues in leatherjackets was 1.2 mg/kg FW at day 10 postspray vs. 0.02 in controls. All earthworms were alive and active when collected. No adverse effects on nesting or feeding territorial birds including carrion crows (<i>Corvus corone</i>), ring-necked pheasant (<i>Phasianus colchicus</i>), magpies (<i>Pica pica</i>), blackbirds (<i>Turdus merula</i>), wood pigeons (<i>Columba palumbus</i>), and buzzards (<i>Buteo buteo</i>). Mammals seemed normal, including brown hares (<i>Lepus capensis</i>), rabbits (<i>Oryctolagus cuniculus</i>), and roe deer (<i>Capreolus capreolus</i>) (Clements and Bole 1988)
Pasturelands where Brent geese (<i>Branta bernicla</i>) and Canada geese (<i>Branta canadensis</i>) were grazing	Single application of 0.72 kg/ha	No perceptible effect on goose behavior (activity, pecking rate) after spraying. Maximum residues in herbage were 20.4 mg/kg 3 days after spraying and 10 mg/kg FW in goose feces 4 days after spraying; residues were <0.05 mg/kg within 10 days (Clements et al. 1992)
Iraqi date palm (<i>Phoenix</i> sp.) orchards	Emulsifiable concentrate applied once after fruiting and infestation with high-pressure ground sprayers at 0.98 kg/ha to control insect pests	Chlorpyrifos residues in dates decreased from 1.28 mg/kg fresh weight at day 1 postapplication to 0.2 mg/kg on day 15, to 0.05 on day 29, and to nondetectable concentrations on day 71. Concentrations of the chlorpyrifos oxygen analog, however, after reaching a peak of 0.5 mg/kg on day 15, were still detectable (0.1 mg/kg) at day 85, suggesting that dates should be harvested at least 8 weeks after chlorpyrifos treatment (Mansour 1985)
Turf	1.12 kg/ha, emulsifiable concentrate, single application, to control chinch bug (<i>Blissus leucopterus listus</i>)	Most arthropods in turf killed immediately after application. Target pest populations remained depressed for 1 year posttreatment, but other insect populations recovered to levels greater than controls after 3.5 months (Streu and Cruz 1972)
Citrus groves; 3 blocks of 4 groves each	One block received up to 3.93 kg/ha of Lorsban 4E postbloom; a second block received up to 6.73 kg/ha postpetal; the third block was not treated	A total of 58 dead vertebrate animals (birds, amphibians, reptiles, mammals) were found on the first block, 39 on the second block, and 50 from the reference site. Authors concluded that risk to wildlife is low (Mortenson et al. 1999)

14.5 RECOMMENDATIONS

Water quality criteria formulated for chlorpyrifos (USEPA 1986; USPHS 1995) and aquatic life protection seem to afford a reasonable degree of safety, at least during short-term exposure. Specifically, the proposed criteria for freshwater are 0.041 µg/L (4-day average concentration) and 0.083 µg/L (1-h average concentration), neither of which should be exceeded more than once every 3 years. For saltwater, these criteria are 0.0056 µg/L and 0.011 µg/L, respectively. Levels of chlorpyrifos in the Sacramento–San Joaquin River system proposed by the state of California to protect aquatic life during chronic exposure are <0.02 µg/L in freshwater and <0.01 µg/L in saltwater (Menconi and Paul 1994). However, concentrations of chlorpyrifos in the San Joaquin River during 1991 to 1993 ranged between 0.01 and 1.6 µg/L (Menconi and Paul 1994) and suggest that California's stringent water quality criteria proposed for chlorpyrifos should be reexamined. Proposed chlorpyrifos drinking water criteria by some agencies to protect human health are significantly higher than those recommended

for aquatic life protection: 21 µg/L in Vermont, 30 µg/L to protect children in lifetime exposure in the United States, 90 µg/L in Canada, and 100 µg/L to protect adults in the United States (USPHS 1995).

The acceptable tolerance level of chlorpyrifos in meat and meat by-products destined for human consumption is 2.0 mg/kg fresh weight (Byford et al. 1986), and for agriculture products it usually ranges between 0.05 and 15.0 mg/kg FW and up to 25.0 mg/kg for citrus oil (USPHS 1995). The significance of these concentrations to animal health, or to consumers other than man, is unknown. More research is needed to establish maximum tolerable chlorpyrifos limits in tissues of sensitive fish and wildlife. Proposed air criteria for chlorpyrifos and human health include 200 µg/m³ in the workplace, and much lower concentrations of 0.48 to 3.3 µg/m³ in nonoccupational settings (USPHS 1995). No air criteria are currently available or proposed for protection of wildlife.

Information is lacking on the effectiveness of chlorpyrifos in large-scale (>40 ha) coldwater ecosystems, typical of those found in Alaska or northern-tier states. Accordingly, initiation of long-term studies in these potential problem areas are recommended. As judged by the available literature, three courses of action now seem warranted.

1. Restrict the use of chlorpyrifos for mosquito control in wetlands, estuaries, and waterfowl breeding areas because recommended treatment levels are demonstrably harmful to nontarget species, including mallard ducklings. The unsuitability of chlorpyrifos for mosquito control is further supported by the finding that certain mosquito populations in California are showing signs of chlorpyrifos resistance, and thus may require more aggressive future treatment programs (Reisen et al. 1984).
2. Curtail agricultural use of chlorpyrifos in watershed areas pending acquisition of additional data on its transport, fate, and effects, including data on chlorpyrifos flux rates from soils and sediments and its resultant bioavailability.
3. Develop suitable replacements for chlorpyrifos in mosquito control programs. These replacement compounds should exhibit a relatively long half-life in aquatic environments while avoiding the broad-spectrum toxicity typical of chlorpyrifos to large numbers of nontarget organisms.

14.6 SUMMARY

Chlorpyrifos (phosphorothioic acid *O,O*-diethyl-*O*-(3,5,6,-trichloro-2-pyridinyl) ester), an organophosphorus compound with an anticholinesterase mode of action, is used extensively in a variety of formulations to control a broad spectrum of agricultural and other pestiferous insects. Domestic use of chlorpyrifos in 1982 was about 3.6 million kg; the compound is used mostly in agriculture, but also to control mosquitoes in wetlands (0.15 million kg applied to about 600,000 ha) and turf-destroying insects on golf courses (0.04 million kg). Accidental or careless applications of chlorpyrifos have resulted in the death of many species of nontarget organisms such as fish, aquatic invertebrates, birds, and humans. Applications at recommended rates of 0.028 to 0.056 kg/surface ha for mosquito control have produced mortality, bioaccumulation, and deleterious sublethal effects in aquatic plants, zooplankton, insects, rotifers, crustaceans, waterfowl, and fish. Adverse effects were also noted in bordering invertebrate populations.

Degradation rate of chlorpyrifos in abiotic substrates varies, ranging from about 1 week in seawater (50% degradation) to more than 24 weeks in soils under conditions of dryness, low temperatures, reduced microbial activity, and low organic content. Intermediate degradation rates reported have been 3.4 weeks for sediments and 7.6 weeks for distilled water. In biological samples, degradation time is comparatively short — usually less than 9 h in fishes and probably the same in birds and invertebrates.

Chlorpyrifos is acutely toxic to some species of aquatic invertebrates and teleosts at nominal water concentrations ranging between 0.04 and 1.1 µg/L. Acute single-dose oral LD₅₀ values of chlorpyrifos to susceptible avian species ranged from 5 to 13 mg/kg body weight. Mammals were comparatively tolerant of chlorpyrifos: acute oral LD₅₀ values were reported to be 151 mg/kg body weight and higher. Lethal dietary concentrations for sensitive species of birds ranged from 30 to

50 mg chlorpyrifos/kg food. Sublethal effects were recorded in all species of organisms examined at concentrations below those causing mortality. These effects included bioconcentration from the medium by teleosts (410 to 1000); cholinesterase activity reduction in brain and hematopoietic tissues; reduced growth; impaired reproduction, including sterility and developmental abnormalities; motor incoordination; convulsions; and depressed population densities of aquatic invertebrates.

Three courses of action are recommended:

1. Restrict the use of chlorpyrifos for mosquito control in wetlands, estuaries, and waterfowl breeding areas because recommended treatment levels are demonstrably harmful to nontarget resident biota.
2. Curtail agricultural use in watershed areas pending acquisition of additional data on chlorpyrifos toxicokinetics.
3. Develop suitable replacements for chlorpyrifos in mosquito control programs; specifically, pesticides with more specificity to target organisms and lower toxicity to nontarget biota.

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CHAPTER 15

Cyanide

15.1 INTRODUCTION

The origin of terrestrial life probably depended on the presence and reactivity of hydrogen cyanide and its derivatives. Paradoxically, hydrogen cyanide is toxic to the majority of living matter (Marrs and Ballantyne 1987). Cyanide is a general respiratory poison — although uptake can also occur through ingestion or dermal absorption — producing reactions within seconds and death within minutes (Towill et al. 1978; U.S. Environmental Protection Agency [USEPA] 1980). The toxic mechanism of cyanide primarily involves the inhibition of cytochrome oxidase, the terminal oxidative enzyme of the mitochondrial electron transport chain, producing blockage of aerobic ATP synthesis (Egekeze and Oehme 1979; Younes and Strubelt 1988). Because of their highly effective lethal potency, cyanides were used for genocidal programs in Germany in World War II, in mass suicides by members of the People's Temple religious sect in Guyana, and in the substitution of medication in Tylenol® capsules in drugstores in various cities in the United States. In fact, cyanides are responsible for more human deaths than any other chemicals known, owing to their deliberate use in suicide, murder, chemical warfare, genocide, and judicial execution (Way 1981, 1984; Ballantyne and Marrs 1987; Gee 1987; Marrs and Ballantyne 1987; Yamamoto 1989). High sublethal doses of cyanide are rapidly detoxified, and accidental acute cyanide poisonings in humans are uncommon (Towill et al. 1978).

Cyanide compounds are useful to society in terms of their key role in synthetic and industrial processes, for certain fumigation and agricultural uses, and for some therapeutic applications (Ballantyne and Marrs 1987). Cyanides are present in effluents from iron and steel processing plants, petroleum refineries, and metal-plating plants, and constitute a hazard to aquatic ecosystems in certain waste-receiving waters (Smith et al. 1979) and to livestock (USEPA 1980; Towill et al. 1978). Cyanide serves no useful purpose in the human body, yet it is present in our food, air, and water (Becker 1985).

Natural sources of cyanide include various species of bacteria, algae, fungi, and higher plants that form and excrete cyanide (Way 1984). The most widely distributed major food crop with a high content of cyanogenic glycosides is cassava (*Manihot esculenta*), also known as manioc. Cassava is a food staple in human diets in over 80 countries, and it is sometimes added to animal feeds as a substitute for more expensive cereal grains (Gomez et al. 1988). In humans, chronic cyanide intoxication caused by consumption of cassava is the main etiological factor in the debilitating tropical ataxic neuropathy (Egekeze and Oehme 1980). Other plants having comparatively elevated cyanide content include fruit pits, sweet potatoes (*Ipomoea batatas*), corn (*Zea mays*), bamboo shoots (*Bambos* spp.), linseed (*Linum* sp.), lima beans (*Phaseolus lunatus*), and millet (*Panicum millaceum*) (Way 1984). In higher plants that contain cyanogenic glycosides, at least 20 of these compounds have been identified (USEPA 1980). Amygdalin — one of the more intensively

studied cyanogenic glycosides — is found in seeds of the cherry (*Prunus* spp.), plum (*Prunus* spp.), peach (*Prunus persica*), apricot (*Prunus armeniaca*), apple (*Malus malus*), pear (*Pyrus communis*), and many parts of the cherry laurel (*Prunus laurocerasus*) (USEPA 1980). Apricot seeds and peach kernels are food delicacies in Turkey and have caused at least nine poisonings (two fatal) in children from that country (Gee 1987). Acute cyanide poisoning has occurred in the United States from the ingestion of almond-flavored milkshakes prepared from apricot kernels (Way 1984). Amygdalin is also the chief ingredient in laetrile, a medication prescribed by some physicians to control tumors. Both laetrile and amygdalin-containing fruit pits have been implicated as the causes of acute cyanide poisoning in humans (USEPA 1980). Another naturally occurring group of organic cyanides (nitriles) is the highly toxic pseudocyanogenic glycosides, especially cycasin, and these have been implicated in a variety of tropical diseases of the nervous system, and partial or total blindness (USEPA 1980). Other nitriles found in plants include the lathyrogenic compounds, glucosinolates, and the cyanopyridine alkaloids (USEPA 1980).

The recognition that certain plants, such as bitter almonds (*Amygdalus communis*), cherry laurel leaves, and cassava, are poisonous if consumed in sufficient quantities has been known for at least 2000 years. But it was not until the 1700s that cyanide was recognized as the basis for their lethal toxicity. The first account of an experimental administration of extract of bitter almonds and other poisons to dogs (*Canis familiaris*) dates from 1679, as reviewed by Sykes (1981) and Ballantyne (1987a). In 1731, two fatal cases of human poisoning in Ireland were caused by drinking cherry laurel water, in this instance used as a flavoring agent in cooking and to dilute brandy. In that same year, it was shown that cherry laurel water administered to dogs by various routes proved rapidly fatal. By 1781, it was well established that mammals, birds, reptiles, amphibians, fish, and insects could all be killed with small doses of laurel water, and that death was more rapid than that produced by other poisons tested. It was also at this time that cyanide was first implicated as a homicidal agent in England. In 1782, hydrocyanic acid was isolated from Prussian blue (a dye) by the Swedish chemist Scheele. In 1786, Scheele accidentally broke a vial of the material and died from vapor poisoning. In 1787, it was determined that hydrocyanic acid contained hydrogen, carbon, and nitrogen, but did not contain oxygen, formerly believed to be an essential component of all acids. Between 1802 and 1815, hydrocyanic acid was found to be lethal in small quantities to birds and dogs, and to act rapidly when given orally, intravenously, or applied to the eye surface. By 1803, it was known that cyanide occurred naturally and could be extracted from apricots or almonds. In 1815, hydrocyanic acid was prepared in a semipure form. Between 1817 and 1948, cyanide, in appropriate doses, was used therapeutically in England for the treatment of pulmonary diseases, tuberculosis, and as a sedative. By 1830, cyanogenic glycosides containing HCN were isolated from cassava. Today, more than 800 species of cyanogenic plants have been identified. In 1876, it was first demonstrated that cyanide inhibited tissue oxidation. In 1894, cobalt compounds were suggested as antidotes due to their marked cyanide-binding capacity. Studies on cyanide detoxification conducted between 1877 and 1894 showed that thiosulfate administration caused the formation of thiocyanate — a relatively harmless metabolite. By the late 1800s, cyanide was regarded as a common plant metabolite rather than as an unusual poison. In 1929, it was conclusively demonstrated that cyanide combines with the trivalent iron atom in cytochrome oxidase, a respiratory enzyme that links the tricarboxylic acid cycle and formation of metabolic water. Many reviews have been published on cyanide in the environment. Particularly useful were those by Doudoroff (1976), Towill et al. (1978), Smith et al. (1979), Egekeze and Oehme (1980), USEPA (1980, 1989), Vennesland et al. (1981), Leduc et al. (1982), Leduc (1984), Way (1984), Ballantyne and Marrs (1987), Evered and Harnett (1988), Eisler (1991), Smith and Mudder (1991), U.S. Public Health Service [USPHS] (1995); Hill and Henry (1996), and Ripley et al. (1996).

Cyanide hazards to fish, wildlife, and livestock are well documented. Massive kills of freshwater fish by accidental discharges of cyanide wastes are fairly common (Holden and Marsden 1964; Leduc 1978; Towill et al. 1978; USEPA 1980; Albersworth et al. 1989; Ripley et al. 1996). In one case, cyanide-containing mine effluents from a Canadian tailings pond released into a nearby creek

killed more than 20,000 steelhead (*Oncorhynchus mykiss*) (Leduc et al. 1982). Many species of birds were found dead near burrows of the black-tailed prairie dog (*Cynomys ludovicianus*) after the burrows had been treated with calcium cyanide to control prairie dog populations; dead birds included the burrowing owl (*Athene cunicularia*), the bald eagle (*Haliaeetus leucocephalus*), and the golden eagle (*Aquila chrysaetos*) (Wiemeyer et al. 1986). An endangered California condor (*Gymnogyps californianus*) found dead in Kern County, California, in November 1983 had particles of a yellow fluorescent tracer in its mouth; these particles were similar to those mixed with sodium cyanide (NaCN) in M-44 spring-loaded ejector mechanism devices used in a U.S. Fish and Wildlife Service Animal Damage Control Program in that vicinity, suggesting that cyanide was a possible cause of death (Krynnitsky et al. 1986). M-44 devices are known to have caused the death of magpies (*Pica* spp.), ravens and crows (*Corvus* spp.), wild turkeys (*Meleagris gallopavo*), and various unidentified species of hawks and vultures (Wiemeyer et al. 1986). Between 1980 and 1989, 519 mammals — mostly rodents (35%) and bats (34%) — were found dead at cyanide-extraction, gold-mine leach ponds in California, Nevada, and Arizona. The list included coyote (*Canis latrans*), foxes, skunks, badger (*Taxidea taxus*), weasels, rabbits, deer, and beavers (Clark and Hothem 1991). Also found dead at these same leach ponds were 38 reptiles, 55 amphibians, and 6997 birds, including many species of waterfowl and songbirds (Allen 1990; Clark and Hothem 1991; Henny et al. 1994; Hill and Henry 1996).

The major threat of cyanide poisoning to livestock and terrestrial mammalian wildlife is through ingestion of plants containing high levels of cyanogenic glycosides (Towill et al. 1978; Marrs and Ballantyne 1987). Plants implicated in cyanide poisoning of animals include the sorghums (Johnson grass, *Sorghum halepense*; Sudan grass, *Sorghum alnum*), arrowgrass (*Triglochin* spp.), elderberry (*Sambucus* spp.), wild cherry (*Prunus* spp.), and the pits of several common fruits, such as apple, peach, and apricot. These plants and fruit pits have the potential of releasing cyanide upon ingestion (Egekeze and Oehme 1980). Domestic goats (*Capra* spp.) died of cyanide poisoning after eating leaves and fruit of the crab apple (*Malus sylvestris*). The crab apple contains cyanogenic glycosides in its leaves and fruit (Shaw 1986). Cyanide poisoning of cattle (*Bos* spp.) by forage sorghums and various hybrid cultivars has been reported in India (Bapat and Abhyankar 1984) and elsewhere (Cade and Rubira 1982; Biehl 1984). Cattle appear to be more vulnerable to cyanide poisoning than sheep (*Ovis aries*), horses (*Equus cabalus*), and pigs (*Sus* spp.) (Cade and Rubira 1982). Equine sorghum cystitis ataxia is a condition observed in horses grazing *Sorghum* or hybrid Sudan grass pastures; it is characterized by urinary incontinence, posterior incoordination, and degenerative central nervous system lesions (Egekeze and Oehme 1980). Grazing cyanogenic plants can induce sulfur deficiency in sheep, presumably because sulfur detoxifies the released cyanide (Towill et al. 1978). The increasing use of cassava and other cyanogenic plants in animal feeding portends a greater exposure to dietary cyanides (Davis 1981).

15.2 CHEMICAL PROPERTIES

The chemical speciation of cyanides varies according to their source. Specific terms used to describe cyanide include free cyanide, cyanide ion, simple cyanides, complex cyanides, nitriles, cyanogens, and total cyanide. The most common forms of cyanide in the environment are free cyanide, metallocyanide complexes, and synthetic nitriles. A brief description of each cyanide species follows (Smith et al. 1978, 1979; Towill et al. 1978; Egekeze and Oehme 1980; USEPA 1980, 1989; Davis 1981; Leduc 1981, 1984; Leduc et al. 1982; Simovic and Snodgrass 1985; Ballantyne 1987a; Homan 1987; Marrs and Ballantyne 1987).

Free cyanide is the primary toxic agent in the aquatic environment. Free cyanide refers to the sum of molecular HCN and the cyanide anion (CN^-), regardless of origin. In aqueous solution with pH 9.2 and lower, the majority of the free cyanide is in the form of molecular HCN. The chemical names for HCN include hydrogen cyanide, hydrocyanic acid, cyanohydric acid, and prussic acid.

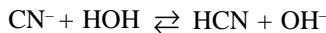
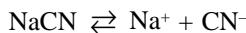
Table 15.1 Some Properties of Potassium Cyanide, Hydrogen Cyanide, and Sodium Cyanide

Property	Potassium Cyanide	Hydrogen Cyanide	Sodium Cyanide
CAS number	151-50-8	74-90-8	143-33-9
Chemical formula	KCN	HCN	NaCN
Molecular weight	65.12	27.03	49.01
Physical state	Solid	Gas or liquid	Solid
Boiling point (°C)	—	25.7	1496
Melting point (°C)	634.5	-13.21	563.7
Specific gravity	1.5	0.7 (liquid)	1.6
Solubility in water (g/L)	716 at 20°C	Miscible	480 at 10°C

Data from U.S. Environmental Protection Agency (USEPA). 1989. Cyanide. *Rev. Environ. Contam. Toxicol.* 107:53-64.

Hydrogen cyanide (Table 15.1) is a colorless, flammable liquid or gas that boils at 25.7°C and freezes at minus 13.2°C. The gas rarely occurs in nature, is lighter than air, and diffuses rapidly. It is usually prepared commercially from ammonia and methane at elevated temperatures with a platinum catalyst. It is miscible with water and alcohol, but is only slightly soluble in ether. In water, HCN is a weak acid with the ratio of HCN to CN⁻ about 100 at pH 7.2, 10 at pH 8.2, and 1 at pH 9.2. HCN can dissociate into H⁺ and CN⁻. Cyanide ion, or free cyanide ion, refers to the anion CN⁻ derived from hydrocyanic acid in solution, in equilibrium with simple or complexed cyanide molecules. Cyanide ions resemble halide ions in several ways and are sometimes referred to as "pseudohalide" ions. For example, silver cyanide is almost insoluble in water, as are silver halides. Cyanide ions also form stable complexes with many metals.

Simple cyanides typically refer to alkali water-soluble salts, such as NaCN, KCN, Ca(CN)₂, and Hg(CN)₂, but also include several cyanide salts of alkali, alkaline earth, or heavy metals, that is, Zn(CN)₂, Cd(CN)₂, Ni(CN)₂, and AgCN, of varying degrees of solubility. In water, NaCN and KCN will completely dissociate to give free cyanide. All simple cyanides ionize in water to release cyanide ion which, depending on pH, will form hydrocyanic acid. For sodium cyanide, the reaction proceeds as follows:



Increased pH will maintain a larger fraction of the cyanide as CN⁻, and acidification will cause the reverse. At pH 7, about 99% of the free cyanide is in the form of HCN; whereas at pH 9.3, HCN composes 50%. Since HCN is extremely water soluble and is also one of the most toxic cyanide species, it is noteworthy that the toxicity of simple cyanides will not be affected measurably below pH 8.3.

Complex cyanides are compounds in which the cyanide anion is incorporated into a complex or complexes. These compounds are different in chemical and toxicologic properties from simple cyanides. In solution, the stability of the cyanide complex varies with the type of cation and the complex that it forms. Some of these are dissociable in weak acids to give free cyanide and a cation, while other complexes require much stronger acidic conditions for dissociation. The least-stable complex metallocyanides include Zn(CN)₄²⁻, Cd(CN)₃⁻, and Cd(CN)₄²⁻; moderately stable complexes include Cu(CN)₂⁻, Cu(CN)₃²⁻, Ni(CN)₄²⁻, and Ag(CN)₂⁻; and the most stable complexes include Fe(CN)₆⁴⁻, and Co(CN)₆⁴⁻. The toxicity of complex cyanides is usually related to their ability to release cyanide ions in solution, which then enter into an equilibrium with HCN; relatively small fluctuations in pH significantly affect their biocidal properties.

Cyanogen [$(CN)_2$] is the simplest compound containing the cyanide group. Cyanogen is an extremely toxic, flammable gas that reacts slowly with water to form HCN, cyanic acid, and other compounds. It is rapidly degraded in the environment. Cyanogen and its halide derivations are comparable to hydrogen cyanide in toxicity.

Nitriles are defined as organic compounds (RCN) containing the cyanide group. Cyanide bound to carbon as nitriles (other than as cyanogenic glycosides) are comparatively innocuous in the environment, are low in chemical reactivity, and are biodegradable. For simple mononitriles, there is a clear progression, with more cyanide being released as chain length increases. A similar pattern exists in dinitriles, but corresponding compounds require a longer carbon chain than mononitriles before free cyanide is produced. Based on studies with chicken liver homogenates (Davis 1981), mononitriles were more toxic than dinitriles, and within each group the order of toxicity was $CH_3 > C_2H_5 > C_3H_7 > C_4H_9 > C_5H_{11} > C_7H_{15}$. Cyanohydrins [$R_2C(OH)CN$] and cyanogenic glycosides [$R_1R_2C(OR_3)CN$] are special classes of nitriles, in that under appropriate conditions they will decompose to HCN and cyanide ions. Cyanogens (not to be confused with cyanogen), such as acrylonitrile, priopionitrile, and succinonitrile, are nitrile-containing materials of varying complexity and lability, and can liberate free and toxicologically available amounts of cyanide. But the non-nitrile portion of the cyanogen molecule may exert an independent or interactive toxicity, causing a complex response.

Cyanates contain the OCN group. Inorganic cyanates that are formed industrially by the oxidation of cyanide salts hydrolyze in water to form ammonia and bicarbonate ion. Alkyl cyanates are insoluble in water and form cyanurates. Alkyl isocyanates contain the OCN radical, are formed from cyanates, and, like cyanates, are readily hydrolyzed. Thiocyanates (SCN group) are formed from cyanides and sulfur-containing materials and are relatively stable.

Total cyanides refers to all cyanide-containing compounds, including simple and complex cyanides, cyanoglycosides, and free cyanide. Total cyanides is a chemical measurement of free cyanide present in solution or released by acidification or digestion. Only free cyanide is considered to be a biologically meaningful expression of cyanide toxicity. Under most circumstances, the concentration of total cyanide will exceed that of HCN. In some waters, however, the total cyanide concentration may consist almost entirely of free cyanide, or it may contain cyanides that readily photodecompose or dissociate to yield HCN. The relation between total cyanide and free cyanide in natural waters varies with receiving-water conditions, type of cyanide compounds present, degree of exposure to daylight, and presence of other chemical compounds.

Hydrogen cyanide has frequently been associated with the odor of bitter almonds (Ballantyne 1983; Gee 1987). The threshold odor for olfactory detection of atmospheric HCN is 1 mg/L, but the odor may not be detected for various reasons, including the presence of other odors and the fact that only 20 to 40% of those tested could detect a cyanide odor.

Analytical methods for determining free and bound cyanide and cyanogenic compounds in biological materials are under revision. Procedures include chromatography; enzymic postcolumn cleavage; electrochemical detection; and ultraviolet, infrared, proton, and carbon-13 nuclear magnetic resonance spectroscopies (Brimer 1988). Proposed newer analytical methodologies include chemiluminescence (Wu et al. 1989); deproteinization techniques (Krynnitsky et al. 1986); thin-film dissociation coupled with preferential ultraviolet irradiation (Kelada 1989); differential pulse polarography (Westly 1988); and modified spectrophotometric (Blago 1989; Ohno 1989), colorimetric (Lundquist and Sorbo 1981), and ion chromatographic determinations (Nonomura and Hobo 1989). Analysis of cyanide and cytochrome oxidase is usually conducted with samples of whole blood, serum, plasma, brain, or ventricular myocardium tissues. Samples should be obtained as soon as possible after cyanide exposure and analyzed immediately; otherwise, erroneous analytical values will result (Towill et al. 1978; Ballantyne 1983). Brain and liver are recommended for cyanide analysis if removed and analyzed within a week (Ballantyne et al. 1974). Cyanide measurements are further confounded by the presence of various antidotal agents (Ballantyne 1983); by various tissue preservatives, such as formaldoxime (Knocke 1981) and sodium fluoride (Curry

et al. 1967); and by the spontaneous postmortem production of cyanide in various tissues (e.g., sterile blood, brain, liver, kidney, uterus, intestines) over time in cases of non-cyanide death (Curry et al. 1967; Ballantyne et al. 1974).

15.3 MODE OF ACTION

Cyanide is a potent and rapid-acting asphyxiant. At lethal doses, inhalation or ingestion of cyanide produces reactions within seconds and death within minutes. Cyanide's toxic effect is due to its affinity for the ferric heme form of cytochrome a_3 , also known as cytochrome c oxidase, the terminal oxidase of the mitochondrial respiratory chain (Towill et al. 1978; Egekeze and Oehme 1980; Solomonson 1981; Way 1981, 1984; Leduc et al. 1982; Biehl 1984; Ballantyne 1987a; Marrs and Ballantyne 1987; Yamamoto 1989; Chew and Ip 1992). Inhibition of the enzyme cytochrome c oxidase is thought to involve a two-step reaction: initial penetration of cyanide into a protein crevice, followed by binding to heme iron. Formation of a stable cytochrome c oxidase-CN complex in the mitochondria produces a blockage of electron transfer from cytochrome oxidase to molecular oxygen and cessation of cellular respiration, causing cytotoxic hypoxia in the presence of normal hemoglobin oxygenation. Tissue anoxia induced by the activation of cytochrome oxidase causes a shift from aerobic to anaerobic metabolism, resulting in the depletion of energy-rich compounds such as glycogen, phosphocreatine, and adenosine triphosphate, and the accumulation of lactate with decreased blood pH. The combination of cytotoxic hypoxia with lactate acidosis depresses the central nervous system — the most sensitive site of anoxia — resulting in respiratory arrest and death. If the absorption rate is significantly greater than the detoxification rate, there will be a rapid accumulation of free cyanide in tissues and body fluids, resulting in the prompt onset of signs of acute cyanide poisoning. Acute cyanide poisoning is frequently encountered as a relatively massive overdose, where the amount of cyanide greatly exceeds the minimal concentration necessary to inhibit cytochrome c oxidase. In such cases, many enzymes and biological systems are disrupted, including various metalloenzymes, nitrate reductase, nitrite reductase, myoglobin, various peroxidases, catalase, and ribulose diphosphate carboxylase, resulting in severe signs of toxicity and rapid death.

The great majority of the absorbed cyanide reacts with thiosulfate in the presence of enzymes to produce thiocyanate, which is excreted in the urine over a period of several days. Owing to this rapid detoxification, animals can ingest high sublethal doses of cyanide over extended periods without harm (Towill et al. 1978; Egekeze and Oehme 1980; USEPA 1980; Davis 1981; Solomonson 1981; Leduc 1984; Ballantyne 1987a; Oh et al. 1987; Marrs and Ballantyne 1987; Westley 1988; Mengel et al. 1989). Authorities are also in general agreement on several points:

- Thiosulfate is usually low in the body, and higher levels can significantly protect against cyanide toxicity.
- Species vary considerably in both the extent to which thiocyanate is formed and the rate at which it is eliminated from the body.
- Thiocyanate metabolites resulting from the transulfuration process are about 120 times less toxic than the parent cyanide compound.
- Thiocyanate can accumulate in tissues and has been associated with developmental abnormalities and other adverse effects.
- The two enzyme systems responsible for the transulfuration process are thiosulfate-cyanide sulfurtransferase — also known as rhodanese — and beta-mercaptopyruvate cyanide sulfurtransferase.

Rhodanese is widely distributed in the body, but activity levels in mammals are highest in the mitochondrial fraction of liver. Rhodanese activity levels in catalyzing the transformation of thiosulfate to thiocyanate are limited by the availability of sulfur. Minor detoxification pathways for cyanide include exhalation in breath as HCN, and as CO₂ from oxidative metabolism of formic

acid; conjugation with cystine to form 2-iminothiazolidene-4-carboxylic acid or 2-aminothiazoline-4-carboxylic acid; combining with hydroxocobalamin (B_{12}) to form cyanocobalamin, which is excreted in urine and bile; and binding by methemoglobin in the blood (Towill et al. 1978; USEPA 1980; Ballantyne 1987a; Marrs and Ballantyne 1987).

Absorption of hydrogen cyanide liquid or gas readily occurs through inhalation, ingestion, or skin contact (Towill et al. 1978; Egekeze and Oehme 1980; USEPA 1980; Homan 1987). Inhalation and skin absorption are the primary hazardous routes in cyanide toxicity in occupational exposure. Skin absorption is most rapid when the skin is cut, abraded, or moist. Inhalation of cyanide salts is also potentially hazardous because the cyanide dissolves on contact with moist mucous membranes. Regardless of route of exposure, cyanide is readily absorbed into the bloodstream and distributed throughout the body. Cyanide concentrates in erythrocytes through binding to methemoglobin (Towill et al. 1978; USEPA 1980), and free cyanide concentrations in plasma are now considered one of the better indicators of cytotoxicity (Ballantyne 1987a). Because of the affinity of cyanide for the mammalian erythrocyte, the spleen may contain elevated cyanide concentrations when compared to blood. Accordingly, spleen should always be taken for analysis in cases of suspected cyanide poisoning (Ballantyne 1975). Cyanide also accumulates in various body cells through binding to metalloproteins or enzymes such as catalase and cytochrome *c* oxidase (USEPA 1980). The brain is probably the major target organ of cytotoxic hypoxia, and brain cytochrome oxidase may be the most active site of lethal cyanide action, as judged by distribution of cyanide, thiosulfate, and rhodanese (Solomonson 1981; Ballantyne 1987a). Significant positive correlations exist between cyanide concentrations in plasma, cerebrospinal fluid, and brain (Ballantyne 1987a). These correlations need further exploration.

Hydrogen cyanide formation may contribute to the toxicity of snake venom, owing to the high levels of L-amino acid oxidase in some snake venoms (Vennesland et al. 1981a). This enzyme is harmless on injection, but the tissue destruction caused by other venom components probably provides the required substrate and cofactor for HCN production. Cyanide inhibits ion transport mechanisms in amphibian skin, gall bladder, and proximal renal tubules (Bello-Reuss et al. 1981). Measurable changes in cell membrane potentials of isolated gall bladder epithelium cells, for example, were induced by NaCN in a salamander (*Necturus maculosus*) (Bello-Reuss et al. 1981). Cyanide-induced hyperpolarization was caused primarily by an increase in permeability of the cell membrane to potassium, which, in turn, was mediated by an elevation of intracellular calcium ion activity, attributable to release from mitochondrial sources. The binding rate of CN to hemeproteins, specifically hemoglobin components III and IV, is 370 to 2300 times slower in a marine polychaete annelid (*Glycera dibranchiata*), when compared to guinea pig (*Cavia* spp.), soybean (*Glycine max*), and sperm whale (*Physeter macrocephalus*). The significance of this observation is unclear but warrants further exploration (Mintorovitch et al. 1989).

15.4 CLINICAL FEATURES

Accidental exposure to cyanides or cyanogens through inhalation, skin exposure, and swallowing occurs in agricultural fumigation, laboratories, industrial operations, domestic abuse, and products of combustion (Ballantyne and Marrs 1987b). Intentional exposure is reported from homicides, suicides (usually uncommon), judicial executions, chemical warfare, and covert activities (Ballantyne and Marrs 1987b). Diagnosis of lethal cyanide poisoning is difficult because of the absence of gross pathology or histology, nonspecific congestion of viscera, and cerebral or pulmonary edema. Sometimes, the blood is bright red, and sometimes the odor of bitter almonds is detected, but neither is sufficiently consistent for diagnostic purposes (Ballantyne and Marrs 1987b). At low lethal doses of cyanide, the effects are principally on cytochrome oxidase in the central nervous system. At higher doses, cardiovascular signs and changes in electrical activity of the brain are among the most consistent changes measured (Way 1981, 1984). Acute and subacute

toxic effects of poisoning with cyanide can vary from convulsions, screaming, vomiting, and bloody frothing to less dramatic events, such as a slow, quiet onset to coma and subsequent death (Way 1981). In the first stage of cyanide poisoning, victims exhibit headache, vertigo, weak and rapid pulse, nausea, and vomiting. In the second stage, there are convulsions, falling, dilated pupils, clammy skin, and a weaker and more rapid pulse. In the final stage, heartbeat becomes irregular and slow, body temperature falls, there is cyanosis of lips, face, and extremities, coma, frothy bloody saliva flow from the mouth, and death (Way 1981). If acute exposure is to a sublethal dose of cyanide, this may lead to signs of toxicity; but as detoxification proceeds, these signs will become less obvious and eventually vanish, and cyanide will be excreted as thiocyanate without accumulating (Ballantyne 1987a).

Chronic cyanide poisoning may develop in individuals who ingest significant quantities of cyanide or cyanide precursors in their diets. Effects are exacerbated by dietary deficiencies in Vitamin B₁₂, iodine, and sulfur amino acids, as well as by low levels and insufficient distribution of detoxifying enzymes such as rhodanese (Solomonson 1981). Cyanide toxicity of dietary origin has been implicated in acute animal deaths and as a major etiologic factor in toxic ataxic neuropathy in man, and as a cause of blindness in humans suffering from tobacco amblyopia and Leber's hereditary optic atrophy (Egekeze and Oehme 1980). An increase in blood plasma cyanide is observed in healthy individuals who smoke cigarettes (Cailleux et al. 1988). An increase in blood plasma thiocyanate is also seen in smokers and in hemodialysis patients just before dialysis (Cailleux et al. 1988). Continuous intake of cyanide causes high levels of plasma thiocyanate and goiters in mammals; the antithyroid action (goiters) results from cyanide interference with iodine transport and thyroxine synthesis (Solomonson 1981; Leduc 1981, 1984). Signs of chronic cyanide poisoning include demyelination, lesions of the optic nerve, decrease in sulfur-containing amino acids, increase in thiocyanate, goiter, ataxia, hypertonia, and depressed thyroid function (Solomonson 1981). These effects are common in areas that depend on cyanogenic plants — such as cassava — as a major dietary component (Solomonson 1981).

Biochemically, cyanide affects the citric acid cycle, strongly inhibits catalases and proteinases, induces glycolysis in protozoans, fish, and mammals, produces Vitamin B₁₂ deficiency, and modifies the phosphorylation mechanism of respiratory mitochondrial enzymes, causing arrested respiration due to inability to use oxygen (Leduc 1984). Cyanide biomagnification or cycling has not been reported, probably because of cyanide's high chemical reactivity and rapid biotransformation (Towill et al. 1978; Marrs and Ballantyne 1987). There is no evidence that chronic exposure to cyanide results in teratogenic, mutagenic, or carcinogenic effects (USEPA 1980). Cyanide possibly has antineoplastic activity, as judged by a low therapeutic success against rat sarcomas (USEPA 1980), but this requires additional documentation.

Confirmatory evidence of cyanide poisoning includes elevated blood thiocyanate levels — except, perhaps, when death was rapid — and reduced cytochrome oxidase activity in brain and myocardium, provided that all tissues were taken within a day or so of death, frozen quickly, and analyzed shortly thereafter (Biehl 1984; Marrs and Ballantyne 1987). Evaluation of cyanide poisoning and metabolism includes signs of toxicity, LD₅₀ values, measurement of cyanide and thiocyanate concentrations, cytochrome *c* oxidase activity, metabolic modification of *in vivo* cyanogenesis, rate of cyanide liberation *in vitro*, and influence of modifying factors such as the animal species, dose, rate and frequency of administration, route of exposure, differential distribution of cyanide, detoxification rates, circadian rhythm interactions, age of the organism, and presence of antidotes (Ballantyne 1987a). For example, the concentration of cyanide measured in body fluids and tissues in man and other animals following lethal administration of cyanide depends on several factors (Ballantyne and Marrs 1987b):

- Route of exposure, with oral route yielding highest residues and inhalation route the lowest
- Amount and duration of exposure
- Nature of the material, with HCN and CN⁻ being most toxic

- Time to death
- Antidotes used; time to autopsy, with marked loss documented from simple evaporation, thiocyanate formation, hydrolysis, and polymerization
- Time from autopsy to sample analysis, wherein cyanide concentrations may increase due to microbial action

15.5 ANTIDOTES

The antagonism of cyanide intoxication has been under investigation for at least 150 years. In 1840, cyanide lethality was reported to be antagonized by artificial respiration. In 1888, amyl nitrite was reported effective in antagonizing lethal effects of cyanide in dogs. In 1894, cobalt was shown to form a stable metal complex with cyanide and was used to antagonize cyanide. In 1933, the use of sodium thiosulfate as the sulfur donor was described (Way 1984). Many compounds are used today as cyanide antidotes, including cobalt salts, rhodanese, sulfur donors, methemoglobin producers, carbohydrates, drugs used to treat acidosis, oxygen, methylene blue, 4-dimethylaminophenol, various aromatic amino- and nitro-compounds (such as aniline, *p*-aminopropiophenone, nitrobenzene), carbonyl compounds, and sodium pyruvate (Egekeze and Oehme 1980; USEPA 1980; Solomonson 1981; Way 1981, 1984; Biehl 1984; Becker 1985; Ballantyne 1987b; Marrs 1987; Marrs and Ballantyne 1987; Way et al. 1988). Different antidotes are preferred in different countries: in the United States, a mixture of sodium nitrite and sodium thiosulfate; in France and the United Kingdom, cobaltedetate, also known as Kelocyanor; and in Germany, a mixture of 4-dimethylaminophenol and sodium thiosulfate.

The classic nitrite-thiosulfate treatment of cyanide poisoning, developed almost 60 years ago, is one of the antidotal combinations still employed (Way 1981). Excess oxygen improves this antidotal combination by potentiating the effectiveness of the nitrite–thiosulfate combination, as confirmed by studies in sheep and rats (Way 1984), although, theoretically, oxygen should serve no useful purpose (Way et al. 1988). This therapeutic regimen protected rats against 20 LD₅₀ doses of cyanide (Towill et al. 1978). Nitrite converts hemoglobin to methemoglobin, which has a high affinity for cyanide. The methemoglobin–HCN complex then slowly releases cyanide, which is converted to thiocyanate by way of rhodanese (Solomonson 1981). Sodium nitrite, administered intravenously, is now considered one of the more rapid therapeutic methods (Way 1984). The injection of sodium thiosulfate provides sulfur for the enzyme rhodanese to mediate the biotransformation of cyanide to the much less toxic thiocyanate (Egekeze and Oehme 1980). Multiple injections of sodium thiosulfate protected mice against death by organic cyanides and were more effective than sodium nitrite (Willhite and Smith 1981). The nitrite–thiosulfate antidotal combination is one of the most effective treatments of cyanide poisoning, although the specific mechanism of action of these two compounds is now being questioned, and concerns have been raised because of the toxicity of nitrite (Way 1981, 1984). One accepted therapy is an intravenous combination of sodium nitrite (1 mL of 20% solution) and sodium thiosulfate (3 mL of 20% solution), giving 4 mL of this mixture per 45 kg of body weight (Egekeze and Oehme 1980). For maximal effectiveness in treating cyanide intoxication in sheep, large doses of sodium thiosulfate (660 mg/kg BW) are given in combination with conventional doses of sodium nitrite (6.6 mg/kg BW) (Egekeze and Oehme 1980). Livestock treatment in cases of suspected cyanide intoxication consists of intravenous administration of 10 to 20 mg sodium nitrite/kg BW followed by 30 to 40 mg sodium thiosulfate/kg BW. However, a sodium thiosulfate dose of 500 mg/kg BW, or more, may be more efficacious (Biehl 1984). Once clinical signs have abated, 1 g of activated charcoal/kg BW may be administered as a drench via a stomach tube (Biehl 1984). A 30-kg female goat (*Capra* sp.) was successfully treated after eating the leaves and fruit of the crab apple (*Malus sylvestris*), a plant that contains high levels of cyanogenic glycosides in leaves and fruits (Shaw 1986). Treatment consisted of four hourly treatments of 100 g of animal charcoal and bismuth subnitrate in water

as a drench, followed by 300 mg sodium nitrite as a 1% aqueous solution, then 25 g of sodium thiosulfate. Another goat died despite identical treatment (Shaw 1986).

Cobalt compounds, such as hydroxocobalamin and its derivatives (i.e., cobalt histidine, cobalt chloride, dicobalt ethylenediamine tetracetic acid) have been used to treat cyanide poisoning for more than 100 years. Their efficacy was confirmed in pigeons (*Columba* sp.) and rabbits (*Oryctolagus* sp.), but cobalt compounds did not receive wide support as cyanide antagonists because of the inherent toxicity of cobalt ion (Way 1981, 1984). Nevertheless, proponents of the use of cobalt compounds (i.e., the United Kingdom, Scandinavia, much of Europe) stress the rapidity of action in forming a stable metal complex with cyanide, thereby preventing its toxic effect (Towill et al. 1978; Way 1984). One of the more frequently used cobalt compounds in cyanide treatment is hydroxocobalamin, which reverses cyanide toxicity by combining with cyanide to form cyanocobalamin (Vitamin B₁₂) (USEPA 1980; Solomonson 1981). Hydroxocobalamin has been used in guinea pigs and baboons (*Papio anubis*) to lower blood cyanide levels, and in humans after inhalation or ingestion of cyanide compounds (Egekeze and Oehme 1980).

Dimethylaminophenol (DMAP) forms methemoglobin by setting up a catalytic cycle inside the erythrocyte, in which oxygen oxidizes the DMAP to *N,N*-dimethylquinoneimine, the latter oxidizing the hemoglobin to methemoglobin (Marrs 1987). Dogs poisoned with KCN and given DMAP intravenously had restored respiration and decreased plasma cyanide levels. The 4-dimethylaminophenol induced ferrihemoglobin production, which combined with the cyanide in the red cells to form ferrihemoglobin cyanide (Christel et al. 1977).

No usable cyanide prophylactic therapy now exists for humans, although sodium thiosulfate, hydroxocobalamin, and other compounds have been used to protect against cyanide toxicity in laboratory animals (Mengel et al. 1989). For example, pyridoxal 5-phosphate, the active form of Vitamin B₆, readily forms complexes with cyanides, and was effective in providing significant protection to rats (Keniston et al. 1987). Fructose fed prior to insult lessens cyanide-induced hepatotoxicity in rats (Younes and Strubelt 1988). L-ascorbic acid and dehydroascorbic acid probably act as protectants against cyanide toxicity by way of nontoxic cyanohydrin formation (Sprine et al. 1982). Carbon tetrachloride pretreatment was effective in protecting mice against death from most nitriles (Willhite and Smith 1981), and pretreatment with *p*-aminopropiophenone serves to protect against cyanide toxicity (D'Mello 1987).

15.6 SOURCES AND USES

Production of cyanides in the United States increased from about 136 million kg in 1963 to 318 million kg in 1976 (Towill et al. 1978; Way 1981; Marrs and Ballantyne 1987). Cyanide consumption in North America was 64 million kg in 1988 and 98 million kg in 1989; about 80% of these amounts was used in gold mining (Knudson 1990). In Canada, more than 90% of the mined gold is extracted from ores with the cyanidation process. This process consists of leaching gold from the ore as a gold–cyanide complex, and recovering the gold by precipitation (Simovic and Snodgrass 1985; Eisler et al. 1999). Heap leaching occurs when crushed ore is stacked on an impermeable plastic pad on the ground surface, with spraying or dripping of an NaCN solution on the flattened top. Large leach heaps may include 272,000 metric tons of ore and tower 100 meters or more (Albersworth et al. 1989). In the milling of gold ores, an NaCN solution is percolated through the crushed ores to dissolve the gold particles (Ripley et al. 1996). In both leaching and milling processes, after the gold is chemically precipitated, the solution is adjusted for pH and cyanide concentration, and recycled to precipitate more gold. Eventually, the remaining solution must be treated to recycle the cyanide or to destroy it to prevent escape into the environment (Ripley et al. 1996). Milling and heap leaching require cycling of millions of liters of alkaline water containing high concentrations of potentially toxic NaCN, free cyanide, and metal cyanide complexes that are frequently accessible to wildlife. Some milling operations result in tailings ponds

of 150 ha and larger. Heap leach operations that spray or drip cyanide solutions onto the top of the ore heap require solution processing ponds of about 1 ha in surface area. Although not intentional or desired, puddles of various sizes may occur on the top of heaps where the highest concentrations of NaCN are found. Exposed solution recovery channels are usually constructed at the base of leach heaps. All of these cyanide-containing water bodies are hazardous to wildlife if not properly managed (Henny et al. 1994; Eisler et al. 1999).

About 84% of domestic HCN production is used to produce organic cyanides, also known as nitriles, including acrylonitriles, methyl methacrylate, and adiponitrile (Towill et al. 1978). Nitriles tend to polymerize, which is the basis for their use in the manufacture of synthetic fibers, resins, plastics, dyestuffs, vitamins, solvents, elastomers, agricultural insecticides, and high-pressure lubricants (Willhite and Smith 1981). The widespread usefulness of HCN is related to its strong tendency and that of its inorganic salts to form complexes with metals. For example, sodium cyanide is used in metallurgy for the extraction of gold and silver from ores and in electroplating baths because it forms stable soluble complexes. Similar behavior makes alkali cyanide solutions excellent for cleaning silverware and other precious metals and is responsible for their general use in industry as metal cleaners (Towill et al. 1978). In Canada, more than 90% of the gold mined is extracted from ores with the cyanidation process. This process consists of leaching gold from the ore as a gold–cyanide complex, and gold being precipitated with the addition of zinc dust. A variety of cyanide compounds are produced during gold cyanidation (Simovic and Snodgrass 1985; Ripley et al. 1996; Eisler et al. 1999). In addition to their primary use in the metals and electroplating industries, and in the manufacture of synthetic fibers and plastics, various cyanide compounds have been used directly or as an intermediate to produce synthetic rubber, fumigants, rodenticides, insecticides, predator control agents, rocket fuels, paints and paint finishes, paper, nylon, pharmaceuticals, photographic chemicals, mirrors, cement, perfume, bleaches, soaps and detergents, riot control agents, fertilizers, and weedicides (Towill et al. 1978; Way 1981; Willhite and Smith 1981; Leduc 1984; Homan 1987).

Hydrogen cyanide vapor, because of its high and rapid acute lethal toxicity and ready diffusion, has been used widely to fumigate buildings, ships, and warehouses; to exterminate rabbits, rodents, and large predators; and in horticultural practice, to control insect pests that have developed resistance to other pesticides (Homan 1987; Ballantyne 1988). Typically, fumigation powders containing either calcium cyanide, Ca(CN)₂, or sodium cyanide, NaCN, are blown into burrows or scattered over the floor in greenhouses. On coming into contact with water, such powders liberate HCN vapor (Ballantyne 1988). Hydrogen cyanide released from Ca(CN)₂ is registered for use on almonds, dried beans, citrus, cocoa beans, grains, nuts, and spices (Towill et al. 1978). Cyanide-containing compounds are used for a variety of agricultural and pesticidal agents. These compounds include cyanogen (NCCN), as an intermediate in the production of some commercial fertilizers; cyanogen chloride (CNCI), in the manufacture of triazine herbicides; cyanogen bromide (CNBr), as a pesticidal fumigant; hydrogen cyanide, in the synthesis of methionine for animal feeds; ammonium thiocyanate (NH₄SCN), as a cotton defoliant; sodium thiocyanate (NaSCN), as a weedkiller; and calcium cyanamide (CaNCN), as a plant fertilizer, herbicide, pesticide, and defoliant of cotton and tomatoes (Homan 1987). Cyanide compounds have also been used as preservatives for raw vegetables (Towill et al. 1978).

Sodium cyanide has been used for about 50 years by the U.S. Fish and Wildlife Service against coyote in attempts to protect livestock, especially sheep. The Service has made extensive use of two NaCN ejector devices: “the coyote getter,” from the late 1930s to 1970; and the M-44, from about 1968 to the present, except for the period 1972 to 1974, when all uses of NaCN for predator control were canceled (USEPA 1976a; Connolly and Simmons 1984). Although both ejectors dispense toxicant when pulled, they differ in the way ejection is achieved. In the coyote getter, the toxicant is in a 0.38-caliber cartridge case and is expelled by the explosive force of the primer plus a small powder charge. The M-44 uses a spring-driven plunger to push out its toxic contents. M-44 capsules weigh about 0.94 grams, and consist of about 89% NaCN, 6% Celatom MP-78 (mostly

diatomaceous silica), 5% potassium chloride, and 0.25% FP Tracerite yellow — used as a fluorescent marker (Connolly and Simmons 1984). Coyote getters and M-44s are set into the ground with only their tops protruding. Fetid scent or lure stimulates a coyote to bite and pull, whereupon a lethal dose of NaCN is ejected into its mouth; coma and death follow in 30 to 60 s. Although coyote getters were about 99% effective against coyotes, compared to 73% for M-44s, the Service decided that spring-driven plungers were less hazardous to operators than were explosive-driven plungers (Connolly and Simmons 1984). The coyote getter was generally much more selective than the trap for the capture of coyotes. It was less destructive than traps to small mammals, birds of prey, ground-nesting birds, deer, antelope, and domestic sheep, but more destructive to dogs, bears, and cattle (Robinson 1943). In a 1-year test period (1940/41) in Colorado, Wyoming, and New Mexico, the following numbers of animals were killed by the coyote getter: 1107 coyotes, 2 bobcats (*Lynx rufus*), 24 dogs, 14 black-billed magpies (*Pica pica*), 7 foxes (*Vulpes* sp.), 8 unidentified skunks, 2 badgers, 2 unidentified eagles, 2 bears (*Ursus* sp.), and 1 each of hawk (unidentified), rockchuck (*Ochotona* sp.), and cow (Robinson 1943).

Cyanide compounds have been used to collect various species of freshwater fish. In England and Scotland, cyanides are used legally to control rabbits, and illegally to obtain Atlantic salmon (*Salmo salar*) and brown trout (*Salmo trutta*) from rivers, leaving no visible evidence of damage to the fish (Holden and Marsden 1964). Sodium cyanide has been applied to streams in Wyoming and Utah to collect fish through anesthesia. Mountain whitefish (*Prosopium williamsoni*) were sensitive to cyanide and died at concentrations that were tolerable to salmon and trout (Wiley 1984). Sodium cyanide was also used as a fish control agent in Illinois, Nebraska, South Dakota, Missouri, and in the lower Mississippi River valley, but was never registered for this use because of human safety concerns (Lennon et al. 1970). The widespread use of NaCN to collect exotic marine fishes is associated with high mortality in aquarium fish stocks in the Philippine Islands and elsewhere (Hall and Bellwood 1995). Cyanide fishing is banned in many Asia-Pacific countries; however, widespread illegal fishing continues, with significant adverse effects on coral reef ecosystems (Jones and Hoegh-Guldberg 1999).

Cyanide compounds have been prescribed by physicians for treatment of hypertension and cancer (Sprine et al. 1982). Sodium nitroprusside ($\text{Na}_2\text{Fe}(\text{CN})_5\text{NO} \cdot 2\text{H}_2\text{O}$) was widely used for more than 30 years to treat severe hypertension and to minimize bleeding during surgery (Solomonson 1981; Vesey 1987). Laetile, an extract of ground apricot kernels, has been used for cancer chemotherapy and, in deliberate high intakes, as an attempted suicide vehicle (Gee 1987).

Road salt in some areas may contribute to elevated cyanide levels in adjacent surface waters (Ohno 1989). In climates with significant snowfall, road salt is applied as a deicing agent. Road salts are commonly treated with anticaking agents to ensure uniform spreading. One anticaking agent, sodium hexacyanoferrate, decomposes in sunlight to yield the highly toxic free cyanide that contaminates surface waters by runoff (Ohno 1989). Another anticaking agent, yellow prussiate of soda (sodium ferrocyanide), has been implicated in fish kills when inadvertently used by fish culturists (Barney 1989).

The military uses of HCN were first realized by Napoleon III, but it was not until World War I (WW I) that this application received widespread consideration. About 3.6 million kg of hydrogen cyanide were manufactured by France as a chemical weapon and used in WW I in various mixtures called Manganite and Bincennite, although its use was not highly successful because of limitations in projectile size and other factors. During WW II, the Japanese were armed with 50-kg HCN bombs, and the United States had 500-kg bombs. More than 500,000 kg of HCN chemical weapons were produced during WW II by Japan, the United States, and the Soviet Union, but it is not known to what extent these weapons were used in that conflict (Way 1981).

Cyanides are widely distributed among common plants in the form of cyanogenic glycosides (Egekeze and Oehme 1980; Solomonson 1981; Way 1981; Biehl 1984; Homan 1987; Marrs and Ballantyne 1987). Their toxicity following ingestion is primarily related to the hydrolytic release of HCN. Ingestion of cyanogenic plants probably has accounted for most instances of cyanide

exposure and toxicosis in man and range animals. Of chief agricultural importance among plants that accumulate large quantities of cyanogenic glycosides are the sorghums, Johnson grass, Sudan grass, corn, lima beans, flax, pits of stone fruits (cherry, apricot, peach), vetch, linseed, sweet potatoes, bamboo shoots, southern mock orange, millet, almonds, and cassava. Factors favoring cyanide buildup in cyanogenic plants include high nitrogen and low phosphorus in soils (Biehl 1984). The potential for high glycoside levels is greatest in immature and rapidly growing plants (Egekeze and Oehme 1980). At present, more than 28 different cyanoglycosides have been measured in about 1000 species of higher plants (Leduc 1984). In cassava, for example, more than 90% of the cyanide is present as linamurin, a cyanogenic glycoside, and the remainder occurs as free (nonglycoside) cyanide (Gomez et al. 1983). Laetrile, a preparation made from apricot kernels, contains high levels of amygdalin, a cyanogenic glycoside that can be degraded in the gut to cyanide and benzaldehyde. Several cases of cyanide poisoning in humans have been reported from intake of laetrile, either orally or anally (Solomonson 1981; Homan 1987). Cyanide formation in higher plants and microorganisms can also occur with compounds other than cyanogenic glycosides, such as glycine, glyoxylate plus hydroxylamine, or histidine (Solomonson 1981; Vennesland et al. 1981a). In some cases, plants may contain cyanide residues resulting from fumigation with HCN (Way 1981).

Many species of plants, including some fungi, bacteria, algae, and higher plants, produce cyanide as a metabolic product (Leduc et al. 1982; Leduc 1984). Some species of soil bacteria suppress plant diseases caused by soil-borne pathogens by producing metabolites with antibiotic activity. Certain strains of *Pseudomonas fluorescens*, a soil bacterium, suppress black root rot of tobacco caused by the fungus *Thielaviopsis basicola* by excreting several metabolites, including HCN (Voisard et al. 1989). A wide variety of bacteria and fungi can degrade cyanide compounds and may be useful in the treatment of cyanide wastes (Towill et al. 1978). For example, several species of fungi known to be pathogens of cyanogenic plants can degrade cyanide by hydration to formamide; dried mycelia of these species are now sold commercially to detoxify cyanide in industrial wastes (Knowles 1988).

Anthropogenic sources of cyanide in the environment include industrial processes, laboratories, fumigation operations, cyanogenic drugs, fires, cigarette smoking, and chemical warfare operations (Marrs and Ballantyne 1987). Cyanides are present in many industrial wastewaters, especially those of electroplaters, manufacturers of paint, aluminum, and plastics, metal finishers, metallurgists, coal gasification processes, certain mine operations, and petroleum refiners (Towill et al. 1978; Egekeze and Oehme 1980; Way 1981, 1984). Electroplaters are a major source. In the United States alone, electroplaters discharge about 9.7 million kg of cyanide wastes annually into the environment from 2600 electroplating plants (Marrs and Ballantyne 1987). Paint residues annually contribute an additional 141,300 kg of cyanide wastes into the environment, and paint sludges 20,400 kg (Way 1981; Marrs and Ballantyne 1987). Cyanide can also originate from natural processes, such as cyanide production by bacteria, algae, and fungi, and from many terrestrial plants that release free HCN when their cellular structure is disrupted (Leduc 1981). Hospital wastewaters usually contain no detectable cyanide, but concentrations up to 64 µg CN⁻/L have been measured after alkali chlorination treatment (Tatsumoto and Hattori 1988). It seems that various compounds common in hospital wastewaters will produce 15 to 25 µg CN⁻/L after alkali chlorination. These compounds include hydantoin (an antiepilepsy agent) and related nitrogenous compounds, such as hydantonic acid, 5,5-diphenylhydantoin, imidazole, and 2-imidazolidinone (Tatsumoto and Hattori 1988).

Free hydrogen cyanide occurs only rarely in nature because of its high reactivity. The gas is sometimes found in the atmosphere, however, as a result of emissions from the petrochemical industry, malfunctioning catalytic converters on automobiles, fumigation of ships and warehouses, incomplete combustion of nitrogen-containing materials, and from tobacco smoke (Towill et al. 1978; Way 1981, 1984). Hydrogen cyanide is known to be produced in fires involving nitrogen-containing polymers and is probably the most important narcotic fire product other than carbon monoxide (Purser et al. 1984). Cyanide-related fire deaths and injuries, as judged by elevated blood

cyanide and thiocyanate concentrations, have been documented in airplanes, jails, and high-rises (Becker 1985; Ballantyne 1987b; Lundquist and Sorbo 1989). In a study of fire victims in Scotland, elevated blood cyanide levels were found in 78% of fatalities, and 31% had blood levels considered to be toxic (Purser et al. 1984). Major factors that influence HCN release include the chemical nature of the material, temperature, oxygen availability, and burning time (Ballantyne 1987b). Substantial quantities of free HCN and organic cyanides are known to be produced in fire settings involving horsehair, tobacco, wool, silk, and many synthetic polymers, such as polyurethane and polyacrylonitriles (Egekeze and Oehme 1980; Purser et al. 1984; Becker 1985; Ballantyne 1987b). Polyacrylonitrile, for example, is used in fabrics, upholstery covers, paddings, and clothing; about 50% of the mass of the polymer is theoretically available as HCN under thermal decomposition (Purser et al. 1984; Homan 1987).

15.7 CONCENTRATIONS IN FIELD COLLECTIONS

The reactivity of HCN, and its ability to condense with itself and other compounds, was probably responsible for the prebiotic formation of the majority of biochemical compounds required for life (Marrs and Ballantyne 1987). Cyanide is now known to be present in a number of foodstuff and forage plants, as a metabolite of certain drugs, in various industrial pollutants, and may be formed by the combustion of cyanide-releasing substances, such as plastics in airplane fires, and tobacco in smoking (Robinson et al. 1985). Hydrogen cyanide production may occur in hepatopancreas of mussels, *Mytilus edulis* (Vennesland et al. 1981a), in rat liver (Solomonson 1981), and in green and blue-green algae during nitrate metabolism (Leduc et al. 1982). Except for certain naturally occurring organic cyanide compounds in plants, it is uncommon to find cyanide in foods consumed in the United States (USEPA 1980).

The cyanide anion is found in a variety of naturally occurring plant compounds as cyanogenic glycosides, glycosides, lathyrogenic compounds, indoleacetonitrile, and cyanopyridine alkaloids. Plants that contain cyanogenic glycosides are potentially poisonous because bruising or incomplete cooking can result in glycoside hydrolysis and release of HCN (Towill et al. 1978). Cyanide concentrations in cyanogenic plants are usually highest in leaves of young plants. Levels drop rapidly after pollination (Biehl 1984). There are about 20 major cyanogenic glycosides, of which usually only one or two occur in any plant. They are synthesized from amino acids and sugars and are found in many economically important plants, such as sorghum, flax, lima bean, cassava, and many of the stone fruits (Table 15.2) (Towill et al. 1978; Shaw 1986). Cassava contains linamurin and lotaustralin, whereas the main cyanogenic glycoside in cereals is dhurrin; consumption of foods containing toxic cyanogens (primarily cassava) has been associated with death or morbidity — on an acute basis — or goiter and tropical ataxic neuropathy on a chronic consumption basis (Okolie and Ugochukwu 1989). Cassava is a perennial shrub, native to the neotropics, grown for its tuberous starchy roots, and a traditional dietary staple of many indigenous populations in Amazonia, especially the Tukanoan Indians in northwestern Amazonia (Dufour 1988). Cassava is one of the few food plants in which the cyanide content may create toxic problems. All varieties of cassava contain cyanogenic glycosides capable of liberating HCN, but amounts vary greatly depending on variety and environmental conditions. Bitter cultivars of cassava provide over 70% of the Tukanoan's food energy, appearing in the diet as bread, meal, a starch drink, and boiled cassava juice. The greatly elevated total cyanide content in bitter varieties (Table 15.2) may contain 5.1 to 13.4% of the total as the toxic free cyanide (Dufour 1988).

The production of HCN by animals is almost exclusively restricted to various arthropods: 7 species of about 3000 species of centipedes; 46 of 2500 species of polydesmid millipedes; and 10 of 750,000 species of insects, including 3 species of beetles, 4 moths, and 3 butterflies (Duffey 1981). Millipedes — which are eaten frequently by toads and starlings — secrete cyanide for

defensive purposes in repelling predators. In zygaenid moths, cyanide seems to be localized in eggs ([Table 15.2](#)) (Duffey 1981).

Cyanide concentrations in fish from streams that were deliberately poisoned with cyanide ranged between 10 and 100 µg total cyanide/kg whole-body FW (Wiley 1984). Total cyanide concentrations in gill tissues of salmonids under widely varying conditions of temperature, nominal water concentrations, and duration of exposure ranged from about 30 µg/kg FW to >7000 µg/kg (Holden and Marsden 1964). Unpoisoned fish usually contained <1 µg/kg FW in gills, although values up to 50 µg/kg occurred occasionally. Lowest cyanide concentrations in gill occurred at elevated (summer) water temperatures. At lower temperatures, survival was greater and residues were higher (Holden and Marsden 1964). Fish retrieved from cyanide-poisoned environments, dead or alive, can probably be consumed by man because muscle cyanide residues were considered to be low (i.e., <1000 mg/kg FW) (Leduc 1984).

Cyanide pollution is likely to occur in many places, ranging from industrialized urban areas to gold mines in the western United States and Northwest Territories of Canada ([Table 15.2](#)). Cyanides are ubiquitous in industrial effluents, and their increasing generation from power plants and from the combustion of solid wastes is expected to result in elevated cyanide levels in air and water (Leduc 1984). However, data are scarce on background concentrations of cyanides in various nonbiological materials. In soils, for example, high concentrations are unusual and are nearly always the result of improper waste disposal (Towill et al. 1978). Cyanides in soils are not absorbed or retained. Under aerobic conditions, microbial metabolism rapidly degrades cyanides to carbon dioxide and ammonia; under anaerobic conditions, cyanides are converted by bacteria to gaseous nitrogen compounds that escape to the atmosphere (Towill et al. 1978). Heat treatment wastes from metal processing operations may contain up to 200 g CN/kg, mostly as NaCN, and are frequently hauled to landfills for disposal (Lagas et al. 1982). The presence of cyanide in landfill waste is potentially hazardous because of the possibility that cyanide may leach to soil and groundwater, release HCN, and disturb natural microbiological degradation of organic materials. Measurements at landfills in England and the Netherlands showed total cyanide levels up to 560 g/kg in soil and 12 µg/L in groundwater (Lagas et al. 1982). However, 7-month-long experimental studies of cyanide in heat treatment wastes in landfills showed that between 72 and 82% of the cyanide was converted, mostly to ammonium and organic nitrogen compounds; between 4 and 22% of the cyanide leached as free or complex cyanide; and up to 11% remained in the landfill (Lagas et al. 1982).

Hydrogen cyanide (HCN) is a common industrial pollutant and frequently occurs in water at concentrations between 0.1 and several mg/L of free HCN (Leduc 1978; Leduc et al. 1982). Total cyanides is the most-often cited measurement in aqueous solutions, owing to limitations in analytical methodologies (Leduc et al. 1982). Cyanides have been identified in freshwaters of rural and wilderness areas in Canada and Germany. Concentrations ranging between 30 and 60 µg total cyanides/L seem related to runoff, with cyanide peaks more frequent in fall and winter during periods of minimal runoff (Leduc et al. 1982). In larger rivers, cyanide was low in winter owing to dilution by high runoff, but peaked in summer because of cyanide production by plants (Leduc 1984). Cyanides do not seem to persist in aquatic environments. In small, cold oligotrophic lakes treated with 1 mg NaCN/L, acute toxicity was negligible within 40 days. In warm shallow ponds, toxicity disappeared within 4 days after application of 1 mg NaCN/L. In rivers and streams, toxicity rapidly disappeared on dilution (Leduc 1984). Cyanide was not detectable in water and sediments of Yellowknife Bay, Canada, between 1974 and 1976, although the bay receives liquid effluents containing cyanides from an operating gold mine. Nondetection was attributed to rapid oxidation (Moore 1981). Several factors contribute to the rapid disappearance of cyanide from water. Bacteria and protozoans may degrade cyanide by converting it to carbon dioxide and ammonia. Chlorination of water supplies can result in conversion to cyanate (USEPA 1980). An alkaline pH favors oxidation by chlorine, and an acidic pH favors volatilization of HCN into the atmosphere (USEPA 1980).

Table 15.2 Concentrations of Cyanide in Field Collections of Selected Living Resources and Nonbiological Materials (Values are in mg total cyanide/kg fresh weight, or mg/L.)

Environmental Compartment	Concentration ^a	Reference ^b
BIOLOGICAL		
Cyanogenic Plants		
Bamboo, (<i>Bambusa</i> , <i>Arundinaria</i> , <i>Dendrocalamus</i>)		
Tip	Max. 8000	1
Stem	Max. 3000	1
Star grass, <i>Cynodon plectostachyum</i> , whole	180	1
Apple family, <i>Malus</i> spp., <i>Pyrus</i> spp.	Max. 200	2
Cassava, <i>Manihot esculenta</i>		
Bitter varieties		
Leaves	347–1000	3, 4
Roots	327–550	1, 4
Dried roots	95–2450	1, 3, 4
Stem	1130	1
Mash	162	5
Bark		
Total cyanide	1351	6
Free cyanide	102	6
Peel		
Total cyanide	1390	6
Free cyanide	255	6
Pulp		
Total cyanide	810	6
Free cyanide	53	6
Sweet varieties		
Leaves	377–500	3, 4
Roots	138	4
Dried roots	46–<100	3, 4
Mash	81	5
Lima bean, <i>Phaseolus</i> spp.		
United States	100–170	1
Burma	2100	1
Puerto Rico	3000	1
Java	3120	1
Almond, <i>Prunus amygdalus</i> , nut		
Bitter	(280–2500)	1
Spicy	(86–98)	1
Sweet	(22–54)	1
Seeds, 4 species, Nigeria, whole, frequently consumed by humans		
<i>Phaseolus</i> sp.	(381–1093)	7
<i>Vigna</i> sp.	(285–1223)	7
<i>Cajanus</i> sp.	(208–953)	7
<i>Canavalia</i> sp.	(285–953)	7
Sorghum, <i>Sorghum</i> spp., young plant, whole		
	Max. 2500	1
Cyanogenic Arthropods		
Millipede, <i>Apheloria corrugata</i> , whole	428	8
Millipede, <i>Apheloria kleinpeteri</i> , whole	18	8
Zygaenid moth, <i>Zygaena filipendulae</i> , whole	668	8
Mammals		
Human, <i>Homo sapiens</i>		
Blood		
Normal	<0.2	9
Afflicted with Leber's optic atrophy	1.4	9

Table 15.2 (continued) Concentrations of Cyanide in Field Collections of Selected Living Resources and Nonbiological Materials (Values are in mg total cyanide/kg fresh weight, or mg/L.)

Environmental Compartment	Concentration ^a	Reference ^b
Plasma		
Nonsmokers	0.05; Max. 0.11	10
Smokers	0.075; Max. 0.3	10
NONBIOLOGICAL		
Air		
Automobile exhaust		
Adverse conditions	Max. 10.0	1
Equipped with catalytic convertor	1.1	1
Sewage Sludge		
From publicly owned treatment works, United States	749 ^c	18
Water, uncontaminated		
Rural watersheds	0.003	11, 12
Industrial areas	0.02	11, 12
Small watersheds, covered with grasslands and forest, uninhabited by humans	0.0007–0.002; Max. 0.005	12
Western and central Canada, 11 rivers, 1974–77	Max. 0.006	12
United States water supplies, 2595 samples nationwide	0.0009; Max. 0.008	1, 13
United Kingdom water supplies	<0.05; Max. 0.1	1
Wastewaters/Runoff		
Electroplaters		
Total cyanide	0.2; Max. 3.0	14, 15
Dissociable cyanide	0.07	15
Complex cyanide	0.2	15
Thiocyanate	0.02	15
Plating wastewater		
Before treatment with alkaline chlorination	0.18	16
After treatment	0.005	16
Road salt dock		
Total cyanide	25.6	15
Dissociable cyanide	2.9	15
Complex cyanide	23.1	15
Thiocyanate	0.0	15
Steel industry		
Plating baths	72 (9–115)	1, 14
Coke oven liquor	6 (0–8)	1
Oil refineries		
Total cyanide	0.01; Max. 4.0	14, 15
Dissociable cyanide	0.0	15
Complex cyanide	0.01	15
Thiocyanate	2.2	15
Coking operations		
Total cyanide	2.1	15
Dissociable cyanide	0.3	15
Complex cyanide	0.8	15
Thiocyanate	23.6	15
Hospital wastewaters		
Before alkaline chlorination	ND	17
After treatment	0.06	17
Gold mills, Canada	0.3–26.5	14
Gold mine cyanide extraction leach ponds, California, Nevada, and Arizona	Usually 200–300, frequently 700, occasionally 9000	19

Table 15.2 (continued) Concentrations of Cyanide in Field Collections of Selected Living Resources and Nonbiological Materials (Values are in mg total cyanide/kg fresh weight, or mg/L.)

Environmental Compartment	Concentration ^a	Reference ^b
<i>Wastewater Treatment Plants, Chicago</i>		
Treated effluent		
Total cyanide	0.005–0.03	15
Dissociable cyanide	0.003–0.007	15
Complex cyanide	0.002–0.02	15
Thiocyanate	0.006–0.03	15
Untreated Wastewater		
Total cyanide	0.02–0.06	15
Dissociable cyanide	0.004–0.05	15
Complex cyanide	0.02–0.08	15
Thiocyanate	0.03–0.27	15
Sludge		
Total cyanide	0.49–3.79	15
Dissociable cyanide	0.06–0.44	15
Complex cyanide	0.43–5.4	15
Thiocyanate	0.2–0.9	15

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).

^b 1, Towill et al. 1978; 2, Shaw 1986; 3, Gomez et al. 1983; 4, Casadi et al. 1984; 5, Ukhun and Dibie 1989; 6, Dufour 1988; 7, Okolie and Ugochukwu 1989; 8, Duffey 1981; 9, Berninger et al. 1989; 10, Egekeze and Oehme 1980; 11, Leduc 1981; 12, Leduc 1984; 13, USEPA 1980; 14, Leduc et al. 1982; 15, Kelada 1989; 16, Nonomura and Hobo 1989; 17, Vennesland et al. 1981a; 18, Beyer 1990; 19, Clark and Hothem 1991.

^c Concentration is in mg/kg dry weight.

15.8 PERSISTENCE IN WATER, SOIL, AND AIR

In water, cyanides occur as free hydrocyanic acid, simple cyanides, easily degradable complex cyanides such as $Zn(CN)_2$, and sparingly decomposable complex cyanides of iron and cobalt; complex nickel and copper cyanides are intermediate between the easily decomposable and sparingly degradable compounds (Towill et al. 1978). Cyanide has relatively low persistence in surface waters under normal conditions but may persist for extended periods in groundwater (Way 1981). Volatilization is the dominant mechanism for removal of free cyanide from concentrated solutions and is most effective under conditions of high temperatures, high dissolved oxygen levels, and at increased concentrations of atmospheric carbon dioxide (Leduc et al. 1982; Simovic and Snodgrass 1985). Loss of simple cyanides from the water column is primarily through sedimentation, microbial degradation, and volatilization (Leduc et al. 1982; Marrs and Ballantyne 1987). Water-soluble strong complexes, such as ferricyanides and ferrocyanides, do not release free cyanide unless exposed to ultraviolet light. Thus, sunlight may lead to cyanide formation in wastes containing iron–cyanide complexes (Towill et al. 1978; Leduc et al. 1982; Simovic and Snodgrass 1985; Marrs and Ballantyne 1987).

Alkaline chlorination of wastewaters is one of the most widely used methods of treating cyanide wastes. In this process, cyanogen chloride, $CNCl$, is formed, which at alkaline pH is hydrolyzed to the cyanate ion, CNO^- . If free chlorine is present, CNO^- can be further oxidized (Way 1981; Leduc et al. 1982; Simovic and Snodgrass 1985; Marrs and Ballantyne 1987). The use of sulfur dioxide in a high dissolved oxygen environment with a copper catalyst reportedly reduces total cyanide in high cyanide rinsewaters from metal plating shops to less than 1 mg/L. This process may have application in cyanide detoxification of tailings ponds (Robbins 1996). Other methods used in cyanide waste management include lagooning for natural degradation, evaporation, exposure

to ultraviolet radiation, aldehyde treatment, ozonization, acidification–volatilization–reneutralization, ion exchange, activated carbon absorption, electrolytic decomposition, catalytic oxidation, and biological treatment with cyanide-metabolizing bacteria (Towill et al. 1978; USEPA 1980; Way 1981; Marrs and Ballantyne 1987; Smith and Mudder 1991). Additional cyanide detoxification treatments include the use of FeSO_4 , FeSO_4 plus CO_2 , H_2O_2 , $\text{Ca}(\text{OCl})_2$ (Henny et al. 1994), dilution with water, FeSO_4 plus H_2O_2 , and $(\text{NH}_4)\text{HSO}_3$ (Eisler et al. 1999). In Canadian gold-mining operations, the primary treatment for cyanide removal is to retain gold mill wastewaters in impoundments for several days to months. Removal occurs through volatilization, photodegradation, chemical oxidation, and, to a lesser extent, microbial oxidation. Microbial oxidation of cyanide is not significant in mine tailing ponds, which typically have $\text{pH} > 10$, a low number of microorganisms, low nutrient levels, large quiescent zones, and cyanide concentrations $>10 \text{ mg/L}$ (Simovic and Snodgrass 1985).

Cyanide seldom remains biologically available in soils because it is either complexed by trace metals, metabolized by various microorganisms, or lost through volatilization (Towill et al. 1978; Marrs and Ballantyne 1987). Cyanide ions are not strongly adsorbed or retained on soils, and leaching into the surrounding groundwater will probably occur. Under aerobic conditions, cyanide salts in the soil are microbially degraded to nitrites or form complexes with trace metals. Under anaerobic conditions, cyanides denitrify to gaseous nitrogen compounds that enter the atmosphere.

Volatile cyanides occur only occasionally in the atmosphere, due largely to emissions from plating plants, fumigation, and other special operations (Towill et al. 1978). Under normal conditions, cyanide has relatively low persistence in air, usually between 30 days and 1 year (Way 1981), although some atmospheric HCN may persist for up to 11 years (Marrs and Ballantyne 1987). Data are lacking on the distribution and transformation of cyanide in the atmosphere (Towill et al. 1978) and should be acquired.

15.9 LETHAL AND SUBLETHAL EFFECTS

15.9.1 Terrestrial Flora and Invertebrates

Bacteria exposed to cyanide may exhibit decreased growth, altered cell morphology, decreased motility, mutagenicity, and altered respiration (Towill et al. 1978). Mixed microbial populations capable of metabolizing cyanide and not previously exposed to cyanide were adversely affected at 0.3 mg HCN/kg; however, these populations can become acclimatized to cyanide and can then degrade wastes with higher cyanide concentrations (Towill et al. 1978). Acclimatized populations in activated sewage sludge can often completely convert nitriles to ammonia, sometimes at concentrations as high as 60 mg total cyanides/kg (Towill et al. 1978). Cyanide can be degraded by various pathways to yield a variety of products, including carbon dioxide, ammonia, beta-cyanoalanine, and formamide (Knowles 1988). Several species of fungi can accumulate and metabolize cyanide, but the products of cyanide metabolism vary. For example, carbon dioxide and ammonia are formed as end products by *Fusarium solani*, whereas alpha-aminobutyronitile is a major cyanide metabolite of *Rhizoctonia solani* (Towill et al. 1978). Significant amounts of cyanide are formed as secondary metabolites by many species of fungi and some bacteria by decarboxylation of glycine (Knowles 1988). Rhizobacteria may suppress plant growth in soil through cyanide production. In one case, volatile metabolites — including cyanide — from fluorescent pseudomonad soil bacteria prevented root growth in seedlings of lettuce, *Lactuca sativa* (Alstrom and Burns 1989). Not all cyanogenic isolates inhibited plant growth. Some strains promoted growth in lettuce and beans by 41 to 64% in 4 weeks vs. 49 to 53% growth reduction by inhibitory strains (Alstrom and Burns 1989).

In higher plants, elevated cyanide concentrations inhibited respiration (through iron complexation in cytochrome oxidase) and ATP production and other processes dependent on ATP, such as

ion uptake and phloem translocation, eventually leading to death (Towill et al. 1978). Cyanide produces chromosomal aberrations in some plants, but the mode of action is unknown (Towill et al. 1978). At lower concentrations, effects include inhibition of germination and growth, but cyanide sometimes enhances seed germination by stimulating the pentose phosphate pathway and inhibiting catalase (Towill et al. 1978; Solomonson 1981). The detoxification mechanism of cyanide is mediated by rhodanese. This enzyme is widely distributed in plants (Solomonson 1981; Leduc 1984). The rate of production and release of cyanide by plants to the environment through death and decomposition is unknown (Towill et al. 1978).

Free cyanide is not found in intact plant cells. Many species of plants, such as cassava, sorghum, flax, cherries, almonds, and beans, contain cyanogenic glycosides that release HCN when hydrolyzed (Towill et al. 1978). Cyanide poisoning of livestock by forage sorghums, such as Sudan grass and various hybrid cultivars, is well known (Cade and Rubira 1982) and has led to the development of several variations of sorghums that have a reduced capability of producing cyanide poisoning (Egekeze and Oehme 1980). Cyanogenesis has an important role in plant defense against predatory herbivores. This herbivore–plant interaction is not simple; the degree of selectivity by herbivores varies among individuals and by differences in hunger and previous diet (Jones 1988).

Cyanide metabolism in higher plants involves amino acids, *N*-hydroxyamino acids, aldoximes, nitriles, and cyanohydrins (Halkier et al. 1988). Cyanide is a coproduct of ethylene synthesis in higher plants. The increase in ethylene production that occurs during the senescence of certain flowers and the ripening of fruits is accompanied by a rise in beta-cyanoalanine activity. The activity of this enzyme correlates closely with that of ACC (1-aminocyclopropane-1-carboxylic acid) oxidase, the last enzyme in the ethylene pathway. Manning (1988) suggested that ACC oxidase reacts with various amino acids to liberate cyanide. Cyanide added to isolated castorbean (*Ricinus communis*) mitochondria significantly enhanced the rate and amount of protein synthesis. Cyanide stimulated mitochondrial protein synthesis in a dose-dependent manner, with an optimal stimulation of over twofold at 26 µg/L; but at this concentration, mitochondrial respiration was inhibited by 90% (Kaderbhai et al. 1989). Cyanide is a weak competitive inhibitor of green bean (*Phaseolus vulgaris*) lipoxygenase, an enzyme that catalyzes the formation of hydroperoxides from polyunsaturated fatty acids (Adams 1989). Because degradation of hydroperoxides causes unacceptable changes in bean flavor and color, compounds that inhibit lipoxygenase may enjoy wide application in the frozen vegetable industry (Adams 1989). Corn seedlings from cold-resistant cultivars were more resistant to 65 mg KCN/L at low temperatures (13°C) than were seedlings from cold-susceptible cultivars (25°C), as judged by respiratory activity of mitochondria (Van De Venter 1985). Results suggest that cyanide-resistant respiration may play a role in cold resistance in maize seedlings, although more evidence is needed to demonstrate that cold-resistant plants actually use their greater potential for alternative respiration at low temperatures (Van De Venter 1985).

The cyanogenic system comprising cyanogenic glycosides, cyanohydrins, beta-glucosidases, and nitrile lyases is widespread in plants but also occurs in several species of arthropods, including the tiger beetle (*Megacephala virginica*), leaf beetle (*Paropsis atomaria*), zygaenid moths, and certain butterflies (Nahrstedt 1988). In *Zygaena trifolii*, cyanide compounds seem to function as protection against predators (Nahrstedt 1988). Defensive secretions of cyanide have also been reported in polydesmid millipedes, and these organisms seem to be more tolerant than other species when placed in killing jars containing HCN (Towill et al. 1978). In a millipede (*Apheloria* sp.), cyanide is generated in a two-compartment organ by hydrolysis of mandelonitrile; cyanide generation occurs outside the gland when the components of the two compartments are mixed during ejection (Towill et al. 1978).

Highly toxic substances, such as cyanides, are sometimes feeding cues and stimulants for specialized insects. For example, instar larvae of the southern armyworm (*Spodoptera eridania*) strongly prefer cyanogenic foods, such as foliage of the lima bean, a plant with comparatively elevated cyanide content — up to 31 mg/kg in some varieties — in the form of linamurin (Brattsten et al. 1983). Feeding was stimulated in southern armyworms at dietary levels up to 508 mg KCN/kg

(208 mg HCN/kg) for first to fourth instar larval stages, and between 1000 and 10,000 mg KCN/kg diet for fifth and sixth instar larvae (Brattsten et al. 1983). Sixth instar larvae preexposed to diets containing 5000 mg KCN/kg showed no adverse effects at dietary levels of 10,000 mg KCN/kg. However, previously unexposed larvae showed reversible signs of poisoning at 10,000 mg/kg diet, including complete inhibition of oviposition and 83% reduction in adult emergence (Brattsten et al. 1983). Experimental studies with southern armyworm larvae and thiocyanate — one of the *in vivo* cyanide metabolites — showed that 5000 mg thiocyanate/kg diet reduced pupation by 77%, completely inhibited oviposition, and reduced adult emergence by 80% (Brattsten et al. 1983), strongly suggesting that thiocyanate poisoning is the primary effect of high dietary cyanide levels in southern armyworms.

Resistant species, such as southern armyworms, require injected doses up to 800 mg KCN/kg BW (332 mg HCN/kg BW) or diets of 3600 mg KCN/kg for 50% mortality (Brattsten et al. 1983), but data are scarce for other terrestrial invertebrates. Exposure to 8 mg HCN/L air inhibits respiration in the granary weevil (*Sitophilus granarius*) within 15 min and kills 50% in 4 h; some weevils recover after cessation of 4-h exposure (Towill et al. 1978).

15.9.2 Aquatic Organisms

Numerous accidental spills of sodium cyanide or potassium cyanide into rivers and streams have resulted in massive kills of fishes, amphibians, aquatic insects, and aquatic vegetation. Sources of poisonings were storage reservoirs of concentrated solutions, overturned rail tank cars, or discharge of substances generating free HCN in the water from hydrolysis or decomposition (Leduc 1984). Data on the recovery of poisoned ecosystems are scarce. In one case, a large amount of cyanide-containing slag entered a stream from the reservoir of a Japanese gold mine as a result of an earthquake (Yasuno et al. 1981). The slag covered the stream bed for about 10 km from the point of rupture, killing all stream biota; cyanide was detected in the water column for only 3 days after the spill. Within 1 month, flora was established on the silt covering the above-water stones, but there was little underwater growth. After 6 to 7 months, populations of fish, algae, and invertebrates had recovered, although species composition of algae was altered (Yasuno et al. 1981). Short-term exposure of 12 days to 10 µg HCN/L — a level frequently encountered in freshwater aquatic ecosystems — has produced cyanide-induced hormonal and physiological balance in sexually mature rainbow trout. Female trout had reduced plasma estradiol levels and reduced oocyte growth and yolk deposition within the ovary (Ruby et al. 1993a). Males had decreased numbers of spermatocytes and selective loss of Type I basophils in the pituitary gland (Ruby et al. 1993b).

Fish were the most sensitive aquatic organisms tested (Eisler 1991). Significant adverse non-lethal effects, including reduced swimming performance and inhibited reproduction, were observed in the range of 5.0 to 7.2 µg free cyanide/L; deaths were recorded for most species between 20 and 76 µg free cyanide/L (Table 15.3). Among invertebrates, adverse nonlethal effects were documented between 18 and 43 µg/L, and lethal effects between 30 and 100 µg/L — although some deaths were recorded in the range 3 to 7 µg/L for the amphipod *Gammarus pulex* (Table 15.3). Algae and macrophytes were comparatively tolerant; adverse effects were reported at >160 µg free cyanide/L (Table 15.3). The high tolerance of mudskippers (*Boleophthalmus boddaerti*), and perhaps other species of fishes, to HCN (LC50 of 290 µg/L in 96 h) is a result of a surplus of cytochrome oxidase and inducible cyanide-detoxifying mechanisms and not to a reduction in metabolic rate or an enhanced anaerobic metabolism (Chew and Ip 1992).

Adverse effects of cyanide on aquatic plants are unlikely at concentrations that cause acute effects to most species of freshwater and marine fishes and invertebrates (USEPA 1980; Eisler 1991). Water hyacinth (*Eichhornia crassipes*) can survive for at least 72 h in nutrient solution containing up to 300 mg CN/L and can accumulate up to 6.7 g/kg DW plant material. On this basis, 1 ha of water hyacinths has the potential to absorb 56.8 kg of cyanide in 72 h, and this property may be useful in reducing the level of cyanide in untreated wastewater from various

electroplating factories, where concentrations generally exceed 200 mg CN/L (Low and Lee 1981). Large-scale use of water hyacinths for this purpose has not yet been implemented, possibly due to disagreement over appropriate disposal mechanisms. Cyanide may also affect plant community structure. Some algae, for example, metabolized cyanide at water concentrations <1 mg CN/L; but at concentrations of 1 to 10 mg/L, algal activity was inhibited, leaving a biota dominated by *Actinomycetes* — a filamentous bacterium (Knocke 1981).

Cyanide adversely affects fish reproduction by reducing the number of eggs spawned, and the viability of the eggs by delaying the process of secondary yolk deposition in the ovary (Lesniak and Ruby 1982; Ruby et al. 1986). Vitellogenin, a glycolipophosphoprotein present in plasma of fish during the process of yolk formation, is synthesized in liver under stimulation of estrogen and subsequently sequestered in the ovary; it is essential for normal egg development. Exposure of naturally reproducing female rainbow trout to as little as 10 µg HCN/L for 12 days during the onset of the reproductive cycle caused a reduction in plasma vitellogenin levels and a reduction in ovary weight. The loss of vitellogenin in the plasma would remove a major source of yolk (Ruby et al. 1986). Reproductive impairment in adult bluegills (*Lepomis macrochirus*) has been reported following exposure to 5.2 µg CN/L for 289 days (USEPA 1980). Fertilized fish eggs are usually resistant to cyanide prior to blastula formation, but delayed effects occur at 60 to 100 µg HCN/L, including birth defects and reduced survival of embryos and newly hatched larvae (Leduc et al. 1982). Concentrations as low as 10 µg HCN/L caused developmental abnormalities in embryos of Atlantic salmon after extended exposure (Leduc 1978). These abnormalities, which were absent in controls, included yolk sac dropsey and malformations of eyes, mouth, and vertebral column (Leduc 1984).

Other adverse effects of cyanide on fish include delayed mortality, pathology, impaired swimming ability and relative performance, susceptibility to predation, disrupted respiration, osmoregulatory disturbances, and altered growth patterns. Free cyanide concentrations between 50 and 200 µg/L were fatal to the more-sensitive fish species over time, and concentrations >200 µg/L were rapidly lethal to most species of fish (USEPA 1980). Cyanide-induced pathology in fish includes subcutaneous hemorrhaging, liver necrosis, and hepatic damage. Exposure of fish for 9 days to 10 µg HCN/L was sufficient to induce extensive necrosis in the liver, although gill tissue showed no damage. Intensification of liver histopathology was evident at dosages of 20 and 30 µg HCN/L and exposure periods up to 18 days (Leduc 1984). Cyanide has a strong, immediate, and long-lasting inhibitory effect on the swimming ability of fish (Leduc 1984). Free cyanide concentrations as low as 10 µg/L can rapidly and irreversibly impair the swimming ability of salmonids in well-aerated water (Doudoroff 1976). Osmoregulatory disturbances recorded at 10 µg HCN/L may affect migratory patterns, feeding, and predator avoidance (Leduc et al. 1982; Leduc 1984). In general, fish experience a significant reduction in relative performance (based on osmoregulation, growth, swimming, and spermatogenesis) at 10 µg HCN/L. And, although fish can survive indefinitely at 30 µg HCN/L in the laboratory, the different physiological requirements necessary to survive in nature could not be met (Leduc 1978, 1981, 1982) (Figure 15.1). Increased predation by green sunfish (*Lepomis cyanellus*) on fathead minnows (*Pimephales promelas*) was noted at sublethal concentrations of HCN, but it was uncertain if fatheads became easier prey or if green sunfish had greater appetites (Smith et al. 1979).

Sodium cyanide has stimulatory effects on oxygen-sensitive receptors in lungfish, amphibians, reptiles, birds, and mammals (Smatresk 1986). Facultative and aquatic air breathers appear to rely on air breathing when external chemoreceptors are stimulated, whereas obligate air-breathing fish are more responsive to internal stimuli (Smatresk 1986). Gill ventilation frequency of longnose gar (*Lepisosteus osseus*), for example, was little affected by external cyanide application but responded strongly when cyanide was administered internally by injection (Smatresk 1986). Cyanide, like many other chemicals, can stimulate growth of fish during exposure to low sublethal levels. This phenomenon, referred to as hormesis, is little understood and warrants additional research (Leduc 1984).

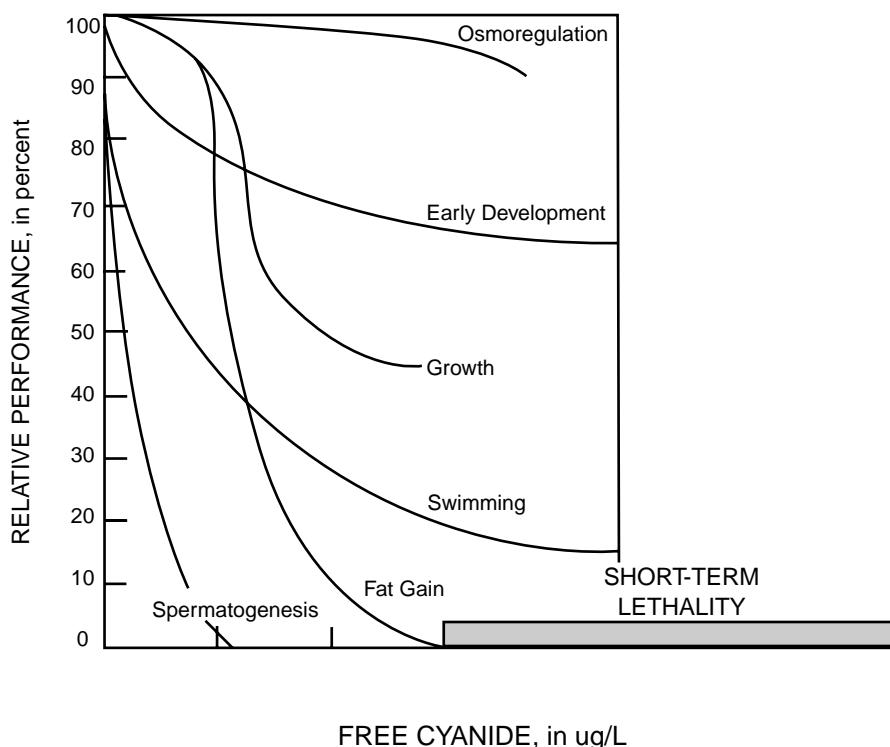


Figure 15.1 Summary of lethal and sublethal effects of free cyanide on freshwater fish. (Modified from Leduc, G., R.C. Pierce, and I.R. McCracken. 1982. The Effects of Cyanides on Aquatic Organisms with Emphasis upon Freshwater Fishes. Natl. Res. Coun. Canada, Publ. NRCC 19246. 139 pp. Avail. from Publications, NRCC/CNRC, Ottawa, Canada K1A OR6.)

The observed toxicity to aquatic life of simple and complex cyanides was attributed almost entirely to molecular (undissociated) hydrocyanic acid (HCN) derived from ionization, dissociation, and photodecomposition of cyanide-containing compounds. The toxicity of the cyanide ion, CN^- , which is a minor component of free cyanide ($\text{HCN} + \text{CN}^-$) in waters that are not exceptionally alkaline is of little importance (Doudoroff 1976; Towill et al. 1978; Smith et al. 1979; USEPA 1980). The acute toxicity of stable silver cyanide and cuprocyanide complex anions is much less than that of molecular HCN, but is nevertheless important. These ions can be the principal toxicants, even in some very dilute solutions. The much lower toxicities of the ferrocyanide and ferricyanide complexes — which are of high stability but subject to extensive and rapid photolysis, yielding free cyanide on direct exposure to sunlight — and the nickelocyanide ion complex are not likely to be of practical importance (Doudoroff 1976). Toxicity to aquatic organisms of organic cyanide compounds, such as lactonitrile, is similar to that of inorganic cyanides because they usually undergo rapid hydrolysis in water to free cyanide (Towill et al. 1978). There is general agreement that total cyanide concentrations in water in most cases will overestimate the actual cyanide toxicity to aquatic organisms, and that the analytically determined HCN concentration in cyanide-polluted waters is considered to be the most reliable index of toxicity (Doudoroff 1976; Smith et al. 1979; USEPA 1980; Abel and Garner 1986).

Cyanide acts rapidly in aquatic environments, does not persist for extended periods, and is highly species selective. Organisms usually recover quickly on removal to clean water. The critical sites for cyanide toxicity in freshwater organisms include the gills, egg capsules, and other sites where gaseous exchange and osmoregulatory processes occur. On passing through a semipermeable membrane, the HCN molecules are usually distributed by way of the circulatory system to various receptor sites where toxic action or detoxification occurs (Leduc 1984). Once in the general

circulation, cyanide rapidly inhibits the electron transport chain of vital organs. Signs of distress include increased ventilation, gulping for air at the surface, erratic swimming movements, muscular incoordination, convulsions, tremors, sinking to the bottom, and death with widely extended gill covers (Leduc 1981, 1989). The acute mode of action of HCN is limited to binding those porphyrins that contain Fe³⁺, such as cytochrome oxidase, hydroperoxidases, and methemoglobin. At lethal levels, cyanide is primarily a respiratory poison and one of the most rapidly effective toxicants known (Leduc et al. 1982). The detoxification mechanism of cyanide is mediated by thiosulfate sulfur transferase, also known as rhodanese. This enzyme is widely distributed in animals, including fish liver, gills, and kidney. Rhodanese plays a key role in sulfur metabolism, and catalyzes the transfer of a sulfane–sulfur group to a thiophilic group (Leduc 1984). Thiosulfate administered in the water with cyanide reduced the toxicity of cyanide to fish, presumably by increasing the detoxification rate of cyanide to thiocyanate (Towill et al. 1978).

Additive or more-than-additive toxicity of free cyanide to aquatic fauna has been reported in combination with ammonia (Smith et al. 1979; Leduc et al. 1982; Alabaster et al. 1983; Leduc 1984) or arsenic (Leduc 1984). However, conflicting reports on the toxicity of mixtures of HCN with zinc or chromium (Towill et al. 1978; Smith et al. 1979; Leduc et al. 1982; Leduc 1984) require clarification. Formation of the nickelocyanide complex markedly reduces the toxicity of both cyanide and nickel at high concentrations in alkaline pH. At lower concentrations and acidic pH, solutions increase in toxicity by more than 1000-fold, owing to dissociation of the metallo-cyanide complex to form hydrogen cyanide (Towill et al. 1978). Mixtures of cyanide and ammonia may interfere with seaward migration of Atlantic salmon smolts under conditions of low dissolved oxygen (Alabaster et al. 1983). The 96-h toxicity of mixtures of sodium cyanide and nickel sulfate to fathead minnows is influenced by water alkalinity and pH. Toxicity decreased with increasing alkalinity and pH from 0.42 mg CN/L at 5 mg CaCO₃/L and pH 6.5, to 1.4 mg CN/L at 70 mg CaCO₃/L and pH 7.5; to 730 mg CN/L at 192 mg CaCO₃/L and pH 8.0 (Doudoroff 1956).

Numerous biological and abiotic factors are known to modify the biocidal properties of free cyanide, including water pH, temperature, and oxygen content; life stage, condition, and species assayed; previous exposure to cyanide compounds; presence of other chemicals; and initial dose tested. There is general agreement that:

- Cyanide is more toxic to freshwater fish under conditions of low dissolved oxygen (Doudoroff 1976; Towill et al. 1978; Smith et al. 1979; USEPA 1980; Leduc 1984)
- pH levels within the range 6.8 to 8.3 had little effect on cyanide toxicity but enhanced toxicity at acidic pH (Smith et al. 1979; USEPA 1980; Leduc et al. 1982; Leduc 1984)
- Juveniles and adults were the most sensitive life stages tested, and embryos and sac fry the most resistant (Smith et al. 1978, 1979; USEPA 1980; Leduc 1984)
- Substantial interspecies variability exists in sensitivity to free cyanide (Smith et al. 1979; USEPA 1980).

Initial dose and water temperature both modify the biocidal properties of HCN to freshwater teleosts. At slowly lethal concentrations (i.e., <10 µg HCN/L), cyanide was more toxic at lower temperatures; at high, rapidly lethal HCN concentrations, cyanide was more toxic at elevated temperatures (Kovacs and Leduc 1982a, 1982b; Leduc et al. 1982; Leduc 1984). By contrast, aquatic invertebrates were most sensitive to HCN at elevated water temperatures, regardless of dose (Smith et al. 1979). Season and exercise modify the lethality of HCN to juvenile rainbow trout (McGeachy and Leduc 1988); higher resistance to cyanide correlated with higher activity induced by exercise and higher temperatures, suggesting a faster detoxification rate or higher oxidative and anaerobic metabolisms. Low levels of cyanide that were harmful when applied constantly may be harmless under seasonal or other variations that allow the organism to recover and detoxify (Leduc 1981). Acclimatization by fish to low sublethal levels of cyanide through continuous exposure might enhance their resistance

to potentially lethal concentrations (Leduc 1981, 1984), but studies with Atlantic salmon and rainbow trout indicate otherwise. Prior acclimatization of Atlantic salmon smolts to cyanide increased their resistance only slightly to lethal concentrations (Alabaster et al. 1983). Juvenile rainbow trout previously exposed to low sublethal concentrations showed a marked reduction in fat synthesis and swimming performance when challenged with higher cyanide doses. Effects were most pronounced at low water temperatures (Kovacs and Leduc 1982a). Experimental evidence is lacking on exposure to lethal concentrations after prior exposure to high sublethal concentrations. Some investigators predict decreased resistance (Leduc 1984), and others increased survival (Towill et al. 1978).

Table 15.3 Cyanide Effects on Selected Species of Aquatic Organisms (All concentrations are shown as g HCN/L [ppb] of medium at start unless indicated otherwise.)

Species, Concentration, and Other Variables	Effect	Reference ^a
ALGAE AND MACROPHYTES		
Alga, <i>Chlorella</i> sp.		
7300	Inhibition of photosynthesis	3
30,000	Enzyme inhibition	2
Water hyacinth, <i>Eichhornia crassipes</i>		
300,000	Nonphytotoxic in 72 h; plants contained 6.7 g total CN/kg dry weight (DW), equivalent to bioconcentration factor (BCF) of 22	5
Freshwater aquatic plants, 9 species, 65,000, 30-min exposure	No effect on respiratory oxygen uptake in 6 species of angiosperms (<i>Myriophyllum</i> sp., <i>Potamogeton</i> spp., <i>Elodea</i> sp., <i>Ruppia</i> sp., <i>Cabomba</i> sp.); some effect on two species of bryophytes (<i>Rhynchostegium ripariooides</i> , <i>Fontinalis antipyretica</i>) and one species of alga (<i>Cladophora glomerata</i>)	4
Alga, <i>Microcystis aeruginosa</i>		
7990	90% kill	2
Alga, <i>Prototricha zopfi</i>		
3000	Inhibition of respiration	2
Alga, <i>Scenedesmus quadricauda</i>		
160, as CN-	Toxic	1
INVERTEBRATES		
Copepod, <i>Acartia clausi</i>		
30	LC50 (96 h)	2
Isopod, <i>Asellus communis</i>		
29–40	MATC ^b	2, 8
1834	LC50 (11 days)	2
Oyster, <i>Crassostrea</i> sp.		
150	Motor activity suppressed after 10 min	2
Daphnid, <i>Daphnia magna</i>		
160	LC50 (96 h)	10
Daphnid, <i>Daphnia pulex</i>		
83	LC50 (96 h)	2
Amphipod, <i>Gammarus pseudolimnaeus</i>		
16–21	MATC ^b	
58	LC50 (96 h) at 20°C	8
184	LC50 (96 h) at 5.2°C	8
Amphipod, <i>Gammarus pulex</i>		
3	LC50 (15 h); 50% dead in 14 days after exposure for only 5 h	6
7.5	LC50 (9 h); exposure for 66 min results in 50% mortality 14 days after exposure	6

Table 15.3 (continued) Cyanide Effects on Selected Species of Aquatic Organisms (All concentrations are shown as g HCN/L [ppb] of medium at start unless indicated otherwise.)

Species, Concentration, and Other Variables	Effect	Reference ^a
15	LC50 (6 h); exposure for 45 min causes 50% mortality 14 days after exposure	6
75	LC50 (3 h); exposure for 18 min results in 50% kill 14 days after exposure	6
Mussel, <i>Mytilus edulis</i>		
18	After exposure for 14 days, growth was reduced and uptake of glycine was inhibited	9
100	LC20 (14 days)	9
Mysid shrimp, <i>Mysidopsis bahia</i>		
11, 20, 43, or 70	Life-cycle (29 days) exposure produced adverse effects on survival at 70 µg/L, and on reproduction at 43 µg/L; no measurable effects at lower doses of 11 and 20 µg/L	7
93–113	LC50 (96 h)	2, 7
Snail, <i>Physa heterostropha</i>		
432	LC50 (96 h)	3, 10
Fiddler crab, <i>Uca tangeri</i>		
Isolated perfused gills subjected to 26,000 CN-/L, as KCN	Inhibited sodium chloride absorption across gill epithelium; effect reversible if exposure <5 min and nonreversible if >30 min; salt absorption effect regulated by (Na ⁺ + K ⁺) ATPase	11
FISHES		
Mudskipper, <i>Boleophthalmus boddarti</i>		
290.0	LC50 (96 h) for adults	33
Mormyrid fishes, <i>Gnathonemus</i> spp.		
5.0–25.0	Significant dose-dependent effect on electric organ activity within 60 min	37
Brown bullhead, <i>Ictalurus nebulosus</i>		
Subjected to steadily increasing concentrations of waterborne cyanide over a 9-h period: 200 at 1 h, 600 at 3 h, 1000 at 5 h, and 1800 at 9 h	Increased heart beat rate at lower concentrations and decreased rate at higher concentrations; hyperventilation in first 3 h, followed by decrease in ventilation rate; oxygen consumption paralleled changes in heart and ventilatory rates; death in 9 h	21
Longnose gar, <i>Lepisosteus osseus</i>		
12 µg CN-/kg BW, as sodium cyanide, equivalent to 10.7 µg CN or 20 µg NaCN, single injection	Hypoxic response and bradycardia; effects appear earlier when administered into the ventral aorta or conus than into the dorsal aorta	27
Bluegill, <i>Lepomis macrochirus</i>		
5.0	Inhibited spawning following chronic exposure	22
5.2	Complete inhibition of spawning after exposure for 57–289 days	2, 8
9.3–19.8	MATC	2
19.4	Reduced survival of fry in 57-day exposure which began with eggs	8
50	Tolerated concentration at higher temperatures, but no reproduction	8
56–227	LC50 (96 h) for juveniles	8, 22
109–218	LC50 (96 h) for fry	8
232–365	LC50 (96 h) for eggs	22
535–690	LC50 (96 h) for eggs at hatching	8
Largemouth bass, <i>Micropterus salmoides</i>		
101	LC50 (96h) for juveniles	8
Cutthroat trout, <i>Oncorhynchus clarkii</i>		
1000 for 20 min	All fish recovered within 12 min and fed and grew normally during the next 6 months	31

Table 15.3 (continued) Cyanide Effects on Selected Species of Aquatic Organisms (All concentrations are shown as g HCN/L [ppb] of medium at start unless indicated otherwise.)

Species, Concentration, and Other Variables	Effect	Reference ^a
Coho salmon, <i>Oncorhynchus kisutch</i>		
7.0	Reduction of 50% in swimming performance during 8-day exposure	13
10	Swimming speed reduced after exposure for 2 h	2
Rainbow trout, <i>Oncorhynchus mykiss</i>		
0.1 or 1.0	No effect on sperm motility or on fertilization rate at lower dose; some effect on sperm motility at higher dose	12
5.0	Reduction of 50% in swimming performance in 20-day exposure	13
10	No effect on growth during 20-day exposure at 6°C	13
10	Increased respiration rate in 4 days, growth reduction and liver damage in 9 days, abnormal oocyte development and reduced spermatogonia production in 18–20 days	2
10	After exposure for 12 days, sexually mature females had significant declines in plasma levels of reproductive and metabolic hormones, and sexually mature males had decreased spermatocytes and selective cell loss in pituitary gland	34, 35
10, 20, or 30 for 7 days, sexually mature females	Exposure to 10 or 20 µg/L caused a reduction in serum calcium to levels insufficient for the production of exogenous yolk; this was not observed in the 30 µg/L group	14
10, 20, or 30 for 18 days, juveniles	Degenerative necrosis of liver hepatocytes at all concentrations in a dose-dependent pattern. Severe initial growth repression at all concentrations followed by a significant increase, but growth remained depressed 40% and 95% in the 20 and 30 µg/L groups, respectively, at 18 days	15
10 or 20, exposure for 20 days during midsummer, sexually maturing females	Both concentrations resulted in abnormal oocytes, delayed development, and significantly reduced the number of eggs for spawning	16
15	No effect on growth during 20-day exposure at 12°C	13
18	No deaths in 96 h at 6°C	13
20	65% reduction in weight gain after 21 days	2
28	LC50 (96 h) at 6°C	10,13,17
30	No effect on growth during 20-day exposure at 18°C	13
32	No deaths in 96 h at 12°C	13
42	LC50 (96 h) at 12°C	13,17
43	LC50 (96 h) for nonexercised juveniles during winter	18
46–75	LC50 (96 h) for juveniles	8,19
52	LC50 (96 h) for exercised juveniles during winter	18
60	No deaths in 96 h at 18°C	13
68	LC50 (96 h) at 18°C	10,13,17
70 for 24 h	Increased susceptibility to mycotic dermal infections by <i>Saprolegnia parasitica</i>	36
96	LC50 (144 h)	20
Subjected to steadily increasing concentrations of waterborne cyanide: 0 at start, 200 at 1 h, 600 at 3 h, 1000 at 5 h, and 1800 at 9 h	Reduction in heart rate, hyperventilation, increased oxygen consumption, death in 9 h	21
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
10	After 64 days, increased growth rate and production when compared to controls	13
20	Growth reduced 27% after exposure for 64 days	2

Table 15.3 (continued) Cyanide Effects on Selected Species of Aquatic Organisms (All concentrations are shown as g HCN/L [ppb] of medium at start unless indicated otherwise.)

Species, Concentration, and Other Variables	Effect	Reference ^a
Yellow perch, <i>Perca flavescens</i>		
76–108	LC50 (96 h) for juveniles	8, 22
288–>389	LC50 (96 h) for eggs and fry	8, 22
Fathead minnow, <i>Pimephales promelas</i>		
12.9–19.6	MATC ^b	8, 22
18–58	Reduction in RNA content in larva in 96 h at 18–36 µg HCN/L, and in DNA and protein at 18–58 µg/L	28
19	Egg reduction of 59% after exposure for 265 days at 25°C	13
35	Reduction in growth rate during chronic exposure	5
44	Hatching reduced 83% after chronic exposure	13
47	Growth reduction in 30 days	28
58	Toxicosis occurred in yolk-sac larvae within 24 h, as judged by significant reductions in content of RNA and protein; however, effects were not measurable in 96 h, suggesting development of partial tolerance	29
>61	Adverse effects on growth and survival during life-time exposure	13
82–113	LC50 (96 h) for fry at 25°C	8
83–137	LC50 (96 h) for juveniles	8, 22
99	LC50 (96 h) for fry at 20°C	8
107	Reduced survival in 96 h	28
121–202	LC50 (96 h) for eggs at 25°C	8
121–352	LC50 (96 h) for eggs; more toxic at low dissolved oxygen	22
122	LC50 (96 h) for fry at 15°C	8
Mixture of NaCN plus CdSO ₄ , equivalent to 170 µg CN/L	LC50 (96 h) for adults	30
Mixture of NaCN plus ZnSO ₄ , equivalent to 180 µg CN/L	LC50 (96 h) for adults	30
230, as NaCN	LC50 (96 h) for adults	30
273	LC50 (96 h) for eggs at 20°C	8
352	LC50 (96 h) for eggs at 15°C	8
Mixture of NaCN plus NiSO ₄ , equivalent to 650 µg CN/L	LC50 (96 h) for adults	8
Black crappie, <i>Pomoxis nigromaculatus</i>		
60	Some deaths in <24 h	3
101	LC50 (96 h) for juveniles	8
Plainfin midshipman, <i>Porichthys notatus</i>		
Isolated photophores exposed to 2600, as KCN	Maximal luminescence induced by KCN; effect inhibited by d-glucose, d-glyceraldehyde 3-phosphate, and 3-phosphoglycerate	32
Atlantic salmon, <i>Salmo salar</i>		
5.0 for 12 days, adult females	Decline in plasma and gonad vitellogenin levels	23
10	Abnormal embryonic development after 58-day exposure	2
10, 80, or 100; newly fertilized eggs continually exposed for 5 months to end of sac-fry stage	Hatching delayed 6–9 days at 80 and 100 µg/L. Hatching success reduced 15–40% at all test concentrations, but no measurable effects on growth or survival after hatching. Abnormalities (mostly defects of eye, mouth, vertebral column) were 6% at 10 µg/L, and 19% at 100 µg/L	24
24	LC50 (24 h) at dissolved oxygen of 3.5 mg/L	25
73	LC50 (24 h) at dissolved oxygen of 10 mg/L	25
5000, 10,000, 25,000, 50,000, or 125,000 for 30 min	Total cyanide residues in gills ranged from 1.0–6.6 mg/kg fresh weight (FW) in a dose-dependent manner	26

Table 15.3 (continued) Cyanide Effects on Selected Species of Aquatic Organisms (All concentrations are shown as g HCN/L [ppb] of medium at start unless indicated otherwise.)

Species, Concentration, and Other Variables	Effect	Reference ^a
50,000 for 10, 15, 20, 25, or 30 min	Residues in gills, in mg total CN/kg FW, ranged from 1.3 (10 and 15 min) to 1.9 (15 and 20 min) to 4.5 (30 min)	26
Brown trout, <i>Salmo trutta</i>		
90	LC50 (96 h)	10
5000, 10,000, 25,000, 50,000, 75,000, or 100,000, as CN ⁻ for 30 min	Residues in gills ranged in a dose-dependent manner from 0.6 mg CN/kg FW in the 5 mg/L group to 3.4 mg/kg FW in the 100 mg/L group	26
50,000 for 10, 15, 20, or 25 min	Residues in tissues, in mg/kg FW, ranged from 0.7–1.8 in gill, 0.6–2.3 in brain, and 1.3–2.5 in liver; concentrations were directly related to length of exposure	26
Brook trout, <i>Salvelinus fontinalis</i>		
5.0	Reduction of 50% in swimming performance in 29-day exposure	13
5.7–11.2	MATC ^b	8, 22
10	75% reduction in swimming endurance after exposure for 26 min	2
10–50	Swimming ability reduced 98% after exposure for 29 days	20
11	Continuous exposure of mature females for 144 days before spawning resulted in 50% reduction in number of eggs produced and 15% reduction in egg viability; however, 90 days after hatch, trout were 18% heavier and 10% longer than controls	13
25	Inhibited oxygen intake after 5 h	2
33	Adverse effects on juvenile growth rate during exposure for 90 days	2, 8
56–112	LC50 (96 h) range for swimup fry and juveniles	8, 22
108–518	LC50 (96 h) for sac-fry	8, 22
>212	LC50 (96 hours) for eggs	8, 22

^a 1, Towill et al. 1978; 2, USEPA 1980; 3, USEPA 1973; 4, Azcon-Bieto et al. 1987; 5, Low and Lee 1981; 6, Abel and Garner 1986; 7, Lussier et al. 1985; 8, Smith et al. 1979; 9, Thompson 1984; 10, Leduc et al. 1982; 11, Drews and Graszynski 1987; 12, Billard and Roubaud 1985; 13, Leduc 1984; 14, Da Costa and Ruby 1984; 15, Dixon and Leduc 1981; 16, Lesniak and Ruby 1982; 17, Kovacs and Leduc 1982b; 18, McGeachy and Leduc 1988; 19, Marking et al. 1984; 20, Ballantyne 1987a; 21, Sawyer and Heath 1988; 22, Smith et al. 1978; 23, Ruby et al. 1987; 24, Leduc 1978; 25, Alabaster et al. 1983; 26, Holden and Marsden 1964; 27, Smatresk et al. 1986; 28, Barron and Adelman 1984; 29, Barron and Adelman 1985; 30, Doudoroff 1956; 31, Wiley 1984; 32, Rees and Baguet 1989; 33, Chew and Ip 1992; 34, Ruby et al. 1993a; 35, Ruby et al. 1993b; 36, Carballo et al. 1995; 37, Lewis et al. 1992.

^b Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

15.9.3 Birds

Free cyanide levels associated with high avian death rates include 0.12 mg/L in air, 2.1 to 4.6 mg/kg body weight (BW) via acute oral exposure, and 1.3 mg/kg BW administered intravenously (Table 15.4). In cyanide-tolerant species, such as the domestic chicken (*Gallus domesticus*), dietary levels of 135 mg total cyanide/kg ration resulted in growth reduction of chicks, but 103 mg total cyanide/kg ration had no measurable effect on these chicks (Eisler 1991; Hill and Henry 1996). First signs of cyanide toxicosis in sensitive birds appeared between 0.5 and 5 min after exposure and included panting, eye blinking, salivation, and lethargy (Wiemeyer et al. 1986). In domestic chickens, signs of cyanide toxicosis began 10 min after exposure. At higher doses, breathing in all species tested became increasingly deep and labored, followed by gasping and shallow intermittent

breathing. Death usually followed in 15 to 30 min, although birds alive at 60 min frequently recovered (Wiemeyer et al. 1986). Elevated cyanide concentrations were found in blood of chickens that died of cyanide poisoning. However, these concentrations overlapped those in survivors. Despite this variability, blood is considered more reliable than liver as an indicator of cyanide residues in exposed birds (Wiemeyer et al. 1986). No gross pathological changes in chickens related to cyanide dosing were observed at necropsy. The rapid recovery of some birds exposed to cyanide may be due to the rapid metabolism of cyanide to thiocyanate and its subsequent excretion. Species sensitivity to cyanide was not related to body size but seemed to be associated with diet (Wiemeyer et al. 1986). Birds that feed predominantly on flesh, such as vultures, kestrels, and owls, were more sensitive to cyanide than were species that feed mainly on plant material — with the possible exception of mallard (*Anas platyrhynchos*) — as judged by acute oral LD₅₀ values (Table 15.4). Mallards given single oral doses of KCN (1.0 mg KCN/kg BW) at cyanide concentrations and amounts similar to those found at gold-mining tailings ponds (40 mg CN⁻/L) had elevated concentrations of creatinine kinase in serum, suggesting tissue damage (Pritsos and Ma 1997). At 0.5 mg KCN/kg BW, mitochondrial function (an indicator of oxygen consumption) and ATP concentrations were significantly depressed in heart, liver, and brain (Ma and Pritsos 1997). Rhodanese and 3-mercaptopyruvate sulfurtransferase — two enzymes associated with cyanide detoxification — were induced in brain but not in heart of KCN-dosed mallards. Although cyanide concentrations as high as 2.0 mg KCN/kg BW (at 80 mg CN⁻/L) were not acutely toxic to mallards, the long-term effects of such exposures were not determined and may have serious consequences for migratory birds exposed sublethally to cyanide at gold-mine tailings ponds.

Many species of migratory birds — including waterfowl, shorebirds, passerines, and raptors — were found dead in the immediate vicinity of gold-mine heap-leach extraction facilities and tailings ponds, presumably as a result of drinking the cyanide-contaminated (>200 mg total cyanide/L) waters (Clark and Hothem 1991; Henny et al. 1994; Hill and Henry 1996). About 7000 dead birds — mostly waterfowl and songbirds — were recovered from cyanide-extraction, gold-mine leach ponds in the western United States between 1980 and 1989. No gross pathological changes related to cyanide were observed in these birds at necropsy (Allen 1990; Clark and Hothem 1991). No gross pathology was evident in cyanide-dosed captive birds (Wiemeyer et al. 1986), and this is similar to the findings of laboratory studies with cyanide and other animal orders that were tested and examined (Eisler 1991). Migratory bird mortality from cyanide toxicosis may be eliminated at these facilities by screening birds from toxic solutions (Hallock 1990) or lowering the cyanide concentrations with hydrogen peroxide to <50 mg total cyanide/L (Allen 1990), although the latter procedure requires verification (Clark and Hothem 1991). Chemical bird repellents used at cyanide ponds with some success against European starlings (*Sturnus vulgaris*) include O-aminoacetophone and 4-ketobenztriazine (Clark and Shah 1993).

Some birds may not die immediately after drinking lethal cyanide solutions. Sodium cyanide rapidly forms free cyanide in the avian digestive tract (pH 1.3 to 6.5), whereas formation of free cyanide from metal cyanide complexes is comparatively slow (Huiatt et al. 1983). A high rate of cyanide absorption is critical to acute toxicity, and absorption may be retarded by the lower dissociation rates of metal-cyanide complexes (Henny et al. 1994). In Arizona, a red-breasted merganser (*Mergus serrator*) was found dead 20 km from the nearest known source of cyanide, and its pectoral muscle tissue tested positive for cyanide (Clark and Hothem 1991). A proposed mechanism to account for this phenomenon involves weak-acid dissociable (WAD) cyanide compounds. Cyanide bound to certain metals, usually copper, is dissociable in weak acids such as stomach acids. Clark and Hothem (1991) suggested that drinking of lethal cyanide solutions by animals may not result in immediate death if the cyanide level is sufficiently low; these animals may die later when additional cyanide is liberated by stomach acid. More research is needed on WAD cyanide compounds.

Cyanide-nutrient interactions are reported for alanine, which appears to exacerbate cyanide toxicity, and for cystine, which seems to alleviate toxicity (Davis et al. 1988). Dietary cyanide — at levels that do not cause growth depression — alleviates selenium toxicity in chickens, but not the reverse (Davis et al. 1988; Elzubier and Davis 1988a). For example, dietary selenium, as selenite, at 10 mg/kg for 24 days, reduced growth, food intake, and food utilization efficiency, and produced increased liver size and elevated selenium residues. The addition of 45 mg CN/kg diet (100 mg sodium nitroprusside/kg) eliminated all effects except elevated selenium residues in liver. The mechanism of alleviation is unknown and may involve a reduction of tissue selenium through selenocyanate formation, or increased elimination of excess selenium by increasing the amount of dimethyl selenide exhaled (Elzubier and Davis 1988a). At dietary levels of 135 mg CN/kg plus 10 mg selenium/kg, chick growth was significantly decreased (Elzubier and Davis 1988a). This interaction can be lost if there is a deficiency of certain micronutrients or an excess of Vitamin K (Davis et al. 1988).

Table 15.4 Cyanide Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effect	Reference ^a
MALLARD, <i>Anas platyrhynchos</i>		
Single oral dose of NaCN		
0.53 mg CN kg body weight (BW), equivalent to 1 mg NaCN/kg BW	No deaths	7
1.1 mg CN/kg BW (2.0 mg NaCN/kg BW)	About 6% dead	7
1.27 mg/CN kg BW (2.4 mg NaCN/kg BW)	About 33% dead	7
1.43 mg CN/kg BW (2.7 mg NaCN/kg BW)	LD50; 95% confidence interval (CI) of 2.2 and 3.2 mg NaCN/kg BW	7, 8
TURKEY VULTURE, <i>Cathartes aura</i>		
Single oral dose of 19.1 mg CN/kg BW, equivalent to 36 mg NaCN/kg BW	Up to 80% of the cyanide in blood was present as free cyanide, and the remainder as bound cyanide	1
Single oral dose of 19.1 mg CN/kg BW, equivalent to 36 mg NaCN/kg BW	Average time to death was about 19 min and ranged between 8 and 41 min. Cyanide residues postmortem, in mg CN/kg fresh weight (FW), were 6.7 in blood (Max. 21) and 0.6 in liver (Max. 2.8)	2
ROCK DOVE, <i>Columba livia</i>		
0.12 mg CN/L air, as HCN	All dead in 10 min	2
1.6 mg CN/kg BW, equivalent to 4.0 mg KCN/kg BW	Minimum lethal dose when administered intravenously or intramuscularly	2
BLACK VULTURE, <i>Coragyps atratus</i>		
Single oral dose, as NaCN		
1.6 mg CN/kg BW	No deaths in 60 min. Mean and maximum blood CN concentrations, in mg/kg FW, were 0.7 and 0.9, respectively	2
2.4 mg CN/kg BW	Some deaths within 30 min.; mean blood CN residues in mg/kg FW, were 0.7 in dead birds vs. 1.2 in those surviving 60 min	2
2.54 mg CN/kg BW	Acute oral LD50; 95% (CI) of 2.3 and 2.8 mg CN/kg BW (4.4–5.3 mg NaCN/kg BW)	2
3.7 and 19.1 mg CN/kg BW	All dead within 16 min; maximum blood CN levels postmortem were 2.1 mg/kg FW in the low-dose group and 4.2 in the high-dose group	2

Table 15.4 (continued) Cyanide Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effect	Reference^a
JAPANESE QUAIL, <i>Coturnix japonica</i>		
Single oral dose, as NaCN 4.5 mg CN/kg BW	Acute oral LD ₅₀ for adult females; 95% CI of 3.1 and 6.5 mg CN/kg BW	2
5.5 mg CN/kg BW	Acute oral LD ₅₀ for adult males; 95% CI of 4.0 and 7.5 mg CN/kg BW	2
AMERICAN KESTREL, <i>Falco sparverius</i>		
2.12 mg CN/kg BW, as NaCN	Acute oral LD ₅₀ , 95% CI of 1.6 and 2.8 mg CN/kg BW	2
DOMESTIC CHICKEN, <i>Gallus domesticus</i>		
Intravenous route 0.01 µg/kg BW	Most of dose recovered in urine as thiocyanate in 6 h; excretion limited by availability of transferable sulfur	3
0.6 mg CN/kg BW, equivalent to 1.5 mg KCN/kg BW	Lethal	2
0.78 mg CN/kg BW, as KCN	Sublethal. Thiocyanate excretion increased 10X after 10 min and returned to normal levels after 3.5 h; the total thiocyanate collected was equivalent to 85% of the administered dose	4
1.3 mg CN/kg BW, as KCN	Lethal	4
Inhalation route 0.12 mg HCN/L air	All survived for at least 60 min	2
Single oral dose, as NaCN 3.2 mg CN/kg BW, equivalent to 6.0 mg NaCN/kg BW	No deaths in 30 min; maximum CN levels, in mg/kg FW, were 1.1 in blood and 0.06 in liver	2
6.4 mg CN/kg BW	Some deaths in 30 min; maximum CN levels, in mg/kg FW, were 1.6 in blood and 0.12 in liver	2
11.1 mg CN/kg BW	Acute oral LD ₅₀ , 95% CI of 6.4 and 19.1 mg CN/kg BW	2
25.4 mg CN/kg BW	Advanced signs of acute poisoning; death probable within 30 min. Maximum CN levels, in mg/kg FW, were 1.5 in blood and 0.6 in liver	2
Dietary route Fed cassava diets containing 4, 37, 70, or 103 mg total cyanide/kg ration to day-old chicks for 8 weeks	At all dietary levels, there was no significant effect on survival, growth, histology, hemoglobin, hematocrit, or lymphocyte number; however, serum thiocyanate levels increased in a dose-dependent manner	5
Fed diets containing 135 mg HCN/kg Chicks, 20-day exposure	Growth and food intake significantly depressed; plasma thiocyanate concentration increased	6
Adults, 14-day exposure	Urinary excretion of thiocyanate increased 5X in laying hens	6
CALIFORNIA condor, <i>Gymnogyps californianus</i>		
Juvenile (8.4 kg), found dead, presumably of cyanide poisoning	No evidence of injuries or disease. Yellow fluorescent particles found in mouth appeared like those placed in NaCN ejector mechanisms used in predator control. However, blood cyanide concentration was similar to that found in nonexposed vultures, including two captive California condors	2
EASTERN SCREECH-OWL, <i>Otus asio</i>		
4.6 mg CN/kg BW, equivalent to 8.6 mg NaCN/kg BW	Acute oral LD ₅₀ , 95% CI of 3.8 and 5.4 mg CN/kg BW	2

Table 15.4 (continued) Cyanide Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effect	Reference^a
CANARY, <i>Serinus canarias</i>		
0.12 mg HCN/L air	All dead in 3 min	2
EUROPEAN STARLING, <i>Sturnus vulgaris</i>		
9.0 mg CN/kg BW, as NaCN	Acute oral LD50, 95% CI of 4.8 and 17 mg CN/kg BW	2
ANDEAN CONDOR, <i>Vultur gryphus</i>		
Single oral dose of 19.1 mg CN/kg BW (36 mg NaCN/kg BW)	Blood sampled immediately after death contained 1.2 mg free CN/L and 0.5 mg bound CN/L	1

^a 1, Krynnitsky et al. 1986; 2, Wiemeyer et al. 1986; 3, Oh et al. 1987; 4, Davis 1981; 5, Gomez et al. 1988; 6, Elzubier and Davis 1988b; 7, personal communication, Dr. E.F. Hill, Patuxent Wildlife Research Center; 8, Henry et al. 1994.

15.9.4 Mammals

Microgold and silver mining are probably the most widespread sources of anthropogenic cyanides in critical wildlife habitat, such as deserts in the western United States (Hill and Henry 1996). Many species of mammals, mostly rodents and bats, were found dead at cyanide-extraction gold-mine tailings and heap leach ponds in California, Nevada, and Arizona, including 10 endangered, threatened, or otherwise protected species of mammals (Clark and Hothem 1991). A similar situation was documented for a vat-leach gold mine in South Carolina with a large tailings pond (Clark 1991).

Much of the toxicological interest in cyanide relating to mammals has focused on its rapid lethal action. However, its most widely distributed toxicologic problems are due to its toxicity from dietary, industrial, and environmental factors (Way 1981, 1984; Gee 1987; Marrs and Ballantyne 1987; Eisler 1991). Chronic exposure to cyanide is correlated with specific human diseases: Nigerian nutritional neuropathy, Leber's optical atrophy, retrobulbar neuritis, pernicious anemia, tobacco amblyopia, cretinism, and ataxic tropical neuropathy (Towill et al. 1978; Way 1981; Sprine et al. 1982; Berninger et al. 1989; Ukhun and Dibie 1989). The effects of chronic cyanide intoxication are confounded by various nutritional factors, such as dietary deficiencies of sulfur-containing amino acids, proteins, and water-soluble vitamins (Way 1981).

Most authorities now agree on five points (Towill et al. 1978; USEPA 1980; Way 1984; Ballantyne and Marrs 1987a; Eisler 1991; Hill and Henry 1996; Eisler et al. 1999) ([Table 15.5](#)):

1. Cyanide has low persistence in the environment and is not accumulated or stored in any mammal studied.
2. Cyanide biomagnification in food webs has not been reported, possibly due to rapid detoxification of sublethal doses by most species, and death at higher doses.
3. Cyanide has an unusually low chronic toxicity, but chronic intoxication exists and, in some cases, can be incapacitating.
4. Despite the high lethality of large single doses or acute respiratory exposures to high vapor concentrations of cyanide, repeated sublethal doses seldom result in cumulative adverse effects.
5. Cyanide, in substantial but sublethal intermittent doses, can be tolerated by many species for long periods, perhaps indefinitely.

The toxicity of cyanogenic plants is a problem for both domestic and wild ungulates. Poisoning of herbivorous ungulates is more prevalent under drought conditions, when these mammals become

less selective in their choice of forage; dry growing conditions also enhance cyanogenic glycoside accumulations in certain plants (Towill et al. 1978). Animals that eat rapidly are at greatest risk, and intakes of 4 mg HCN/kg BW can be lethal if consumed quickly (Egekeze and Oehme 1980). In general, cattle are most vulnerable to cyanogenic plants; sheep, horses, and pigs — in that order — are more resistant than cattle (Cade and Rubira 1982). Deer (*Odocoileus* sp.) and elk (*Cervus* sp.) have been observed to graze on forages that contain a high content of cyanogenic glycosides; however, cyanide poisoning has not been reported in these species (Towill et al. 1978). Ruminant and nonruminant ungulate mammals that consume forage with high cyanogenic glycoside content, such as sorghums, Sudan grasses, and corn, may experience toxic signs due to microbes in the gut that hydrolyze the glycosides, releasing free hydrogen cyanide (Towill et al. 1978). Signs of acute cyanide poisoning in livestock usually occur within 10 min and include initial excitability with muscle tremors, salivation, lacrimation, defecation, urination, and labored breathing, followed by muscular incoordination, gasping, and convulsions; death can occur quickly, depending on the dose administered (Towill et al. 1978; Cade and Rubira 1982). Thyroid dysfunction has been reported in sheep grazing on star grass (*Cydonia plectostachyum*), a plant with high cyanogenic glycoside and low iodine content. Sheep developed enlarged thyroids and gave birth to lambs that were stillborn or died shortly after birth (Towill et al. 1978). Cyanogenic foods can exacerbate selenium deficiency, as judged by the increased incidence of nutritional myopathy in lambs on low-selenium diets (Elzubier and Davis 1988a). A secondary effect from ingesting cyanogenic glycosides from forage is sulfur deficiency as a result of sulfur mobilization to detoxify the cyanide to thiocyanate (Towill et al. 1978).

Cyanide poisonings of livestock by forage sorghums and other cyanogenic plants are well documented (Cade and Rubira 1982). Horses in the southwestern United States grazing on Sudan grass and sorghums developed posterior muscle incoordination, urinary incontinence, and spinal cord histopathology. Offspring of mares that had eaten Sudan grass during early pregnancy developed musculoskeletal deformities (Towill et al. 1978). Salt licks containing sulfur (8.5%) have been used to treat sheep after they failed to gain weight when grazing on sorghum with high HCN content (Towill et al. 1978). Sugar gum (*Eucalyptus cladocalyx*) and manna gum (*Eucalyptus viminalis*) contain high levels of cyanogenic glycosides, and both have been implicated as the source of fatal HCN poisoning in domestic sheep and goats that had eaten leaves from branches felled for drought feeding, or after grazing sucker shoots on lopped stumps (Webber et al. 1984). In one case, 10 goats died and 10 others were in distress within 2 h after eating leaves from a felled sugar gum. Dead goats had bright red blood that failed to clot and subepicardial petechial hemorrhages. Rumens of dead goats contained leaves of *Eucalyptus* spp. and smelled of bitter almonds. The 10 survivors were treated intravenously with 3 mL of a 1-L solution made to contain 20 g sodium nitrite and 50 g sodium thiosulfate; four recovered and six died. Of 50 afflicted goats, 24 died within 24 h and the remainder recovered (Webber et al. 1984). In rare instances, HCN poisoning occurs when animals are exposed to chemicals used for fumigation or as a fertilizer (Webber et al. 1984), but there is general agreement that ingestion of plants containing high levels of cyanogenic glycosides is the most frequent cause of cyanide poisoning in livestock.

Cassava, also known as manioc, tapioca, yucca, or guacamate, is one of the very few — and, by far, the most important — food crops in which the cyanide content creates toxic problems (Cooke and Coursey 1981). Cassava is a major energy source for people and livestock in many parts of the world. It accounts for an average of 40% of the human caloric intake in Africa (Casadi et al. 1984) and ranges to more than 70% in some African diets (Way 1984). In comparison to other tropical crops, it produces the highest yield per hectare (Okeke et al. 1985). Cassava is native to tropical America from southern Mexico to northern Argentina and probably has been under cultivation there for 4000 to 5000 years. It has been introduced to east Africa, Indian Ocean islands, southern India, and the Far East (Cooke and Coursey 1981). The global production of cassava roots was estimated at 50 million tons in 1950, and 100 million tons in 1980; about 44.2 million tons are grown annually in Africa, 32.7 in tropical America, and 32.9 in Asia (Cooke and Coursey 1981).

Linamurin is the principal cyanogenic glycoside in cassava; its toxicity is due to hydrolysis by intestinal microflora releasing free cyanide (Padmaja and Panikkar 1989). Rabbits (*Oryctolagus cuniculus*) fed 1.43 mg linamurin/kg BW daily (10 mg/kg BW weekly) for 24 weeks showed effects similar to those of rabbits fed 0.3 mg KCN/kg BW weekly. Specific effects produced by linamurin and KCN included elevated lactic acid in heart, brain, and liver; reduced glycogen in liver and brain; and marked depletion in brain phospholipids (Padmaja and Panikkar 1989).

The use of cassava in animal feed presents two major problems: the presence of cyanogenic glycosides in the tuber, and the remarkably low protein levels in fresh and dried cassava. Pigs fed low-protein cassava diets for 8 weeks had reduced food consumption and lowered liver weight; addition of protein supplement to the diet reversed these trends (Tewe 1982a). Removal of cyanogenic glycosides from cassava tubers, mash, peels, and root meal is accomplished with several techniques. Usually, the cassava root is dried in the sun for several weeks, and this process removes most of the cyanogenic glycosides. However, under conditions of famine or food shortage, this process cannot be carried out properly (Cliff et al. 1984). Long fermentation periods, especially under conditions of high moisture content, may be effective in substantial detoxification of cassava mash (Ukhun and Dibie 1989). Cassava peels containing as much as 1061 mg HCN/kg FW can be rendered suitable for feeding to livestock (4 to 625 mg/kg) by boiling for 7 min, roasting for 30 min, soaking for 15 h, or drying in the sun for 7.6 days (Okeke et al. 1985). Cassava root meal (up to 40% of cassava meal) is satisfactory as a diet supplement for domestic pigs, provided that cyanide content is <100 mg/kg ration (Gomez et al. 1983).

Neuropathies associated with cassava ingestion (i.e., cyanide intoxication) can develop into a syndrome in humans and domestic animals, characterized by nerve deafness, optic atrophy, and an involvement of the sensory spinal nerve that produces ataxia. Other symptoms include stomatitis, glossitis, and scrotal dermatitis (Way 1981). Potentially more serious are long-term effects such as ataxic neuropathy, goiter, and cretinism, which have been attributed to high cassava content in diets. Thiocyanate — one of the detoxification products — inhibits iodine absorption and promotes goiter, a common ailment in tropical countries (Cooke and Coursey 1981). At high dietary cyanide intakes, there is an association with diabetes and cancer (Cliff et al. 1984), but this requires verification. The first case of cassava toxicity occurred almost 400 years ago (Cooke and Coursey 1981). The toxic principle was later identified as a cyanogenic glycoside, shown to be identical with flax linamurin (2-(beta-D-glucopyranosyloxy)-isobutyronitrile). All parts of the plant, except possibly the seeds, contain the glycoside together with the enzyme linamarase. This enzyme affects hydrolysis of the nitrile to free HCN when the tissue cellular structure is damaged (Cooke and Coursey 1981). Mantakassa disease is related to chronic cyanide intoxication associated with a diet consisting almost exclusively of cassava. In times of famine and sulfur-poor diets, Mantakassa effects were more pronounced (Casadi et al. 1984). Symptoms of Mantakassa disease include the sudden onset of difficulty in walking, increased knee and ankle reflexes, elevated serum thiocyanate levels, fever, pain, headache, slurred speech, dizziness, and vomiting. Women of reproductive age and children were the most seriously affected. Symptoms persisted for up to 4 months after treatment with hydroxycobalamin, vitamin supplements, and a high-protein, energy-rich diet (Cliff et al. 1984). Mantakassa was reported in 1102 victims in Mozambique in 1981 from a drought-stricken cassava staple area; from Zaire in 1928, 1932, 1937, and again in 1978 to 1981; in Nigeria; and in the United Republic of Tanzania. The mean serum thiocyanate level in patients with Mantakassa is 2.6 times higher than in non-Mantakassa patients in Nigeria, and 3.5 times higher than in Tanzanian patients. Pesticides, infection, viruses, and consumption of food other than cassava were eliminated as possible causative agents in Mantakassa disease. Still unresolved is whether the disease is triggered when a threshold level of thiocyanate is reached, or when a critical combination of cyanide intoxication plus nutritional deficiency occurs (Cliff et al. 1984).

Routes of administration other than dietary ingestion should not be discounted. Livestock found dead near a cyanide disposal site had been drinking surface water runoff from the area that contained up to 365 mg HCN/L (USEPA 1980). The use of cyanide fumigant powder formulations may be

hazardous by contact of the powder with moist or abraded skin, contact with the eye, swallowing, and inhalation of evolved HCN (Ballantyne 1988). In rabbits, lethal systemic toxicity was produced by contamination of the eye, moist skin, or abraded skin (but not dry skin) with cyanide powder formulations (40% NaCN plus 60% kaolin) administered at 1 to 5 g powder/m³ (Ballantyne 1988). Hydrogen cyanide in the liquid state can readily penetrate the skin, and skin ulceration has been reported from splash contact with cyanides among workers in the electroplating and gold extraction industries — although effects in those instances were more likely due to the alkalinity of the aqueous solutions (Homan 1987). In one case, liquid HCN ran over the bare hand of a worker wearing a fresh air respirator; he collapsed into unconsciousness in 5 min, but ultimately recovered (USEPA 1980).

Use of poisons in livestock collars is both specific and selective for animals causing depredations, as is the case for cyanide collars to protect sheep against coyotes (Steiner 1979) (**Table 15.5**). These collars contain a 33% NaCN solution and are usually effective against coyotes. However, field results indicate that some coyotes kill by means other than neck attack, and some exhibit great wariness in attacking collared sheep (Savarie and Sterner 1979).

Calcium cyanide in flake form was used in the 1920s to kill black-tailed prairie dogs and pocket gophers (*Geomys bursarius*) in Kansas, and various other species of rodents in Nova Scotia (Wade 1924). For prairie dog control, the usual practice was to place 43 to 56 g calcium cyanide 0.3 to 0.7 m below the rim of the burrow and close to the entrances. The moisture in the air liberated HCN gas, which remained in the burrow for several hours, producing 100% kill. A lower dose of 28 g per burrow was only about 90% effective (Wade 1924). Control of prairie dogs with cyanide sometimes resulted in the death of burrowing owls that lived in the prairie dog burrows (Wade 1924). Some animals can develop an aversion to food associated with sodium cyanide-induced illness (Clapperton et al. 1996). For example, sodium cyanide-containing baits used in New Zealand against the brushtail possum (*Trichosurus vulpecula*) produced bait shyness through conditioned food aversion induced by sublethal (4 to 5 mg NaCN/kg BW) cyanide ingestion, effectively reducing NaCN poisoning operations in that country (Warburton and Drew 1994; O'Connor and Matthews 1995; Clapperton et al. 1996).

Clinical signs of acute cyanide poisoning in mammals last only a few minutes after ingestion and include rapid and labored breathing, ataxia, cardiac irregularities, dilated pupils, convulsions, coma, and respiratory failure. Death may occur quickly, depending on the dose administered (Towill et al. 1978; Egekeze and Oehme 1980; Cade and Rubira 1982; Ballantyne 1983). Despite the high lethality of large single exposures, repeated sublethal doses — especially in diets — are tolerated by many species for extended periods, perhaps indefinitely (Eisler 1991). Cyanide poisoning causes cardiovascular changes as well as its better known effects on cellular respiration. Cyanide increases cerebral blood flow in rabbits and cats, and disrupts systemic arterial pressure in dogs (Robinson et al. 1985). Cyanide affects mammalian behavior, mostly motor functions, although these effects have not been quantified. Cyanide-induced motor alterations observed in rats and guinea pigs include muscular incoordination, increased whole-body locomotion, disrupted swimming performance, and altered conditioned avoidance responses (D'Mello 1987). As a consequence of the cytotoxic hypoxia in acute cyanide poisoning, there is a shift from aerobic to anaerobic metabolism, and the development of lactate acidosis. A combination of rapid breathing, convulsions, and lactate acidosis is strongly suggestive of acute cyanide poisoning (Ballantyne 1983). As with other chemical asphyxiants, the critical organs that are most sensitive to oxygen depletion are the brain and heart (Egekeze and Oehme 1980). The only consistent postmortem changes found in animals poisoned by cyanide are those relating to oxygenation of the blood. Because oxygen cannot be utilized, venous blood has a bright-red color and is slow to clot (Egekeze and Oehme 1980). Bright-red venous blood is not a reliable indicator of cause of death, however, because it is also associated with chemicals other than cyanide (Ballantyne 1983).

Cyanide poisoning is associated with changes in various physiological and biochemical parameters. The earliest effect of cyanide intoxication in mice seems to be inhibition of hepatic rhodanese

activity, due to either blockage by excess binding to the active site or to depletion of the sulfane–sulfur pool. These changes do not seem to occur in blood, where rhodanese functions at its maximal rate, thus preventing cyanide from reaching the target tissues and causing death (Buzaleh et al. 1989). Cyanide causes dose- and species-dependent responses on vascular smooth muscle. Studies with isolated aortic strips indicate that rabbits are 80 times more sensitive than dogs or ferrets (*Mustela putorius*) (Robinson et al. 1985). Rabbits killed with HCN had higher concentrations of cyanide in blood and other tissues and lower tissue cytochrome oxidase activities than did those killed with KCN (Ballantyne et al. 1972). Cyanide promotes dose- and calcium-dependent release of dopamine from tissues in the domestic cat, and reductions in adenosine triphosphate (ATP) content of the carotid body (Obeso et al. 1989). Cyanide-induced hypoxia is believed to produce decreases in the ATP content of Type I glomus cells. The decrease in the phosphate transfer potential is a crucial step in the overall transduction process, that is, the activation of the transmitter release from Type I cells, with resultant release and activation of sensory nerve endings (Obeso et al. 1989). Studies with isolated heart of the domestic ferret demonstrate that cyanide affects intracellular ionic exchange of H⁺, Na⁺, and Ca²⁺ (Fry et al. 1987); inhibits cardiac action potential (Elliott et al. 1989); and inhibits oxidative phosphorylation accompanied by an intracellular acidosis, a decrease in phosphocreatinine, and a rise in inorganic phosphate (Eisner et al. 1987). When oxidative phosphorylation is inhibited in cardiac muscle, there is a rapid decrease of developed force or pressure. Most of the decrease of developed pressure produced by cyanide in ferret heart is not produced by intracellular acidosis and may result from increased inorganic phosphate (Eisner et al. 1987). Observed changes in rat cerebral oxidative responses to cyanide may be due to redistribution of intracellular oxygen supply to mitochondria respiring in an oxygen-dependent manner or by branching effects within brain mitochondria (Lee et al. 1988). Hyperammonemia and the increase of neutral and aromatic amino acids may also be important in loss of consciousness induced by cyanide (Yamamoto 1989). Rats exposed for 30 days to 100 or 500 mg KCN/L drinking water had mitochondrial dysfunction, depressed ATP concentrations in liver and heart, and a depressed growth rate. Little effect was observed at 50 mg KCN/L (Pritsos 1996). The adverse effect on growth is consistent with the biochemical indicators of energy depletion. However, the concentrations should be viewed with caution as CN may have volatilized from the water solutions prior to ingestion by the rats, due to presumed neutral pH (Pritsos 1996).

Organic cyanide compounds, or nitriles, have been implicated in numerous human fatalities and signs of poisoning — especially acetonitrile, acrylonitrile, acetone cyanohydrin, malonitrile, and succinonitrile. Nitriles hydrolyze to carboxylic acid and ammonia in either basic or acidic solutions. Mice (*Mus sp.*) given lethal doses of various nitriles had elevated cyanide concentrations in liver and brain; the major acute toxicity of nitriles is CN release by liver processes (Willhite and Smith 1981). In general, alkyl nitriles release CN much less readily than aryl alkyl nitriles, and this may account for their comparatively low toxicity (Davis 1981).

No human cases of illness or death due to cyanide in water supplies are known (USEPA 1980). Accidental acute cyanide poisonings in man are uncommon (Towill et al. 1978). However, a man accidentally splashed with molten sodium cyanide died about 10 h later (Curry 1963). Human cyanide deaths usually involve suicides, where relatively large amounts of sodium cyanide or potassium cyanide are ingested and the victims die rapidly in obvious circumstances. Recovery after oral ingestion is rare. In one case, a spouse emptied capsules containing medicine and repacked them with 40% solid NaCN. The victim took one capsule and ingested about 0.05 g, but vomited and recovered completely (Curry 1963). Human deaths are increasing from gas or smoke inhalation from urban fires, possibly owing to the increased toxicity of fire atmospheres caused by the use of organocyanide plastics in modern construction and furnishings (Egekeze and Oehme 1980). Hydrogen cyanide may be important in some fires in producing rapid incapacitation, causing the victims to remain in the fire and die from carbon monoxide or other factors, although HCN concentrations of 60 mg/L air and lower had minimal effects (Purser 1984). Exposure to the mixture of HCN and carbon monoxide, with accompanying changes in cerebral blood flow during attempts to escape

from fires, may be a cause of collapse and subsequent death (Purser 1984). For example, cynomolgus monkeys (*Macaca* spp.) exposed to pyrolysis products of polyacrylonitrile (PAN) and to low-level HCN gas had similar physiological effects in both atmospheres: specifically, hyperventilation, followed by loss of consciousness after 1 to 5 min; and bradycardia, with arrhythmias and T-wave abnormalities. Recovery was rapid following cessation of exposure (Purser et al. 1984). Because HCN is the major toxic product formed by the pyrolysis of PAN, Purser et al. (1984) suggested that HCN may produce rapid incapacitation at low blood levels of cyanide in fires, while death may occur later due to carbon monoxide poisoning or other factors.

Finally, cyanide does not appear to be mutagenic, teratogenic, or carcinogenic in mammals (USEPA 1980; Ballantyne 1987a). In fact, there has been a longstanding hypothesis for an anticancer effect of the cyanogenic glycoside amygdalin (also called laetrile). The hypothesis is based on amygdalin's selective hydrolysis by a beta glucosidase, liberating cyanide and benzaldehyde at the neoplastic site. The cyanide then selectively attacks the cancer cell, which is presumed to be low in rhodanese, whereas normal cells are assumed to possess sufficient rhodanese and sulfur to detoxify the cyanide (Way 1981). However, many tumors are neither selectively enriched in beta glucosidase nor low in rhodanese (Way 1981).

Table 15.5 Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference ^a
CATTLE, <i>Bos</i> sp.		
Fed hybrid sorghum Sudan grass cross 988 at 15–20 kg/animal daily for 3–8 days	Of 180 cows, 21 were affected and 13 died; toxic cyanide levels were measured in fodder, and in liver and ruminal contents of dead cows	44
DOG, <i>Canis familiaris</i>		
Administered doses up to 2 mg NaCN/kg body weight (BW), once or twice daily for 15 months	Acute toxic signs evident after each administration, but complete recovery within 30 min; no measurable adverse effects after 15 months	1
5.4 mg NaCN/kg BW, single subcutaneous injection	LD50	2
24 mg KCN/kg BW, single oral or slow intravenous injection route	Lethal. At time of respiratory arrest, blood plasma concentration was 1.0 mg total CN/L or about 0.4 mg free cyanide/L	3
Fed diets containing 150 mg NaCN/kg for 30 days	No measurable effect on food consumption, blood chemistry, behavior, or organ histology	1
COYOTE, <i>Canis latrans</i>		
Single forced oral dose of NaCN, in mg/kg BW		
4	Immobilized in 13 min, but all survived for at least 30 days. Some sacrificed after 30 min: NaCN residues in mg/kg fresh weight (FW) were 0.03 in blood and 0.9 in stomach	2
4.1 (2.1–8.3)	LD50	2
8	Immobilization in 9 min, death within 41 min	2
16, 32, or 64	All immobilized in less than 1 min and all died in less than 8 min; maximum NaCN residues were 0.14 mg/L in blood and 13.0 mg/L FW in stomach	2
"Toxic" collars attached to neck of sheep and camouflaged with wool. Each collar contained 50 mL of a 33% NaCN solution. Toxic action commences when coyote attacks sheep and punctures collar. All coyotes tested were known to attack sheep in laboratory pens	Of three coyotes tested, one was immobilized in 1 min and died within 18 min; the other two coyotes recovered. The dead coyote had mouthed the collar for about 2 s: residues, in mg NaCN/kg, were 0.026 in blood and <0.1 in stomach. The other two coyotes had mouthed the collar for 3–15 s and had NaCN	

Table 15.5 (continued) Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Toxic collar, as above. Each coyote tested was known to have fatally attacked at least 3 domestic sheep within a 30-day period	levels, in mg/kg FW, of 0.014 and 0.029 in blood, and 0.6 and <0.1 in stomach Of the 12 coyotes that attacked the neck region of the sheep and punctured the collar, 9 received lethal doses and became immobilized in 1–3 min and died 3–25 min later. The mean time to death was 11.6 min. One of the three sublethally dosed coyotes survived at last three successful attacks in which the collar was punctured, and two survived two attacks. In all cases, contact with NaCN produced shaking of the head, pawing at the mouth, rubbing the snout on the ground, and ataxia	2 4
AFRICAN GIANT RAT, <i>Cricetomys gambianus</i>		
Weanlings fed diets for 16 weeks containing zero mg HCN/kg (maize), 110 mg HCN/kg (cassava pulp), 150 mg HCN/kg (cassava tuber), or 597 mg HCN/kg (cassava peel)	Food consumption was similar in all diets. No pathology was observed in any organ of animals on all treatments. Rats on maize and cassava pulp diets had significantly increased growth rate, feed efficiency, and protein efficiency. Rats on cassava peel and tuber diets had significantly increased thiocyanate levels in serum, organs, and urine	5
Juveniles, age 10–14 weeks, fed cassava peel diets for 2 weeks containing 720 mg HCN/kg Weanlings fed 1000 mg CN/kg diet, as KCN, for 12 weeks	Adverse effects on growth when cassava peel exceeds 7.8% of the ration Reduction in feed intake, reduced body weight, elevated thiocyanate concentrations in serum (37.4 mg/L vs. 12.6), urine (341 mg/L vs. 25), liver (1.7 g/kg FW vs. 0.4), kidney (2.4 g/kg FW vs. 0.4), and spleen (2.1 g/kg FW vs. 0.3)	6 7
HUMAN, <i>Homo sapiens</i>		
Intentional oral ingestion of unknown amount of NaCN or KCN, three cases	Death between 5 and 30 min; stomach cyanide concentrations ranged between 100 and 164 mg; tissue residues postmortem, in mg cyanide/kg FW, were 0.3–1.1 in blood, 0.3–1.0 in liver, and 0.2–0.3 in brain	8
Found dead, four cases, time to death unknown	Maximum cyanide burden in stomach was 230 mg; maximum tissue residues, in mg cyanide/kg FW were 3.5 in blood, 6.3 in liver, and 0.5 in brain	8
Attempted suicide by 39-year-old male, unknown amount of NaCN	Severe tremors and progressive loss of muscle tone — representing the first case of cyanide intoxication with delayed onset of symptoms	9
Inhalation of HCN gas, in mg/m ³ , for various time intervals		
140 for 60 min	Calculated LC50	10
220 for 30 min	Calculated LC50	10
504 for 10 min	Calculated LC50	10
680 for 5 min	Calculated LC50	10
1500 for 3 min	Calculated LC50	10
4400 for 1 min	Calculated LC50	10
Inhalation of 2000 mg HCN/L	First breath results in deep, rapid breathing, with collapse, convulsions, and death within 1 min	11
Inhalation of cyanogen chloride, in mg/L, for various time intervals		
1, 10 min	Irritant	1
48, 30 min	Fatal	1
159, 10 min	Fatal	1

Table 15.5 (continued) Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Inhalation of cyanogen bromide, in mg/L, for various time intervals		
1.4, no time given	Irritant to eyes and nose	1
92, 10 min	Fatal	1
Single oral dose		
0.5–3.5 mg HCN/kg BW	Lethal	12, 41
0.7–3.5 mg KCN/kg BW, equivalent to 50–250 mg KCN/adult	Fatal	10
2 mg HCN/kg BW, or total of about 150 mg HCN	Acute LD ₅₀ for adults	13
1–5 g NaCN or KCN, equivalent to 0.2 g/adult or 3 mg/kg BW	Minimum lethal dose	14
Tissue residues		
Whole blood, 1–2 mg free cyanide/L	Usually lethal	42
Whole blood, 2.6–3.1 mg total CN/L	Minimum cyanide concentration associated with death in an otherwise healthy individual	13
Whole blood, 4–45 mg total CN/L	Levels measured in known suicides	13
Whole body, 7 mg HCN/kg BW	Residue associated with minimum lethal dose	11
Daily dietary intake of 15–31.5 mg hydrogen cyanide from cassava	Mantakassa disease (see text for discussion)	15
100 mg HCN/kg BW applied to skin surface	LD ₅₀	11
Clothing inundated with 10% NaCN solution, pH 11.4	Clinical signs of toxicity within 25 min and death in about 60 min	13
LIVESTOCK		
>200 mg HCN/kg plant materials in diet	Potentially dangerous	13
CYNOMOLGUS MONKEYS, <i>Macaca</i> spp.		
Given multiple sublethal doses of KCN (5–18 mg) for 23 days	Brain histopathology	3
Exposed to HCN gas produced from combustion of polyacrylonitrile materials at various temperatures		
300°C, 87–170 mg HCN/L air	Incapacitated in 16–30 min, blood cyanide of 4.3 mg/L	16
600°C, 120–174 mg HCN/L air	Incapacitated between 6 and 24 min; blood cyanide of 2.96 mg/L	16
900°C, 166–196 mg HCN/L air	Incapacitated between 2 and 13 min; blood cyanide concentration of 3.1 mg/L	16
Exposed to HCN gas at air concentrations of 60, 80, or 150 mg HCN/L for 30 min	At 60 mg/L, HCN had only a slight depressive effect on the central nervous system; at 80 and 150 mg/L, severe CNS depression and incapacitation occurred	17
Exposed to HCN gas at air concentrations of 100, 102, 123, 147, or 156 mg HCN/L air	Incapacitated in 8 min at higher doses, to 19 min at lowest dose tested. Blood cyanide after 30 min exposure ranged between 1.7 mg/L at 100 mg HCN/L and 3.2 mg/L at 156 mg HCN/L; after recovery for 60 min, blood CN ranged between 2.0 and 2.9 mg/L	16
HOUSE MOUSE, <i>Mus musculus</i>		
Single oral dose of 8.7 (8.2–9.3) mg NaCN/kg BW, equivalent to 4.6 mg CN/kg BW	LD ₅₀	45
DOMESTIC MOUSE, <i>Mus</i> spp.		
Single intraperitoneal injection		
HCN, 2.8 mg/kg BW	LD ₅₀	10
NaCN, 4.6–5.9 mg/kg BW	LD ₅₀	10

Table 15.5 (continued) Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference^a
KCN, 5.3–6.7 mg/kg BW	LD50	10
Acetone cyanohydrin, $(\text{CH}_3)_2\text{C}(\text{OH})\text{CN}$, 8.7 mg/kg BW	LD50 (7 days); first death in 5 min	18
Malononitrile, NCCH_2CN , 18 mg/kg BW	LD50 (7 days); first death in 4.8 h	18
Propiononitrile, $\text{CH}_3\text{CH}_2\text{CN}$, 28 mg/kg BW	LD50 (7 days); first death in 21 h	18
N-butyronitrile, 38 mg/kg BW	LD50 (7 days); first death in 2.2 h	18
Acrylonitrile, $\text{CH}_2=\text{CHCN}$, 46 mg/kg BW	LD50 (7 days); first death in 2.3 h	18
Succinonitrile, $\text{NCCH}_2\text{CH}_2\text{CN}$, 62 mg/kg BW	LD50 (7 days); first death in 5.1 h	18
Acetonitrile, CH_3CN , 175 mg/kg BW	LD50 (7 days); first death in 7.1 h	18
Single subcutaneous injection		
HCN, 7.8–12.0 mg/kg BW	LD50	10
KCN, 10 mg/kg BW	Loss of consciousness in 100%; blood ammonia levels increased 2.5X; brain amino acid levels (i.e., leucine, isoleucine, tyrosine, phenylalanine) increased by 1.5–3.0X. Alpha ketoglutarate, at 500 mg/kg BW by intraperitoneal injection, completely blocked the development of cyanide-induced loss of consciousness and hyperammonemia	19
Single oral dose		
8.5 mg KCN/kg BW, equivalent to 3.4 mg CN ⁻ /kg BW	LD50	10, 20
Drinking water, 1000 mg KCN/L, exposure for 40 days	Marked inhibition of cytochrome oxidase activity in liver, brain, and blood; increased cyanide concentrations in all tissues; inhibition of rhodanese activity; diminished labile sulfur tissue levels	43
LITTLE BROWN BAT, <i>Myotis lucifugus</i>		
Single oral dose of NaCN of 8.4 (5.9–11.9) mg/kg BW, equivalent to 4.4 (3.1–6.3) mg CN/kg BW	LD50	45
RABBIT, <i>Oryctolagus</i> spp.		
Isolated aorta strips, 0.00014 µg NaCN/L–140 µg/L	Small contractions measured at lowest dose tested, ED50 at 70 µg/L, and maximum response at 140 µg/L. Higher doses up to 14 mg/L produced relaxation	21
Single intramuscular injection, in mg/kg BW		
0.5–1.5	LD50 for HCN	10
1.6	LD50 for NaCN	10
3.1–3.3	LD50 for KCN	10
8.0		
Killed with KCN	Cyanide concentrations, in mg/kg FW, were 1.6 in serum, 5.3 in blood, and <0.4 in other tissues sampled	22
Killed with HCN	Cyanide concentrations, in mg/kg FW, were 9.3 in blood, 2.1 in brain, 2.0 in serum, 0.5 in myocardium, and <0.4 in other tissues	22
Single intravenous injection, in mg/kg BW		
0.6	LD50 for HCN	10
1.2	LD50 for NaCN	10
1.9	LD50 for KCN	10
Single dose administered to eye surface, in mg/kg BW		
1.0	LD50 for HCN	10
4.5–5.1	LD50 for NaCN	10
7.9	LD50 for KCN	10
11.2	Signs of NaCN poisoning in 3 min; death in 7 min	23

Table 15.5 (continued) Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Single intraperitoneal injection, in mg/kg BW		
1.7–2.0	LD50 for HCN	10
2.8–2.9	LD50 for NaCN	10
3.6–4.0	LD50 for KCN	10
Administered as solution to skin, in mg/kg BW		
2.3	LD50 for HCN and abraded skin	10
6.9	LD50 for HCN and intact skin	10
14.3	LD50 for KCN and abraded skin	10
19.3	Abraded skin. Signs of NaCN poisoning evident in 25 min, death in 41 min	23
22.3	LD50 for KCN and intact skin	10
29.5	Moist skin. Signs of NaCN poisoning evident in 79 min, death in 117 min	23
>110	Dry skin. No signs of NaCN poisoning, no deaths	23
Single oral dose, in mg/kg BW		
2.5	LD50 for HCN	10
5.1	LD50 for NaCN	10
5.8	LD50 for KCN	10
12.8	Signs of NaCN poisoning in 4 min, death in 22 min	23
Single oral dose, NaCN, 10–15 mg/kg BW	All dead in 14–30 min; blood cyanide ranged between 3.7 and 5.4 mg/L	24
Inhalation of HCN from combustion of 20 g polyacrylonitrile	All dead in 12–16 min; blood cyanide ranged between 1.6 and 3.1 mg/L	24
Interval between death and removal of tissues for analysis in rabbits killed by KCN		
Brain	Concentrations dropped from 1.6 mg/kg FW immediately after death to 1.2 in 1 day, 0.92 in 3 days, and 0.04 in 7 days	25
Blood	Residues, in mg/kg FW, were 5.7 immediately after death, and 2.3 after 21 days	25
Lung	Cyanide concentrations dropped from 2.0 mg/kg FW just after death, to 0.8 in 7 days	25
DOMESTIC SHEEP, <i>Ovis aries</i>		
Intravenous or intraarterial injection, fetal lambs 80% through gestation (120 days), NaCN, 50–400 µg	Slowing of fetal heart rate, disruption of respiratory movements, significant but inconsistent changes in arterial blood pressure	26
Single intramuscular injection of 10 mg KCN/kg BW	All dead within 17 min; cyanide concentrations postmortem, in mg/kg FW, were 3.3 in blood, 1.5 in plasma, 1.6 in serum, 1.4 in cerebrospinal fluid, 0.9 in brain grey matter, and 1.0 in brain white matter	3, 10, 27
WHITE-FOOTED MOUSE, <i>Peromyscus leucopus</i>		
Single oral dose of 28 mg NaCN/kg BW, equivalent to 14.8 mg CN/kg BW	LD50	45
LABORATORY WHITE RAT, <i>Rattus</i> spp.		
Single intraperitoneal injection		
0.1–10 mg CN/kg BW	LD50	28
5 mg NaCN or KCN/kg BW	50% decrease in brain cytochrome oxidase activity within 5–10 min	14
5 mg KCN/kg BW	Reversible intracellular metabolic changes including acidosis and increased lactate levels — typical of cellular anoxia	29

Table 15.5 (continued) Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Intravenous injection, constant infusion of 0.15–0.20 mg CN/kg BW per min	LD50 in about 20 min; rapid progressive reduction in cerebrocortical cytochrome oxidase (cytochrome aa ₃) concomitant with increases up to 200% in cerebral blood flow	30
Single intracarotid artery injection of KCN 1–2 mg/kg BW	Modest acute clinical dysfunction and incomplete suppression of brain electroencephalographic (EEG) activity	31
2.5 mg/kg BW	Some deaths. Survivors showed rapid abolition of brain EEG activity, 52% reduction in brain cytochrome oxidase activity, 600% increase in lactate, 85% decrease in glycogen, 32% reduction in ATP, and 73% increase in ADP. All values returned to normal in 6–24 h, and remained normal for balance of 7-day observation period	31
3.5–5 mg/kg BW	High incidence of cardiovascular collapse and death within minutes	31
Tissue residues 2.6–2.9 mg HCN/kg FW	Minimum lethal concentrations in rats poisoned orally with KCN	13
Inhalation exposure route, HCN vapor, in mg/m ³ , for various periods 3778 for 10 s 1128 for 1 min 493 for 5 min 151–173 for 30–60 min	LC50 LC50 LC50 LC50	10 10 10 10
Single oral dose 3.4 mg KCN/kg BW 3.6–4.2 mg HCN/kg BW 5.1–5.7 mg NaCN/kg BW 5.7 mg KCN/kg BW 6, 10, or 14 mg KCN/kg BW	LD25 LD50 LD50 LD50 Some deaths in all groups; all dead at higher doses within 60 min. Those killed 10 min postadministration had higher blood CN concentrations than those killed near death or at survival at 60 min	32 10 10 32 13
6.4 mg NaCN/kg BW 7.5–10 mg KCN/kg BW 8.6 mg KCN/kg BW 10 mg KCN/kg BW, equivalent to 4 mg HCN/kg BW 13.2 mg NaCN/kg FW or 7 mg HCN/kg BW	LD50 LD50 LD98 LD50 Dead in 10.3 min. Tissue cyanide levels, in mg/kg FW, were 8.9 in liver, 5.9 in lung, 4.9 in blood, 2.1 in spleen, and 1.5 in brain	13 10, 13 32 20 33
40 mg NaCN/kg BW, equivalent to 21 mg HCN/kg BW	Dead in 3.3 min	33
Drinking water exposure Equivalent to 8 mg CN/kg BW daily for 21 days Equivalent to 21 mg CN/kg BW daily for 21 days 200 mg CN/L for 4 weeks Drinking water of adults contained 150 mg CN/L, as KCN, for 2 weeks, followed by injection with radioselenium-75 and observed for 15 days	Liver normal Significantly increased liver weight Reduced growth Cyanide-treated rats excreted significantly more radioselenium in urine than did controls. Half-time persistence of radioselenium in treated group was 28 days vs. 38 days in controls	20 20 34 35
Drinking water of weanling males contained 150 mg CN/L for 9 weeks	Significant reduction in glutathione activity, and in selenium concentrations in blood, kidney, liver, and muscle	35

Table 15.5 (continued) Cyanide Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effect	Reference ^a
Dietary exposure		
Fed 12 mg CN/kg BW daily for 2 years, equivalent to 300 mg HCN/kg ration	No measurable adverse effects on blood chemistry, growth, survival, or histology; elevated thiocyanate levels in liver and kidneys	1
Fed 500 mg HCN/kg ration to pregnant rats through gestation and lactation	No effect on reproduction	20
Weanlings fed diets of raw lima beans containing 727 mg CN/kg for 3 weeks, or 727 mg CN/kg diet as KCN for 3 weeks	Lima bean diet alone increased hepatic glutamate dehydrogenase (GLDH) and decreased isocitrate dehydrogenase (ICDH) activities. But KCN diet had no effect on GLDH and increased ICDH activity, emphasizing the importance of dietary components when evaluating CN-containing diets	36
750 mg CN/kg diet (1875 mg KCN/kg diet) for 8 weeks, adequate protein	No measurable effect on food consumption or growth rate. Significantly increased serum and urinary thiocyanate concentrations	37
As above, protein-deficient diet	Reduction in body weight gain, reduction in serum thiocyanate concentration	37
Weanling males fed diets containing 1500 mg KCN/kg, or 2240 potassium thiocyanate (KSCN) for 50 weeks	No deaths or clinical signs of toxicity. Both groups had decreased thyroid gland activity. Cyanide, but not thiocyanate, caused reduction in growth rate	38
Isolated liver segments from starved rats exposed to 100 mg KCN/L	Oxygen consumption reduced 80%, and evidence of hepatotoxicity as judged by enzyme release, glutathione depletion, and calcium accumulation in liver. Hepatotoxicity prevented by feeding rats fructose	39
DOMESTIC PIG, <i>Sus</i> spp.		
Fed diet containing 96 mg CN/kg ration, as cassava peel, for 72 days	No effect on food consumption or protein metabolism	40

^a 1, USEPA 1980; 2, Sterner 1979; 3, Christel et al. 1977; 4, Savarie and Sterner 1979; 5, Tewe 1984; 6, Tewe 1988; 7, Tewe 1982; 8, Curry 1963; 9, Grandas et al. 1989; 10, Ballantyne 1987a; 11, Towill et al. 1978; 12, Ukhun and Dibie 1989; 13, Egekeze and Oehme 1980; 14, Way 1981; 15, Casadi et al. 1984; 16, Purser et al. 1984; 17, Purser 1984; 18, Willhite and Smith 1981; 19, Yamamoto 1989; 20, USEPA 1989; 21, Robinson et al. 1985; 22, Ballantyne et al. 1972; 23, Ballantyne 1988; 24, Yamamoto et al. 1979; 25, Ballantyne et al. 1974; 26, Itskovitz and Rudolph 1987; 27, Ballantyne 1975; 28, Brattsten et al. 1983; 29, Lotito et al. 1989; 30, Lee et al. 1988; 31, MacMillan 1989; 32, Keniston et al. 1987; 33, Yamamoto et al. 1982; 34, Palmer and Olson 1981; 35, Beilstein and Whanger 1984; 36, Aletor and Fetuga 1988; 37, Tewe and Maner 1985; 38, Philbrick et al. 1979; 39, Younes and Strubelt 1988; 40, Tewe and Dessu 1982; 41, Way 1984; 42, Marrs and Ballantyne 1987a; 43, Buzaleh et al. 1989; 44, Bapat and Abhyanker 1984; 45, Clark et al. 1991.

15.10 RECOMMENDATIONS

Proposed free cyanide criteria suggest that sensitive species of aquatic organisms are protected at <3 µg/L; birds and livestock at <100 mg/kg diet; and human health at concentrations of <10 µg/L drinking water, <50 mg/kg diet, and <5 mg/m³ air (Eisler 1991) ([Table 15.6](#)). In aquatic systems, research is needed in several areas:

1. Long-term effects of cyanide on life cycles, growth, survival, metabolism, and behavior of a variety of aquatic organisms and microorganisms in addition to fish (Towill et al. 1978; Leduc et al. 1982)
2. Effects of seasonal pulses of cyanide on aquatic organisms in rural and wilderness areas (Leduc 1984)

3. Influence of various environmental parameters (e.g., oxygen, pH, temperature), if any, on adaptive resistance to cyanide (Leduc 1981, 1984)
4. Usefulness of various biochemical indicators of cyanide poisoning, such as cytochrome oxidase inhibition (Gee 1987), estradiol and thyroxine levels in fish plasma (Ruby et al. 1986, 1993a), and pituitary gland histology (Ruby et al. 1993b)

To protect vertebrate wildlife from mine water poisoning with certainty, it is necessary to exclude them from cyanide solutions or to reduce cyanide concentrations to nontoxic levels (Henny et al. 1994). More research is needed on chemical repellents and physical screening methods. Mortality of avian and terrestrial wildlife from cyanide toxicosis may be curtailed at small ponds associated with leach heaps by screening wildlife from toxic solutions (Hallock 1990) or covering small solution ponds with polypropylene netting, provided that the fencing and netting are properly maintained (Henny et al. 1994). Some mines in Nevada are now covering surfaces of small ponds with 4-inch (10.2-cm) diameter high-density polyethylene balls; birds are no longer attracted to these ponds as water sources (Eisler et al. 1999). Gold mine operators in southern California and Nevada used plastic sheeting to cover the cyanide leach pond, resulting in a cessation of wildlife mortality. The comparatively high cost of this process was soon recouped through reduced evaporation of water and cyanide (Eisler et al. 1999). To reduce the potential for puddling on ore heaps, more research is recommended on physical exclusionary devices, chemical repellents, and monitoring of solution application rates (Henny et al. 1994; Hill and Henry 1996; Eisler et al. 1999).

Analytical methodologies need to be developed that differentiate between free cyanide (HCN and CN^-) and other forms of cyanide, and that are simple, sensitive (i.e., in the $\mu\text{g/L}$ range), and accurate (Smith et al. 1979; Leduc et al. 1982). Procedures need to be standardized that ensure prompt refrigeration and analysis of all samples for cyanide determination because some stored samples generate cyanide, while others show decreases (Gee 1987). Periodic monitoring of cyanide in waterways is unsatisfactory for assessing potential hazards because of cyanide's rapid action, high toxicity, and low environmental persistence. A similar case is made for cyanide in the atmosphere. Development of a continuous monitoring system of cyanides in waterways and air is recommended, with emphasis on point source dischargers, such as industrial and municipal facilities (Towill et al. 1978; Egekeze and Oehme 1980; Leduc et al. 1982). Information is needed on the fate of cyanide compounds in natural waters, relative contributions of natural and anthropogenic sources, and critical exposure routes for aquatic organisms (Leduc et al. 1982). Additional research is needed on the origin of cyanide in wilderness and rural watershed areas, specifically the roles of organic wastes and their associated bacterial flora, aquatic vegetation induced by nutrient enrichment, and terrestrial plant cover in the watershed (Leduc 1984).

The use of M-44 sodium cyanide capsules for predator control was suspended and canceled by the U.S. Environmental Protection Agency on March 9, 1972. M-44 use was again permitted by the U.S. Environmental Protection Agency beginning on February 4, 1976, provided that "each authorized or licensed applicator shall carry an antidote kit on his person when placing or inspecting M-44 devices. The kit shall contain at least 6 pearls of amylnitrite and instructions on their use. Each authorized or licensed applicator shall also carry on his person instructions for obtaining medical assistance in the event of accidental exposure to sodium cyanide" (USEPA 1976a, b). The use of cyanide-containing paste baits to control pestiferous mammals is practiced widely in New Zealand; however, some species are repelled by these baits and more research is needed to improve their effectiveness (Warburton and Drew 1994).

Farmers need to be aware of factors that influence the cyanogenic potential of forage crops and conduct regular inspections of grazing fields for cyanogenic plants. Moreover, hay and silage should be properly cured in order to minimize cyanide content before feeding to livestock (Egekeze and Oehme 1980). Selective breeding of plants with low cyanide content will help reduce livestock

poisoning, but the most advisable prevention method at present is to prohibit grazing on fields where cyanogenic plants are present (Egekeze and Oehme 1980). More research seems needed on:

1. Effects of drought and other factors that may increase the concentration of cyanogenic glycosides in livestock forage plants
2. Mechanisms of cyanide liberation by plants
3. Effects of cyanide on wildlife and range animals that graze foliage with high cyanogenic glycoside content (Towill et al. 1978)

Research is needed on low-level, long-term cyanide intoxication in mammals by oral and inhalation routes in the vicinities of high cyanide concentrations, especially on the incidence of skin dermatitis, nasal lesions, and thyroid dysfunction, and on urinary thiocyanate concentrations. These types of studies may provide a more valid rationale in establishing standards and threshold limit values for HCN and inorganic cyanide (Towill et al. 1978; Egekeze and Oehme 1980). Data are scarce on the carcinogenic, teratogenic, and mutagenic properties of cyanide, and on the distribution and transformation of cyanides in air, land, or water. Additional analysis of available information and more research in these areas are recommended. Finally, more research is needed on cyanide toxicokinetics because cyanide is a very reactive nucleophile that distributes widely through the body, is permeable to cell membranes, and may accumulate in the fetus (Towill et al. 1978; Eisler et al. 1999).

Table 15.6 Proposed Free Cyanide Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
FRESHWATER ORGANISMS (g/L medium)		
Minimal impairment, most species of fish		
Reduced survival, amphipods	3–5	1–6
Safe, most fish species	>3–34	1, 7
Significant impairment, most species of fish	3.5 (24-h average, not to exceed 52.0 at any time)	7
Hazardous	8–16, exposure for at least 20 days	6, 7
Most fish species	>11	1, 4
Microorganisms	>300	8
Reduced survival, chronic exposure		
Bivalve molluscs, larvae	>14	1
Fish, many species	30–150	1, 5
Impaired reproduction, sensitive species of fish	>25	2
Impaired swimming ability, growth, development, and behavior	>100	3, 6
Lethal to rapidly lethal, acute exposure	300–1000	5
Great Lakes		
Acute exposure, safe	<22	23
Chronic exposure, safe	<5.2	23
MARINE ORGANISMS (g/L seawater)		
Acceptable		
Acute	<1.0	23
Chronic	<1.0	23
Adverse effects, chronic exposure	>2	7
Minimal risk	<5	1
Hazardous	>10	1
Lethal	>30	7

Table 15.6 (continued) Proposed Free Cyanide Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
SEDIMENTS, GREAT LAKES (mg total cyanide/kg dry weight = DW)		
Nonpolluted		
Moderately polluted	<0.10	20
Heavily polluted	0.1–0.25	20
Heavily polluted		
BIRDS		
Domestic chickens		
Diet, safe level (mg total cyanide/kg ration FW)	90–<100	9, 10
Waterfowl		
Drinking water, safe level (mg total cyanide/L)	<50	21, 22
LIVESTOCK (mg/kg FW)		
Diet, safe level		
Free cyanide	<100	9
Total cyanide	<625	11
Forage, hazardous level	>200	8
Drinking water ($\mu\text{g}/\text{L}$)	<200	23
LABORATORY WHITE RAT		
Diet, safe level (mg/kg ration FW)	<1000	19
Blood (mg/L)		
Normal	0.25–0.45	12
Minimum lethal concentration	2.6–2.9	12
Liver		
Minimum lethal concentration (mg/kg FW)	0.5–6.1	12
HUMAN HEALTH		
Drinking water ($\mu\text{g}/\text{L}$)		
Recommended	<5–<10	1, 6, 8, 13
United States nationwide survey	Maximum 8.0	7
Safe	<10	1
Goal, United States	<10	7, 14
Maximum allowable limit		
United States	10	13
Goal, Canada	<20	7
Lifetime health advisory	<154–200	14, 23
World Health Organization, acceptable	<100	23
United States and Canada		
Acceptable	<200	7
Mandatory limit	200	13
Rejected	>200	1, 8
10-day health advisory		
Child	<220	14
Adult	<770	14
Diet		
Acceptable daily intake		
Water	1.5 mg, equivalent to 0.02 mg/kg BW daily for 70-kg adult	15
Food (mg/kg BW)	8.4	7
Food (mg/kg FW ration)	<50	15
Food (mg total cyanide/kg FW ration)	<415	11

Table 15.6 (continued) Proposed Free Cyanide Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
Cassava, <i>Manihot esculenta</i> , roots, total cyanide (mg/kg FW)		
Safe	<50	16
Moderately toxic	50–100	16
Very poisonous	>100	16
Food items (mg/kg)		
Cocoa	<20 DW	13
Beans, nuts	<25 DW	1
Cereals, grains	<25 DW	13
Citrus fruits	<50 FW	1
Uncooked pork	<50 FW	13
Grains	<75 FW	1
Cereal flours	<125 DW	13
Spices	<250 FW	1, 13
Frozen meat	<950 FW	1, 13
Bakery products, yeast	<1500 DW	13
Egg white solids	<1000 DW	13
Tissue residues		
Blood and spleen (µg/L or µg/kg FW)		
Normal	77	17
Suspected poisoning	>1000	17
Whole blood (µg/L)		
Usually fatal	1000–2000	15
Whole body (mg/kg BW)		
Fatal	4, if taken rapidly	18
Air (mg/m ³)		
Recommended safe levels		
Soviet Union, Romania, Hungary, Bulgaria, Czechoslovakia	<0.3	1
United States	<5	14
Most countries	<11	1, 15
Occupational exposure		
Proposed safe level, United States	<3	15
Safe ceiling concentration	<5	1
Hazardous levels	4.2–12.4	1
Soils (mg/kg DW)		
Free cyanide		
Background	1	20
Moderate contamination	10	20
Requires cleanup	100	20
Complex cyanide		
Background	5	20
Moderate contamination	50	20
Requires cleanup	100	20

^a 1, Towill et al. 1978; 2, Smith et al. 1979; 3, Doudoroff 1976; 4, Leduc 1981; 5, Leduc 1984; 6, Leduc et al. 1982; 7, USEPA 1980; 8, Egekeze and Oehme 1980; 9, Gomez et al. 1983; 10, Gomez et al. 1988; 11, Okeke et al. 1985; 12, Egekeze and Oehme 1979; 13, USEPA 1973; 14, USEPA 1989; 15, Marrs and Ballantyne 1987; 16, Dufour 1988; 17, Gee 1987; 18, Shaw 1986; 19, Tewe 1982; 20, Beyer 1990; 21, Allen 1990; 22, Clark and Hothem 1991; 23, USPHS 1995.

15.11 SUMMARY

Cyanides are used widely and extensively in the manufacture of synthetic fabrics and plastics, in electroplating baths and metal mining operations, as pesticidal agents and intermediates in agricultural chemical production, and in predator control devices. Elevated cyanide levels are normally encountered in more than 1000 species of food plants and forage crops, and this probably

represents the greatest source of cyanide exposure and toxicosis to humans and to range animals. Anthropogenic sources of cyanide in the environment include certain industrial processes, laboratories, fumigation operations, cyanogenic drugs, fires, cigarette smoking, and chemical warfare. Although cyanide is ubiquitous in the environment, levels tend to be elevated in the vicinity of metal processing operations, electroplaters, gold-mining facilities, oil refineries, power plants, and solid waste combustion.

Many chemical forms of cyanide are present in the environment, including free cyanide, metallocyanide complexes, and synthetic organocyanides, also known as nitriles. But only free cyanide (i.e., the sum of molecular hydrogen cyanide, HCN, and the cyanide anion, CN⁻) is the primary toxic agent, regardless of origin. Cyanides are readily absorbed through inhalation, ingestion, or skin contact and are readily distributed throughout the body via blood. Cyanide is a potent and rapid-acting asphyxiant. It induces tissue anoxia through inactivation of cytochrome oxidase, causing cytotoxic hypoxia in the presence of normal hemoglobin oxygenation. Diagnosis of acute lethal cyanide poisoning is difficult because signs and symptoms are nonspecific, and numerous factors modify its biocidal properties, such as dietary deficiencies in Vitamin B₁₂, iodine, and sulfur amino acids. Among the more consistent changes measured in acute cyanide poisoning are inhibition of brain cytochrome oxidase activity, and changes in electrical activity in heart and brain. At sublethal doses, cyanide reacts with thiosulfate in the presence of rhodanese to produce the comparatively nontoxic thiocyanate, most of which is excreted in the urine. Rapid detoxification enables animals to ingest high sublethal doses of cyanide over extended periods without harm. Antidotes in current use to counteract cyanide poisoning include a combination of sodium nitrite and sodium thiosulfate (United States), cobalt edetate (United Kingdom, Scandinavia, France), or a mixture of 4-dimethylaminophenol and sodium thiosulfate (Germany).

All available evidence suggests that cyanides are neither mutagenic, teratogenic, nor carcinogenic. Moreover, there are no reports of cyanide biomagnification or cycling in living organisms, probably owing to its rapid detoxification. Cyanide seldom persists in surface waters and soils owing to complexation or sedimentation, microbial metabolism, and loss from volatilization. More data are needed on cyanide distribution and transformation in the atmosphere. Analytical methods for the determination of free and bound cyanides and cyanogenic compounds in biological materials are under constant revision. Further, unless tissue samples are obtained promptly after cyanide exposure and analyzed immediately, erroneous analytical values will result.

Higher plants are adversely affected by cyanide through cytochrome oxidase inhibition; the rate of production and release of cyanide by plants to the environment through death and decomposition is unknown. Nonacclimatized soil bacteria are adversely affected at 0.3 mg HCN/kg; acclimatized populations, however, can degrade wastes containing up to 60 mg total cyanide/kg. In some cases, soil bacteria and fungi produce cyanides as secondary metabolites, with adverse effects on certain plants. Several species of arthropods normally contain elevated whole-body cyanide concentrations, and these confer protection against predators and allow consumption of cyanogenic plants.

Fish were the most sensitive aquatic organisms tested. Adverse effects on swimming and reproduction were observed between 5 and 7.2 µg free cyanide/L; lethal effects usually occurred between 20 and 76 µg/L. Biocidal properties of cyanide in aquatic environments were significantly modified by water pH, temperature, and oxygen content; life stage, condition, and species assayed; previous exposure to cyanides; presence of other chemicals; and initial dose tested. Birds that feed predominantly on flesh were more sensitive to cyanide than were herbivores. Free cyanide levels associated with high avian death rates include 0.12 mg/L in air, 2.1 to 4.6 mg/kg body weight (BW) via acute oral exposure, and 1.3 mg/kg BW administered intravenously. Dietary levels of 135 mg total cyanide/kg ration resulted in growth reduction of chicks, but 103 mg total cyanide/kg ration had no measurable effect on domestic chickens. Cyanogenic plants represent a problem for various range animals and wildlife, primarily among species that eat rapidly. Intakes of 4 mg HCN/kg BW are lethal to these species if it is consumed quickly. Cassava (*Manihot esculenta*) is a cyanogenic plant that accounts for up to 70% of human caloric intake in some areas, and this is

associated with serious, long-term toxic effects including ataxia, optic nerve lesions, altered thyroid function, demyelination, and increases in tissue thiocyanate levels. Acute oral LD₅₀ values for representative species of mammals ranged between 2 and 3.6 mg HCN/kg BW. Despite the high lethality of large single exposures, repeated sublethal doses — especially in diets — can be tolerated by many species for extended periods, perhaps indefinitely. Mammalian deaths were also recorded at air concentrations of 140 mg HCN/m³ (exposure for 60 min) and 4400 mg HCN/m³ (exposure for 1 min), and at dermal applications between 2.3 mg HCN/kg BW for abraded skin and 100 mg HCN/kg BW for intact skin. Adverse nonlethal effects were noted at drinking water concentrations >150 mg HCN/L and at dietary concentrations >720 mg HCN/kg ration.

Free cyanide criteria currently proposed for natural resource protection include <3 µg/L medium for aquatic life, and <100 mg/kg diet for birds and livestock. For human health protection, free cyanide values are <10 µg/L drinking water, <50 mg/kg diet, and <5 mg/m³ air.

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CHAPTER 16

Diazinon

16.1 INTRODUCTION

Diazinon, an organophosphorus compound with an anticholinesterase mode of action, was released for experimental evaluation in the early 1950s. Diazinon is now used extensively by commercial and home applicators in a variety of formulations to control flies, cockroaches, lice on sheep, insect pests on ornamental plants and food crops (especially corn, rice, onions, and sweet potatoes), forage crops such as alfalfa, and nematodes and soil insects in turf, lawns, and croplands (Anonymous 1972; Meier et al. 1976; Allison and Hermanutz 1977; Berg 1984; Stone and Gradoni 1985; Eisler 1986; Wan 1989; Menconi and Cox 1994; Moore and Waring 1996). Diazinon is the most widely used organophosphorus pesticide in Pakistan to control cabbage root fly and carrot fly (Alam and Maughan 1992). In 1992, more than 612,000 kg diazinon were used in California on alfalfa, nuts, stone fruits, vegetables, and other crops (Menconi and Cox 1994).

Avian and terrestrial wildlife can acquire diazinon by drinking contaminated water, by absorbing it through legs and feet, by consuming treated grass or grain, or by ingesting pesticide-impregnated carrier particles (Stone and Knoch 1982; Stone and Gradoni 1985). Diazinon was detected at low concentrations (<0.2 mg/kg) in tissues of 29% of loggerhead shrikes (*Lanius ludovicianus*) collected in Virginia between 1985 and 1988 (Blumton et al. 1990). Diazinon poisonings of birds — involving 54 incidents in 17 states — have been recorded for at least 23 species, especially among waterfowl feeding on recently treated turfgrass. Incidents involving agricultural applications may be less conspicuous, and thus not as well-documented (Stone and Gradoni 1985). Kills of Canada geese (*Branta canadensis*), brant (*Branta bernicla*), mallard (*Anas platyrhynchos*), American black duck (*Anas rubripes*), American wigeon (*Anas americana*), other species of waterfowl, and songbirds have all been associated with consumption of grass or grain shortly after diazinon application (Schobert 1974; Zinkl et al. 1978; Stone 1980; Stone and Knoch 1982; Anderson and Glowa 1985; Littrell 1986; Stone and Gradoni 1986; Brehmer and Anderson 1992; Kendall et al. 1992, 1993). Fatal diazinon poisonings have also been recorded in humans (Soliman et al. 1982; Lox 1983), domestic chickens (*Gallus gallus*) (Sokkar et al. 1975), domestic ducklings (*Anas* spp.) and goslings (*Anser* spp.) (Egyed et al. 1974, 1976), in laboratory monkey colonies of the tamarin (*Saguinus fuscicollis*) and the common marmoset (*Callithrix jacchus*) (Brack and Rothe 1982), and the honeybee (*Apis mellifera*) (Anderson and Glowa 1984). Mammals seem to be less sensitive than birds to diazinon poisoning (Stone and Gradoni 1985). The lack of reported mammalian mortalities (only one suspected case of a pocket gopher, *Thomomys* sp., found dead in a park at Yakima, Washington, following aerial spraying of diazinon on shade trees) is consistent with the general findings of Grue et al. (1983) for organophosphorus insecticides. Sublethal effects such as reduced food consumption and egg production in the ring-necked pheasant (*Phasianus colchicus*) (Stromborg 1977), and behavioral modifications, reduced food intake, alterations in liver enzyme activities,

reductions in vitamin concentrations, reduced body temperature, and lowered resistance to cold stress in white-footed mice (*Peromyscus leucopus*) (Montz and Kirkpatrick 1985) have been noted at diazinon concentrations markedly lower than those causing acute mortality. It has been suggested — but not proven — that wildlife partially disabled in the field as a result of diazinon poisoning would be more likely to die of exposure, predation, starvation, or dehydration, or face behavioral abnormalities, learning impairments, and reproductive declines than would similarly treated domestic or laboratory animals (Montz 1983; Montz and Kirkpatrick 1985). Sublethal effects of diazinon on fish populations include vertebral malformations, altered blood chemistry, inhibition of acetylcholinesterase activity, reduced larval and adult growth, impaired swimming, abnormal pigmentation, histopathology of muscle and gills, and reduction of liver RNA, DNA, and protein content (Allison and Hermanutz 1977; Eisler 1986; Moore and Waring 1996).

16.2 ENVIRONMENTAL CHEMISTRY

Diazinon is a broad-spectrum insecticide that is effective against a variety of orchard, vegetable, and soil pests, ectoparasites, flies, lice, and fleas. It exists as technical-grade product, wettable powder, emulsifiable concentrate, granules, and in a variety of other formulations (Negherbon 1959; Anonymous 1972; Eberle 1974; Berg 1984; Menconi and Cox 1994). The active ingredient in diazinon is phosphorothioic acid *O,O*-diethyl *O*-(6-methyl-2-1(methylethyl)-4-pyrimidinyl) ester (Figure 16.1). Its molecular formula and molecular weight are $C_{12}H_{21}N_2O_3PS$ and 304.35, respectively. The technical grade is light amber to dark brown and boils at 83° to 84°C. Diazinon is soluble in water to 60 mg/L and dissolves readily in aliphatic and aromatic solvents, alcohols, and ketones. Diazinon can be stored on the shelf for at least 3 years with negligible degradation. Diazinon is also known as G-24480, Sarolex, Spectracide (Anonymous 1972), AG-500, Alfa-tox, Basudin, Dazzel, Diazajet, Diazide, Diazol, ENT 19507, Gardentox, Neocidol, Nucidol, CAS 333-41-5 (Hudson et al. 1984), Diagran, Dianon, DiaterrFos, Diazatol, Dizinon, Dyzol, D.z.n., Fezudin, Kayazinon, Kayazol, Knox Out, and Nipsan (Berg 1984).

Some diazinon formulations contain 0.2 to 0.7% (2000 to 7000 mg/kg) of Sulfotep (tetraethyl dithiopyrophosphate) as a manufacturing impurity. Sulfotep is reportedly at least 100 times more toxic than diazinon to some organisms (Jarvinen and Tanner 1982). It seems that additional research is warranted on diazinon/Sulfotep interactions.

Diazinon degrades rapidly in plants, with half-time persistence usually less than 14 days. However, persistence increases as temperatures decrease, and is longer in crops with a high oil content (Table 16.1). In water, diazinon breaks down to comparatively nontoxic compounds with little known hazard potential to aquatic species (Meier et al. 1976; Jarvinen and Tanner 1982), although the degradation rate is highly dependent on pH (Table 16.1). The half-time persistence of

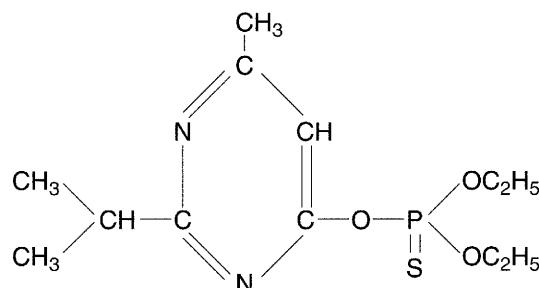


Figure 16.1 Structural formula of diazinon.

diazinon on sandy loam soil exposed to sunlight is 2.5 to 10 days (Menconi and Cox 1994). In most soils, diazinon seldom penetrates below the top 1.3 cm (Kuhr and Tashiro 1978; Branham and Wehner 1985). But diazinon may remain biologically available in soils for 6 months or longer at low temperature, low moisture, high alkalinity, and lack of suitable microbial degraders (Anonymous 1972; Bartsch 1974; Meier et al. 1976; Allison and Hermanutz 1977; Menzie 1978; Forrest et al. 1981; Branham and Wehner 1985). Bacterial enzymes, derived from *Pseudomonas* sp., can be used to hydrolyze diazinon in soil, although costs are prohibitive except in treating emergency situations involving spills of concentrated diazinon solutions. In one case, diazinon was enzymatically hydrolyzed within 24 h in an agricultural sandy soil at concentrations as high as 10,000 mg/kg (Barick and Munnecke 1982).

In almost every instance of diazinon poisoning, there has been a general reduction in cholinesterase activity levels, especially in brain and blood. Diazinon exerts its toxicity by binding to the neuronal enzyme acetylcholinesterase (AChE) for a considerable time postexposure (Montz 1983; Kendall et al. 1992; Decarie et al. 1993). It is emphasized that all organophosphorus pesticide compounds, in sufficient dose, inhibit AChE *in vivo*, and all share a common mechanism of acute toxic action (Murphy 1975). AChE inhibition results in the accumulation of endogenous acetylcholine in nerve tissues and effector organs, resulting in signs that mimic the muscarinic, nicotinic, and central nervous system (CNS) actions of acetylcholine. The immediate cause of death in fatal organophosphorus compound poisonings, including diazinon, is asphyxia resulting from respiratory failure. Contributing factors are the muscarinic actions of bronchoconstriction and increased bronchial secretions, nicotinic actions leading to paralysis of the respiratory muscles, and the CNS action of depression and paralysis of the respiratory center (Murphy 1975).

Diazinon is not a potent inhibitor of cholinesterase and must be converted to its oxygen analogues (oxons), especially diazoxon (diethyl-2-isopropyl-6-methylpyrimidin-4-yl phosphate) *in vivo* before poisoning can occur (Wahla et al. 1976). Diazoxon is about 10,000 times more effective in reducing cholinesterase activity levels than diazinon (Fog and Asaka 1982). At least eight diazinon metabolites have been identified in vertebrates, of which four are oxons (Machin et al. 1975; Menzie 1978; Seguchi and Asaka 1981). It is generally agreed that diazinon is metabolized to diazoxon through the action of liver mixed-function oxidases and nicotinic adenine nucleotide phosphate (Menzie 1978; McLean et al. 1984). Diazinon toxicity will depend to some extent on the relation between the rates of activation of diazinon to diazoxon, and of decomposition of the latter to harmless products (Fujii and Asaka 1982). Birds are more sensitive to diazinon than mammals, probably because mammalian blood enzymes hydrolyze diazoxon rapidly, whereas bird blood has virtually no hydrolytic activity. It seems that diazoxon stability in blood is a major factor affecting susceptibility of birds and mammals to diazinon poisoning (Machin et al. 1975).

Diazinon poisoning effects in animals can be delayed or prevented by treatment with a variety of compounds. For example, AChE in diazinon-stressed birds can be reactivated by pralidoxime (Egyed et al. 1976; Fleming and Bradbury 1981; Misawa et al. 1982). Furthermore, pretreatment of large white butterfly (*Pieris brassicae*) larvae with methylene dioxyphenyl compounds will inhibit the diazinon-to-diazoxon activation (Wahla et al. 1976). Added tryptophan and its metabolites may prevent teratogenic defects by maintaining nicotinic adenine nucleotide (NAD) levels in diazinon-treated chicken embryos; diazinon reportedly acts to decrease the availability of tryptophan to bird embryos, subsequently interfering with NAD metabolism and causing birth defects (Henderson and Kitos 1982). NAD metabolism in diazinon-stressed birds can also be maintained with nicotinamide (Misawa et al. 1982). In contrast to many other organophosphorus insecticides, organisms that survive diazinon-inhibited cholinesterase levels can undergo considerable spontaneous reactivation (dephosphorylation), indicating that its dephosphorylation occurs more readily than that of cholinesterase inhibited by other organophosphorus compounds (Fleming and Bradbury 1981).

Table 16.1 Persistence of Diazinon in Plants, Soil, and Water

Sample Type and Other Variables	Time for 50% Persistence	Reference ^a
PLANTS		
Cabbage leaves		
Summer	14 days	1
Winter	>14 days	1
Leafy vegetables, forage crops	<2 days	2
Other vegetables, cereal products	<7 days	2
Fruits	4 days	2
Carrots, oil seed plants	>4 days	2
Grass	7 days	3
SOIL		2–4 weeks
WATER		
Lake Superior	30 days (14–184 days)	5
River water	39 days	6
Effect of pH		
3.1	12 h	7
5.0	4–12 days	9
6.0	2 weeks	8
7.0	78–138 days	8
7.4	6 months	8
9.0	1.5–4 months	8, 9
10.4	6 days	7

^a **1**, Montz 1983; **2**, Bartsch 1974; **3**, Kuhr and Tashiro 1978; **4**, Branham and Wehner 1985; **5**, Jarvinen and Tanner 1982; **6**, Arthur et al. 1983; **7**, Meier et al. 1976; **8**, Allison and Hermanutz 1977; **9**, Menconi and Cox 1994.

16.3 LETHAL EFFECTS

16.3.1 General

Diazinon toxicity varies widely within and among species, and is modified by organism age, sex, body size, climatic conditions, pesticide formulation, chemistry of the environment, and other factors (Montz 1983). Nevertheless, several trends are apparent, as judged by available data. Among aquatic organisms, for example, freshwater cladocerans and marine shrimps were the most sensitive species tested, with LC50 (96 h) values of less than 5 µg/L; freshwater teleosts were more resistant, with the lowest LC50 (96 h) value recorded being 90 µg/L. Diazinon has considerable potential for causing acute avian poisoning episodes. Sensitive species of birds, including ducks, turkey (*Meleagris gallopavo*), and red-winged blackbird (*Agelaius phoeniceus*), died at single oral doses of 2 mg of diazinon/kg body weight. Mammals are more resistant than birds to diazinon; the lowest LD50 (acute oral) value recorded is 224 mg/kg body weight for female rats (*Rattus rattus*). Chronic oral toxicity tests with mammals suggest that daily intake exceeding 5 or 10 mg diazinon/kg body weight is probably fatal over time to swine (*Sus scrofa*) and dogs (*Canis familiaris*), respectively. Finally, 9 mg/kg of dietary diazinon fed during gestation to pregnant mice (*Mus musculus*) was associated with significant mortality of pups prior to weaning.

16.3.2 Aquatic Organisms

Freshwater cladocerans and marine crustaceans were the most sensitive groups tested, with LC50 (96 h) values of less than 2 µg/L for the more sensitive species (Table 16.2). European eels (*Anguilla anguilla*), rainbow trout (*Oncorhynchus mykiss*), and bluegills (*Lepomis macrochirus*) seemed to be the most sensitive freshwater teleosts tested, with LC50 (96 h) values between 80

and 120 µg/L; however, the postlarval and juvenile stages of the striped knifejaw (*Oplegnathus fasciatus*) — a marine fish cultured intensively in Japan — were unusually sensitive (Table 16.2). In general, technical grade formulations of diazinon seem to be more toxic than emulsifiable concentrates, dusts, and oil solutions (Table 16.2). Also, large variations in acute toxicity values were evident, even among closely related species (Table 16.2).

Outward signs of diazinon poisoning in fish included lethargy, forward extension of pectoral fins, darkened areas on posterior part of body, hyperexcitability when startled, sudden rapid swimming in circles, and severe muscular contractions (Goodman et al. 1979; Alam and Maughan 1992). Internally, physiological mechanisms in teleosts preceding death involved the following sequence: cholinesterase inhibition, acetylcholine accumulation, disruption of nerve functions, respiratory failure, and asphyxia (Sastry and Sharma 1980). Closely related species of fishes differ markedly in their sensitivity to diazinon. Guppies (*Poecilia reticulata*) are 5 times more sensitive to diazinon than are zebrafish (*Brachydanio rerio*), as judged by LC50 (96 h) values (Keizer et al. 1991, 1993). Differences of resistance and accumulation between guppies and zebrafish are related to the rate of oxidative metabolism. Preexposure of guppies to a high sublethal concentration of diazinon increases resistance to diazinon by a factor of 5 when compared to non-pretreated guppies; zebrafish similarly pretreated were not more resistant. Pretreatment of guppies resulted in a strong inhibition of diazoxon formation and pyrimidinol during incubations of diazinon with the hepatic postmitochondrial supernatant. It was concluded that toxicity of diazinon in the guppy is due to its metabolism to a highly toxic metabolite, likely diazoxon. And in zebrafish or pretreated guppies having low rates of diazinon metabolism, toxicity is due to the accumulation of the parent compound (Keizer et al. 1991, 1993). Limited data indicated that the yellowtail (*Seriola quinqueradiata*), a marine teleost, was 84 times more sensitive to diazinon than were four species of freshwater fishes, as judged by LC50 (48 h) values, and by its inability to biotransform diazinon to nontoxic metabolites within 1 h (Fujii and Asaka 1982). Diazinon has not been detected in marine waters, but the potential exists for contamination of estuarine areas from agricultural and urban runoff (Goodman et al. 1979).

Table 16.2 Acute Toxicity of Diazinon to Aquatic Organisms (All values shown are in micrograms of diazinon [active ingredients] per liter of medium fatal to 50% in 96 h.)

Ecosystem, Taxonomic Group, Organism, and Other Variables	LC50 (96 h) (g/L)	Reference ^a
FRESHWATER		
<i>Aquatic Plants</i>	>1000	14
Invertebrates		
Amphipod, <i>Gammarus fasciatus</i>	0.2	2, 14
Cladoceran, <i>Ceriodaphnia dubia</i>	0.5	14
Daphnid, <i>Daphnia magna</i>		
Dust (27%)	1.2	1
Emulsifiable concentrate (47.5%)	1.3	1
Technical grade (91.9%)	2.0	1
Oil solution (0.5%)	13.0	1
Cladoceran, <i>Simocephalus serrulatus</i>	1.4 ^b	2
Stonefly, <i>Pteronarcys californica</i>	25	2
Daphnid, <i>Daphnia pulex</i>	800 ^b	2
Rotifer, <i>Brachionus calyciflorus</i>	29,200	14
Fish		
European eel, <i>Anguilla anguilla</i>	80 (60–100)	11, 12, 15–17
Rainbow trout, <i>Oncorhynchus mykiss</i>	90–400	2, 3

Table 16.2 (continued) Acute Toxicity of Diazinon to Aquatic Organisms
 (All values shown are in micrograms of diazinon [active ingredients] per liter of medium fatal to 50% in 96 h.)

Ecosystem, Taxonomic Group, Organism, and Other Variables	LC50 (96 h) (g/L)	Reference ^a
Technical grade	110	1
Emulsifiable concentrate	3000	1
Dust	3200	1
Oil solution	19,000	1
Bluegill, <i>Lepomis macrochirus</i>	90–670	2–4, 14
Technical grade	120	1
Emulsifiable concentrate	530	1
Dust	170	1
Oil solution	160	1
Lake trout, <i>Salvelinus namaycush</i>	602	2
Brook trout, <i>Salvelinus fontinalis</i>	770	4
Guppy, <i>Poecilia reticulata</i>	800	14, 20
Flagfish, <i>Jordanella floridae</i>	1600	4
Cutthroat trout, <i>Oncorhynchus clarki</i>	1700	2
Freshwater fish, <i>Barilus vagra</i>	1900–2900	18
Murrel, <i>Channa punctatus</i>	3100	5
Common carp, <i>Cyprinus carpio</i>	3400–5000	18, 19
Fathead minnow, <i>Pimephales promelas</i>	5100–15,000	4, 6
Goldfish, <i>Carassius auratus</i>	9000	3
Zebrafish, <i>Brachydanio rerio</i>	8000	20
Tilapia, <i>Tilapia nilotica</i>	20,000	13
Amphibians		
Bullfrog, <i>Rana catesbeiana</i>	>2,000,000 ^c	7
MARINE		
Invertebrates		
Mysid shrimp, <i>Mysidopsis bahia</i>	4.8	8
Penaeid shrimp, <i>Penaeus aztecus</i>	28 ^b	8
Fish		
Sheepshead minnow, <i>Cyprinodon variegatus</i>	1470	9
Striped knifejaw, <i>Opelognathus fasciatus</i>		
Egg	3200 ^d	10
Prelarvae	5500 ^d	10
Postlarvae	25.1 ^d	10
Juvenile	27.8 ^d	10

^a 1, Meier et al. 1976; 2, Johnson and Finley 1980; 3, Anonymous 1972; 4, Allison and Hermanutz 1977; 5, Sastry and Malik 1982; 6, Jarvinen and Tanner 1982; 7, Hudson et al. 1984; 8, Nimmo et al. 1981; 9, Goodman et al. 1979; 10, Seikai 1982; 11, Sancho et al. 1993a; 12, Sancho et al. 1992b; 13, Sakr and Gabr 1992; 14, Menconi and Cox 1994; 15, Ferrando et al. 1991; 16, Sancho et al. 1992a; 17, Sancho et al. 1993b; 18, Adam and Maughan 1993; 19, Adam and Maughan 1992; 20, Keizer et al. 1991.

^b 48 h value.

^c Single oral dose, in mg/kg body weight.

^d 24 h value.

16.3.3 Birds

Diazinon adversely affects survival of developing mallard embryos when the eggshell surface is subjected for 30 seconds to concentrations 25 to 34 times higher than recommended field application rates. Mortality patterns were similar for solutions applied in water or in oil (Table 16.3).

Table 16.3 Mortality of Mallard Embryos after Immersion for 30 seconds in Graded Strength Diazinon Solutions

Age of Eggs (days)	Solution Vehicle (water or oil)	Diazinon Conc. (mg/L)	Percent Dead	Approximate Field Application Rate
3	Water	11	None	0.5
3	Water	110	3	5
3	Water	542	50	25
8	Water	597	50	27
3	Oil	13	None	0.6
3	Oil	133	7	6
3	Oil	648	50	29
8	Oil	741	50	34

Modified from Hoffman, D.J. and W.C. Eastin, Jr. 1981. Effects of malathion, diazinon, and parathion on mallard embryo development and cholinesterase activity. *Environ. Res.* 26:472-485.

This laboratory finding suggests that eggs of mallards, and probably other birds, are protected when diazinon is applied according to label directions. Chickens dipped in solutions containing 1000 mg of diazinon/L, an accidentally high formulation, experienced 60% mortality within 3 days; no other deaths occurred during the next 4 months (Sokkar et al. 1975). Results of 5-day feeding trials with 2-week-old Japanese quail (*Coturnix japonica*), followed by 3 days on untreated feed, showed an LD₅₀ of 167 mg diazinon/kg diet — a concentration considered “very toxic.” No deaths were observed at dietary levels of 85 mg diazinon/kg, but 53% died at 170 mg/kg, and 87% at 240 mg/kg (Hill and Camardese 1986).

Diazinon has a potential for causing acute avian poisoning episodes (Schafer et al. 1983). Ingestion of 5 granules of Diazinon 14G (14.3% diazinon) killed 80% of house sparrows (*Passer domesticus*), and all red-winged blackbirds to which they were administered (Balcomb et al. 1984). Ingestion of fewer than 5 granules of Diazinon 14G, each containing about 215 µg diazinon, could be lethal to sparrow-sized birds (i.e., 15 to 35 g body weight), especially juveniles of seed-eaters (Hill and Camardese 1984). Acute oral LD₅₀ values indicate that 15 mg diazinon/kg body weight is fatal to virtually all species tested, and that 2 to 5 mg/kg is lethal to the more sensitive species (Table 16.4). Signs of diazinon poisoning in birds included muscular incoordination, wing spasms, wing-drop, hunched back, labored breathing, spasmodic contractions of the anal sphincter, diarrhea, salivation, lacrimation (tear production), eyelid drooping, prostration, and arching of the neck over the back (Hudson et al. 1984). Most of these signs have been observed in birds poisoned by compounds other than diazinon; these compounds also act via an anticholinesterase mode of action (Hudson et al. 1984).

16.3.4 Mammals

Signs of diazinon poisoning in mammals included a reduction in blood and brain cholinesterase activity, diarrhea, sweating, vomiting, salivation, cyanosis, muscle twitches, convulsions, loss of reflexes, loss of sphincter control, and coma (Anonymous 1972). Other compounds that produce their toxic effects by inhibiting AChE, such as organophosphorus pesticides and many carbamates, show similar effects (Murphy 1975). Two species of marmoset accidentally poisoned by diazinon exhibited — prior to death — high-pitched voices, trembling, frog-like jumping, a stiff gait, and pale oral mucous membranes. Internally, bone marrow necrosis and hemorrhages in several organs were evident (Brack and Rothe 1982). Internal damage was also observed in swine and dogs that died following controlled administration of diazinon. Swine showed histopathology of liver and intestinal tract, and duodenal ulcers; dogs showed occasional rupture of the intestinal wall and testicular atrophy (Earl et al. 1971).

Results of acute oral toxicity tests indicated that the rat was the most sensitive mammalian species tested, with an acute oral LD50 of 224 mg diazinon/kg body weight (Table 16.4). It is clear that mammals are significantly more resistant to acute oral poisoning by diazinon than birds (Table 16.4). Diazinon was also toxic to mammals when administered dermally, through inhalation, and in the diet (Table 16.5). The lowest dermal LD50 recorded was 600 mg diazinon/kg body weight for rabbits (*Lepus* sp.) using an emulsifiable (4E) formulation. The single datum for inhalation toxicity indicated that 27.2 mg of diazinon/L of air killed 50% of test rabbits after exposure for 4 h (Table 16.5). Pregnant mice fed diets containing 9 mg of diazinon/kg during gestation all survived, but some pups died prior to weaning (Table 16.5). Results of chronic oral toxicity tests of diazinon indicated that death was probable if daily doses exceeded 5 mg/mg body weight for swine, or 10 mg/kg for dogs (Table 16.5).

Table 16.4 Acute Oral Toxicity of Diazinon to Birds and Mammals (All values shown are in milligrams of diazinon/kg body weight fatal to 50% after a single oral dose.)

Taxonomic Group, Organism, and Other Variables	LD50 (range) (mg/kg body weight)	Reference ^a
BIRDS		
Turkey, <i>Meleagris gallopavo</i>	2.5	1
Red-winged blackbird, <i>Agelaius phoeniceus</i>		
Age 0–3 days	2.4 (1.3–6.1)	9
Age unspecified	2.6	2
Age 4–7 days	3.4	9
Age 8–11 days	8.3 (6.6–10.0)	9
Adults	9.1 (3.9–15.9)	9
Goslings, <i>Anser</i> spp.	2.7	1
Turkey	3.5	3
Ducks, <i>Anas</i> spp.	3.5	3
Mallard, <i>Anas platyrhynchos</i>	3.5 (2.4–5.3)	4, 5
European quail, <i>Coturnix coturnix</i>	4.2	2
Ring-necked pheasant, <i>Phasianus colchicus</i>	4.3 (3.0–6.2)	4, 5
Northern bobwhite, <i>Colinus virginianus</i>	5.0 ^b	6
Chicks, <i>Gallus gallus</i>	5.0 ^c	1
Chicken, <i>Gallus gallus</i>	9.0	3
Turkey	10.0 ^c	1
European starling, <i>Sturnus vulgaris</i>		
Age 0–3 days	12.7 (10.9–15.1)	9
Age 8–11 days	93.2	9
Age unspecified	213	2
Adults	602	9
Ducklings	14.0	1
Northern bobwhite	14.7	6
Northern bobwhite	25.0 ^c	6
MAMMALS		
Rat, <i>Rattus rattus</i>	425	3, 5
Technical grade	350	7
AG 500 (granule)	327	7
4 E (emulsion)	542	7
4 S (spray)	735	7
50 W (wettable)		
Males	521	7
Females	224	7
Pig, <i>Sus scrofa</i>	400	3
Guinea pig, <i>Cavia cobaya</i>	450	3

Table 16.4 (continued) Acute Oral Toxicity of Diazinon to Birds and Mammals
 (All values shown are in milligrams of diazinon/kg body weight fatal to 50% after a single oral dose.)

Taxonomic Group, Organism, and Other Variables	LD50 (range) (mg/kg body weight)	Reference ^a
Dog, <i>Canis familiaris</i>	>500	8
Sheep, <i>Ovis aries</i>	>1000	3

^a 1, Egyed et al. 1974; 2, Schaefer et al. 1983; 3, Machin et al. 1975; 4, Hudson et al. 1984; 5, Zinkl et al. 1978; 6, Hill et al. 1984; 7, Anonymous 1972; 8, Earl et al. 1971; 9, Wolf and Kendall 1998.

^b No mortality seen.

^c All animals tested died.

Table 16.5 Toxicity of Diazinon to Laboratory Animals via Dermal, Inhalation, Dietary, and Chronic Oral Routes of Administration

Mode of Administration, Units, Organism, Formulations, and Other Variables	Dose	Effect	Reference ^a
DERMAL, mg/kg body weight			
Rabbit, <i>Lepus</i> sp.			
AG-500 (granule)	900	LD50	1
4 E (emulsion)	600	LD50	1
4 S (spray)	735	LD50	1
14 G (granule)	>15,400	LD50	1
50 W (wettable)	>2000	LD50	1
Mice, <i>Mus musculus</i>			
Technical diazinon	2750	LD50	2
INHALATION, mg/L air			
Rabbit ^b	27.2	LC50	1
DIETARY, mg/kg diet, during gestation only			
Mice	0.18	No pup deaths at weaning	3
Mice	9	12% of pups dead prior to weaning	3
CHRONIC ORAL, mg/kg body weight daily			
Dog, <i>Canis familiaris</i>	10	None dead in 8 months	4
Dog	20	All dead in 30 days	4
Dog	25	None dead in 15 days	4
Dog	50	None dead in 4 days	4
Swine, <i>Sus scrofa</i>	5	None dead in 8 months	4
Swine	10	75% dead in 30 days	4

^a 1, Anon., 1972; 2, Skinner and Kilgore 1982; 3, Barnett et al. 1980; 4, Earl et al. 1971.

^b Exposure for 4 h to 4% aqueous suspension.

16.3.5 Terrestrial Invertebrates

Accidental spraying of beehives in Connecticut with diazinon resulted in a complete kill of resident honeybees. Dead bees contained up to 3 mg diazinon/kg (Anderson and Glowa 1984). Diazinon is an effective insecticide. LD50 values for diazinon and adult houseflies (*Musca domestica*), applied topically, were 0.4 µg/insect, or 4.6 mg/kg body weight (Negherbon 1959). LD50 values for larvae of the large white butterfly, applied topically, were 8.8 mg/kg body weight for diazinon, and 11.0 mg/kg body weight for diazoxon (Wahla et al. 1976). Pretreatment of larvae

with methylene dioxyphenyl compounds antagonized the action of diazinon by a factor of about 2, but synergized the action of diazoxon by an order of magnitude (Wahla et al. 1976).

16.4 SUBLETHAL EFFECTS

16.4.1 General

Among sensitive species of aquatic organisms, diazinon was associated with reduced growth and reproduction in marine and freshwater invertebrates and teleosts, spinal deformities in fish, reduced emergence in stream insects, measurable accumulations in tissues, increased numbers of stream macroinvertebrates carried downstream by currents (drift), possible mutagenicity in fish, and interference with algal–invertebrate interactions. In birds, diazinon is a known teratogen. It is also associated with reduced egg production, decreased food intake, and loss in body weight. Diazinon fed to pregnant mice resulted in offspring with brain pathology, delayed sexual maturity, and adverse behavioral modifications that became apparent late in life. For all groups tested, diazinon directly or indirectly inhibited cholinesterase activity.

16.4.2 Aquatic Organisms

Atlantic salmon (*Salmo salar*) exposed to 0.3 to 45.0 µg diazinon/L for 120 h had reduced levels of reproductive steroids in blood plasma at all concentrations. Exposure to 2 µg/L for only 30 min produced a significant reduction in olfactory response to prostaglandin F_{2a} (Moore and Waring 1996). Carp and other species of freshwater teleosts that survived high sublethal concentrations of diazinon had impaired swimming and abnormal pigmentation (Alam and Maughan 1992). Spinal deformities, mostly lordosis and scoliosis, were among the more insidious effects documented for diazinon. Malformations were observed in fathead minnows (*Pimephales promelas*) after 19 weeks in water containing 3.2 µg diazinon/L (Allison and Hermanutz 1977), in yearling brook trout (*Salvelinus fontinalis*) within a few weeks at 4.8 µg/L (Allison and Hermanutz 1977), and in various species of freshwater teleosts after exposure for 7 days to 50 µg diazinon/L (Kanazawa 1978). Exposure of bluegills (*Lepomis macrochirus*) to 15 µg diazinon/L for only 24 h resulted in mild hyperplasia of the gills that increased in severity with increasing concentration (30 to 75 µg/L) and may lead to death (Dutta et al. 1993).

Diazinon is a noncarcinogen and reportedly has no significant mutagenic activity in microbial systems, yeast, and mammals, including humans (as quoted in Vigfusson et al. 1983). However, Vigfusson et al. (1983) have measured a significant increase in the frequency of sister chromatid exchange in central mud minnows (*Umbra limi*) that were exposed *in vivo* for 11 days to solutions containing 0.16 to 1.6 µg diazinon/L. This finding requires verification.

In general, diazinon does not bioconcentrate to a significant degree and is rapidly excreted after exposure (Menconi and Cox 1994; Tsuda et al. 1995). Diazinon in water is bioconcentrated by brook trout at levels as low as 0.55 µg/L, but tissue residues for all aquatic organisms seldom exceeds 213 times that of ambient water, even after months of continuous exposure (Table 16.6). Common carp (*Cyprinus carpio*) exposed to 1.5 to 2.4 µg/L for 168 h had bioconcentration factors of 12 in muscle, 12 in gallbladder, 50 in kidney, and 51 in liver; almost all was excreted in 72 h on transfer to clean water, except for kidney, which is the major organ for excretion (Tsuda et al. 1990). High bioconcentration factors of 800 in liver, 1600 in muscle, 2300 in gill, and 2730 in blood are reported for juvenile European eels (*Anguilla anguilla*) after exposure to 42 to 56 µg/L for 96 h. However, diazinon residues in tissues were usually not detected in tissues after 24 h in clean water (Sancho et al. 1992b, 1993a). The half-time persistence of diazinon in tissues of European eels was estimated at 17 to 31 h in liver, 32 to 33 h in muscle, and 27 to 38 h in gill

Table 16.6 Accumulation of Diazinon by Aquatic Organisms

Ecosystem, Taxonomic Group, Organism, and Other Variables	Diazinon Concentration in Water (g/L)	Exposure Period ^a	Concentration Factor	Reference ^b
FRESHWATER				
Invertebrates				
Crayfish, <i>Procambarus clarkii</i>				
Whole	10	7 d	5	1
Pond snail, <i>Cipangopoludina malleata</i>				
Whole	10	7 d	6	1
Red snail, <i>Indoplanorbis exustus</i>				
Whole	10	7 d	17	1
Shrimp, <i>Penaeopsis joyneri</i>				
Whole	20	14 d	3	2
Whole	20	14 d + 7 d pt ^a	<1	2
Fish				
4 spp., whole	10	7 d	18–152	1
3 spp., whole	20	14 d	26–120	2
3 spp., whole	20	14 d + 7 d pt	<1	2
Medaka, <i>Oryza latipes</i> , whole	4.5	3 d	27	5
Topmouth gudgeon, <i>Pseudorasbora parva</i>				
Whole	10	14 d	173	1
Whole	10	14 d + 1 d pt	72	1
Whole	10	14 d + 4 pt	8	1
Whole	10	14 d + 8 d pt	<1	1
Brook trout, <i>Salvelinus fontinalis</i>				
Adult				
Muscle	0.55	8 m	25	3
Blood	1.1	6 m	17	3
Muscle	1.1	8 m	25	3
Muscle	2.4	8 m	35	3
Blood	4.8	6 m	13	3
Muscle				
Mature male	4.8	8 m	24	3
Spawned female	4.8	8 m	19	3
Immature male	4.8	8 m	51	3
Adult female				
Egg	9.6	8 m	151	3
Muscle	9.6	8 m	34	3
MARINE				
Fish				
Sheepshead minnow, <i>Cyprinodon variegatus</i>				
Whole	1.8	4 d	147	4
Whole	3.5	4 d	147	4
Whole	6.5	4 d	213	4
Whole	6.5	4 d + 8 d pt	<1	4
Whole	6.5	108 d	<1	4
Egg	<0.98	LC ^a	<1	4
Egg	1.8–6.5	LC ^a	10–13	4

^a d = days; m = months; pt = posttreatment observation period; LC = life cycle

^b 1, Kanazawa 1978; 2, Seguchi and Asaka 1981; 3, Allison and Hermanutz 1977; 4, Goodman et al. 1979; 5, Tsuda et al. 1995.

(Sancho et al. 1992a, 1992b, 1993b). Whole guppies exposed to high sublethal concentrations of diazinon show bioconcentration factors of 59 after 48 h and 188 after 144 h; the half-time persistence of diazinon was 10 h after 48-h exposure and 23 h after 144-h exposure (Keizer et al. 1993). Diazinon and its metabolites are excreted rapidly posttreatment; the loss rate is approximately linear (Kanazawa 1978). The enzyme system responsible for diazinon metabolism in fish liver microsomes required NADPH and oxygen for the oxidative desulfuration of diazinon to diazoxon (Hogan and Knowles 1972). Fish with high fat content contained greater residues of diazinon in fatty tissues than did fish with comparatively low lipid content (Seguchi and Asaka 1981), and this could account, in part, for inter- and intraspecies variations in uptake and depuration. Some organisms, such as the sheepshead minnow (*Cyprinodon variegatus*), have measurable diazinon residues during initial exposure to 6.5 µg/L, but no detectable residues after lengthy exposure (Goodman et al. 1979), suggesting that physiological adaptation resulting in rapid detoxification is possible.

Freshwater and marine alga were unaffected at water diazinon concentrations that were fatal (i.e., 1000 µg/L) to aquatic invertebrates (Stadnyk and Campbell 1971; Shacklock and Croft 1981). However, diazinon at 1.0 µg/L induced extensive clumping of a freshwater alga (*Chlorella pyrenoidosa*) onto the antennae of *Daphnia magna* within 24 h (Stratton and Corke 1981). The affected daphnids were immobilized and settled to the bottom of the test containers. The causes of particulate matter adhesion are open to speculation, and additional research is merited.

Freshwater macroinvertebrates were comparatively sensitive to diazinon (Table 16.7). Results of large-scale experimental stream studies (Arthur et al. 1983) showed that dose levels of 0.3 µg diazinon/L caused a five- to eightfold reduction in emergence of mayflies and caddisflies within 3 weeks. After 12 weeks, mayflies, damselflies, caddisflies, and amphipods were absent from benthic samples. Elevated (and catastrophic) drift of stream invertebrates was also documented in diazinon-treated streams, especially for amphipods, leeches, and snails (Arthur et al. 1983). Short-term tests of 5-h duration with rotifers (*Brachionus calyciflorus*) show a 50% reduction in feeding

Table 16.7 Lowest Tested Diazinon Concentrations in Medium that Produced Significant Nonlethal Biological Effects to Aquatic Organisms

Ecosystem and Taxonomic Group	Concentration (g/L)	Effect	Reference ^a
FRESHWATER			
<i>Invertebrates</i>			
Insects	0.3	Lowered emergence	1
Amphipods	0.3	Elevated drift	1
Daphnids	1.0	Immobilization	2
<i>Fish</i>			
Brook trout, <i>Salvelinus fontinalis</i>	0.55	Reduced growth of progeny	3
Fathead minnow, <i>Pimephales promelas</i>	3.2	Reduced hatching success	3
Flagfish, <i>Jordanella floridae</i>	14.0	Reduced larval growth	4
Bluegill, <i>Lepomis macrochirus</i>	15.0	Gill histopathology	6
MARINE			
<i>Invertebrates</i>			
Mysid shrimp, <i>Mysidopsis bahia</i>	3.2	Reduced growth and reproduction	5
<i>Fish</i>			
Sheepshead minnow, <i>Cyprinodon variegatus</i>	0.47	Reduced fecundity	3

^a 1, Arthur et al. 1983; 2, Stratton and Corke 1981; 3, Goodman et al. 1979; 4, Allison and Hermanutz 1977; 5, Nimmo et al. 1981; 6, Dutta et al. 1993.

rate on alga (*Nannochloris oculata*) at 14.2 mg/L (Fernandez-Casalderry et al. 1992), with long-term implications to population stability.

Freshwater fish populations can be directly damaged by prolonged exposure to diazinon at concentrations up to several hundred times lower than those causing acute mortality (Sastry and Sharma 1980; Sastry and Malik 1982; Saker and Gabr 1992; Dutta et al. 1997; [Table 16.7](#)). Impaired reproduction and AChE inhibition occurs concurrently in teleosts during long-term exposure to diazinon, but reproduction can be impaired for at least 3 weeks after fish are placed in uncontaminated water, even though AChE is normal and they contained no detectable diazinon residues (Goodman et al. 1979). Furthermore, diazinon exposure during spawning caused complete, but temporary, inhibition of reproduction at concentrations that did not produce this effect in fish exposed since hatch (Allison 1977). This could severely impact aquatic species with a short reproductive period (Allison 1977).

16.4.3 Birds

Diazinon produces visible Type I and II teratisms when injected into chicken embryos (Misawa et al. 1981, 1982; Henderson and Kitos 1982; Wyttenbach and Hwang 1984). Type I teratisms (related to tissue NAD depression) included abnormal beaks, abnormal feathering, and shortened limbs. Type II teratisms, which included short and wry neck, leg musculature hypoplasia, and rumplessness were associated with disruptions in the nicotinic cholinergic system. The severity of effects depended on embryo age and was dose related. Chick embryos (age 48 h) receiving 25 µg or more of diazinon/embryo had cervical notochord and neural tube malformations at 96 h, and short neck at 19 days (Wyttenbach and Hwang 1984). Wry neck occurred at doses ranging from 6.2 to 100 µg/embryo, but was more frequent at higher doses. Type II teratisms were attributed to disruption of notochord sheath formation. Coinjection of 2-pyridinealdoxime methochloride (2-PAM) along with 200 µg diazinon/embryo markedly reduced notochord and neural tube deformations (Wyttenbach and Hwang 1984). Similarly, the co-presence of tryptophan — or its metabolites L-kynurenine, 3-hydroxyanthronilic acid, quinolinic acid — maintained NAD levels of diazinon-treated embryos close to, or above, normal, and significantly alleviated the symptoms of Type I teratisms (Henderson and Kitos 1982).

Reduced egg production, depressed food consumption, and loss in body weight have been observed in ring-necked pheasants at daily diazinon intakes greater than 1.05 mg/bird; a dose-related delay in recovery of egg laying was noted after termination of diazinon treatment (Stromborg 1977, 1979). Threshold levels in ring-necked pheasants of 1.05 and 2.1 mg diazinon daily corresponded to 1/16 and 1/8 of daily ration (70 g) treated at commercial application rates. Food consumption of ring-necked pheasants was reduced significantly when only food treated with diazinon was available; pheasants avoided diazinon-treated food if suitable alternatives existed (Stromborg 1977; Bennett and Prince 1981). Dietary levels above 50 mg/kg were associated with reduced food consumption, weight loss, and reduction in egg production in northern bobwhites (Stromborg 1981). If food reduction is important, then diets containing more than 17.5 mg diazinon/kg (based on empirical calculations) were potentially harmful to bobwhites (Stromborg 1981). The mechanisms accounting for reduction in egg deposition are not clear, but are probably related primarily to decreased food intake. They may also be associated with diazinon-induced pituitary hypofunction at the level of the hypothalamus, resulting in reduced synthesis and secretion of gonadotrophic, thyrotrophic, and adrenocorticotropic hormones (Sokkar et al. 1975).

16.4.4 Mammals

Diazinon exerts its toxic effects by binding to the neuronal enzyme acetylcholinesterase (AChE) for long periods after exposure. Diazinon, in turn, is converted to diazoxon, which has a higher affinity for AChE (and thus greater toxicity) than the parent compound. There is a latent period in

white-footed mice in reduction of cholinesterase activities, sometimes up to 6 h, until diazinon is converted to diazoxon (Montz 1983). Effects of multiple doses of diazinon to mammals are not clear; for example, rats exposed to a high dose of diazinon did not respond fully to a second dose until 1 month later (Kikuchi et al. 1981). It is difficult to ascertain when complete recovery of diazinon-poisoned animals has occurred. It is speculated, but not verified, that wildlife recovering from diazinon poisoning may face increased predation, aberrant behavior, learning disabilities, hypothermia, and reproductive impairments (Montz 1983). Data are lacking on recovery aspects of diazinon-poisoned native mammal populations (Montz and Kirkpatrick 1985).

Diazinon is rapidly biotransformed and excreted in mammals. Estimated half-times of diazinon persistence were 6 to 12 h in rats (Anonymous 1972) and dogs (Iverson et al. 1975). Most of the diazinon metabolites were excreted in the urine as diethyl phosphoric acid and diethyl phosphorothioic acid in dogs (Iverson et al. 1975), and as hydroxy diazinon and dehydrodiazinon in sheep (Machin et al. 1974).

Determination of AChE activity in selected tissues following diazinon exposure provided an estimate of potential toxicity, but tissue sensitivity varied widely between and among taxa. In sheep, brain cholinesterase inhibition was pronounced after diazinon insult, and metabolism of diazinon in, or close to, the brain was the most likely source of toxicologically effective diazoxon (Machin et al. 1974, 1975). In rat, diazinon effectively reduced blood cholinesterase levels, with inhibition significantly more evident in erythrocytes than in plasma (Tomokuni and Hasegawa 1985). All mammalian bloods hydrolyze diazoxon rapidly, whereas birds have virtually no hydrolytic activity in their blood, and, as a result, were more susceptible than mammals. The stability of diazoxon in the blood appears to be a primary factor in susceptibility to diazinon poisoning (Machin et al. 1975). In species lacking blood oxonases, the liver was probably the most important site of diazinon metabolism (Machin et al. 1975). Diazinon that accumulated in rat liver was biotransformed, usually within 24 h, by microsomal mixed-function oxidases and glutathione S-transferases. However, diazinon residues in rat kidney were almost 500 times those in liver (and 11 times brain), and were measurable in kidney but not in liver (Tomokuni and Hasegawa 1985). It now seems that diazinon residues in kidney and cholinesterase inhibition in erythrocytes are the most useful indicators of acute diazinon poisoning in mammals.

Sublethal effects of diazinon have been recorded in rodents, the most sensitive mammal group tested. Effects were measured at 0.5 mg diazinon/kg in diets of rats for 5 weeks, at 0.18 mg/kg body weight administered daily to pregnant mice, and at single doses of 1.8 mg/kg body weight for rat and 2.3 mg/kg body weight for white-footed mice (Table 16.8). Many variables modify diazinon-induced responses, including the organism's sex. For example, female rats and dogs were more sensitive to diazinon than males (Earl et al. 1971; Davies and Holub 1980a, 1980b; Kikuchi et al. 1981), but male swine were more sensitive than females (Earl et al. 1971).

Behavioral deficits observed in offspring of mice exposed to diazinon during gestation indicated that prenatal exposure may produce subtle dysfunctions not apparent until later in life (Spyker and Avery 1977). Pregnant mice given a daily dose of 0.18 or 9 mg diazinon per kg body weight throughout gestation gave birth to viable, overtly normal, offspring. But, pups born to mothers of the 9 mg/kg groups grew more slowly than controls and were significantly smaller at 1 month than controls (Spyker and Avery 1977). Offspring of mothers receiving 0.18 mg/kg body weight exhibited significant delays in the appearance of the contact placing reflex and in descent of testes or vaginal opening. Mature offspring of mothers exposed to either dose level displayed impaired endurance and coordination on rod cling and inclined plane tests of neuromuscular function (Table 16.8). In addition, offspring of the 9-mg/kg-dose group had slower running speeds and less endurance in a swimming test than controls. At 101 days, forebrain neuropathology was evident in the 9-mg/kg group but not in the 0.18-mg/kg group. The mechanisms responsible for these effects are unknown (Spyker and Avery 1977).

Diazinon is nonmutagenic to mammals, as judged by its inability to induce sister chromatid exchanges (SCE) in Chinese hamster ovary cells (CHOC) at 80 mg/kg culture medium. Most organophosphorus insecticides tested induced SCE in CHOC at this concentration (Nishio and

Table 16.8 Sublethal Effects of Diazinon in Selected Mammals

Organism and Dose^a	Exposure Period	Effect	Reference^b
RAT, <i>Rattus rattus</i>			
0.009 (BW)	5 weeks	No effect	1
0.1 (D)	5 weeks	No effect	1
0.5 (D)	5 weeks	Depressed plasma cholinesterase	1
1.8 (BW)	Single dose	Elevated serum glucuronidase	2
2 (D)	1 week	Depressed plasma cholinesterase (females only)	3
3.8 (BW)	Single dose	Altered blood chemistry	4
10 (D)	2 years	Cholinesterase inhibition	5
1000 (D)	2 years	Reduced growth	5
1000 (D)	3 generations	No malformations, no effect on reproduction	5
MOUSE, <i>Mus musculus</i>			
(pregnant)			
0.18 (BW)	2.8 weeks	Altered behavior and delayed sexual maturity of progeny	6
9 (BW)	Throughout gestation	Reduced growth and altered serum immunoglobulins of progeny; some deaths	7
MOUSE (juveniles)			
0.18 (BW)	14.4 weeks	Impaired endurance and coordination	6
9 (BW)	14.4 weeks	Brain pathology	6
WHITE-FOOTED MICE, <i>Peromyscus leucopus</i>			
2.3 (BW)	Single dose	9% depression in brain AChE in 24 h	8
17.3 (BW)	Single dose	60% depression in brain AChE in 6 h	9
DOG, <i>Canis familiaris</i>			
4 (BW)	Single dose	39% reduction in serum cholinesterase in 10 min; 50% reduction in 3.5 h	10
4.3–5.3 (BW)	43 weeks	Cholinesterase inhibition	5
10 (BW)	8 months	Testicular atrophy, cholinesterase inhibition	11
75 (BW)	Single dose	Acute pancreatitis	12
SWINE, <i>Sus scrofa</i>			
5 (BW)	8 months	Cholinesterase inhibition, duodenal ulcers, liver pathology	11
SHEEP, <i>Ovis aries</i>			
Sprayed with 100 mg/L diazinon solutions	4 min	Effective lice control for 3 weeks, partial protection for 8.6 weeks	13
450–650 (BW)	Single dose	Flesh unfit for human consumption for several weeks (high fat residues of 333–520 mg/kg)	14
MONKEYS, several species			
0.5 (BW)	2.04 years	None	5
5 (BW)	2.04 years	Cholinesterase inhibition	5

^a D = mg/kg diet; BW = mg/kg body weight daily.^b 1, Davies and Holub 1980a; 2, Kikuchi et al. 1981; 3, Davies and Holub 1980b; 4, Lox 1983; 5, Anonymous 1972; 6, Spyker and Avery 1977; 7, Barnett et al. 1980; 8, Montz 1983; 9, Montz and Kirkpatrick 1985; 10, Iverson et al. 1975; 11, Earl et al. 1971; 12, Dressel et al. 1982; 13, Wilkinson 1980; 14, Machin et al. 1974.

Uyeki 1981; Chen et al. 1982). Diazoxon, an oxygen analog of diazinon, did produce SCE at 304 mg/kg, but was 3 to 10 times less effective than oxygen analogues of other organophosphorus compounds screened (Nishio and Uyeki 1981).

16.4.5 Terrestrial Invertebrates

Tobacco hornworms (*Manduca sexta*) from a field sprayed with 840 mg diazinon/ha contained no detectable residues of diazoxon. Only one sample, collected about 4 h after spraying, exceeded 1.0 mg diazinon/kg body weight. No diazinon residues in these insects were detectable after 18 days.

It was concluded that the potential hazard to birds eating hornworms was minimal (Stromborg et al. 1982). In contrast, diazinon residues in molluscan slugs (*Agriolimax reticulatus*), collected from plats of spring wheat sprayed with 8000 mg diazinon/ha, increased linearly to about 200 mg/kg at 6 weeks postapplication, then declined to background levels after 16 weeks (Edwards 1976). During this same period, soil residues decreased from about 4 mg/kg immediately after application, to about 1 mg/kg at 6 weeks, and were not detectable after 12 weeks. The high residues observed in slugs may be due, in part, to physical adsorption of diazinon to slug mucus. Edwards (1976) concluded that slugs heavily contaminated by diazinon constituted a serious danger to birds and mammals feeding on them.

Depuration rates of diazinon differed significantly for two species of nematodes, *Panagrellus redivivus* and *Bursaphelenchus xylophilus* (Al-Attar and Knowles 1982). Both species showed maximum uptake of radiolabeled diazinon between 6 and 12 h, and both metabolized diazinon to diazoxon and pyrimidinol. By 96 h, 95% of the diazinon in *P. redivivus* had been metabolized, but only 26% was transformed in *B. xylophilus*, again demonstrating variability in diazinon metabolism between related species.

16.5 RECOMMENDATIONS

As shown earlier, certain aquatic organisms were impacted by diazinon water concentrations between 0.3 and 1.2 µg/L; effects included lowered emergence and elevated drift of stream insects (0.3 µg/L), reduced fecundity of marine minnows (0.47 µg/L), accumulations in freshwater teleosts (0.55 µg/L), and daphnid immobilization (1.0 µg/L) and death (1.2 µg/L). These comparatively low levels are of concern because transient peak water concentrations of 4 to 200 µg diazinon/L have been recorded near diazinon sheep-dipping sites in England (Moore and Waring 1996), and 36.8 µg/L in the Sacramento–San Joaquin River, California (Menconi and Cox 1994). For protection of sensitive aquatic organisms, Arthur et al. (1983) recommended that water diazinon levels should not exceed 0.08 µg/L. This value represents a safety factor of about 4 over the lowest recorded adverse effect level of 0.3 µg/L. For protection of freshwater aquatic life, Menconi and Cox (1994) recommend an average 4-day concentration of 0.04 µg diazinon/L provided that this value is not exceeded more than once every 3 years and the maximum 1-h concentration does not exceed 0.08 µg/L more than once every 3 years. Safety factors may require adjustment as additional data become available. Establishment of safe levels is complicated by the fact that diazinon can persist for many months in neutral or basic waters, including seawater (Kanazawa 1978), but hydrolyzes rapidly in acidic waters (Allison and Hermanutz 1977). Data on chronic effects of fluctuating and intermittent exposures of fishes and invertebrates to diazinon are also needed, and these will aid in the establishment of safe concentrations for this organophosphorus pesticide (Allison and Hermanutz 1977).

Granular formulations were especially hazardous to seed-eating birds; ingestion of fewer than 5 granules of a Diazinon 14G formulation could be lethal (Hill and Camardese 1984). A reduction in diazinon content of existing granular formulations may become necessary in application areas frequented by high densities of seed-eating birds. Stone and Gradoni (1985) recommend that diazinon should not be used in areas where waterfowl feed, especially turfgrass. Suggested alternatives to diazinon for turfgrass use include Dursban (*O,O*-diethyl *O*-(3,5,6-trichloro-2-pyridyl)-phosphorothioate), Dylox (dimethyl (2,2,2-trichloro-1-hydroxyethyl) phosphonate), Carbaryl (1-naphthyl *N*-methylcarbamate), and Lannate (*S*-methyl-*N*-((methylcarbamoyl)oxy)-thioacetimidate) (Stone 1980; Stone and Gradoni 1985). Diazinon should be used with caution in large-scale spray applications — such as grasshopper control — as judged by some deaths of horned larks (*Eremophila alpestris*), lark buntings (*Calamospiza melanocorys*), western meadowlarks (*Sturnella neglecta*), and chestnut-collared longspurs (*Calciarius ornatus*) when used for this purpose in Wyoming (McEwen et al. 1972). Diazinon applications to agricultural crops comprised a relatively

small percentage of the reported mortality incidents, but it is likely that this category is under-reported since such incidents were probably less conspicuous than those noted on lawns and golf courses (Stone and Gradoni 1985). Also, diazinon interactions with other agricultural chemicals, such as Captan (*cis*-*N*-((trichloromethyl)thio)-4-cyclohexene-1,2-dicarboximide), may produce more-than-additive (but reversible) adverse effects on food consumption and egg production of ring-necked pheasants (Stromborg 1977). More research is needed on complex mixtures of agricultural pesticides that contain diazinon.

In female rats, the no-observable-effect level (NOEL) is 0.1 mg/kg of dietary diazinon. At 0.5 mg/kg, there was a marked lowering of plasma cholinesterase activity in 5 weeks (Davies and Holub 1980a). But studies with male rats indicate that the NOEL is 2 mg/kg of dietary diazinon, or about 20 times higher than female rats (Davies and Holub 1980b). Accordingly, future studies should consider sex as a variable in toxicity evaluation of diazinon. It is generally agreed that mammals are more resistant than birds to diazinon owing, in part, to their ability to rapidly metabolize diazoxon. However, data are missing on the effects of diazinon on native mammals under field conditions, and this should constitute a priority research area. No diazinon criteria to protect human health have been proposed by the U.S. Food and Drug Administration or the state of California (Menconi and Cox 1994).

16.6 SUMMARY

Diazinon (phosphorothioic acid *O,O*-diethyl *O*-(6-methyl-2-(1-methylethyl)-4-pyrimidinyl) ester) is an organophosphorus compound with an anticholinesterase mode of action. It is used extensively to control flies, lice, insect pests of ornamental plants and food crops, as well as nematodes and soil insects in lawns and croplands. Diazinon degrades rapidly in the environment, with half-time persistence usually less than 14 days. But under conditions of low temperature, low moisture, high alkalinity, and lack of suitable microbial degraders, diazinon may remain biologically active in soils for 6 months or longer.

At recommended treatment levels, diazinon-related kills have been noted for songbirds, honeybees, and especially waterfowl that consume diazinon-treated grass. However, incidents involving agricultural applications may be underreported. Accidental deaths through misapplication of diazinon have also been recorded in domestic poultry, monkeys, and humans. It has been suggested, but not yet verified, that wildlife partially disabled in the field as a result of diazinon poisoning would be more likely to die of exposure, predation, starvation, or dehydration, or face behavioral modifications, learning impairments, and reproductive declines than would similarly treated domestic or laboratory animals.

Among sensitive aquatic organisms, LC50 (96 h) values of 1.2 to 2.0 µg/L were derived for freshwater cladocerans, and 4.1 to 5.9 µg/L for marine shrimps; freshwater teleosts were comparatively resistant, with all LC50 (96 h) values greater than 80 µg/L. Sublethal effects were recorded at 0.3 to 3.2 µg diazinon/L and included reduced emergence of stream insects (0.3 µg/L), reduced fecundity of a marine fish (0.47 µg/L), significant accumulations in freshwater teleosts (0.55 µg/L), daphnid immobilization (1.0 µg/L), potential mutagenicity in a freshwater fish (1.6 µg/L), and spinal deformities in teleosts (3.2 µg/L). Exposure to diazinon during spawning caused temporary, but complete, inhibition of reproduction at concentrations that did not produce this effect in fish exposed continuously since hatch.

Acute oral LD50 values of about 2500 to 3500 µg diazinon/kg body weight were determined for goslings (*Anser* spp.), ducks (*Anas* spp.), domestic turkey (*Meleagris gallopavo*), and the red-winged blackbird (*Agelaius phoeniceus*), the most sensitive birds tested. A dietary LD50 of 167,000 µg diazinon/kg was determined for Japanese quail (*Coturnix japonica*). Diazinon produced marked teratogenic effects in embryos of the domestic chicken (*Gallus gallus*) at 6.2 to 25 µg/embryo, reduced egg deposition in the ring-necked pheasant (*Phasianus colchicus*) at more

than 1050 µg/bird, and (empirically) decreased food consumption and increased weight loss in the northern bobwhite (*Colinus virginianus*) at greater than 17,500 µg diazinon/kg diet.

The rat (*Rattus rattus*) was the most sensitive mammal tested in acute oral toxicity screenings, with an LD₅₀ of 224,000 µg diazinon/kg body weight. Chronic oral toxicity tests with swine (*Sus scrofa*) indicated that death was probable if daily intakes were greater than 5000 µg diazinon/kg body weight. Measurable adverse effects of diazinon have been recorded in rodents, the most sensitive mammalian group tested: at 500 µg/kg in diets fed to rats for 5 weeks, causing blood cholinesterase inhibition; 180 µg/kg body weight administered daily to pregnant mice (*Mus musculus*) during gestation, inducing behavioral modifications and delayed sexual maturity of progeny; and single oral doses of 1800 and 2300 µg/kg body weight in rats and white-footed mice (*Peromyscus leucopus*), respectively, producing altered blood chemistry and brain cholinesterase inhibition.

For protection of sensitive aquatic organisms, diazinon concentrations in water should not exceed 0.08 µg/L. However, more data are needed on effects of fluctuating and intermittent chronic exposures of diazinon on reproduction of fish and aquatic invertebrates. Granular formulations of diazinon seem to be especially hazardous to seed-eating birds, suggesting a need to control or eliminate granular applications when these species are present. For additional protection of birds, diazinon should be used with extreme caution in areas where waterfowl feed, and in large-scale spray applications such as grasshopper control. Diazinon in combination with some agricultural chemicals produced more-than-additive adverse effects on bird growth and fecundity; accordingly, more research is needed on effects of complex mixtures of pesticides that contain diazinon. Most investigators agreed that mammals were less susceptible to diazinon than were birds, at least under controlled environmental regimens. Data are lacking on diazinon impacts to mammals under field conditions; acquisition of these data should constitute a priority research area.

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CHAPTER 17

Diflubenzuron

17.1 INTRODUCTION

Compounds collectively known as insect growth regulators have been recognized in recent years as important new insecticides. These compounds include juvenile hormone mimics, antijuvenile hormone analogs, and chitin synthesis inhibitors. The most widely studied chitin synthesis inhibitor, and the only one currently registered for use against selected insect pests in the United States, is diflubenzuron (1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea), also known as dimilin (Christiansen 1986; Touart and Rao 1987; Eisler 1992). Chitin is a major component of the tough outer covering, or cuticle, of insects. As insects develop from immature larvae to adults, they undergo several molts, during which new cuticles are formed and old ones are shed. Diflubenzuron prevents successful development by inhibiting chitin synthetase, the final enzyme in the pathway by which chitin is synthesized from glucose (Marx 1977; Ivie 1978).

Diflubenzuron is highly effective against larval stages of many species of nuisance insects. It has been used extensively to control mosquitoes, midges, gnats, weevils (including the cotton boll weevil, *Anthonomus grandis*), various beetles, caterpillars of moths and butterflies (especially the gypsy moth, *Lymantria dispar*), flies, and rust mites (Marx 1977; Ivie 1978; Veech 1978; Schaefer et al. 1980; Opdycke et al. 1982a; Mazzarelli 1986). In Maryland, for example, more than 30,000 ha are sprayed annually to control gypsy moths (Swift et al. 1988a). In general, less than 140 g/ha (2 ounces/acre) of diflubenzuron is sufficient to control susceptible species, although affected larvae do not die until they molt (Marx 1977).

Most authorities agree that diflubenzuron has low mammalian toxicity, is not highly concentrated through vertebrate food chains or by absorption from water, remains stable on foliage, and seldom persists for extended periods in soil and water (Marx 1977; Ivie 1978; Schaefer et al. 1980). Chitin synthesis inhibitors, however, are not specific to insect pests. Beneficial insects also produce chitin, as do all arthropods, including spiders, crabs, crayfish, lobsters, shrimp, daphnids, mayflies, stoneflies, barnacles, copepods, and horseshoe crabs. All of these groups are adversely affected by diflubenzuron, including effects on survival, reproduction, development, limb regeneration, and population growth (Farlow 1976; Marx 1977; Christiansen 1986; Cunningham 1986; Mazzarelli 1986; Touart and Rao 1987; Weis et al. 1987; Eisler 1992; Fischer and Hall 1992).

17.2 ENVIRONMENTAL CHEMISTRY

17.2.1 General

Diflubenzuron breakdown by hydrolysis, soil degradation, or plant and animal metabolism initially yields 2,6-difluorobenzoic acid and 4-chlorophenylurea. Ultimately, the end products are

either conjugated into mostly water-soluble products or are biologically acylated and methylated. At extremely low doses, diflubenzuron selectively inhibits the ability of arthropods to synthesize chitin at the time of molting, producing death of the organism from rupture of the cuticle or starvation. Other organisms that contain chitin (i.e., some species of fungi and marine diatoms), or polysaccharides similar to chitin (i.e., birds and mammals), seem unaffected. Mobility and leachability of diflubenzuron in soils is low, and residues are usually not detectable after 7 days. Degradation is most rapid when small-particle (2 to 5 µm) formulations are applied and soil bacteria are abundant. In water, diflubenzuron usually persists for only a few days. Degradation is most rapid under conditions of high organic and sediment loadings, and elevated water pH and temperature.

17.2.2 Chemical and Biochemical Properties

Selected chemical properties of diflubenzuron are listed in [Table 17.1](#). Diflubenzuron degradative pathways are almost entirely through cleavage between the carbonyl and amide groups of the urea bridge. Ultimately, the end products are either conjugated into predominantly water-soluble products or are acylated and methylated biologically (Metcalf et al. 1975). Hydrolysis, soil degradation, and plant and animal metabolism of diflubenzuron yield the same initial products: 2,6-difluorobenzoic acid and 4-chlorophenylurea. Soil degradation and plant and animal metabolism involve further conversion of these compounds to 2,6-difluorobenzamide and 4-chloroaniline (Schaefer et al. 1980; Gartrell 1981) ([Figure 17.1](#)). Interspecies variations in ability to metabolize diflubenzuron are common, as judged by metabolic patterns in rat (*Rattus spp.*), cow (*Bos bovis*), and sheep (*Ovis aries*). In all three species, hydroxylation of either aromatic ring and scission of the ureido bridge constituted the main metabolic pathways. In cow and rat, the prevailing route was ring hydroxylation; in sheep, it was the scission reaction. In cow and sheep, about half the 2,6-difluorobenzoyl moiety excreted in urine was conjugated to glycine, but in rat the acid was excreted largely unchanged. In sheep, where cleavage-splitting of the diflubenzuron molecule was the primary metabolic route, there was no evidence of 4-chlorophenylurea or 4-chloroaniline in

Table 17.1 Chemical and Other Properties of Diflubenzuron

Variable	Data
Chemical names	1-(4-Chlorophenyl)-3-(2,6-difluorobenzoyl)urea; <i>N</i> -[(4-chlorophenyl)amino]carbonyl]-2,6-difluorobenzamide; 1-(2,6-difluorobenzoyl)-3-(4-chlorophenyl)urea
Alternate names	Deflubenzon, Diflubenzuron, Dimilin, DU, DU 112307, Duphar BV, ENT-29054, Largon, Micromite, OMS 1804, PDD 6040-I, PH 60-40, TH 6040, Vigilante
Action	Insecticide, larvicide, ovicide; insect growth regulator acting by interference with deposition of insect chitin
CAS number	35367-38-5
Empirical formula	C ₁₄ H ₉ ClF ₂ N ₂ O ₂
Molecular weight	310.68
Formulations	Granular; oil-dispersible concentrate; wettable powder
Manufacturing process and impurities	Produced by reaction of 2,6-difluorobenzamide with 4-chlorophenyl isocyanate. The technical product is 95% pure. Impurities are of low toxicological concern in terminal residues
Stability	Stable under sunlight and in neutral or mildly acidic solutions; unstable in strong basic solutions
Physical state	White crystalline solid
Melting point	210–230°C (technical); 230–232°C (pure)
Solubility	
Water	0.1–0.2 mg/L at 20°C; 1.0 mg/L at 25°C
Polar organic solvents	Moderate to good
K _{ow}	3500

Data from Metcalf et al. 1975; Farlow 1976; Johnson and Finley 1980; Gartrell 1981; Hudson et al. 1984; Mayer 1987; Poplyk 1989; Fischer and Hall 1992.

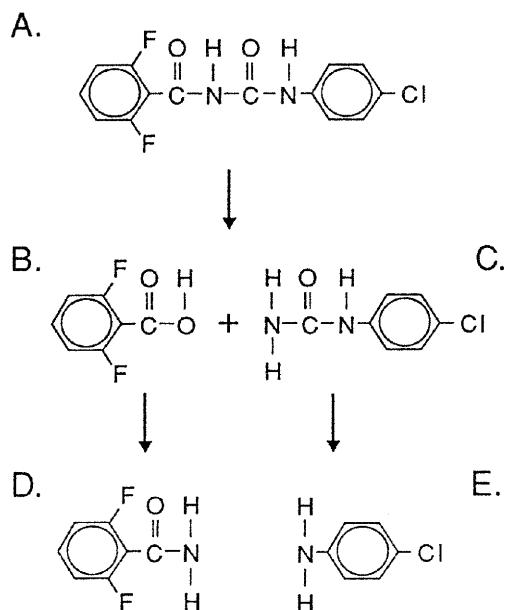


Figure 17.1 Generalized degradation pattern for diflubenzuron. Diflubenzuron (**A**) degrades initially to 2,6-difluorobenzoic acid (**B**) and 4-chlorophenylurea (**C**). 2,6-Difluorobenzoic acid (**B**) degrades to 2,6-difluorobenzamide (**D**) and 4-chlorophenylurea (**C**) degrades to 4-chloroaniline (**E**).

urine (Willems et al. 1980). More information on degradation and metabolic pathways of diflubenzuron is given in Metcalf et al. (1975), Schooley and Quistad (1979), Ivie et al. (1980), Willems et al. (1980), Franklin and Knowles (1981), and Jenkins et al. (1986).

The benzoylphenylureas — including diflubenzuron — control target insect populations at extremely low doses by selectively inhibiting their ability to synthesize chitin-bearing parts. Ingested diflubenzuron has no apparent adverse effects until the molting process is under way. Diflubenzuron caused increases in cuticle chitinase and cuticle phenoloxidase activity, producing a softened endocuticle through reduction of its chitin content and a hardened exocuticle as a result of increased phenoloxidase activity (Farlow 1976). Diflubenzuron inhibits serine protease, thus blocking the conversion of chitin synthetase zymogen into an active enzyme (Cunningham 1986; Mazzarelli 1986). Insect larvae treated with diflubenzuron develop cuticles that are unable to withstand the increased turgor occurring during ecdysis and that fail to provide sufficient muscular support during molting. These larvae are unable to cast their exuviae, resulting in death from starvation or rupture of the new, delicate, malformed cuticle (Farlow 1976). In addition to terrestrial insects, diflubenzuron is toxic to a wide variety of aquatic insects and crustaceans (Swift et al. 1988a, 1988b), but it does not seem to affect other organisms that contain chitin, including fungi (Mazzarelli 1986) and marine diatoms (Montgomery et al. 1990).

Chitin is a polymer of *N*-acetylglucosamine (AGA), and it rivals cellulose as the most abundant biopolymer in nature. Measured chitin concentrations in marine waters range between 4 and 21 µg/L, and planktonic crustaceans are the most significant source of chitin in the sea (Montgomery et al. 1990). Insect chitin is synthesized during phosphorylation by uridine dispospho-*N*-acetyl glucosamine (UDPGA) — the immediate precursor of chitin (Crookshank et al. 1978). Diflubenzuron inhibits the incorporation of chitin precursors into chitin, with a resultant accumulation of UDPGA (Crookshank et al. 1978). Chitin is not found in vertebrates, although several important polysaccharides similar to chitin are found, including hyaluronic acid (HA). Hyaluronic acid is found in skin, synovial fluid, connective tissue, vitreous humor, and the covering of the ovum.

Hyaluronic acid is a polysaccharide compound of alternating groups of glucuronic acid and AGA. The immediate precursor for glucuronic acid is uridine diphospho-glucuronic acid and that for AGA is UDPAGA. Because UDPAGA is used in the synthesis of chitin by insects and of HA by vertebrates, and because diflubenzuron interferes with the incorporation of UDPAGA into chitin by insects, diflubenzuron may interfere with the formation of HA in birds (Crookshank et al. 1978) (to be discussed later).

17.2.3 Persistence in Soil and Water

Mobility and leachability of diflubenzuron in soils is low, and residues are usually not detectable after 7 days. In water, half-time persistence (T_b 1/2) is usually less than 8 days and lowest at elevated temperatures, alkaline pH, and high sediment loadings (Fischer and Hall 1992) (Table 17.2). Increased concentrations of diflubenzuron in soils and waters are associated with increased application frequency, flooding of treated supratidal areas, wind drift, and excessive rainfall (Cunningham 1986).

Diflubenzuron is persistent in postharvest soils during winter and spring months, especially if associated with plant litter. Concentrations decline rapidly with the onset of high summer temperatures to <0.3 mg/kg DW soil in summer (Bull and Ivie 1978; Bull 1980). Diflubenzuron particle size and soil flora may be important in the soil degradation process. Diflubenzuron adsorbed to smaller particles of 2 μm diameter had a short T_b 1/2 of 3 to 7 days; diflubenzuron adsorbed to larger particles (10 μm diameter) persisted for 8 to 16 weeks. Diflubenzuron adsorbed to particles of 2 μm diameter had a low rate of degradation in sterile soils (<6% in 4 weeks), but in nonsterile soils 98% degraded in the same period, suggesting that soil bacteria are important in the degradation process (Cunningham 1986). In Canada, data on mobility of a pesticidal chemical in forest soil must be collected before it can be registered for use under the Canadian Pest Control Products Act in order to assess its potential for groundwater contamination (Sundaram and Nott 1989). Diflubenzuron used properly in forest management is unlikely to be leached into groundwater from a site of application (Sundaram and Nott 1989).

Water concentrations of diflubenzuron in treated ponds are significantly higher in surface and middle samples than in bottom samples during the first 5 h after treatment. However, after 24 h, distribution is about the same for all depths (Colwell and Schaefer 1980). Diflubenzuron persists for only a few days in pasture waters at 22 to 45 g/ha applied to control pasture mosquitoes (*Aedes nigromaculatus*, *A. melanimon*); hydrolysis and adsorption onto organic matter limit persistence in water (Schaefer and Dupras 1977). Aerial spraying of 70 g/ha in a forest ecosystem resulted in pondwater concentrations of 5.9 to 13.8 $\mu\text{g}/\text{L}$, which declined to <0.05 $\mu\text{g}/\text{L}$ within 16 to 20 days (Sundaram et al. 1991; Tanner and Moffett 1995). Water temperature and pH significantly affect persistence of diflubenzuron. Degradation is most rapid at elevated temperatures and alkaline pH values. Half-time persistence of diflubenzuron at pH 7.7 and various thermal regimes is 8 days at 38°C, 35 days at 24°C, and 29 days at 10°C. At pH 10, T_b 1/2 values are 2 days at 38°C, 14 days at 24°C, and 32 days at 10°C; degradation is negligible at pH 4 and at low temperatures regardless of pH (Cunningham 1989). In water, as in soil, small-particle (2 to 5 μm diameter) diflubenzuron formulations, such as WP-25%, degrade rapidly, usually in 2 to 8 days (Cunningham 1986). Larger-particle sand-granule formulations, developed for use in mosquito control programs wherein the compound needs to penetrate thick vegetation to reach the water, reduce drift during application and also provide slower release of diflubenzuron into aquatic habitats (Cunningham 1986).

The presence of sediments in diflubenzuron marine microcosms results in rapid removal from seawater and ultimately a reduction in mortality of larval crustaceans (Table 17.2) (Cunningham et al. 1987). But marine sediments that exceed 200 μg diflubenzuron/kg — levels normally encountered at application rates for control of salt marsh mosquitoes — could be detrimental to juvenile and adult crustaceans that consume detritus and organic matter on the surface of the marsh or at the water-sediment interface (Cunningham and Myers 1986; Cunningham et al. 1987).

Table 17.2 Diflubenzuron Persistence in Soil and Water

Sample, Initial Concentration, and Other Variables	Persistence	Reference ^a
SOIL		
0.08 g/ha, aerial spray, single application	Values always <0.05 mg/kg up to 14 days after spraying	1
22.4 g/ha (0.02 pounds/acre) applied 4 times, 1 month between treatments	Residues, in mg/kg, after first treatment were 0.2 at 1 day and 0.016 at 7 days. Residues at time of fourth treatment were nondetectable (ND) at start, 0.01 at 1 h, 0.02 at 1 day, and ND between days 3 and 56	2
44.9 g/ha (0.04 pounds/acre, applied 4 times, 2 weeks between treatments	Maximum residues, in mg/kg, after first treatment were 0.07 at 1 day and 0.05 at 7 days. After fourth treatment, residues were 0.04 at start, 0.09 at 3 days, and ND between days 7 and 56	2
70, 210, or 630 g/ha applied once to sandy loam forest soil or clay loam forest soil, plus water equivalent to 50.8 cm of precipitation	Mobility of diflubenzuron was low and did not increase with dosage. No residues detected below 10 cm or in leachates in either soil type at all dosage levels. At 70 g/ha, all residues were found in the top 2.5 cm; at 630 g/ha, 4–9% moved below 2.5 cm in sandy loam (mobility was lower in clay loam)	3
DISTILLED WATER		
100 µg/L, 37°C	No degradation at pH 4 in 8 weeks; Tb 1/2 was about 7 days at pH 6 and <3 days at pH 10. Major degradation products were 4-chlorophenylurea and 2,6-difluorobenzoic acid; small amounts of 2,6-difluorobenzamide and a quinazolininedione product were also formed	4
PASTURE WATER		
22–45 g/ha (0.02–0.04 pounds/acre), single application	Maximum concentrations, in µg/L, were 8.8 in 1 h, 7.1 in 24 h, 3.9 in 48 h, and 2.6 in 72 h; most treatments produced ND (<1 µg/L) residues in 24 h	5
45 g/ha (0.04 pounds/acre), single application	Concentrations, in µg/L, were 4 at start, 36 at 1 h, 9 at 24 h, and 6 at 14 days	1
45 g/ha, applied 4 times at 2-week intervals	Maximum concentrations, in µg/L, were 7.4 at 1 h after first treatment, 1.3 at 1 h after second application, 2.9 at 1 h after third treatment, and 6.4 at 1 h and 0.9 at 1 day after last treatment	2
80 g/ha, single application	Concentrations, in µg/L, of diflubenzuron declined from 20.3 at 1 h to 2.4 at 4 days; 4-chlorophenylurea increased slightly from 5.6 to 7.2 during this interval; 4-chloroaniline increased from 0.7 at 1 h to 2.6 at 4 days	6
POND WATER		
2.5 µg/L	Concentration after treatment was 1.9 µg/L; after 2 weeks, it was 0.5 µg/L	7
5 µg/L	Concentration immediately after treatment was 4.6 µg/L; after 2 weeks, it was 0.3 µg/L	7
10 µg/L	Initial concentration in medium declined from 9.8 µg/L to 0.2 µg/L after 2 weeks	7
13.8 µg/L	Concentration 1 h after aerial spraying of 70 g/ha; this declined to 6.3 µg/L at 12 h, 3.4 in 2 days, 1.0 in 10 days, 0.2 in 15 days, and was not detectable after 20 days	10
SEAWATER		
10 µg/L, sediments present	Tb 1/2 of 5.3 days; <0.7 µg/L in 19 days; <0.5 µg/L in 22 days	8
10 µg/L, sediments absent	Tb 1/2 of 17.8 days	8

Table 17.2 (continued) Diflubenzuron Persistence in Soil and Water

Sample, Initial Concentration, and Other Variables	Persistence	Reference ^a
100 µg/L	Tb 1/2 of 7.9 days at 38°C, and 35 days at 24°C	9
45 g/ha	Tb 1/2 of 10 days	9

^a 1, Booth and Ferrell 1977; 2, Schaefer and Dupras 1977; 3, Sundaram and Nott 1989; 4, Ivie et al. 1980; 5, Schaefer and Dupras 1976; 6, Schaefer et al. 1980; 7, Apperson et al. 1978; 8, Cunningham et al. 1987; 9, Cunningham and Myers 1986; 10, Sundaram et al. 1991.

17.3 USES

Diflubenzuron effectively inhibits molting in many species of insect pests, especially among the lepidoptera, coleoptera, and diptera. In the United States, diflubenzuron was approved for use by the U.S. Environmental Protection Agency (USEPA) against the gypsy moth in 1976, the cotton boll weevil in 1979, and foliar feeders on soybeans in 1982. By 1989 diflubenzuron was also registered for domestic use against mosquitoes, forest lepidoptera, mushroom flies, and certain leaf-eating insect pests of citrus, woody ornamentals, vegetables, and fruits (Bull 1980; Nimmo et al. 1980; Gartrell 1981; Cunningham 1986; Mazzarelli 1986; Webb and Wildey 1986; Wilson and Costlow 1987; Martinat et al. 1988; Poplyk 1989). In 1990, over 269,000 ha of forest were treated with diflubenzuron to suppress gypsy moth and tent caterpillar (*Malacosoma disstria*) populations (Whitmore et al. 1993).

In Europe and elsewhere, diflubenzuron is used in a variety of ways not permitted in the United States. For example, diflubenzuron and other insect growth regulators are fed as admixtures to rations of chickens, cattle, and swine in order to control fly larvae breeding in their manures, and also as a spray directly on manures prior to disposal (Opdycke et al. 1982b; Opdycke and Menzer 1984; Giga 1987). Diflubenzuron has been administered orally as a bolus to beef cattle for control of face flies (*Musca autumnalis*) and horn flies (*Haematobia irritans*), two serious pests of cattle in North America. Immature insects develop in fresh manure on open pasture. A single bolus released diflubenzuron into feces that killed horn and face fly larvae for 8 weeks and remained partially effective for 16 weeks (Scott et al. 1986).

Three diflubenzuron formulations are now in general use: an oil dispersible concentrate, a wettable powder (WP), and granules (Bull 1980; Cunningham 1986; Poplyk 1989). Granular formulations are produced by applying diflubenzuron to sand granules. Since technical diflubenzuron (99.5% pure) is a crystalline material that is almost insoluble in water (i.e., 0.1 mg/L at 20°C), it is usually dispersed in an organic solvent carrier. Wettable powders (25% active ingredients), however, are dispersed in water for use in many commercial applications; diflubenzuron particle size in WP-25 formulations usually ranges between 2 and 5 microns.

17.4 LETHAL AND SUBLETHAL EFFECTS

17.4.1 General

Diflubenzuron applied to foliage of terrestrial plants tends to remain adsorbed for several weeks with little or no absorption or translocation from plant surfaces; loss is mainly by wind abrasion, rain washing, or shedding of senescent leaves. Among insect species, there is great variability in sensitivity to diflubenzuron. In general, diflubenzuron is toxic to early life stages of insects at concentrations as low as 0.1 mg/kg diet and at topical applications between 0.003 and 0.034 µg/larvae. Among aquatic organisms, early developmental stages of crustaceans and insects are the most sensitive groups tested. Adverse effects on growth, survival, reproduction, and behavior

occur between 0.062 and 2.0 µg/L. Groups highly resistant to diflubenzuron include the algae, gastropods, fishes, and amphibians. Birds are comparatively resistant: acute oral LD₅₀ values exceed 2000 mg diflubenzuron/kg body weight (BW), and dietary levels of 4640 mg/kg ration are tolerated for 8 days. Also, forest birds seem unharmed by recommended diflubenzuron application procedures to control pestiferous insects. No data are available on mammalian wildlife. However, studies with small laboratory animals and domestic livestock suggest a high degree of resistance. No observable adverse effects occur in cows given 0.25 mg/kg BW daily for 4 months, in rabbits given 4 mg/kg BW daily on days 6 to 18 of gestation, in dogs fed diets containing 40 mg/kg for 13 weeks (equivalent to 1.6 mg/kg BW daily), in rats fed diets containing 160 mg/kg for 2 years, and in rabbits and rodents given single oral or dermal doses <2000 mg/kg BW. All of these points are discussed later.

17.4.2 Terrestrial Plants

There is little to no absorption and translocation of diflubenzuron residues from plant surfaces (Gartrell 1981). Due to its stability and low volatility, diflubenzuron residues adhering to plant surfaces are removed primarily through physical effects such as wind abrasion, rain washing, or the loss of dead leaves (Bull 1980). A greenhouse study with corn (*Zea mays*), soybeans (*Glycine max*), cabbage (*Brassica oleracea capitata*), and apples (*Malus* sp.) showed no significant degradation of diflubenzuron residues in leaves for up to 16 weeks after treatment (Gartrell 1981). In a study with radiolabeled diflubenzuron, a single dose applied to a cotton (*Gossypium hirsutum*) leaf showed <5% photodegradation in 4 weeks, <7% absorption in 7 weeks, <50% loss to weathering or volatilization in 4 weeks in samples not exposed to rain, and 77% loss in 3 weeks after a heavy rainfall (Bull and Ivie 1978; Bull 1980). Edible portions of rotational crops treated repeatedly with diflubenzuron at recommended application levels had low, but detectable, residues. Maximum concentrations, in mg/kg DW, were always <0.01 in wheat (*Triticum* spp.), <0.02 in cotton, <0.09 in collards (*Brassica* spp.), and <0.16 in radish (*Raphanus* spp.) (Bull and Ivie 1978; Bull 1980).

Diflubenzuron applied aerially to forest leaves in the spring growing season did not persist when the leaves were placed in stream water (Harrahy et al. 1993). Residues on oak leaves decreased 36% in July, and 23% in August within the first 48 h of stream incubation, reaching >90% loss within 3 weeks. However, in December, after 54 days in the stream, there was no significant loss from leaves of red maple, oak, or poplar. The persistence of diflubenzuron to forest leaves under winter conditions is attributed to the increased stability of diflubenzuron at cold temperatures, the greater retention to leaves at low temperatures, and the reduction in microbial degradation. In view of the persistence of diflubenzuron on hardwood leaves at low stream temperatures, nontarget aquatic organisms that consume these leaves may be exposed for extended periods with possible adverse effects (Harrahy et al. 1993).

Foliage of cotton that initially contained 100 mg/kg DW contained about 60 mg/kg after 7 weeks; leaf residues consisted entirely of the parent diflubenzuron (Gartrell 1981). Diflubenzuron applied topically to lima bean (*Phaseolus lunatus*) foliage was not absorbed by the plant, as expected. Injected diflubenzuron, however, was metabolized, and certain metabolites were similar to those isolated from mites (Franklin and Knowles 1981).

Diflubenzuron mixed into compost layers of the cultivated mushroom (*Agaricus bisporus*) at 30 mg/kg compost to control dipteran pests of mushroom resulted in increased yield and size. However, at higher concentrations of 180 mg/kg and 1080 mg/kg, mushroom yield and number were reduced, and this became more severe over time (White 1986). Frequent applications of diflubenzuron to agricultural soils are not detrimental to nitrogen-fixing bacteria (i.e., *Azotobacter vinelandii*), and high concentrations could stimulate nitrogenase activity in soils. This conclusion is based on a study by Martinez-Toledo et al. (1988) using nonsterile agricultural soils and sterilized soils inoculated with *A. vinelandii*. At diflubenzuron loadings between 100 and 500 mg/kg, all concentrations tested had a stimulatory effect on nitrogen fixation in both soils.

17.4.3 Terrestrial Invertebrates

Diflubenzuron is most toxic to early life stages of some insects at 0.1 mg/kg diet, 0.034 µg/larvae (about 3.1 mg/kg BW), or in combination with various chemicals (Table 17.3). Some beneficial insects, such as the honey bee (*Apis mellifera*), are adversely affected at dietary concentrations of 1 mg/kg for 12 weeks, 10 mg/kg for 10 weeks, or 59 mg/kg for 10 days (Table 17.3). At 28 to 56 g/ha (0.025 to 0.05 pounds/acre), diflubenzuron effectively controls mosquitoes for 8 to 15 days (Schaefer and Dupras 1977; Booth and Ferrell 1977), especially organophosphorus insecticide-resistant strains of salt marsh mosquitoes in California (Lee and Scott 1989). Diflubenzuron was also effective in controlling strains of house fly (*Musca domestica*) that were resistant to organochlorine, organophosphorus, carbamate, and pyrethroid insecticides on a United Kingdom pig farm; 416 mg/m² to slurry pots of pig weaning rooms gave effective control 2 to 4 weeks after application (Webb and Wildey 1986).

Chemical control of larvae of gypsy moth and other forest-insect defoliators may cause indiscriminate reduction of nontarget arthropods, which, in turn, may affect food resources of forest birds and small mammals. This problem is of special concern in West Virginia, where two species of endangered bats (Indiana bat, *Myotis sodalis*; eastern big-eared bat, *Plecotus phyllotis*) occur in areas threatened by gypsy moth defoliation (Martinat et al. 1988). Diflubenzuron applications, usually at 70 g/ha on two consecutive days, controlled gypsy moth larvae and also significantly reduced populations of canopy macrolepidoptera and nonlepidopteran mandibulate herbivores. Sucking herbivorous insects, microlepidoptera, and predaceous arthropods, however, were relatively unaffected, which suggests that although diflubenzuron can potentially affect food supply of forest birds and small mammals, these effects are probably minimal (Martinat et al. 1988).

Researchers generally agree that diflubenzuron causes incomplete ecdysis by interfering with chitin synthesis. However, diflubenzuron at lethal concentrations causes an effect in chironomid larvae (*Chironomus decorus*, *Tanypus grodhausi*) other than inhibition of chitin synthetase, as judged by histopathology of the alimentary canal, especially the ventriculus. Dysfunction of the ventriculus, an organ that normally lacks chitin, results in a general breakdown of the digestive apparatus of exposed chironomid larvae (Pelsue 1985). Exposure of nematodes and of adults of several insect species, including boll weevil, housefly, and stable fly (*Stomoxys calcitrans*), to diflubenzuron results in deposition of eggs that appear normal but fail to hatch. This effect seems to be due to an ovicidal action and not to sterility of the treated adults, since the larvae appear to undergo normal development within the egg. Secretion of unmetabolized diflubenzuron into the eggs apparently accounts for observed ovicidal effects (Ivie and Wright 1978; Veech 1978; Ivie et al. 1980). Treated female boll weevils began to lay viable eggs 12 days after treatment and became as productive as controls in 24 days; additional treatment is required to maintain a significant suppression of egg hatch (Bull 1980).

Diflubenzuron is the most investigated benzoylphenylurea and has shown excellent potency for controlling mosquitoes and certain lepidopterous and coleopterous pests. Some insect species, however, cannot be controlled efficiently by diflubenzuron. For example, the cotton leafworm (*Spodoptera littoralis*) is comparatively resistant because of reduced penetration through the exoskeleton, rapid elimination of unchanged diflubenzuron, and rapid metabolism, which occurs mainly through hydrolysis (El Saidy et al. 1989). To combat *Spodoptera* and other resistant pests, new benzoylphenylurea compounds have been developed, including chlorfluazuron, teflubenzuron, and hexafluron (El Saidy et al. 1989).

Beneficial insects associated with fruit orchards show different responses to diflubenzuron treatment (Broadbent and Pree 1984). Lacewings (*Chrysopa oculata*) in contact with leaves containing 300 mg/kg DW had reduced survival and inhibited molting of first instar larvae, but the assassin bug (*Acholla multispinosa*) was not affected by contact with treated leaves. Lacewings and other beneficial predator insects fed diflubenzuron-treated, two-spotted spider mites (*Tetranychus urticae*) for 3 days showed no adverse effects after 14 days (Broadbent and Pree 1984).

Spraying of diflubenzuron at 28 g/ha to control gypsy moth did not affect *Cotesia melanoscela*, a hymenopterid predator of the gypsy moth. However, another natural enemy, a virus, was adversely affected (Webb et al. 1989). Certain arthropod predators were unaffected by diflubenzuron at 70 mg/ha applied four times in 3 weeks to control the boll weevil; these include the convergent lady bug beetle (*Hippodamia convergens*), the big-eyed bug (*Geocoris punctipes*), and various species of *Coleomegilla*, *Orius*, *Nabis*, and *Chrysopa* (Deakle and Bradley 1982).

Diflubenzuron can be either hydrolyzed at the urea bridge or oxidized by ring hydroxylation followed by conjugation. Hydrolytic cleavage seems to be a major route for diflubenzuron metabolism in many insect species (El Saidy et al. 1989). Two-spotted spider mites showed <10% absorption in 96 h of topically applied diflubenzuron. Of the amount absorbed, about 27% was metabolized in 96 h to 4-chlorophenylurea, 2,6-difluorobenzoic acid, 4'-chloroformanilide, 2,6-difluorobenzamide, and other metabolites (Franklin and Knowles 1981). Effects of diflubenzuron were synergized by profenofos (El Saidy et al. 1989) in cotton leafworm fourth instar larvae, and they were antagonized by 20-hydroxyecdysone (Soltani et al. 1987) in beetle (*Tenebrio molitor*) pupae. More information is needed on interaction effects of diflubenzuron with other chemicals.

Table 17.3 Diflubenzuron Effects on Selected Terrestrial Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
NEMATODE, <i>Acrobeloides</i> sp.		
Fed diet containing 100 mg/kg for 10 days	Population reduction of 97%	1
BOLL WEEVIL, <i>Anthonomus grandis</i>		
1 µg/female weevil, applied topically	After 8 days, about 62% was not absorbed, 3% was absorbed, and 35% was metabolized and excreted	2
113.4 g/ha, applied 5 times during winter	Reduced heavy infestations by >70% in upper Gulf Coast area of Texas	3
HONEYBEE, <i>Apis mellifera</i>		
Fed sucrose syrup/sugar cake diets containing 0.01, 0.1, 1, or 10 mg/kg for 12 weeks	Adult colony survival reduced at 10 mg/kg; inhibited reproduction at 1 and 10 mg/kg; no measurable effect on survival or reproduction at 0.01 or 0.1 mg/kg	4
Fed diet containing 10 mg/kg for 10 weeks	No reduction in consumption of pollen or in quantity of brood reared, but >50% reduction in amount of sucrose syrup stored	5
Fed sucrose syrup containing 59 mg/kg for 10 days	Inhibited reproduction	6
Fed sucrose syrup containing 60 mg/L and drinking water containing 100 mg/L for 40 days	Treated bees consumed significantly less water and pollen and produced significantly less comb, brood, and new workers	7
GERMAN COCKROACH, <i>Blattella germanica</i>		
Nymphs fed diets containing 4, 20, 100, or 500 mg/kg for 4 weeks	None dead at 4 mg/kg, 15% at 20 mg/kg, 88% at 100 mg/kg, and all dead at 500 mg/kg	8
APHID LION, <i>Chrysoperla carnea</i>		
0.5 g/L spray	Reduced incubation period, reduced hatch, and reduced survival	9
2.0 g/L spray	No hatch	9
TERMITES, <i>Coptotermes heimi</i>		
Nymphs fed diets containing 100, 500, or 1000 mg/kg	All dead in 24 days at 200 mg/kg, 20 days at 500 mg/kg, or 16 days at 1000 mg/kg. Some nymphs developed blister-like swellings on the abdomen and failed to molt into the next instar	10

Table 17.3 (continued) Diflubenzuron Effects on Selected Terrestrial Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
MOSQUITO, <i>Culex pipiens quinquefasciatus</i>		
Adults fed 500 or 1000 mg/kg diet for 2 days	At both doses, 40% of eggs failed to hatch or hatched abnormally; at the high dose, ovarian histopathology recorded	11
CAT FLEA, <i>Ctenocephalides felis</i>		
Larvae, held in rearing medium for 5–6 weeks		
90 µg/kg	LC50, 1.5-day-old larvae	12
2220 µg/kg	LC50, 2.5-day-old larvae	12
>100 mg/kg	LC50, 3.5-day-old larvae	12
TERMITE, <i>Heterotermes indicola</i>		
Nymphs fed diets containing 100, 500, or 1000 mg/kg feed	All dead in 14–16 days at 100–1000 mg/kg diet	10
GYPSY MOTH, <i>Lymantria dispar</i>		
100 µg/kg diet	100% lethal to larvae	13
CABBAGE MOTH, <i>Mamestra brassicae</i>		
2.2 mg/L spray	LC90, third instar larvae	14
NEMATODES, various species		
Fed diet containing 1 mg/kg for 10 days	No effect on reproduction	1
Fed diet containing 10 mg/kg for 10 days	53% population reduction in <i>Panagrellus redvirus</i> , and 95% reduction in <i>Pelodera</i> sp.	1
AMERICAN COCKROACH, <i>Periplaneta americana</i>		
Nymphs fed diets containing 100 or 800 mg/kg for 4 weeks	17% dead at low dose and 52% dead at high dose	8
LARGE WHITE BUTTERFLY, <i>Pieris brassicae</i>		
0.39 mg/L spray	LC50, third instar larvae	14
COTTON LEAFWORM, <i>Spodoptera littoralis</i>		
Fourth instar larvae, topical application 3, 10, 30, or 100 ng/larva	Incorporation of N-acetyl glucosamine into chitin was inhibited by 23% at 3 ng/larva, 75% at 10 ng, 90% at 30 mg, and 98% at 100 ng	14
34 ng/larva, equivalent to 3.1 mg/kg BW	LD50, applied in combination with profenofos	15
468 ng/larva, equivalent to 42.5 mg/kg BW	LD50	15
4.3 mg/L, spray	LC90, third instar larvae	14
TERMITES		
Nymphs, 3 species, given 100–1000 mg/kg diet	All dead in 14–24 days	10
Adults, 2 species, given 1000 mg/kg diet	Fecundity reduced and eggs failed to develop	10

^a 1, Veech 1978; 2, Bull 1980; 3, Cole 1980; 4, Stoner and Wilson 1982; 5, Nation et al. 1986; 6, Muzzarelli 1986; 7, Barker and Waller 1978; 8, Tsuji and Taneike 1988; 9, Zaki and Gesraha 1987; 10, Ahmad et al. 1986; 11, Mittal and Kohli 1988; 12, El-Gazzar et al. 1988; 13, Martinat et al. 1988; 14, Grosscurt et al. 1988; 15, El Saidy et al. 1989.

17.4.4 Aquatic Organisms: Laboratory Studies

Studies with diflubenzuron and representative aquatic organisms under controlled conditions (Table 17.4) show several trends:

1. Crustaceans are the most sensitive group of nontarget organisms tested. Adverse effects on growth, survival, reproduction, and behavior of copepods, shrimp, daphnids, amphipods, and crabs occur between 0.062 and 2.0 µg/L medium, and early developmental stages were the most vulnerable.
2. Next in sensitivity are aquatic insects, including mayflies, chironomids, caddisflies, and midges. Diflubenzuron concentrations between 0.1 and 1.9 µg/L medium produce low emergence and survival.
3. Other groups tested are comparatively resistant (i.e., adverse effects occur at >45 µg/L). In fish, for example, death occurred at >33,000 µg/L.
4. Elevated accumulations occur in aquatic plants during exposure to 100 µg/L and in fish during exposure between 1 and 13 µg/L. All species in these groups, however, seemed unaffected by elevated body burdens, as judged by normal growth and metabolism.

The major degradation products of diflubenzuron in water are 4-chlorophenylurea and 2,6-difluorobenzoic acid (Metcalf et al. 1975; Ivie et al. 1980). These compounds are less toxic to aquatic organisms than the parent chemical (Julin and Sanders 1978; Schaefer et al. 1979, 1980; Gattavecchia et al. 1981). A minor metabolite, 4-chloroaniline, which is classified as a mutagen by The National Cancer Institute, and the Cancer Assessment group of the U.S. Environmental Protection Agency (Schaefer et al. 1980), is significantly more toxic to fish and *Euglena gracilis* than is diflubenzuron. For example, LC50 (96 h) values for 4-chloroaniline and four species of freshwater teleosts are 16 to 56 times lower than comparable data for diflubenzuron (Julin and Sanders 1978), but 4-chloroaniline is 76 times less toxic than diflubenzuron to *Chironomus* midge larvae in 48 h (Julin and Sanders 1978). There is a dose-dependent effect of 4-chloroaniline on *Euglena* growth inhibition and glycine metabolism in the range of 1 to 200 mg/L during exposure for 30 h (Gattavecchia et al. 1981). The most sensitive organism to 4-chloroaniline was bluegill (*Lepomis macrochirus*) with an LC50 (96 h) value of 2.3 mg/L (Julin and Sanders 1978). It is highly unlikely, however, that this concentration will be encountered under recommended diflubenzuron application practices.

Diflubenzuron inhibits several enzyme systems in crab and insect larvae, resulting in disrupted glucose metabolism, reduced *N*-acetylglucosamine incorporation into cuticle, and ultrastructural deformities of chitinous components of the cuticle (Christiansen and Costlow 1982; Christiansen et al. 1984; Christiansen 1986). Specifically, diflubenzuron inhibits chitin synthetase, a magnesium-requiring enzyme that catalyzes the transfer of *N*-acetyl-*D*-glucosamine to chitin; the final result is relatively large accumulations of *N*-acetylglucosamines (Horst 1981; Machado et al. 1990).

Diflubenzuron acts specifically on insects and crustaceans as a larvicide by interfering with chitin deposition into cuticles during juvenile development through ecdysis (Horst 1981; Antia et al. 1985; Cunningham 1986; Machado et al. 1990). The biosynthesis of chitin in arthropods is under hormonal control. Arthropods increase in size by resorbing a portion of the shell and initiating the secretion of a new exoskeleton under the old cuticle. At this time, chitin synthesis is maximal. After completion of about half the new shell, molting occurs, the old shell is discarded, and the new shell is synthesized. Diflubenzuron exposure produces disturbances in the cuticular structure, weakening the cuticle so that it fails mechanically during ecdysis of insects and crustaceans. In general, treated larvae appear healthy during the entire intermolt period until molting commences, at which time many larvae are unable to cast their molts completely and die within a few hours. Several genera of diatoms, including *Thalassiosira* and *Skeletonema*, produce up to 33% of their biomass as chitin. These diatoms synthesize chitin strands that extend outside their frustules to increase buoyancy (Montgomery et al. 1990). Chitin-producing diatoms, as well as nonchitanaceous

diatoms, are seemingly unaffected at elevated concentrations of 1 mg/L for periods up to 14 days (Antia et al. 1985). Some species of algae, especially *Plectonema boryanum*, are reported to efficiently degrade diflubenzuron (Schooley and Quistad 1979), but this requires verification.

Studies with laboratory stream communities dosed for 5 months confirm that insects and crustaceans are the most severely affected groups. Adverse effects occur in the range of 1.0 to 1.1 µg diflubenzuron/L. Fish and molluscs, however, show no adverse effects at 45 µg/L (Hansen and Garton 1982). Freshwater clams (*Anodonta cygnea*) exposed to high concentrations of diflubenzuron for lengthy periods may experience blocked polycondensation reactions to chitin chains in the outer mantle epithelium secretory cells, producing unstabilized chitin and increasing shell fragility. On this basis, the comparatively resistant burrowing bivalve molluscs may be at risk if exposed over several calcification periods (Machado et al. 1990). Fish accumulated diflubenzuron from water up to 160 times water levels, but tissue concentrations during exposure declined steadily over time (Schaefer et al. 1980).

Exposure of *Aedes albopictus*, a mosquito vector of dengue and encephalitis in Taiwan, for 24 h to 0.00025 to 25 µg/L diflubenzuron resulted in dose-dependent aberrations in larvae, pupae, and adults (Ho et al. 1987) (Table 17.4). In general, most treated second and third instar *Aedes* larvae died during molting, while most fourth instar larvae developed abnormally (Ho et al. 1987). Unfortunately, levels of diflubenzuron used to control saltwater mosquitoes and other insects are also toxic to zoeal stages of crustaceans (Costlow 1979) and adversely affect growth and reproduction of adults (Mazzarelli 1986). Treated larvae of estuarine crustaceans are characterized by the following (Table 17.4) (Cunningham 1986):

- Histological alterations in the cuticular layers of the exoskeleton at concentrations as low as 1 µg/L
- Higher mortality associated with molting and gross morphological deformities at concentrations as low as 0.5 µg/L
- Behavioral modifications at concentrations as low as 0.1 µg/L

Behavioral effects in fiddler crabs (*Uca pugilator*) were the most sensitive indicator of diflubenzuron stress, and these effects potentially may influence the ability of juvenile crabs to avoid predation, construct burrows, or feed adequately in nature (Cunningham and Myers 1987). Behavioral effects on cladocerans that can result in latent mortality include reduced filter feeding rates, reduced body movements, and inability to exhibit positive phototaxis, a characteristic of untreated individuals (Cunningham 1986) (Table 17.4). Shrimp larvae exposed to >2.5 µg/L will not undergo daily vertical migration, and those exposed to 1 µg/L undergo only limited migration, which could affect horizontal transport and dispersal of populations and reduce recruitment to benthopelagic adult populations (Wilson et al. 1987). In addition to its inhibitory effect on cuticle synthesis, diflubenzuron affects hormone balance by delaying or arresting the molt cycle, and it inhibits limb regeneration by inhibiting mitosis and differentiation (Touart and Rao 1987). Regenerated limbs of diflubenzuron-stressed crabs that survived ecdysis had lesions in the form of black areas in which the cuticle was improperly developed (Weis et al. 1987). Also, diflubenzuron caused a reduction in metabolism of beta-ecdysone in larval insects, leading to an excess of this molting hormone in the tissues. Treatment of decapod crustaceans with ecdysones frequently causes high mortality and molt acceleration (Gulka et al. 1982).

Toxicity and persistence of diflubenzuron in aquatic environments depend on formulation, frequency of application, quantity of organic matter, sediment type, and water pH and temperature. Biological variables are more important than physical variables in assessing diflubenzuron toxicity, especially the age of the test organism and frequency and synchrony of molting during the exposure period (Cunningham 1986). Crustaceans and other organisms that molt do not demonstrate a typical survival dose-response curve against diflubenzuron because death occurs only when molting is blocked (Nebeker 1983; Cunningham 1986; Cunningham and Myers 1987; Wilson and Costlow 1987). In general, the most sensitive species had comparatively short larval or nymphal periods,

and the organism molted frequently (Rodrigues and Kaushik 1986). Susceptible species include mayflies (*Leptophlebia* sp., *Baetis pygmaeus*), while more-resistant species include a stonefly (*Paragnetina media*) and caddisfly (*Hydropsyche bettani*). Amphipods were especially sensitive at 25°C, but not at 10°C, 15°C, or 20°C (Rodrigues and Kaushik 1986).

Mortality patterns of megalops larvae of blue crab (*Callinectes sapidus*) were elevated at higher temperatures but were seemingly unaffected by water salinity (Costlow 1979). In studies on larvae of black fly (*Simulium vittatum*), diflubenzuron was more effective (1) against earlier larval instar stages than later ones, (2) against rapidly growing larvae than starved, slow-growing larvae, and (3) at 25°C than at 20°C (Rodrigues and Kaushik 1986). Among diflubenzuron-stressed barnacles (*Balanus eburneus*), mortality was higher in fed groups than in starved groups, perhaps due to an increased uptake from contaminated food or to an increased molting rate due to feeding (Gulka et al. 1980). Increased fragility of cast exuviae from diflubenzuron-treated barnacles suggests mechanical weakening of the cuticle due to a decrease in chitin content (Gulka et al. 1982).

Table 17.4 Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
ALGAE AND MACROPHYTES		
Diatom, <i>Cyclotella cryptica</i> 5000	No effect on photosynthesis during 14-day exposure	1
Blue-green alga, <i>Plectonema boryanum</i> 100	Residues, in µg/kg dry weight, during exposure for 4 days were 144,700 at 1 h, 85,700 at 1 day, 56,900 at 2 days, 11,700 at 3 days, and 8300 at 4 days; <i>Plectonema</i> growth rate was unaffected	2
Alga, <i>Selenastrum capricornutum</i> 45	No effect on growth during exposure for 120 h	3
Diatoms, 3 species (<i>Skeletonema costatum</i> , <i>Thalassiosira nordenskioldii</i> , <i>T. weissflogii</i>) 1000	No effect on photosynthesis during exposure for 11–14 days	1
5000	Photosynthesis inhibited 70–80% in 11–14-day exposure	1
COELENTERATA		
Hydra, <i>Hydra oligactis</i> 0.1–0.12 (estimated)	After 24-h exposure, asexual budding rate significantly increased over controls during 20-day posttreatment period; some histopathology. Second-generation hydras not significantly different from controls	4
PLATYHELMINTHES		
Planarian, <i>Dugesia dorotocephala</i> 5	No effect on survival, behavior, or asexual reproductive capacity after 24-h exposure	23
AQUATIC INSECTS		
Mosquito, <i>Aedes aegypti</i> , 4th instar larvae 20 (equivalent to 0.056 kg/ha)	Fatal to 100% within 24 h, about 50% after 4 days, and <20% after 8 days	5
Mosquito, <i>Aedes albopictus</i> 0.00025	LC30 (24 h), 2nd instar larvae	6
0.0028	Adult emergence inhibited when 2nd instar larvae exposed for 24 h	6
0.025	LC67 (24 h), 2nd instar larvae	6

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
0.125	Histopathology of cuticle and anal gills in 4th instar larvae after 24-h exposure of 3rd instar larvae	6
0.21	Adult emergence inhibited when 3rd instar larvae exposed for 24 h	6
0.25	LC67 (24 h), 3rd instar larvae	6
12.5	No histopathology of 4th instar larvae after 24-h exposure	6
25	LC16 (24 h), 4th instar larvae	6
39.6	Adult emergence inhibited when 4th instar larvae exposed for 24 h	6
Mosquito, <i>Aedes nigromaculatus</i>		
0.5	LC50 (48 h), larvae	7
Aquatic beetles		
<i>Hydrophilus triangularis</i>		
100	LC50 (48 h), larvae	7
<i>Laccophilus</i> spp.		
250	No deaths of adults in 216 h	7
<i>Thermonectus basillaris</i>		
250	No deaths of adults in 168 h	7
<i>Tropisternus lateralis</i>		
250	No deaths of adults in 48 h	7
Mayfly, <i>Callibaetis</i> sp.		
10	LC90 (168 h), nymphs	7
Chironomid, <i>Chironomus decorus</i> , 4th instar		
1.9	LC50	8
6.0	LC90	8
Midge, <i>Chironomus plumosus</i>		
560	50% of larvae immobilized in 48 h	9, 10
Caddis fly, <i>Clistoronia magnifica</i>		
0.1	Adult emergence inhibited during 4-week exposure	11
Midge, <i>Cricotopus</i> spp.		
1.6	No adult emergence in 96-h exposure	11
4.9	Molting and survival adversely affected during exposure for 96 h	11
Mosquito, <i>Culex pipiens</i> , exposed as 4th instar larvae for 24 h		
8	50% reduction in adult emergence	12
100	74% reduction in adult emergence	12
1000	No adult emergence	12
Mosquito, <i>Culex pipens quinquefasciatus</i>		
1.0	Fourth instar larval dip had no effect on adult sterility	13
Chironomid, <i>Glyptotendipes paripes</i> , 4th instar		
1.8	LC50	8
4.1	LC90	8
Midge, <i>Goeldichironomus holoprasinus</i>		
10	LC90 (168 h), larvae	7
Dragonfly, <i>Orthemis</i> spp., <i>Pantala</i> sp.		
50	LC50 (168 h)	7
Blackfly, <i>Simulium vittatum</i> , larvae		
80 for 30 min at various water temperatures		
10°C	50% dead in 21 days	14
20°C	53% dead in 13 days	14
25°C	92% dead in 3 days	14
500 for 15 min	98% dead in 18 days at 10.5°C	14
1000 for 30 min	All dead in 10 days at 15°C	14

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
Stonefly, <i>Skwala</i> sp. 57,500	LC50 (96 h)	15
Midge, <i>Tanytarsus dissimilis</i> 1.0 4.9	LC50, period between 2nd and 3rd instar larvae Molting and survival adversely affected during 5-day exposure	3 11
ARACHNOIDS		
Horseshoe crab, <i>Limulus polyphemus</i> 5 50	Larvae exposed for 24 days showed slight delay in molting at 14 days; survival as in controls Larvae exposed for 24 days showed molt rate as in controls, but high mortality immediately after ecdysis; reduced growth of survivors	6 16
MOLLUSCS		
Clam, <i>Anodonta cygnea</i> 200,000	After exposure for 3 months, all clams survived and appeared healthy. But normal calcification process disrupted on lamellar layer of the shell, producing fragile shell	17
Snail, <i>Juga plicifera</i> 36–45	No effect on survival, growth, or reproduction during 3-week exposure	3, 11
Snail, <i>Physa</i> spp. 45	No measurable effect on growth, survival, or reproduction during 3-week exposure	3, 11
CRUSTACEANS		
Copepod, <i>Acartia tonsa</i> Adults exposed following terminal molt 1 10 100 1000	Hatch of viable nauplii reduced by 50% after 12-h exposure; no hatch after 36-h exposure. Effect not reversible for at least 30 h after exposure Hatch of nauplii reduced by >95% after exposure for 24 h and 100% after 36 h. Effect not reversible for at least 26 h after exposure No effect on egg production during 14-day exposure No adverse effect on survival during exposure for 5 days	18 18 18 18
Brine shrimp, <i>Artemia salina</i> Adults exposed to 1, 2, 5, or 10	During exposure for 80 days, there was a significant reduction in reproductive lifespan at 2, 5, and 10 µg/L. Nauplii produced viviparously by mated pairs were comparable to controls — except for the 10-µg/L group, which produced fewer nauplii. Cysts produced oviparously by treated pairs, however, had lower mean hatchability	19
Nauplii exposed to 1, 10, or 100	All dead within 30 days in the 100 µg/L group; survival same as controls in 12 days for the 1 and 10 µg/L groups	19
Barnacle, <i>Balanus eburneus</i> 50 50–100 100 750 or 1000	Some deaths when exposure exceeds 10 days Significant acceleration of intermolt cycle at low dose, and among survivors at high dose No deaths of adults in 28 days High mortality during 10-day exposure; prolonged premolt; histopathology of cuticle-secreting epidermal cells	20 21 21 20

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
1000 for 48 h plus clean seawater for 26 days	No deaths of adults	21
1000 for 72 h plus clean seawater for 25 days	High mortality of adults, especially on days 7–14 postexposure	21
Copepods, 2 species		
100	Negligible mortality in 144 h	7
Blue crab, <i>Callinectes sapidus</i>		
1	High survival of megalops	22
3	Low survival of megalops	22
Ostracod, <i>Cypicerus</i> sp., <i>Cypridopsis</i> sp.		
500	Negligible mortality in 72 h	7
Daphnid, <i>Daphnia magna</i>		
0.062	Survival and reproduction adversely affected in full life cycle (21-day exposure)	3
2	All dead within 6 days	11
4.4–15	50% immobilized or dead in 48 h	3,9,10,15
Daphnids, 2 species		
1.5	LC50 (48 h)	7
Clam shrimp, <i>Eulimnadia</i> spp.		
0.15	LC50 (48 h)	7
Copepod, <i>Eurytemora affinis</i>		
0.75–1.00	MATC ^b	49
2.2	LC50 (48 h) for nauplii	49
Scud (amphipod), <i>Gammarus pseudolimnaeus</i>		
25–45	LC50 (96 h)	9, 10, 15
1000	After exposure for 30 min, 22% dead in 55 days at 15°C	14
1000	After 30-min exposure, 91% dead in 9 days at 25°C	14
Amphipod, <i>Hyalella azteca</i>		
1.8	LC50 (96 h)	3
2	LC60 (96 h)	11
1000	After 30-min exposure, 3–7% dead in 19–21 days at 15°C	14
1000	After 30-min exposure, 62–99% dead in 7–12 days at 25°C	14
Stone crab, <i>Menippe mercenaria</i>		
0.5	LC50 (48 h), larvae	22, 24
Copepod, <i>Mesocyclops thermocyclopoides</i>		
1–15	Impaired fertility of ovigerous females	25
2–1000	Prolongation of copepodite stage for 3–4 days, followed by death without molting, in most cases. At 125 µg/L and higher, partial molting occurred but all died	25
500	No larval deaths in 48 h	25
1000	LC50 (48 h) for copepodites. No effect on mating behavior of adults but abnormal ovisac development and decreased fecundity in some females	25
Mysid shrimp, <i>Mysidopsis bahia</i>		
0.075	Reduction in number of young per female after exposure for 21 days	26
0.075	Reduced survival and reproductive success after exposure for 28 days	24
1.2	LC50 (21 days)	26

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
1.9	Exposure for 24 h resulted in 65% mortality 3 days after treatment; progeny produced before death had a significantly lower reproduction rate than controls, as did those in the next generation at nanogram/L (ppt) concentrations	27
2.0–2.1	LC50 (96 h)	24, 26–28
Grass shrimp, <i>Palaemonetes pugio</i>		
0.1–0.5	No effect on duration of molt cycle, but dose-related inhibition of regenerative limb growth noted (EC50 = 0.11 µg/L for left 5th periopod)	29
0.3–0.5	MATC ^b	30
0.3–0.5	Loss of positive phototaxis in embryos exposed for 96 h	31
0.3–1.0	Dose-dependent increase in swimming speed in light-adapted larvae	30
0.65	LC50 (7–14 days) intermolt-molt stage; deaths noted during or immediately after molting	29
<1.0	Almost all larvae that survived to day 15 eventually metamorphosed successfully to postlarvae	32
1.0 (initial), medium aged for 71 days, with or without sediments	No deaths of larvae in 22 days when sediments present; all larvae died within 22 days when sediments absent	34
1.0	Limited vertical migration of larvae	30
1.1	LC50 (96 h), early premolt stage	29
1.4	LC50 (96 h) larvae, 95% confidence interval (CI) 1.27–1.54, for wettable powder (WP-25) in water	32
1.6	LC50 (96 h), postlarvae	33
1.8	LC50 (96 h), larvae, 95% CI for technical grade in acetone is 1.64–2.08	32
2.5	All dead by day 15, regardless of formulation tested	32
2.5–5	Morphological abnormalities, both positive and negative phototaxis suppressed	29
3.4	LC50 (24-h exposure, held until molting complete in 24–48 h)	29
1.0 (initial)	Fatal to larvae exposed to medium aged for 71 days without sediments; no deaths of larvae after exposure for 22 days to medium aged for 71 days with sediments (about 0.5 µg/L)	34
202	LC50 (96 h), adult males and nonovigerous females	33
2000	Negligible mortality of late premolt stage during exposure for 96 h	29
6985	LC50 (96 h), adult ovigerous females	33
Crab, <i>Rithropanopeus harrisi</i>		
0.05	No effect on positive phototaxis response of stage IV larvae	35
0.1	Reduced positive phototaxis of stage IV larvae	35
0.3–0.5	Increased swimming speed of stage I, II, and III larvae	35
0.5	No adverse effects on larval survival during exposure for 20 days	36
1.0	Decreased larval survival during 20-day exposure	36
10	All larvae died during 32-day exposure in containers without sediments; containers with sediments were no longer toxic after 19 days	34
Crab, <i>Sesarma reticulatum</i>		
1	No adverse effects on larval survival during 40-day exposure	36
3	Decreased larval survival during 40-day exposure	36
10	All larvae died during 40-day exposure	36

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
Copepod, <i>Tigriopus californicus</i> 0.1–100	During 72-day exposure, no adverse effects were noted on adult survival and juvenile development at 0.1 µg/L. Reproduction was inhibited at 1 and 5 µg/L. Copepods exposed to 10 or 100 µg/L did not reproduce, were moribund, and had decreased survival.	1
Tadpole shrimp, <i>Triops longicaudatus</i> 0.75	LC40 (24 h)	7
Fiddler crab, <i>Uca pugilator</i> Juveniles exposed for 24 h once a week for 10 weeks, then held in clean seawater for an additional 14 weeks 0.2	No adverse effects on survival or ability to escape from test containers	37
2	No effect on survival, but reduced ability to escape from container	37
20	All died in 23 weeks; reduced mobility prior to death	37
200	All dead in 8 weeks; most deaths occurred in first 4 weeks	37
Adults exposed to 0.5, 5, or 50 after multiple autotomy of one chela and 5 walking legs	Continuous exposure for 18 days produced a dose-dependent retardation of regeneration and deaths during molt at 5 and 50 µg/L. The presence of sediment in test containers lessened effects, but did not eliminate them	38
Adults exposed for 1–3 weeks 0.5–50	Some reduction in number of burrows dug at 15 and 60 min after exposure	39
Unknown	Burrowing activity normal on sediments containing 1 mg/kg	39
FISH		
Mummichog, <i>Fundulus heteroclitus</i> 29,800 33,000–255,000	No deaths in 96 h LC50 (96 h)	40 5, 40
Mosquitofish, <i>Gambusia affinis</i> Unknown	Fish exposed to radiolabeled diflubenzuron for 33 days contained about 6% of the parent diflubenzuron vs. 54% for alga (<i>Oedogonium cardiacum</i>), 82% for snail (<i>Physa sp.</i>), and 94% for larvae of mosquito (<i>Culex pipiens quinquefasciatus</i>)	42
200 for 8 days followed by 300 until day 14 1000	Fish were 2.5 times more hyperactive than controls within 2 days, 4 times more during days 4–8, and no different from controls at day 14 No deaths in 10 days	43 7
Brown bullhead, <i>Ictalurus nebulosus</i> 13.2 in pond surface layer 1 h after treatment, <0.2 after 14 days	Maximum concentrations, in µg/kg whole-body fresh weight (FW), were 387 at day 1, 190 at day 2, 42 at day 4, and ND at day 7	44
Channel catfish, <i>Ictalurus punctatus</i> Unknown	Runoff from soil containing 0.55 mg diflubenzuron/kg at start produced maximum residues during 28 days, in µg/kg FW, of 4 in muscle and 10 in viscera	2
>100,000 370,000	LC50 (96 h) LC50 (96 h)	10, 15 9
Bluegill, <i>Lepomis macrochirus</i> 1–10 2.5	Bioconcentration factor of 13–20 after 24-h exposure Growth reduction of 56–86% for young of year held in large enclosures for 3 months — attributed to reduction in food items	45 51

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

Taxonomic Group, Organism, and Concentration in Medium (g/L [ppb])	Effect	Reference ^a
10	After exposure for 24 h, residues 24 and 48 h later were 848 and 8 µg/kg FW whole fish (less tail and viscera)	45
30	Growth reduction of 88–97% after exposure for 3 months	51
200 (initial); diflubenzuron concentrations ranged from 1.3–5.1 between 3 h and 19 days; for 4-chlorophenyl-urea, they were 0.6–3.1; and for 4-chloroaniline they were <0.1–0.4	Maximum concentrations in µg/kg whole-fish FW, for diflubenzuron were 119 at 3 h, 812 at 1 day, 55 at 5 days, 196 at 12 days, and 86 at 19 days. For the metabolite 4-chlorophenylurea, these values were 1.6 at 3 h, 8 at 1 day, 40 at 50 days, and 33 at 19 days; and for 4-chloroaniline, 0.8 at 3 h, 2.1 at 1 day, and 1.1–1.3 for days 5–19	46
135,000–660,000	LC50 (96 h)	5, 9
Cutthroat trout, <i>Oncorhynchus clarki</i>		
57,000–75,000	LC50 (96 h)	10, 15
Coho salmon, <i>Oncorhynchus kisutch</i>		
150,000	No deaths in 96 h	47
1,000,000	No deaths in 96 h after 15-min exposure	47
Rainbow trout, <i>Oncorhynchus mykiss</i>		
29–300	No adverse effects on eyed eggs or fingerlings in 30-day flowthrough exposure	10
625–10,000	Dose-dependent decrease in serum glutamate oxalacetate transaminase (GOT) activity in 96 h, but values overlapped normal GOT range from this hatchery	50
150,000	No deaths in 96 h	47
240,000 (95% CI 201,000–286,000)	LC50 (96 h)	9, 10
1,000,000	No deaths in 96 h after 15-min exposure	47
Yellow perch, <i>Perca flavescens</i>		
>50,000	LC50 (96 h)	15
Fathead minnow, <i>Pimephales promelas</i>		
36–45	Embryo-larval exposure for 30 days had no effect on survival, egg hatch, or growth	3, 11
>100,000	LC50 (96 h)	10, 15
430,000	LC50 (96 h)	9
White crappie, <i>Pomoxis annularis</i>		
5 (nominal), 3.3 (measured), 0.4 after 5 weeks	Whole-body residues, in µg/kg FW, were 133 at 1 day, 355 at 4 days, 197 at 14 days, and 62 at 21 days	48
10	Fish exposed for 24 h in uncontaminated media contained 822 µg/kg FW whole fish less tail and viscera. Exposure for 48 or 72 h plus 24 h in uncontaminated media produced residues of 533 and 630 µg/kg FW	45
Atlantic salmon, <i>Salmo salar</i>		
10	Avoided medium when given choice in 10-min trials	41
>50,000	LC50 (96 h)	15
Brook trout, <i>Salvelinus fontinalis</i>		
>50,000	LC50 (96 h)	15

^a 1, Antia et al. 1985; 2, Booth and Ferrell 1977; 3, Hansen and Garton 1982; 4, Kalafatic and Znidaric 1987; 5, Madder and Lockhart 1980; 6, Ho et al. 1987; 7, Miura and Takahashi 1974; 8, Ali and Lord 1980b; 9, Julin and Sanders 1978; 10, Johnson and Finley 1980; 11, Nebeker et al. 1983; 12, Kelada et al. 1980; 13, Mittal and Kohli 1988; 14, Rodrigues and Kaushik 1986; 15, Mayer and Ellersiek 1986; 16, Weis and Ma 1987; 17, Machado et al. 1990; 18, Tester and Costlow 1981; 19, Cunningham 1976; 20, Gulka et al. 1982; 21, Gulka et al. 1980; 22, Costlow 1979; 23, Levy and Miller 1978; 24, Nimmo et al. 1981; 25, Rao and Paul 1988; 26, Nimmo et al. 1979; 27, Nimmo et al. 1980; 28, Mayer 1987; 29, Touart and Rao 1987; 30, Wilson et al. 1987; 31, Wilson et al. 1985; 32, Wilson and Costlow 1986; 33, Wilson and Costlow 1987; 34, Cunningham et al. 1987; 35, Foward and Costlow 1978; 36, Christiansen et al. 1978; 37, Cunningham and Myers 1987; 38, Weis et al. 1987; 39, Weis and Perlmutter 1987; 40, Lee and Scott 1989; 41, Granett et al. 1978; 42, Metcalf

Table 17.4 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Laboratory Studies

et al. 1975; **43**, Ellgaard et al. 1979; **44**, Colwell and Schaefer 1980; **45**, Schaefer et al. 1979; **46**, Schaefer et al. 1980; **47**, McKague and Pridmore 1978; **48**, Apperson et al. 1978; **49**, Savitz 1991; **50**, Madder and Lockhart 1978; **51**, Tanner and Moffett 1995.

^b Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

17.4.5 Aquatic Organisms: Field Studies

Field use of diflubenzuron in aquatic habitats for control of pestiferous insects also affects other species (Table 17.5). Diflubenzuron applications in marshes, ponds, streams, lakes, and rice fields routinely cause population reductions — sometimes irreversible — in many species of nontarget organisms, especially crustaceans and aquatic insects. Taxonomic groups that seem comparatively tolerant to diflubenzuron include algae, turbellarians, rotifers, aquatic beetles, molluscs, annelid worms, ostracods, and fish (Table 17.5). Following multiple applications to lake and pond ecosystems, diflubenzuron was not measurable in water, sediment, and aquatic vegetation after several days (Booth and Ferrell 1977). Algae (*Plectonema boryanum*) reportedly degrade 80% of absorbed diflubenzuron in 1 h, primarily to 4-chlorophenylurea and 4-chloroaniline (Booth and Ferrell 1977).

Most authorities agree on four points:

1. Rates as low as 28 to 56 g diflubenzuron/surface ha (0.025 to 0.05 pounds/surface acre), or 2.5 to 16 µg/L, are highly effective against pestiferous dipterans, including many species of chaoborids, chironomids, and culicids (Mulla et al. 1975; Julin and Sanders 1978; Ali and Lord 1980a, 1980b; Cunningham 1986; Ali et al. 1988).
2. These same dosages suppress nontarget populations of cladocerans, copepods, mayfly nymphs, corixids, and springtails (Miura and Takahashi 1975; Mulla et al. 1975; Booth and Ferrell 1977; Julin and Sanders 1978; Ali and Lord 1980a; Cunningham 1986; Ali et al. 1988).
3. Moderately resistant to diflubenzuron are larvae of diving beetles, dragonfly adults and naiads, ostracods (*Cybericercus*, *Cyprinotus*), backswimmers, and water boatmen; highly resistant species include mosquitofish (*Gambusia affinis*), frogs and toads, snails, and algae (Miura and Takahashi 1974; Mulla et al. 1975; Nimmo et al. 1980).
4. All populations of survivors begin to recover within days or weeks, and recovery is usually complete within 80 days after the last treatment (Mulla et al. 1975; Booth and Ferrell 1977; Ali and Lord 1980a; Nimmo et al. 1980; Cunningham 1986).

Unlike laboratory studies, diflubenzuron does not bioaccumulate markedly in fish or biomagnify through food chains, although altered feeding habits may occur. Under field conditions, marsh or pond sediments usually contain <50 µg/kg FW. This concentration presents negligible risk to channel catfish (*Ictalurus punctatus*) over a 28-day period, suggesting little hazard to catfish during multiple mosquito control applications of diflubenzuron (Booth and Ferrell 1977). Bioaccumulation of diflubenzuron from marsh applications is minimal, as judged by results of uptake studies using marsh sediments containing 550 µg/kg. Maximum residues in fish tissues after 3 days were 4 µg/kg FW in muscle and 10 µg/kg DW in viscera (Schooley and Quistad 1979). Diflubenzuron residues are moderately persistent in algae, snails, salt marsh caterpillars (*Estigmene* spp.), and mosquito larvae, but are not biomagnified in food chains ending in fish (Schooley and Quistad 1979). Maximum diflubenzuron concentrations range from 50 to 720 µg/kg FW in whole body of three species of freshwater teleosts exposed to water treated up to 8 times with 135 g/ha (Gartrell 1981). Feeding habits of freshwater fishes change in ponds showing marked reductions (94 to 99%) in copepod and cladoceran populations after diflubenzuron treatment (Colwell and Schaefer 1980), perhaps due to availability of various food items. In one study, black crappie (*Pomoxis nigromaculatus*) and brown bullhead (*Ictalurus nebulosus*) altered their diets for 1 month after treatment,

eating about 3 times more insects and ostracods, and almost no cladocerans and copepods (usually, major items), than before treatment (Colwell and Schaefer 1980).

Although diflubenzuron is not sprayed directly on fresh waters in gypsy moth control, aerial spraying of large forest tracts may result in exposure of streams by way of leaf litter (Swift et al. 1988a). Residual diflubenzuron was present for at least 4 months on leaves submerged in flowing water, and it was toxic to various invertebrates. For example, treated leaves of the tulip poplar (*Liriodendron tulipifera*) that contain 10 mg diflubenzuron/m² after 4 months of submersion produce adverse effects on survival and growth when fed to craneflies (*Tipula abdominalis*, *Platycentropus radiatus*) (Swift et al. 1988b). The effects of diflubenzuron on leaf-litter processing rates in streams is unresolved and merits additional research (Swift et al. 1988a, 1988b).

Table 17.5 Diflubenzuron Effects on Selected Aquatic Organisms: Field Studies

Ecosystem, Dose, and Other Variables	Effect	Reference ^a
COASTAL MARSH, LOUISIANA		
6 applications, each of 28 g/ha, over 18-month period	Severe reduction in populations of amphipods, dragonfly naiads, corixid nymphs, and some adult beetles. Increased populations of snails, aquatic insect adults, and 2 species of fish. No change in 27 taxa. Results confounded by severe drought in experimental and control areas	1, 2
FARM POND		
2.5, 5, or 10 µg/L; single application	Inhibited adult emergence by 95–100% of a gnat (<i>Chaoborus astictopus</i>), 2–7 days after treatment. Crustacean zooplankton suppressed at all treatment levels, especially cladocerans and copepods. Rotifers and algae were not affected. Bluegills that fed predominantly on cladocerans and copepods switched to chironomid midges and terrestrial insects after treatment, with no adverse effects	3
LABORATORY STREAM COMMUNITIES		
0.1, 1, 10, or 50 µg/L for 5 months	Aquatic insect populations were the most sensitive group, especially mayflies, stoneflies, and dipterans. These, and other invertebrates, showed rapid and permanent reductions in biomass and diversity at 1.0 µg/L and higher. Diversity showed an apparent dose-response relation, with no effect at 0.1 µg/L, intermediate reductions at 1 µg/L, and maximal reductions at 10 and 50 µg/L	4
LAKE		
110 g/ha (3.7 µg/L), or 220 g/ha (7.4 µg/L); single application	At low dose, amphipods (<i>Hyalella azteca</i>) had 97% population reduction that remained depressed; temporary reduction in cladoceran and copepod populations. At high dose, marked population reductions in cladocerans, copepods, and ostracods (<i>Cyrinofus</i> sp.). Oligochaete worms were tolerant to both doses	5
110–280 g/ha	Effectively suppressed adult emergence of nuisance midges (<i>Tanytarsus</i> , <i>Procladius</i>) for up to 2 weeks; ineffective against a more pestiferous midge species (<i>Chironomus decorus</i>)	6
156 g/ha to lake surface, equivalent to 12 µg/L on April 26 and again on August 24	After first treatment, reduction within 1 week of 3 species of cladocerans (<i>Daphnia laevis</i> , <i>Ceriodaphnia</i> sp., <i>Bosmina longirostrus</i> sp.), and 2 species of copepods (<i>Cyclops</i> sp., <i>Diaptomus</i> sp.). No recovery of <i>Daphnia</i> and <i>Ceriodaphnia</i> for 6 months, but <i>Bosmina</i> reappeared 11 weeks later. <i>Diaptomus</i> was depleted for 4 months, but <i>Cyclops</i> recovered in 6–7 weeks. The amphipod <i>Hyalella azteca</i> was eliminated within 4 weeks, and no recolonization was evident after 6 months. No adverse effects on oligochaetes, snails (<i>Physa</i> sp.), or ostracods (<i>Cypridopsis</i> sp.). After second treatment, temporary reduction in <i>Cyclops</i> and <i>Bosmina</i> , and no significant effects on ostracods, snails, or worms	7

Table 17.5 (continued) Diflubenzuron Effects on Selected Aquatic Organisms: Field Studies

Ecosystem, Dose, and Other Variables	Effect	Reference ^a
PASTURE POND		
280 g/ha, single application	Controlled pasture mosquitoes, <i>Aedes nigromaculatus</i> and <i>Aedes melanimon</i> , and caused temporary reductions of cladoceran and mayfly nymph populations. Many cladocerans and mayflies died during the posttreatment ecdysis, characteristically with signs of incomplete cleavage of the middorsal ecdysial suture. More-tolerant groups included corixid and notonectid nymphs, and adult aquatic beetles. No effects on the most tolerant groups: turbellarians (<i>Mesotoma</i> , <i>Bothromestoma</i>), rotifers (<i>Asplanchna</i>), ostracods, algae, and spiders (<i>Pardosa</i> spp., <i>Lycosa</i> spp.)	8
POND		
13.2 µg/L in pond surface layer 1 h after treatment; <0.2 µg/L after 14 days	Residues, in µg/kg whole-body FW, in black crappie (<i>Pomoxis nigromaculatus</i>) were 426 at day 1, 194 at day 2, 56 at day 4, and not detectable at day 7	9
13.8 µg/L 1 h after forest was sprayed with 70 g/ha; this declined to not detectable in 20 days	Zooplankton populations were reduced 3 days after treatment and remained suppressed for 2–3 months; low survival of caged amphipods and immature corixids 1–6 days after treatment; littoral insects were reduced in abundance 21–34 days after treatment, but recovered; manna grass (<i>Glyceria borealis</i>) concentrations declined from 0.3 mg/kg FW 1 h post spray to not detectable in 10 days; sediment residues were 0.1 mg/kg FW after 12 h and not detectable in 10 days	14
16 µg/L (estimated from application of 56 g/ha)	Caused declines in 3rd and 4th instar larvae of <i>Culex tarsalis</i> mosquito 2–8 days after treatment, but not at 11 days	10
80 µg/L (estimated from application of 280 g/ha)	Adult <i>C. tarsalis</i> emergence from treated larvae almost completely inhibited for at least 11 days posttreatment	10
RICE FIELD, FLOODED		
1.1–28 g/ha	100% control of massive rice field populations of 4th instar larvae of the mosquito <i>Psorophora columbiiae</i> 3–5 days after treatment. Significant reductions in certain nontarget aquatic insect populations	11
About 1000 µg/L (as judged by 280 g/ha in rice field water 10 cm deep)	Significant reductions in immature populations of the rice water weevil (<i>Lissorhopterus oryzophilus</i>) 4–5 days after rice emergence in a continuously flooded field	12
About 1500 µg/L (420 g/ha)	<i>Lissorhopterus</i> population reduced 75% when applied 7 days after rice emergence	12
RIVER		
1250 µg/L added for 1 h to control simuliid flies	After initial depression, target dipteran insects, including simuliids, increased 4–40 times over pretreatment levels after 3–4 weeks, suggesting that one-time applications are useless. No adverse effects on adults and fry 3–4 weeks after exposure of dace (<i>Phoxinus lagowski</i>) and minnow (<i>Leuciscus hakonensis</i>)	13

^a 1, Farlow 1976; 2, Farlow et al. 1978; 3, Apperson et al. 1978; 4, Hansen and Garton 1982; 5, Ali and Mulla 1978a; 6, Johnson and Mulla 1981; 7, Ali and Mulla 1978; 8, Miura and Takahashi 1975; 9, Colwell and Schaefer 1980; 10, Mulla et al. 1975; 11, Steelman et al. 1975; 12, Smith et al. 1988; 13, Satake and Yasuno 1987; 14, Sundaram et al. 1991.

17.4.6 Birds

Birds are comparatively resistant to diflubenzuron, as judged by the ability of the mallard (*Anas platyrhynchos*) to tolerate single oral doses up to 2000 mg/kg BW or dietary loadings up to 4640 mg/kg ration for 8 days (Table 17.6). Poisoning of insectivorous birds by diflubenzuron, after

spraying in orchards as recommended, is highly improbable (Muzzarelli 1986). This conclusion is based on the maximum possible daily intake of insects by wild nestlings (15 mg/kg BW in Great tit, *Parus major*; 10 mg/kg BW in tree sparrow, *Passer montanus*), on a maximum whole-body loading of 0.5 mg diflubenzuron/kg FW in insect prey, and on observations of normal growth and subsequent breeding of nestlings in orchards sprayed with diflubenzuron (Muzzarelli 1986).

Despite the apparent absence of direct effects in forest birds, the widespread use of diflubenzuron in the suppression of forest insect defoliators may lead to potentially harmful effects by reducing populations of immature lepidoptera and other mandibulate herbivorous insects upon which they feed. All field evidence collected to date, however, is either inconclusive or negative. In one study, 70.75 g diflubenzuron/ha was applied to an oak forest (*Quercus rubra*, *Q. velutina*, *Q. prinus*) in West Virginia to control first and second instars of gypsy moths (Martinat et al. 1987) (Table 17.6). The maximum diflubenzuron residue recorded in a wide variety of canopy forager birds (great crested flycatcher, *Myiarchus crinitus*; eastern wood peewee, *Contopus virens*; black-capped chickadee, *Parus atricapillus*; tufted titmouse, *Parus bicolor*; blue-gray gnatcatcher, *Polioptila caerulea*; red-eye vireo, *Vireo olivaceus*; warblers, *Dendroica* spp.; scarlet tanager, *Piranga olivacea*) was 0.21 mg/kg whole-body FW. A similar value, 0.20 mg/kg whole-body FW, was recorded in ground or low foragers, including wood thrush (*Hylocichla mustelina*), ovenbird (*Seiurus aurocapillus*), rufous-sided towhee (*Pipilo erythrorthalmus*), chipping sparrow (*Spizella passerina*), song sparrow (*Melospiza melodia*), and indigo bunting (*Passerina cyanea*) (Martinat et al. 1987). Neotropical migrants breeding in a diflubenzuron-treated forest had significantly lower fat reserves on a dry weight basis than did conspecifics from reference sites, possibly due to a reduction in food availability and quality (Whitmore et al. 1993). In another study, up to 280 mg diflubenzuron/ha applied to control the Douglas-fir tussock moth (*Orygia pseudotsugata*), an important defoliator of true firs (*Abies* spp.) and Douglas-fir (*Pseudotsuga menziesii*) in western North America, had no adverse effects on forest birds, as judged by population censuses, nesting studies, and bird behavior (Richmond et al. 1979) (Table 17.6).

Domestic chickens (*Gallus* sp.) metabolize diflubenzuron to a greater extent than insects, but less than rodents and ruminants. The main pathway of diflubenzuron degradation in chickens is through cleavage of the urea bridge, whereas rats and cows tend to hydroxylate and conjugate the parent molecule (Opdycke and Menzer 1984). Metabolism studies in chickens showed that major residues in tissues and eggs were unchanged diflubenzuron and 4-chlorophenylurea; also present were 2,6-difluorobenzoic acid and 4-chloroaniline (Gartrell 1981). Metabolites in chicken excreta included 4-chlorophenylurea, 4-chloroaniline, 2,6-difluorobenzamide, 2,6-difluorobenzoic acid, and several unidentified compounds (Opdycke and Menzer 1984). At high dietary loadings of 50 to 500 mg/kg ration, diflubenzuron accumulates in fat, egg, and muscle tissues of chickens; however, excretion is rapid and residues are usually negligible after 5 weeks on a clean diet (Table 17.6). Diflubenzuron fed at levels up to 250 mg/kg ration to male broiler chickens for 98 days had no effect on hyaluronic acid (HA) concentration in the combs and wattles (Crookshank et al. 1978). Both chitin and HA are polysaccharides and have a common biochemical precursor, uridine diphospho N-acetyl-glucosamine (UDPGA) (Crookshank et al. 1978), which is used in the synthesis of chitin by insects and in the production of HA by vertebrates. Since diflubenzuron interferes with the incorporation of UDPGA into chitin by insects but not with HA production, it would seem that diflubenzuron is relatively harmless to birds. However, more research is needed for verification.

Intraspecies differences in diflubenzuron metabolism are reported for domestic chickens. The White Leghorn breed, for example, produced eggs with significantly higher residues than other breeds tested after 3 weeks on a diet containing 50 mg diflubenzuron/kg, and it had elevated concentrations in fat tissues after 15 weeks on a 10-mg/kg diet (Opdycke et al. 1982b; Opdycke and Menzer 1984). In chickens, diflubenzuron is usually eliminated more rapidly in feces than in eggs, but in the White Leghorn breed, the major route of elimination is via egg production. The White Leghorn breed also differed significantly from the Rhode Island Red/Barred Plymouth Rock

(RIR/BPR) breed in ability to metabolize diflubenzuron administered orally or intravenously (Table 17.6). White Leghorn chickens accumulated diflubenzuron to a greater extent than RIR/BPR chickens, and they retained residues for longer periods. Also, White Leghorn chickens produced a higher percentage and greater number of diflubenzuron metabolites in their excreta than other breeds tested (Opdycke et al. 1982b). Differences in ability to metabolize diflubenzuron between different strains of domestic chickens may be due to differences in lipid metabolism associated with egg production (Opdycke and Menzer 1984). No comparable database exists for avian wildlife, and one should be developed through research.

Table 17.6 Diflubenzuron Effects on Selected Birds

Species, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
RED-WINGED BLACKBIRD, <i>Agelaius phoeniceus</i>		
Oral, single dose, 3700 mg/kg body weight (BW)	Insufficient to kill 50%	12
MALLARD, <i>Anas platyrhynchos</i>		
Oral, single dose, 2000 mg/kg BW	Insufficient to kill 50%; anorexia observed on day after treatment	1
Dietary, 4640 mg/kg ration	Insufficient to kill 50% in 8 days	2
FOREST BIRDS		
From oak (<i>Quercus</i> spp.) forest sprayed aerially with 70.75 g diflubenzuron/ha to control gypsy moth instars; samples collected 3 days prior to spraying, and up to 21 days after spraying	Maximum concentrations, in mg/kg fresh weight (FW) whole body, were 0.21 in canopy birds 3 days postspray (0.09 at day 21); 0.20 in understory birds 1 day postspray, and nondetectable (ND) at day 21; 0.45 in foliage 1 day postspray (0.18 at day 21); 0.49 in foliage arthropods at day 3, and 0.1 at day 21; ND in litter at all times; 0.11 in litter arthropods at day 10 and 0.03 at day 21. Controls, in all cases, contained <0.03, except litter arthropods, which contained 0.06 mg/kg	3
From fir (<i>Abies</i> sp., <i>Pseudotsuga menziesii</i>) forest sprayed aerially with 140 or 280 mg/ha to control Douglas-fir tussock moth; effects evaluated in year of spraying and 1 year later	No significant changes in species diversity, brain cholinesterase activity, survival, morbidity, or behavior at either dose. Significant increases in total breeding pairs noted 1 year later in Townsend's warbler (<i>Dendroica townsendi</i>), MacGillivray's warbler (<i>Oporornis tolmiei</i>), and mountain chickadee (<i>Parus gambeli</i>). Some reductions in populations of golden-crowned kinglet (<i>Regulus satrapa</i>), lazuli bunting (<i>Passerina amoena</i>), and warbling vireo (<i>Vireo gilvus</i>), but all differences were attributed to biological variability rather than to insecticide effects	4
DOMESTIC CHICKEN, <i>Gallus</i> spp.		
Intravenous injection		
1 mg/kg BW, White Leghorn breed, single dose	Half-time (T _b 1/2) persistence in blood of 14.7 h, 12% of dose excreted in 24 h	5
1 mg/kg BW, Rhode Island Red/Barred Plymouth Rock breed (RIR/BPR), single dose	T _b 1/2 of 8.4 h in blood; 29% of dose excreted in 24 h	5
Oral route		
5 mg/kg BW, White Leghorn breed, single dose	Maximum residues after dosing, in mg/kg FW, were 0.25 in egg, 0.4 in eggshell, 0.19 in kidney, and 0.16 in ovary. Excretion of 50% in 8–12 h	5, 6
5 mg/kg BW, RIR/BPR breed, single dose	Maximum residues after dosing were 0.14 mg/kg FW in eggs and ND in eggshell, kidney, and ovary. Excretion of 51% in 30–36 h and 82–91% in 13 days	5, 6

Table 17.6 (continued) Diflubenzuron Effects on Selected Birds

Species, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
White Leghorn and RIR/BPR strains given 5 mg/kg BW daily for 11 days; residues measured in egg during dosing and for 10 days after dosing	Residues, in mg/kg FW egg, for White Leghorn strain were highest at days 9 (3.5) and 11 (2.6). Values were 0.04 at day 20, and ND at day 21. Residues in RIR/BPR were lower: 1.7 at day 9, 1.1 at day 11, 0.02 at day 20, and ND at day 21. Tb 1/2 for egg residues ranged between 34 and 38 h	5
Dietary route		
0.05 mg/kg for 28 days	Fat contained 0.018 mg/kg FW at 28 days and <0.0006 mg/kg 7 days after withdrawal	7
0.5 mg/kg for 28 days	Fat contained 0.033 mg/kg FW at 28 days and less than 0.005 mg/kg 7 days after withdrawal	7
1.6 mg/kg for 3 weeks	Minor effects on larvae of house fly (<i>Musca domestica</i>) in manure; egg residue of 0.05 mg/kg FW	8
3.1 mg/kg for 3 weeks	Killed 85% of fly larvae in manure; egg residue of 0.25 mg/kg FW	8
5 mg/kg for 28 days	Fat contained 1.16 mg/kg FW at 28 days and <0.032 mg/kg 7–14 days after withdrawal	7
6.2 mg/kg for 3 weeks	Complete inhibition of fly larvae in manure; egg residue of 0.55 mg/kg FW	8
12.5, 25, or 50 mg/kg for 3 weeks	All diets completely inhibited fly larval development in manure; white egg residues, in mg/kg FW, were 1.0 for 12.5 mg/kg diet, 2.1 for 25-mg/kg group, and 2.9 for the 50-mg/kg group; residues in brown eggs were half those of white eggs	8
Mature White Leghorn hens fed diets containing 10, 50, 100, or 500 mg diflubenzuron/kg for 8 weeks	No adverse effects of any diet on feed consumption, growth, egg production, egg weight, eggshell thickness, fertility, hatchability, or progeny performance. Maximum concentrations in tissues after 8 weeks, in mg/kg FW, in the 500-mg/kg diet group, were 53 in fat, 10 in egg, 9 in liver, and 0.9 in muscle; for the 100-mg/kg group, these values were 21 in fat, 10 in liver, 3 in egg, and 0.5 in muscle; for the 50-mg/kg group, residues were 1.5 in fat, 1 in egg, 0.8 in liver, and 0.2 in muscle. Five weeks after withdrawal from all diets, diflubenzuron was <0.05 mg/kg FW in all tissues	9
Male broiler and layer breed chickens fed 205 mg/kg ration for 98 days beginning at age 1 day	No significant effect on body weight, food consumption, or weight of testes, liver, comb, and feet	10
Male and female layer-breed chickens were fed diets containing up to 250 mg/kg for 58 weeks, including a 26-week laying cycle. Progeny were reared to age 2 weeks	No significant effect of any dose level on survival, egg production, egg weight, eggshell weight, fertility, hatchability, or hatch weight and body weight of progeny. No gross abnormalities in progeny; growth and feathering as in controls	11

^a 1, Hudson et al. 1984; 2, Farlow 1976; 3, Martinat et al. 1987; 4, Richmond et al. 1979; 5, Opdycke and Menzer 1984; 6, Opdycke et al. 1982b; 7, Gartrell 1981; 8, Miller et al. 1975; 9, Cecil et al. 1981; 10, Kubena 1981; 11, Kubena 1982; 12, Whitmore et al. 1993.

17.4.7 Mammals

No data are available on effects of diflubenzuron on mammalian wildlife. However, results of studies on small laboratory animals and domestic livestock are available (Table 17.7), and these indicate several trends. Adverse effects levels occurred in dogs fed diets containing 160 mg/kg (6.2 mg/kg BW daily) for 13 weeks (abnormal blood chemistry), in mice given 125 mg/kg BW daily for 30 days (hepatocellular changes), in rabbits fed diets containing 640 mg/kg for 3 weeks

(abnormal hemoglobin), and in rats given 5000 mg/kg BW daily for 13 weeks (abnormal hemoglobin). Accumulations of diflubenzuron occurred in several species. Elevated tissue residues — but no other measurable effects — occurred in cows given 0.05 to 0.5 mg/kg ration for 28 days or 1 to 16 mg/kg BW for 4 months, in pigs given a single oral dose of 5 mg/kg BW; and in sheep given a single oral dose of 10 mg/kg BW (Table 17.7). No observable adverse effect levels occurred in cows given 0.25 mg/kg BW daily for 4 months; in rabbits given 4 mg/kg BW daily on days 6 to 18 of gestation, in dogs fed diets containing 40 mg/kg for 13 weeks (equivalent to 1.6 mg/kg BW daily); in rats fed diets containing 160 mg/kg for 2 years; and in rabbits and rodents given single oral or dermal doses <2000 mg/kg BW (Table 17.7).

All available data indicate that diflubenzuron is not a mutagen, teratogen, or carcinogen. Diflubenzuron is not mutagenic, as judged by the results of:

1. The mouse lymphoma forward mutation test at the thymidine kinase locus (detects mutations to a nonfunctional thymidine kinase in a line of culture mouse lymphoma cells).
2. The Ames *Salmonella typhimurium* microsome reverse mutation test (ability to produce point gene mutations of a base pair).
3. The mouse micronucleus test (which detects chromosome breakage or chromosome loss from mitotic abnormalities in bone marrow erythrocytes) (MacGregor et al. 1979).
4. A DNA damage study with yeast, *Saccharomyces cerevisiae* (Gartrell 1981).

No teratogenicity or reproductive effects were associated with elevated doses of diflubenzuron in all species of mammals tested (Gartrell 1981). Diflubenzuron suppresses melanogenesis and uptake of nucleosides in mouse melanoma cells (Jenkins et al. 1986), and it inhibits growth of experimental tumors in mice, either alone or in combination with CoCl₂ (Table 17.7). Mixed function oxidase, induced by 3-methylcholanthrene, enhances the antitumor properties of diflubenzuron, suggesting that aromatic hydroxylation may be required for tumor growth regulation (Jenkins et al. 1986). The most likely diflubenzuron metabolite that affects tumor growth regulation is the form oxidized at the 2 carbon of the phenyl ring; other metabolites tested (i.e., 4-chlorophenylurea, 3-OH-diflubenzuron) are only marginally effective (Jenkins et al. 1986). Diflubenzuron did not produce tumors in fetal cells of hamsters (*Cricetus* spp.) at whole-body doses of 500 mg/kg, and this also suggests a relatively low oncogenic potential (Quarles et al. 1980). Diflubenzuron is not cytotoxic and does not inhibit the synthesis of complex carbohydrates in animal cells, as judged by results of studies with cultured rat glial cells, wherein diflubenzuron was not metabolized to any measurable extent, and more than 98% could be recovered from particulate fractions of whole cells (Bishai and Stoolmiller 1979).

Intestinal absorption of diflubenzuron in laboratory rats, measured as the sum of urinary and biliary excretion, decreases with increasing dose: from 50% at a single oral dose of 4 mg/kg BW to 4% at 900 mg/kg BW. Excretion is almost complete after 75 h; at that time, up to 4% of the administered dose is recovered from skinned carcasses (Willems et al. 1980). About 80% of diflubenzuron metabolites excreted by rats seem to have the basic diflubenzuron structure intact. Three metabolites are largely excreted as conjugates in the bile. One metabolite, 2,6-difluorobenzoic acid, is excreted largely in urine. Its counterpart, 4-chlorophenylurea, was not present in urine or bile in appreciable quantity, nor was 4-chloroaniline detected (Willems et al. 1980). Lifetime feeding studies of 4-chloroaniline, a relatively common diflubenzuron metabolite, showed no compound-related effects in laboratory mice and rats (Gartrell 1981).

Oral treatment of sheep and cattle (*Bos* spp.) with diflubenzuron is followed by absorption of the compound through the gastrointestinal tract, metabolism, and elimination of residues through the urine, feces, and, to a very limited extent, milk. Intact diflubenzuron is eliminated in the feces of orally dosed cattle and sheep (Ivie 1978). Major metabolites of diflubenzuron excreted by cattle and sheep result from hydroxylation on the difluorobenzoyl and chlorophenyl rings, and by cleavage between the carbonyl and amide groups to produce metabolites that are excreted free or as conjugates (Ivie 1978). Cattle dosed repeatedly with diflubenzuron had detectable residues only in liver

and milk. The parent compound, 4-chlorophenylurea, 2,6-difluorobenzoic acid, and 4-chloroaniline compose only 15% of the total residue in liver. The bulk of the residue is not extractable (Gartrell 1981). Dietary levels of 5 mg/kg ration produce low (13 µg/L), but detectable, diflubenzuron concentrations in milk of cattle (Gartrell 1981). The major hydroxylated diflubenzuron metabolite in cow milk (*N*-[[(4-chlorophenyl)amino]carbonyl]-2,6-difluoro-3-hydroxybenzamide) when fed to white rats is rapidly excreted with little biotransformation (Ivie 1978).

Metabolism of diflubenzuron by mammals and birds probably occurs by way of hydroxylation, conjugation, and cleavage of the urea moiety (Opdycke et al. 1982a); however, interspecies differences are considerable. In cows, for example, the major identified metabolic transformation is hydroxylation at the 3-position of the 2,6-difluorobenzoyl ring. In sheep, however, major metabolites arise through cleavage of the amide bond at the benzoyl carbon to produce 2,6-difluorobenzoic acid, which is excreted in the urine either free or conjugated with glycine (Ivie 1978). The major diflubenzuron metabolite in cow urine is 2,6-difluoro-3-hydroxydiflubenzuron, accounting for 45%, and in feces 18%; unchanged diflubenzuron accounts for 43% of the administered dose in cow feces. In sheep urine, 2,6-difluorobenzoic acid and 2,6-difluorohippuric acid account for 57%; in sheep feces, unchanged diflubenzuron is 97% (Ivie 1978). In swine, the great majority of the administered dose is eliminated in feces unchanged; the urine contains mostly metabolites, indicating that most of the absorbed diflubenzuron is metabolized (Opdycke et al. 1982a).

Table 17.7 Diflubenzuron Effects on Selected Mammals

Species, Mode of Administration, Dose, and Other Variables	Effect	Reference ^a
CATTLE, <i>Bos</i> sp.		
Dermal 0.125 mg/cm ² hide, single application, 1% solution to 400 cm ² skin surface	No absorption through skin; rapid disappearance. Maximum residues in hair, in mg/kg fresh weight (FW), were 128 after 1 week, 19 after 2 weeks, and 4 after 4 weeks. For skin, these values were 0.4, 0.1, and <0.1	1
Diet 0.05 mg/kg ration for 28 days	No detectable residues in milk and tissues, except liver (0.01 mg/kg FW); liver residues remained detectable after a 7-day withdrawal period	2
0.5 mg/kg ration for 28 days	No detectable residues in milk and tissues, except liver (0.08 mg/kg FW); liver residues remained detectable after a 7-day withdrawal period	2
5 mg/kg ration for 28 days	Liver residue of 0.54 mg/kg FW remained elevated after a 7-day withdrawal period; residues in milk reached 0.013 mg/L within the first few days of feeding and declined to nondetectable (ND) levels after a 4-day withdrawal period	2
Fed diets equivalent to 0.25 mg/kg body weight (BW) daily for 4 months, single animal	No detectable residues in any tissue. Tb 1/2 of 4–5 days in manure; manure gave >95% control of larvae of the face fly, <i>Musca autumnalis</i>	3
Fed diet equivalent to 1 mg/kg BW daily for 4 months, single animal	No detectable residues in any tissue except omental fat (0.1 mg/kg FW). No houseflies (<i>Musca domestica</i>) or face flies developed in manure	3
Fed diet that increased from 1 mg/kg BW daily to 8 mg/kg BW over a 2-month period, then 16 mg/kg BW daily for 3 months	No detectable diflubenzuron residues in heart, muscle, or kidney; 130 µg/kg FW in liver; about 250 µg/kg FW in subcutaneous fat	3
Holstein bull calves fed diet equivalent to 2.8 mg/kg BW daily for first 7 months, then 1 mg/kg BW daily for 6–12 months	No effect on weight gain, serum testosterone at age 11 months, libido, sperm mobility, semen volume, and sperm concentration. No histopathology of liver, lung, kidney, or spleen. No tissue residues — except for one bull slaughtered at age 5 months: <20 µg/kg FW in muscle, 20 in liver and kidney, 40 in subcutaneous fat, and 80 in renal and omental fat	4

Table 17.7 (continued) Diflubenzuron Effects on Selected Mammals

Species, Mode of Administration, Dose, and Other Variables	Effect	Reference^a
Fed diet equivalent to 8 mg/kg BW daily for 4–5 months, single animal	No detectable residues in milk	3
Fed diet equivalent to 16 mg/kg BW daily for 4–5 months, single animal	Maximum concentrations recorded were 20 µg/L in milk and 250 µg/kg FW in body fat. No obvious adverse effects on feeding behavior	3
Oral 10 mg/kg BW, single-dose to a lactating cow	Extensively metabolized in 4 days; almost all totally excreted in 7 days: about 85% in feces, 15% in urine, 0.2% in milk. At 7 days, liver contained 2.9 mg/kg FW, skin 0.4, and all other tissues <0.4	1
DOG, <i>Canis familiaris</i>		
Fed diets containing 10, 20, 40, or 160 mg/kg (equivalent to 0.42, 0.84, 1.64, or 6.24 mg/kg BW daily) for 13 weeks	Abnormal hemoglobin levels in 160 mg/kg group after 6 weeks; no other abnormal findings or histopathology observed in any group at 13 weeks	2
ANGORA GOAT, <i>Capra</i> sp.		
30 mL of 2% diflubenzuron solution applied dermally 6 weeks after shearing, 25-kg females	Protected against Angora goat-biting lice (<i>Bovicola limbatus</i>) for up to 18 weeks	5
DOMESTIC MOUSE, <i>Mus</i> sp.		
Diet 4, 8, 16, or 50 mg/kg ration for 80 weeks	Increase in tumors in females at the 16 mg/kg level	2
Intraperitoneal injection 3 daily injections of 1.2 mg, equivalent to 144 mg/kg BW, tumor-bearing strain	Tumors conditioned with CoCl ₂ then treated with diflubenzuron showed a 75% reduction in rate of tumor increase	6
5 daily injections of 20 mg (total of 100 mg, equivalent to 4000 mg/kg BW), C57BL/6 strain with B16 melanomas 2150 mg/kg BW	Initial antitumor activity, as judged by 11–20% decrease in tumor volume, and a 2–3 day increase in tumor doubling time. But at midtreatment, tumors regained control rate of volume increase	6
Oral Adult males given 125, 500, or 2000 mg/kg BW daily for 30 days	Insufficient to kill 50%	7
>4640 mg/kg BW	Hepatocellular changes at all dose levels, including histopathology and altered activities of glutathione S-transferase enzymes	8
	Acute oral LD ₅₀	2, 7, 8
RABBIT, <i>Oryctolagus</i> sp.		
Dermal 2000 mg/kg BW	Insufficient to kill 50%	7
Diet Males given 640 mg/kg feed for 18–21 days	Abnormal hemoglobin	2
<i>In vitro</i> studies Up to 5 mg/L	Protein and RNA synthesis rates were significantly stimulated in liver, and inhibited in muscle in a dose-dependent manner. Maximum effect in both tissues occurred at 5 mg/L for protein synthesis and 0.2 mg/L for RNA synthesis	9
Oral Females given 1, 2, or 4 mg/kg BW daily on days 6–18 of gestation	No compound-related maternal toxicity or birth defects	2

Table 17.7 (continued) Diflubenzuron Effects on Selected Mammals

Species, Mode of Administration, Dose, and Other Variables	Effect	Reference ^a
SHEEP, <i>Ovis aries</i>		
Dermal		
Merino sheep exposed to mass-released gravid females of the sheep blowfly (<i>Lucilia cuprina</i>) — a severe ectoparasite in Australia that may kill — in a fly-proof animal house after dermal application of 1000, 1500, or 2500 mg diflubenzuron/L; sheep thoroughly wetted twice during 4 days	1000 mg/L protected against fly strike for at least 110 days; 1500 mg/L protected until end of trial at 170 days; 2500 mg/L provided excellent protection against severe infestation. No resistance to diflubenzuron was acquired by blowflies	10
Oral		
Single dose of 10 mg/kg BW	Residues after 7 days, in mg/kg FW, were about 3 in liver, 0.4 in kidney, and <0.2 in all other tissues	1
Single dose of 500 mg/kg BW	In 4 days, bile accounted for 36% of diflubenzuron metabolites excreted, feces 32%, and urine 24%; in 7 days, feces were the major pathway	1
LABORATORY WHITE RAT, <i>Rattus sp.</i>		
Diet		
Fed 10, 20, 40, or 160 mg/kg ration for three generations	No effect on fetotoxicity or teratogenicity	2
Fed 10, 20, 40, or 160 mg/kg ration for 2 years	No compound-related effects	2
Oral		
Females given 1, 2, or 4 mg/kg BW daily on days 6–15 of gestation	No compound-related maternal toxicity or birth defects	2
4 mg/kg BW, single dose	Intestinal absorption of 50%	11
5 mg/kg BW, single dose	72–93% excreted in 6 days, mostly in feces	11
900 mg/kg BW, single dose	Intestinal absorption of 4%	11
>4640 mg/kg BW	Acute oral LD ₅₀	2, 7
Males given 5000 mg/kg BW daily for 13 weeks	Abnormal hemoglobin on days 1–4, and on day 8	2
SWINE, <i>Sus sp.</i>		
Adult female pig given single oral dose of 5 mg/kg BW and observed for 11 days	By 11 days, 82% of dose was excreted unchanged in feces, and 5% in urine as metabolites (4-chlorophenylurea, 2, 6-difluorobenzoic acid, 4-chloroaniline, and 2,6-difluorobenzamide). Tissue residues, in mg/kg FW, ranged from ND in bone to 0.04–0.09 in stomach wall, brain, pancreas, small intestine, blood, heart, muscle and ovary; from 0.11–0.2 for large intestine, subcutaneous fat, lymph, lung, and kidney; and from 0.23–0.4 in liver, omental fat, and gall bladder	12

^a 1, Ivie 1978; 2, Gartrell 1981; 3, Miller et al. 1976; 4, Miller et al. 1979; 5, Miller et al. 1985; 6, Jenkins et al. 1986; 7, Poplyk 1989; 8, Young et al. 1986; 9, El-Sebae et al. 1988; 10, Hughes and Levot 1987; 11, Willems et al. 1980; 12, Opdycke et al. 1982a.

17.5 RECOMMENDATIONS

Since diflubenzuron toxicity seems to be similar in both insects and crustaceans, extreme care must be taken when this compound and other chitin synthesis inhibitors are used for insect control in areas where aquatic crustaceans occur. Otherwise, ecological instability may result, with consequences

for feeding, metabolism, growth, reproduction, and survival of numerous nontarget organisms (Christiansen 1986). Specifically, diflubenzuron use in saltmarsh mosquito breeding areas or on agricultural lands less than 5 km from coastal areas is not recommended because of concerns that runoff may reach the adjacent estuaries, which are the primary hatcheries for many economically important species of crustaceans (Costlow 1979; Cunningham 1986; Cunningham and Myers 1986; Fischer and Hall 1992). Also, diflubenzuron concentrations in seawater should not exceed 0.1 µg/L, the minimum concentration known to produce measurable behavioral changes in estuarine crustacean larvae (Cunningham and Myers 1986). Concentrations of 2.5 µg diflubenzuron/L and higher in freshwater are known to reduce arthropod populations by 67 to 71%, resulting in reduced growth of young of year bluegills. Growth inhibition, in turn, may result in greater starvation, increased predation, reduction in over-winter survival, and diminished to poor recruitment (Tanner and Moffett 1995). If diflubenzuron and other insect growth regulators continue to be used near productive aquatic habitats, then food chain transfer studies are recommended (Fischer and Hall 1992). High accumulations of diflubenzuron by aquatic algae — up to 4.5 mg/kg DW in some cases (Booth and Ferrell 1977) — strongly implicate food chain transfer as a potential mechanism of contaminant transfer in aquatic invertebrate food webs. To protect certain fishes, diflubenzuron use to control copepod vectors of human disease — including various species of *Cyclops* — is not recommended in areas where these fishes breed or feed on *Cyclops* (Rao and Paul 1988).

For control of cotton pests, including the boll weevil, a maximum recommended treatment schedule is 421 g diflubenzuron/ha, applied 6 times, usually weekly, during the growing season (Bull 1980). Honeybees (*Apis mellifera*) in heavily sprayed areas, however, may experience adverse effects if their diets exceed 1 mg diflubenzuron/kg FW (Stoner and Wilson 1982). Diflubenzuron inhibits house fly development in poultry manure. A recommended cost-effective fly control program in poultry houses involves the feed-through method (5 mg diflubenzuron/kg FW poultry diet) during hot, wet summers for 3 to 4 months, coupled with good sanitation and good manure management (Giga 1987).

For protection of domestic cattle, feeds should contain <0.05 mg diflubenzuron/kg FW. Cottonseed may be added to cattle diets provided that diflubenzuron concentrations in the seed do not exceed 0.2 mg/kg FW and that cottonseed composes <17% of the total diet bulk (Gartrell 1981). Diflubenzuron causes biochemical upset, as judged by lowered testosterone levels in chickens and rats (USEPA 1979), altered glutathione S-transferase activity in mouse liver (which adversely affects the ability to detoxify foreign substances by way of conjugation; Young et al. 1986), and disrupted hydroxylamine activity in human infants (USEPA 1979). Additional research seems needed on biochemical alterations induced by diflubenzuron. No diflubenzuron criteria are currently recommended for protection of avian and mammalian wildlife. All data available suggest that wildlife species are about as tolerant to diflubenzuron as are domestic poultry and livestock; however, the wildlife database seems inadequate for practicable criteria formulation.

Anti-cancer properties of diflubenzuron require elucidation. The indication that one or more hydroxylated forms of diflubenzuron can regulate growth of mouse tumor cells provides a basis for further studies to identify and isolate the most active analog of this compound, and it suggests that other benzoylphenyl ureas may have similar properties (Jenkins et al. 1986).

Diflubenzuron has a Surveillance Index Classification of Class IV, indicating a sufficiently low hazard potential to human health from toxicological and exposure standpoints to justify only minimal monitoring efforts (Gartrell 1981). Human cancer risk of lifetime dietary exposure to diflubenzuron in a worst-case scenario is considered slight (USEPA 1979). Diflubenzuron has little potential for human dietary exposure because of its limited use on cotton and the low residues measured on cottonseed, meat, milk, poultry, and eggs (Gartrell 1981). For protection of human health, tolerances of <0.05 mg/kg FW have been set for fat, meat, meat by-products, poultry, milk, dairy products, and eggs, and <0.2 mg/kg FW for cottonseed (USEPA 1979). These foods compose about 45% of the average human diet. If all of these foods bore residues at the tolerance level, they would contribute 0.035 mg daily on the basis of 1.5 kg food eaten daily. For a 60-kg adult, the

theoretical maximum residue concentration would be 0.6 µg/kg BW daily. Tolerances would be approached only when maximum quantities of cottonseed fraction (i.e., hulls, meal, soapstock), all bearing tolerance-level residues, are incorporated into livestock diets. At present, however, no acceptable daily intake level in humans has been established (Gartrell 1981).

17.6 SUMMARY

Diflubenzuron (1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea), also known as dimilin, is a potent broad-spectrum insect growth regulator that interferes with chitin synthesis at time of molting and is effective in controlling immature stages of insects. Diflubenzuron was approved for domestic use in 1976 to control gypsy moth (*Lymantria dispar*), and in 1979 against the cotton boll weevil (*Anthonomus grandis*). By 1989 this compound was also registered for domestic use against mosquitoes, forest lepidoptera, mushroom flies, and leaf-eating insect pests of citrus, woody ornamentals, vegetables, and fruit.

Diflubenzuron seldom persists for more than a few days in soil and water. When used properly in forest management, it is unlikely to be leached into groundwater from the application site. Degradation in water and soil is most rapid when small-particle formulations are applied, micro-organisms are abundant, and at elevated pH, temperature, and organic loading. Chemical and biological processes initially yield 2,6-difluorobenzoic acid and 4-chlorophenylurea. Soil degradation processes and plant and animal metabolism involve further conversion of these compounds to 2,6-difluorobenzamide and 4-chloroanaline. Ultimately, the end products are either conjugated into mostly water-soluble products or are biologically methylated.

Diflubenzuron applied to foliage of terrestrial plants tends to remain adsorbed for several weeks with little or no absorption or translocation from plant surfaces; loss occurs mainly from wind abrasion, rain washing, or shedding of senescent leaves. Among terrestrial insects, there is great variability in sensitivity to diflubenzuron. Sensitive pestiferous species of insects die at topical applications of 0.003 to 0.034 µg/larvae or after consuming diets containing 0.1 mg/kg. Some beneficial insects, such as the honey bee (*Apis mellifera*), are adversely affected at 1 mg/kg fresh weight (FW) of diet.

Diflubenzuron application rates between 28 and 56 g/ha (0.025 to 0.05 pounds/acre) or 2.5 to 16 µg/L are highly effective against pestiferous aquatic dipterans, including representative chironomids, chironomids, and culicids. These same dosages temporarily suppress nontarget populations of cladocerans, copepods, mayfly nymphs, corixids, and springtails; population recovery is usually complete within 80 days. In general, crustaceans were the most sensitive nontarget aquatic organisms tested. Adverse effects on crustacean growth, survival, reproduction, and behavior occur between 0.062 and 2 µg/L. Next in sensitivity are mayflies, chironomids, caddisflies, and midges; concentrations between 0.1 and 1.9 µg/L produce low emergence and survival. Moderately resistant to diflubenzuron are larvae of diving beetles, dragonfly adults and naiads, ostracods, spiders, backswimmers, and water boatmen. Relatively tolerant of diflubenzuron (i.e., no observable adverse effects at ≤45 µg/L) are the algae, molluscs, fishes, and amphibians. High accumulations occur on some aquatic plants during exposure to 100 µg/L and in fish during exposure to 1 to 13 µg/L, but all species in these groups seem unaffected by elevated body burdens and grow and metabolize normally.

Birds seem comparatively resistant to diflubenzuron: acute oral LD₅₀ doses exceed 2000 mg/kg body weight (BW); dietary concentrations <4640 mg/kg FW are tolerated for at least 8 days; and forest birds seem unharmed by recommended diflubenzuron application procedures to control pestiferous insects, except for a possible loss in fat reserves. Intraspecies differences in ability to metabolize diflubenzuron are probably large; different strains of domestic chickens show significant differences in ability to accumulate and retain this compound.

No data were found on diflubenzuron effects on mammalian wildlife. However, studies on small laboratory animals and domestic livestock indicate no observable effects in cows (*Bos bovis*) given

0.25 mg/kg BW daily for 4 months; in rabbits (*Oryctolagus cuniculus*) given 4 mg/kg BW daily on days 6 to 18 of gestation; in dogs (*Canis familiaris*) fed diets containing 40 mg/kg for 13 weeks (equivalent to 1.6 mg/kg BW daily); in rats (*Rattus spp.*) fed diets containing 160 mg/kg for 2 years; and in rabbits and rodents given single oral or dermal doses <2000 mg/kg BW. All experimental studies conducted with laboratory animals indicate that diflubenzuron is nonmutagenic, nonteratogenic, and noncarcinogenic. Adverse effects occur in dogs fed diets containing 160 mg/kg (6.2 mg/kg BW daily) for 13 weeks (abnormal blood chemistry); in mice (*Mus spp.*) given 125 mg/kg BW daily for 30 days (hepatocellular changes); in rabbits fed diets of 640 mg/kg for 3 weeks (abnormal hemoglobin), and in rats given 5000 mg/kg BW daily for 13 weeks (abnormal hemoglobin). Elevated tissue residues — but no other measurable effects — occur in cows given 0.05 to 0.5 mg/kg ration for 28 days or 1 to 16 mg/kg BW for 4 months; in pigs (*Sus spp.*) given a single oral dose of 5 mg/kg BW; and in sheep (*Ovis aries*) given a single oral dose of 10 mg/kg BW.

Criteria now recommended for protection of various species include the following: dietary loadings, in mg/kg FW ration, of <0.05 for human health, <0.05 for livestock, <1 for honey bees, and <5 for poultry; seawater concentrations <0.1 µg/L for estuarine crustacean larvae; and, for all aquatic life, restricted or prohibited use of diflubenzuron in saltmarsh mosquito breeding areas and on agricultural lands less than 5 km from coastal areas. No criteria are available or proposed for protection of avian and mammalian wildlife against diflubenzuron, probably because of an incomplete toxicological database.

17.7 LITERATURE CITED

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CHAPTER 18

Dioxins

18.1 INTRODUCTION

Accidental contamination of the environment by polychlorinated dibenzo-*para*-dioxins (PCDDs), especially 2,3,7,8-tetrachlorodibenzo-*para*-dioxin (2,3,7,8-TCDD), is the cause of poor reproduction of herring gulls (*Larus argentatus*) in Lake Ontario (Stolzenburg and Sullivan 1983), and of other fish-eating birds in the Great Lakes and on Canada's west coast (Boddington et al. 1990). Humans exposed to herbicides contaminated with 2,3,7,8-TCDD and higher chlorinated dioxins may experience an increase in overall cancer risk and in risk for specific tumors (Kogevinas et al. 1997). The sale of striped bass (*Morone saxatilis*) and blue crabs (*Callinectes sapidus*) from Newark Bay, New Jersey, was prohibited because levels of 2,3,7,8-TCDD exceeded 50 ng/kg (parts per trillion = ppt), a level of concern established by the U.S. Food and Drug Administration (Prince and Cooper 1995a). PCDDs are associated with the closure of selected rivers in Missouri (Powell 1984) and Arkansas (Johnson et al. 1996) to anglers because of high residues in fish, with the destruction of fish and wildlife in Vietnam during military defoliation operations using phenoxy herbicides (Rappe 1984), and with the death of livestock and wildlife in Missouri (Powell 1984) and Italy (Fanelli et al. 1980b). For example, in 1976, massive kills of small animals (predominantly rabbits and poultry) occurred within the first few weeks after a chemical plant explosion in Seveso, Italy, in which 2,3,7,8-TCDD was released; many humans were hospitalized (Fanelli et al. 1980b). Levels of 2,3,7,8-TCDD in milk from dairy cows and tissues of pigs, chickens, cattle, goats, and sheep from Seveso were sufficiently elevated to pose a risk to human health. Accordingly, all domestic livestock in the most seriously afflicted areas were destroyed. In eastern Missouri during 1971, waste oil contaminated with 2,3,7,8-TCDD was applied to control road dust (Powell 1984). Later, hundreds of horses kept in riding arenas became sick, and 75 died; deaths were also observed among dogs, rodents, chickens, cats, and birds near the treated areas. Soils in Times Beach, Missouri were so heavily contaminated with 2,3,7,8-TCDD that it was permanently evacuated in December 1982. The U.S. Environmental Protection Agency [USEPA] had earlier announced it would buy the dioxin-contaminated city of Times Beach; once purchase is completed, the city will no longer exist officially (Powell 1984). Approximately 22 kg (48.4 pounds) of 2,3,7,8-TCDD were involved in the Times Beach incident (Westing 1978).

PCDDs are present as trace impurities in some commercial herbicides and chlorophenols. They can be formed as a result of photochemical and thermal reactions in fly ash and other incineration products. Their presence in manufactured chemicals and industrial wastes is neither intentional nor desired. The chemical and environmental stability of PCDDs, coupled with their potential to accumulate in fat, has resulted in their detection throughout the global ecosystem. The number of chlorine atoms in PCDDs can vary between one and eight to produce up to 75 positional isomers. Some of these isomers are extremely toxic, while others are believed to be relatively innocuous.

The most toxic and extensively studied PCDD isomer is 2,3,7,8-TCDD. In fact, it is the most toxic synthetic compound ever tested under laboratory conditions. This isomer is produced during the synthesis of 2,4,5-trichlorophenol, which is used in the manufacture of the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), other trichlorophenoxy acids, and the germicide hexachlorophene. There is general agreement that 2,3,7,8-TCDD is exceedingly stable, readily incorporated into aquatic and terrestrial ecosystems, extraordinarily persistent, and virtually impossible to destroy. PCDD-contaminated phenoxy herbicides are not the only sources of 2,3,7,8-TCDD; others include polychlorinated biphenyls and pentachlorophenols. The other 74 isomers enter the biosphere from a variety of sources (National Research Council of Canada [NRCC] 1981). The fate and effects of PCDDs — with special reference to 2,3,7,8-TCDD and its role in poisonings of humans, aquatic organisms, wildlife, livestock, poultry, and its contamination of vegetation, soils, and sediments — have been extensively reviewed (Blair 1973; Cattebeni et al. 1978; Ramel 1978; Nicholson and Moore 1979; NRCC 1981; Hay 1982; Kociba and Schwetz 1982a, 1982b; Choudhary et al. 1983; Josephson 1983; Long et al. 1983; Stolzenburg and Sullivan 1983; Tucker et al. 1983; NIOSH 1984; Nriagu and Simmons 1984; Rappe 1984; U.S. Environmental Protection Agency [USEPA] 1984, 1993; Webb 1984; Kamrin and Rodgers 1985; Stalling et al. 1985a, 1985b; Young and Cockerham 1985; Eisler 1986; Cooper 1989; World Health Organization [WHO] 1989; Boddington et al. 1990; Clement et al. 1990; Ahlborg et al. 1992; Damstra et al. 1992; Cook et al. 1993; Fletcher and McKay 1993; Sijm and Opperhuizen 1996; U.S. Public Health Service [USPHS] 1998).

18.2 ENVIRONMENTAL CHEMISTRY

The PCDDs consist of 75 isomers that differ in the number and position of attached chlorine atoms. Each isomer has its own unique identity and toxicological properties. The most toxic of the chlorinated dioxin isomers is 2,3,7,8-TCDD (Figure 18.1). It is one of 22 possible congeners of tetrachlorodibenzo-*p*-dioxin. There is general agreement that PCDDs, including 2,3,7,8-TCDD, are (or were, until recently) found in chlorophenols, especially trichlorophenol and pentachlorophenol (Table 18.1), in certain phenoxy pesticides (2,4,5-T; 2,4-D; Fenoprop; Silvex; Ronnel; Erbon; Agent Orange), in hexachlorophene, and in polychlorinated biphenyls (used in electrical transformers and capacitors, and contaminated with trichlorobenzenes). PCDDs enter the environment naturally through forest fires and volcanoes, and through human activities such as accidental release during chlorophenol production, aerial application of some phenoxy herbicides, and through improper disposal of wastes into terrestrial and aquatic ecosystems from municipal incinerators and pulp and

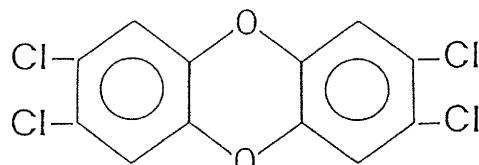
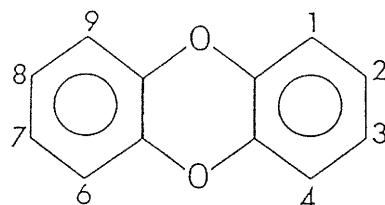


Figure 18.1 Upper: numbering system used for identification of individual PCDD isomers. Lower: the isomer 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD).

Table 18.1 Levels of PCDDs in Commercial Chlorinated Phenols, and Levels of 2,3,7,8-TCDD in 2,4,5-T Acid and Ester Formulations

Formulation	Geographic Locale (year)	Concentration (mg/kg)	
		PCDDs	2,3,7,8-TCDD
2,4,5-T acid	Sweden (1952)	—	1.10
2,4,5-T ester	Sweden (1960)	—	0.40
2,4,5-T ester	Finland (1962)	—	0.95
2,4,5-T ester	Finland (1967)	—	0.22
2,4,5-T acid	U.S. (1964)	—	4.8
2,4,5-T acid	U.S. (1969)	—	6.0
Agent orange	U.S. (—)	—	0.12
Agent orange	U.S. (—)	—	5.1
2,4,6-Trichlorophenol	Sweden (—)	3.0	—
2,4,6-Trichlorophenol	U.S. (—)	0.3	—
2,3,4,6-Tetrachlorophenol	England (—)	12.0	—
Pentachlorophenol	U.S. (—)	1900–2625	—
Pentachlorophenol	Germany (—)	6.8	—

Data from Hardell, L. 1983. Epidemiological studies on soft-tissue sarcoma, malignant lymphoma, nasal and nasopharyngeal cancer, and their relation to phenoxy acid or chlorophenol exposure. Pages 367-374 in G. Choudhary, L.H. Keith, and C. Rappe (eds.). *Chlorinated Dioxins and Dibenzofurans in the Total Environment*. Butterworth, Woburn, MA.

paper mills that use chlorine for the bleaching process (Ramel 1978; NRCC 1981; Ogilvie 1981; Choudhary et al. 1983; Josephson 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Rappe 1984; Kamrin and Rodgers 1985; USEPA 1988; WHO 1989; Boddington et al. 1990; Schell et al. 1993; Allinson et al. 1994; Blus et al. 1998; Elliott et al. 1998; Lynam et al. 1998). In Japan, major PCDD sources include waste incineration and the herbicide chlornitofen with metabolites of chlornitofen that include 1,3,6,8-TCDD and 1,3,7,9-TCDD (Ishizuka et al. 1998). The PCDD content of technical products varies between manufacturers, between lots and grades, and between various formulations of pesticidal chemicals (NRCC 1981). PCDDs have been identified in effluents from combustion products of municipal and industrial incinerators, including fly ash and flue gas (Czuczwa and Hites 1984). These PCDDs may be associated with small particles that have long residence times in the atmosphere and can become distributed over large areas. For example, in the Great Lakes, atmospheric transport of combustion products is the major source of PCDDs (mostly octa-, hepta-, and hexa-CDDs) in sediments (Czuczwa et al. 1984). Increased retentive capacity of the higher chlorinated PCDDs may account for the pattern of increasing dioxin concentrations in sediments with increasing chlorine substitution observed in the Great Lakes and other aquatic environments (Servos et al. 1992a). High-temperature combustion of bituminous coal in an oxidized and chlorinated atmosphere (produced experimentally) yielded chlorodioxins, mostly octa-, hepta-, and hexa-CDDs, and measurable quantities of tetra-CDDs (Mahle and Whiting 1980). Other potential sources of PCDDs include microbial by-products in activated sludge basins fed with chlorophenol-containing wastes (Lynam et al. 1998), fossil fuel power plants, internal combustion engines, home fireplaces, and cigarette smoke (Kociba and Schwetz 1982a, 1982b).

In general, PCDDs exhibit a relative inertness to acids, bases, oxidation, reduction, and heat. With increasing halogen content, they become more environmentally and chemically stable (NRCC 1981; WHO 1989). PCDDs are usually destroyed at temperatures greater than 1000°C. They are resistant to biological breakdown, concentrated in fat, not readily excreted, extremely toxic to some animals, and the cumulative effects of small doses to both animals and humans are a source of increasing concern (Stolzenburg and Sullivan 1983). Most PCDDs are relatively insoluble in water, sparingly soluble in organic solvents, and will decompose on exposure to UV light, including sunlight (NIOSH 1984), or to hydroxyl compounds (Josephson 1983). The isomer 2,3,7,8-TCDD is a colorless crystalline solid at room temperature and decomposes when heated to more than 700°C (Table 18.2).

Table 18.2 Chemical and Physical Properties of 2,3,7,8-TCDD, Also Known as CAS Registry No. 1746-01-6

Criterion	Property
Empirical formula	C ₁₂ H ₄ Cl ₄ O ₂
Percent by weight	
Carbon	44.70
Oxygen	9.95
Hydrogen	1.25
Chlorine	44.1
Molecular weight	322
Vapor pressure, mmHg at 25°C	1.7 × 10 ⁻⁶
Melting point	305°C
Decomposition temperature	>700°C
Solubilities, g/L	
o-Dichlorobenzene	1.4
Chlorobenzene	0.72
Benzene	0.57
Chloroform	0.37
n-Octanol	0.05
Methanol	0.01
Acetone	0.11
Water	2.0 × 10 ⁻⁷

Data from NIOSH. 1984. Current Intelligence Bulletin 40: 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD, "dioxin"). U.S. Dep. Health Human Serv., NIOSH Publ. 84-104. 20 pp.

Data on the bioavailability of PCDDs are limited. It is known that PCDDs incorporated into wood as a result of chlorophenol (preservative) treatment are bioavailable. Swine and poultry using chlorophenol-treated wooden pens or litter have been found to be contaminated with PCDDs (NRCC 1981). Toxicities of individual PCDD isomers can vary by a factor of 1000 to 10,000 for isomers as closely related as 2,3,7,8-TCDD and 1,2,3,8-TCDD, or 1,2,3,7,8-penta-CDD and 1,2,4,7,8-penta-CDD (Rappe 1984). Isomers with the highest biological activity and acute toxicity have four to six chlorine atoms, and all lateral (i.e., 2,3,7, and 8) positions substituted with chlorine. On this basis, the most toxic PCDD isomers are 2,3,7,8-TCDD, 1,2,3,7,8-penta-CDD, 1,2,3,6,7,8-hexa-CDD, 1,2,3,7,8,9-hexa-CDD, and 1,2,3,4,7,8-hexa-CDD (Rappe 1984). Ishizuka et al. (1998) have assigned toxic equivalencies for various PCDDs, with 2,3,7,8-TCDD given a value of 1 (highest biological activity), followed by a value of 0.5 for 1,2,3,7,8-penta-CDD; a value of 0.1 for three PCDD isomers (1,2,3,4,7,8-hexa-CDD, 1,2,3,4,7,8-hexa-CDD, 1,2,3,7,8,9-hexa-CDD), a value of 0.01 for 1,2,3,4,6,7,8-hepta-CDD; and a value of 0.001 for 1,2,3,4,6,7,8,9-octa-CDD.

Although PCDDs are highly persistent, volatilization and photolysis are major removal processes (NRCC 1981). In soils, 2,3,7,8-TCDD undergoes photolysis rapidly on the surface in a few hours, but more deeply buried 2,3,7,8-TCDD could have a chemical half-time greater than 10 years (NRCC 1981). When more than one degradation pathway was possible, microbial dechlorination of dioxins occurred at the most positively charged atom in the ring, which was usually a lateral carbon atom (Lynam et al. 1998). Microbial degradation of 2,3,7,8-TCDD in soils is slow, with biological half-times estimated at 1.0 to 1.5 years (Ramel 1978). However 2,3,7,8-TCDD was detected in northwestern Florida from samples of soils, rodents, birds, lizards, fishes, and insects 12 years after application. This half-time in soil was estimated at 2.9 years (Westing 1978). Uptake of 2,3,7,8-TCDD from soils by vegetation is considered negligible (Blair 1973; Ramel 1978).

The half-time persistence of 1,3,6,8-TCDD and OCDD in freshwater is short, of the order of 2.6 to 4 days; the rapid partitioning to dissolved and particulate organic matter in the water column and sediments limited their bioavailability (Servos et al. 1992a). Techniques are now available to

measure 2,3,7,8-TCDD at the part-per-quadrillion (0.1 parts per trillion) level in foods with high fat content (La Fleur et al. 1990) and human blood (Boddington et al. 1990), and in fish tissues to 1 ppt (Marquis et al. 1994). Analyses at such low levels are complicated by interference from a multitude of other compounds, as well as by the large number of PCDD isomers and their differences in chemical properties (Rappe 1984). Although 2,3,7,8-TCDD is the most extensively studied PCDD isomer, data on its fate and persistence are generally poor, interpretations are frequently absent, and extrapolations from case to case usually impossible. The general result is a qualitative concept of this compound's behavior in environmental situations (NRCC 1981). This issue is further confounded by the presence in biological and abiotic samples of chemicals of similar structure and toxicological properties to that of 2,3,7,8-TCDD. These isosteric compounds include: 2,3,6,7-tetrachlorobiphenylene; 2,3,7,8-chlorine substituted dibenzofurans; and 3,3',4,4'-tetra-, 3,3',4,4',5-penta-, and 3,3',4,4',5,5'-hexachlorobiphenyl (Stalling et al. 1985a, 1985b). For example, analytical results of fish, birds, and sediments indicated that every sample that was positive for 2,3,7,8-TCDD also contained 2,3,7,8-chlorine-substituted dibenzofurans (Stalling et al. 1985a, 1985b).

In mammals, biochemical and pathological responses of 2,3,7,8-TCDD are mediated through binding to a cytoplasmic protein, the Ah receptor. Many of the toxic responses to 2,3,7,8-TCDD are associated with alterations of cell proliferation in affected tissues. Common examples of 2,3,7,8-TCDD-mediated differentiation and proliferation in both fishes and mammals include dermal hyperkeratinization (fin necrosis in fish), teratogenicity, lymphoid involution, immunotoxicity, and carcinogenesis (Newsted and Giesy 1992). Lipid peroxidation in liver, kidney, thymus, and testes is induced in rats by 2,3,7,8-TCDD in a dose- and time-dependent manner. The enhanced lipid peroxidation by microsomes from 2,3,7,8-TCDD-treated rats may be associated with an increase in hydrogen peroxide production in conjunction with a decrease in glutathione peroxidase activity and an increase in free iron (Al-Bayati et al. 1987).

18.3 CONCENTRATIONS IN FIELD COLLECTIONS

PCDDs are ubiquitous in the environment and have been measured in air, water, soil, sediments, and foods. In Canada, all animals have been and continue to be exposed to these substances (Boddington et al. 1990). Plasma dioxin levels of Canadian villagers are about 8 times higher than levels in urban residents, and this is attributed to consumption of contaminated wildlife (Ryan et al. 1997). Many PCDDs, in addition to 2,3,7,8-TCDD, are present in biological and abiotic samples (NRCC 1981; O'Keefe et al. 1983; Petty et al. 1983; Stalling et al. 1983; Czuczwa et al. 1984; Lamparski et al. 1984; Kamrin and Rodgers 1985; Stalling et al. 1985a; Ryan et al. 1997). In general, wherever high levels of dioxins have been detected in the environment, a local application of 2,3,7,8-TCDD-contaminated herbicide, hazardous waste site, or industrial discharge has usually been implicated as the source (Stolzenburg and Sullivan 1983; Eisler 1986; USEPA 1987, 1988; WHO 1989). Aside from direct deposition, observed increases in 2,3,7,8-TCDD concentrations may result from microbial dechlorination as modified by the action of humic constituents such as resorcinol, 3,4-dihydroxybenzoic acid, and catechol (Barkovskii and Adriaens 1998).

At Eglin Air Force Base (EAFB), located in northwestern Florida, contamination of a 208-hectare section with 2.8 kg of 2,3,7,8-TCDD (equivalent to 13 mg/ha) occurred between 1962 and 1970 as a result of repeated, massive herbicide applications (Young and Cockerham 1985). The 2,3,7,8-TCDD isomer was present as an impurity in 76,740 kg of 2,4-D and 73,010 kg of 2,4,5-T applied to this section of EAFB during the 9-year span. Ecological surveys conducted between 1970 and 1975 showed an apparently healthy and diverse wildlife fauna, although soil levels of 520 ppt (ng/kg) of 2,3,7,8-TCDD were frequently encountered, and 2,3,7,8-TCDD residues were elevated in some species examined. The highest residues recorded in various trophic levels were 283 ppt in whole beetle grubs; up to 1360 ppt in whole southern toads (*Bufo terrestris*); 360 ppt in viscera and 430 ppt in carcass of a lizard, the six-lined racerunner (*Cnemidophorus sexlineatus*);

18 ppt in gonad and 85 ppt in gut contents of the spotted sunfish (*Lepomis punctatus*); 100 to 1200 ppt in stomach contents of the southern meadowlark (*Sturnella magna argutula*); and 300 to 2900 ppt in liver and 130 to 200 ppt in the pelt of a beachmouse (*Peromyscus polionotus*) (Young and Cockerham 1985). The significance of these elevated residues is discussed later.

In some cases, 2,3,7,8-TCDD has constituted up to 95% of the total body PCDD burden, as was true in lake trout, *Salvelinus namaycush* (O'Keefe et al. 1983), and rainbow trout, *Oncorhynchus mykiss* (Petty et al. 1983) from Lake Ontario. Concentrations of 2,3,7,8-TCDD in whole carp (*Cyprinus carpio*), varied from 24% of total body PCDDs in Saginaw Bay, Michigan (Stalling et al. 1983), to 45 to 56% in the Niagara River (NRCC 1981). In herring gulls from Saginaw Bay, 2,3,7,8-TCDD comprised 40 to 60% of the whole-body PCDD content (NRCC 1981; Petty et al. 1983), and 72 to 78% in gulls from Lakes Huron and Ontario (Stalling et al. 1983, 1985a). In 1983, Forster's tern (*Sterna forsteri*) from Green Bay, Wisconsin, contained 114 ppt of PCDDs in egg, of which 41% was 2,3,7,8-TCDD. Double-crested cormorants (*Phalacrocorax auritus*) from the same area contained 25 to 214 ppt of PCDDs in whole body, of which only 10 to 31% was 2,3,7,8-TCDD (Stalling et al. 1985a). The causes of the observed variations are not known but may be associated with localized inputs from municipal sewage treatment plants (Lamparski et al. 1984) and with atmospheric transport of incinerated domestic and industrial chemical wastes (Czuczwa et al. 1984). For example, the PCDD composition of sewage sludge from Milwaukee, Wisconsin, was relatively constant, as judged by analysis of samples from 1933, 1981, and 1982 (Lamparski et al. 1984). Total PCDD content in sewage sludge samples ranged between 60,950 and 70,191 ppt, of which the great majority was in the form of octa-CDDs (82 to 86%), hepta-CDDs (11.0 to 15.4%), and hexa-CDDs (1.3 to 2.1%). However, the tetra-CDDs increased from 34 ppt in 1933, to 138 in 1981, and to 222 in 1982. Corresponding values for the 2,3,7,8-TCDD isomer in 1933, 1981 and 1982 were 2.2, 11.0, and 16.0 ppt, respectively. Other TCDD isomers also showed increases from 6 ppt in 1933 to 22 ppt in 1982 (1,3,7,8-TCDD), and during that same period from 2.2 ppt to 140 ppt (1,2,3,7-, and 1,2,3,8-TCDD). It seems that chlorinated dibenzodioxins have been present in dried sludge from this plant for at least 50 years. Their presence in this material suggests that they may have been formed by the condensation of chlorophenols resulting from the chlorination of naturally occurring phenolic compounds (Lamparski et al. 1984). PCDDs were also found in sediments from Siskiwit Lake on Isle Royale in Lake Superior, a location that can receive only atmospheric inputs. The source of these compounds is the atmospheric transport of dioxins formed by combustion of domestic and chemical wastes. For example, particulates from a chemical waste incinerator in Midland, Michigan, had 260,000,000 ppt octa-CDDs and 170,000,000 ppt hepta-CDDs; lower, but still elevated levels of 440,000 ppt octa-CDDs and 310,000 ppt hepta-CDDs were measured in municipal trash incinerator particulates (Czuczwa et al. 1984).

Mussels and fish can accumulate 2,3,7,8-TCDD and other PCDDs from the medium and may be used as sentinel organisms. Mussels (*Elliptio complanata*) from an uncontaminated site exposed for 21 days in the contaminated Rainy River, Ontario, were sensitive monitors of PCDD sources, such as kraft pulp and paper mills (Hayton et al. 1990). Fish in Maine rivers contaminated by the effluent of bleached kraft paper mills accumulated 2,3,7,8-TCDD from the medium by factors as high as 24,600 in muscle of smallmouth bass (*Micropterus dolomieu*); 28,300 in muscle of brown trout (*Salmo trutta*); 7500 in white perch (*Morone americana*) fillets; and 106,000 in whole white suckers (*Catostomus commersoni*) (Frakes et al. 1993). High levels of PCDDs were found in edible tissues of mountain whitefish (*Prosopium williamsoni*) exposed to effluent from bleached kraft pulp mills in Canada; uptake was attributed to the food prey selection of filter-feeding invertebrates that ingest suspended sediments (Law and Gudaitis 1994; Owens et al. 1994). The primary route of exposure of 2,3,7,8-TCDD for pelagic fish is the diet, which accounts for 75% or more of the total uptake in lake trout (Tietge et al. 1998). Food chain biomagnification of PCDDs is reported for fish to birds (de Wit et al. 1992), fish to turtle (Ryan et al. 1986), and in Great Lakes food chains of phytoplankton to zooplankton to forage fish to lake trout (Whittle et al. 1992). But food chain biomagnification has not been observed in a complex Baltic Sea food chain using sophisticated

stable nitrogen isotope techniques (Broman et al. 1992), and in fish to seal, and fish to bird (guillemot, *Uria aalge*) food chains (de Wit et al. 1992). To confound matters, PCDD patterns in different fish species collected at the same site are highly variable, indicating species differences in accumulation (de Wit et al. 1992). PCDD sources from pulpmill effluents, combustion, and magnesium production can now be recognized in aquatic fauna by analysis of profiles of 2,3,7,8-substituted chlorinated dibenzodioxins using statistical principal component analysis techniques (Zitko 1992).

Eggs of the lake trout (*Salvelinus namaycush*) from Lake Ontario had higher 2,3,7,8-TCDD toxic equivalents (10.7 ppt) than eggs from Lake Superior or a hatchery (0.3 ppt), but these were below the levels considered fatal to lake trout eggs (LD₅₀ of 42 to 72 ppt) or harmful (NOAEL of 30 to 45 ppt) (Guiney et al. 1996). Concentrations of 2,3,7,8-TCDD in whole fish collected nationwide in the United States in 1983 from 395 sites usually contained 0.5 to 2.0 ppt FW, with a maximum of 85 ppt; concentrations were highest in predatory fish collected near pulp and paper manufacture discharge sites and lowest in estuarine areas (Kuehl et al. 1989) (Table 18.3). In the Great Lakes area, fish from the Tittabawasee and Saginaw Rivers, two tributaries of Lake Huron's Saginaw Bay, contained up to 695 ppt of 2,3,7,8-TCDD (Stolzenburg and Sullivan 1983). High 2,3,7,8-TCDD levels (87 to 162 ppt) were also recorded in fish from the Niagara River, New York, and from parts of Lake Ontario; lower concentrations (2 to 28 ppt) were noted in fish from Lakes Erie, Huron, Michigan, and Superior (Stolzenburg and Sullivan 1983). Muscle from larger specimens of commercial fish collected from Lake Ontario in 1980 had higher levels of 2,3,7,8-TCDD than smaller fish (Ryan et al. 1984), suggesting that accumulation increases with age. The larger fish also contained high concentrations (1.2 to 4.9 mg/kg, fresh weight) of polychlorinated biphenyls (Ryan et al. 1984), demonstrating a need to elucidate TCDD interaction kinetics with other contaminants. Bottom-feeding fish, such as carp and catfish, from rivers in Michigan during 1978 contained higher 2,3,7,8-TCDD residues than surface feeders (Marless et al. 1982), indicating an association with contaminated sediments. Marine amphipods (*Ampelisca abdita*) held on sediments containing as much as 25 µg 2,3,7,8-TCDD/kg DW for 10 days had normal survival and growth (Barber et al. 1998), although the authors did not measure 2,3,7,8-TCDD residues in amphipods. Sediments from the Spring River, Missouri, contained 12 ppt of 2,3,7,8-TCDD immediately downstream of a now defunct hexachlorophene facility (Kleopfer and Zirscky 1983). Concentrations in fish were measurable 111 km downstream from this disposal site (Table 18.3). Fish from the Spring River (and also the Meremac River, Missouri) contained inordinately high levels of 18 to 78 ppt 2,3,7,8-TCDD, prompting the U.S. Food and Drug Administration to issue a health advisory in 1982 against fish consumption from these areas (Powell 1984). In Massachusetts, six ponds were surveyed for 2,3,7,8-TCDD in 1983 after prior treatment with phenoxy herbicides between 1958 and 1978 (Anonymous 1984). Only one fish, a brown bullhead (*Ictalurus nebulosus*), age 3+ years, contained measurable (25 ppt) dioxin levels. Residues were not detectable in other species of fish sampled, including several species of ictalurid catfish, yellow perch (*Perca flavescens*), and chain pickerel (*Esox niger*). Negative results (less than 10 ppt 2,3,7,8-TCDD) were also documented in freshwater fish from Arkansas and Texas following spraying of the herbicide 2,4,5-T (Shadoff et al. 1977).

In general, high PCDD concentrations in avian tissues were correlated with poor growth, survival, and reproduction. Nest success, hatching success, and duckling production of wood ducks (*Aix sponsa*) were suppressed at nesting sites within 58 km of a PCDD point source (a former chemical plant that manufactured the herbicide 2,4,5-T). Egg toxicity equivalent factors were inversely correlated with productivity in nests, and teratogenic effects occurred in ducklings at the most contaminated sites (White and Seginak 1994). High PCDD levels in yolk-sacs of cormorant (*Phalacrocorax carbo*) hatchlings may have been responsible for the observed low breeding success of Dutch colonies in 1989 (Van den Berg et al. 1994). The endangered Forster's tern (*Sterna forsteri*) population on Green Bay, Wisconsin, showed signs of embryotoxicity, congenital deformities, and poor hatching success Kubiak et al. 1989). Eggs from this population contained 215 (90 to 245)

ppt FW of 2,3,7,8-TCDD equivalents vs. 23 (14 to 34) ppt from a reference population (Baumann and Whittle 1988; Tillitt et al. 1993). Great blue herons (*Ardea herodias*) located near a pulp mill in British Columbia failed to fledge young in 1987, with a concurrent sharp increase in PCDD levels in their eggs. In 1988, levels in heron eggs were — in ppt FW — 211 for 2,3,7,8-TCDD, 263 for 1,2,3,7,8-penta CDD, and 430 for 1,2,3,6,7,8-hexa-CDD. These values were significantly higher than eggs from other sites, although other factors may have contributed to the decline of the heron population (Boddington et al. 1990; Hart et al. 1991). Eggs of the osprey (*Pandion haliaetus*), however, collected near a bleached kraft mill facility in Wisconsin between 1992 and 1996 hatched and fledged normally despite 2,3,7,8-TCDD concentrations as high as 162 ppt on a fresh weight basis (Woodford et al. 1998).

Proposed indicators of 2,3,7,8-TCDD contamination in bird eggs include changes in yolk retinoid concentrations and EROD enzyme activity levels. Changes in yolk retinoids, as measured by Vitamin A concentrations, of herring gulls (*Larus argentatus*) from the Great Lakes during 1986/87 were associated with increasing concentrations of 2,3,7,8-TCDD, and this may be an early indicator of survival and teratogenesis in birds from the Great Lakes (Spear et al. 1990). Eggs of the great blue heron (*Ardea herodias*) from British Columbia in 1990 to 1992 had decreased concentrations of 2,3,7,8-TCDD when compared to 1988. Decreases in 2,3,7,8-TCDD content in eggs was associated with decreased EROD activity in eggs and resultant chicks, decreased incidence of chick edema, and increased growth rate of chicks (Sanderson et al. 1994a). The use of avian hepatic microsomal EROD activity is a useful index of cytochrome P4501A1 induction by polychlorinated aromatic hydrocarbons, including PCDDs. A significant regression of hepatic microsomal EROD activity on TCDD-toxic equivalent was measured in chicks of the double-crested cormorant (*Phalacrocorax auritus*) (Sanderson et al. 1994b).

Fish-eating birds usually have the highest concentrations of PCDDs of all birds measured (Baumann and Whittle 1988; Ankley et al. 1993; Jones et al. 1993). Diet is the major route of PCDD accumulation in livers of fish-eating birds. Fish-eating birds and their food from the Netherlands are contaminated with 2,3,7,8-substituted PCDDs and polychlorinated dibenzofurans (PCDFs); pentachlorophenol and polychlorinated biphenyls are the two major contaminating sources of PCDDs and PCDFs (Van den Berg et al. 1987). A linear relation exists between the retained PCDDs and PCDFs in the livers of cormorants (*Phalacrocorax carbo*), probably caused by continuous exposure to a relatively stable mixture of these compounds in their fish diet. Biomagnification of 2,3,7,8-TCDD and 1,2,3,6,7,8-hexa CDD probably occurs from the European eel (*Anguilla anguilla*) to the cormorant (Van den Berg et al. 1987). In birds, the levels of 2,3,7,8-TCDD have been decreasing, according to analysis of herring gull eggs from Lake Ontario. During the decade 1970 to 1980, there was a reduction of about 50% in 2,3,7,8-TCDD levels every 2 years (Ogilvie 1981; NRCC 1981; Nriagu and Simmons 1984). The reasons for the decline are unknown, and the relevance to higher-chlorinated PCDDs has not yet been determined. Until these questions are resolved and more substantive data are acquired on dioxin residues in birds, the current predictive trends on decline rates should be interpreted with caution.

Some information on 2,3,7,8-TCDD levels in wildlife and domestic livestock are from the vicinity of Seveso, Italy (Table 18.3). There, on July 10, 1976, a thick cloud of chemicals — including at least 34 kg 2,3,7,8-TCDD, and perhaps as much as 250 kg — was released into the atmosphere when a runaway reaction accidentally occurred in a trichlorophenol-producing facility (di Domenico et al. 1990). Its wind-driven settling contaminated large inhabited areas. It contaminated the food (hay, grass, cut-up corn) of dairy cows (Fanelli et al. 1980a). Grossly elevated levels (7900 ppt) were measured in milk from these herds at concentrations considered hazardous to human health (i.e., more than 7000 ppt) (Fanelli et al. 1980a). Wildlife from the most heavily contaminated area appeared to accumulate 2,3,7,8-TCDD. Field mice (*Microtus arvalis*), for example, contained very high whole-body concentrations of 2,3,7,8-TCDD (up to 49,000 ppt) almost 2 years after the critical contamination. The mechanisms for this phenomenon included ingestion of contaminated soil and licking of their dioxin-contaminated pelt (Fanelli et al. 1980c). In 1996,

humans from the most heavily contaminated area of Seveso (based on soil 2,3,7,8-TCDD concentrations) had 53 ppt of 2,3,7,8-TCDD in plasma on a fresh weight basis compared to 4.9 ppt in a reference population; women had significantly higher plasma 2,3,7,8-TCDD concentrations than men, especially women closest to the accident site and who consumed meat regularly (Landi et al. 1997). In another study, no 2,3,7,8-TCDD was detected in livers of mountain beavers (*Aplodontia rufa*) that fed for 45 to 60 days in Oregon forests that had been sprayed with 2.2 kg of 2,4,5-T/ha (Newton and Snyder 1978). Although it was presumed that the herbicide was heavily contaminated with dioxins, no chemical analysis of the 2,4,5-T was performed.

In Germany, humans ingest an average of 85 pg daily of 2,3,7,8-TCDD equivalents per person or 1.2 pg/kg BW daily, mostly from fish and fish products (32%), beef (20%), and cow's milk (16%) (Furst et al. 1990). In the United States, there is a potential for 2,3,7,8-TCDD to migrate from paperboard-based food packaging on contact with food. The migration rate of 2,3,7,8-TCDD from bleached paperboard cartons into whole milk was linear with the square root of exposure time. After 12 days of storage, 6.7% of the 2,3,7,8-TCDD in the paperboard carton migrated into the milk (La Fleur 1990). The amount of 2,3,7,8-TCDD formed in the U.S. bleached kraft industry in 1988 was estimated at 0.64 kg annually (Whittemore et al. 1990). In Vietnam, 2,3,7,8-TCDD concentrations in food and wildlife in 1985 to 1987 were higher in South Vietnam than in North Vietnam, with elevated values attributed to the increased industrialization of South Vietnam (Olie et al. 1989).

Table 18.3 Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
AQUATIC ORGANISMS		
Molluscs		
South Vietnam, during military defoliation operations with 2,4,5-T Various species, whole	Max. 810 FW	2
Arthropods		
Freshwater crab, <i>Eriocheir japonicus</i> ; Tone River, Japan; hepatopancreas; females; August–October		
Total PCDDs	310 LW	52
2,3,7,8-TCDD	5.3 LW	52
1,2,3,7,8-penta-CDD	16 LW	52
All tetra-CDDs	39 LW	52
All penta-CDDs	42 LW	52
Hexa-CDDs	120 LW	52
Hepta-CDDs	84 LW	52
OCDD	31 LW	52
Fish		
United States; 1983; 395 sites; whole	0.5–2.0 FW; Max. 85 FW	28
Lake trout, <i>Salvelinus namaycush</i>		
Great Lakes; liver; 1993		
2,3,7,8-TCDD	<0.2–16.8 FW	51
1,2,3,7,8-penta-CDD	<0.3–7.0 FW	51
1,2,3,4,7,8-hexa-CDD	<0.08 FW	51
1,2,3,6,7,8-hexa-CDD	<0.07–4.9 FW	51

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
1,2,3,7,8,9 hexa-CDD	<0.07–0.6 FW	51
1,2,3,4,6,7,8 hepta-CDD	<0.8–3.0 FW	51
OCDD	1–43 FW	51
Massachusetts, 1983		
Lake Winthrop		
Muscle with skin		
Brown bullhead, <i>Ictalurus nebulosus</i>	25 FW	3
Other fish species	ND	3
Other bodies of water (5)		
Muscle with skin, 8 spp.	ND	3
Missouri, 1982		
Spring River		
Whole fish	26 FW	4
Fillets	18 FW	4
Meremac River		
Whole	78 FW	4
Missouri, 1981		
Spring River, whole		
Distance, in km, downstream from hexachlorophene manufacturing facility		
1	19 FW	5
5	37 FW	5
9	36 FW	5
74	1.1 FW	5
111	0.8 FW	5
Niagara River, New York, 1981		
Spottail shiner, <i>Notropis hudsonius</i> , whole	(4–60) FW	6
Cayuga Creek, New York, 1980		
Fillets, 4 spp.	(12–27) FW	7
Coho salmon, <i>Oncorhynchus kisutch</i>		
Fillet	21 FW	7
Lake Michigan		
Eggs, <i>Oncorhynchus</i> spp.; 1990	92 FW	22
Eggs, chinook salmon, <i>Oncorhynchus tshawytscha</i> ; 1986	29–514 FW; correlated with total PCB concentrations but not correlated to egg or fry mortality	23
Lake Ontario, 1990		
Eggs, <i>Oncorhynchus</i> spp.	88–320 FW; associated with 24–46% mortality	22
Lake trout, <i>Salvelinus namaycush</i> , whole vs. whole forage fish		
2,3,7,8-TCDD	44 FW vs. 10 FW	26
1,2,3,7,8-penta-CDD	<2 FW vs. <2 FW	26
1,2,3,4,7,8-hexa-CDD	7 FW vs. <3 FW	26
Lake Ontario, 1980		
Muscle fillet, skinless		
White sucker, <i>Catostomus commersoni</i>	3 (2–4) FW	8
Yellow perch, <i>Perca flavescens</i>	3.8 (3.2–4.3) FW	8
Brown bullhead, <i>Ictalurus nebulosus</i>	6.0 (3.4–8.6) FW	8
Channel catfish, <i>Ictalurus punctatus</i>	15.5 (12.8–17.7) FW	8
American eel, <i>Anguilla rostrata</i>	19.8 (6.4–38.5) FW	8
Rainbow smelt, <i>Osmerus mordax</i>	20.0 (11.3–32.9) FW	8
Rainbow trout, <i>Oncorhynchus mykiss</i>	32 FW	7
Lake trout	41 FW	9

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
Lake trout, whole Lake Ontario, 1979	51 FW	7
Rainbow trout, muscle Lake Ontario, 1978	17 FW	7
Lake trout, muscle Brown trout, <i>Salmo trutta fario</i> , muscle	107 FW 162 FW	9 9
Michigan Rivers, 1978		
Muscle, edible		
Lake trout	ND	10
Smallmouth bass, <i>Micropterus dolomieu</i>	8 (7–8) FW	10
Catostomids	11 (4–21) FW	10
Yellow perch	14 (10–20) FW	10
Carp, <i>Cyprinus carpio</i>	55 (20–153) FW	10
Channel catfish	157 (28–695) FW	10
Cayuga Creek, New York 1978		
Coho salmon, fillet	20 FW	7
Ontario, Canada; summer 1991; near pulp mills; white sucker, <i>Catostomus commersoni</i> ; liver vs. muscle, maximum values		
2,3,7,8-TCDD	84 FW vs. 2 FW	25
Total penta-CDDs	11 FW vs. ND	25
Total hexa-CDDs	32 FW vs. ND	25
Total hepta-CDDs	20 FW vs. ND	25
OCDD	58 FW vs. ND	25
Amsterdam, Netherlands		
Eel, <i>Anguilla anguilla</i>		
From sediments containing 5000 ng/kg DW		
Whole	1.1 FW	11
Fat	3.9 FW	11
Sweden; 1988		
Baltic herring, <i>Clupea harengus</i> ; muscle		
2,3,7,8-TCDD	1.9 FW	27
1,2,3,7,8-penta-CDD	4.4 FW	27
1,2,3,4,7,8-hexa-CDD	0.5 FW	27
1,2,3,6,7,8-hexa-CDD	2.0 FW	27
1,2,3,7,8,9-hexa-CDD	0.3 FW	27
OCDD	0.7 FW	27
Burbot, <i>Lota</i> sp.; liver; maximum values		
2,3,7,8-TCDD	74 FW	27
1,2,3,7,8-penta-CDD	46 FW	27
1,2,3,6,7,8-hexa-CDD	90 FW	27
1,2,3,7,8,9-hexa-CDD	8 FW	27
OCDD	0.8 FW	27
Amphibians		
Seveso, Italy, 1978		
Toad, <i>Bufo</i> sp., whole	200 FW	1
Reptiles		
Snapping turtle, <i>Chelydra serpentina</i>		
Upper St. Lawrence River near Lake Ontario; June 1984–85		
2,3,7,8-TCDD		
Fat	232–474 FW	29
Liver	37–107 FW	29

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
1,2,3,7,8-penta-CDD		
Fat	33–104 FW	29
Liver	5–22 FW	29
Total hexa-CDDs		
Fat	Max. 102 FW	29
Liver	Max. 18 FW	29
1,2,3,4,6,7,8-hepta-CDD		
Fat	Max. 69 FW	29
Liver	Max. 5 FW	29
OCDD		
Fat	Max. 34 FW	29
Liver	Max. 27 FW	29
Ontario, Canada; Hamilton Harbor; 1984; eggs		
2,3,7,8-TCDD	67 FW	30
2,3,4,7,8-penta-CDD	14 FW	30
1,2,3,6,7,8-hexa-CDD	4 FW	30
1,2,3,7,8,9-hexa-CDD	1 FW	30
1,2,3,4,6,7,8-hepta-CDD	2 FW	30
OCDD	ND	30
St. Lawrence River, New York; total PCDDs		
Fat	334–597 FW	31
Liver	47–154 FW	31
Mammals		
Beluga whale, <i>Delphinapterus leucas</i>		
Found dead in St. Lawrence River estuary; 1987–90; blubber 2,3,7,8-TCDD equivalents (due primarily to planar PCBs)		
Females	330 FW	35
Males	1400 FW	35
Total PCDDs	<1 FW	35
Northern hemisphere; 1983–87; blubber; 2,3,7,8-TCDD vs. 1,2,3,7,8-penta-CDD		
Grey seal, <i>Halichoerus grypus</i>	3–7 LW vs. 9–15 LW	32
Harp seal, <i>Pagophilus groenlandicus</i>	<2 LW vs. 4 LW	32
Ringed seal, <i>Phoca hispida</i>	<7–68 LW vs. 7–196 LW	32
Common seal, <i>Phoca vitulina</i>	2–4 LW vs. 3–9 LW	32
Harbor seal, <i>Phoca groenlandica</i> ; Greenland Sea; 1991; age 1–18 years; blubber vs. brain		
2,3,7,8-TCDD	0.6–1.3 FW vs. <0.4 FW	33
1,2,3,7,8-penta-CDD	1.7–5.2 FW vs. <0.2 FW	33
1,2,3,4,7,8-hexa-CDD	0.3–1.2 FW vs. <0.4 FW	33
1,2,3,6,7,8-hexa-CDD	1.8–4.3 FW vs. <0.2 FW	33
1,2,3,7,8,9-hexa-CDD	0.3–0.8 FW vs. <0.3 FW	33
1,2,3,4,6,7,8-hepta-CDD	0.4–1.0 FW vs. <0.3 FW	33
OCDD	1.3–6.6 FW vs. 0.8–2.0 FW	33
Harbor porpoise, <i>Phocoena phocoena</i> ; found dead on Dutch coast; 1990–93; blubber; maximum values		
2,3,7,8-TCDD	0.3 LW	34
1,2,3,7,8-penta-CDD	0.5 LW	34
1,2,3,4,7,8-hexa-CDD	0.2 LW	34
1,2,3,6,7,8-hexa-CDD	0.5 LW	34
1,2,3,7,8,9-hexa-CDD	0.1 LW	34
1,2,3,4,6,7,8-hepta-CDD	0.6 LW	34
OCDD	4.6 LW	34

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
TERRESTRIAL ORGANISMS		
Higher plants		
Seveso, Italy, 1976 Various species, leaves	Max. 50,000,000 FW	2
Annelids		
Seveso, Italy, 1978 Earthworms, whole	12,000 FW	1
Reptiles		
Seveso, Italy, 1978 Snakes, various spp. Liver	2700 FW	1
Adipose tissue	16,000 FW	1
Mammals		
Seveso, Italy, 1978 Field mouse, <i>Microtus arvalis</i> Whole	1200 (70–49,000) FW	1
Rabbit, <i>Lepus</i> sp. Liver	7700 (2700–13,000) FW	1
Seveso, Italy, 1976 Domestic goat, <i>Capra</i> sp. Liver	1253 FW	12
Rabbit Liver		
Precontamination	13 (0.3–55) FW	12
Postcontamination	85 (3.7–633) FW	12
Cow, <i>Bos</i> sp. Milk		
July 9	ND	13
July 28	7900 FW	13
August 2	5100 FW	13
August 10	2500 FW	13
Sweden, 1988; wolf; <i>Canis lupus</i> ; muscle		
2,3,7,8-TCDD	0.05 FW	27
1,2,3,7,8-penta-CDD	0.18 FW	27
OCDD	0.23 FW	27
Humans, <i>Homo sapiens</i>		
Quebec, Canada; 1990–94; plasma lipids From fishing villages on lower north shore of the St. Lawrence River		
2,3,7,8-TCDD	14 FW	43
1,2,3,7,8-penta-CDD	19 FW	43
Total 2,3,7,8-hexa-CDDs	113 FW	43
Urban residents		
2,3,7,8-TCDD	2 FW	43
1,2,3,7,8-penta-CDD	4 FW	43
Total 2,3,7,8-hexa-CDDs	69 FW	43

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
Seveso, Italy; 1996; plasma; from most heavily soil-contaminated area in 1976 vs. reference population	53 (1–90) FW vs. 5 FW	44
Germany; diet; maximum concentrations		
Cow's milk		
2,3,7,8-TCDD	1.9 LW	45
1,2,3,7,8-penta-CDD	2.5 LW	45
1,2,3,7,8,9-hexa-CDD	3.0 LW	45
1,2,3,6,7,8-hexa-CDD	10.0 LW	45
1,2,3,4,7,8-hexa-CDD	2.0 LW	45
1,2,3,4,6,7,8-hepta-CDD	29.0 LW	45
OCDD	25.0 LW	45
Beef muscle vs. chicken muscle		
2,3,7,8-TCDD	5 LW vs. 16 LW	45
1,2,3,7,8-penta-CDD	4 LW vs. 5 LW	45
1,2,3,7,8,9-hexa-CDD	2 LW vs. 0.6 LW	45
1,2,3,6,7,8-hexa-CDD	3 LW vs. 2 LW	45
1,2,3,4,7,8-hexa-CDD	2 LW vs. 0.6 LW	45
1,2,3,4,6,7,8-hepta-CDD	2 LW vs. 1 LW	45
OCDD	<0.5 LW vs. <0.5 LW	45
United States, 1980s		
Whole cow's milk		
Unpackaged	1.8 FW	46
In paperboard carton for 288 h	8.5 FW	46
Canned corned beef hash	8–20 FW	46
Ground beef		
South	17 FW	46
Midwest	18 FW	46
Northwest	62 FW	46
Beef hot dogs		
South	37 FW	46
Midwest	12 FW	46
Northwest	15 FW	46
North Vietnam; 1985–87; maximum concentrations		
Pork fat	0.4 FW	47
Chicken fat	0.8 FW	47
Fish	0.2 FW	47
Cow fat	0.9 FW	47
South Vietnam; 1985–87; food and wildlife; maximum concentrations		
Fish liver	2.5 FW	47
Chicken fat	3.1 FW	47
Pork fat	3.1 FW	47
Turtle liver	19.1 FW	47
Turtle gall bladder	2.2 FW	47
Turtle ovaries	60.2 FW	47
Snake	11.6 FW	47
BIRDS		
Wood duck, <i>Aix sponsa</i> ; Arkansas; 1988–90; eggs; PCDD-contaminated site vs. reference site		
2,3,7,8-TCDD	36 (2–482) FW vs. 0.01 FW	36
Tetra-CDDs	53 (2–727) FW vs. 0.3 FW	36

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
Penta-CDDs	3 (0–24) FW vs. 0.4 FW	36
Hexa-CDDs	6 (0–22) FW vs. 3 FW	36
Hepta-CDDs	9 (0–45) FW vs. 6 FW	36
OCDD	46 (16–268) FW vs. 26 (0–84) FW	36
Great blue heron, <i>Ardea herodias</i> British Columbia; eggs; near kraft mill on Vancouver Island (no young raised); 1986 vs. 1987		
2,3,7,8-TCDD	66 (32–134) FW vs. 210 (136–351) FW	39
1,2,3,7,8-penta-CDD	252 FW vs. 257 FW	39
1,2,3,6,7,8-hexa-CDD	337 FW vs. 402 FW	39
1,2,3,7,8,9-hexa-CDD	21 FW vs. 27 FW	39
1,2,3,4,6,7,8-hepta-CDD	3 FW vs. 3 FW	39
OCDD	3 FW vs. 4 FW	39
Total 2,3,7,8-TCDD equivalents	79 (38–164) FW vs. 230 (139–381) FW	39
As above except some young raised; 1990–92; maximum values		
2,3,7,8-TCDD	42 FW	40
1,2,3,7,8-penta-CDD	45 FW	40
1,2,3,4,7,8-hexa-CDD	3 FW	40
1,2,3,6,7,8-hexa-CDD	57 FW	40
1,2,3,7,8,9-hexa-CDD	3 FW	40
1,2,3,4,6,7,8-hepta-CDD	4 FW	40
OCDD	5 FW	40
British Columbia; eggs; reference site; 1986 vs. 1987		
2,3,7,8-TCDD	(2–34) FW vs. (25–55) FW	39
Total 2,3,7,8-TCDD equivalents	11–14 FW vs. 34–64 FW	39
Great Lakes area, Green Bay and Lake Michigan Black-crowned night-heron, <i>Nycticorax nycticorax</i>		
Whole		
1982	21 FW	14
1978	(12–59) FW	14
Double-crested cormorant, <i>Phalacrocorax auritus</i>		
Whole, 1983	4 FW	14
Forster's tern, <i>Sterna forsteri</i> Wisconsin, 1983, egg		
Green Bay	47 FW	14
Lake Poygan	9 FW	14
Herring gull, <i>Larus argentatus</i>		
Egg		
Lake Ontario		
1983	90 FW	14
1980	(44–68) FW	15
1971–72	(800–1000) FW	15
1970	1200 FW	16
Other Great Lakes		
1980	(2–14) FW	15
Saginaw Bay		
1980	(43–86) FW	15

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
Osprey, <i>Pandion haliaetus</i>		
Eggs; Pacific Northwest; 1991–97; near bleached kraft pulp mills vs. reference site; maximum values		
2,3,7,8-TCDD	19 FW vs. 26 FW	54
1,2,3,7,8-penta-CDD	30 FW vs. 9.2 FW	54
1,2,3,6,7,8-hexa-CDD	47 FW vs. 11 FW	54
1,2,3,4,6,7,8-hepta-CDD	1811 FW vs. 109 FW	54
OCDD	7000 FW vs. 345 FW	54
Eggs; Wisconsin; 1992–96; near bleached kraft mill facilities vs. reference site		
2,3,7,8-TCDD	29–162 FW vs. ND–24 FW	53
Chicks; plasma; near bleached kraft pulp mill; June–July 1992; upstream vs. downstream		
2,3,7,8-TCDD	<0.1 FW vs. <0.1 FW	54
1,2,3,7,8-penta-CDD	As above	54
1,2,3,6,7,8-hexa-CDD	As above	54
1,2,3,4,6,7,8-hepta-CDD	1.2 FW vs. 1.4 FW	54
OCDD	4.3 FW vs. 5.8 FW	54
Cormorant, <i>Phalacrocorax carbo</i> ; the Netherlands; April–May 1989; two colonies; yolk-sac of hatchlings		
2,3,7,8-TCDD	666–908 (278–1469) LW	37
1,2,3,7,8-penta-CDDs	742–1021 (385–1231) LW	37
1,2,3,6,7,8-hexa-CDD	579–1348 (330–1790) LW	37
Forster's tern, <i>Sterna forsteri</i> ; whole eggs; 1983; Green Bay, Wisconsin (contaminated site) versus Lake Poygan, Wisconsin (reference site)		
2,3,7,8-TCDD	37 (14–105) FW vs. 8 (<2–20) FW	42
Penta-CDDs	102 (71–84) FW vs. 25 (9–44) FW	42
Hexa-CDDs	37 (11–46) FW vs. 3 (<3–16) FW	42
Common tern, <i>Sterna hirundo</i>		
Europe; yolk-sac of eggs; 1991; maximum values		
Tetra-CDDs	ND	41
1,2,3,7,8-penta-CDD	400 LW; 88 FW	41
1,2,3,6,7,8-hexa-CDD	1090 LW; 342 FW	41
Wisconsin; 1988; Green Bay and Fox River; whole egg (less shell) vs. whole chick (less stomach contents, beaks, feathers, and feet), maximum values		
Red-winged blackbird, <i>Agelaius phoeniceus</i>		
2,3,7,8-TCDD	0.4 FW vs. 0.7 FW	38
OCDD	29 FW vs. 111 FW	38
Common tern, <i>Sterna hirundo</i>		
2,3,7,8-TCDD	11 FW vs. 5 FW	38
1,2,3,7,8-penta-CDD	8 FW vs. 4 FW	38
1,2,3,4,7,8-hexa-CDD	3 FW vs. 3 FW	38
1,2,3,6,7,8-hexa-CDD	19 FW vs. 8 FW	38
1,2,3,4,6,7,8-hepta-CDD	12 FW vs. 9 FW	38
OCDD	108 FW vs. 18 FW	38
Forster's tern, <i>Sterna forsteri</i>		
2,3,7,8-TCDD	20 FW vs. 4 FW	38
1,2,3,7,8-penta-CDD	9 FW vs. 5 FW	38

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
1,2,3,6,7,8-hex-a-CDD	16 FW vs. 7 FW	38
1,2,3,4,6,7,8-hepta-CDD	9 FW vs. 11 FW	38
OCDD	163 FW vs. 27 FW	38
Tree swallow, <i>Tachycineta bicolor</i>		
2,3,7,8-TCDD	5 FW vs. 3 FW	38
1,2,3,7,8-penta-CDD	24 FW vs. 12 FW	38
1,2,3,4,7,8-hex-a-CDD	24 FW vs. 12 FW	38
1,2,3,6,7,8-hex-a-CDD	101 FW vs. 48 FW	38
1,2,3,4,6,7,8-hepta-CDD	109 FW vs. 71 FW	38
OCDD	140 FW vs. 25 FW	38

NONBIOLOGICAL MATERIALS

Kraft and sulfite mills; United States; 1988; 104 mills

P脉		
Hardwood Kraft	5 FW, Max. 33	21
Softwood Kraft	12 FW, Max. 116	21
Sulfite	1 FW, Max. 15	21
Effluents		
Kraft mills	0.059 FW, Max. 0.6 FW	21
Sulfite mills	0.006 FW, Max. 0.02 FW	21
Sludge		
Kraft mills	95 FW, Max. 1390 FW	21
Sulfite mills	16 FW, Max. 58 FW	21

Sediments

Alberta, Canada; 1990; near bleached-kraft mill	Max. 11 DW	24
Newark Bay, New Jersey, (total deposition estimated at 4–8 kg of 2,3,7,8-TCDD), 1980s	260–430 DW	20
Massachusetts, 1983		
Lake Winthrop	5.9 FW	3
Other ponds (5)	ND	3

Soils

Seveso, Italy		
1978	3500 (10–12,000) FW	1
1976		
Precontamination	ND	12
Postcontamination	2300 (<0.75–51,000) FW	12
Southwest Missouri		
1974	(220,000–440,000) FW	17
1971	(31,800,000–33,000,000) FW	17

Municipal sewage sludge

Milwaukee, Wisconsin		
1933	2 FW	18
1981	11 FW	18
1982	16 FW	18

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Ecosystem, Taxonomic Group, Collection Locale, Year of Collection, Species, Tissue, and Other Variables	Concentration ^a (ppt)	Reference ^b
Industrial chemical and sludge samples		
Trichlorophenol process		
Still, bottom	111,000,000 FW	19
Sump fluid		
Upper layer	63 FW	19
Lower layer	676,000 FW	19
Sludge		
Liquid	445,000 FW	19
Solid	374,000 FW	19
Process	79 FW	19
Discharge	22,000 FW	19
INTEGRATED STUDIES		
Florida; St. Johns River; downstream from a bleach-kraft mill; 1988–89		
Effluent	0.016 FW; Max. 0.033 FW	48
Sediment	53 FW	48
Bowfin, <i>Amia calva</i>		
Liver	Max. 19 FW	48
Ovary	46 FW	48
Largemouth bass, <i>Micropterus salmoides</i>		
Gonads	9 FW	48
Liver	Max. 3 FW	48
Brown bullhead, <i>Ictalurus nebulosus</i> ; liver	Max. 3 FW	48
Blue crab, <i>Callinectes sapidus</i> ; hepatopancreas	8 FW	48
Arkansas, Bayou Meto (250-km section contaminated with 2,3,7,8-TCDD from a chemical plant in the 1970s)		
Sediments		
1970s	Max. 12,400 FW	49
mid-1980s	2500 FW	49
1991	>1 FW; Max. 276 FW	49
Duck eggs, 1970s	Max. 482 FW	49
Fish, muscle		
mid-1980s	Max. 1900 FW	49
1991	>25 FW; Max. 123 FW	49
Fish, whole		
1982	(18–863) FW	49
1987	(22–1900) FW	49
1991	Max. 296 FW	49
Baltic Sea		
Phytoplankton	(8–58) DW	50
Seston	(32–38) DW	50
Zooplankton	25 DW	50
Common mussel, <i>Mytilus edulis</i> ; soft parts	28 DW	50
Fish muscle		
Baltic herring, <i>Clupea harengus</i>	4 DW	50
Atlantic cod, <i>Gadus morhua</i>	2 DW	50
Eider duck, <i>Somateria mollissima</i> ; various tissues	1.2–2.9 DW	50

Table 18.3 (continued) Concentrations of PCDDs Measured in Selected Organisms and Nonbiological Materials Collected from Various Locales (Unless indicated otherwise, all values are in parts per trillion [ppt] 2,3,7,8-TCDD [ng/kg] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

^a Concentrations are listed as mean (minimum–maximum), maximum = Max., or nondetectable = ND.
^b 1, Fanelli et al. 1980c; 2, Ramel 1978; 3, Anonymous 1984; 4, Powell 1984; 5, Kleopfer and Zirschy 1983; 6, Suns et al. 1983; 7, O'Keeffe et al. 1983; 8, Ryan et al. 1984; 9, NRCC 1981; 10, Harless et al. 1982; 11, Heida 1983; 12, Fanelli et al. 1980b; 13, Fanelli et al. 1980a; 14, Stalling et al. 1985a; 15, Ogilvie 1981; 16, Nriagu and Simmons 1984; 17, Kimbrough 1984; 18, Kamparski et al. 1984; 19, Van Ness et al. 1980; 20, Prince and Cooper 1995a; 21, Whittemore et al. 1990; 22, Smith et al. 1994; 23, Williams and Giesy 1992; 24, Owens et al. 1994; 25, Servos et al. 1994; 26, Whittle et al. 1992; 27, de Wit et al. 1990; 28, Kuehl et al. 1989; 29, Ryan et al. 1986; 30, Struger et al. 1993; 31, Meyers-Schone and Walton 1994; 32, Bignert et al. 1989; 33, Oehme et al. 1995; 34, Van Scheppingen et al. 1996; 35, Muir et al. 1996; 36, White and Seginak 1994; 37, Vand den Berg et al. 1994; 38, Ankley et al. 1993; 39, Elliott et al. 1989; 40, Sanderson et al. 1994a; 41, Bosveld et al. 1995; 42, Kubiak et al. 1989; 43, Ryan et al. 1997; 44, Landi et al. 1997; 45, Furst et al. 1990; 46, La Fleur et al. 1990; 47, Olie et al. 1989; 48, Schell et al. 1993; 49, Johnson et al. 1996; 50, Broman et al. 1992; 51, Whyte et al. 1998; 52, Ishizuka et al. 1998; 53, Woodford et al. 1998; 54, Elliott et al. 1998.

18.4 LETHAL AND SUBLETHAL EFFECTS

18.4.1 General

Information is lacking or scarce on the biological properties of PCDD isomers, except 2,3,7,8-TCDD. The latter has been associated with lethal, carcinogenic, teratogenic, reproductive, mutagenic, histopathologic, and immunotoxic effects. There are substantial inter- and intraspecies differences in sensitivity and toxic responses to 2,3,7,8-TCDD. Typically, animals poisoned by 2,3,7,8-TCDD exhibit weight loss, atrophy of the thymus gland, and eventually death. The toxicological mechanisms are imperfectly understood.

18.4.2 Terrestrial Plants and Invertebrates

Higher plants, such as corn (*Zea mays*) and beans (*Phaseolus vulgaris*), grown on soil contaminated with 2,3,7,8-TCDD (12 to 2750 ng 2,3,7,8-TCDD/kg FW) accumulated the toxin in the aerial parts progressively over time with increasing soil burdens of 2,3,7,8-TCDD. In hydroponic tests, TCDD uptake occurred only in light (Sacchi et al. 1986). Aerial parts of beans grown in soil containing 12 ng 2,3,7,8-TCDD/kg had 0.09 ng 2,3,7,8-TCDD/kg FW after 7 days; beans grown in soils with 2750 ng 2,3,7,8-TCDD/kg had 7.2 ng/kg FW after 7 days. After 57 days, beans contained a maximum of 5 ng/kg FW. Aerial parts of corn had 0.74 to 10 ng 2,3,7,8-TCDD/kg FW after 17 days; after 57 days, this range was 1.2 to 3.2 ng/kg FW (Sacchi et al. 1986).

Reinecke and Nash (1984) reported that two species of earthworms (*Allolobophora caliginosa* and *Lumbricus rubellus*) showed no adverse effects when held for 85 days in soils containing grossly elevated levels of 5 mg/kg of 2,3,7,8-TCDD, but both species died at 10 mg/kg. In soils containing lower concentrations of 50 µg/kg of 2,3,7,8-TCDD, earthworms accumulated 5 times the soil levels in 7 days. There was no avoidance of soils contaminated with 2,3,7,8-TCDD, suggesting indifference. No surface penetration of dioxins into the body of earthworms was noted, and there was no biological breakdown of 2,3,7,8-TCDD during digestion as judged by the absence of mono-, di-, and tri-CDDs in excrement. Worm-worked soils had 2,3,7,8-TCDD retention times of 80 to 400 days, suggesting that earthworms may significantly alter half-time patterns of 2,3,7,8-TCDD in soils (Reinecke and Nash 1984).

Mutagenic responses were produced in *Escherichia coli* and certain strains of *Salmonella typhimurium* bacteria by 2,3,7,8-TCDD, but not by octa-CDD (Vos 1978). Further, chromosomal aberrations were induced in at least one species of higher plant and mammal (Ramel 1978). It must be concluded at this time that 2,3,7,8-TCDD is mutagenic or has mutagenic potential.

18.4.3 Aquatic Organisms

Limited data are available on lethal and sublethal effects of any PCDD isomer to aquatic organisms, except for 2,3,7,8-TCDD and freshwater biota (Table 18.4); 2,3,7,8-TCDD and liver microsomal enzyme activities in two marine species: winter flounder, *Pleuronectes americanus*, and the little skate, *Raja erinacea* (Pohl et al. 1976); and 1,3,6,8-TCDD uptake and elimination by fathead minnows (*Pimephales promelas*) and rainbow trout (Corbet et al. 1983). Lymphomyeloid and epithelial tissues are the primary target organs for TCDD-induced pathologic lesions in rainbow trout (Spitsbergen et al. 1988a). Cardiovascular systems seem to be the initial tissue affected in both the TCDD toxicity syndrome and in blue-sac disease of developing lake trout. Lesions in other organs, including brain, retina, and liver, develop as a result of circulatory derangements, anemia, and hypoxia (Spitsbergen et al. 1991). The mode of action of 2,3,7,8-TCDD in rainbow trout and mammals on the epidermal growth factor is mediated, in part, through protein kinase C activity (Newsted and Giesy 1993).

Tissue residues of 55 ng 2,3,7,8-TCDD/kg FW in sac fry of the lake trout (*Salvelinus namaycush*) were lethal (Walker et al. 1991), and water concentrations of 0.038 ng 2,3,7,8-TCDD/L caused a reduction in feeding activity and general activity levels of rainbow trout (Mehrle et al. 1988; Newsted and Giesy 1992). Less-sensitive species of teleosts exhibited reduced growth and fin necrosis at concentrations as low as 0.1 ppt of 2,3,7,8-TCDD after exposure for 24 to 96 h. Concentrations of 1.0 ppt and higher were eventually fatal, and exposure to lower concentrations of 0.01 ppt for 24 h had no measurable effect (Table 18.4). A typical 2,3,7,8-TCDD poisoning sequence in guppies (*Poecilia reticulatus*) and coho salmon (*Oncorhynchus kisutch*) during a postexposure observation period included: declining interest in feeding (5 to 8 days postexposure); skin discoloration and fin necrosis (30 days), with caudal fin most severely affected; reduced resistance to fungal infestations; reduced swimming; and, finally, death several weeks to months after exposure (Miller et al. 1973). In general, older and larger fish die last, and smaller or younger specimens succumb first (Norris and Miller 1974).

In brook trout (*Salvelinus fontinalis*), feces was the most important egestion route, and spawning was not an important source of chemical elimination of 2,3,7,8-TCDD (Nichols et al. 1998). However, Tietge et al. (1998) disagree and, using radioisotope techniques, show 39% maternal transfer of 2,3,7,8-TCDD to eggs in brook trout, and suggest the need for additional research in this area.

Histopathologic and teratogenic effects were noted in fry of rainbow trout (*Oncorhynchus mykiss*) exposed to 10 ppt 2,3,7,8-TCDD for 96 h as eggs, or as yolk-sac fry (Helder 1981). Some fry showed extensive degeneration and necrosis of the liver, and subsequently developed edema prior to death. The remaining fry showed a high incidence of teratogenic changes, including opercular defects, and foreshortened maxillas. Invertebrates, plants, and amphibians were comparatively resistant to 2,3,7,8-TCDD. For example, there were no adverse effects on growth, reproduction, or food consumption of algae, daphnids, and snails during immersion for 32 days in solutions containing 2.4 to 4.2 ppt 2,3,7,8-TCDD (Yockim et al. 1978). Populations of the mummichog (*Fundulus heteroclitus*) from New Jersey coastal waters contaminated with 2,3,7,8-TCDD are unusually resistant to dioxins when compared to reference populations (Prince and Cooper 1995a). Mummichogs from a TCDD-contaminated site were resistant to the toxicity of 2,3,7,8-TCDD and the ability of 2,3,7,8-TCDD to induce P4501A activity, which may imply an alteration in the Ah receptor complex of TCDD-contaminated mummichogs (Prince and Cooper 1995b).

Bioconcentration factors of dioxins in fishes are relatively low compared to other chlorinated aromatic compounds because of the low metabolic conversion of dioxins, their low available concentrations in test systems, and their highly variable uptake rates (de Voogt et al. 1990). In general, bioconcentration factors for persistent superlipophilic chemicals, such as OCDD, derived for freshwater fishes from supersaturated solutions may seriously underestimate the true BCF (Geyer

et al. 1992). BCF values for OCDD in various fish species are about 4.3×10^6 on a fresh weight basis and 8.5×10^7 on a lipid weight basis. However, these values are several orders of magnitude higher than those reported for guppies, rainbow trout, and fathead minnows because the lower values were derived from OCDD concentrations that exceeded the water solubility of OCDD (Geyer et al. 1992). Although uptake from food predominates over direct uptake of dioxins from water (de Voogt et al. 1990), the accumulation of 2,3,7,8-TCDD from the aquatic environment occurred in all species examined (Table 18.4). The isomer 1,3,6,8-TCDD was also accumulated from the environment by freshwater teleosts, but accumulations were much lower than predicted when compared to 2,3,7,8-TCDD, and elimination was 10 to 15 times more rapid than 2,3,7,8-TCDD (Corbet et al. 1983). Of seven chlorinated dibenzodioxins tested, 2,3,7,8-TCDD was concentrated by rainbow trout and fathead minnows to the greatest extent (de Voogt et al. 1990). In outdoor pond studies, a major portion of the added 2,3,7,8-TCDD concentrated in aquatic plants and at the sediment–water interface (Tsushimoto et al. 1982); however, most (85 to 99%) of the 2,3,7,8-TCDD originally added to the ecosystem remained in the sediments at the end of the study (Isensee and Jones 1975), with significant reduction in bioavailability of PCDDs to fishes (Loonen et al. 1994a). Among teleosts, body burdens of 2,3,7,8-TCDD increased with increasing concentration in the water column and with increasing duration of exposure. On removal to uncontaminated water, less than 50% was lost in 109 days (Miller et al. 1979). Accumulation of PCDDs in biota shifted from direct equilibrium partitioning during the first few days when concentrations in the water column were relatively high, to a detrital food chain transfer as the freely available PCDDs in the water column declined (Servos et al. 1992b).

Table 18.4 Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
ALGAE AND MACROPHYTES		
Alga, <i>Odegonium cardiacum</i> ; 2.4–4.2 parts per trillion (ng/L) 2,3,7,8-TCDD for 32 days	Bioconcentration factor (BCF) of 6 at day 1, 654–2083 at days 3–32, 500 at day 7 postexposure (pe), and 230 at day 14 pe. Residues of 7000 ng/kg fresh weight (FW) in 5 days, and 2500 ng/kg FW in 30 days	1, 11
Pondweeds, <i>Elodea</i> sp. and <i>Ceratophyllum</i> sp.; 53.7 ng/L 2,3,7,8-TCDD for 30 days	Residues of 7000 ng/kg in 5 days and 2500 in 30 days	2
Duckweed, <i>Lemna minor</i> ; 710 ng/L 2,3,7,8-TCDD for 30 days	No adverse effects	11
MOLLUSCS		
Snail, <i>Helisoma</i> sp.; 2.4–4.2 ng/L 2,3,7,8-TCDD for 32 days	Maximum BCF of 3731	1
Snail, <i>Physa</i> sp.; 200 ng/L 2,3,7,8-TCDD for 36 days	Reduced reproduction at day 12 pe	3
ANNELIDS		
Worm, <i>Paranais</i> sp.; 200 ng/L 2,3,7,8-TCDD for 55 days	Reduced reproduction	3
ARTHROPODS		
Mosquito, <i>Aedes aegypti</i> ; larvae exposed to 200 ng/L 2,3,7,8-TCDD for 17 days	No effect at day 30 pe	3
Daphnid, <i>Daphnia magna</i> 2.4–4.2 ng/L 2,3,7,8-TCDD for 32 days 1030 ng/L 2,3,7,8 TCDD for 48 h, then observed for 7 days	Maximum BCF of 7125 No adverse effects	3 12

Table 18.4 (continued) Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
FISHES		
Zebrafish, <i>Brachydanio rerio</i> ; females fed diets equivalent to a single exposure of 1, 5, 10, or 20 ng 2,3,7,8-TCDD per fish. A value of 5 ng 2,3,7,8-TCDD/fish = 1.7–2.0 µg 2,3,7,8-TCDD/kg BW	No significant toxic effects at 1 ng/fish. Doses of 5 ng/fish and higher led to dose-related reduction of egg numbers and to lethal developmental abnormalities in their offspring; ovaries of parents were abnormal histologically	13
Common carp, <i>Cyprinus carpio</i> ; juveniles given single intraperitoneal (ip) injection of 10, 30, 50, 270, 570, or 2930 ng 2,3,7,8-TCDD/kg BW and observed for 6 weeks	Dose-dependent induction of EROD activity at 30 ng/kg BW and higher; lymphocyte depletion at 270 ng/kg and higher. The 270- and 570-ng/kg groups had reduced food intake, severe cutaneous hemorrhages, and swollen eyes. The 570- and 2930-ng/kg groups had liver histopathology. The high-dose group had 60% dead; survivors had reduced growth	14
Northern pike, <i>Esox lucius</i> ; eggs and fry exposed to 0.1 or 10.0 ng/L 2,3,7,8-TCDD for 96 h	Low-dose group had reduced growth that persisted for 21 days; in high-dose group, most died within 23 days	5, 11
Freshwater fishes		
2,3,7,8-TCDD concentrations in eggs of seven species after exposure as fertilized eggs to nominal concentrations of 9–285 ng 2,3,7,8-TCDD/L for up to 540 h. Lowest observed effect concentration (LOEC) in ng/kg FW associated with adverse effects on survival or growth 32 days post exposure vs. no observed effect concentration (NOEC) in ng/kg FW		
Lake herring, <i>Coregonus artedi</i> ; 270 vs. 175	LOEC (after 100 days) vs. NOEC	37
Fathead minnow, <i>Pimephales promelas</i> ; 435 vs. 235	LOEC vs. NOEC	37
Channel catfish, <i>Ictalurus punctatus</i> ; 855 vs. 385	LOEC vs. NOEC	37
Medaka, <i>Oryzias latipes</i> ; 949 vs. 455	LOEC vs. NOEC	37
White sucker, <i>Catostomus commersoni</i> ; 1220 vs. 848	LOEC vs. NOEC	37
Northern pike, <i>Esox lucius</i> ; 1800 vs. 1190	LOEC vs. NOEC	37
Zebrafish, <i>Brachydanio rerio</i> ; 2000 vs. 424	LOEC vs. NOEC	37
Single intraperitoneal injection of 2,3,7,8-TCDD 3–5 µg/kg BW	Estimated LD ₅₀ (80 days postexposure) for sensitive species; fin necrosis in all species	15
10–16 µg/kg BW	Estimated LD ₅₀ (80 days postexposure) for resistant species; fin necrosis in all species	15
60 µg/kg BW radiolabeled 2,3,7,8-TCDD; 6 species	At least 3 TCDD metabolites in addition to the parent compound were found in gall bladder bile of all 6 species and at least 2 metabolites were glucuronide conjugates	15
Mosquitofish, <i>Gambusia affinis</i> ; 2.4–4.2 ng/L 2,3,7,8-TCDD for 15 days	BCF of 676 at day 1 and 1482 at day 7. All dead at day 15, with death preceded by nasal bleeding and listless swimming	1
Channel catfish, <i>Ictalurus punctatus</i> ; 2.4–4.2 ng/L 2,3,7,8-TCDD for 20 days	Fin necrosis, erratic swimming, hemorrhaging from anus and lower jaw, BCF of 2181; all dead between days 15 and 20	1

Table 18.4 (continued) Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Radiolabeled 1,3,6,8-TCDD; 4–211 ng/L for 5 days; depuration for 24–48 days	Whole fish BCF at equilibrium of 2100; highest concentration in bile; half-time persistence of 6–9 days	20, 25
Radiolabeled OCDD; 9–415 ng/L for 5 days; depuration for 24–48 days	Whole fish BCF at equilibrium was 85; highest concentration in bile; Tb 1/2 of 5–13 days	20, 25
Whole fish bioconcentration factors at equilibrium		
2,3,7,8-TCDD	7762–9270	25
1,2,3,4,7-penta-CDD	810	25
1,2,3,4,7,8-hexa-CDD	2278	25
1,2,3,4,6,7,8-hepta-CDD	1413	25
Single intraperitoneal injection		
0.006, 0.03, 0.06, 0.3, 0.6, or 3.06 µg 2,3,7,8-TCDD/kg BW; juveniles; killed 3, 6, or 12 weeks after injection	The high-dose group had 20% dead at week 12, with lethargy and growth inhibition evident in survivors at week 6. A dose-related increase in EROD activity and total cytochrome P450 content was observed after 3 weeks at dose levels of 0.3 µg/kg BW and higher; the ED50 for EROD activity was 0.8 µg/kg. Six weeks after single injections of 0.3 µg/kg BW and higher, trout had hemorrhages in fins and the skin and significant enzyme induction in spleen and liver	26
0.1 µg 2,3,7,8-TCDD/kg BW; juveniles	Increase in hepatic EROD and AHH activity	28
0.1, 1, 5, 10, 25, or 125 µg 2,3,7,8-TCDD/kg BW; fingerlings and yearlings	Doses of 25 and 125 µg/kg BW resulted in 85% dead 2–4 weeks after injection. Gross and microscopic lesions found in the 10-µg/kg and higher groups. The 5-µg/kg group had reduced growth and 20% dead after 11 weeks. The 1-µg/kg group had leukopenia and thrombocytopenia	27
0.91 µg 2,3,7,8-TCDD/kg BW; juveniles	50% increase in hepatic ethoxresorufin O-deethylase (EROD) activity	28
10.0 µg 2,3,7,8-TCDD/kg BW; fingerlings and yearlings	LD50, single ip injection	27
10.0 µg 2,3,7,8-TCDD/kg BW; juveniles	Maximum reduction in epidermal growth factor receptor in liver plasma membranes 10–40 days after injection	29
Fingerlings given single ip injection of 60 µg 2,3,7,8-TCDD/kg BW	One week after injection, the bile contained at least 3 TCDD metabolites plus the parent compound; at least one of the metabolites was a glucuronide conjugate	31
Oral dose		
4 µg 2,3,7,8-TCDD/kg BW twice with 4-day interval, for a total dose of 8 µg/kg BW	EROD activity increased by 1450% at day 9	33
Single oral dose of 30 µg 2,3,7,8-TCDD/kg BW to seawater-adapted juveniles	Highest TCDD accumulations in visceral and extravisceral fat deposits. But Atlantic cod, <i>Gadus morhua</i> , treated similarly, accumulated TCDDs in liver and brain and to a significantly greater extent than did seawater-adapted rainbows	32
Isolated liver membranes; 0.17 or 0.79 µg 2,3,7,8-TCDD/kg FW	Low dose caused 50% reduction in epidermal growth factor receptor; high dose caused 50% increase in EROD activity	29

Table 18.4 (continued) Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
Juveniles (0.4 g BW) exposed for 28 days to 0.038, 0.079, 0.176, 0.382, or 0.789 ng 2,3,7,8-TCDD/L (parts per trillion) followed by 28 days in clean water	Significant adverse effects on survival, growth, and behavior during exposure and depuration at all concentrations tested. The lowest concentration group tested (0.038 ng/L) — which was the least affected — had 45% dead after day 28 of depuration and a whole-body BCF of 39,000 after exposure and about 26,000 after depuration. Controls had 93% survival	30
Eggs held in 0.1 ng/L 2,3,7,8-TCDD for 96 h Yolk-sac fry exposed to 1.0 ng 2,3,7,8-TCDD/L for 96 h	Growth retardation of fry at day 72 pe Growth retarded for 23 weeks	6 11
Juveniles held in 10.0 ng/L 2,3,7,8-TCDD for 96 h	Growth retardation, edema; 26% dead at day 72 pe	6
Immatures held in 107.0 ng/L 2,3,7,8-TCDD for 2 h Immatures held in 107.0 ng/L 2,3,7,8-TCDD for 6 h	Whole-body residues of 1010 ng/kg FW Some deaths beginning at day 78 pe. At day 136 pe, survivors had reduced growth and enlarged livers; tissue residues, in ng/kg FW, were 650 in whole trout, 260 in muscle, 3710 in liver, and 3800 in fat	7 7
Fingerlings fed a diet containing 494 ng radiolabeled 2,3,7,8-TCDD/kg ration for 13 weeks followed by a clean diet for 13 weeks	No overt signs of toxicity. After 13 weeks, more than 90% of the 2,3,7,8-TCDD recovered was in fatty tissues; 98% of the 2,3,7,8-TCDD had not been metabolized. Time for 50% depuration from whole body was 15 weeks and for individual organs 8–19 weeks	31
Coho salmon, <i>Oncorhynchus kisutch</i> ; juveniles 0.56 ng/L 2,3,7,8-TCDD for 48 h 2.05 ng/L 2,3,7,8-TCDD for 96 h	12% dead in 60 days Whole-body residues of 125 ng/kg at day 114 pe	3 9
5.6 ng/L 2,3,7,8-TCDD for 96 h 56.0 ng/L 2,3,7,8-TCDD for 24 h 10.53 ng/L 2,3,7,8-TCDD for 96 h	55% dead in 60 days All dead in 40 days Whole-body residues of 2117 ng/kg at day 114 pe; reduced growth and survival	3, 11 3 9
Medaka, <i>Oryzias latipes</i> Exposed to radiolabeled 2,3,7,8-TCDD for as long as 12 days and then transferred to uncontaminated media for up to 175 days	The predicted steady-state BCF for 2,3,7,8-TCDD in medakas is 510,000. But observed whole-body BCF after 12 days was only 24,000 times the water concentration; this decreased by 47% after 175 days in uncontaminated media	16
Fed diets containing 0.04, 0.4, 1, 4, 10, 40, 100, or 400 mg 1,3,6,8-TCDD/kg ration for 28 days and observed for an additional 60 days. Snails (<i>Indoplanorbis exustus</i>) were given medaka detritus in their diets	No harmful effects in fish, even at highest dose fed of 400 mg 1,3,6,8-TCDD/kg ration. Absorption ranged between 0.05 and 0.1% and almost all was excreted within 8 weeks. Snails, however, were more efficient at absorbing 1,3,6,8-TCDD and their populations were reduced dramatically, even at the lowest dioxin dose fed. Medaka whole-body concentrations, in µg 1,3,6,8-TCDD/kg FW, at day 28 were 13 in the 40 mg/kg group, 65 in the 100 mg/kg group, and 354 in the 400 mg/kg group; by day 84, it was less than 2 µg/kg FW (<17 µg/kg lipid weight) in all groups. Snails at	17

Table 18.4 (continued) Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
Yellow perch, <i>Perca flavescens</i> Fed diet containing 424 ng 2,3,7,8-TCDD/kg ration for 13 weeks, then fed clean diet for another 13 weeks	day 28 had 4 µg/kg BW fresh weight (80 µg/kg BW lipid weight) from detritus in the 0.04-mg/kg group and 6534 µg/kg FW (130,680 µg/kg lipid weight) at 400 mg/kg ration	18
Single intraperitoneal injection of 1, 5, 25, or 125 µg 2,3,7,8-TCDD/kg BW	No overt signs of toxicity. After 13 weeks, 78% of the total 2,3,7,8-TCDD was in carcass and visceral fat, and the rest in liver (9%), gill (5%), skin (3%), muscle (2%), and GI tract, pyloric caeca, kidney, spleen, and heart. At least 96% of the 2,3,7,8-TCDD was not metabolized; however, gall bladder bile had 4 TCDD metabolites. The half-time persistence for 2,3,7,8-TCDD in whole body was 18 weeks, and for individual organs 6–19 weeks	19
3 (2–4) µg 2,3,7,8-TCDD/kg BW, single intraperitoneal injection	Hepatocyte lipidosis in all groups. Dose-related splenic lymphoid depletion in perch given 5 µg/kg BW and higher. The 5-µg/kg group had progressive loss of body weight and 80% mortality by day 80 postinjection. The 25- and 125-µg/kg groups had 95% dead within 28 days postinjection. Groups given 5 µg/kg and higher had fin necrosis, ascites, and petechial cutaneous hemorrhage	19
Fathead minnow, <i>Pimephales promelas</i> Half-time persistence of various PCDDs 1,2,3,7-TCDD 1,3,6,8-TCDD 2,3,7,8-TCDD 1,2,3,4,7,8-hexa-CDD 1,2,3,4,6,7,8-hepta-CDD OCDD 9–415 ng/L OCDD for 5 days and depuration for 48 days	LD50 (80 days postinjection) 2.7 days 6.9 days 14.5–58 days 3.1 days 17.3 days 13.9 days BCF for whole minnows was 2200 with highest concentrations in bile; half-time persistence of 5–13 days	19 12 12 12 12 12 20
4–211 ng/L 1,3,6,8-TCDD for 5 days and depuration for up to 48 days	Whole fish BCF of 5702 with highest concentrations in bile; half-time persistence of 6–9 days	20
0.9 ng/L 2,3,7,8-TCDD for 28 days, then uncontaminated media for 28 days	Whole-body BCF was 5840 and whole-body residue of 15–25 µg/kg DW on day 28; steady state not achieved	12
1.7 ng/L 2,3,7,8-TCDD 53.7 ng/L 2,3,7,8-TCDD for 40 days	LC50 (28 days) Survivors had whole-body residues of 8500 ng/kg in 10 days, 2500 ng/kg in 40 days	12 2
Guppy, <i>Poecilia reticulatus</i> ; adults Exposed to a complex mixture of radiolabeled PCDDs and dibenzofurans for 21 days 0.01 ng/L 2,3,7,8-TCDD for 24 h 1.0 ng/L 2,3,7,8-TCDD for 24 h	Highest uptake was by 2,3,7,8-substituted isomers; whole-body BCF values were log 5.24 for 2,3,7,8-TCDD and log 5.27 for 1,2,3,7,8-penta-CDD No effect at day 32 pe LC50 at day 42 pe	21 9 9

Table 18.4 (continued) Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
1.1 ng/L 2,3,7,8-TCDD for 24 h	Fin disease after 42 days	9
10.0 ng/L 2,3,7,8-TCDD for 24 h	10% dead within 41 days pe	11
100.0 ng/L 2,3,7,8-TCDD for 24 h	Fin necrosis in 10 days; all dead at day 32 pe	10
Brook trout, <i>Salvelinus fontinalis</i>		
Adults fed various dietary concentrations of 2,3,7,8-TCDD for extended period to produce eggs that contain 0, 41, 84, 156, 285, or 517 ng 2,3,7,8-TCDD/kg FW	No effect on adult fertility and growth or on juvenile sex ratios. All exposed groups had edema in free embryos at hatch. Egg concentrations of 41 and 117 ng/kg caused 13.8% and 50% exophthalmia in juveniles, respectively; 138 ng/kg egg caused 50% kill at swimup	36
Newly fertilized eggs exposed to various concentrations of 2,3,7,8-TCDD for 48 h to produce 101–470 ng 2,3,7,8-TCDD/kg FW egg, then transferred to clean water until hatch	Dose-related increases in sac-fry mortality associated with yolk-sac edema hemorrhages and arrested development; signs resembled blue-sac disease	22
135 ng 2,3,7,8-TCDD/kg FW egg	NOEL for sac-fry mortality	22
185 ng 2,3,7,8-TCDD/kg FW egg	LOEL for increased mortality	22
200 (179–215) ng 2,3,7,8-TCDD/kg FW egg	LD50, sac fry	22
324 (283–488) ng 2,3,7,8-TCDD/kg FW egg	LD100, sac fry	22
Adults, age 18 months, fed diets containing stable and radiolabeled 2,3,7,8-TCDD for various periods to produce whole-body concentrations as high as 1200 ng/kg BW	At 600 ng/kg BW, no adverse effects on survival, growth, or reproduction. At 1200 ng/kg BW, spawning was delayed 13 days. Dietary assimilation of 2,3,7,8-TCDD is high at 89% and is independent of time and whole-body TCDD burdens. Regardless of dose, ovarian tissues of adult females had 74% of the whole-body 2,3,7,8-TCDD concentration on a lipid weight basis and 61% on a nonlipid basis. Spawning eggs had 39% of the whole-body 2,3,7,8-TCDD concentration on a nonlipid basis	34
Lake trout, <i>Salvelinus namaycush</i>		
Fertilized eggs were exposed for 48 h to graded concentrations (0, 0.1, 1, 10, or 100 ng 2,3,7,8-TCDD/L) to achieve egg concentrations of 0, <15, 40, or 400 ng 2,3,7,8-TCDD/kg FW egg. Eggs were then transferred to flowing uncontaminated media through hatch	Development normal in all groups until 1 week prior to hatch. At this time, embryos and sac fry in the 400-nug/kg group had a variety of hemorrhages and experienced low survival at hatch; survivors developed severe subcutaneous edema and all died prior to swimup. Blue sac disease occurred at 2% frequency in the 40 ng/kg group versus 1% in the <15 and control groups	23
Fertilized eggs were exposed for 48 h to 10, 20, 40, 62, or 100 ng 2,3,7,8-TCDD/L to produce 2,3,7,8-TCDD concentrations in eggs of 34, 55, 121, 226, or 302 ng/kg FW, then transferred to uncontaminated media through hatching	TCDDs were not eliminated by eggs or sac fry, but were rapidly eliminated (Tb 1/2 of 35–37 days) from fry. Hatchability was reduced at 226 and 302 ng/kg egg, with greatest mortality at the sac-fry stage. In all TCDD groups, sac fry that died developed subcutaneous yolk-sac edema. There were no deaths at egg concentrations of 34 ng/kg and some deaths at 55 ng/kg	24
Egg concentrations of 50 ng 2,3,7,8-TCDD/kg FW and higher, regardless of route of transfer (injection, ambient medium, internal transfer)	Fry exposed as eggs show pericardial and yolk-sac edema, subcutaneous hemorrhaging, craniofacial alterations, arrested development, and frequently death	35

Table 18.4 (continued) Effects of 2,3,7,8-TCDD and Other PCDDs on Representative Species of Freshwater Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effects	Reference ^a
Egg concentrations of 65 ng 2,3,7,8-TCDD/kg FW Adult whole-body concentrations of 78 ng 2,3,7,8-TCDD/kg FW	Associated with 50% mortality by swimup Reproduction inhibited	34 34
AMPHIBIANS		
Bullfrog, <i>Rana catesbeiana</i>		
Tadpoles; single intraperitoneal (ip) injection of 500 ng/kg BW 2,3,7,8-TCDD	No effect through metamorphosis	4
Adults; single ip injection of 500 ng/kg BW 2,3,7,8-TCDD	No effect at day 35 pe	4

^a 1, Yockim et al. 1978; 2, Tushimoto et al. 1982; 3, Miller et al. 1973; 4, Neal et al. 1979; 5, Helder 1980; 6, Helder 1981; 7, Branson et al. 1985; 8, Vodicnik et al. 1981; 9, Miller et al. 1979; 10, Norris and Miller 1974; 11, USEPA 1984; 12, Adams et al. 1986; 13, Wannemacher et al. 1992; 14, Van der Weiden et al. 1994; 15, Kleeman et al. 1988; 16, Schmeider et al. 1995; 17, Allinson et al. 1994; 18, Kleeman et al. 1986b; 19, Spitsbergen et al. 1988b; 20, Muir et al. 1986; 21, Loonen et al. 1994b; 22, Walker and Peterson 1994; 23, Spitsbergen et al. 1991; 24, Walker et al. 1991; 25, Fletcher and McKay 1993; 26, Van der Weiden et al. 1992; 27, Spitsbergen et al. 1988a; 28, Newsted et al. 1995; 29, Newsted and Giesy 1993; 30, Mehrle et al. 1988; 31, Kleeman et al. 1986a; 32, Hektoen et al. 1992; 33, Hektoen et al. 1994; 34, Tietge et al. 1998; 35, Walker et al. 1994; 36, Johnson et al. 1998; 37, Elonen et al. 1998.

18.4.4 Birds

LD50 values computed 37 days after a single oral dose of 2,3,7,8-TCDD varied from 15 µg/kg body weight in northern bobwhite (*Colinus virginianus*), with 95% confidence limits of 9.2 and 24.5 µg/kg, to more than 810 µg/kg body weight for the ringed turtle-dove (*Streptopelia risoria*). Mallards (*Anas platyrhynchos*) were intermediate in sensitivity, with an acute oral LD50 value of more than 108 µg/kg body weight (Hudson et al. 1984). For all three species, death occurred 13 to 37 days after treatment. Remission in survivors had apparently occurred by day 30 posttreatment. Gross necropsy of ringed turtle-doves that survived treatment showed enlarged livers, about twice normal size. Bobwhites showed severe emaciation, high accumulations of uric acid salts in connective tissues, and fluid accumulations in the pericardial and abdominal cavities (Hudson et al. 1984). Some birds regurgitated within a few minutes after treatment. Signs of intoxication that began 7 days after treatment included excessive drinking, loss of appetite, hypoactivity, emaciation, weakness, debility, muscular incoordination, increased reaction to stimuli, fluffed feathers, huddled position, unkempt appearance, falling, tremors, spasms, convulsions, and immobility (Hudson et al. 1984).

In ovo exposure to dioxins is associated with development of grossly asymmetric avian brains, especially the forebrain and tectum. Brain asymmetry was observed in herons, cormorants, eagles, and chickens exposed to 2,3,7,8-TCDD under controlled conditions. Asymmetry appears with increasing frequency and severity in embryos and hatchlings exposed to increasing doses of 2,3,7,8-TCDD, beginning early in development (Henshel 1998). Injection of 1.3 to 11.7 µg 2,3,7,8-TCDD/kg FW egg into yolks of the double-crested cormorant (*Phalacrocorax auritus*) prior to incubation produced an LD50 at hatch of 4.0 µg/kg; hepatic EROD activities were elevated in all treatment groups when compared to controls, but development was normal (Powell et al. 1998).

Studies with 2,3,7,8-TCDD and various life stages of the ring-necked pheasant (*Phasianus colchicus*) by Nosek and co-workers (Nosek et al. 1992a, 1992b, 1993) showed several trends:

1. Hens given a single intraperitoneal (ip) injection of 25 µg/kg BW and higher had reduced growth and survival during an 11-week observation period.
2. Hens given weekly ip injections of 1.0 µg/kg BW for 10 weeks had reduced egg production and hatchability, and a wasting disease that proved fatal to 100% by 13 weeks after the last injection.
3. Hens given weekly ip injections for 10 weeks prior to egg laying of 0.1 µg/kg BW had no adverse effects on growth, reproduction, or survival; translocation of 2,3,7,8-TCDD to egg yolks indicates that egg laying is an important route of elimination.
4. The half-time persistence of 2,3,7,8-TCDD in hatchlings exposed as embryos is about 13 days; for adult hens not producing eggs, the half-time persistence of radiolabeled 2,3,7,8-TCDD is 378 days.
5. The most sensitive effect of *in ovo* exposures was induction of hepatic ethoxyresorufin O-deethylase (EROD) activity in 1-day-old chicks, with an ED50 dose of 0.312 µg/kg FW egg.
6. LD50 values for embryos were 1.35 µg/kg egg when injected into the egg albumin and 2.18 µg/kg when injected into the egg yolk.
7. No adverse effects on 1-day-old hatchlings and 28-day-old chicks on growth, survival, development, and metabolism were observed at egg 2,3,7,8-TCDD doses up to and including 1.0 µg/kg.
8. Embryo mortality is the most sensitive sign of 2,3,7,8-TCDD toxicity in the ring-necked pheasant; pheasant embryos were more sensitive to 2,3,7,8-TCDD than were embryos of the eastern bluebird (*Sialia sialis*), but less sensitive than embryos of the domestic chicken (*Gallus* sp.).

Domestic chickens were relatively sensitive to PCDDs, especially 2,3,7,8-TCDD, with an estimated 2,3,7,8-TCDD oral LD50 range of 25 to 50 µg/kg body weight (Kociba and Schwetz 1982a, 1982b). EROD induction by 2,3,7,8-TCDD in avian hepatocytes of five species followed a concentration-response relation in livers of hatchlings. Chickens were the most sensitive species tested, followed by the double-crested cormorant, ring-billed gull (*Larus delawarensis*), herring gull, and Forster's tern (Sanderson et al. 1998). Chickens fed 1 or 10 µg 2,3,7,8-TCDD, 1,2,3,7,8,9-hexa-CDD, or hepta-CDDs per kilogram body weight daily for 21 days showed signs of chick edema disease, that is, pericardial, subcutaneous, and peritoneal edema; liver enlargement and necrosis with fatty degeneration; and frequently died (NRCC 1981; Gilbertson 1983). Autopsies of poultry killed by 2,3,7,8-TCDD in Seveso, Italy, in 1976 showed signs characteristic of chick edema disease (Fanelli et al. 1980b). Pathological signs of chick edema disease were also seen in herring gull chicks on the lower Great Lakes in the early 1970s (Gilbertson 1983). Concentrations of 2,3,7,8-TCDD in eggs of the herring gull declined from about 1000 ppt in 1971 to less than 80 ppt in 1981. This was accompanied by a decrease in the frequency of chick edema disease (Gilbertson 1983). Decreases in levels of other contaminants — notably mirex — were probably more important to the survival of gulls in these colonies than 2,3,7,8-TCDD (Eisler 1985). However, little data exist on the interaction of PCDDs, including 2,3,7,8-TCDD, with other contaminants appearing concomitantly in bird tissues or their diets. Although there presently is no evidence of biomagnification of PCDDs in birds (Gilbertson 1983), it is speculated that piscivorous birds have a greater potential to accumulate PCDDs than the fish that they eat (NRCC 1981).

18.4.5 Mammals

Many industrial accidents involving malfunctioning reaction vessels used to manufacture chlorinated phenols or phenoxy herbicides have exposed more than 1300 workers to short-term, high-level doses of the dioxins that occur as contaminants of these substances (Boddington et al. 1990). Exposures have frequently been associated with acne-like skin lesions, dermatitis, altered liver enzyme concentrations, pulmonary deficiency, numbness, nausea, headache, hearing loss, sleep disturbance, tiredness, sexual dysfunction, depression, and appetite loss. Populations exposed to dioxin-contaminated materials through nonoccupational sources — including dioxin-contaminated soils in Missouri, a trichlorophenol reactor explosion in Italy, a dioxin-containing herbicide in Vietnam, and assorted laboratory accidents — have all experienced similar effects (WHO 1989; Boddington et al. 1990).

The International Agency for Research on Cancer (IARC) concludes that there is inadequate human data but sufficient animal data for 2,3,7,8-TCDD to be a possible human carcinogen (Boddington et al. 1990). In rats, carcinomas in liver, pharynx, skin, lung, and thyroid were documented at daily dosages of 0.01 to 0.1 µg 2,3,7,8-TCDD/kg body weight; comparable values for mice were 0.03 to 0.07 µg/kg body weight (Kociba and Schwetz 1982a, 1982b; Rappe 1984; WHO 1989; Andersen et al. 1993). No response occurred at continuous daily dose levels of 0.001 to 0.0014 µg/kg body weight in rats and 0.001 to 0.03 in mice. Carcinogenic or cocarcinogenic effects were also induced in rodents by 1,2,3,6,7,8-hexa-CDD and 1,2,3,7,8,9-hexa-CDD, but only at high dose levels (Rappe 1984). In rodents, 2,3,7,8-TCDD was a potent tumor promoter and inducer of the cytochrome P-450 1A family, especially in liver, lungs, and kidneys (Beebe et al. 1992; Andersen et al. 1993). In Seveso, Italy, a follow-up study of the human population between 1976 and 1986 showed an increased cancer incidence of soft tissue sarcoma, and hepatobiliary and hematologic neoplasms (Pesatori et al. 1992). Workers exposed to 2,3,7,8-TCDD or higher chlorinated dioxins had an increased risk for all neoplasms, especially soft tissue sarcomas, compared with workers from the same cohort exposed to phenoxy herbicides and chlorophenols but with minimal or no exposure to 2,3,7,8-TCDD and higher chlorinated dioxins (Kogevinas et al. 1997). In 1997, the IARC reclassified 2,3,7,8-TCDD as a Group 1 human carcinogen (USPHS 1998).

The greater toxic potential of certain PCDD isomers involves two properties: halogen atoms occupying at least three of the four lateral ring positions (2,3,7,8 positions) and at least one of the adjacent ring positions being nonhalogenated (Kociba and Schwetz 1982a, 1982b). Comparative toxicity data for selected PCDD isomers to the guinea pig (*Cavia* sp.) and the mouse (*Mus* sp.) confirmed this generalization and demonstrated significant interspecies differences in sensitivity (Table 18.5). Other PCDD isomers tested (2,8-di CDD, octa-CDD) were relatively nontoxic to mice and guinea pigs (NRCC 1981). In marmoset monkeys (*Callithrix jacchus*) given a subcutaneous injection of a mixture of PCDDs and PCDFs, only the 2,3,7,8-substituted congeners were detected at high concentrations in liver and fat, equivalent to 25% of the administered dose for 2,3,7,8-TCDD to 74% for 2,3,4,6,7,8-hexa-CDD (N. Neubert et al. 1990). The half-time persistence of 2,3,7,8-TCDD was about 8 weeks in hepatic tissues and 11 weeks in adipose tissue. Half-time persistence increased with increasing chlorination and, in the case of OCDD, there was no loss of accumulated OCDD after 28 weeks (N. Neubert et al. 1990; 1992).

Table 18.5 Acute Toxicities of Selected PCDD Isomers to the Guinea Pig and the Mouse

PCDD Isomer	Oral LD50 (g/kg body weight)	
	Guinea Pig	Mouse
2,8-di-CDD	>300,000	—
2,3,7-tri-CDD	29,444	>3000
2,3,7,8-TCDD	2	284
1,2,3,7,8-penta-CDD	3	338
1,2,4,7,8-penta-CDD	1125	>5000
1,2,3,4,7,8-hexa-CDD	73	825
1,2,3,6,7,8-hexa-CDD	70–100	1250
1,2,3,7,8,9-hexa-CDD	60–100	>1440
1,2,3,4,6,7,8-hepta-CDD	>600	—

Data from Kociba, R.J. and B.A. Schwetz. 1982b. A review of the toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) with a comparison to the toxicity of other chlorinated dioxin isomers. *Assoc. Food Drug Off. Quart. Bull.* 46:168-188.

Acute toxicity studies with 2,3,7,8-TCDD have shown marked differences — up to 8400 times — between the single oral LD50 dose for the guinea pig and the hamster (*Cricetus* sp.) (Table 18.6). The acute oral LD50 value of 0.6 µg/kg body weight for guinea pigs suggests that 2,3,7,8-TCDD

may be the most toxic compound ever tested on small laboratory animals. The unusual resistance of hamsters may be associated with its enhanced rate of metabolism and excretion of 2,3,7,8-TCDD relative to other PCDD isomers examined (Olson et al. 1980b; NRCC 1981; WHO 1989). Poisoning in mammals by 2,3,7,8-TCDD is typically characterized by loss of body weight, shrinkage of the thymus, and delayed lethality; large interspecies differences exist in lethal dosages and toxic effects (Vos 1978; Neal et al. 1979; Kociba and Schwetz 1982a, 1982b; Josephson 1983; Matsumura 1983; Kimbrough 1984; Seefeld et al. 1984; WHO 1989; Boddington et al. 1990). For example, 2,3,7,8-TCDD produces prominent chloracne-type skin lesions in man and monkeys, edema formation in birds, and severe liver damage in rats, mice, and rabbits.

Studies with mink (*Mustela vison*) indicate that route of administration, age, and sex of the animal influence 2,3,7,8-TCDD toxicity. Adult male minks given a single oral dose showed a dose-dependent decrease in food consumption and body weight, and a calculated LD₅₀ after 28 days of 4.2 µg/kg BW (Hochstein et al. 1988). Livers, spleens, and kidneys were discolored after a single oral dose of 2,3,7,8-TCDD and, at high sublethal doses, the brain, kidneys, heart, thyroid, and adrenals were enlarged (Hochstein et al. 1988). Newborn mink kits given 0.1 or 1.0 µg/kg BW daily by intraperitoneal injection for 12 consecutive days had mortality in excess of 50% in the high-dose group and growth rate reduction at 0.1 µg/kg BW daily (Aulerich et al. 1988). Adult minks fed diets containing 1.0 to 80.8 ng 2,3,7,8-TCDD equivalents/kg ration for 85 days (equivalent to total ingestion of 23 to 1019 ng 2,3,7,8-TCDD) prior to and throughout the reproductive period had impaired reproduction with reduced body weights and survival in a dose-dependent manner (Heaton et al. 1995). Females in the highest dose group whelped the fewest number of kits, all of which were stillborn or died with 24 h. For adult females, a value of 3.6 ng 2,3,7,8-TCDD equivalents/kg BW daily was determined for the lowest observable adverse effect level (Heaton et al. 1995). Adult females fed diets containing 0.001, 0.01, 0.1, 1, 10, or 100 µg 2,3,7,8-TCDD/kg ration for up to 125 days showed a dose-dependent decrease in food consumption and body weight (Hochstein et al. 1998). At day 125, 63% of the 1-µg/kg group, and 100% of the 10- and 100-µg/kg groups had died. Calculated LD₅₀ values were 4.8 µg 2,3,7,8-TCDD/kg diet at day 28 and 0.85 µg/kg diet at day 125, equivalent to 0.264 µg 2,3,7,8-TCDD/kg BW daily for the 28-day exposure and 0.047 µg/kg BW daily for the 125-day exposure (Hochstein et al. 1998).

Table 18.6 Acute Oral Toxicities of 2,3,7,8-TCDD to Mammals

Organism	LD ₅₀ (g/kg body weight [ppb])	Reference ^a
Guinea pig, <i>Cavia</i> sp.	0.6–2.0	1, 2, 5
In corn oil	2.5	3
In aqueous methyl cellulose	19.0	3
Mink, <i>Mustela vison</i> ^b	4.2	7, 8
Rat, <i>Rattus</i> sp.	22–45	2, 5
Rhesus monkey, <i>Macaca mulatta</i>	<70	4, 6
Dog, <i>Canis familiaris</i>	100–200	2, 5
Mouse, <i>Mus</i> sp.	114–284	2, 5
Rabbit, <i>Oryctolagus</i> sp.	115	4, 6
Hamster, <i>Cricetus</i> sp.	1157–5051	2, 5

^a 1, Harless et al. 1982; 2, Kociba and Schwetz 1982a; 3, Silkworth et al. 1982; 4, Olson et al. 1980a; 5, Kociba and Schwetz 1982b; 6, Olson et al. 1980b; 7, Hochstein et al. 1988; 8, Boddington et al. 1990.

^b Calculated LD₅₀ values for adult females fed 2,3,7,8-TCDD diets were 0.264 µg 2,3,7,8-TCDD/kg BW daily for a 28-day exposure period and 0.047 µg/kg BW daily for a 125-day exposure period (Hochstein et al. 1998).

Intraspecies differences in sensitivity to 2,3,7,8-TCDD — up to 14-fold — are reported among three strains of mice; no reasons were given to account for these differences. Oral LD₅₀ (30-day) values varied from 182 µg 2,3,7,8-TCDD per kg body weight in strain C57, the most sensitive

strain tested, to 296 for strain BD6, to 2570 for strain DBA (Chapman and Schiller 1985). All three strains of mice evidenced a 25 to 34% weight loss prior to death; however, there was no measurable decline in food consumption.

Atrophy of the thymus is a consistent finding in mammals poisoned by 2,3,7,8-TCDD, and suppression of thymus-dependent cellular immunity, particularly in young animals, may contribute to their death. Although the mechanisms of 2,3,7,8-TCDD toxicity are unclear, research areas include the role of thyroid hormones (Rozman et al. 1984); interference with plasma membrane functions (Matsumura 1983); alterations in ligand receptors (Vickers et al. 1985); the causes of hypophagia (reduced desire for food) and subsequent attempts to alter or reverse the pattern of weight loss (Courtney et al. 1978; Seefeld et al. 1984; Seefeld and Peterson 1984); and excretion kinetics of biotransformed metabolites (Koshakji et al. 1984).

Teratogenic and fetotoxic effects of 2,3,7,8-TCDD are well documented in several species of animals (Marless et al. 1982; Kociba and Schwetz 1982a, 1982b; Kimbrough 1984; Weber et al. 1985). Cleft palate in young mice was associated with daily dosages of 1.0 µg 2,3,7,8-TCDD per kg body weight in pregnant females (no-effect level at 0.1 µg/kg), and intestinal hemorrhage was found in sensitive strains of rats given daily dosages of 0.125 µg/kg body weight (no-effect level at 0.03 µg/kg) (Kociba and Schwetz 1982a, 1982b). Developing mammalian fetuses are especially sensitive to 2,3,7,8-TCDD, and maternal exposure results in increased frequencies of stillbirths. Among live births, exposure to 2,3,7,8-TCDD produces teratogenic effects such as cystic kidney, cleft palate, and spinal column deformities (Ramel 1978). Effects of 2,3,7,8-TCDD on reproduction are reported for rats (McNulty 1977; Murray et al. 1979; Kociba and Schwetz 1982a, 1982b; WHO 1989; Boddington et al. 1990) and monkeys (Ramel 1978; Barsotti et al. 1979; NRCC 1981; Kociba and Schwetz 1982a, 1982b; WHO 1989; R. Neubert et al. 1990). In a three-generation study with rats, daily dose levels of 0.01 µg 2,3,7,8-TCDD/kg body weight (equivalent to 120 to 290 ppt or ng/kg in the diet) produced decreased litter size at birth, increased the number of stillborns, and reduced the survival and growth of young in both the F1 and F2 generations. In rats, no adverse effect occurred at daily dosages of 0.001 µg/kg BW — equivalent to 12 to 30 ng/kg 2,3,7,8-TCDD in the diet — on growth, survival, reproduction, metabolism, or cancer incidence during exposure for three generations. Abortion and weight loss were reported in rhesus monkeys (*Macaca mulatta*) at dietary levels as low as 50 ppt 2,3,7,8-TCDD (about 0.0017 µg/kg body weight daily) after 7 to 29 months. However, comparatively high dosages (200 ppt in diets equivalent to 0.0095 µg/kg body weight daily) could be tolerated by monkeys for short periods (three times weekly for 3 weeks) with no adverse effects on reproduction. Higher dose levels for extended periods (i.e., 500 ppt in diets equivalent to about 0.011 µg/kg body weight daily for 9 months) caused death (63%) or, among survivors, abortion, chloracne, nail loss, scaly and dry skin, and progressive weakness. Most treated monkeys remained fairly alert to external stimuli until just prior to death. On removal from the 500-ppt 2,3,7,8-TCDD diet and transfer to an uncontaminated diet, a severely affected monkey became pregnant and gave birth to a well-developed infant after an uneventful gestation. This suggests that some 2,3,7,8-TCDD damage effects are not permanent.

Androgenic deficiency in male rats given a single oral dose of 15 µg 2,3,7,8-TCDD/kg BW was evident as early as 2 days posttreatment, with persistence up to 12 days. These deficiencies may account for male reproductive pathology and dysfunction in rats treated with overtly toxic doses of TCDD. Findings included depression in plasma testosterone concentrations, as well as decreased weight of seminal vesicles (by 68%), ventral prostate gland (by 48%), testes, and epididymis (Moore et al. 1985).

Accumulation of 2,3,7,8-TCDD is reported in the liver of rats during lifetime exposure to diets containing 0.022 µg 2,3,7,8-TCDD/kg (Newton and Snyder 1978), or when administered orally at 0.01 µg/kg body weight once a week for 45 weeks (Cantoni et al. 1981). Liver residues of rats fed 2,3,7,8-TCDD were 0.54 µg/kg, or about 25 times dietary levels; livers of rats dosed orally contained 1.05 µg/kg, or about 2.3 times the total dose received on a unit weight basis. Unlike toxicity, elimination rates of accumulated 2,3,7,8-TCDD were within a relatively narrow range. The estimated retention times of 2,3,7,8-TCDD in small laboratory mammals (rats, mice, guinea pigs, and

hamsters) extended from 10.8 to 30.2 days for 50% elimination and seemed to be little influenced by species, concentration administered, duration of dose, or route of administration (Blair 1973; Olson et al. 1980b; NRCC 1981; Koshakji et al. 1984). Half-time persistence in primates is usually lengthy: about 1 year in most species of monkeys and 5.8 years in humans (Boddington et al. 1990), although the half-time persistence of 2,3,7,8-TCDD in marmoset monkeys (*Callithrix jacchus*) is only 6 to 8 weeks (N. Neubert et al. 1992).

Histopathological effects have been reported in rabbits and horses poisoned by 2,3,7,8-TCDD. Rabbits surviving exposure to an industrial accident in Seveso, Italy, in which 2,3,7,8-TCDD was released, had edema, hemorrhagic tracheitis, pleural hemorrhage, and dystrophic lesions of hepatic tissue (Fanelli et al. 1980b). Horses from Missouri that died after waste oil contaminated with 2,3,7,8-TCDD was applied as a dust control agent in riding arenas had liver lesions, skin hyperkeratosis, gastric ulcers, and lung and kidney lesions (Kimbrough 1984). Since 2,3,7,8-TCDD is an extremely potent porphyrogenic agent, it is probable that these animals also exhibited porphyria, a condition characterized by fragility of the skin, photosensitivity, and accumulation of porphyrins in the liver (Cantoni et al. 1981).

Thermoregulatory function and Vitamin A metabolism in rodents are altered by 2,3,7,8-TCDD. Perinatal exposure to 2,3,7,8-TCDD alters thermoregulatory function in adult rats and hamsters, as judged by a reduced body temperature during sleep; however, normal behavioral regulation suggests that hypothalamic thermoregulatory centers are not permanently altered (Gordon and Miller 1998). For example, pregnant rats exposed on gestational day 15 to 1 µg 2,3,7,8-TCDD/kg BW by gavage produced male offspring with reduced body temperature during nocturnal phases; TCDD-treated rats given endotoxins had higher fevers than controls (Gordon and Miller 1998). Rats given a single oral dose of 10 µg 2,3,7,8-TCDD/kg BW had altered Vitamin A turnover and inhibited hepatic accumulation of dietary Vitamin A, and this is attributed to a combination of inhibited retinol esterification in hepatic cells, increased release of endogenous Vitamin A, and increased hepatic catabolism of retinoids (Hansberg et al. 1998).

Interaction effects of PCDDs with other polychlorinated compounds or mixtures are not extensively documented. For example, certain polychlorinated hexachlorobiphenyls (PCBs) have a low toxic potency to induce cleft palate deformities in mice (Birnbaum et al. 1985). However, mixtures of 2,3,7,8-TCDD and 2,3,4,5,3',4'-hexachlorobiphenyl resulted in a tenfold increase in incidence of cleft palate in mice. Thus, the toxicity of compounds such as 2,3,7,8-TCDD may be enhanced by compounds of relatively low acute toxicity, such as selected PCBs. Birnbaum et al. (1985) concluded that the widespread environmental occurrence of such combinations suggests a need for further evaluation of the mechanism of this interaction.

18.5 RECOMMENDATIONS

No criteria or standards have been promulgated for any of the 75 PCDD isomers by any regulatory agency for the protection of sensitive species of wildlife and aquatic organisms — except 2,3,7,8-TCDD (Table 18.7). Data are scarce or missing on the distribution and upper limits of background levels of PCDDs in natural resources (except 2,3,7,8-TCDD), on the identification of fish and wildlife resources potentially at risk, on the relative importance of PCDD sources, and on the comparative toxicities of various PCDDs to fish and wildlife, especially reproductive and immunosuppressive toxicities (NRCC 1981; Eisler 1986; WHO 1989; USEPA 1993). Multigeneration reproductive studies are recommended for the most widespread PCDDs, including 1,2,3,7,8-penta-CDD and -OCDD (WHO 1989). Improved analytical accuracy and standardized protocols are needed in PCDD sampling techniques to account for the organic content of sediments, dissolved organic content of water, and lipid content of samples (WHO 1989; Fletcher and McKay 1993). The stability and mobility of organic-associated PCDDs and their partitioning between substrates need clarification (Fletcher and McKay 1993).

Lethality of 2,3,7,8-TCDD to freshwater teleosts is documented at concentrations as low as 0.038 ng/L in water and 55 ng/kg FW in sac fry ([Table 18.7](#)). It is noteworthy that water column concentrations of 2,3,7,8-TCDD immediately downstream of 89% of 104 chlorine-bleaching pulp and paper mills exceeded 0.038 ng/L (USEPA 1990). More research is needed on dietary routes of PCDD exposure to aquatic organisms. A simple apparatus for loading 2,3,7,8-TCDD and other chemicals onto commercially available, pelletized fish food is now available (Fernandez et al. 1998). Recommended safe levels for aquatic life protection are 0.01 ng/L in water and 34 ng/kg FW tissue, and these confer a degree of protection — based on lethal action — of 1.6 to 3.8 times ([Table 18.7](#)). Values for 2,3,7,8-TCDD protection of freshwater aquatic life are in sharp contrast to those recommended for birds and mammals, which were usually derived from the highest concentration tested that produced no observed adverse effect, and on uncertainty factors of 100 or more ([Table 18.7](#)). Proposed 2,3,7,8-TCDD criteria for birds include <12 ng/kg FW ration, whole-body concentrations of <1 ng/kg BW in domestic chickens and <6 ng/kg BW in woodcocks, and <20 ng/kg FW in wood duck eggs ([Table 18.7](#)). Concentrations of 2,3,7,8-TCDD as high as 50 ng/kg in soil were not likely to produce adverse effects in woodcocks, nor does this soil concentration present a significant risk to humans who may consume game birds inhabiting these sites (Keenen et al. 1990). Proposed criteria for non-human mammals include <0.01 ng/kg BW daily from all sources and 10 to 30 ng/kg ration ([Table 18.7](#)). To protect human health, edible fish tissues should contain <25 ng/kg FW in most states and <10 ng/kg FW in New York; dairy cattle need to be grazed on soils containing <6 ng/kg FW; drinking water should contain <0.015 ng/L and ambient air <0.03 ng/m³. Food items containing more than 50 ng/kg FW are considered unsafe for human consumption, but fish fillets containing between 25 and 50 ng/kg of 2,3,7,8-TCDD may be eaten once weekly by occasional consumers of fish, and twice monthly for those who eat contaminated fish year-round ([Table 18.7](#)). It is not known at this time whether residues of 10 to 50 ng/kg (or higher) of 2,3,7,8-TCDD in fish flesh represent an unacceptable risk to the growth, survival, reproduction, metabolism, or behavior of the teleost, or to its predators; clearly, this is a high-priority research topic. Also, mechanisms of PCDD toxicity need to be established in mammals, birds, and poikilotherms to support extrapolation to humans and other species (WHO 1989; USEPA 1993).

More research is needed on factors that alter bioconcentration, toxicokinetics, and metabolism of PCDDs (Cooper 1989). For example, field bioconcentration factors (BCF) for 2,3,7,8-TCDD in fish from contaminated rivers in Maine ranged from 3000 to 106,000, and most exceeded the value of 5000 recommended by the U.S. Environmental Protection Agency. BCF values between 15,000 and 25,000 are now considered a reasonable estimate of the BCF for use in regulatory purposes in the state of Maine (Frakes et al. 1993). Mixtures of 2,3,7,8-TCDD and PCB 77 were slighter greater than additive in toxicity to rainbow trout (Newsted et al. 1995), indicating a need for more research on chemical interactions. Daily intakes of PCDDs vary substantially between and within species, and this needs to be incorporated into future models of risk assessment (Law and Gudaitis 1994). In humans, for example, daily intake of 2,3,7,8-TCDD — on a ng/kg BW basis — is 78 times higher in neonates than adults, and 2.3 times higher in children and 5.2 times higher in infants than adults (Boddington et al. 1990).

In the past, the major source of 2,3,7,8-TCDD in the environment was as a contaminant in phenoxy herbicides (such as 2,4,5-T; Silvex; 2,4-D; and Agent Orange), in hexachlorophene, and in other chlorophenol-type compounds. Concentrations of 2,3,7,8-TCDD in some of these products exceeded 60,000 µg/kg. This situation has been largely corrected by new manufacturing processes and by increasingly stringent federal regulations (NRCC 1981; Choudhary et al. 1983; Stolzenburg and Sullivan 1983; NIOSH 1984; Rappe 1984). For example, the 2,3,7,8-TCDD level in 2,4,5-T has decreased from 60,000 µg/kg in 1957 to 2000 µg/kg in 1965 as a result of new manufacturing processes, and it was limited to 500 µg/kg in 1970 by the Canadian federal government. In 1970, the U.S. Department of Defense halted the spraying of Agent Orange. In 1972, the U.S. Food and Drug Administration banned the use of hexachlorophene in nonprescription soaps and deodorants.

In 1978, 7 of 14 major producers of 2,4,5-T no longer manufactured this product, and the remainder claimed that their products contained less than 100 µg/kg of 2,3,7,8-TCDD. In 1979, production of 2,4,5-T and Silvex ceased in the United States, although stockpiles of both are still being distributed and permitted for use on rice fields, sugarcane fields, orchards, fence rows, vacant lots, and lumber yards. In 1982, the USEPA required some industries to certify that chlorophenol-type compounds would no longer be used as slime control agents. On October 18, 1983, the USEPA published its intent to cancel the registration of pesticide products containing 2,4,5-T and Silvex, and to prohibit the transfer, distribution, sale, or importation of any unregistered product containing 2,4,5-T, Silvex, or their derivatives (NIOSH 1984). Continued monitoring is recommended of food, air, and sediments, including time trends and determinations of isomer patterns (WHO 1989).

Burning or heating of commercial and purified chlorophenates, and pyrolysis of polychlorinated biphenyls contaminated with trichlorobenzenes can result in the production of 2,3,7,8-TCDD and other PCDDs (NIOSH 1984). These sources, together with discharges from various municipal and industrial incinerators of chlorinated compounds, probably constitute the largest source of PCDDs in the environment today. In 1983, the U.S. Environmental Protection Agency proposed to monitor 2,3,7,8-TCDD in the environment (Stolzenburg and Sullivan 1983; WHO 1989). Specific goals of the monitoring program included:

- Determination of 2,3,7,8-TCDD concentrations in soils and biota, with emphasis on geographic areas where PCDDs may have been manufactured, used, or stored — and where concentrations may be in excess of 1000 ng/kg
- Monitoring of industrial and municipal incinerators for 2,3,7,8-TCDD emissions
- Establishment of background levels for PCDDs in areas where these compounds are not expected to occur in high levels.

Information is also needed on the toxicological interactions of groups of polychlorinated chemicals (such as certain biphenyls, biphenylenes, and dibenzofurans) known to be isosteric with 2,3,7,8-TCDD and that frequently coexist with 2,3,7,8-TCDD in environmental samples. Acquisition of these data should provide the basis of a risk assessment analysis for dioxin and fishery and wildlife resources.

Table 18.7 Proposed 2,3,7,8-TCDD Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective 2,3,7,8-TCDD Concentration	Reference ^a
AQUATIC ORGANISMS, FRESHWATER		
Water		
Acceptable	<0.01 ng/L (ppt) ^b	1
Safe	0.01 ng/L ^c	2
No observed adverse effects on rainbow trout, <i>Oncorhynchus mykiss</i> , juveniles	<0.038 ng/L	3
Safe	<0.038 ng/L	7
Unacceptable		
Adverse effects on growth, survival and swimming of rainbow trout juveniles	0.038 ng/L	3
Adverse effects expected in sensitive species	0.1–1.0 ng/L and higher	1, 4, 24
Death observed in sensitive species several weeks after exposure for 6 days	10.0 ng/L	2
Death expected in sensitive species shortly after exposure	>1000 ng/L	2
Tissue residues		
Lake trout, <i>Salvelinus namaycush</i>		
Egg and sac fry		
No effect on survival	34 ng/kg fresh weight (FW)	6
Some deaths	55 ng/kg FW	6
50% dead by swimup	65 ng/kg FW	6, 23, 25

Table 18.7 (continued) Proposed 2,3,7,8-TCDD Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective 2,3,7,8-TCDD Concentration	Reference ^a
Whole body		
Reproduction inhibited	78 ng/kg FW	25
Rainbow trout; adverse effects expected; egg	More than 0.4 µg/kg FW	23
BIRDS		
Diet		
Safe	10–12 ng/kg FW ration	8, 9
Adverse effects		
Domestic chicken, <i>Gallus</i> sp.	Equivalent to about 1.0 ng/kg body weight (BW) daily	10, 11
Woodcock, <i>Philohela minor</i> ; adults; Maine	Daily intake of >6 ng/kg BW, and half-time persistence of 7.2 days	12
Soils, Maine		
No adverse effects expected in woodcocks after consuming earthworms and insects from 2,3,7,8-TCDD-contaminated soils	<50 ng/kg FW soil	12
Adverse effects observed in woodcocks	>27–250 ng/kg FW soil	12
Tissue residues		
Wood duck, <i>Aix sponsa</i> ; eggs; adverse effects on survival	>20–50 ng/kg FW	13
MAMMALS		
Diet		
No effect on carcinogenicity or reproduction in laboratory white rat, <i>Rattus</i> sp.	Equivalent to <1.0 ng/kg BW daily	5
Safe; laboratory white rat; exposure for 3 generations	12–30 ng/kg FW ration, equivalent to about 1.0 ng/kg BW daily	9
Safe; mammalian wildlife	10–12 ng/kg FW ration	8, 9
Acceptable; daily intake; lifetime exposure	<0.01 ng/kg BW ^d	5
Unacceptable, monkeys	>50 ng/kg FW ration equivalent to >1.7 ng/kg BW daily	10, 14, 15
Subcutaneous injection; marmoset monkey, <i>Callithrix jacchus</i> ; adverse sublethal effects	Persistent altered blood chemistry after single injection of 10 ng/kg BW	16, 17
HUMAN HEALTH		
Daily intake, minimum risk level		
Acute	0.0002 µg	26
Intermediate	0.00002 µg	26
Chronic	0.000001 µg	26
Diet, acceptable		
Fish muscle		
New York	<10 ng/kg FW fillet	21
Canada	<20 ng/kg FW fillet	5, 21
Most U.S. states	<25 ng/kg FW fillet	2, 18, 20, 22
Diet, limited		
Fish muscle; may be eaten once weekly by occasional consumers of fish and up to twice monthly for those who eat contaminated fish year-round	25–50 ng/kg FW fillet	18, 22
Diet, unacceptable	>50 ng/kg FW ration	2, 20, 22, 26
Soils, acceptable		
Residential areas	<1000 ng/kg FW	20
Of grazing dairy cattle	<6 ng/kg FW	20
Cancer risk		
Lifetime cancer risk increases from drinking water and eating fish from 2,3,7,8-TCDD-contaminated waters		
Cancer risk of 1 in a million	0.000013 ng/L water	20

Table 18.7 (continued) Proposed 2,3,7,8-TCDD Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective 2,3,7,8-TCDD Concentration	Reference ^a
Cancer risk of 1 in 100,000	1.0 ng/L water	20
Drinking water, acceptable	<0.01–<0.02 ng/L	5, 26
Ambient water, acceptable	<0.01 ng/L	5
Ambient air, acceptable	<0.03 ng/m ³	5
Total daily intake from all sources; maximum allowed	<160 ng/kg BW	18
Total daily intake from all sources; recommended	<61–<100 ng/kg BW	5, 18, 19
Total daily intake from all sources; lifetime exposure; acceptable	<0.01 ng/kg BW ^d	5

^a 1, Miller et al. 1979; 2, USEPA 1984; 3, Mehrle et al. 1988; 4, Helder 1980; 5, Boddington et al. 1990; 6, Walker et al. 1991; 7, USEPA 1990; 8, McNulty 1977; 9, Murray et al. 1979; 10, NRCC 1981; 11, Gilbertson 1983; 12, Keenen et al. 1990; 13, White and Seginak 1994; 14, Ramel 1978; 15, Barsotti et al. 1979; 16, R. Neubert et al. 1990; 17, N. Neubert et al. 1990; 18, Boyer et al. 1991; 19, Law and Gudaitis 1994; 20, USEPA 1987; 21, Kleopfer and Zirscky 1983; 22, Stolzenburg and Sullivan 1983; 23, Sijm and Opperhuizen 1996; 24, Cook et al. 1993; 25, Tietge et al. 1998; 26, USPHS 1998.

^b 0.01 ng/L was the highest 2,3,7,8-TCDD concentration tested that had no measurable adverse effect on freshwater teleosts.

^c Based on bioconcentration factor of 5000.

^d Based on no-observable-adverse effect concentration of 1.0 ng/kg BW daily in a three-generation rat study and an uncertainty factor of 100.

18.6 SUMMARY

Polychlorinated dibenzo-*para*-dioxins (PCDDs) are present as trace impurities in some manufactured chemicals and industrial wastes. The chemical and environmental stability of PCDDs and their tendency to accumulate in fat have resulted in their detection within many ecosystems. In general, wherever high levels of PCDDs have been detected, the source has been a hazardous waste dump, an industrial discharge, or an application of PCDD-contaminated herbicide. There are 75 PCDD isomers; some are extremely toxic, while others are believed to be relatively innocuous. The most toxic and most extensively studied PCDD isomer is 2,3,7,8-tetrachlorodibenzo-*para*-dioxin (2,3,7,8-TCDD). In the United States and elsewhere, accidental contamination of the environment by 2,3,7,8-TCDD has resulted in deaths of many species of wildlife and domestic animals. High residues of 2,3,7,8-TCDD in fish (i.e., more than 50 ppt wet weight), have resulted in closing rivers to fishing. In the most seriously affected areas, hospitalization and permanent evacuation of humans have been necessary. Laboratory studies with birds, mammals, aquatic organisms, and other species have demonstrated that exposure to 2,3,7,8-TCDD can result in acute and delayed mortality as well as carcinogenic, teratogenic, mutagenic, histopathologic, immunotoxic, and reproductive effects. These effects varied greatly among species. No regulations governing PCDD contamination exist at present to protect sensitive species of wildlife and aquatic organisms. Data available suggest that 2,3,7,8-TCDD concentrations in water should not exceed 0.01 ppt to protect aquatic life, or 10 to 12 ppt in food items of birds and other wildlife. Additional data are needed in several areas:

- Concentrations of PCDDs in natural systems
- Identification of fish and wildlife populations at risk
- Relative importance of PCDD sources
- Toxicological effects of various PCDDs to aquatic biota and wildlife, especially reproductive and immunosuppressive effects
- Toxic and other interaction effects of PCDDs with other groups of polychlorinated chemicals having similar structure and properties, such as biphenyls, dibenzofurans, and biphenylenes.

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CHAPTER 19

Famphur

19.1 INTRODUCTION

Famphur (phosphorothioic acid, *O*-[4-[(dimethylamino)sulfonyl], phenyl] *O,O*-dimethyl ester) also known as Warbex, is a systemic organophosphorus insecticide found effective against lice, grubs, flies, and gastrointestinal nematodes of ruminants. Introduced commercially in 1961, the compound is especially effective against cattle grubs (*Hypoderma* spp.) when fed in the diet, injected subcutaneously or intramuscularly, or applied as a pour-on and oral drench treatment (Gatterdam et al. 1967; Kaemmerer and Buntenkotter 1973; Black et al. 1979; Felton et al. 1981; Gallo and Lawryk 1991; Eisler 1994).

Many dead birds, including robins, hawks, and magpies were found after cattle were treated with pour-on applications of famphur (Henny et al. 1985; Smith 1987). The black-billed magpie (*Pica pica*) was especially sensitive; ranchers reported observations of magpies dying after famphur use on cattle as early as 1973 (Henny et al. 1985). Dead magpies usually had famphur in the gizzard contents and severely depressed brain cholinesterase activity — a characteristic of organophosphorus poisoning. Populations of the black-billed magpie in western states declined between 1968 and 1979, which coincides with widespread use of famphur in that region; however, factors other than famphur may have caused the decline (Henny et al. 1985).

19.2 USES

The cholinesterase-inhibiting and intoxicating properties of organophosphorus compounds have been known since these products were first synthesized about 60 years ago (Randell and Bradley 1980). During World War II, the more toxic organophosphorus compounds — such as soman, tabun, and sarin — were stockpiled for use as potential chemical warfare agents. More than 50,000 organophosphorus compounds have been synthesized and screened for possible insecticidal and antihelminthic activity, and several dozen, including famphur, are available commercially (Randell and Bradley 1980). During the 1970s, most organochlorine insecticides were removed from common use in North America, Europe, and most developed countries, and the removal increased reliance on carbamate and organophosphorus compounds, the two major classes of cholinesterase-inhibiting pesticides (Mineau 1991). The relative lack of target specificity of these compounds and their high acute toxicity to many nontarget organisms were ignored in favor of their short-term environmental persistence and lack of accumulation in organisms. The anticholinesterase insecticides now account for the majority of globally registered insecticides (Mineau 1991).

Famphur is not now applied to forests or crops but is used almost exclusively as a veterinary chemical (Smith 1987). A single treatment controls cattle grubs and reduces cattle-lice infestations

(American Cyanamid Company 1984). Famphur is especially effective against maggots of the botfly and warble fly (*Hypoderma* spp.) and of other oestrid dipterous flies (Seel 1985). Eggs from this group of insects are laid on the feet and legs of cattle and other mammals and licked off by the host and hatch in the mouth or esophagus. The resultant larvae burrow through the tissues to the skin of the animal's back where they live until ready to pupate and cause warbles or swellings (Seel 1985; Tarry 1986). When applied carelessly, famphur and other systemic insecticides are highly toxic and frequently produce acute poisonings in ruminants (Ballantyne and Marrs 1992). Famphur is not now registered or regulated by the U.S. Environmental Protection Agency.

Cholinesterase-inhibiting agents such as famphur vary widely in their effectiveness in controlling target pests and depend on the route of administration, dose rate, formulation, and timing and frequency of applications (Mineau 1991). Famphur can be administered to livestock by intramuscular injection, orally in the diet, as a dermal pour-on, or as a bolus. Intramuscular injections of a 35% famphur concentrate are usually given in the gluteal muscle (Loomis and Schock 1978). When fed in the diet, famphur is formulated as a 33.3% liquid feed premix (Pasarela et al. 1967; Smith 1987). The topical use of famphur as a systemic insecticide was recommended in 1970. As a pour-on over part of the backline of cattle at dosages between 15 and 35 mg/kg body weight (BW), 12.5 to 13.2% w/v famphur applied in the autumn controls warbles before they develop into grubs the following year (Henny et al. 1985) and controls various species of lice (Annand et al. 1976). When used as a pour-on for cattle-tick control, famphur may be transferred from treated cattle to untreated animals (Annand et al. 1976), presumably through body contact. The solvent used in preparing dermal formulations of famphur significantly affects absorption hazards. In the case of the laboratory white rat (*Rattus* spp.), corn oil proved to be the least hazardous solvent and acetone the most hazardous; benzene was intermediate (Durham 1967). Famphur can also be administered in a rumen bolus as a systemic insecticide against ticks in cattle. Boluses have been designed to release 200 mg famphur/bolus daily over a 65- to 75-day postingestion period; actual release rates range from 207 to 308 mg daily (Hair et al. 1979).

Technical information by the American Cyanamid Company (1984) lists five precautions and warnings for the use of famphur.

1. Famphur is "Toxic to fish, birds, and other wildlife. Keep out of lakes, ponds, and streams. Do not apply to areas where run-off occurs. Do not contaminate water by cleaning of equipment or disposal of wastes."
2. After use, all containers should be drained and rinsed several times with a solution of water, detergent, and lye ("bury rinse solution deeply in an isolated location with 18 inches [7 cm] of cover"); the empty container should be punctured and crushed to prevent reuse.
3. Famphur should not be used in combination with any compound having cholinesterase-inhibiting activity, either simultaneously or within a few days before or after treatment.
4. Famphur use on livestock is contraindicated for less than 3-month-old calves; animals stressed from castration, dehorning, or overexcitement; and sick or convalescent animals. Brahman and Brahman crossbreeds are less tolerant of cholinesterase-inhibiting insecticides than other breeds, and Brahman bulls are especially sensitive and should not be treated with famphur. Cattle should not be slaughtered for at least 35 days after treatment with famphur.
5. For humans, famphur is considered harmful or fatal if swallowed or absorbed through the skin, especially by children. If poisoning should occur, physicians are advised that atropine is antidotal and that pralidoxime chloride may be effective as an adjunct to atropine. Pour-on formulations are flammable, and users should keep them away from heat, sparks, and open flames including hot branding irons and cautery dehorning devices (American Cyanamid Company 1984).

19.3 CHEMISTRY AND METABOLISM

Some physical and chemical properties of famphur are listed in [Table 19.1](#). Gas chromatography is used to measure famphur and its oxygen analog famoxon in bovine milk, blood, and edible

tissues; detection limits are 0.005 mg/L milk and <0.01 mg/kg tissue (Pasarela et al. 1967; Annand et al. 1976). The main degradation routes of famphur in mammals occur through hydrolysis of the P-O phenyl, P-O methyl, and N-methyl bonds; oxidative desulfuration and N-demethylation take place to a small extent (Figure 19.1) (Kaemmerer and Buntenkotter 1973; Eto 1974). In the metabolic scheme for famphur in mammals (Figure 19.1), only famphur and its oxygen analog, famoxon, were of toxicological significance, as judged by acute oral toxicity in mice (Gatterdam et al. 1967). In studies with mice, acute oral LD₅₀ values in mg/kg BW were 27 for famphur; 18 for famoxon; 2270 for *O*-desmethylfamphur; 860 for *O,N*-bisdesmethylfamphur; 2290 for *p*-(*N,N*-dimethylsulfamoyl)phenol; 2500 for *p*-(*N*-methylsulfamoyl)phenol; 6400 for *p*-hydroxybenzenesulfonic acid; and >5000 for *p*-(*N,N*-dimethylsulfamoyl)phenyl glucuronide.

Table 19.1 Chemical and Other Properties of Famphur

Variable	Datum
Chemical names	Phosphorothioic acid <i>O</i> -[4-[(dimethylamino) sulfonyl], phenyl] <i>O,O</i> -dimethyl ester; Phosphorothioic acid, <i>O</i> , <i>O</i> -dimethyl-, <i>O</i> -ester with <i>p</i> -hydroxy- <i>N,N</i> -dimethylbenzene sulfonamide; Phosphorothioic acid, <i>O</i> , <i>O</i> -dimethyl <i>O</i> - <i>p</i> -(dimethylsulfamoyl) phenyl ester; <i>O</i> -Dimethyl hydrogen phosphorothioate, <i>O</i> -ester with <i>p</i> -hydroxy- <i>N,N</i> -dimethylbenzenesulfonamide; <i>O</i> -[4-1 (Dimethylamino) sulfonyl] phenyl phosphorothioic acid <i>O</i> , <i>O</i> -dimethyl ester; <i>O</i> , <i>O</i> -Dimethyl <i>O</i> , <i>p</i> -(<i>N,N</i> -dimethylsulfamoyl) phenyl phosphorothioate; <i>O</i> , <i>p</i> -(Dimethylsulfamoyl)phenyl <i>O</i> , <i>O</i> -dimethyl phosphorothioate; <i>p</i> -(Dimethylsulfamoyl)phenyl dimethyl phosphorothioate; <i>O</i> , <i>O</i> -dimethyl <i>O</i> -[<i>p</i> -(dimethylsulfamoyl)-phenyl] phosphorothioate; Dimethyl <i>p</i> -(dimethylsulfamoyl) phenyl phosphorothioate; <i>O</i> , <i>O</i> -dimethyl- <i>O</i> , <i>p</i> -(dimethylsulfamoyl) phenyl phosphorothionate
Alternate names	AC 38023, American Cyanamid 38023, Bo-Ana, CL 38023, Cyflee, Dovip, ENT 25644, Famaphos, Famfos, Famophos, Famphos, Fanfos, Warbex, 38023
Primary use	Systemic livestock insecticide
CAS Number	52-85-7
Empirical formula	C ₁₀ H ₁₆ NO ₅ PS ₂
Molecular weight	325.36
Melting point, crystals vs. powder	52.5–53.5°C vs. 55°C
Solubility	
Chlorinated hydrocarbons	Highly soluble
Water	~100 mg/L
Polar solvents	Slightly soluble
Aliphatic hydrocarbons	Insoluble

^a O'Brien et al. 1965; Gatterdam et al. 1967; Pasarela et al. 1967; Tucker and Crabtree 1970; Schafer 1972; Kaemmerer and Buntenkotter 1973; Eto 1974; Black et al. 1979; Ryan and McLeod 1979; Hudson et al. 1984; Hill and Camardese 1986; Smith 1987; Gallo and Lawryk 1991.

Famphur residues of 1 to 3 mg/kg fresh weight (FW) are common in cattle tissues after normal pour-on applications of the chemical (Annand et al. 1976). The half-time persistence of famphur in subcutaneous fat of cattle after a single pour-on application was 0.9 days and was independent of dose within the range of 25 to 150 mg/kg BW or initial tissue residues between 1.8 and 12.3 mg/kg FW; fat residues were <0.08 mg/kg FW 5 days after treatment and <0.01 mg/kg FW after 11 days. These observations suggest that famphur tissue residues are near or below detection levels within 1 week after treatment, even with gross misuse of the chemical (Annand et al. 1976). However, because famphur persists on cattle hair for >90 days at concentrations >1000 mg/kg, this has serious implications for local populations of birds (Henny et al. 1985).

Famphur and other organophosphorus compounds are metabolized and excreted with greater efficiency by mammals than the target pests before these compounds can bind to and ultimately inhibit the cholinesterase enzyme (Randell and Bradley 1980). Mice, for example, degrade famphur rapidly. Less than 1 h after an intraperitoneal injection of 1 mg famphur/kg BW, only 8.34% of

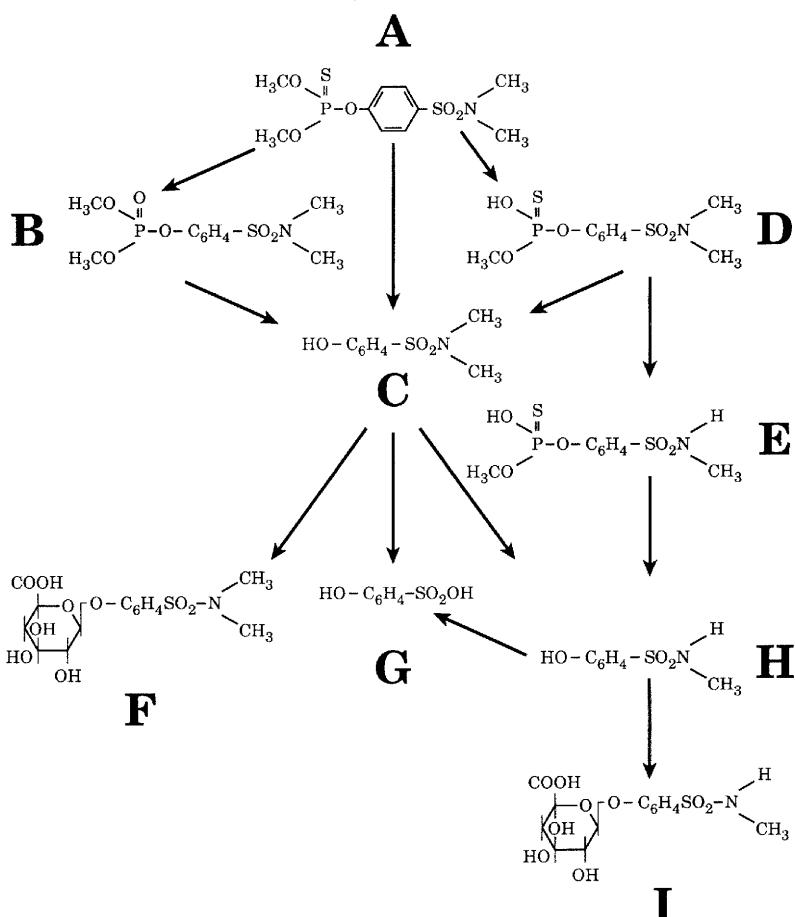


Figure 19.1 Metabolic scheme for famphur in mammals. (Adapted from Gatterdam, P.E., L.A. Wozniak, M.W. Bullock, G.L. Parks, and J.E. Boyd. 1967. Absorption, metabolism, and excretion of tritium-labeled famphur in the sheep and calf. *Jour. Agricul. Food Chem.* 15:845-853.) Major metabolic routes are indicated by an asterisk (*). **A**, famphur; **B**, famoxon; **C**, *p*-(*N,N*-dimethylsulfamoyl)phenol; **D**, *O*-desmethylfamphur; **E**, *O,N*-bisdesmethylfamphur; **F**, *p*-(*N,N*-dimethylsulfamoyl)phenyl glucuronide; **G**, *p*-hydroxybenzene sulfonic acid; **H**, *p*-(*N*-methylsulfamoyl)phenol; and **I**, *p*-(*N*-methylsulfamoyl)phenyl glucuronide. According to this scheme, famphur (**A**) initially undergoes oxidation at the P=S bond to yield famoxon (**B**), hydrolysis at the P-O-phenyl bond to yield the transitory *p*-(*N,N*-dimethylsulfamoyl)phenol (**C**)*, or hydrolysis at one of the P-O-methyl bonds to yield *O*-desmethylfamphur (**D**)*. *p*, *N,N*-dimethylsulfamoylphenol (**C**) may also arise by hydrolysis of famoxon (**B**) or *O*-desmethylfamphur (**D**)*. *p*-(*N,N*-dimethylsulfamoyl)phenol (**C**) is immediately conjugated to form *p*-(*N,N*-dimethylsulfamoyl)phenyl glucuronide (**F**)* or transformed to *p*-hydroxybenzene sulfonic acid (**G**) or *p*-(*N*-methylsulfamoyl)phenol (**H**). *O*-desmethylfamphur (**D**) can also give rise to *O,N*-bisdesmethylfamphur (**E**)* by removal of one of the methyl groups of the sulfonamide moiety. *O,N*-bisdesmethylfamphur (**E**) is hydrolyzed to the corresponding transitory *p*-(*N*-methylsulfamoylphenol) (**H**)* which is immediately conjugated to yield the corresponding glucuronide, *p*-(*N*-methylsulfamoyl)phenyl glucuronide (**I**)*.

the original administered dose remained in the mouse: 8.11% as the parent famphur, 0.22% as famoxon, and 0.01% as desmethylfamphur (Kaemmerer and Buntenkotter 1973). Famphur's biocidal properties are associated with its ability to inhibit cholinesterase activity, blocking synapses at the neuromuscular junction. Useful reviews of ecological and toxicological properties of cholinesterase-inhibiting agents in the environment — including organophosphorus insecticides — are given by Gallo and Lawryk (1991), Mineau (1991), and Ballantyne and Marrs (1992). Brain cholinesterase inhibition is often used to diagnose death of wildlife after exposure to famphur and

other organophosphorus insecticides (Mineau 1991). It is emphasized that the type and number of cholinesterase compounds and cholinesterase activities vary widely between species and tissues, and activities are further modified by metabolic factors, age, genotype, circadian rhythms, sex, reproductive status, nutritional status, ambient temperature, and disease (Mineau 1991).

19.4 LETHAL AND SUBLETHAL EFFECTS

19.4.1 General

Famphur controls many species of pestiferous insects that afflict poultry and livestock. The LD₅₀ values for target insects ranged from 2.4 to 4.1 mg/kg BW from a dermal route and 8.0 to 11.8 mg/kg BW from abdominal injection. Toxicity of famphur is often associated with differential degradation and cholinesterase sensitivity among various species of target pests. Famoxon is more effective than famphur in producing cholinesterase inhibition and death, and this confirms the generalization that the corresponding oxons are the more potent anticholinesterase agents.

No published data were available on famphur toxicity to aquatic life. Other data, however, suggest that acute famphur toxicity to fishes may be comparable to that of other phosphorothioate insecticides. Among birds, sensitive species had reduced survival after single oral doses of 1.8 to 3.0 mg famphur/kg BW or when fed diets containing 35 to 49 mg famphur/kg ration. Daily oral doses as low as 0.3 mg famphur/kg BW caused depressed cholinesterase activity in the brain and in plasma. Secondary poisoning of eagles and hawks foraging on famphur-killed vertebrates and tertiary poisoning of a great horned owl (*Bubo virginianus*) feeding on a famphur-poisoned hawk are documented. Famphur has also been used illegally to kill birds — including migratory waterfowl and other federally protected species — thought to be depredating crops. Famphur-induced mortality in mammals was documented at concentrations as low as 11.6 mg/kg BW in intraperitoneal injection (mouse), 27 mg/kg BW in oral exposure (mouse), >33.3 mg/kg BW in intramuscular injection (Brahman cattle), and 400 mg/kg BW in dermal application (rat). In reindeer, altered blood chemistry was evident 1 year after famphur exposure. Famphur is metabolized rapidly by mammals; residues in animal tissues and milk — regardless of mode of administration, length of exposure, or dose — were usually not detectable within 4 days of final exposure.

19.4.2 Terrestrial Invertebrates

Famphur controls many species of pestiferous insects that afflict poultry and livestock, especially warble flies (*Hypoderma* spp.). Famphur is one of the most toxic compounds for the control of adults and late instars of the lesser mealworm (*Alphitobius diaperinus*), the most abundant beetle inhabiting poultry litter and manure (Vaughan and Turner 1984). *Alphitobius* can transmit several diseases to poultry, including avian leukosis — one of the most costly diseases for the poultry industry. By tunneling, *Alphitobius* can destroy polyurethane and polystyrene panels adjacent to manure. Famphur also controls the lesser mealworm in nests of birds and in bat roosts (Vaughan and Turner 1984). The northern fowl mite (*Ornithonyssus sylviarum*) is the most important ectoparasite of commercial breeders and laying hens in the United States. However, attempts to control northern fowl mite with famphur were ineffective regardless of tested mode of administration (De Vaney and Ivie 1980).

Cattle lice (*Haematopinus* spp.) were controlled when the equivalent of 2.5 mg famphur/kg BW in diets was fed to cattle for at least 30 days (Ivey et al. 1976); 40.5 mg/kg BW were applied as a topical pour-on (Randell and Bradley 1980). Famphur was used in 1971 to control cattle lice at pour-on applications equivalent to 15 to 35 mg/kg BW (Annand et al. 1976). Pour-on treatments of Australian yearling heifers were especially effective in controlling the long-nosed sucking louse (*Linognathus vituli*) and the short-nosed sucking louse (*Haematopinus eurysternus*); untreated heifers grew more slowly than famphur-treated heifers (Bailey et al. 1984). Larvae of the hornfly

(*Haematobia irritans*) were controlled in manure of cattle fed famphur at 2.5 to 5.0 mg/kg BW daily (Ivey et al. 1976). Manure of treated cows contained low concentrations of famphur (as much as 0.14 mg/kg FW) 1 day after diet cessation, but residues were nondetectable thereafter (Henny et al. 1985).

In Alaska, reindeer (*Rangifer tarandus*) infested with reindeer warble fly (*Oedemagena tarandi*) produced hides of little value and low quality meat. Reindeer warble flies were not controlled by pour-on applications of famphur because the product was unable to penetrate the hair coat of reindeer; however, intramuscular injections were effective (Ivey et al. 1976). In Norway, Sweden, and Finland, famphur was the most promising control agent against reindeer warble fly and reindeer nostril fly (*Cephenomyis trompe*) — two parasites that together caused a 15 to 20% annual loss of total yield in reindeer husbandry (Niemenen et al. 1980).

Famphur was not very effective in the control of ticks. The tropical horse tick (*Anocentor nitens*) is a species of serious concern to horse breeders and raisers in Florida mainly because it transmits *Babesia caballi*, the causative agent of equine piroplasmosis. A secondary concern is that heavy tick infestations may cause injury to the ears of the horse (Gladney et al. 1972). Data were unavailable on famphur control of ticks in horses; however, famphur was 99.9 to 100% effective in controlling *A. nitens* in Hereford steers and heifers when fed in the diet at 5 mg/kg BW for 14 to 21 days. Famphur at 2.5 mg/kg BW in cattle diets for 7 days was only partially effective (39 to 87.5%) in controlling horse ticks (Gladney et al. 1972). Famphur — despite multiple treatments — was not effective in controlling cattle ticks (*Haemaphysalis longicornis*) when used as a pour-on at recommended application rates in weaned Hereford calves (Heath et al. 1980).

Results of selected studies of famphur and insects indicate several trends:

- Males are more sensitive than females
- The oxygen analog, famoxon, is more toxic than the parent chemical
- Dermal LD₅₀ values range from 2.4 to 4.1 mg/kg BW
- Abdominal injection LD₅₀ values range from 8.0 to 11.8 mg/kg BW
- Metabolic degradation rates vary widely between species ([Table 19.2](#)).

Famoxon is about 100 times more effective than famphur in controlling houseflies (*Musca* spp.), which confirms the generalization that the corresponding oxons are the most effective anticholinesterase agents and are, in fact, the actual toxicants (O'Brien et al. 1965).

Differences in toxicity of organophosphorus compounds among species is often associated with differential degradation rates, pathways, and metabolites. Although injections of famphur were equally toxic to mice (*Mus* sp.), the American cockroach (*Periplaneta americana*), and the milkweed bug (*Oncopeltus fasciatus*), famphur was rapidly degraded by mice (91.7% degraded within 1 h after injection) and cockroaches (81.5% in 1 h); however, milkweed bug degraded only 15.4% during a similar period (O'Brien et al. 1965). The variations in degradation rate among mice and cockroaches were relatively small, about 1.9-fold. Despite the great similarity in famphur toxicity to mice and cockroaches, net famoxon production — like famphur persistence — was very low in the mouse but 10 times higher in the milkweed bug. The cholinesterase activity in the milkweed bug was 32 times more resistant to inhibition by famoxon than either mouse or cockroach cholinesterase, and this could account for the comparatively slow breakdown of famphur by the milkweed bug (O'Brien et al. 1965).

There is a correlation among cholinesterase activity depression in rabbit blood, depression of cholinesterase activity in ectoparasites feeding on the blood of the host, and mortality of ectoparasites (Smith and Goulding 1970). In one case, rabbits (*Oryctolagus* sp.) parasitized by the yellow fever mosquito (*Aedes aegypti*) and Rocky mountain wood tick (*Dermacentor andersoni*) were treated with 5 to 50 mg of famphur/kg BW administered orally, subcutaneously, or intravenously. Regardless of dose or route of administration, tick and mosquito mortality was related to cholinesterase activity levels in rabbit plasma and erythrocytes. Some ectoparasite deaths were noted when

cholinesterase levels in rabbits were depressed 32%; ectoparasite mortality increased to 90% at 33% depression and to 100% at 68% cholinesterase inhibition. In general, wood ticks and mosquitoes reflected cholinesterase activity levels of the host rabbit. Surviving female ticks that fed on dosed hosts laid no eggs during a 32-day postremoval observation period. Mosquitoes that had fed on famphur-dosed hosts were more susceptible to cold than those that fed on control hosts (Smith and Goulding 1970).

Table 19.2 Famphur Effects on Selected Terrestrial Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
LESSER MEALWORM, <i>Alphitobius diaperinus</i>, topically applied		
3.44 mg/kg body weight (BW), 95% confidence interval (CI) 2.4–3.8 mg/kg BW	LD50 (24 h), adults	1
3.61 (95% CI of 3.32–4.08) mg/kg BW	LD50 (24 h), late instars	1
MILKWEED BUG, <i>Oncopeltus fasciatus</i>		
Abdominal injection, various doses		
Famoxon, 3.0 mg/kg BW	LD50	2
Famphur, 8.0 mg/kg BW	LD50	2
Single abdominal injection of 1 mg famphur/kg BW; whole-body residues of famphur, famoxon, and N-desmethylfamphur measured 1 h after injection	Of total amount injected, 84.6% remained after 1 h: 79.4% famphur, 2.2% famoxon, and 3.1% N-desmethylfamphur	2
AMERICAN COCKROACH, <i>Periplaneta americana</i>		
Abdominal injection, various doses		
Famoxon, 4.6 (males) or 8.6 (females) mg/kg BW	LD50	2
Famphur, 9.0 (males) or 11.8 (females) mg/kg BW	LD50	2
Single abdominal injection of 1 mg famphur/kg BW; whole-body residues of famphur, famoxon, and N-desmethylfamphur measured 1 h after injection	Of total amount injected, 18.5% remained after 1 h: 16.8% famphur, 0.5% famoxon, and 1.2% N-desmethylfamphur	2

^a 1, Vaughan and Turner 1984; 2, O'Brien et al. 1965.

19.4.3 Aquatic Organisms

An extensive literature search revealed no published data on famphur toxicity to aquatic animals. Unpublished studies of acute lethality were, however, conducted with the bluegill (*Lepomis macrochirus*) and rainbow trout (*Oncorhynchus mykiss*). In those studies, the range in LC50 values at 96 h was 18 to 21 mg/L in bluegills and 4.9 to 5.3 mg/L in rainbow trout. The no-observable-effect concentration at 96 h ranged from 14 to 18 mg/l in bluegills and was 2.1 mg/L in rainbow trout (U.S. Environmental Protection Agency, OPPTS/OPP/EFED/EEB, personal communication, 30 June 1993).

Although no data were available on the effects of famphur in aquatic ecosystems, there is a substantial database on other organophosphorus insecticides. For example, methyl parathion (*O,O*-dimethyl *O*-(*p*-nitrophenyl)phosphorothioate), another phosphorothioate organophosphorus insecticide, had LC50 (96 h) values for bluegills and rainbow trout that were similar to those of famphur: 5.7 mg/L and 2.7 mg/L, respectively (Khan 1977). But exposure for 96 h is not sufficient to satisfactorily evaluate the aquatic toxicity of organophosphorus insecticides. The mortality of adult northern puffers (*Sphaeroides maculatus*) continuously exposed to 20.2 mg/L of methyl parathion was <5% in 96 h but 100% in 40 days. Puffers refused to eat during exposure, and survivors between days 10 and 40 showed complete inhibition of serum esterase activity, zinc-depleted liver and gills, and altered blood chemistry (Eisler 1967, 1972). In another study, male guppies (*Poecilia reticulata*)

held in sublethal concentrations (0.01 to 1.0 mg/L) of methyl parathion for 40 days or longer showed a dose-dependent decrease in spermatogenesis (Billard and de Kinkelin 1970). Pesticide-induced mortality patterns of representative organophosphorus compounds are also modified by water temperature, pH, and salinity. The mummichog (*Fundulus heteroclitus*), an estuarine cyprinodontiform teleost, was most sensitive to organophosphorus compounds at elevated temperatures, reduced salinities, and low pH (Eisler 1970b). Duration of exposure to organophosphorus compounds also affects mummichog survival: fish exposed to high (LC₇₅, 24-h) concentrations of representative insecticides for more than 30 min died by day 21 postexposure. Some insecticides were as much as 8.3 times more toxic after exposure for 240 h than 96 h, as judged by LC₅₀ values (Eisler 1970b). In general, crustaceans were more sensitive than teleosts — sometimes by several orders of magnitude — to organophosphorus insecticides in 96-h tests. Grass shrimp (*Palaemonetes vulgaris*) and fishes were most sensitive to organophosphorus insecticides at high salinities in the 1.2 to 3.6% test range and high temperatures in the 10 to 30°C test range (Eisler 1969; 1970c, 1972). Marine clams and gastropods were comparatively resistant to organophosphorus insecticides; none died in 96-h exposure to 25 mg/L of five organophosphorus insecticides, including methyl parathion. But during a postexposure observation of 133 days, some bivalves and gastropods died (Eisler 1970a), and these deaths are similar to the delayed mortality for some species of mammals and invertebrates after exposure to certain organophosphorus insecticides (Negherbon 1959).

The expected continued use of famphur in the environment and its vehicular transport along roads that border navigable waters suggest a need for aquatic toxicity data. Famphur data — like those on other organophosphorus insecticides — should reflect the influence of dose, exposure duration, formulation, and other biological and abiotic variables on growth, survival, and metabolism of representative species of aquatic organisms.

19.4.4 Birds

The avian acute oral LD₅₀ of famphur is usually between 1 and 9.5 mg/kg BW (Schafer 1972; Hill and Mendenhall 1980). Laboratory studies with sensitive species of birds show reduced survival after a 5-day consumption of diets containing 35 to 49 mg famphur/kg ration (Hill et al. 1975) (Table 19.3). Depressed cholinesterase activity in the brain and in plasma of European starling (*Sturnus vulgaris*) nestlings occurred after 15 daily oral exposures of concentrations as low as 0.3 mg famphur/kg BW (Powell and Gray 1980) (Table 19.3). Signs suggesting famphur poisoning in mallards (*Anas platyrhynchos*) included regurgitation, goose-stepping, ataxia, wing drop, tremors, and tonic seizures (Tucker and Crabtree 1970; Hudson et al. 1984).

Famphur is considered a Class II toxic compound to the Japanese quail (*Coturnix japonica*) according to the classification of Hill and Camardese (1986). Class II compounds (very toxic) kill 50% of the test organisms on diets containing 40 to 200 mg chemical/kg ration for 5 days followed by a 3-day observation. By comparison, the 50% kill in other classes (in mg/kg diet) is <40 in Class I (highly toxic), >200 to 1000 in Class III (moderately toxic), >1000 to <5000 in Class IV (slightly toxic), and >5000 in Class V (practically nontoxic) (Hill and Camardese 1986). Smith (1987) rates famphur as a Class I toxic compound, as judged by results of dietary tests with mallards.

Birds killed by organophosphorus compounds in the wild consistently show 80 to 95% depression of brain cholinesterase activity (Hill 1992). Depression of brain cholinesterase activity by >20% in birds has been used as a conservative criterion to indicate significant exposure to organophosphorus chemicals. Depression of brain cholinesterase activity by >50% and confirmation of suspected organophosphorus chemical residues in tissues or ingesta are criteria for cause–effect diagnosis of death in birds exposed to cholinesterase-inhibiting chemicals (Henny et al. 1985; Hill 1992). Death occurs in many avian species when brain-cholinesterase inhibition is 60 to 90%. However, no barn owls (*Tyto alba*) died or showed signs of intoxication after consuming famphur-poisoned Japanese quail, although 70% of the owls had brain cholinesterase inhibition within these lethal bounds (Hill and Mendenhall 1980). Barn owls fed famphur-poisoned quail, the digestive

tracts of which had been removed, showed significant but lesser brain cholinesterase activity inhibition than owls fed intact poisoned quail, indicating that famphur or cholinesterase-inhibiting metabolites were most heavily concentrated in digestive tracts (Table 19.3).

The black-billed magpie seems unusually sensitive to famphur. Dead famphur-poisoned magpies contained as much as 290 mg famphur/kg liver FW, 4770 mg/kg gizzard FW, and <0.2 mg/kg muscle or fat (Hill and Mendenhall 1980). There is a growing body of literature on adverse effects on magpies from pour-on (13.2% famphur) applications along the backline of cattle to control cattle warbles at the recommended rate of 0.326 mL/kg BW, not to exceed 118 mL/animal — equivalent to 43 mg/kg BW, not to exceed 15.6 g/animal (Felton et al. 1981; Henny et al. 1985; Seel 1985; Smith 1987). Felton et al. (1981) documented three occasions when dead birds were found after pour-on-famphur treatment of cattle against warble flies:

1. 12 black-billed magpies in a nearby field 2 to 3 days after cattle were treated
2. 6 magpies during a 14-day period (although other species of corvids were present, only magpies were affected)
3. 8 robins (*Erythacus rubecula*) and a single dunnock (*Prunella modularis*) near a cattle crush a few days after famphur treatment.

The dead birds had no measurable brain-cholinesterase activity, and famphur was detected in the gizzards of birds in all three incidents (Felton et al. 1981). Partially paralyzed magpies containing as much as 3500 mg famphur/kg gizzard contents were found in the vicinity of cattle recently treated with a pour-on formulation of famphur to control an infestation by warble flies; another 20 to 30 dead magpies were found in the immediate area (Seel 1985). Magpies and one red-tailed hawk (*Buteo jamaicensis*) were the only birds found dead where cattle had been topically treated with famphur, although several other species, including killdeers (*Charadrius vociferus*) and European starlings, were common in these pastures (Henny et al. 1985). Famphur residues were detected in all dead magpies and hawks, and brain cholinesterase activity depression ranged from 70 to 92%. Based on residue concentrations in the gizzards, dead magpies contained 5.2 to 6.1 mg famphur/kg whole body; these values were above the acute oral LD₅₀ values for several species of birds (Henny et al. 1985) (Table 19.3).

The most probable explanation for the sensitivity of magpies to famphur is associated with the contents of the poisoned magpies, which consisted of as much as 12% cattle hair (Henny et al. 1985). Although most organophosphorus compounds degrade rapidly, famphur persists for >90 days on hair of Hereford bulls and steers and Angus yearlings. Famphur concentration in hair of a Hereford bull averaged 38,000 mg/kg FW 1 week after a single pour-on treatment and a maximum of 12,000 mg/kg FW 60 days posttreatment. High concentrations of famphur in the gizzards of magpies indicated that the material was ingested and not from dermal contact or inhalation. Tissue residues, in mg famphur/kg FW, in famphur-poisoned magpies were as much as 550 in the upper GI tract, 4.3 in the lower GI tract, and 3 in the whole body. Cow hair from gizzards of dead magpies averaged 4600 mg famphur and famoxon/kg FW; other animal matter in the gizzard contained 620 mg famphur and famoxon/kg FW and plant matter 340 mg famphur and famoxon/kg FW. A potentially lethal dose to magpies would be 8 to 19 mg of treated hair at day 7 and 26 to 60 mg of treated hair after 60 days. Coincidentally, magpie mortality persisted for more than 3 months; most deaths occurred 5 to 13 days after cattle were treated (Henny et al. 1985). The manure-insect-bird pathway of famphur translocation is untenable because of extremely low (<0.14 mg/kg FW) concentrations of famphur in cow manure (Henny et al. 1985).

Secondary poisoning of flesh-eating birds foraging on famphur-killed vertebrates is well documented. The degree of hazard to the predator is related to the amount and type of consumed tissues and famphur concentrations in the prey tissues (Heinz et al. 1979; Hill and Mendenhall 1980; Henny et al. 1985, 1987; Hill 1992). Secondary poisoning of raptors killed by famphur that was topically applied to livestock include the bald eagle (*Haliaeetus leucocephalus*) — after eating

cattle that died within 100 days of famphur treatment or famphur-poisoned brown-headed cowbirds (*Molothrus ater*) and European starlings — and a red-tailed hawk after eating famphur-poisoned black-billed magpies or European starlings (Henny et al. 1987). In one case, an adult female bald eagle that was unable to fly near Lewes, Delaware, was brought to a national wildlife refuge where it died after a few days (Franson et al. 1985). Stomach contents included one lead shot and remains of brown-headed cowbirds and European starlings. A necropsy showed no signs of lead poisoning. Clinical signs, physical examination, and presence of a full crop suggested acute poisoning. Crop and stomach contents were analyzed for a variety of pesticides, metals, and herbicides, but only famphur was elevated at 1.9 mg/kg FW. As judged by famphur residues in the GI tract and by brain cholinesterase activity inhibition of 85%, the authors concluded that famphur was the probable cause of death (Franson et al. 1985). There is also a case of tertiary poisoning in which a great horned owl (*Bubo virginianus*) died after consuming a dead famphur-poisoned red-tailed hawk. In all of these cases, brain cholinesterase activity of poisoned birds was depressed >50% and undigested remains contained famphur (Henny et al. 1987).

Famphur has also been used to intentionally kill birds, including migratory waterfowl and other protected species, and should be added to the list of other toxic organophosphorus insecticides, such as monocrotophos, dicrotophos, and parathion, that have been used for this purpose (White et al. 1989). In 1988, for example, famphur was used illegally by farmers in Georgia and West Virginia to kill birds thought to be depredating crops. Corn and grain at the mortality sites contained between 4240 and 8500 mg famphur/kg. Dead birds at these locations included Canada geese (*Branta canadensis*), mallards, American black ducks (*Anas rubripes*), American crows (*Corvus brachyrhynchos*), common grackles (*Quiscalus quiscula*), red-winged blackbirds (*Agelaius phoeniceus*), sandhill cranes (*Grus canadensis*), and a single red-tailed hawk. Most of the poisoned waterfowl, cranes, raptors, corvids, and songbirds from the five sites had severely depressed brain cholinesterase activity (i.e., >50%), poisoned bait in the gizzards, and famphur concentrations in the gastrointestinal tracts ranging from 5 mg/kg FW in the red-tailed hawk to 1480 mg/kg FW in Canada geese. It was concluded that all birds died from direct ingestion of the poisoned bait, except the red-tailed hawk that had eaten one or more famphur-poisoned crows (White et al. 1989).

Table 19.3 Famphur Effects on Birds

Route of Administration, Organism, Dose, and Other Variables	Effect	Reference ^a
DIETARY EXPOSURE		
Treated feed for 5 days, then untreated feed for 3 days		
Mallard, <i>Anas platyrhynchos</i> ; 35 mg/kg diet Japanese quail, <i>Coturnix japonica</i> ; 69 mg/kg diet, 95% confidence interval (CI) of 49–97 mg/kg diet	About 50% survived; ducklings age 10 days 50% dead; 14-day-old quail	1 2
Ring-necked pheasant, <i>Phasianus colchicus</i> ; 49 mg/kg diet, 95% CI of 40–61 mg/kg diet	50% dead; 10-day-old chicks	1
Domestic chicken, <i>Gallus</i> sp. Fed 50 mg/kg ration for 10 days (in attempt to control northern fowl mite, <i>Ornithonyssus sylviarum</i>)	Ineffective in controlling mites. Feed consumption, body weight, and egg production significantly decreased	3
Barn owl, <i>Tyto alba</i> , adults, 475 g body weight (BW)	Owls did not avoid famphur-poisoned <i>Coturnix</i> , fed normally, and did not lose weight. By the tenth day, plasma-cholinesterase activities in owls were depressed 45–81%, and brain cholinesterase activities were depressed 32–73%	4
Owls were fed whole famphur-poisoned Japanese quail. Quail received multiple doses of famphur (a total of 1 mg over a 3-day period). One poisoned <i>Coturnix</i> was fed daily for 10 days. If no famphur was lost or metabolized by <i>Coturnix</i> prior to death, then owls received a maximum of 21 mg/kg BW for the 10-day period or 2.1 mg famphur/kg BW daily		

Table 19.3 (continued) Famphur Effects on Birds

Route of Administration, Organism, Dose, and Other Variables	Effect	Reference ^a
As above, except digestive tract was removed from famphur-poisoned <i>Coturnix</i> before presentation to owls	Owls had brain cholinesterase activity values intermediate between controls and those fed poisoned whole <i>Coturnix</i>	4
MULTIPLE ORAL DOSES		
Japanese quail; dosing by gavage over 3 days: 300 µg on days 1 and 2 and 400 µg on day 3; mean weight of 120 g	Some deaths; cumulative dose received at day 3 = 8.33 mg/kg BW	4
Domestic chicken; 2.5 mg/kg BW once daily for 8 days; observed for 10 days posttreatment	Egg production, body weight, and feed consumption decreased significantly; ineffective in controlling northern fowl mite	3
European starling, <i>Sturnus vulgaris</i> , free-living nestlings, age 4 days. Dosed perorally with famphur dissolved in corn oil at 0.3, 1.0, or 3.0 mg famphur/kg BW daily for 15 days, then killed at age 19 days	At 0.3 mg/kg BW, 1 nestling died after the second dose (age 6 days) and another after the fifth dose vs. no deaths in controls; at day 19, brain cholinesterase activity was depressed 51% and plasma activity 49%. At 1.0 mg/kg BW, 1 died after the third dose; at day 19, brain cholinesterase activity level was depressed 75% and plasma cholinesterase 25%. At 3.0 mg/kg BW, 9 of 11 tested nestlings died within 8 h of the first dose, another within 8 h of the second dose, and the last was killed by a predator after the second dose. The 2 nestlings that survived a single dose were moribund and their brain cholinesterase activity was depressed 85%	5
SINGLE ORAL DOSE		
Red-winged blackbird, <i>Agelaius phoeniceus</i> ; 1.8 mg/kg BW, 95% CI of 1.0–3.2 mg/kg BW	LD50	6, 9
Mallard; 9.87 mg/kg BW, 95% CI of 5.88–16.6 mg/kg BW	LD50 for 3–4-month-old hens	7, 8
Domestic chicken; 10 mg/kg BW in gelatin capsule to control northern fowl mite; observed for 10 days posttreatment	Ineffective in controlling mites. On day 2 posttreatment, 1 of 12 chickens had died and 9 others showed muscular incoordination, especially in the legs. By day 3 posttreatment, most of the 9 were again standing and feeding and feces had reverted from a greenish diarrheic discharge to the normal consistency. By day 10 posttreatment, body weight and egg production was significantly decreased, although egg weight was unaffected	3
European starling; 4.2 mg/kg BW, 95% CI of 1.99–9.50 mg/kg BW	LD50	6, 9

^a 1, Hill et al. 1975; 2, Hill and Camardese 1986; 3, DeVaney and Ivie 1980; 4, Hill and Mendenhall 1980; 5, Powell and Gray 1980; 6, Smith 1987; 7, Tucker and Crabtree 1970; 8, Hudson et al. 1984; 9, Schafer 1972.

19.4.5 Mammals

Famphur is a group-D compound that is not classifiable as a human carcinogen (Sine 1991). However, a study of leukemia risk among males in Iowa and Minnesota indicated a slight but significant elevation in risk — especially chronic lymphocyte leukemias — for farmers but not for nonfarmers. Moreover, a significantly elevated leukemia risk was seen from exposure to specific animal insecticides, including famphur (Brown et al. 1990). It is clear that more research is needed on the potential carcinogenicity of famphur.

Signs of famphur toxicosis in cattle include ataxia, muscular fasciculations, general weakness, lacrimation, salivation, and diarrhea (Randell and Bradley 1980). In comparison with European breeds of cattle (*Bos taurus*), the Brahman (*Bos indicus*) and European X Brahman hybrids are more sensitive to famphur, and Brahman bulls are more sensitive than cows (Johnson et al. 1972; Randell and Bradley 1980) (Table 19.4). At a comparatively low dose of 16.6 mg famphur/kg BW, both *B. taurus* and *B. indicus* are tolerant of intramuscular injectable famphur. However, *B. indicus* is more sensitive, and bulls sometimes died when treatment levels exceeded 33.3 mg/kg BW (Randell and Bradley 1980) (Table 19.4). In addition to cattle, famphur-induced mortality in other species of mammals has been documented (Table 19.4). Single exposures of famphur, in mg/kg BW, killed rabbits (*Oryctolagus* sp.) at 2730 in dermal exposure; mice (*Mus* sp.) at 27 in oral dose or 11.6 by intraperitoneal injection; domestic sheep (*Ovis aries*) at 400 in oral dose; and laboratory white rats (*Rattus* sp.) at 400 dermal exposure or >28 in oral dose (Table 19.4). Mice receiving fatal or near-fatal intraperitoneal injections of famphur or famoxon began to convulse 10 to 20 min postinjection; death came within 45 min postinjection, usually from respiratory failure. Mice remaining alive at 60 min postinjection usually recovered (O'Brien et al. 1965).

Latent effects of famphur exposure in reindeer hinds (Nieminen et al. 1980) strongly indicate a need for additional studies in this subject area. Intramuscular injections of reindeer hinds and their 4-week-old calves controlled warble-fly infection in treated animals. Treated calves did not differ significantly from controls during the following year in body weight, body temperature, or blood chemistry. Treated hinds, however, had significantly lower erythrocyte sedimentation rates and serum gamma-globulin concentrations and significantly higher hemoglobin, serum calcium, serum inorganic phosphorus, and serum magnesium than untreated hinds 1 year after treatment (Nieminen et al. 1980).

Reduced brain cholinesterase activity in avian and mammalian wildlife is associated with adverse effects on metabolism, reproduction, sensory behavior, motor activity, food and water intake, learning, and memory (Mineau 1991). Cholinesterase activity in mammals regenerates rapidly after a cessation from treatment with famphur (Kaemmerer and Buntenkotter 1973). In humans, typical symptoms of organophosphorus-induced cholinesterase inhibition include headache, giddiness, nervousness, blurred vision, weakness, nausea, cramps, diarrhea, chest discomfort, sweating, salivation, vomiting, and tremors (Gallo and Lawryk 1991). In severe cases, victims show muscular weakness, convulsions, coma, loss of reflexes, loss of sphincter control, and eventually death. Effects of cholinesterase-inhibiting agents in humans are usually counteracted with repeated intravenous injections of atropine sulfate (2 to 4 mg), intravenous injections of pralidoxime chloride (1 g), and oxygen (Gallo and Lawryk 1991). Rats had depressed plasma cholinesterase activity when fed diets containing as little as 1 mg famphur/kg for as many as 90 days, although growth and appetite seemed normal (Black et al. 1979). Brahman bulls had maximum erythrocyte cholinesterase inhibition 14 days after intramuscular injection of famphur. Cholinesterase activity levels recovered toward normal during the next 14 days, and recovery correlated with the formation of new erythrocytes (Randell and Bradley 1980). Except for cholinesterase activity inhibition, there were no signs of organophosphate intoxication in Brahman heifers and steers given single dermal doses of 20 to 61 mg famphur/kg BW. Cholinesterase activity was inhibited for as many as 14 days posttreatment at the lower (20 to 41 mg/kg BW) doses and for at least 7 weeks at 61 mg/kg BW (Table 19.4).

Famphur is metabolized rapidly in mammals. In cattle, famphur controlled target insect pests when administered as a bolus, in the diet, as an oral paste, by intramuscular injection, or by pour-on. Regardless of mode of administration, length of exposure, or dose, famphur residues in tissues and milk were usually nondetectable within 4 days of final exposure. A similar pattern was evident in other species of mammals (Table 19.4). Rats and sheep metabolize famphur differently. During the first 24-h postdosing period, urine of rats contained as much as 2 times more of the unchanged *O*-desmethyl compound than urine of sheep, about the same amount of dimethylsulfamoylphenyl glucuronide, about 0.3 times as much *O,N*-bisdesmethylfamphur, and about 0.5 times less methylsulfamoylphenyl glucuronide (Gatterdam et al. 1967). With the exception of the oxon, metabolites of famphur were considerably less toxic to mammals than the parent chemical. In general, famoxon

was 100 times more effective than famphur in depressing erythrocyte cholinesterase activity (Kaemmerer and Buntenkotter 1973).

Famphur in pour-on applications penetrates skin at different rates, depending on the solvent. In rat skin, penetration was most rapid when the solvent was acetone and least rapid in corn oil and benzene; the percent of remaining famphur in rat skin 3 h after a single dermal application was 38% from the acetone mixture, and 67% from both benzene and corn oil solvents (O'Brien and Dannelley 1965). The penetrability of famphur pour-on formulations used in lice control on Angora goats was enhanced when applied in combination with a liquid-detergent wetting agent (Fuchs and Shelton 1985). Laboratory screening tests in which small mammals are treated with chemicals and parasitized by insects are now used to predict the effectiveness of systemic insecticides. Tests with mice and rodent botfly (*Cuterebra* sp.) were useful in predicting the effectiveness of famphur against larvae of the common cattle grub (*Hypoderma lineatum*) in cattle (Gingrich et al. 1972) (Table 19.4), and show promise for screening additional chemicals.

Table 19.4 Famphur Effects on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
CATTLE, <i>Bos</i> spp.		
Bolus		
Given to 180-kg heifer calves 12 days before infestation by 30–60-day-old larvae of ticks. Sustained release equivalent to 3, 5, or 6.8–10.1 mg famphur/kg body weight (BW) daily	Ineffective at 3 mg/kg BW against fever ticks (<i>Boophilus annulatus</i> , <i>B. microloplus</i>) and the American dog tick (<i>Dermacentor variabilis</i>). At 5 mg/kg BW, famphur was effective (87–97%) against fever ticks but ineffective against the dog tick. At the highest daily release rate, famphur was 100% effective against fever ticks between days 12 and 41, but remained ineffective against the dog tick	1
7 mg/kg BW daily (range 4.5–11.5 mg/kg BW daily)	Bolus was 99–100% effective against Gulf Coast tick (<i>Amblyomma maculatum</i>) and 60–86% effective against the lone star tick (<i>A. americanum</i>). Heifers showed no signs of organophosphorus insecticide poisoning, but had slight reduction in erythrocyte cholinesterase activity	2
Diet		
Lactating cows fed diets equivalent to 3.3 mg famphur/kg BW for 90 days	Concentrations in milk on day of withdrawal were 0.025 mg famphur/L and 0.023 mg famoxon/L. During the next four milkings (i.e., through day 8 posttreatment), famphur and famoxon residues in milk were always <0.005 mg/L	3
Calves fed rations equivalent to 3.3 or 9.9 mg famphur/kg BW for 90 days	Within 2 days of cessation of the low-dose-contaminated diet all calf tissues were free of famphur and famoxon; this value was 4 days for the 9.9-mg/kg BW group. Concentrations of famphur (famoxon) in mg/kg FW in the high-dose group at the end of the 90-day feeding study were 0.31 (0.03) in muscle, 1.6 (0.23) in fat, 5.6 (0.5) in liver, and 0.49 (0.19) in kidney	3
Adult rations contained equivalent of 5 mg famphur/kg BW daily	99.5–100% effective in control of Gulf Coast tick and lone star tick; ineffective against the American dog tick	1
Adults given equivalent of 5 mg famphur/kg BW daily	Effective against tropical horse tick (<i>Anocentor nitens</i>), but not completely effective against 3 other species of ticks	2
Adults given equivalent of 5 mg/kg BW daily for 10 days, administered as a 33%-feed premix	>90% control of cattle grubs (<i>Hypoderma</i> spp.). Manure from treated cattle controlled larvae of horn fly (<i>Haematobis irritans</i>), but was ineffective against larvae of the house fly (<i>Musca domestica</i>)	4
Intramuscular injection		
15 mg/kg BW; Hereford steers and calves, Angus cows; to control cattle grubs (<i>Hypoderma lineatum</i> , <i>H. bovis</i>)	97% grub reduction in calves, 93% in cows, 94% in steers	5

Table 19.4 (continued) Famphur Effects on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
16.6, 33.3, or 49.9 mg/kg BW, single injection; Brahman bulls, steers, and heifers 6–8 months old, 169–200 kg BW. Observed for 28 days posttreatment	All doses inhibited erythrocyte cholinesterase levels by 45–95%. All groups tolerated 16.6 mg/kg BW. Severe toxicosis in the two high-dose groups (9 of 20) in bulls but not in heifers and steers; 7 of the 9 bulls died or had to be euthanized; necropsy showed severe pulmonary edema	6
18 mg/kg BW, single injection	Residues <0.7 mg/L in blood 2 h postinjection	7
36 mg/kg BW, single injection	Residues in blood >0.7 mg/L 2 h postinjection, but <0.7 mg/L after 4 h	7
54 mg/kg BW, single injection	Residues in blood >0.7 mg/L 1–2 h postinjection, but <0.7 mg/L after 4 h	7
60.7 mg/kg BW, single injection of radiolabeled famphur	Blood plasma levels in mg/kg fresh weight (FW) were 0.4 after 4 h and 0.18 after 72 h; for famoxon, these values were not detectable at 4 h and 0.05 at 72 h. Plasma and urine radioactivity levels reached maxima after 24 h	7, 8
83.2 mg/kg BW; Brahman bulls and Angus bulls, 7–9 months old, 174–184 kg BW	5 of 6 injected Brahman bulls showed severe signs of toxicosis and 4 died within 48 h; recovery of the 5th bull took 10 days. Only 1 of 5 Angus bulls showed clinical signs of toxicosis, but it recovered	6
Oral		
9.9 mg/kg BW; single application, residues measured 24 h posttreatment; control values always <0.05 mg/kg FW of famphur and famoxon		
Fat; famphur vs. famoxon (mg/kg FW)	0.14 vs. <0.05	3
Kidney; famphur vs. famoxon (mg/kg FW)	<0.05 vs. <0.05	3
Liver; famphur vs. famoxon (mg/kg FW)	0.08 vs. 0.05	3
Muscle; famphur vs. famoxon (mg/kg FW)	<0.05 vs. <0.05	7
18 mg/kg BW	Residues in blood >0.7 mg/L 18–24 h after ingestion	7
20, 30, or 40 mg/kg BW, each with 8 mg levamisole/kg BW; administered as a paste to cattle yearlings in California, Nebraska, and Kentucky	As much as 85% reduction in cattle grubs and nematode gastrointestinal worms at 20 mg/kg BW + levamisole; as much as 98.2% reduction in 30 or 40 mg/kg BW groups	9
36 mg/kg BW, single dose	Residues in blood >0.7 mg/L 6–72 h after intake, but <0.7 mg/L after 96 h	7
Pour-on		
15–35 mg/kg BW, cows	Controls cattle-biting lice (<i>Damalinia bovis</i>), long-nosed cattle lice (<i>Linognathus vituli</i>), and short-nosed cattle lice (<i>Haematopinus eurysternus</i>)	10
20.25, 40.5, or 60.75 mg/kg BW; Holstein Friesian calves; blood cholinesterase activity levels measured up to 49 days posttreatment	At the 2 lowest doses, significant depression from day 2 through day 14; blood cholinesterase normal at day 21. At 60.75 mg/kg, blood cholinesterase decreased for entire 49-day posttreatment. No outward signs of organophosphate intoxication and normal food intake and demeanor	11
23 mg/kg BW, cows	At 24 h, whole milk had 0.24 mg famphur/L of which 76% was in the butterfat fraction; after 72 h, residues in milk were <0.008 mg/L	10
25 mg/kg BW, cows	After 24 h, mean residue of famphur in subcutaneous fat was 1.8 mg/kg FW, maximum was 2.46 mg/kg FW	10
40 mg/kg BW; Hereford steers and calves, Angus cows	87% effective in controlling cattle grubs in calves; 100% effective in cows and steers	5
40 mg/kg BW, cattle yearlings	100% effective in controlling cattle grubs and nematode gastrointestinal worms	9

Table 19.4 (continued) Famphur Effects on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
40 or 50 mg/kg BW; yearling steers; Canada, late autumn; single treatment	Although not completely satisfactory for control of <i>Hypoderma</i> spp. (52–68% reduction in grubs) — possibly because of low absorption associated with low ambient temperatures at time of treatment — and some inhibition in blood cholinesterase activity (maximum inhibition of 31–38% reached 15 days after treatment), both groups of treated steers gained significantly more weight than a control group during the posttreatment of 181 days and were otherwise normal	12
Brahman bulls, steers, and heifers; mean weight of 117 kg		
40 mg/kg BW	Erythrocyte cholinesterase depression after 24 h was 43% in bulls and 33–34% in steers and heifers	13
80 mg/kg BW	After 5 h, 1 of 13 bulls was anorexic and salivating	13
209 mg/kg BW	After 48 h, erythrocyte cholinesterase depression was 56% in bulls, 55% in steers, and 51% in heifers	13
40.5 mg/kg BW, Brahman bull calves	2 of 3 famphur-treated calves died	11
45 mg/kg BW, cows	Famphur concentrations, in mg/kg FW, after 24 h were <0.05 in liver and kidney, 1.25 in fat, and 1.41 in muscle. After 7 days, these values were 0.53 in fat and 0.71 in muscle. By day 14, maximum values were 0.11 mg/kg FW in fat and <0.02 in other tissues	10
50 mg/kg BW, cows	After 24 h, mean residue of famphur in subcutaneous fat was 2.08 mg/kg FW, maximum was 3.00 mg/kg FW	10
150 mg/kg BW, cows	After 24 h, famphur concentrations in subcutaneous fat ranged from 6.3–12.3 mg/kg FW	10
ANGORA GOAT, <i>Capra</i> sp.		
Pour-on, 4.1–4.8 mg/kg BW; nannies 27–41 kg; single application	100% effective in 14-day control of Angora goat-biting louse (<i>Bovicola limbatus</i>) and hairy goat louse (<i>B. crassipes</i>); significant protection after 45 days	14
LABORATORY MOUSE, <i>Mus</i> sp.		
Dermal		
Mice infected nasally or orally with rodent botfly (<i>Cuterebra</i> sp.) were dipped 48 h postinfestation for 30 s in 25% emulsifiable famphur solutions (0.001–10%) and examined 1 week later. Entire body was submersed, except head	50% kill of larvae after immersion in 0.0072% solution (18 mg famphur/L); 90% control in 0.051% solution (127.5 mg/L)	16
Oral		
Male mice, 8–12 weeks old, orally and nasally infected with 1st-stage larvae of rodent botfly. Two days after infection, mice were given single doses of 1.46 or 3.38 mg famphur/kg BW	Low dose killed 50% of larvae; high dose killed 90%	17
As above, except that mice were given 1.5 mg famphur/kg BW at 1, 2, or 3 days after infestation	Most effective control (71% dead larvae) when administered at 3 days	17
18 mg/kg BW	Acute LD50, famoxon	7
27–30 mg/kg BW	Acute LD50, famphur	7, 15

Table 19.4 (continued) Famphur Effects on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference^a
Intraperitoneal injection		
Single injection of 1 mg famphur/kg BW; residues of famphur, famoxon, and <i>N</i> -desmethylfamphur measured 1 h postinjection	Only 8.3% of the injected dose was measurable 1 h postinjection: 8.1% as the parent famphur, 0.2% as famoxon, and 0.01% as <i>N</i> -desmethylfamphur	18
5.8 mg famoxon/kg BW	LD50	18
11.6 mg famphur/kg BW	LD50	18
RABBIT, <i>Oryctolagus</i> sp.		
50 mg/kg BW; oral, subcutaneous, or intravenous route	No effect on reproduction	25
2730 mg/kg BW, dermal route	LD50	15
DOMESTIC SHEEP, <i>Ovis aries</i>		
Bolus; sustained release of 7 mg famphur/kg BW daily	Completely effective against Gulf Coast tick, partial control of lone star tick, ineffective against American dog tick	2
Intravenous injection		
Single injection of radiolabeled famphur equivalent to 22.3 mg famphur/kg BW. Sheep killed at 96 h and tissues analyzed for residual radioactivity	More than 50% of the administered dose was excreted within 6 h and 98% within 48 h. About 97% was excreted in urine and <3% in feces. Residues, in mg/kg FW, were 1.4 in blood; 0.3–0.6 in kidney, liver, spleen, lung, and cerebrospinal fluid; and <0.1 in bile, fat, brain, and muscle	7, 8
Single injection, 22.3 mg/kg BW	Famphur (famoxon) residues in blood plasma in mg/kg FW were 0.6 (5.6) at 2 h, and nondetectable (0.01) at 24 h	7
Intravenous or intramuscular injection; urine collected over 24-h period after single application of radiolabeled famphur	Urinary radioactivity was due to the unchanged O-desmethyl compound (13–24%); <i>N,N</i> -dimethyl sulfamoylphenyl glucuronide (32–33%); <i>O,N</i> -bisdesmethylfamphur (31–34%); and <i>N</i> -methyl sulfamoylphenyl glucuronide (8–15%)	8
Intramuscular injection		
Single injection of radiolabeled famphur, equivalent to 55.1 mg/kg BW. Sheep killed at 72 h and tissues analyzed for residual radioactivity	About 64% of the administered dose was recovered in excreta after 72 h. Residues in mg/kg FW were 15 at the muscle injection site; 5–8 in kidney, bile, and fat; 1.6–2.3 in liver, spleen, lung, and blood; and 0.7–0.9 in brain, muscle, and cerebrospinal fluid.	7, 8
Single injection, 55.1 mg/kg BW	Famphur (famoxon) residues in blood plasma, in mg/kg FW, were 0.9 (0.1) at 2 h and 0.06 (0.01) at 72 h	7, 8
Oral, single dose; 400 mg/kg BW	LD50	15, 19, 20
Rumen infusion; peroral administration by cannulation for 72 h of ewes given doses equivalent to 5 or 7 mg famphur/kg BW daily. After infusion for 72 h, sheep were challenged by various blood-sucking arthropods	At 5 mg/kg BW, famphur caused a significant increase in mortality and decrease in percent egg hatch of adult Gulf Coast ticks and complete control of the bedbug (<i>Cimex lectularius</i>). At 7 mg/kg BW daily, Gulf Coast ticks were completely controlled, but dose was ineffective against the lone star tick and the American dog tick	21
REINDEER, <i>Rangifer tarandus</i>		
Intramuscular injection		
15 mg/kg BW, single injection	At 24 h residues were highest (8.1–9.1 mg/kg FW) in fatty tissues; at muscle injection site, residues ranged as high as 635 mg/kg FW vs. 0.6 mg/kg FW in normal muscle. At 7 days posttreatment, residues in mg/kg FW, were 0.03–0.19 in fat,	22

Table 19.4 (continued) Famphur Effects on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
30 mg/kg BW, single injection	0.03 in injection-site muscle, and 0.03 in liver. At 5 weeks, famphur was detectable only in fat; by 7 weeks, no famphur was detectable in any tissue. Famoxon was not found in any tissue at any time	22
30 mg/kg BW, single injection	Residues at 24 h in mg/kg FW were as high as 38 in fat, 8 in muscle, 5 in liver and 2.5 in kidney	23
Accidental overdose (usually double-dosed), 60 mg/kg BW	90–95% reduction in larvae of warble fly (<i>Oedemagena tarandi</i>) and nostril fly (<i>Cephenomyia trompe</i>)	23
	Atropine sulfate is recommended antidote	23
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Dermal		
Single application, mg/kg BW		
400	LD50, adult males	19
533	LD50, adult females	19
Diet		
Rations containing 1, 3, or 25 mg famphur/kg for as many as 90 days	At 90 days, all groups had depressed plasma cholinesterase, although growth and appetite seemed normal. Whole-blood cholinesterase was depressed in the 3- and 25-mg/kg groups; brain cholinesterase was significantly reduced in the 25-mg/kg group	24
Diet containing 25 mg famphur/kg for 90 days, then famphur-free diet for 42 days	Blood chemistry and histology normal at necropsy on day 132. Rats avoided diets during famphur-free phase	24
Oral		
Single dose, in mg/kg BW		
28	LD50, adult males	19
35	LD50	7, 20
36–62	LD50	15
51	LD50, adult females	19
73	LD50, weanling males	19
Subcutaneous injection; urine collected during 24-h period after single application of radiolabeled famphur	Urinary radioactivity was due to the unchanged O-desmethyl compound (>50%); <i>N,N</i> -dimethyl sulfamoylphenyl glucuronide (30%); (O, <i>N</i> -bisdesmethylfamphur (12%), and <i>N</i> -methyl sulfamoylphenyl glucuronide (7%)	8

^a **1**, Hair et al. 1979; **2**, Teel et al. 1979; **3**, Pasarela et al. 1967; **4**, Drummond 1968; **5**, Loomis and Schock 1978; **6**, Randell and Bradley 1980; **7**, Kaemmerer and Buntenkotter 1973; **8**, Gatterdam et al. 1967; **9**, Campbell et al. 1987; **10**, Annand et al. 1976; **11**, Watson and Black 1981; **12**, Khan and Kozub 1981; **13**, Johnson et al. 1972; **14**, Fuchs and Shelton 1985; **15**, Smith 1987; **16**, Drummond and Gingrich 1972; **17**, Gingrich et al. 1972; **18**, O'Brien et al. 1965; **19**, Gallo and Lawryk 1991; **20**, Eto 1974; **21**, Teel et al. 1977; **22**, Ivey et al. 1976; **23**, Nordkvist 1975; **24**, Black et al. 1979; **25**, Smith and Goulding 1970.

19.5 RECOMMENDATIONS

The four primary areas of concern about famphur use are:

1. Mortality of birds associated with topical applications to cattle
2. Latent effects on domestic livestock
3. The absence of aquatic toxicity data
4. Potential carcinogenicity

Because of its high toxicity to birds and field and experimental evidence of primary and secondary poisoning of birds, famphur is considered hazardous to avian wildlife — especially magpies — where cattle are topically treated with this insecticide (Felton et al. 1981; Henny et al. 1985, 1987). The pour-on application for cattle is now preferred to systematic dipping or intramuscular injection; dipping is reportedly labor intensive and costly (Hair et al. 1979). Intramuscular injection is more labor intensive, causes greater tissue damage and higher famphur absorption at the injection site, and produces a greater depression in blood cholinesterase levels and a lower rate of weight gain in cattle than pour-on application (Loomis and Schock 1978). Nevertheless, famphur-induced mortality of magpies and other birds can be significantly reduced or eliminated by changing the insecticide application from the present pour-on method to other, now-available modes of administration such as by diets, bolus, and intramuscular injection (Henny et al. 1985, 1987). Furthermore, a warning should be added to famphur labels; livestock dying within 3 months of famphur treatment should be removed from the range or farmland; this would offer partial protection to carrion-feeding raptors such as eagles and vultures (Henny et al. 1987).

Reindeer are considered safe for human consumption 6 to 7 weeks after famphur treatment by intramuscular injection (dermal applications of famphur seldom penetrate the thick hair coat of reindeer). Treated reindeer had no detectable residues in liver, kidney, and muscle after 3 weeks (Ivey et al. 1976) and none in fat and other tissues after 6 to 7 weeks (Nordkvist 1975; Ivey et al. 1976). However, treated hinds during the following year had a significantly altered blood chemistry profile when compared to untreated hinds (Nieminen et al. 1980), suggesting a need for additional research on latent effects of famphur exposure. A safe dosage for cattle (*Bos* spp.) is 7 to 25 mg/kg BW by intramuscular injection or 40 to 55 mg/kg BW by pour-on (Loomis and Schock 1978). The maximum concentration of famphur and famoxon allowed in cattle meat, fat, and meat by-products in the United States is 0.1 mg/kg (Kaemmerer and Buntenkotter 1973; Ryan and McLeod 1979). In Australia, the maximum value is 0.05 mg/kg FW (Annand et al. 1976). The recommended minimum time between famphur treatment and slaughter of Australian cattle is 14 days. The half-time persistence of famphur in cattle tissues is 0.9 days, implying that even with gross misuse of the chemical, residues fall to low levels within a week (Annand et al. 1970). At present, no published studies are available on the latent effects of famphur to cattle. Evidence of latent effects of famphur in reindeer (Nieminen et al. 1980) strongly suggest initiation of research into this subject area with cattle and other treated livestock.

No published data were available on effects and fate of famphur in aquatic ecosystems. This seems to be a high-priority research need in view of the increasing and illegal use of famphur to kill migratory waterfowl (White et al. 1989). In the absence of these data, it is recommended that concentrations of famphur and famoxon in water and in tissues of aquatic organisms not exceed current analytical detection limits of 0.005 mg/L in water or 0.01 mg/kg FW tissue.

The carcinogenicity of famphur has not been satisfactorily resolved. Studies indicate a significantly elevated risk for leukemias among farmers handling famphur (Brown et al. 1990), but this needs verification.

19.6 SUMMARY

Famphur (phosphorothioic acid, *O*-[4-[(dimethylamino)sulfonyl], phenyl] *O,O*-dimethyl ester), also known as Warbex, is a systemic organophosphorus insecticide used almost exclusively as a veterinary chemical to control parasites in livestock. Famphur has proven effective in controlling maggots of the botfly and warble fly (*Hypoderma* spp.), lice (*Haematopinus* spp., *Linognathus* spp.), hornfly (*Haematobia* spp.), reindeer warble fly (*Oedemogena* spp.), reindeer nostril fly (*Cephanomyia* spp.), and mealworms (*Alphitobius* spp.). The LD₅₀ values for target insects ranged from 2.4 to 4.1 mg/kg body weight (BW) from a dermal route and 8.0 to 11.8 mg/kg BW from abdominal injection.

Only famphur and its oxygen analog, famoxon, were of toxicological significance. Other famphur metabolites were 31 to 237 times less toxic, as judged by acute oral toxicity tests in the mouse (*Mus* sp.). Famoxon was more effective than famphur in producing cholinesterase inhibition and death and confirms the generalization that the corresponding oxons are the more effective anticholinesterase agents. Differential toxicity of famphur to target pests and nontarget species was often associated with differential degradation and cholinesterase sensitivity.

Famphur is administered to livestock by intramuscular or subcutaneous injection, through the diet, as a dermal pour-on, or as an oral bolus. In mammals, famphur induced mortality at concentrations as low as 11.6 mg/kg BW in intraperitoneal injection (mouse), 27 mg/kg BW in a single oral exposure (mouse), >33.3 mg/kg BW in an intramuscular injection (Brahman cattle, *Bos indicus*), and 400 mg/kg BW in a dermal application (rat, *Rattus* sp.). Latent effects of famphur exposure were reported in reindeer (*Rangifer tarandus*) hinds 1 year posttreatment (altered blood chemistry). Famphur is rapidly metabolized by mammals. The half-time persistence of famphur and famoxon in subcutaneous fat of cattle after a single pour-on application is 0.9 days and is independent of dose between 25 and 150 mg/kg BW or initial tissue residues between 1.8 and 2.3 mg/kg BW.

Famphur has been used illegally by U.S. farmers to kill wild birds — including migratory waterfowl — thought to be depredating crops. Pour-on applications of famphur to cattle at recommended doses are sometimes associated with bird die-offs, especially the black-billed magpie (*Pica pica*). Magpie mortality — which persisted for 3 months — was probably associated with the lengthy persistence (>90 days) of famphur on cattle hair, and the ingestion of cattle hair by magpies. Cattle hair comprised as much as 12% of gizzard contents of dead magpies, and hair in the gizzards of dead magpies averaged 4600 mg famphur and famoxon/kg. Secondary poisoning of eagles and hawks foraging on famphur-killed vertebrates and tertiary poisoning of a great horned owl (*Bubo virginianus*) feeding on a famphur-poisoned hawk are documented. In the laboratory, sensitive species of birds died after single oral doses of 1.8 to 3.0 mg famphur/kg BW or when fed diets containing 35 to 49 mg famphur/kg ration. Depressed cholinesterase activity in the brain and in plasma occurred in nestlings at daily oral concentrations as low as 0.3 mg famphur/kg BW.

No published data were available on the fate or effects of famphur in aquatic ecosystems. In the absence of aquatic toxicity data on famphur, it is recommended that famphur and famoxon concentrations do not exceed the analytical detection limits of these compounds in water (0.005 mg/L) or in tissues of aquatic organisms (<0.01 mg/kg fresh weight).

Current recommendations include the discontinuance of topical applications of famphur to cattle because of its association with primary and secondary poisoning of birds — especially magpies, hawks, and eagles — and more research on famphur in the three areas of latent effects on treated livestock, fate and effects in aquatic ecosystems, and carcinogenicity evaluation.

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CHAPTER 20

Fenvalerate

20.1 INTRODUCTION

Synthetic pyrethroids, including fenvalerate [(*RS*) α -cyano-3-phenoxybenzyl (*RS*) 2-(4-chlorophenyl)-3-methylbutyrate]^{*}, are broadly recognized as a major class of synthetic organic insecticides (Gray and Soderlund 1985). Introduced commercially less than 40 years ago, synthetic pyrethroids now account for more than 30% of insecticide use worldwide (Flannigan et al. 1985; Gilbert et al. 1989), in household, agricultural, and veterinary applications (Haya 1989; Williamson et al. 1989). More than 1000 pyrethroids have been synthesized since 1973 (Flannigan et al. 1985). They include compounds containing nitrogen, sulfur, fluorine, chlorine, and bromine, in addition to carbon, hydrogen, and oxygen (Glickman and Casida 1982). The most potent synthetic pyrethroid insecticides are the cyanophenoxybenzyl pyrethroids (Casida and Lawrence 1985); and fenvalerate is the most widely used compound in this group (Clark et al. 1985).

Pyrethroid insecticides are synthetic analogs of natural pyrethrins. Natural pyrethrins were widely used in Europe during the 19th century when few effective insecticides were available (Elliott and Janes 1978). Natural pyrethrins, which contain six insecticidally active components extracted from the dried heads of the pyrethrum flower (*Chrysanthemum cinariaefolium*), have high insecticidal properties and low mammalian toxicity. However, they are expensive to produce and have low photostability and high biodegradability (Wouters and Bercken 1978; Gray and Soderlund 1985; Haya 1989; Williamson et al. 1989). Modern synthetic pyrethroids have been designed to provide enhanced residual activity through greater photostability and greater resistance to chemical and biological degradation, greater insecticidal activity, diminished mammalian toxicity, and greater cost effectiveness (Elliott and Janes 1978; Vijverberg and Bercken 1982; Gray and Soderlund 1985; Smith and Stratton 1986; Coats et al. 1989; Haya 1989). The first synthetic pyrethroids — allethrin and cycloethrin — were produced around 1950, but lacked adequate photostability and were not as effective insecticidally as the natural pyrethrins. Tetramethrin was introduced in 1964, but it had inferior insecticidal activity. The first synthetic pyrethroids with greater insecticidal activity than natural pyrethrins were resmethrin and cismethrin, produced in 1968. Photostable pyrethroids were produced in the mid-1970s and included deltamethrin, cypermethrin, fenpropathrion, and fenvalerate (Smith and Stratton 1986).

Pyrethroid insecticides are generally recognized as potent neurotoxicants that interfere with nerve membrane function by interaction with the sodium channel (Elliott and Janes 1978; Vijverberg et al. 1982; Gilbert et al. 1989; Haya 1989). Synthetic pyrethroids are more toxic against insect pests, up to 10 times more potent in some cases, than other insecticides now in general use (Bradbury

* The technical fenvalerate formulation is no longer being manufactured by the Dupont Company, although existing stocks may be used until exhausted. The new fenvalerate formulation is sold as Asana or Esfenvalerate, and contains only the 2S, α S isomer (A. Stavola, U.S. Environmental Protection Agency, personal communication, January 28, 1991).

and Coats 1989a). However, the stereochemical structure of pyrethroid insecticides greatly influences their toxicity to insects and mammals, and this phenomenon is especially pronounced for fenvalerate (Bradbury et al. 1987b).

As broad-spectrum insecticides, the synthetic pyrethroids are necessarily toxic to a wide range of arthropods. Most insect orders are extremely susceptible, including many types of beneficial predator and parasite species (Bradbury and Coats 1989a). Synthetic pyrethroids are also toxic to fish and nontarget aquatic insects and crustaceans (Muir et al. 1985). Fenvalerate, for example, enters freshwater aquatic environments in runoff from food crop use, in drift from forest-spray procedures, and by direct spraying of water bodies (Haya 1989). Estuarine organisms may be exposed to fenvalerate and other pyrethroids after applications to corn, cotton, rice, and vegetables in coastal areas or by discharges from pyrethroid manufacturers or formulating and distribution centers (Clark et al. 1989). Fenvalerate has been implicated in kills of coastal organisms in South Carolina, primarily from agricultural runoff into estuarine tidal creeks (Scott et al. 1987).

Detailed information on ecological and toxicological aspects of fenvalerate and other synthetic pyrethroid insecticides is provided in reviews by Elliott (1977), Elliott and Janes (1978), Wouters and Bercken (1978), Glickman and Casida (1982), Vijverberg and Bercken (1982), Gray and Soderlund (1985), Leahey (1985), Smith and Stratton (1986), Coats et al. (1989), Bradbury and Coats (1989a), and Eisler (1992).

20.2 ENVIRONMENTAL CHEMISTRY

20.2.1 General

Synthetic pyrethroids now account for at least 30% of the world insecticide market and are rapidly replacing other agricultural chemicals for control of insect pests. Fenvalerate is one of the more widely used synthetic pyrethroid insecticides. It is derived from a combination of α -cyano-3-phenoxybenzyl alcohol and α -isopropyl phenylacetate ester. Technical fenvalerate is a mixture of four optical isomers, each occurring in equal amounts but with different efficacies against insect pests. Fenvalerate does not usually persist in the environment for >10 weeks, and it does not accumulate readily in the biosphere. Time for 50% loss (T_b 1/2) in fenvalerate-exposed amphibians, birds, and mammals was 6 to 14 h; for reptiles, terrestrial insects, aquatic snails, and fish it was >14 h to <2 days; and for various species of crop plants, it was 2 to 28 days. Fenvalerate degradation in water is due primarily to photoactivity, and in soils to microbial activity. Half-time persistence in nonbiological materials is variable, but may range up to 6 days in freshwater, 34 days in seawater, 6 weeks in estuarine sediments, and 9 weeks in soils.

20.2.2 Chemical Properties

Synthetic pyrethroid insecticides are photostable analogs of the natural pyrethrins of botanical origin. They consist of a series of related esters derived from alcohols and acids that maintain critical isosteric relations with the natural product prototype (Glickman and Casida 1982; Bradbury and Coats 1989a). Small changes in substituents and stereochemistry are sufficient to produce compounds differing in their insecticidal potency, spectrum of activity, and mammalian toxicology (Gray and Soderlund 1985). These halogenated, lipophilic, photostable compounds are exceptionally active against many species of insects. Although these compounds are relatively safe to birds and mammals, they are usually extremely toxic to certain freshwater and marine groups, including fish (Leahey 1985; Coats et al. 1989).

The first significant success in creating a photostabilized pyrethroid with high insecticidal activity was achieved through use of the 3-phenoxybenzyl alcohol moiety. A further step was the finding that 2-aryl-3-methylbutyric acid esters of pyrethroid alcohols were both photostable and

Table 20.1 Chemical and Other Properties of Fenvalerate^a

Variable	Data
Chemical name	(RS)- α -cyano-3-phenoxybenzyl(RS)-2-(4-chlorophenyl)-3-methylbutyrate; cyano(3-phenoxyphenyl) methyl 4-chloro- α -(1-methylethyl) benzeneacetate; α -cyano-3-phenoxybenzyl 2-(4-chlorophenyl)-3-methylbutyrate; 4-chloro- α -(1-methylethyl) benzeneacetic acid cyano(3-phenoxyphenyl) methyl ester; α -cyano-3-phenoxybenzyl α -(4-chlorophenyl) isovalerate
Alternate names	Agmatrin, Belmark, Ectrin, Fenkill, Phenvalerate, Pydrin, S-5602, Sanmarton, SD 43775, Sumicidin, Sumifly, Sumipower, Sumitox, WL 43775
CAS Number	51630-58-1
Chemical formula	C ₂₅ H ₂₂ CINO ₃
Molecular weight	419.92
Physical state	Clear yellow, viscous, liquid at 23°C
Purity	Technical grade compound is about 92% pure; nature and extent of impurities unknown
Vapor pressure at 25°C	1.1 × 10 ⁻⁸ mm mercury
Density at 23°C	1.17 g/mL
Stability	Stable in most solvents except alcohols at ambient temperature. Unstable in alkaline media. No significant breakdown after 100 h at 75°C; gradual degradation occurred in range 150–300°C
Degradation	Cleavage of the ester linkage is the primary route
Formulations	Emulsifiable concentrate, dust, granules, wettable powder
Log K _{ow}	6.2
Solubility at 20°C	
Acetone	>450 g/L
Chloroform	>450 g/L
Methanol	>450 g/L
Hexane	77 g/L
Water	2–85 µg/L
Seawater	24 µg/L

Data from Elliott 1977; Coats and O'Donnell-Jefferey 1979; Reed 1981; Tagatz and Ivey 1981; Akhtar 1983; Schimmel et al. 1983; Windholtz et al. 1983; Clark et al. 1987, 1989; Crofton and Reiter 1988; Sine 1988.

insecticidal (Gray and Soderlund 1985). Fenvalerate is one of the more recently developed and widely used synthetic pyrethroid insecticides, and it is a highly active phenylacetate ester of known pyrethroid alcohols, specifically, a combination of α -isopropyl phenyl acetate ester and α -cyano-3-phenoxybenzyl alcohol (Wouters and Bercken 1978). The phenoxybenzyl group and the halogenated phenyl ring increase the photostability of the molecule. The cyano group, substituted on the benzylic carbon, stabilizes the ester bond against hydrolysis (Coats et al. 1989).

Fenvalerate, like most other synthetic pyrethroids, is a halogenated, lipophilic, stable compound with low solubility in water and high solubility in organic solvents (Table 20.1). Technical fenvalerate is a racemic mixture of four isomers, composed of equal amounts of dextrorotatory and levorotatory forms. However, the four optical isomers (Figure 20.1) have very different efficacies against pest species. In general, fenvalerate stereoisomers with *S*-configurations in both the acid and alcohol moieties are more active pharmacologically and toxicologically than those with *R*-configurations (Wouters and Bercken 1978). Fenvalerate can be isolated and concentrated from pond water and other solutions using solid-phase extraction, and analyzed to 1.0 µg/L on a capillary gas chromatograph equipped with an electron-capture or flame photometric detector (Swineford and Belisle 1989).

20.2.3 Uses

Pyrethroids are used primarily for the control of household and agricultural insect pests, and secondarily in industrial, stored product, and veterinary applications. They are especially advantageous for use in northern climates because their toxicity is enhanced at low temperatures (Smith and Stratton 1986). Synthetic pyrethroid insecticides, including fenvalerate, are used as alternatives

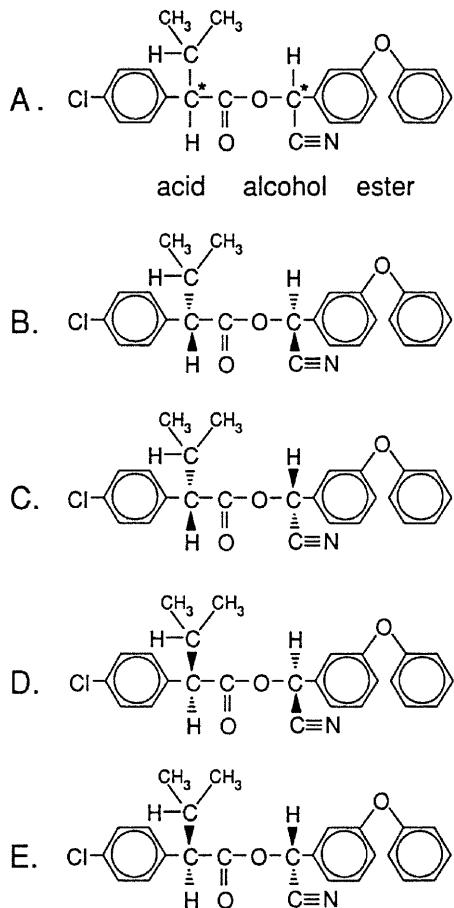


Figure 20.1 Fenvalerate and its isomers (Ohkawa et al. 1979; Hill 1981; Kaneko et al. 1981, 1986; Vijverberg and Bercken 1982; Miyamoto et al. 1986; Bradbury et al. 1987; Bradbury and Coats 1989a, 1989b; Coats et al. 1989). **A.** Chemical structure of fenvalerate denoting two asymmetric carbon atoms (*): the 2C position of the acid moiety, and the αC position of the α-cyano-3-phenoxybenzyl alcohol moiety. These two chiral centers, at the 2C and αC positions, yield a mixture of four stereoisomers, in approximately equal amounts, but with greatly different biological properties. **B.** (2S)-α-cyano-3-phenoxybenzyl (αS)-2-(4-chlorophenyl)-3-methylbutyrate. The 2S,αS-isomer is extremely toxic to insects, and is the most active form of fenvalerate. **C.** (2S)-α-cyano-3-phenoxybenzyl (αR)-2-(4-chlorophenyl)-3-methylbutyrate. The 2S,αR-isomer has markedly reduced insecticidal activity when compared with the 2S,αS-isomer, but is greatly elevated in this respect when compared with fenvalerate stereoisomers with an *R* configuration in the acid moiety, that is, the 2R,αS- and the 2R,αR-isomers. **D.** The 2R,αS-isomer is the only fenvalerate isomer that caused granulomatous changes in liver, spleen, and mesenteric lymph node in rodents. **E.** The 2R,αR-isomer has greatly reduced biological and toxicological properties when compared with other fenvalerate isomers. Isomers with an *R* configuration in the acid moiety degraded slightly faster than the insecticidally active 2S,αS- and 2S,αR-isomers.

to organochlorine, organophosphorus, carbamate, and natural pyrethrum insecticides because they are highly toxic to insect pests, low to intermediate in persistence, and low in toxicity to warm-blooded organisms, although extremely toxic to many aquatic organisms (Hansen et al. 1983; Coats et al. 1989). By 1982, more than 30% of the world market for insecticides consisted of synthetic pyrethroids, and this percentage is increasing (Smith and Stratton 1986).

Outside of the United States, fenvalerate is used on cotton (*Gossypium hirsutum*) in Australia, Greece, and South Africa, and on apples (*Malus* sp.), pears (*Pyrus* sp.), and potatoes (*Solanum* sp., *Ipomea* sp.) in Canada (Reed 1981); uses in other countries, including Mexico, are anticipated (Reed 1981), as is increased use against agricultural, poultry, dairy, and household pests (Mumtaz

and Menzer 1986). In agricultural use, recommended application rates of fenvalerate range between 0.055 and 0.224 kg/ha for control of a broad spectrum of pestiferous insects (Bennett et al. 1983).

Domestically, about 6500 kg fenvalerate were used in 1979; all of this amount was imported (Reed 1981). In 1980, in addition to registered use, the U.S. Environmental Protection Agency (USEPA) allowed an additional 80,000 kg for crisis and experimental use (Reed 1981). By 1981, fenvalerate had been registered for domestic use on apples, cotton, peanuts (*Arachis* sp.), pears, and potatoes. Additional uses were allowed under various experimental or crisis exemptions on beans (*Phaseolus* spp.), peppers (*Piper* spp.), broccoli, cabbage, cauliflower (*Brassica* spp.), celery (*Apium* sp.), corn (*Zea mays*), cucumbers (*Cucumis* sp.), eggplant (*Solanum melongena*), grapes (*Vitis* spp.), lettuce (*Lactuca* sp.), peas (*Pisum* sp.), squash (*Cucurbita* spp.), and tomatoes (*Lycopersicon esculentum*) (Reed 1981). By 1989, this list was expanded to include tobacco (*Nicotiana tabacum*), soybeans (*Glycine max*), sugarcane (*Saccharum* sp.), a wide variety of nuts, fruits, and vegetables, pine seed orchards, forest tree nurseries, mosquitoes, biting insects, insect vectors of disease, mite control in poultry, and fly and tick control in cattle (Spehar et al. 1982; Akhtar 1983; Bennett et al. 1983; Hansen et al. 1983; Sine 1988; Clark et al. 1989; Smith et al. 1989).

The delivery vehicle of fenvalerate-containing insecticide may account for wide variations in toxic action. For example, fenvalerate microcapsules used to control caterpillar pests (*Plutella xylostella*, *Spodoptera litura*) were most effective with thin-walled capsules and small particles. However, significant protection to nontarget organisms, such as fish, occurred with thicker-walled capsules and larger particles (Ohtsubo et al. 1989). The popularity of commercial synthetic pyrethroids and their widespread replacement of older, more-toxic compounds in various settings mandates a thorough understanding of the formulation used and of the active and inert components (Williamson et al. 1989).

20.2.4 Persistence

In nonbiological samples, half-time persistence of fenvalerate is variable, but frequently ranged between 2 and 6 days in freshwater, between 27 and 34 days in seawater, between 3 and 9 weeks in soils, and up to 6 weeks in estuarine sediments (Table 20.2). Persistence was longer at higher initial application rates and under conditions of reduced light, low microbial activity, and high organic content (Table 20.2). Fenvalerate is not readily transported from upland field application sites into the aquatic environment. Fenvalerate that directly enters the aquatic environment by way of runoff has limited bioavailability to aquatic organisms, owing to rapid adsorption onto soil particles, organic matter, or plants, and to chemical hydrolysis and photodecomposition (Ohkawa et al. 1980). Under acidic conditions, fenvalerate in water is stable to hydrolysis for 100 h at 75°C; Tb 1/2 at elevated recommended application rates is about 21 days, primarily as a result of photo-degradation (Reed 1981).

Fenvalerate is one of the more persistent synthetic pyrethroids in soils (Klaassen et al. 1986). In agricultural soils, fenvalerate is tightly adsorbed to soil particles, does not easily move laterally or to lower soil layers with groundwater, and almost always localizes in the application site because of its extremely low solubility in water (Ohkawa et al. 1980; Hill 1981; Miyamoto 1988). Fenvalerate degradation rates from mineral soil surfaces are dependent on soil type, moisture, temperature, and microbial activity. Half-time persistence in soils usually ranged between 2 and 18 days, but 3 months has also been recorded (Harris et al. 1981; Reed 1981; Bennett et al. 1986). Although fenvalerate is susceptible to chemical degradation by hydrolysis and oxidation, most authorities agree that degradation in soils is due primarily to microbial activity, that microbial degradation is most rapid under aerobic conditions, and that transformed products do not persist longer than the parent compound (Ohkawa et al. 1980; Chapman et al. 1981; Bennett et al. 1986).

In biological samples, fenvalerate neither persists for lengthy periods nor is readily accumulated (Smith and Stratton 1986; Cooper 1991). In general, fenvalerate is rapidly (i.e., Tb 1/2 of 6 to 14 h) excreted by amphibians, birds, and mammals; has low persistence in various reptiles, terrestrial

Table 20.2 Fenvvalerate Persistence in Water, Sediments, and Soils

Sample and Other Variables	Persistence	Reference ^a
FRESHWATER		
Various concentrations	Half-time persistence (Tb 1/2) of 3.2 days (range 1.9–5.8 days); longer for higher initial doses	1
0.1 µg/L	Tb 1/2 of 4.1 days; 90% loss in 13.5 days	11
3.9 µg/L	Maximum concentration was 2.3 µg/L 48 h after application; at 168 h it was 0.6 µg/L	1
8.3 µg/L	Concentration declined from 5.3 µg/L at 24 h to 1.8 µg/L at 168 h	1
16.5 µg/L	Concentration declined from 17.6 µg/L at 24 h to 9.1 µg/L at 168 h	1
30.6 µg/L	Concentration declined from 54.4 µg/L at 24 h to 21.2 µg/L at 168 h	1
SEAWATER	Tb 1/2 of 8 days in light, >14 days in dark; 27–34 days under alternating light and dark	2, 3
ESTUARINE SEDIMENTS		
Sterilized	No degradation in 28 days	2
Natural "Low" concentrations	Tb 1/2 of 4.5–9 days	1, 3
"Various" concentrations	Tb 1/2 of 24–42 days	2, 4–6
0.1–10 mg/kg dry weight (DW)	73% loss in 8 weeks at initial nominal concentration of 0.1 mg/kg DW, 78% at 1.0 mg/kg, and 96% loss in 8 weeks at 10 mg/kg DW	4
SOILS		
Initial concentration of 1.0 mg/kg DW soil		
Natural mineral, pH 8.0–8.1	12% remaining after 8 weeks; about 5% after 16 weeks	7
Sterilized mineral, pH 7.7–8.1	91% remaining after 8 weeks, 87% after 16 weeks	7
Natural organic, pH 7.1–7.2	58% remaining at 8 weeks, about 32% after 16 weeks	7
Sterilized organic, pH 6.5–6.9	100% remaining after 16 weeks	7
Various (clay, silt, sand), dose unknown	Tb 1/2 of 22–40 h	8
Mineral soils, dose unknown	Tb 1/2 of 6 weeks	9
Moist sand, dose unknown	Tb 1/2 of 9 weeks; 88% loss in 48 weeks	9
Lethbridge surface soil, agricultural, British Columbia		
Field conditions, initial application of 150 g/ha	Tb 1/2 of 6 weeks; 89% loss in 45 weeks	10
Laboratory study, 70 g/ha equivalent	Tb 1/2 of 5.2 weeks	10

^a 1, Coulon 1982; 2, Schimmel et al. 1983; 3, Smith and Stratton 1986; 4, Tagatz et al. 1987; 5, Tagatz and Ivey 1981; 6, Hansen et al. 1983; 7, Chapman et al. 1981; 8, Muir et al. 1985; 9, Harris et al. 1981; 10, Hill 1981; 11, Day et al. 1987.

insects, aquatic snails, and fish; and has moderate (i.e., Tb 1/2 of 2 to 28 days) persistence in various species of target plants (Reed 1981; Mumtaz and Menzer 1986; Bradbury and Coats 1989a, 1989b; Muir et al. 1994) (Table 20.3). Animals collected after 5 days from a cotton field sprayed with 0.112 kg/ha, or from the immediate vicinity, had very low fenvvalerate residues (Table 20.3) (Bennett et al. 1983). In that study fenvvalerate was detected in one of nine bird species sampled, in one of four mammals, in the western ribbon snake (*Thamnophis* sp.), in one of four amphibian species, and in fish and insects. The bird was a male dickcissel (*Spiza americana*) that had established a breeding territory within the sprayed cotton field. Carnivorous ground beetles, found moribund on the ground, contained the highest mean fenvvalerate residue of 0.55 mg/kg fresh weight (FW) whole body; large numbers of dead insects were found in the fields during collection. The highest residues (0.32 to 0.55 mg/kg) in fish and invertebrates were in those collected from a small pool in a drainage ditch, which compares with 0.92 mg/kg found in common carp (*Cyprinus carpio*) after exposure in the laboratory for 7 days to 0.8 µg fenvvalerate/L (Bennett et al. 1983).

Fenvalerate is not significantly absorbed or translocated in plants. Cotton, apples, and lettuce treated with fenvalerate contained surface residues of parent fenvalerate 8 weeks after treatment (Reed 1981). In addition to the parent compound, which accounted for 80% of all residues, identified metabolites included 3-phenoxybenzaldehyde, 3-phenoxybenzyl methylbutyric acid, and conjugates of these compounds. Half-time persistence of fenvalerate on plant surfaces is between 2 and 4 weeks, and degradation is primarily a result of weathering (Reed 1981).

Various plants sprayed with 0.25 kg fenvalerate/ha all had measurable residues 7 days after application, and nondetectable residues 15 to 30 days after treatment (Jain et al. 1979). Washing plants in cold water to remove the pesticide was effective only on the initial day of application, removing 30 to 50%. Afterward, only 3 to 13% could be removed by washing. Cooking removed 71 to 88% of the fenvalerate residues on the initial day of treatment; but in later samplings, removal was 68 to 70% in spinach (*Spinacea oleracea*) and tomatoes, and 38 to 40% in okra (*Abelmoschus esculentus*) and cauliflower (*Brassica oleracea botrytis*) (Jain et al. 1979).

Adsorption and persistence in plants can be modified by other chemicals or by selected carriers, although mechanisms to account for these phenomena are unclear. The application mixture influences adsorption and persistence of fenvalerate. For example, interception and persistence in sugarcane were increased when fenvalerate was applied in a 25% water/75% soybean oil mixture vs. water or soybean oil alone (Smith et al. 1989). Also, biocidal properties of fenvalerate residues on cotton foliage were increased up to 100% due to enhanced persistence of fenvalerate in the presence of toxaphene (Brown et al. 1982).

Fenvalerate photoproducts merit consideration, as some may be comparatively toxic. Decarboxyfenvalerate is a major degradation product of fenvalerate that is formed by photochemical reactions in water and on plant foliage (Mikami et al. 1985). This photoproduct comprises up to 10% of the total residues in forage crops that have been exposed to prolonged sunlight and drying. Decarboxyfenvalerate did not persist in tissues of hens, rats, and cows when consumed with feed for extended periods; its residue levels in ova, milk, and meat were negligible (Mikami et al. 1985).

Photolysis of fenvalerate in various solvents by sunlight yields products resulting from ester cleavage, primarily decarboxyfenvalerate, but also 15 other products. All sunlight photoproducts were relatively harmless to mice; LD₅₀ values were >500 mg/kg body weight (Holmstead et al. 1978). When photolysis was by way of ultraviolet light, however, two of the photoproducts formed (3-phenoxybenzoyl cyanide and 3-phenoxybenzyl cyanide) were considerably more toxic than fenvalerate. LD₅₀ values for intraperitoneal injection in mice were >500 mg/kg BW for fenvalerate, 2 mg/kg BW for 3-phenoxybenzoyl cyanide, and 105 mg/kg BW for 3-phenoxybenzyl cyanide (Holmstead et al. 1978). This finding strongly suggests a need for additional research on fenvalerate photoproduct persistence and toxicity.

Table 20.3 Fenvalerate Persistence in Plants and Animals under Field Conditions

Sample and Other Variables	Persistence	Reference ^a
Alfalfa, <i>Medicago sativa</i>	Half-time persistence (Tb 1/2) of 9–11 days	1
Cotton (<i>Gossypium hirsutum</i>) treated with 0.224 kg/ha, residues on foliage 12 days later		
In combination with 2.24 kg/ha toxaphene	Fenvalerate residues were 11.6 mg/kg	2
Fenvalerate alone	Residues were 5.9 mg/kg	2
Cotton, foliage	Tb 1/2 of 2 days, 96% lost in 17 days	3, 7
Cotton field sprayed with 0.112 kg/ha (0.1 pound/acre), Garland, Arkansas, July 1979. Animals collected from field 5 days later		
Mammals		
Deer mouse, <i>Peromyscus maniculatus</i> ; white-footed mouse, <i>P. leucopus</i> ; cotton rat, <i>Sigmodon hispidus</i>	<0.01 mg/kg whole-body fresh weight (FW), less skin and GI tract	3
House mouse, <i>Mus musculus</i>	0.01 mg/kg whole-body FW, less skin and GI tract	3

Table 20.3 (continued) Fenvalerate Persistence in Plants and Animals under Field Conditions

Sample and Other Variables	Persistence	Reference^a
Birds		
Cardinal, <i>Richmondena cardinalis</i> ; red-winged blackbird, <i>Agelaius phoeniceus</i> ; meadowlark, <i>Sturnella magna</i> ; brown-headed cowbird, <i>Molothrus ater</i> ; purple martin, <i>Progne subis subis</i> ; horned lark, <i>Eremophila alpestris</i> ; little blue heron, <i>Florida coerulea</i> ; green heron, <i>Butorides virescens</i>	<0.01 mg/kg whole-body FW, less skin and GI tract	3
Dickcissel, <i>Spiza americana</i>	0.02 mg/kg whole-body FW, less skin and GI tract	3
Reptiles		
Western ribbon snake, <i>Thamnophis proximus</i>	0.12 mg/kg whole-body FW, less skin and GI tract	3
Animals collected from location near cotton field 5 days later		
Insects		
Cicada, Cicadidae	<0.01 mg/kg FW whole body	3
Short-horned Acrididae	0.18–0.24 mg/kg FW whole body	3
Ground beetle, <i>Calosoma</i> sp.	0.55 mg/kg FW whole body	3
Molluscs		
Aquatic snail, unidentified	0.53 mg/kg FW soft parts	3
Fish		
Mosquitofish, <i>Gambusia affinis</i>	0.3 mg/kg FW whole body	3
Golden shiner, <i>Notemigonus crysoleucas</i>	0.47 mg/kg FW whole body	3
Amphibians		
Southern leopard frog, <i>Rana utricularia</i> ; green frog, <i>Rana clamitans</i> ; green treefrog, <i>Hyla cinerea</i>	<0.01 mg/kg FW whole body, less skin and GI tract	3
Fowler's toad, <i>Bufo fowleri</i>	0.02 mg/kg FW whole body, less skin and GI tract	3
Old field site, Iowa, 0.112 kg/ha (0.1 pound/acre) applied on June 9, 1980, and again on August 5, 1980, June 10, 1981, and July 21, 1981		
Vegetation	Maximum immediately after each application was 12.1 mg/kg FW; residues after 24 days were always <1 mg/kg FW	1
Short-horned grasshopper, whole		
Applied June 9, 1980	Residues were 0.03 mg/kg FW after 36 days, and nondetectable (ND) in 49 days	1
Applied August 5, 1980	Residues were 0.33 mg/kg FW after 7 days, 0.19 after 14 days, and 0.12 after 21 days	1
Ground beetles, Carabidae, whole		
Applied June 1980	After 10 days, beetles contained 0.12 mg/kg FW; after 17 days, residues were ND	1
Applied August 5, 1980	After 6 days, residues were 0.14 mg/kg FW, and ND in 17 days	1
Applied July 21, 1981	Maximum residue after 24 days was 0.15 mg/kg FW	1
Deer mice, <i>Peromyscus maniculatus</i> , whole		
Applied July 21, 1988	Residues were 0.1 mg/kg FW after 2 days, and 0.01 after 21 days	1
Meadow vole, <i>Microtus pennsylvanicus</i> , whole		
Applied July 21, 1988	Residues were variable: 0.07 mg/kg FW after 2 days, 0.12 after 4 days, 0.46 after 8 days, and 0.04 after 21 days	1
Plants, 4 species, sprayed with 0.05% emulsifiable concentrate equivalent to 0.25 kg/ha		
Okra, <i>Abelmoschus esculentus</i> , initial concentration of 4 mg/kg FW	After 5 days, residue was 1.6 mg/kg FW, after 7 days it was 0.8, and after 15 days it was ND	4

Table 20.3 (continued) Fenvalerate Persistence in Plants and Animals under Field Conditions

Sample and Other Variables	Persistence	Reference ^a
Cauliflower, <i>Brassica oleracea botrytis</i> , initial deposit of 0.86 mg/kg FW	Initial deposit degraded to 0.3 mg/kg in 7 days, and was ND in 15 days	4
Tomato, <i>Lycopersicon esculentum</i> , initial residue of 0.85 mg/kg FW	Initial residue degraded to 0.67 mg/kg in 5 days, 0.3 in 15 days, and ND in 30 days	4
Spinach, <i>Spinacea oleracea</i> , initial residue of 9.5 mg/kg FW	Initial residue degraded to 2.8 mg/kg in 15 days, and ND in 30 days	4
Plants, various, foliage	Mean Tb 1/2 of 8.2 days, range 2.8–14 days	6
Bean, <i>Phaseolus</i> , sp.	Tb 1/2 of 14 days, essentially no translocation from leaf surface	1
Sugarcane, <i>Saccharum officinarum</i>, initial residue immediately after application was 18.8–28.2 mg/kg dry weight leaf	Residues after 7 days were 2.1–5.4 mg/kg DW; Tb 1/2 of 2.2–2.4 days	5

^a 1, Bennett et al. 1986; 2, Brown et al. 1982; 3, Bennett et al. 1983; 4, Jain et al. 1979; 5, Smith et al. 1989; 6, Willis and McDowell 1987; 7, Buck et al. 1980.

20.3 MODE OF ACTION

20.3.1 General

Two types of synthetic pyrethroids have been identified, as judged by different behavioral, neurophysiological, chemical, and biochemical profiles:

- Type I: those pyrethroids lacking the α -cyano group
- Type II: those possessing the α -cyano group (i.e., fenvalerate)

Induction of repetitive activity in the nervous system is the principal effect of pyrethroids. Repetitive activity originates from a prolongation of the transient increase in sodium permeability of the nerve membrane associated with excitation. All pyrethroids affect sodium channel gating in a similar manner, although Type II pyrethroids are significantly more neurotoxic than Type I pyrethroids.

Metabolism of fenvalerate proceeds by way of oxidation and hydrolysis to produce metabolites considered pharmacologically inactive or inferior to the parent compound. Insects and fish are extremely susceptible to fenvalerate when compared to mammals and birds. Interspecies differences are associated with rates of metabolism, excretion, absorption, esterase activity, and neurosensitivity.

Fenvalerate is neither mutagenic nor teratogenic. Tumor-like growths in rodent tissues, however, were associated with the $2R,\alpha S$ isomer — heretofore believed innocuous — more specifically, with its cholesterol conjugate.

20.3.2 Types of Pyrethroids

Two distinct types of synthetic pyrethroids have been identified, as judged by different behavioral, neurophysiological, chemical, and biochemical profiles in rodents (Wouters and Bercken 1978; Verschoyle and Aldridge 1980; Glickman and Casida 1982; Gray 1985; Gray and Soderlund 1985; Klaassen et al. 1986; Crofton and Reiter 1988; Bradbury and Coats 1989a; Gilbert et al. 1989; Williamson et al. 1989):

- Type I, also known as Class 1, or T — for tremor
- Type II, also known as Class 2, or CS — for choreoathetosis/salivation

In general, these authorities agree that pyrethroids containing both a halogenated acid esterified with the α -cyano-3-phenoxybenzyl alcohol — such as fenvalerate, deltamethrin, and cyper-

methrin — produce the Type II poisoning syndrome, and that pyrethroids lacking either or both of these moieties (i.e., permethrin, resmethrin, cismethrin, allethrin, bromphenothrin, phenothrin, kadeithrin, and tetramethrin) tend to produce the Type I syndrome. Type I is characterized by sparring, aggressive behavior (in rats, but not mice), rapid onset of tremor in the extremities, increased body temperatures, and whole-body tremors. As toxicity progresses, mice show hyperactivity, whereas rats become prostrate and die with immediate onset of rigor mortis; in mice, death is often associated with spasmodic seizures. The Type I syndrome is very similar to that produced by *p,p'*-DDT. Type II is characterized by pawing and burrowing behavior, profuse salivation, a decrease in body temperature of rats (due partially to evaporation of saliva), tremors progressing to choreoathetosis (i.e., a sinuous, writhing movement), muscular contractions and seizures, and death. With repeated high doses sufficient to kill some rats, degenerative changes in sciatic and posteriad tibial nerves were observed. The same two types of pyrethroid actions are also evident among insects.

Regardless of route of administration, signs of fenvalerate poisoning in rodents were similar. Doses administered by intercerebroventricular injection of comparatively low concentrations were more toxic than higher doses given orally, or by intravenous or intraperitoneal injection, suggesting greater central nervous system involvement in Type II than in Type I poisoning. In fact, pyrethroids that produce the Type II syndrome — including fenvalerate — are 5 to 10 times more potent neurotoxicants than Type I pyrethroids, which suggests different sites of action in the central nervous system.

20.3.3 Sodium Gating Kinetics

Pyrethroids have an action at or near the sodium channel in the nerve, resulting in greatly altered ionic currents and disrupted nerve function through membrane depolarization. Based on studies with insects, crustaceans, frogs, and small mammals, there is general agreement that (Wouters and Bercken 1978; Gammon et al. 1981; Vijverberg and Bercken 1982; Vijverberg et al. 1982; Parker et al. 1984b; Flannigan et al. 1985; Gray and Soderlund 1985; Ruigt and Bercken 1986; Eells and Dubocovich 1988; Flodstrom et al. 1988; Clark and Brooks 1989; Gilbert et al. 1989; Holloway et al. 1989; Salgado et al. 1989; Theophilidis et al. 1997):

- The sodium channel in the nerve membrane is the major target site for all synthetic pyrethroid insecticides (and many other neurotoxicants)
- Synthetic pyrethroids prolong the transient increase in sodium permeability of the nerve membrane during excitation, resulting in spontaneous depolarization and repetitive discharges
- Persistent repetitive discharges lead to muscular fasciculations, acetylcholine depletion, and muscular weakness
- Effects are enhanced at lower temperatures
- α -cyano (Type II) pyrethroids are more potent neurotoxicants than noncyano (Type I) pyrethroids, differences in neurotoxic effects being attributed solely to the α -cyano substituent

Most authorities agree that fenvalerate was the most effective pyrethroid tested for inducing pronounced repetitive activity in nerve fibers and that the 2S, α S-isomer was up to 15 times more potent than other fenvalerate isomers. Pyrethroids induce the sodium channels to close more slowly than normal, resulting in a gradually decaying inward sodium current (called a tail current) after termination of membrane depolarization. Type I pyrethroids induce tail currents with time constants of decay in milliseconds, but Type II pyrethroids result in time constants of decay that are orders of magnitude longer and contain thousands of impulses, inducing a quickly reversible, frequency-dependent suppression of the action potential. Depolarization of axons by synthetic pyrethroids was most effective at low temperatures; the negative temperature dependence of the steady-state current seems to be due to the stabilizing effect of low temperature on the open-modified channel.

Myelinated nerves of vertebrates are thought to sequester the pyrethroid molecules, known to be soluble in the myelin sheath, thereby preventing a portion of their chemical effect on the nerve axon (Flannigan et al. 1985). Fenvalerate, unlike other α -cyano pyrethroids, had little effect on the electrophysiological function of single myelinated nerve fibers in the frog (*Rana esculenta*), suggesting that additional research is needed on mechanisms other than membrane sodium transport (Tippe 1987).

The role of calcium in pyrethroid interaction with nerve tissue is under active investigation. Fenvalerate affects calcium-ATPase enzyme and calmodulin-activated enzyme activities, such as phosphodiesterase (Flodstrom et al. 1988). Fenvalerate inhibits calcium uptake by nerve cord of crayfish (*Procambarus clarkii*) and axon of spiny lobster (*Panulirus japonicus*), an action that seems to be related to its lipophilic properties (Doherty et al. 1986). Fenvalerate enhances the calcium-dependent, potassium-stimulated release of norepinephrine from rat brain and could lead to an overall depletion of brain stores of this neurotransmitter, producing a convulsive state typical of Type II pyrethroid poisoning (Brooks and Clark 1987; Clark and Brooks 1989). Fenvalerate evoked a calcium-dependent release of dopamine and acetylcholine from rabbit brain that was concentration related and specific for the 2S, α S-isomer; release of dopamine and acetylcholine was antagonized completely by tetrodotoxin, a sodium channel blocker (Eells and Dubocovich 1988). The relatively low potency of fenvalerate and other Type II pyrethroids on potassium-stimulated calcium uptake in rat brain and other responses suggests that neither the sodium–calcium exchanger nor the voltage-dependent calcium channels are primary targets for pyrethroid toxicity (Ramadan et al. 1988).

Toxic isomers of Type II pyrethroids usually antagonize γ -aminobutyric acid (GABA) by interacting with the *t*-butyl-bicyclicphosphorothionate/picrotoxin binding site in brain; antagonism of GABA leads to a reduction in inhibition (Casida and Lawrence 1985). Fenvalerate seems to increase inhibition, however, and this may be explained by a differential effect on sodium channel kinetics (Gilbert et al. 1989). Fenvalerate also inhibits perhydrohistrionicotonin binding with electric organ membrane of the electric ray (*Torpedo* sp.) (Abassy et al. 1983) and interacts with binding sites for dihydropicrotoxin and kainic acid in the brain (Gammon et al. 1982), but the significance of these observations is unclear.

20.3.4 Metabolism

The most important metabolic degradation pathways for synthetic pyrethroids are oxidation on the phenoxy ring, hydrolysis of the ester linkage, and conjugation of metabolites. Rates and pathways differ among taxonomic animal groupings, resulting in large differences in sensitivity (Holmstead et al. 1978; Kaneko et al. 1981; Akhtar 1983; Miyamoto 1988; Bradbury and Coats 1989a).

All metabolic degradation products of fenvalerate are pharmacologically inactive or inferior to the parent compound, implying that metabolic modifications lead to detoxication (Miyamoto 1988). Fenvalerate and other α -cyano pyrethroids, however, are consistently more resistant to oxidative attack than their non-cyano analogs (Gray and Soderlund 1985). Liver is the predominant site of fenvalerate metabolism via hydrolysis by one or more hepatic microsomal esterases. Inhibition of these enzymes results in enhanced toxicity (Ghiasuddin and Soderlund 1984). Hydrolysis has also been demonstrated in plasma, kidney, stomach, and brain tissues. Except for brain, however, these tissues were relatively unimportant in the detoxification process (Ghiasuddin and Soderlund 1984; Gray and Soderlund 1985).

Metabolism of the 2S-isomers proceeds sequentially: hydroxylation at the phenoxy group, hydrolysis of the cyano group, and cleavage of the ester linkage (Coats et al. 1989). Fenvalerate and the 2S-isomers yield two ester metabolites in feces from hydroxylation at the 4'- and 2'-phenoxy positions. Other significant metabolites were 3-phenoxybenzoic acid and its hydroxy derivatives from the alcohol moiety, 3-(4-chlorophenyl) isovaleric acid and its hydroxy derivatives from the acid moiety, and thiocyanate and carbon dioxide from the cyano moiety (Ohkawa et al. 1979). A slow elimination rate characterizes fenvalerate and other α -cyano pyrethroids when compared with

non-cyano pyrethroids; it seems to be due to the release of the cyano group during ester cleavage, which is then incorporated into the body thiocyanate pool and retained in the skin and stomach (Gray and Soderlund 1989). Decarboxyfenvalerate, a photolysis product of fenvalerate, is present in water and on plant surfaces, but it is extensively hydroxylated in mammals, and excreted rapidly and completely into feces, with no apparent toxic effects (Miyamoto 1988).

Signs of fenvalerate intoxication are similar in birds, fish, mammals, and insects, but insects and fish are extremely sensitive when compared with warm-blooded organisms, frequently by one to three orders of magnitude (Bradbury and Coats 1989a,b). Increased resistance to fenvalerate and other synthetic pyrethroid insecticides in mammals and birds, when compared with aquatic organisms and terrestrial insects, is attributed to their higher metabolism, more rapid excretion, lower absorption from diet or the surrounding envirosphere, higher esterase activity, higher fat content, and lower neurosensitivity (Wouters and Bercken 1978; Ohkawa et al. 1979; Glickman and Casida 1982; Flannigan et al. 1985; Gray and Soderlund 1985; Klaassen et al. 1986; Bradbury and Coats 1989a,b; Coats et al. 1989). For example, rainbow trout (*Oncorhynchus mykiss*) — one of the more sensitive aquatic species — have significantly lower rates of metabolism and elimination of fenvalerate than those reported for birds and mammals (Bradbury et al. 1986; Bradbury and Coats 1989a,b); show little or no esterase activity toward pyrethroids and substantially lower oxidative activity than warm-blooded animals (Bradbury and Coats 1989a,b); efficiently accumulate fenvalerate from the medium (Gray and Soderlund 1985), and show greater intrinsic sensitivity of the central nervous system when compared with birds and mammals (Gray and Soderlund 1985; Bradbury and Coats 1989a).

Fenvalerate effects are antagonized or synergized by various compounds or chemicals. Dermal exposure to fenvalerate in mammals may produce a skin sensory response, most frequently on the face, characterized by itching and tingling. Administration of Vitamin E up to 29 h before fenvalerate exposure partially reduced the fenvalerate-mediated skin sensation in guinea pigs (*Cavia* sp.; Malley et al. 1985). The effectiveness of Vitamin E may be associated with its membrane stabilizing property, although the exact mode of action is unknown. Fenvalerate skin sensations were also reduced by piperonyl butoxide when applied directly to the skin or in conjunction with fenvalerate (Malley et al. 1985). Delayed toxic effects in rodents and insects were produced with various muscle relaxants, including propranolol and diazepam, perhaps through depolarization of nerve terminals (Gammon et al. 1982; Gray 1985; Gray and Soderlund 1985). Mice given profenofos, an esterase inhibitor, were up to 27 times more susceptible than were nontreated animals (Glickman and Casida 1982).

20.3.5 Mutagenicity, Teratogenicity, and Carcinogenicity

Fenvalerate and other synthetic pyrethroids caused no oncogenic, reproductive, mutagenic, or teratogenic effects, as judged by results of 2-year feeding studies with rodents at 250 to 300 mg/kg diet, three-generation rodent reproduction studies at 250 mg/kg diet, various mutagenicity assays, bone marrow cytogenicity up to 150 mg/kg BW, the dominant lethal bioassay at 100 mg/kg, and a host-mediated bioassay in mice at 50 mg/kg BW (Reed 1981; Pluijmen et al. 1984; Flannigan et al. 1985; Gray and Soderlund 1985). Some chromosomal aberrations and alterations in the mitotic index were noted, however, in bone marrow and testis cells of rats given 100 mg fenvalerate/kg BW orally, a dose that killed 71% of the rats (Gray and Soderlund 1985). A similar pattern was noted in mice (Flodstrom et al. 1988; Pati and Bhunya 1989), indicating that additional research is needed to establish the mutagenicity of fenvalerate.

The carcinogenic potential of fenvalerate is based on negative or inconclusive evidence and centers on its ability to produce microgranulomas in various tissues, especially liver, in dogs and rodents. Beagle dogs exposed to 250, 500, or 1000 mg fenvalerate/kg diet for 6 months showed treatment-related microscopic effects, including histiocytic cell infiltrates in mesenteric lymph nodes and multifocal microgranulomas in liver (Parker et al. 1984b). Female rats fed a diet containing 1000 mg fenvalerate/kg ration for 2 years showed a statistically significant increase in the

incidence of mammary tumors; however, this was judged by the authors (Parker et al. 1984a) to be of unlikely biological significance. Their unusual conclusion was based on four points:

1. None of the mammary tumor incidences exceeded those expected or reported on aged female rats of this strain
2. Time and appearance of tumors in control and treated groups were unchanged by treatment
3. The benign:malignant ratio of mammary tumors was the same in control and treated groups
4. The tumors were common in this strain of rat and did not seem to be related to treatment

Fenvalerate inhibits intercellular communication between fibroblast cells and enhances the development of hepatocyte foci in rat liver at nonhepatotoxic dose levels. Chemicals that possess these properties are likely to be tumor promoters (Flodstrom et al. 1988). Fenvalerate alone induced no hepatotoxic effects in rat liver, as judged by transaminase activities and histology. However, some rats that were partially hepatectomized and insulted with nitrosodiethylamine — a carcinogen and tumor initiator — had significantly elevated numbers of liver foci after administrations of fenvalerate. This response suggests that fenvalerate is a potential tumor promoter (Flodstrom et al. 1988).

Linkage of the tumor-like formations in rodents with a specific fenvalerate stereoisomer was an important breakthrough (Kaneko et al. 1986; Okuno et al. 1986; Miyamoto et al. 1986; Miyamoto 1988). Granulatomous cells in spleen, lymph node, and liver of fenvalerate-stressed rats and mice tended to fuse, forming large multinucleated cells called giant cells. Researchers convincingly demonstrated that the $2R,\alpha S$ -isomer, heretofore believed innocuous, was solely responsible for the observed microgranulomas. The residual metabolite in this instance is the cholesterol conjugate [cholesterol ($2R$)-2-(4-chlorophenol) isovalerate] known as CPIA-cholesterol ester. This lipophilic conjugate forms rapidly, usually peaking within 60 min, and tends to persist in tissues, especially in adrenal, spleen, liver, and mesenteric lymph node. Of the four fenvalerate isomers, only the $2R,\alpha S$ -isomer yielded CPIA-cholesterol ester in tissue homogenates of mice, rats, dogs, and monkeys. Mouse tissues showed relatively higher activities than those of other animals. Kidney, brain, and spleen of mice showed relatively higher capacities to form CPIA-cholesterol ester when compared with other mouse tissues; in all cases, enzyme activity localized mainly in microsomal fractions. Researchers concluded that stereoselective formation of the CPIA-carboxyesterase complex only from the $2R,\alpha S$ -isomer, which subsequently undergoes cleavage by cholesterol to yield the CPIA-cholesterol ester that produced giant cells in mice (Kaneko et al. 1986; Okuno et al. 1986; Miyamoto et al. 1986; Miyamoto 1988). These findings strongly support the need for more research on the carcinogenic potential of fenvalerate stereoisomers.

20.4 EFFECTS

20.4.1 General

Fenvalerate is extremely toxic to representative nontarget aquatic organisms and to some beneficial terrestrial arthropods at concentrations substantially lower than those recommended to control pestiferous insects. Toxic effects are associated primarily with the $2S,\alpha S$ -isomer and are exacerbated at low temperatures. Birds, mammals, and terrestrial plants are normally tolerant.

Target insect species are usually killed at fenvalerate concentrations of 0.015 µg whole body, 0.11 kg/ha by way of aerial application, 5.4 mg/kg in the soil, or 50 mg/kg in the diet. Adverse effects on survival of sensitive aquatic organisms occur at 0.003 to 0.03 µg/L for crustaceans and 0.09 to 1.1 µg/L for fish and amphibians. Younger stages of sensitive birds had reduced survival at acute oral doses >500 mg/kg BW, and reduced growth at diets containing >750 mg/kg ration; poultry diets containing <50 mg fenvalerate/kg feed produced no appreciable residues in eggs and

meat of exposed birds. Among sensitive mammals, adverse effects on survival were noted at acute oral doses of 50 to 450 mg/kg BW, dietary concentrations of 50 to 1000 mg/kg, and dermal applications of 1800 mg/kg BW.

20.4.2 Terrestrial Plants and Invertebrates

Terrestrial plants are relatively unaffected by fenvalerate at recommended application rates, as judged by negligible uptake of fenvalerate from treated soils, formation of numerous fenvalerate conjugates that are pharmacologically inactive, and metabolism of the liberated cyano group into amino acids and eventually carbohydrate and protein (Miyamoto 1988).

Adverse effects of fenvalerate on survival of terrestrial arthropods were observed at 0.002 to 0.015 µg whole-body topical application, 0.11 kg/ha aerial application, 5.4 mg/kg in the soil, 50 mg/kg in the diet, and 1.4 g/ant mound (Table 20.4). Synthetic pyrethroids are more effective in biological systems at low temperatures. The relative sensitivity of insects when compared with mammals is attributed in part to this negative temperature coefficient. Thus, warm-blooded animals are less affected than insects and other poikilotherms (Klaassen et al. 1986). Fenvalerate, for example, showed a negative correlation between temperature and toxicity to crickets (*Acheta pennsylvanicus*), being up to 1.9 times more toxic at 15°C than at 32°C (Harris et al. 1981). A similar case is made for honey bees (*Apis mellifera*) (Mayer et al. 1987) and for many species of aquatic invertebrates and fish (Mayer 1987).

Signs of lethal pyrethroid poisoning in insects and other arthropods generally include hyperexcitation, tremors, and convulsions, culminating in paralysis and death (Wouters and Bercken 1978). At sublethal doses, equivalent to about 10% of a lethal dose, signs of poisoning in sensitive insects include cessation of feeding, wandering, hyperactivity, restlessness, and flushing out of hiding (Bradbury and Coats 1989a). The American cockroach (*Periplaneta americana*) exposed to topical lethal concentrations of fenvalerate had uncoordinated rapid movements followed by inactivity, appearance of water drops under wings and abdomen, and blackening of the abdomen (Yellamma and Reddy 1987). Signs appeared in <1 h at lethal concentrations and <3 h at sublethal concentrations. Roaches exposed to sublethal doses began recovery 6 h after exposure, attaining full recovery at 24 h (Yellamma and Reddy 1987).

Field application rates of 0.05 to 0.2 kg fenvalerate/ha are recommended for insect control on many food crops. Under these conditions, fenvalerate remained completely effective for 5 days against adults and nymphs of aphids (*Lipaphis erysimi*), jassids (*Amrasca biguttula biguttula*), and white fly (*Bemisia tabaci*) (Jain et al. 1979). Fenvalerate, applied as a drench to mounds, shows promise as an effective control agent of the fire ant, *Solenopsis invicta* (Phillips et al. 1984). Foliar applications of fenvalerate sprays at 135 mg/L effectively controlled various pests in pear orchards of northern California, including pear psylla (*Psylla pyricola*), codling moth (*Laspeyresia pomonella*), and pear rust mite (*Epitrimerus pyri*); populations of spider mites increased, especially the two-spotted spider mite, *Tetranychus urticae* (Riedl and Hoying 1980).

A concentration of 2 mg fenvalerate/L is frequently applied to soils to control insect pests (Schreiber and Brink 1989). However, several species of soil protozoans (*Blepharisma undulans*, *Colpoda cucullus*, *Oikomonas termo*) have LC10 (9 h) values in the range of 0.1 to 0.18 mg/L, suggesting that some damage occurs to this group under recommended application protocols (Schreiber and Brink 1989). In fact, all fenvalerate treatments applied to control insect pests of crops also reduced populations of beneficial nontarget organisms, including spiders, ground beetles, and crickets (Smith et al. 1989). For example, spiders (*Chiracanthium mildei*) exposed for 48 h to grapefruit leaves that had been dipped 1 h previously for 5 s in aqueous emulsions of fenvalerate at field-recommended application rates all died within 2 days postexposure (Mansour 1987).

Fenvalerate-tolerant strains of arthropods include insect vectors of disease, flies and cockroaches, arthropods of veterinary importance, and agricultural pests (Sawicki 1985). But serious

control problems are restricted to only a few areas, such as Central America and Thailand, where insecticidal usage is often excessive (Sawicki 1985). The exact mechanisms of resistance are unknown, although tolerance to fenvvalerate in the diamondback moth (*Plutella xylostella*), a worldwide pest of cabbage-type crops, is about 20% genetic, involving several genes and multiple loci (Tabashnik and Cushing 1989). Estimates of heritability in tolerance of insects to all biocides ranges between 14 and 47% (Tabashnik and Cushing 1989). Tolerant insect species, such as larvae of the common green lacewing, and resistant strains of houseflies and lepidopterous larvae may hydrolyze fenvvalerate faster than sensitive species or susceptible strains (Glickman and Casida 1982). Fenvvalerate-resistant strains of domestic houseflies (*Musca domestica*), for example, when compared with susceptible strains, absorbed up to 3 times less fenvvalerate, had a metabolic rate up to 8 times faster, began excretion of metabolites 5 times faster, and were twice as resistant to piperonyl butoxide, a synergist applied with fenvvalerate (Golenda and Forgash 1989).

The alfalfa leaf cutter bee (*Megachile rotundata*) is the most important insect pollinator of alfalfa grown for seed production in France. Alfalfa is parasitized by many insects, including the flower midge (*Contarinia medicaginis*). Fenvvalerate, at 0.05 kg/ha, controls the flower midge without harm to alfalfa leaf cutter bees (Tasei and Debray 1985). In general, fenvvalerate-treated plants were usually nontoxic to bees after 24 h (Mayer et al. 1987). Fenvvalerate does not poison bees when they are in contact with contaminated (100 mg/kg) wax in combs (Stoner et al. 1985). Fenvvalerate does not pose a serious threat to honey bees except when dietary levels exceed 50 mg fenvvalerate/kg (Stoner et al. 1984). Field application of 0.22 kg fenvvalerate/ha on blooming alfalfa, pollen-shedding corn, and blooming red raspberry resulted in reduced honey bee visitation and low-to-moderate adult bee mortality (Mayer et al. 1987). Caged honey bees exposed to an equivalent dose of 0.11 kg fenvvalerate/ha experienced >50% mortality within 24 h (Table 20.4). However, field studies showed that 0.11 kg/ha caused no observable adverse effects to bee colonies located adjacent to a treated alfalfa field; researchers concluded that fenvvalerate temporarily repelled bees, as judged by a 70% reduction in bee visits to the alfalfa field in the afternoon after application when compared with periods 24 h before and after application (Moffett et al. 1982). Impaired response to scent stimuli, in addition to repellency, may account for a reduction in bee visits. Studies by Taylor et al. (1987) suggested that bees surviving LD₅₀ doses of fenvvalerate were unable to distinguish odor-mediated learned responses for up to 6 days after treatment. This finding indicates that more research is needed on fenvvalerate-associated olfactory inhibition.

Table 20.4 Lethal and Sublethal Effects of Fenvvalerate on Terrestrial Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
CRICKET, <i>Acheta pennsylvanicus</i>		
5.4 mg/kg mucky soil	LD ₅₀ (18 h)	1
6.5 mg/kg moist sand	LD ₅₀ (18 h)	1
MOSQUITO, <i>Anopheles stephensi</i>		
0.002 µg whole body	LD ₅₀	12
INDIAN HIVE BEE, <i>Apis cerama indica</i>		
0.128–0.14 µg/bee	LD ₅₀ , topical application	2
HONEY BEE, <i>Apis mellifera</i>		
0.11 kg/ha, caged bees	57% dead in 24 h	3
Bees caged with alfalfa treated previously with 0.22 kg/ha, and held under various photothermal regimens for 24 h	Bees held at 10°C in the dark experienced 96% mortality; bees held at 29°C in the dark had 58% dead; those held at 18–35°C with normal photoperiod had 40% dead	3
0.22 kg/ha	Repelled bees for 10 h	4

Table 20.4 (continued) Lethal and Sublethal Effects of Fenvalerate on Terrestrial Invertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
0.4 kg/ha	Increased mortality for 3 days after exposure	4
0.43 kg/ha, caged bees	All dead in 24 h	3
0.9 kg/ha	Hazardous for 2 h after application	5
Fed sucrose syrup for 7–8.5 weeks containing 0.1, 1, 10, 50, or 100 mg fenvalerate/kg	At 100 mg/kg, survival was lower and honey production declined. At 50 mg/kg diet, bees consumed less syrup, suggesting repellency. No measurable effect at 10 mg/kg diet, and lower. Queens were not affected at any dose level	5
Colonies exposed for several weeks to 1, 10, 100, or 1000 mg/kg incorporated into beeswax foundation	Adverse effects noted only at 1000 mg/kg, namely, lower egg hatch and survival. Fenvalerate degradation in beeswax was 11% in 15 days, 21% in 75 days, and 81% in 130 days	6
MITE, <i>Chorioptes bovis</i>		
0.05% dip (500 mg/L) for 1 min	Kills all mites and their eggs on Angora goats (<i>Capra</i> sp.) within 7 days	7
ALFALFA LEAFCUTTING BEE, <i>Megachile rotundata</i>		
0.05 kg/ha	No effect on survival or reproduction	8
0.11 kg/ha	82% dead in 24 h	3
0.22 kg/ha	92% dead in 24 h	3
0.43 kg/ha	All dead within 24 h	3
HOUSEFLY, <i>Musca domestica</i>		
Susceptible strain		
0.013–0.015 µg/fly	LD5, topical dose	12, 13
0.028 µg/fly	LD30, topical dose	13
Resistant strain		
0.150 µg/fly	LD5, topical dose	13
ALKALI BEE, <i>Nomia melanderi</i>		
0.11 kg/ha	64% dead in 24 h	3
0.43 kg/ha	All dead in 24 h	3
AMERICAN COCKROACH, <i>Periplaneta americana</i>		
3.5 µg/roach	Nonlethal	9
10.5 µg/roach	LD50, topical	9
100 µg/kg BW	LD50, topical	12
200 µg/kg BW	LD95, topical. Diazepam delayed onset of action	10
FIRE ANT, <i>Solenopsis invicta</i>		
0.73–1.4 g/mound, applied as drench	All mounds viable after 4 weeks; 70–100% of mounds nonviable after 8 weeks	11
112 or 224 g/ha, aerial application	Ineffective control. After 4 weeks, population levels were 29–35% of controls	11

^a 1, Harris et al. 1981; 2, Lingappa et al. 1985; 3, Mayer et al. 1987; 4, Moffett et al. 1982; 5, Stoner et al. 1984; 6, Stoner et al. 1985; 7, Wright et al. 1988; 8, Tasei and Debray 1985; 9, Yellamma and Reddy 1987; 10, Gammon et al. 1982; 11, Phillips et al. 1984; 12, Abassy et al. 1983; 13, Golenda and Forgash 1989.

20.4.3 Aquatic Organisms

“Supertoxic” compounds are those with LC50 (96 h) values <10 µg/L (Scott et al. 1987). Fenvalerate is considered supertoxic, as judged by LC50 (96 h) values of <1.0 µg/L for sensitive aquatic organisms, and <10 µg/L for representative aquatic species (Table 20.5).

Signs of fenvalerate poisoning in fish include loss of schooling behavior, swimming near the water surface, hyperactivity, erratic swimming, seizures, loss of buoyancy, elevated cough rate, increased gill mucus secretions, flaring of the gill arches, head shaking, and listlessness prior to death (Bradbury and Coats 1989a, 1989b). Fenvalerate mainly affects the nervous system in fishes, as discussed earlier. It also produces osmoregulatory imbalance, as judged by altered calcium uptake (Symonik et al. 1989), abnormal sodium and potassium excretion rates, and elevated urine osmolality (Bradbury et al. 1987a; Bradbury and Coats 1989a, 1989b). Histological damage to gill surfaces by fenvalerate is attributed to high accumulations in gills, irritation due to elevated mucus secretion, increased ventilation volume, and decreased gill-oxygen uptake efficiency (Bradbury et al. 1986, 1987a; Bradbury and Coats 1989a,b). In fish, as in mammals, fenvalerate toxicity is primarily dependent on the *2S,αS*-component of the technical mixture. Studies with individual isomers and various freshwater fishes indicate that the *2S,αS*-isomer is 96 times more toxic than the *2S,αR*-isomer, and at least 1766 times more toxic than the *2R,αS*- or *2R,αR*-isomers ([Table 20.5](#)).

Laboratory studies with fenvalerate and aquatic organisms indicate marked differences in sensitivity among taxonomic groups ([Table 20.5](#)). Crustaceans were the most sensitive group: reduced survival was evident between 0.0032 and 0.03 µg/L, and impaired feeding and reproduction between 0.0016 and 0.01 µg/L. Fish and amphibians were more tolerant to fenvalerate than were crustaceans. Increased mortality was evident between 0.088 and 1.1 µg/L, and no adverse effects were demonstrated in several species between 0.062 and 0.083 µg/L, although certain salmonids showed high uptake at concentrations as low as 0.0003 µg/L. Algae, molluscs, and chordates were comparatively resistant to fenvalerate ([Table 20.5](#)). Survival patterns of fenvalerate-stressed aquatic organisms are significantly altered, sometimes by an order of magnitude or greater, by selected biological, chemical, and physical variables. In general, increased mortality was associated with the following:

- Reduced metabolism and excretion (Bradbury et al. 1986; Bradbury and Coats 1989a; Coats et al. 1989; Haya 1989)
- Depleted glycogen stores due to starvation (Haya 1989)
- Larval and juvenile stages of development (Spehar et al. 1982; Bradbury and Coats 1989a; Haya 1989)
- Low concentrations of humic acid and other dissolved materials (Coats et al. 1989)
- Low particulate loadings (Coulon 1982; Coats et al. 1989; Fairchild et al. 1992)
- Increased water hardness (Dyer et al. 1989; Coats et al. 1989)
- Increased exposure time and bioavailability (Spehar et al. 1982; Curtis et al. 1985)
- Emulsifiable formulations (Trim 1987; Haya 1989)
- Low temperatures (Cole and Casida 1983; Bradbury and Coats 1989a; Coats et al. 1989; Materna 1991)
- The *2S,αS*-component (Ohkawa et al. 1980; Bradbury and Coats 1989a; Coats et al. 1989; Haya 1989).

Fenvalerate intoxication effects may be reversible. Tadpoles of the northern leopard frog (*Rana pipiens*) that survived LC₅₀ concentrations of the *S,S*-isomer for 96 h appeared normal 7 days after being placed in clean water (Materna 1991). Fenvalerate-protective agents include diazepam and endosulfan. Diazepam provides up to 14-fold protection to frogs against toxic doses of fenvalerate (Cole and Casida 1983); endosulfan provides limited protection to estuarine fish and shrimp (Scott et al. 1987; Trim 1987).

Bioaccumulation factors for fenvalerate by representative freshwater and estuarine organisms during exposure for 28 to 30 days to various sublethal doses ranged from 40 to 570 for fish, 356 to 4700 for invertebrates, and 477 to 933 for algae (Smith and Stratton 1986). Because of its unusually high lipophilicity, fenvalerate is accumulated at only 30% efficiency by aquatic fauna, and uptake is not dose dependent (Coats et al. 1989). Contamination of algal food of daphnids with fenvalerate does not seem to contribute to an increase in whole-body burdens, although reduced filtration rates

due to toxicity could also account for a reduced intake of fenvalerate adsorbed to algae ([Table 20.5](#)) (Day and Kaushik 1987b,c).

Fenvalerate applications of 0.055 to 0.220 kg/ha are recommended for control of pestiferous crop insects, but these levels are rapidly fatal to nontarget organisms if introduced accidentally into aquatic environments (Day et al. 1987). In one study, large earthen ponds containing red crawfish (*Procambarus clarkii*) were treated with fenvalerate at concentrations equivalent to 28, 56, 112, or 224 g/ha. All crawfish died within 24 h at all concentrations tested (Coulon 1982). After 3 days, ponds dosed with 112 g/ha and lower were not lethal to crawfish exposed for 24 h. The 224-g/ha pond remained toxic to crawfish after 72 h (71% dead) and 120 h (32% dead); mortality was negligible (<10%) after 168 h (Coulon 1982). Fenvalerate applications of 28 to 112 g/ha (0.025 to 0.1 pounds/acre) usually control 90 to 100% of floodwater mosquitoes and stagnant water mosquitoes. But at 2 to 11 g/ha equivalent, the following effects are reported (Mulla et al. 1978, 1980; Tagatz and Ivey 1981; Anderson 1982; Spehar et al. 1982; Hansen et al. 1983; Smith and Stratton 1986; Day et al. 1987; Bradbury and Coats 1989a; Day 1989):

- Mayfly naiads are eliminated
- Populations of diving beetles, cladocerans, and dragonfly naiads are suppressed for up to 3 weeks
- Zooplankton filtration rates are reduced
- Colonization processes are altered
- Algal and rotifer populations increase due to lack of cladoceran grazing and competition

Several large-scale mesocosm studies were conducted with esfenvalerate, the most active form of fenvalerate (Fairchild et al. 1992; Heinis and Knuth 1992; Lozano et al. 1992; Webber et al. 1992). These investigators demonstrated that:

1. The half-time persistence of fenvalerate in the water column is about 10 h
2. Initial concentrations of 1.0 or 5.0 µg/L were not detectable in the water column after 2 and 4 days, respectively
3. In the first 2 days after application, the water column contained the majority of the fenvalerate
4. By day 4 postapplication, the sediments and macrophytes were the major reservoirs of fenvalerate
5. Fish usually contained less than 1% of the esfenvalerate at any time
6. Sensitive species of some copepod and insect genera showed declines in abundance at 0.08 to 0.2 µg/L and were unable to recover
7. Most species of zooplankton and benthic invertebrates decreased in abundance at 0.25 µg/L and higher
8. At 1.0 to 5.0 µg/L, there were drastic reductions or elimination of most species of crustaceans and chironomids, juvenile bluegills, and larval cyprinid fishes.

Sediment/water interactions are important to the understanding of fenvalerate toxicokinetics. Addition of soil to fenvalerate-treated waters reduced toxicity to channel catfish (*Ictalurus punctatus*) through adsorption of fenvalerate to clay and organic components of soil; however, crayfish (*Procambarus spp.*) were not protected (Coulon 1982). Chironomid larvae held in water on sand initially spiked with 50 µg fenvalerate/kg accumulated up to 15 times more fenvalerate than did larvae held in water above spiked silt or clay. A similar pattern was evident at an initial concentration of 5 µg/kg (Muir et al. 1985). This phenomenon is attributed to the greater bioavailability of fenvalerate in sand, as judged by elevated sediment interstitial water concentrations in sand when compared with those of silt or clay ([Table 20.5](#)) (Muir et al. 1985). Mortality was observed in systems where fenvalerate concentrations in sediments were sufficient to establish lethal concentrations in the overlying water through sediment/water partitioning; lethal effects at nominal sediment concentrations of 0.1 mg fenvalerate/kg were observed for mysids (*Mysidopsis bahia*) and grass shrimp (*Palaemonetes pugio*), and at 10 mg/kg for pink shrimp (*Penaeus duorarum*) (Clark et al. 1989). Because fenvalerate readily sorbs and binds to organic and inorganic particulate matter, it is difficult to predict its toxic effects on aquatic biota after runoff from agricultural areas or from discharges into particulate-laden habitats (Clark et al. 1989).

Table 20.5 Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
ALGAE		
Alga, <i>Chlamydomonas reinhardtii</i> 0.109–5.17 µg/L	Up to 93% of all fenvalerate was adsorbed by algae in 48 h in a biomass-dependent manner when cells increased from 100/mL to 2 million/mL. In absence of alga, up to 33% of fenvalerate added to glass containers was adsorbed to container walls in 48 h	1
Marine algae, 4 species: <i>Isochrysis galbana</i> , <i>Skeletonema costatum</i> , <i>Thalassiosira pseudonana</i> , <i>Nitzchia angularis</i> 1000 µg/L	Insufficient to produce 50% growth inhibition in 96 h	2
INVERTEBRATES		
Mosquito, <i>Aedes nigromaculatus</i> Multi-resistant strain, fourth-stage larvae 5.6 g/ha (0.005 pounds/acre) 11.2 g/ha (0.01 pounds/acre) 28.0 g/ha (0.025 pounds/acre)	58% reduction 6 h after treatment 81% reduction 6 h after treatment 88% reduction 6 h after treatment	3 3 3
Mosquito, <i>Aedes</i> spp. 0.9–10.0 µg/L 1.5–4.0 µg/L	LC50–LC90 range for fourth-stage larvae LC50–LC90 range for 24-h-stage pupae	4 4
Rhagionid fly, <i>Atherix</i> sp. 0.021 µg/L 0.029 µg/L 0.032 µg/L	LC30 (28 days) LC50 (28 days) LC50 (96 h)	5 5 5
Cladoceran, <i>Ceriodaphnia lacustris</i> 0.01 µg/L 0.05 µg/L 0.21 µg/L	Filtration rate of alga (<i>Chlamydomonas reinhardtii</i>) significantly decreased after 24-h exposure Decreased food assimilation rate, 24-h exposure 50% immobilization of adults in 48 h	6 6 6
Chironomids 4.2–18.0 µg/L 4.2–80.0 µg/L	LC50 (24 h), 3 species LC50 (24 h), 8 species	7 7
Midge, <i>Chironomus tentans</i> , fourth-instar larvae 0.015–0.93 µg/L; exposed for 24 h in different sediment types containing initial concentration of 50 µg fenvalerate/kg fresh weight (FW) or 48 h in water above sediment; depuration for 96 h in each case	Normal burrowing behavior	8
Sand (water column and sediment interstitial water concentrations after 24 h were 1.02 and 4.82 µg/L, respectively) Silt (water column 0.17 µg/L, interstitial water 0.15 µg/L) Clay (water column 0.3 µg/L, interstitial water 0.34 µg/L)	Bioconcentration factor (BCF) of 69 for those held in water column and 102 for those held in sand BCF of 74 for water column, 116 for silt BCF of 32 for water column, 152 for clay	8 8 8
Snail, <i>Cipangopaludina japonica</i> 0.4–0.7 µg/L	BCF of 617 in 30 days	9
Sand shrimp, <i>Crangon septemspinosa</i> 0.04 µg/L	LC50 (96 h)	10, 11
American oyster, <i>Crassostrea virginica</i> 1.0 µg/L	BCF of 4700 in 28 days; depuration to nondetectable levels in <7 days	12

Table 20.5 (continued) Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
>1000 µg/L	Abnormal shell growth in 50% of larvae surviving exposure for 48 h	2, 11
Mosquito, 3 species of <i>Culex</i>		
1.2–30.0 µg/L	LC50–LC90 range for 24-h-stage pupae	4
4.0–10.0 µg/L	LC50–LC90 range for fourth-stage larvae	4
Mosquito, <i>Culex pipiens pipiens</i> , larvae		
0.45 µg/L	LC50 (24 h), technical grade	13
30.0 µg/L	LC50 (24 h), emulsifiable formulation	13
11.0 mg/kg diet	LC50 (24 h)	13
Mosquito, <i>Culex quinquefasciatus</i>		
7–8 µg/L	LC50–LC90 range for fourth-stage larvae	3
Daphnid, <i>Daphnia galeata mendotae</i>		
0.005 µg/L	Life cycle (28-day) exposure produced increased longevity but decreased production of young	1
0.01 µg/L, and higher	Decreased survival, reproduction, and generation time in lifetime exposure	1
0.042–0.084 µg/L	Whole-body fenvalerate residues in presence of alga (<i>Chlamydomonas reinhardtii</i>) ranged from 0.51–1.08 mg/kg FW after 48-h exposure	14
0.05 µg/L	Decreased filtering rate and assimilation rate of algae after exposure for 24 h; decrease in population numbers in 28-day exposure	1, 6
0.051–0.109 µg/L	In absence of algae, whole-body residues ranged from 1.46–2.66 mg/kg FW after 48 h	14
0.16 µg/L	50% of immatures immobilized in 48 h	6, 15
0.29 µg/L	50% of adults immobilized in 48 h	6, 15
Daphnid, <i>Daphnia magna</i>		
0.25 µg/L	No measurable effect after exposure for 21 days	16, 17
0.27 µg/L	LC50 (48 h)	50
0.5 µg/L	After 21 days, reduced survival and inhibited reproduction	16
0.83 µg/L	50% immobilization of immatures in 48 h	6
2.1–2.5 µg/L	50% immobilization of adults in 48 h	6, 18
Daphnid, <i>Daphnia pulex</i>		
0.4–0.7 µg/L	BCF of 683 in 30 days	19
Copepod, <i>Diaptomus oregonensis</i>		
0.05 µg/L	Decreased filtration rate and food assimilation rate after 48-h exposure	6
0.12 µg/L	50% of adults immobilized in 48 h	6
Mayfly, <i>Ephemerella</i> sp.		
0.022 µg/L	LC80 (14 days)	5
0.07 µg/L	50% reduction in swimming ability in 96 h	20
0.08 µg/L	LC50 (96 h)	20
0.93 µg/L	LC50 (24 h)	5, 20
Amphipod, <i>Gammarus pseudolimnaeus</i>		
0.022 µg/L	LC65 (6 days)	5
0.03 µg/L	LC50 (96 h), adults	5
0.05 µg/L	LC50 (96 h), juveniles	5
0.93 µg/L	All dead or immobilized within 5 h	5
Snail, <i>Helisoma trivolis</i>		
0.021 µg/L	BCF of 1167 in 28 days	5, 7
0.054 µg/L	BCF of 592 in 28 days	5, 7
0.79 µg/L	BCF of 386 in 28 days; no adverse effects on survival or behavior	5, 7
American lobster, <i>Homarus americanus</i>		
0.14 µg/L	LC50 (96 h)	10, 11
Mosquito, 4 species, larvae		
0.9–28.0 µg/L	LC50 (24 h)	7, 21

Table 20.5 (continued) Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
Mysid shrimp, <i>Mysidopsis bahia</i>		
0.008–0.021 µg/L	LC50 (96 h)	2, 11, 12, 18, 22
97–190 µg/kg sediment, equivalent to 0.03 µg/L water column	58% dead in 4 days, 70% dead in 10 days	23
1200–1600 µg/kg sediment, equivalent to 0.06–0.17 µg/L water column	All dead in 4 days	23
Copepod, <i>Nitocra spinipes</i>		
0.38 µg/L	LC50 (96 h)	23
Rusty crayfish, <i>Orconectes rusticus</i>		
20 µg/L	LC100 (96 h)	24
Grass shrimp, <i>Palaemonetes pugio</i>		
0.0016 µg/L	No deaths of larvae in 20 days; larval development prolonged by 2 days	25
0.003–0.013 µg/L	LC50 (96 h)	18, 26
0.0032 µg/L	Larvae exposed for 20 days had reduced survival and inhibited metamorphosis	25
0.007 µg/L	LC50 (96 h), emulsifiable concentrate, zoeae, 10‰ salinity	27
0.02 µg/L	LC50 (96 h), emulsifiable concentrate, zoeae, 20‰ salinity	27
0.040 µg/L	LC50 (96 h), adults, emulsifiable concentrate	27
0.044 µg/L	LC50 (96 h), adults, technical grade	27
0.046 µg/L	Maximum tolerated dose in 6-h exposure, adults	27
0.1–0.15 µg/L	LC50, 90 h after 6-h exposure, adults	27
10 µg/kg sediment	After exposure for 28 days, body burdens of carbon and nitrogen were reduced	56
88–200 µg/kg sediment	LC50 (96 h)	18, 23
97–190 µg/kg sediment	48% dead in 4 days	18, 23
100 µg/kg sediment	After exposure for 28 days, larval metamorphosis of survivors was inhibited and growth reduced	56
1000–1200 µg/kg sediment	LC100 (96 h)	18, 23
Pink shrimp, <i>Penaeus duorarum</i>		
0.84 µg/L	LC50 (96 h)	12, 22
1200–1600 µg/kg sediment, equivalent to 0.06–0.17 µg/L	None dead in 10 days	23
10,000–13,000 µg/kg sediment equivalent to 0.2–1.9 µg/L water column	All dead in 4 days	23
Red crawfish, <i>Procambarus clarkii</i>		
0.37 µg/L	LC50 (24 h), juveniles	28
Mosquito, <i>Psorophora columbiae</i>		
28–50 µg/L	LC50–LC90 range for fourth-stage larvae	4
53–82 µg/L	LC50–LC90 range for 24-h-stage pupae	4
Stonefly, <i>Pteronarcys dorsata</i>		
0.11 µg/L	38% immobilized in 72 h	5
0.13 µg/L	50% immobilized in 72 h	5
0.44 µg/L	38% immobilized in 24 h; 25% dead in 72 h	5
1.02 µg/L	All immobilized in <4 h; most dead in 72 h	5
CHORDATES		
Amphioxus, <i>Branchiostoma caribaeum</i>		
760 µg/L	LC10 (10 days)	18
1000 µg/L	No deaths in 96 h	18
1600 µg/L	LC50 (96 h)	18
2500 µg/L	LC100 (96 h)	18, 23
100–1000 µg/kg sand	Effectively colonized in 8 weeks	29
10,000 µg/kg sediments	No deaths in 10 days	18
10,000 µg/kg sand	Unable to effectively colonize during 8-week study	29

Table 20.5 (continued) Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
VERTEBRATES		
Bleak, <i>Alburnus alburnus</i> 0.3 µg/L	LC50 (96 h)	23
Topsmelt, <i>Atherinops affinis</i> 0.14 µg/L	Survival normal of embryos and fry after exposure for 30 days	51
0.34 µg/L	Survival 86% of embryos and fry after exposure for 30 days; bioaccumulation factor of 315	51
0.66 µg/L	LC50 (96 h) for juveniles	51
0.82 µg/L and higher	All fry dead within 96 h of hatch	51
3.2 µg/L	Normal hatch on day 7 of exposure	51
Desert pupfish, <i>Cyprinodon macularis</i> 25 µg/L	LC50 (48 h)	20
Sheepshead minnow, <i>Cyprinodon variegatus</i> 0.3–5.0 µg/L	Whole-body BCF values in fish surviving 28-day exposure were 460 (0.31 µg/L), 360 (0.62 µg/L), 500 (1.2 µg/L), 700 (2.5 µg/L), and 820 (5.0 µg/L)	22
0.56 µg/L	No effect on hatchability, survival or growth in 28-day exposure	17, 22
2.2 µg/L	Growth reduction in 28-day exposure	22
4.4–5.0 µg/L	LC50 (96 h), flowthrough assay	2, 12, 22, 30
120 µg/L	LC50 (96 h), static assay	2
Common carp, <i>Cyprinus carpio</i> 0.4–0.7 µg/L	BCF of 69–117 in 30-day exposure	19
0.8 µg/L	After exposure for 7 days, 50% excreted 5 days after exposure and 87% in 25 days	19
0.9 µg/L	No deaths in 48 h	31
3.8 µg/L	LC10 (48 h)	31, 32
10 µg/L	At 48 h, hypoproteinemia and altered enzyme activity in gills	31, 32
10 µg/L for 6–48 h	No deaths. Exposure-dependent decrease in tissue acetylcholinesterase activity and increase in acetylcholine content	54
21–30 µg/L	LC50 (48–96 h)	31, 32, 54
117 µg/L	LC90 (48 h)	31
Mummichog, <i>Fundulus heteroclitus</i> 1.2–1.8 µg/L	LC50 (96 h)	23, 26
Mosquitofish, <i>Gambusia affinis</i> 15.0 µg/L	LC50 (48 h)	20
Channel catfish, <i>Ictalurus punctatus</i> 1.8–1.9 µg/L	LC50 (24 h)	19, 28
16.5 µg/L, equivalent to 112 g/ha	Muscle residues in dead fish ranged up to 70 µg/kg FW	28
30.6 µg/L, equivalent to 224 g/ha	Muscle residues in dead fish collected 24 h after treatment ranged up to 160 µg/kg FW	28
Bluegill, <i>Lepomis macrochirus</i> 0.2 µg/L	Significant decline in adenylate energy charge in gills after 10 days exposure; normal by day 30 of exposure	52
0.3–1.1 µg/L	LC50 (96 h)	19, 50
0.7 µg/L	Elevated whole-body calcium content after 48 h	34
0.9–1.9 µg/L	LC50 (48 h) range for water hardnesses between 6 and 309 mg CaCO ₃ /L, or between 4.2 and 13.6‰ salinity	35
10 µg/L	LC100 (96 h)	24

Table 20.5 (continued) Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
Intraperitoneal injection, in mg/kg body weight (BW)		
0.12	LD50 (48 h); 2S, α S-isomer	17, 36, 37
0.67	LD50 (48 h); technical fenvalerate — mixture of all isomers	13, 17, 36, 37
11.5	LD50 (48 h); 2S, α R-isomer	17, 36, 37
216	No deaths in 48 h; 2R, α S-isomer	17, 36, 37
264	No deaths in 48 h; 2R, α R-isomer	17, 36, 37
Crimson-spotted rainbow fish, <i>Melanotaenia fluviatilis</i> ; larvae		
0.32 µg/L	Some deaths after 1-h exposure to esfenvalerate	55
1.18 µg/L	LC50 (96 h); technical esfenvalerate	55
1.99 µg/L	LC50 (96 h); emulsified esfenvalerate	55
4.5 µg/L	Some deaths after exposure for 1 min to esfenvalerate	55
12.75 µg/L	LC50 (96 h); technical fenvalerate	55
30.25 µg/L	LC50 (96 h); emulsified fenvalerate	55
Freshwater fish, <i>Labeo rohita</i>		
10 µg/L for 6–48 h	Exposure-dependent decrease in respiration rate and content of sodium, potassium, and calcium in gill, brain, muscle and liver. At 48 h, whole animal respiration rate decreased 51%, tissue Na content by 28–40%, tissue K content by 28–34%, and tissue Ca content by 19–36%	53
30 µg/L	LC50 (48 h)	53
California grunion, <i>Leuresthes tenuis</i>		
0.06 µg/L	No-observable-effect concentration in 28-day early life history exposure	23
0.3–0.6 µg/L	LC50 (96 h)	2, 30
Inland silverside, <i>Menidia beryllina</i>		
1.0 µg/L	LC50 (96 h)	30
Atlantic silverside, <i>Menidia menidia</i>		
0.062 µg/L	No-observable-effect concentration in 28-day early life history exposure	23
0.31–0.69 µg/L	LC50 (96 h)	12, 17, 22
Tidewater silverside, <i>Menidia peninsulae</i>		
0.083 µg/L	No-observable-effect concentration in 28-day early life history exposure	23
1.0 µg/L	LC50 (96 h)	30
Striped mullet, <i>Mugil cephalus</i>		
0.58 µg/L	LC50 (96 h)	2, 12, 22
African catfish, <i>Mystus vittatus</i>		
0.13 µg/L	Safe concentration	38
6.3 µg/L	LC50 (96 h)	38
Rainbow trout, <i>Oncorhynchus mykiss</i>		
0.00028 µg/L, exposure for 48 h followed by depuration for 48 h	Tissue residues, in µg/kg FW, were 7.06 in bile; 0.2 in fat; 0.02–0.05 in blood, brain, carcass, gill, kidney, liver, muscle, ovary, erythrocytes, and spleen; and <0.02 in heart, plasma, and testes	39
0.23–2.1 µg/L	LC50 (96 h)	17–20, 41, 50
3.6 µg/L	Hyperactivity in 48 h	41
4.7–76 µg/L	LC50 (24 h)	20, 42
300 µg/L	All dead in 10 h. At death, brain residues of 150–160 µg/kg FW. Similar brain residues reported via lethal intraperitoneal and intravenous injection routes	13, 39, 43

Table 20.5 (continued) Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
412 µg/L	All dead in 11 h. Prior to death, trout displayed elevated cough rate, tremors, seizures, elevated urine Na and K, and abnormal blood chemistry. At death, gill histopathology evident, and residues, in µg/kg FW, were 160 in brain, 250 in carcass, and 3620 in liver	40
Steelhead trout, <i>Oncorhynchus mykiss</i>		
Steelhead embryos and larvae exposed intermittently (4.5 h daily) or continuously for 70 days after fertilization to nominal concentrations of 0.018, 0.04, 0.08, 0.135, or 0.505 µg/L		
0.018 µg/L	No deaths. Whole-body BCF values at 70 days were 400 for intermittent exposure and 4100 for continuous exposure	40
0.04 µg/L, tested at intermittent exposure only	No deaths; BCF of 3200	40
0.08 µg/L	For continuous exposure, no effect on survival or growth; BCF of 3000. For intermittent exposure 32% dead, 50% reduction in growth, BCF of 10,700	40
0.135 µg/L, continuous exposure only	More than 90% dead, with most dying after 56 days; BCF of 11,800	40
0.505 µg/L, continuous exposure	All dead. Most died after 49 days	40
Steelhead juveniles exposed intermittently (4.5 h daily) or continuously		
0.088 µg/L	LC50 (96 h), intermittent exposure	40
0.172 µg/L	LC50 (96 h), continuous exposure	17, 40
Gulf toadfish, <i>Opsanus tau</i>		
1.2 µg/L	No observable effect concentration in 28-day early life history exposure	23
2.4–5.4 µg/L	LC50 (96 h)	2, 12, 23
Fathead minnow, <i>Pimephales promelas</i>		
0.14–0.19 µg/L	Whole-body residues of larvae in 28-day exposure ranged from 230 to 880 µg/kg FW. BCF values ranged from 1643 to 4631, in a dose-dependent manner	21
0.19 µg/L	No effect on larval survival or growth in 30-day exposure	45
0.33 µg/L	50% of larvae exposed for 96 h developed abnormally	45
0.34 µg/L	LC50 (48 h), adults, mixture of 2S,αS and 2S,αR-isomers	36, 37
0.36–0.43 µg/L	Exposure of eggs and resultant larvae for 30 days had no effect on hatchability, but adversely affected larval growth, survival, and swimming ability	21, 45
0.37 µg/L	Mean whole-body residue of survivors at 96 h was 598 µg/kg FW, equivalent to BCF of 1616	46
0.49 µg/L	After 96 h, survivors contained 911 µg/kg whole body, or BCF of 1859	46
0.75 µg/L	After 96 h, survivors contained 1680 µg/kg BW, or BCF of 2240	46
0.85 µg/L	LC50 (96 h), larvae	45
1.69 µg/L	LC50 (48 h), adults, technical fenvalerate	37
2.5 µg/L	Schooling behavior absent after 48 h exposure, adults	41
2.85 µg/L	Exposure of larvae for 5 h resulted in 50% deformities 96 h later	45

Table 20.5 (continued) Lethal and Sublethal Effects of Fenvalerate on Aquatic Organisms

Taxonomic Group, Organism, Dose or Concentration, and Other Variables	Effect	Reference ^a
3.6 µg/L	Hyperactivity after 48 h, adults	41
5.4 µg/L	LC50 (96 h), adults	17
>140 µg/L	LC50 (48 h), adults, mixture of 2R,αS- and 2R,αR-isomers	36, 37
1.0 mg/kg FW whole body	Residue at death of fenvalerate-poisoned fish	13
Northern leopard frog, <i>Rana pipiens</i> ; tadpoles		
1.0 µg/L and lower	Normal activity after 96 h	57
1.3 µg/L	Up to 40% had decreased activity in 96 h	57
3.6 µg/L	20% had spasms, uncoordinated swimming in 96 h	57
7.3 µg/L	LC50 (96 h)	57
Northern grassfrog, <i>Rana pipiens pipiens</i>		
3 µg/L	All dead in 72 h at 4°C	47
9 µg/L	None dead in 72 h at 20°C	47
130 µg/kg BW	LD50 (24 h), subcutaneous injection (sc)	47
1800 µg/kg BW	LD50 (24 h). Initially pretreated with sc dose of 10 mg diazepam/kg BW followed by sc dose of fenvalerate	47
Frog, <i>Rana</i> sp.		
450 mg/kg BW	Acute oral LD50	58
Atlantic salmon, <i>Salmo salar</i>		
0.8 µg/L	Some deaths during 96-h exposure; BCF of 200	10
1.2 µg/L	LC50 (96 h)	10
2.0–4.1 µg/L	Some deaths during 54-h exposure; BCF about 125	10
9.3 µg/L	Some deaths during 16-h exposure; BCF of 40	10
Mozambique tilapia, <i>Tilapia mossambica</i>		
9 µg/L	No deaths in 20 days, but significant decreases in activity of catalase superoxide dismutase in liver, gill, and muscle, and significant increases in activity (and presumably metabolism) of fructose-1, 6-diphosphate aldolase in liver, gill, kidney, and brain	48, 49
45 µg/L	LC50 (48 h)	48, 49

^a 1, Day and Kaushik 1987a; 2, Mayer 1987; 3, Mulla et al. 1978; 4, Mulla et al. 1980; 5, Anderson 1982; 6, Day and Kaushik 1987c; 7, Anderson 1989; 8, Muir et al. 1985; 9, Ohkawa et al. 1980; 10, McLeese et al. 1980; 11, Tagatz and Ivey 1981; 12, Schimmel et al. 1983; 13, Coats et al. 1989; 14, Day and Kaushik 1987b; 15, Day 1989; 16, McKee and Knowles 1986; 17, Bradbury and Coats 1989b; 18, Clark et al. 1987; 19, Mayer and Ellersiek 1986; 20, Smith and Stratton 1986; 21, Spehar et al. 1982; 22, Hansen et al. 1983; 23, Clark et al. 1989; 24, Bills and Marking 1988; 25, McKenney and Hamaker 1984; 26, Scott et al. 1987; 27, Baughman et al. 1989; 28, Coulon 1982; 29, Tagatz et al. 1987; 30, Clark et al. 1985; 31, Jagan et al. 1989; 32, Reddy and Bashamohideen 1988; 33, Trim 1987; 34, Symonik et al. 1989; 35, Dyer et al. 1989; 36, Haya 1989; 37, Bradbury et al. 1987b; 38, Verma et al. 1981; 39, Bradbury et al. 1986; 40, Curtis et al. 1985; 41, Holcombe et al. 1982; 42, Coats and O'Donnell-Jeffery 1979; 43, Bradbury and Coats 1989a; 44, Bradbury et al. 1987a; 45, Jarvinen et al. 1988; 46, Bradbury and Coats 1985; 47, Cole and Casida 1983; 48, Radhaiah and Reddy 1989; 49, Radhaiah et al. 1989; 50, Fairchild et al. 1992; 51, Goodman et al. 1992; 52, Hohreiter et al. 1991; 53, Reddy and Philip 1992; 54, Reddy et al. 1992; 55, Holdaway et al. 1994; 56, McKenney et al. 1998; 57, Materna 1991; 58, Theophilidis et al. 1997.

20.4.4 Birds

Birds that died of fenvalerate poisoning contained residues of 0.1 to 1.26 mg/kg brain fresh weight (FW) and 0.74 mg/kg liver FW, based on acute oral doses of 500 to 4000 mg/kg BW (Table 20.6); juveniles were more sensitive than adults (Bradbury and Coats 1989a). When compared to other synthetic pyrethroids tested in laying hens, fenvalerate provided higher, more persistent residues in tissues (Saleh et al. 1986). Birds given single oral doses as low as 250 mg

fenvalerate/kg BW experienced significant weight loss (adults) or a reduction in the rate of weight gain (immatures). Similar signs were noted at dietary levels of 15,000 mg/kg ration, but not at 7500 mg/kg feed (Bradbury and Coats 1982). Poultry diets that contain <50 mg fenvalerate/kg feed do not produce an appreciable concentration of residues in eggs or meat of exposed birds (Akhtar et al. 1989).

Adult Japanese quail (*Coturnix japonica*) given a single oral dose of 4000 mg/kg BW started feeding normally (Mumtaz and Menzer 1986); but in about 90 min, they became hyperactive. Hyperactivity increased until 2 h postdosing, at which time feeding ceased. At 4 h, they had convulsions, irregular movements, jerking, and twitching; they became progressively ataxic and uncoordinated. One quail died at 4 h, another at 8 h. By 24 h, most of the survivors had resumed feeding, but they had an odd standing posture: head held high above the body, legs extended as far straight as possible, and wings held in an upright position close to the body. By 48 h, the survivors seemed to be feeding and drinking regularly; growth was normal 14 days after exposure (Mumtaz and Menzer 1986). Signs of intoxication in fenvalerate-poisoned bobwhites (*Colinus virginianus*) usually appeared within 2 h and included hyperactivity, irregular locomotion, ataxia, and spastic muscle contractions (Bradbury and Coats 1982, 1989a). Bobwhites use croplands for feeding, and insects are an important dietary item of chicks and adults in summer months. Little potential exists for adverse effects of fenvalerate on bobwhite and other gallinaceous bird populations from dietary exposures, however, because insects from sprayed fields had maximum whole-body residues of only 0.5 mg/kg — a level far below that associated with adverse effects (Table 20.6) (Bradbury and Coats 1982).

Birds rapidly and efficiently metabolize fenvalerate by hydrolytic cleavage of the ester bond, followed by extensive hydroxylation of the acid moiety at the carbon adjacent to the carboxyl group, the methyl group, or both. Major metabolites identified in liver preparations were 2-(4-chlorophenyl)-3-methylbutyric acid, 4-hydroxyfenvalerate, 3-phenoxybenzaldehyde, and 3phenoxybenzoic acid (Akhtar 1983; Mumtaz and Menzer 1986; Akhtar et al. 1989; Bradbury and Coats 1989a). Liver microsomal drug-metabolizing enzymes usually play an important role in pesticide metabolism; however, fenvalerate and other synthetic pyrethroids are very weak inducers of avian microsomal enzymes (Riviere et al. 1983). Birds are more resistant to fenvalerate than are mammals, as judged by studies with Japanese quail and rats (*Rattus* sp.). Quail excreted fenvalerate more rapidly, had lower absorption, and faster metabolism; the oral LD₅₀ for quail was >4000 mg/kg BW vs. 450 mg/kg BW for rat, almost an order of magnitude higher (Mumtaz and Menzer 1986).

Table 20.6 Lethal and Sublethal Effects of Fenvalerate on Birds

Organism, Dose, and Other Variables	Effect	Reference ^a
COMMON BOBWHITE, <i>Colinus virginianus</i>		
0.1–1.26 mg/kg fresh weight (FW), brain	Residues in dead birds following single oral exposure; residues increased in dose-dependent manner in dose range of 500–4000 mg/kg body weight (BW)	1
0.74 mg/kg FW, liver	Mean residue in dead birds following single oral exposure; residue seemingly independent of dose	1
250 mg/kg BW, single oral dose, immatures, age 5 weeks	No deaths in 14 days	1
500 mg/kg BW, single oral dose, immatures	20% dead within 25 h	1
1785 mg/kg BW, single oral dose, immatures	LD ₅₀ . All deaths occurred 3–25 h after dosing	1
4000 mg/kg BW, single oral dose, immatures	70% dead within 24 h; remainder survived at least 14 days	1
4000 mg/kg BW, single oral dose, adults, age 19 weeks	No deaths in 14 days; all appeared normal 24 h after dosing	1
15,000 mg/kg diet, 5 days of exposure plus 3 days of clean feed	Insufficient to kill 50% of 2-week-old chicks	1

Table 20.6 (continued) Lethal and Sublethal Effects of Fenvalerate on Birds

Organism, Dose, and Other Variables	Effect	Reference ^a
JAPANESE QUAIL, <i>Coturnix japonica</i>		
4 daily treatments of 100 mg/kg BW, oral route	Maximum tissue residues 72 h after the last dose, in mg/kg FW, were 3.1 in fat, 0.9 in skin, 0.7 in liver, 0.2 in heart and kidney, 0.1 in lung, and 0.02 in brain	2
2000 mg/kg diet, 6-week-old females, 7-day feeding period	Increased liver aldrin epoxidase, intestinal cytochrome P-450, and intestinal ethoxyresorufin dealkylase	3
4000 mg/kg BW, single oral dose, 14-day observation period	75% excreted in <6 h, 90% within 24 h. Tissue residues were highest at 3 h in liver (9 mg/kg FW) and gradually declined, while in blood it peaked within 2 h and fell quickly to an equilibrium level of 1.5 mg/L	2
AMERICAN KESTREL, <i>Falco sparverius</i>		
Oral dose of 1000, 2500, or 4000 mg/kg BW; maintained at 22°C or minus 5°C for 10 h after dosing	No deaths. Mild intoxication and elevated plasma alanine amino-transferase activity; holding temperature did not affect toxicity	8
DOMESTIC CHICKEN, <i>Gallus</i> sp.		
0.03 mg/kg diet for 32 days	No detectable residues in tissue or eggs	6
5 mg/kg BW, single oral dose, residues measured in egg albumin and yolk, and various tissues during observation period of 144 h	Up to 85% of administered dose eliminated in 24 h, 88% in 72 h. Maximum residues, in mg/kg FW, were 0.5 in kidney (24 h), 0.48 in yolk (96 h), 0.46 in liver (24 h), 0.25 in plasma (24 h), 0.19 in abdominal fat (96 h), 0.18 in albumin (24 h), 0.14 in blood cells (24 h), 0.07 in both leg muscle and heart at 144 h, and not detectable in subcutaneous fat and breast muscle	4
10 mg/kg BW, single oral dose, laying hens, residues measured over 14 days	Maximum residues, in mg/kg FW, were 4.7 in blood (24 h), 4.0 in brain (7 days), 1.0 in kidney (48 h), 1.0 in heart (3 days), 0.3 in egg yolk (5 days), 0.25 in kidney (14 days), 0.23 in egg white (5 days), 0.2 in skin (5 days), 0.18 in liver (48 h), and <0.15 in fat and ovary	5
Oral doses of 1000 mg/kg BW for 5 days, and again at 21 days	No neurotoxic effects observed in hens	6
1500 mg/kg BW	Acute oral LD50	7

^a 1, Bradbury and Coats 1982; 2, Mumtaz and Menzer 1986; 3, Riviere et al. 1983; 4, Akhtar et al. 1989; 5, Saleh et al. 1986; 6, Reed 1981; 7, Smith and Stratton 1986; 8, Rattner and Franson 1984.

20.4.5 Mammals

In general, fenvalerate administered to mammals was rapidly eliminated and had little tendency to accumulate in tissues (Table 20.7). Fenvalerate killed sensitive species of mammals at a brain injection concentration of 1.0 mg/kg FW brain (equivalent to 14 µg/kg body weight = BW), an intraperitoneal injection concentration of 3.9 mg/kg BW, acute oral doses of 50 to 450 mg/kg BW, dietary levels of 50 to 1000 mg/kg feed, and an acute dermal concentration of 1800 mg/kg BW. In all cases, the 2S,αS-isomer was the most toxic (Table 20.7). Measurable residues of fenvalerate were detected in tissues of sensitive mammals at 0.15 mg/kg diet, 0.15 mg/kg BW applied dermally six times over a 3-week period, and at 2.5 mg/kg BW given orally; in all cases the 2R,αS-isomer was taken up 9 to 16 times over other isomers (Table 20.7). Behavioral alterations (e.g., change in drinking water preference) occurred in mice after a single oral dose of 0.3 mg/kg BW (Table 20.7). No significant adverse effects were observed in dogs on diets equivalent to 12.5 mg/kg BW daily for 90 days, or in rats on diets containing 250 mg fenvalerate/kg (equivalent to 12.5 mg/kg BW) for 2 years (Table 20.7).

At sublethal doses in rodents (i.e., 100 mg/kg BW), fenvaleate produces neurological toxicity but no histological damage. At higher doses, pathological alterations in peripheral nerves occur (Bradbury and Coats 1989a). Rats given acutely toxic doses of fenvaleate showed histopathological changes such as axonal swelling and degeneration, and myelin fragmentation of the sciatic nerve; the significance of these findings is unclear (Gray and Soderlund 1985).

Route of administration may account for wide variations in the toxic action of fenvaleate. Most authorities agree that fenvaleate is most toxic to rodents when administered by intercerebroventricular injection relative to other routes — indicating the importance of the brain in the Type II poisoning syndrome. Fenvaleate was decreasingly toxic when administered intravenously, intraperitoneally, orally, and dermally (Lawrence and Casida 1982; Flannigan et al. 1985; Grissom et al. 1985; Bradbury and Coats 1989a; Williamson et al. 1989).

Differences in fenvaleate metabolism occur, even among closely related species such as rats and mice (Kaneko et al. 1981). In both species, regardless of sex, dose level, or chiral isomer, fenvaleate is metabolized primarily by oxidation at the 2'-, 4'-phenoxy positions of the alcohol moiety and at the C-2 and C-3 positions of the acid moiety, by cleavage of the ester linkage, by conversion of the CN group to SCN⁻ and CO₂, and by conjugation of the resultant carboxylic acids and phenols with glucuronic acid, sulfuric acid, and amino acids. However, the taurine conjugate of 3-phenoxybenzoic acid was found in mice but not in rats; 4'-hydroxylation of the alcohol moiety and the sulfate conjugate of 3-(4'-hydroxyphenoxy) benzoic acid occurred to a greater extent in rats than in mice; and more thiocyanate was excreted in mice than in rats (Kaneko et al. 1981). Dogs (*Canis familiaris*) are remarkably different from rodents in their ability to metabolize fenvaleate (Kaneko et al. 1984). Four major differences have been observed:

1. Rats and mice show hydroxylation of the 2'-position of the alcohol moiety, whereas dogs do not.
2. Dogs produce 3-phenoxybenzyl alcohol and 3-(4'-hydroxyphenoxy) benzyl alcohol, whereas rodents do not.
3. The predominant conjugate of the alcohol moiety in dogs is 3-phenoxybenzoyl glycine, but this is only a minor conjugate in rodents.
4. Dogs produced more glucuronides of acid moiety and their hydroxy derivatives than did rats and mice.

The proposed fenvaleate metabolic pathways in dogs (Kaneko et al. 1984) suggest that species differences and pathways are important and require more research.

Cattle (*Bos* spp.) protected against various insect pests by fenvaleate-impregnated ear tags grow better than unprotected cattle. Beef cattle were protected against hornflies (*Haematobia irritans*) and other blood-sucking dipterans by fenvaleate-impregnated ear tags. During a 115-day grazing period, protected cattle had greater weight gain than unprotected cattle (Haufe 1982). This technique may have application in protecting fly-infested threatened or endangered species of mammals. Dairy cows tagged with 8% fenvaleate ear tags showed a 99.9% reduction in hornflies over a 16-week trial (Block and Lewis 1986). But other species of flies (housefly, *Musca domestica*; stablefly, *Stomoxys calcitrans*; facefly, *Musca autumnalis*) were not controlled to the same extent, and they increased as hornfly populations decreased. Protected cows produced 117 kg more milk in 16 weeks than did unprotected cows; fat and protein percentages in milk were the same for both groups. The higher milk production in the fenvaleate-tagged group was attributed to more uninterrupted forage time, greater forage consumption, and more efficient energy utilization because less energy was expended on avoiding or removing flies (Block and Lewis 1986). Similar results were reported in dairy cows in a 12-week study (Harris et al. 1987). Fenvaleate was adequately distributed over the entire body and persisted for at least 80 days on the hair of cattle with one ear tag containing 10.5 g active ingredients (Yeung et al. 1989). Residues in hair were highest at 14 days (18.4 mg/kg FW) and lowest at 80 days (1.3 to 3.0 mg/kg FW). All four stereoisomers were present

on cattle hair, and no stereoselective degradation occurred. Hair contained 14.8 mg/kg FW fenvalerate after 30 days with two ear tags (Yeung et al. 1989).

Cows fed fenvalerate in grain at 10 mg/kg diet for 4 days excreted most of the fenvalerate, essentially unchanged, in urine (Wszolek et al. 1981b). A secondary excretion route is feces, accounting for about 25% of the ingested dose. Milk accounted for 0.44 to 0.64% of the total excreted (Wszolek et al. 1980). Half-time persistence of fenvalerate in milk of treated cows is about 6.4 days (Frank et al. 1984). Effects of low concentrations (1.14 to 6.8 µg/L) of fenvalerate in milk of treated cows on newborn suckling calves are unknown and merit additional research (Frank et al. 1984).

Fenvalerate toxicity is antagonized by atropine sulfate or methocarbamol, which may be effective in treating severe cases of poisoning (Hiromori et al. 1986). Conversely, some compounds exacerbate the toxicity of fenvalerate and interfere with a desired use. Domestic cats (*Felis domesticus*) treated with Fendeet (an aerosol mixture of fenvalerate and *N,N*-diethyl-*m*-toluamide) to control fleas and ticks sometimes show signs of toxicosis, such as tremors, hypersalivation, ataxia, vomiting, depression, and seizures. Signs usually appeared within hours of topical application, and females and juveniles seem to be the most sensitive groups. The demonstrated ability of *N,N*-diethyl-*m*-toluamide to enhance the dermal absorption of fenvalerate is the probable cause of toxicosis (Dorman et al. 1990).

In occupational settings, fenvalerate produces temporary irritation and itching (Bradbury and Coats 1989a). Among human fenvalerate applicators, sensitive individuals complain of a burning and tingling skin sensation after using the insecticide, and sometimes they substitute a more toxic insecticide to nontarget species in order to avoid this uncomfortable sensation (Flannigan et al. 1985). This practice, if widespread, may compromise existing or proposed natural resource management practices.

Table 20.7 Lethal and Sublethal Effects of Fenvalerate on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
CATTLE, <i>Bos</i> spp.		
Diet		
Fed 0.15 mg/kg feed for 21 days	Residues ranged up to 0.002 mg/L in milk, 0.022 mg/L in cream, 0.014 mg/kg fresh weight (FW) in fat, 0.006 mg/kg FW in liver, and <0.01 mg/kg FW in bone, brain, muscle, kidney, or lung	1
Dairy cows fed 5 or 15 mg/kg ration daily for 4 days; milk and feces collected during exposure and 6 days after exposure	Maximum concentrations of fenvalerate in milk during exposure were 48 µg/L (377 µg/kg dry weight = DW) in the 5 mg/kg group, and 250 µg/L (1950 µg/kg DW) in the 15 mg/kg group; fenvalerate was not detectable 2 days after exposure in the low-dose group and 6 days after exposure in the high-dose group. In feces, the maximum concentrations ranged between 34.9 and 50.4 mg/kg DW during exposure; detectable concentrations in both groups were evident 6 days after exposure	2
Fed 10.9 mg/kg feed for 28 days	Maximum residues, in mg/kg FW, were 0.13 in whole milk, 1.0 in cream, 0.8 in fat, and 0.06 in muscle	1
Dermal		
Dairy cows of mean weight 671 kg given 0.1 g topically (0.1 mg/kg body weight = BW) in 6 consecutive treatments at intervals of 3 or 4 days (total 0.6 g)	After last application, no detectable fenvalerate residues were found in milk after 6 h; maximum residues in milk were 1.14 µg/L after 3 days, 0.42 in 4 days, and not detectable after 7 days	3

Table 20.7 (continued) Lethal and Sublethal Effects of Fenvalerate on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference^a
Dairy cows given three consecutive topical treatments of 0.5 g (0.5 mg/kg BW; total 1.5 g) at 2-week intervals	Maximum residues in milk, in µg/L, after last treatment were 6.8 after 6 h, 2.9 after 3 days, 2.5 at 7 days, 1.3 at 14 days, and <0.2 at 3 weeks. About 0.05% of the applied fenvalerate appeared in the milk as the intact insecticide over the 59-day study period	3
DOG, <i>Canis familiaris</i>		
Oral		
Male beagles, 7 months old, 1.7 mg/kg, single dose	About 84% eliminated from body within 3 days via urine and feces. Half-time persistence of 2 h in blood, and 0.7–1.0 day in whole body	4
Diet		
Fed up to 12.5 mg/kg BW equivalent for 90 days	No evidence of toxicity at any level	1
Groups of 12 beagles (6 males, 6 females), 5 months old, fed 250, 500, or 1000 mg fenvalerate/kg feed for 6 months	For all groups, dose-dependent increase in emesis, head shaking, biting of the extremities, blood chemistry alterations, ataxia, tremors, and hepatic multifocal microgranulomas. Some males in the 1000-mg/kg-group were killed after 2 weeks while in coma. Sex-related differences were noted: increased cholesterol and alkaline phosphatase in males; poor growth and enlarged adrenals, ovaries, liver, and kidneys in females. Lymph node histopathology was observed in female 500- and 1000-mg/kg-group and in the male 1000-mg/kg-group	5
HAMSTER, <i>Cricetus</i> sp.		
<i>In vitro</i>		
5–40 mg/L	Nontoxic to isolated cells	6
Oral		
12.5 or 25 mg/kg BW for 2 days	No chromosomal aberrations in bone marrow	1
DOMESTIC CAT, <i>Felis domesticus</i>		
Dermal		
Topical aerosol treatment of fenvalerate plus Deet (<i>N,N</i> -diethyl- <i>m</i> -toluamide) to control fleas and ticks	Kitten, 3 months old, died in 6 h following hypersalivation, ataxia, depression, and seizures. No histopathology at necropsy; brain AChE activity normal. Fenvalerate residues, in µg/kg, were 345,000 in skin, 230 in kidney, 150 in liver, 10 in brain. Adult (4-year-old) showed signs of toxicosis 4 h after topical application; by 30 h, animal had lowered body temperature, bradycardia, and other signs of fenvalerate poisoning. At death, shortly thereafter, fenvalerate residues were 1000 µg/kg in skin and 20 µg/kg in liver	7
DOMESTIC MOUSE, <i>Mus</i> spp.		
Intercerebroventricular injection		
0.2 mg/kg BW	95% dead; 50% show signs of poisoning within 6 min of brain injection	8
1.0 mg/kg FW brain, equivalent to 14 µg/kg BW	LD50; 2S,α-S-isomer	9
Oral, single dose		
0.3, 3, or 30 mg/kg	No deaths in any group. The 30 mg/kg group was hyperactive for 4 h after dosing. All mice preferred 0.3% saccharin solution to water	10

Table 20.7 (continued) Lethal and Sublethal Effects of Fenvalerate on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
2.5 mg/kg BW of each of the 4 chiral isomers; tissue residues measured 6 days later	Residues of the <i>2R,αS</i> -isomer were 9–16 times higher in adrenal than the other 3 isomers (<i>2S,αS</i> ; <i>2S,αR</i> ; <i>2R,αR</i>), at least 20 times higher in heart, 6–14 times higher in kidney, 17–28 times higher in liver, at least 15 times higher in lung, 3–6 times higher in mesenteric lymph node, and >30 times higher in spleen	11
7 mg/kg BW, residues measured 6 days later	Maximum concentrations, in mg/kg FW, were 7.3 in hair, 0.9 in fat, 0.5 in skin, 0.3 in blood, and 0.08 in liver	12
8.4 mg/kg BW, residues measured 7 days later	Maximum concentrations, in mg/kg FW, were 2.3 in hair, 0.8 in fat, 0.3 in stomach contents, 0.1 in skin, and 0.05 in blood	12
50 mg/kg BW	LD50; <i>2S,αS</i> -isomer	13
72–845 mg/kg BW, various laboratory strains	LD50	1, 13–16
200 mg/kg BW	Slight increase in frequency of chromosome aberrations in bone marrow cells	17
>600 mg/kg BW	LD50; <i>2S,αR</i> isomer	13
>5000 mg/kg BW	LD50; <i>2R,αR</i> isomer	13
Dermal		
1 mg/kg BW, single application	Penetration through skin was 1.9% at 60 min, 2.2% at 6 h, and 9.1% at 24 h. Of penetrated dose, maximum percent distribution was 83% in carcass at 60 min, 1.3% in blood at 6 h, 11.5% in liver at 6 h, 2.2% in kidney at 6 h, 0.7% in fat at 6 h, and 73% in feces at 24 h	18, 19
60, 600, or 1800 mg/kg BW, single application	At 1800 mg/kg BW, 20% died in 96 h; no deaths in other groups. Survivors in 600 and 1800 mg/kg groups were hyperactive. All survivors preferred 0.3% saccharin solution to water	10
Intraperitoneal injection		
3.9 mg/kg BW	LD50; <i>2S,αS</i> -isomer	9
62 mg/kg BW	LD50	14
89 mg/kg BW	LD99	14
Diet		
Fed 5, 15, or 50 mg/kg on days 6–15 of gestation	Maternal toxicity at 50 mg/kg BW, but no effect on embryonic development	1
Fed 10, 50, 250, or 1250 mg/kg feed for 2 years	Increased mortality, reduced growth, disrupted enzyme activity at 1250 mg/kg. Nonneoplastic microgranulomas in lymph, liver, and spleen of 250 and 1250 mg/kg male mice; less severe microgranulomatous changes in mesenteric lymph node of 50 and 250 mg/kg groups; no observable effect at 10 mg/kg diet	34
Fed 50, 250, or 1250 mg/kg feed for 2 years	Nonneoplastic pathological changes diagnosed as multifocal microgranulomas in lymph nodes, liver, and spleen of males at all dose levels, and in females at the 250 and 1250 mg/kg diet level	20
Fed 100, 300, 1000, or 3000 mg/kg feed for 78 weeks	No evidence of carcinogenicity at any dose tested. No-observable-effect-level (NOEL) was 100 mg/kg diet (equivalent to 15 mg/kg BW); dose-related effects noted in liver at 300 mg/kg diet and higher	1
125 mg/kg diet, 8 weeks, <i>2R,αS</i> isomer	No deaths; 70% incidence of microgranulomas in liver	20
Fed 500 mg/kg diet of three isomers (<i>2S,αS</i> ; <i>2R,αS</i> ; <i>2R,αR</i>) for 2 weeks	Residues, in µg/kg FW, of the <i>2R,αS</i> isomer were significantly higher than that of other isomers tested in adrenal (173 vs. 10–21), heart (15 vs. 2), kidney (22 vs. 9–10), liver (105 vs. 13); lung (31 vs. 2–5), mesenteric lymph nodes (86 vs. 8–12), and spleen (21 vs. 1)	11

Table 20.7 (continued) Lethal and Sublethal Effects of Fenvalerate on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
500 mg/kg diet, 13 weeks	No deaths; 100% incidence of microgranulomas or giant cell infiltration	20
500 mg/kg diet, 52 weeks, 2S, α S-isomer	No microgranulomas or giant cell infiltration in liver, spleen, or lymph nodes	20
500 or 1000 mg/kg diet, 52 weeks, 2S, α R isomer	No deaths; no microgranulomas	20
1000 mg/kg diet, 2 weeks, 2S, α S isomer	Severe hyperexcitability and tremors and 100% kill. No microgranulomas present	20
1000 mg/kg diet, 4 weeks, 2R, α S isomer	No deaths; 100% incidence of microgranulomas	20
1000 mg/kg diet, 13 weeks, 2R, α R isomer	No deaths; no microgranulomas or giant cell infiltration	20
2000 mg/kg diet, 2 weeks, 2S, α R isomer	All dead; no microgranulomas	20
Intraperitoneal (ip) injection		
40 mg/kg BW, 5 daily doses (total of 100 mg/kg BW)	Significant increase in frequency of chromosome aberrations induced in bone marrow cells — but frequency lower than single-dose ip injection of 200 mg/kg BW	17
Subcutaneous injection		
Given 5 daily doses totaling 100, 150, or 200 mg/kg BW	After 35 days, incidence of sperm abnormalities was significantly increased over controls: 3.3% abnormal sperm in 100-mg/kg-group, 5.9% in 150-mg/kg-group, and 6.3% in 200-mg/kg-group vs. 2.3% in controls	17
RABBIT, <i>Oryctolagus</i> spp.		
Dermal		
0.13 mg/cm ² skin, applied 5 days weekly for 16 weeks	Minor increases in cutaneous blood flow, skin reddening, and skin thickening	22
<i>In vitro</i>		
0.2–10 mg/L, liver and muscle tissues	Synthesis of protein and RNA inhibited in muscle in a dose-dependent manner; maximum inhibition was 0.2 mg/L for RNA synthesis and 10 mg/L for protein. The reverse was observed in liver; maximum stimulation was at 2 mg/L	23
DOMESTIC SHEEP, <i>Ovis aries</i>		
Diet		
3-month-old lambs fed 45 mg/kg feed for 10 days, equivalent to 20 mg daily	Tissue residues, in mg/kg DW, were 3.6–4.4 in renal fat, 0.2 in leg muscle, and 0.1 in liver	24
LABORATORY WHITE RAT, <i>Rattus</i> spp.		
Diet		
Fed 1, 5, 25, or 250 mg/kg ration for up to 2 years	No measurable effect on body weight, food consumption, hematology, clinical chemistry, or organ weights of any diet	25
Fed diets containing 1, 5, 25, or 250 mg/kg feed for 3 generations	No teratogenic or fetotoxic effects. Females in third generation fed highest dose had reduced growth	1
Fed 1, 5, 25, 250, or 500 mg/kg ration for 2 years	NOEL at 250 mg/kg, equivalent to 12.5 mg/kg BW; growth suppression at 500 mg/kg diet	1
Fed 50, 150, 500, or 1500 mg/kg feed for 15 months	NOEL at 50 mg/kg, equivalent to 2.5 mg/kg BW. Higher doses had adverse effects on growth, food consumption, and behavior	1
Fed 1000 mg/kg ration for 2 years	Growth inhibited; organ/BW ratios increased in brain, liver, spleen, kidney, heart (females), and testes. Mammary and pituitary tumors commonly observed in treated and in control groups. No statistically significant difference in number or type of neoplasms, except for mammary tumors	25

Table 20.7 (continued) Lethal and Sublethal Effects of Fenvalerate on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect	Reference ^a
Oral		
1.7 mg/kg BW daily for 5 consecutive days, or single dose of 8.4 mg/kg BW. Technical fenvalerate and 2S, α S-isomer tested separately	No apparent differences in the nature and amount of metabolites and in the pattern of excretion and tissue residues between the racemic mixture and the 2S, α S isomer	26
Single dose, 2.5 mg/kg BW; residues, in μ g/kg FW, in tissues measured 6 days after exposure		
2R, α S isomer	Residues in tissues were usually much higher than those of other isomers tested: adrenal, 371; fat, 304; heart, 40; kidney, 25; liver, 72; lung, 25; mesenteric node, 318; and spleen, 62	11
2S, α S isomer	Residues were 511 in fat, 45 in mesenteric lymph node, and <22 in other tissues	11
2S, α R isomer	Fat contained 326, mesenteric lymph node 68, and other tissues <20	11
2R, α R isomer	Fat contained 756, in mesenteric lymph node 94, and other tissues <23	11
Single dose of 3 mg/kg BW, individual isomers tested, fat analyzed periodically during 21-day observation period	Half-time persistence of all 4 isomers in fat ranged between 7 and 10 days; mean residues at 24 h and 21 days after exposure were 0.64 and 0.08 mg/kg FW, respectively	27
Decarboxyfenvalerate, single dose, 4 mg/kg BW	Almost completely eliminated in a few days, mainly via the feces; little translocation from GI contents and liver to other tissues; Tb 1/2 of 10 h in pancreas and <7 h in all other tissues	28
Single dose, 7 mg/kg BW, residues measured 6 days later	Residues, in μ g/kg FW, were about 1250 in blood, 1200 in fat, 2300 in hair of females, 37,000 in hair of males, 370 in liver, and 5800 in skin	12
Single doses between 15–200 mg/kg BW	At 90 min, rats showed a dosage-dependent decrease in locomotor activity and operant response rates	29
Adults given 25 or 75 mg/kg BW, 5 days a week for 10 weeks	At low dose, no signs of neurotoxicity or significant hepatotoxicity. At high dose, neurotoxicity evident only during first week; liver contained significantly elevated number of foci/cm ² and a larger percentage of liver tissue occupied by foci when compared to controls	30
450–3000 mg/kg BW	LD50; variability due to solvent	1
451 mg/kg BW	LD50	15, 21, 31
Single dose of 850 mg/kg BW, observed for 7 days	Signs of toxicosis appeared in 2 h; if untreated, 80% died. Intraperitoneal injection of 400 mg/kg BW of methocarbamol followed by repeated doses of 200 mg/kg BW at every onset of signs eliminated signs of poisoning within 17 h and prevented mortality	32
Dermal		
31, 155, or 310 mg/kg BW, 5 days weekly for 2 weeks; observed for 2 weeks after last treatment	No deaths. Altered blood chemistry that returned to normal during observation period, except for elevated serum alkaline phosphatase activity	33
Intravenous injection		
50–100 mg/kg BW	LD50	21

^a 1, Reed 1981; 2, Wszolek et al. 1980; 3, Frank et al. 1984; 4, Kaneko et al. 1984; 5, Parker et al. 1984b; 6, Pluijmen et al. 1984; 7, Dorman et al. 1990; 8, Gammon et al. 1982; 9, Lawrence and Casida 1982; 10, Mitchell et al. 1988; 11, Kaneko et al. 1986; 12, Kaneko et al. 1981; 13, Bradbury and Coats 1989a; 14, Williamson et al. 1989; 15, Bradbury and Coats 1989b; 16, El-Sewedy et al. 1982; 17, Pati and Bhunya 1989; 18, Grissom et al. 1985; 19, Grissom et al. 1987; 20, Okuno et al. 1986; 21, Gray and Soderlund 1985; 22, Flannigan et al. 1985; 23, El-Sebae et al. 1988; 24, Wszolek et al. 1981a; 25, Parker et al. 1984a; 26, Ohkawa et al. 1979; 27, Marei et al. 1982; 28, Mikami et al. 1985; 29, Crofton and Reiter 1988; 30, Flodstrom et al. 1988; 31, Smith and Stratton 1986; 32, Hiromori et al. 1986; 33, Saleh et al. 1986a; 34, Parker et al. 1983.

20.5 RECOMMENDATIONS

Fenvalerate is listed under the Class IV Surveillance Index Classification, indicating a low hazard potential to humans from toxicological and exposure standpoints. This classification requires only nominal monitoring (Reed 1981). Monitoring efforts of regulatory agencies to the present time, however, have been limited and of marginal worth in evaluating background concentrations of fenvalerate. Additional monitoring is recommended to measure fenvalerate residues in tissues of birds and mammals of U.S. Fish and Wildlife Service concern.

Products that contain fenvalerate and are registered for use on corn, wheat, soybeans, sorghum, oats, barley, rye, or cotton are subject to the provisions of the Endangered Species Act (Sine 1988). The Endangered Species Act requires that actions of federal agencies not jeopardize threatened or endangered species or their habitats. Specifically, the U.S. Environmental Protection Agency, in consultation with the U.S. Fish and Wildlife Service, determines whether use of fenvalerate poses a threat to listed species of animals and plants in various locations (Sine 1988). Clearly, fenvalerate and other synthetic pyrethroid insecticides should be used with extreme caution in habitats of endangered species.

No regulations exist for protection of sensitive natural resources against fenvalerate, although current application rates to control pestiferous crop insects are lethal to many species of nontarget organisms, including bees, fish, and crustaceans ([Table 20.8](#)). Proposed fenvalerate guidelines for protection of livestock, poultry, and human health are as follows: <5 mg/kg in diets of livestock; <50 mg/kg in diets of poultry; <3 mg/kg in human diets (<1 mg/kg for vegetables, <0.5 mg/kg for meat, <0.25 mg/kg for milkfat); and <0.125 mg/kg BW for acceptable daily intake in man ([Table 20.8](#)).

Despite the high toxicity of fenvalerate and other pyrethroids to aquatic organisms, few environmental problems have been documented, presumably due to the very low application levels needed to control insects, adsorption onto soil and organic matter, and comparatively rapid degradation (Gray and Soderlund 1985). Nevertheless, fenvalerate is extremely toxic to aquatic organisms ([Table 20.8](#)), has high bioaccumulation, and is persistent in sediments. These patterns are most pronounced in estuaries and other wetland environments. Fenvalerate use in areas adjacent to estuarine systems poses unacceptable risks to those ecosystems at concentrations not detectable by analytical methods (Schimmel et al. 1983). It seems reasonable to prohibit all uses of fenvalerate directly into aquatic environments, and to severely restrict usage in areas adjacent to drainage systems.

Additional research is needed on sublethal effects of fenvalerate in the following areas:

1. Impaired response to scent stimuli as demonstrated in bees (Taylor et al. 1987)
2. Genotoxic potency as shown in positive genotoxic effects on mice bone marrow (Pati and Bhunya 1989)
3. Photoproduct formation — especially those formed through ultraviolet irradiation — wherein at least two photoproducts were more toxic than the parent chemical (Holmstead et al. 1978)
4. Enhanced tumor formation in rodent liver (Flodstrom et al. 1988)
5. Development of analytical procedures to detect minute and short-lived reactive metabolites (Miyamoto 1988)
6. Development of simplified and reliable laboratory test systems more representative of total natural ecosystems (Miyamoto 1988)
7. Interaction effects of fenvalerate degradation products with other chemicals (Smith and Stratton 1986).

More research is also needed on indirect effects on wildlife due to reductions in nontarget insects, and on bioavailability of fenvalerate to aquatic organisms from sediments and the sediment–water interface.

Table 20.8 Proposed Fenvalerate Criteria for the Protection of Natural Resources and Human Health

Resource and Other Variables	Criterion	Reference ^a
BEES (<i>Apis spp.</i>, <i>Megachile</i> sp.)		
Adverse effects		
Whole body	>0.1 µg/bee	1
Diet	>10 mg/kg fresh weight (FW)	2
Aerial application	0.05–>0.11 kg/ha	3, 4
AQUATIC ORGANISMS		
Crustaceans, decreased survival		
Water column	0.003–0.022 µg/L	5–12
Sediments	97–190 µg/kg FW	13
Fish		
Water column		
Persistent residues	>0.00028 µg/L	14
No adverse effects on growth, survival, or reproduction	0.062–0.083 µg/L	13
Lethal	0.088–0.31 µg/L	5, 10, 11, 13, 15–20
Brain residues at death	>0.16 mg/kg FW	20
BIRDS		
Acute oral exposure, single dose		
No deaths	<250 mg/kg body weight (BW)	21
Some deaths	>500 mg/kg BW	21
Persistent residues	>5 mg/kg BW	22
Tissue residues at death		
Brain	0.1–1.26 mg/kg FW	21
Liver	0.74 mg/kg FW	21
Dietary exposure		
Sublethal		
No residues in eggs or meat	<50 mg/kg diet	22
Biochemical upset	>2000 mg/kg diet	24
Lethal	>15,000 mg/kg diet	21
MAMMALS		
Dietary exposure		
Sublethal		
Persistent residues	0.15–15 mg/kg feed	23, 25
Temporary tolerance level, livestock, dried apple pomace	5 mg/kg feed	23
No significant effects	12.5–15 mg/kg BW daily, 100–250 mg/kg diet	23, 26
Significant adverse effects	250–1000 mg/kg diet	27
Lethal	>50 mg/kg BW, >1250 mg/kg diet	23, 28
Single oral exposure		
Sublethal		
Behavioral changes	0.3–30 mg/kg BW	29
Persistent residues	>2.5 mg/kg BW	30
Lethal	50–450 mg/kg BW	20, 23, 31
Dermal exposure		
Sublethal		
Persistent residues	0.15–1.0 mg/kg BW	32–34
No deaths	310 mg/kg BW daily for 2 weeks	35
Lethal	1800 mg/kg BW, single application	29
HUMAN HEALTH		
Permanent tolerance level		
Meat and milk fat	<0.02 mg/kg FW	23

Table 20.8 (continued) Proposed Fenvalerate Criteria for the Protection of Natural Resources and Human Health

Resource and Other Variables	Criterion	Reference ^a
Temporary tolerance level		
Milk fat	<0.25 mg/kg FW	23
Meat	<0.5 mg/kg FW	23
Total diet	<3 mg/kg FW	23
Vegetables, "safe" level	<1 mg/kg FW	36
Acceptable daily intake (ADI), 60-kg person, 1.5 kg food daily	0.125 mg/kg BW	23
Theoretical daily exposure from diet		
Minimum	0.015 mg, 0.00025 mg/kg BW, 0.2% of ADI	23
Maximum	0.334 mg, 0.0056 mg/kg BW, 4.5% of ADI	23

^a 1, Lingappa et al. 1985; 2, Stoner et al. 1984; 3, Tasei and Debray 1985; 4, Mayer et al. 1987; 5, Clark et al. 1987; 6, Scott et al. 1987; 7, Day and Kaushik 1987c; 8, Day and Kaushik 1987a; 9, Anderson 1982; 10, Schimmel et al. 1983; 11, Mayer 1987; 12, Tagatz and Ivey 1981; 13, Clark et al. 1989; 14, Bradbury et al. 1986; 15, Curtis et al. 1985; 16, Mayer and Ellersiek 1986; 17, Clark et al. 1985; 18, Holcombe et al. 1982; 19, Hansen et al. 1983; 20, Bradbury and Coats 1989b; 21, Bradbury and Coats 1982; 22, Akhtar et al. 1989; 23, Reed 1981; 24, Riviere et al. 1983; 25, Wszolek et al. 1980; 26, Parker et al. 1984a; 27, Parker et al. 1984b; 28, Parker et al. 1983; 29, Mitchell et al. 1988; 30, Kaneko et al. 1986; 31, Bradbury and Coats 1989a; 32, Frank et al. 1984; 33, Grissom et al. 1985; 34, Grissom et al. 1987; 35, Saleh et al. 1986a; 36, Jain et al. 1979.

20.6 SUMMARY

Synthetic pyrethroids are the newest major class of broad-spectrum organic insecticides used in agricultural, domestic, and veterinary applications, and now account for more than 30% of global insecticide use. Fenvalerate [(*RS*) α -cyano-3-phenoxybenzyl (*RS*) 2-(4-chlorophenyl)-3-methylbutyrate] is one of the newer synthetic pyrethroid insecticides, and the one most widely used. Technical fenvalerate is a mixture of four optical isomers, each occurring in equal amounts, but with different efficacies against insect pests. Insecticidal properties are largely associated with the *2S,αS*-isomer, and to a minor extent with the *2S,αR*-isomer. Isomers with a *2R* configuration have negligible biocidal properties. However, tumor-like growths in rodent liver are associated with the comparatively innocuous *2R,αS*-isomer. Pyrethroid insecticides are potent neurotoxicants that interfere with nerve membrane function by interaction with the sodium channel. Fenvalerate is among the most effective pyrethroid neurotoxicants tested, and the *2S,αS*-isomer is up to 15 times more potent than other fenvalerate isomers.

Fenvalerate persists for <10 weeks in the environment and does not accumulate readily in the biosphere. Time for 50% loss (T_b 1/2) in fenvalerate-exposed amphibians, birds, and mammals is 6 to 14 h. For reptiles, terrestrial insects, aquatic snails, and fish, it is usually >14 h to <2 days; and for crop plants, it is 2 to 28 days. In nonbiological compartments, T_b 1/2 is up to 6 days in freshwater, 34 days in seawater, 6 weeks in estuarine sediments, and 9 weeks in soils.

At recommended application rates to control pestiferous crop insects, fenvalerate and other synthetic pyrethroids are relatively harmless to birds, mammals, and terrestrial plants. However, certain nontarget species, including bees, crustaceans, and fish, are at considerable risk, especially at low temperatures. Target insect species are usually killed at fenvalerate concentrations of 0.015 µg/insect, 0.11 kg/ha by way of aerial application, 5.4 mg/kg in soil, or 50 mg/kg in diet. Fenvalerate is especially toxic to aquatic organisms (e.g., crustaceans died at 0.003 to 0.03 µg/L and fish and amphibians at 0.09 to 1.1 µg/L), and its use in or near aquatic environments now seems contraindicated. Birds and mammals are significantly more resistant than fish and invertebrates. Adverse effects on birds occur at acute oral doses >500 mg/kg body weight (BW), and 750 mg/kg ration; <50 mg fenvalerate/kg feed produced no appreciable residues in eggs and meat of exposed birds. Among sensitive mammals, adverse effects on survival occur at acute oral doses of 50 to

450 mg/kg BW, dietary loadings of 50 to 1000 mg/kg feed, and dermal applications of 1800 mg/kg BW.

Criteria have not yet been formulated by regulatory agencies for protection of sensitive fish and wildlife resources against fenvalerate. Guidelines for protection of poultry, livestock, and human health include <50 mg/kg in poultry diets, <5 mg/kg in livestock diets, <3 mg/kg in human diets, and <0.125 mg/kg BW daily in humans.

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CHAPTER 21

Mirex

21.1 INTRODUCTION

Fish and wildlife resources associated with approximately 51 million ha (125 million acres) in the southeastern United States, and with the Great Lakes, especially Lake Ontario, have been negatively affected by intensive or widespread use of mirex, a chlorinated hydrocarbon compound (Waters et al. 1977; Bell et al. 1978; Kaiser 1978; National Academy of Sciences [NAS] 1978; Lowe 1982; Eisler 1985; Hill and Dent 1985; Sergeant et al. 1993; Blus 1995; U.S. Public Health Service [USPHS] 1995). Contamination of the Southeast and of Lake Ontario by mirex probably occurred between 1959 and 1978. During that period, mirex was used as a pesticide to control the red imported fire ant (*Solenopsis invicta*) and the black imported fire ant (*Solenopsis richteri*), which infested large portions of Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, and Texas. Under the trade name of Dechlorane, mirex was used as a fire retardant in electronic components, fabrics, and plastics; effluents from manufacturing processes resulted in the pollution of Lake Ontario. Regulatory agencies, environmentalists, and the general public became concerned as evidence accumulated demonstrating that mirex was associated with high death rates, numerous birth defects, and tumors, and that it disrupted metabolism in laboratory mammals, birds, and aquatic biota. Mirex also tends to bioaccumulate and to biomagnify at all trophic levels of food chains. Field studies corroborated the laboratory findings and showed that mirex appeared to be one of the most stable and persistent organochlorine compounds known, being resistant to chemical, photolytic, microbial, metabolic, and thermal degradation processes. Upon degradation, a series of potentially hazardous metabolites are formed, although it is generally acknowledged that the fate and effects of the degradation products are not fully understood. Mirex was also detected in human milk and adipose tissues at low concentrations, the levels related to the degree of environmental contamination. In 1978, the U.S. Environmental Protection Agency banned all uses of mirex. It is probable that mirex and its metabolites will continue to remain available to living organisms in this country for at least 12 years, although some estimates range as high as 600 years.

21.2 CHEMICAL PROPERTIES

Mirex is a white, odorless, free-flowing, crystalline, nonflammable, polycyclic compound composed entirely of carbon and chlorine. The empirical formula is $C_{10}Cl_{12}$, and the molecular weight 545.54 (Hyde 1972; Waters et al. 1977; Bell et al. 1978; NAS 1978; Menzie 1978; Kaiser 1978). In the United States, the common chemical name is dodecachlorooctahydro-1,3,4-metheno-2H-cyclobuta[c,d]pentalene. The systematic name is dodecachloropentacyclo 5.3.0.0^{2,6}.0^{3,9}.0^{4,8}decane. Mirex was first prepared in 1946, patented in 1955 by Allied Chemical Company, and introduced

in 1959 as GC 1283 for use in pesticidal formulations against hymenopterous insects, especially ants. It was also marketed under the trade name of Dechlorane for use in flame-retardant coatings for various materials. Mirex is also known as ENT 25719 (Tucker and Crabtree 1970), CAS 2385-85-5 (Schafer et al. 1983), Dechlorane 510, and Dechlorane 4070 (Kaiser 1978). Technical-grade preparations of mirex consist of 95.19% mirex and less than $2.58 \times 10^{-7}\%$ contaminants, mostly kepone $C_{10}Cl_{10}O$ (NAS 1978). Mirex is comparatively soluble in various organic solvents, such as benzene, carbon tetrachloride, and xylene, with solubilities ranging from about 4000 to 303,000 mg/L. However, mirex has very low solubility in water, not exceeding 1.0 µg/L in freshwater or 0.2 µg/L in seawater (Bell et al. 1978). In biological systems, mirex lipophilicity would account for the high concentrations observed in fatty tissues and reserves.

Mirex, which is composed of 22% carbon and 78% chlorine, is highly resistant to chemical, thermal, and biochemical degradation. It is reportedly unaffected by strong acids, bases, and oxidizing agents, and is resistant to photolysis in hydrocarbon solvents, but less so in aliphatic amines. Thermal decomposition begins at about 550°C and is rapid at 700°C. Degradation products include hexachlorobenzene, hexachlorocyclopentadiene, and kepone. Several additional degradation products of mirex have been isolated, but not all have been identified (Holloman et al. 1975; Menzie 1978). At least one photodegradation product, the 8-monohydro analogue, sometimes accumulates in sediments and animals, but the fate and effects of these photoproducts are unclear (Cripe and Livingston 1977).

Mirex is rapidly adsorbed onto various organic particles in the water column, including algae, and eventually removed to the sediments. Not surprisingly, mirex has a long half-life in terrestrial and aquatic sediments; large fractional residues were detected at different locations 12 and 5 years after initial application (Bell et al. 1978). Some degradation of mirex to the 10-monohydro analogue was reported in anaerobic sewage sludge after 2 months in darkness at 30°C (Menzie 1978). Other studies with mirex-contaminated anaerobic soils, anaerobic lake sediments, and soil microorganisms showed virtually no bacterial degradation over time (Jones and Hodges 1974). In Lake Ontario, mirex from contaminated sediments remained available to lake organisms for many years and, as judged by present sedimentation rates, mirex may continue to be bioavailable for 200 to 600 years in that system (Scrudato and DelPrete 1982). Disappearance of mirex from baits over a 12-month period was about 41% for those exposed on the ground, 56% from those exposed in soil, and 84% from those exposed in pond water (de la Cruz and Lue 1978b). Mirex disappearance is probably related to uptake by biological organisms, as has been demonstrated in marine ecosystems contaminated with mirex (Waters et al. 1977), and not to degradation.

Mirex is a highly stable chlorinated hydrocarbon with lipophilic properties, and its accumulation and persistence in a wide variety of nontarget biological species has been well documented. The biological half-life of mirex reportedly ranges from 30 days in quail to 130 days in fish and to more than 10 months in the fat of female rats (Menzie 1978); this subject area is further developed later. At this juncture, it is sufficient to state that most authorities agree on two points: there is little evidence of significant mirex metabolism, and mirex ranks among the more biochemically stable organic pesticides known.

21.3 LETHAL EFFECTS

21.3.1 Aquatic Organisms

Aquatic organisms are comparatively resistant to mirex in short-term toxicity tests. Among various species of freshwater biota, LC₅₀ (96 h) values were not obtained at the highest nominal concentrations tested of 1000 µg/L for insects, daphnids, and amphipods (Johnson and Finley 1980; Sanders et al. 1981) and 100,000 µg/L for five species of fish (Johnson and Finley 1980). Similar results were reported for other species of freshwater invertebrates (Muncy and Oliver 1963; Lue and de la Cruz 1978) and fishes (Van Valin et al. 1968), although waterborne mirex at concentrations of 1000 µg/L was lethal to postlarval freshwater prawns (*Macrobrachium rosenbergerii*) in 24 h

(Eversole 1980). It is probable that bioavailable concentrations from the water in each test did not exceed 1.0 µg/L. However, delayed mortality frequently occurs for extended periods after exposure, and the potential for adverse effects at the population level remains high (NAS 1978). Latent biocidal properties of mirex were documented for fish (Van Valin et al. 1968; Koenig 1977) and crustaceans (Ludke et al. 1971; Hyde 1972; Cripe and Livingston 1977). Crustaceans were the most sensitive group examined. For example, the crayfish (*Procambarus blandus*) immersed in nominal concentrations of 0.1 to 5.0 µg mirex/L for periods of 6 to 144 h died 5 to 10 days after initial exposure (Ludke et al. 1971). Immature crayfish were more sensitive than adults, and mortality patterns were similar when mirex was administered in the water or in baits (Ludke et al. 1971).

21.3.2 Birds and Mammals

Acute oral toxicity of mirex to warm-blooded organisms was low, except for rats and mice, which died 60 to 90 days after treatment with 6 to 10 mg mirex/kg body weight (Table 21.1). Birds were comparatively resistant. The red-winged blackbird (*Agelaius phoeniceus*) was unaffected at 100 mg mirex/kg body weight, although it was considered the most sensitive of 68 species of birds tested with 998 chemicals for acute oral toxicity, repellency, and hazard potential (Schafer et al. 1983).

Mortality due to dietary mirex is variable among species, although high death rates were usually associated with high dietary concentrations and long exposure periods (Table 21.2). One significant effect of mirex fed to breeding adult chickens, voles, and rats was a decrease in survival of the young (Naber and Ware 1965; Shannon 1976; Waters et al. 1977; Chu et al. 1981). Prairie voles (*Micropterus ochrogaster*) fed diets containing 15 mg mirex/kg ration bred normally, but all pups died by day 21 (Shannon 1976). Survival of the pups of prairie voles decreased in the first litter when the diet of the parents contained 10 mg mirex/kg ration, in the second litter when it contained 5 mg/kg, and in the third litter when it contained 0.1, 0.5, 0.7, or 1.0 mg/kg (Shannon 1976).

Table 21.1 Acute Oral Toxicity of Mirex to Birds and Mammals

Organism	Dose (mg/kg body weight)	Mortality	Reference ^a
Mice, <i>Mus</i> sp.	5	None, 60 days posttreatment	1
Rat, <i>Rattus</i> sp.; female	6	50%, 90 days posttreatment	1
Mice	10	100%, 60 days posttreatment	1
Red-winged blackbird, <i>Agelaius phoeniceus</i>	100	None	2
Mice	100–132	50% in 10 days	3
Common quail, <i>Coturnix coturnix</i>	300	12–30%	4
Rat, male	306	Some	5
Mice	330	50%	6
Rat, female	365	50%, 14 days posttreatment	2
Rat, male	400	Lowest fatal dose	7
Rat, female	500	Lowest fatal dose	7
European starling, <i>Sturnus vulgaris</i>	562	None	8
Rat, female	600	Some	5
Rabbit, <i>Lepus</i> sp.	800 ^b	50%	6
Dog, <i>Canis</i> sp.	1000	None	9
Dog	1250	60%	11
Ring-necked pheasant, <i>Phasianus colchicus</i>	1400–1600	50%	6
Mallard, <i>Anas platyrhynchos</i>	2400	None	10
Japanese quail, <i>Coturnix coturnix japonica</i>	10,000	50%	6

^a 1, Gaines and Kimbrough 1969; 2, Schafer et al. 1983; 3, Fujimori et al. 1983; 4, Stickel 1963; 5, Hyde 1972; 6, Waters et al. 1977; 7, NAS 1978; 8, Schafer et al. 1983; 9, Larson et al. 1979; 10, Tucker and Crabtree 1970; 11, USPHS 1995.

^b Dermal.

Table 21.2 Dietary Toxicity of Mirex to Vertebrate Organisms

Organism	Mirex Dietary Concentration (mg/kg ration)	Exposure Interval	Percent Mortality	Reference ^a
Mallard, <i>Anas platyrhynchos</i>	1.0	25 weeks	6.2	1
Old-field mouse, <i>Peromyscus polionotus</i>	1.8	60 weeks	20.0	2
Mice, <i>Mus</i> sp.	5.0	30 days	Some	3
Prairie vole, <i>Micropterus ochrogaster</i>	5–15	90 days	Some	4
Old-field mouse	17.8	60 weeks	91.7	2
Beagle dog, <i>Canis</i> sp.	20	13 weeks	None	5
Pinfish, <i>Lagodon rhomboides</i>	20	20 weeks	None	6
Prairie vole	25	90 days	100	4
Rat, <i>Rattus</i> sp.	25	30 days	Some	3
Rat	50	14 days	None	7
Mice	50	14 days	100	7
Coho salmon, <i>Oncorhynchus kisutch</i>	50	12 weeks	None	8
Beagle dog	100	13 weeks	Some	5
Mallard	100	25 weeks	27.4	1
Channel catfish, <i>Ictalurus punctatus</i>	400	4 weeks	None	9
Ring-necked pheasant, <i>Phasianus colchicus</i>	1540	5 days	50.0	10
Common bobwhite, <i>Colinus virginianus</i>	2511	5 days	50.0	10
Japanese quail, <i>Coturnix coturnix japonica</i>	5000	5 days	20.0	10
Mallard ducklings	5000	5 days	None	10

^a 1, Hyde 1972; 2, Wolfe et al. 1979; 3, Chernoff et al. 1979; 4, Shannon 1976; 5, Larson et al. 1979; 6, Lowe 1982; 7, NAS 1978; 8, Leatherland et al. 1979; 9, McCorkle et al. 1979; 10, Heath et al. 1972.

21.4 SUBLETHAL EFFECTS

21.4.1 Aquatic Organisms

The maximum acceptable toxicant concentration (MATC) values calculated for mirex and various freshwater species were:

- <2.4 µg/L for amphipods (*Gammarus* sp.), based on growth inhibition at higher concentrations (Sanders et al. 1981)
- 2 to 3 µg/L for fathead minnows (*Pimephales promelas*), as judged by disruption of swim bladder hydroxyproline content, Vitamin C metabolism, and bone collagen (Mehrle et al. 1981)
- 34 µg/L for fathead minnows, based on impaired reproduction (Buckler et al. 1981)
- >34 µg/L for daphnids (*Daphnia* sp.) and midges (*Chaoborus* sp.), predicated on daphnid reproduction and midge emergence (Sanders et al. 1981)

Other mirex-induced sublethal effects included reduced photosynthesis in freshwater algae (Hollister et al. 1975), gill and kidney histopathology in the goldfish (*Carassius auratus*) (Van Valin et al. 1968), reduced growth in the bluegill (*Lepomis macrochirus*) (Van Valin et al. 1968), cessation of reproduction in *Hydra* sp. (Lue and de la Cruz 1978), and disrupted behavior in the blue crab (*Callinectes sapidus*) (Shannon 1976) and the marine annelid (*Arenicola cristata*) (Schoor and Newman 1976). McCorkle et al. (1979) showed that channel catfish (*Ictalurus punctatus*) are particularly resistant to high dietary concentrations of mirex; juveniles fed 400 mg mirex/kg ration for 4 weeks showed no significant changes in enzyme-specific activities of brain, gill, liver, or muscle. However, yearling coho salmon (*Oncorhynchus kisutch*) fed 50 mg mirex/kg ration for 3 months showed significant reduction in liver weight and whole-body lipid content (Leatherland

et al. 1979). Additional studies with coho salmon and rainbow trout (*Salmo gairdneri*) fed 50 mg mirex/kg ration for 10 weeks demonstrated a significant depression in serum calcium, and significant elevation of skeletal magnesium in salmon; trout showed no measurable changes in calcium and magnesium levels in serum, muscle, or skeleton, although growth was reduced, muscle water content was elevated, and muscle lipid content was reduced (Leatherland and Sonstegard 1981). Interaction effects of mirex with other anthropogenic contaminants are not well studied, despite the observations of Koenig (1977) that mixtures of DDT and mirex produced more than additive deleterious effects on fish survival and reproduction.

21.4.2 Birds

Among captive American kestrels (*Falco sparverius*) fed 8 mg mirex/kg ration for 69 days by Bird et al. (1983), there was a marked decline in sperm concentration and a slight compensatory increase in semen volume, but an overall net decrease of 70% in sperm number. These investigators believed that migratory raptors feeding on mirex-contaminated food organisms could ingest sufficient toxicant to lower semen quality in the breeding season which, coupled with altered courtship, could reduce the fertility of eggs and the reproductive fitness of the individual. Altered courtship in ring-necked doves (*Streptopelia capicola*) fed dietary organochlorine compounds was reported by McArthur et al. (1983).

Most investigators, however, agree that comparatively high dietary concentrations of mirex had little effect on growth, survival, reproduction, and behavior of nonraptors, including chickens (*Gallus* sp.), mallards, several species of quail, and red-winged blackbirds. For domestic chickens, levels up to 200 mg mirex/kg ration were tolerated without adverse effects on various reproductive variables (Waters et al. 1977), but 300 mg mirex/kg diet for 16 weeks was associated with reduced chick survival, and 600 mg/kg for 16 weeks reduced hatching by 83% and chick survival by 75% (Naber and Ware 1965). Mallard ducklings experienced temporary mild ataxia and regurgitation when given a single dose of 2400 mg/kg body weight, but not when given 1200 mg/kg or less (Tucker and Crabtree 1970). Mallards fed diets containing as much as 100 mg mirex/kg ration for prolonged periods showed no significant differences from controls in egg production, shell thickness, shell weight, embryonation, hatchability, or duckling survival (Hyde 1972). However, in other studies with mallards fed 100 mg mirex/kg diet, eggshells were thinned and duckling survival was reduced (Waters et al. 1977), suggesting that 100 mg mirex/kg ration may not be innocuous to mallards. No adverse effects on reproduction were noted in the common bobwhite at 40 mg mirex/kg diet (Kendall et al. 1978), or in two species of quail fed 80 mg mirex/kg ration for 12 weeks (Waters et al. 1977). Red-winged blackbirds were not repelled by foods contaminated with mirex, but consumed normal rations (Schafer et al. 1983); a similar observation was recorded for bobwhites (Baker 1964).

21.4.3 Mammals

Mirex has considerable potential for chronic toxicity because it is only partly metabolized, is eliminated very slowly, and is accumulated in the fat, liver, and brain. The most common effects observed in small laboratory mammals fed mirex included weight loss, enlarged livers, altered liver enzyme metabolism, and reproductive failure. Mirex reportedly crossed placental membranes and accumulated in fetal tissues. Among the progeny of mirex-treated mammals, developmental abnormalities included cataracts, heart defects, scoliosis, and cleft palates (NAS 1978; Blus 1995).

Mirex has caused liver tumors in mice and rats and must be considered a potential human carcinogen (Waters et al. 1977; NAS 1978). Long-term feeding of 50 and 100 mg mirex/kg ration to rats of both sexes was associated with liver lesions that included neoplastic nodules and hepatocellular carcinomas; neither sign was found in controls (Ulland et al. 1977).

Adults of selected mammalian species showed a variety of damage effects of mirex:

- Enlarged livers in rats at 25 mg mirex/kg diet (Gaines and Kimbrough 1969) or at a single dose of 100 mg/kg body weight (Ervin 1982)
- Liver hepatomas in mice at 10 mg mirex/kg body weight daily (Innes et al. 1969)
- Decreased incidence of females showing sperm in vaginal smears, decreased litter size, and thyroid histopathology in rats fed 5 mg mirex/kg diet since weaning (Chu et al. 1981)
- Elevated blood and serum enzyme levels in rats fed 0.5 mg mirex/kg ration for 28 days (Yarbrough et al. 1981)
- Diarrhea, reduced food and water consumption, body weight loss, decreased blood glucose levels, and disrupted hepatic microsomal mixed function oxidases in mice receiving 10 mg/kg body weight daily (Fujimori et al. 1983).

In studies of field mice, decreased litter size was observed at 1.8 mg mirex/kg diet, and complete reproductive impairment at 17.6 mg/kg diet after 6 months (Wolfe et al. 1979). At comparatively high sublethal mirex concentrations, various deleterious effects were observed: thyroid histopathology and decreased spermatogenesis in rats fed 75 mg mirex/kg diet for 28 days (Yarbrough et al. 1981); abnormal blood chemistry, enlarged livers, reduced spleen size, and loss in body weight of beagles fed 100 mg mirex/kg ration for 13 weeks (Larson et al. 1979); and decreased hemoglobin, elevated white blood cell counts, reduced growth, liver histopathology, and enlarged livers in rats fed 320 mg/kg ration for 13 weeks (Larson et al. 1979).

Cataract formation, resulting in blindness, in fetuses and pups from maternal rats fed comparatively low concentrations of dietary mirex is one of the more insidious effects documented. Mirex fed to maternal rats at 6 mg/kg body weight daily on days 8 to 15 of gestation, or at 10 mg/kg body weight daily on days 1 to 4 postpartum, caused cataracts in 50% of fetuses on day 20 of gestation, and in 58% of pups on day 14 postpartum (Rogers 1982). Plasma glucose levels were depressed in fetuses with cataracts, and plasma proteins were depressed in neonates; both hypoproteinemia and hypoglycemia are physiological conditions known to be associated with cataracts (Rogers 1982). Mirex-associated cataractogenicity has been reported in female pups from rats fed 5 mg mirex/kg ration since weaning (Chu et al. 1981), in rat pups from females consuming 7 mg mirex/kg ration on days 7 to 16 of gestation or 25 mg/kg diet for 30 days prior to breeding (Chernoff et al. 1979), and in mice fed 12 mg mirex/kg ration (Chernoff et al. 1979). Offspring born to mirex-treated mothers, but nursed by nontreated mothers showed fewer cataracts (Waters et al. 1977). Other fetotoxic effects in rats associated with dietary mirex included:

- Edema and undescended testes (Chernoff et al. 1979)
- Lowered blood plasma proteins, and heart disorders, including tachycardia and blockages (Grabowski 1981)
- Hydrocephaly; decreases in weight of brain, lung, liver, and kidney; decreases in liver glycogen, kidney proteins and alkaline phosphatase; and disrupted brain DNA and protein metabolism (Kavlock et al. 1982)

In prairie voles exposed continuously to dietary mirex of 0.5, 0.7, 1.0, 5.0, or 10.0 mg/kg ration, the numbers of litters produced decreased (Shannon 1976). Maximum number of litters per year were four at 1.0 mg mirex/kg ration, three at 5.0 mg/kg, and two at 10.0 mg/kg ration. Furthermore, the number of offspring per litter also decreased progressively. Concentrations as low as 0.1 mg mirex/kg ration of adults were associated with delayed maturation of pups and with an increase in number of days required to attain various behavioral plateaus such as bar-holding ability, hind-limb placing, and negative geotaxis (Shannon 1976). On the basis of residue data from field studies, as is shown later, these results strongly suggest that mirex was harmful to the reproductive performance and behavioral development of prairie voles at environmental levels approaching 4.2 g mirex/ha, a level used to control fire ants before mirex was banned.

21.5 BIOACCUMULATION

21.5.1 Aquatic Organisms

All aquatic species tested accumulated mirex from the medium and concentrated it over ambient water levels by factors ranging up to several orders of magnitude. Uptake was positively correlated with nominal dose in the water column (Table 21.3). Other investigators have reported bioconcentration factors from water of 8025 in daphnids (Sanders et al. 1981), 12,200 in bluegills (Skaar et al. 1981), 56,000 in fathead minnows (Huckins et al. 1982), and 126,600 in the digestive gland of crayfish (Ludke et al. 1971). Rapid uptake of mirex by marine crabs, shrimps, oysters, killifishes, and algae was reported after the application of mirex baits to coastal marshes (Waters et al. 1977; Cripe and Livingston 1977). Mirex was also accumulated from the diet (Table 21.3) (Ludke et al. 1971; Zitko 1980), but not as readily as from the medium. Dietary bioaccumulation studies with guppies and goldfish show that mirex and other persistent hydrophobic chemicals are retained in the organism and biomagnify through food chains because of their hydrophobicity (Gobas et al. 1989, 1993; Clark and Mackay 1991). Mirex may also be accumulated from contaminated sediments by marine teleosts (Kobylinski and Livingston 1975), but such accumulation has not been established conclusively. Although terrestrial plants, such as peas and beans, accumulate mirex at field application levels, mangrove seedlings require environmentally high levels of 11.2 kg mirex/ha before accumulation occurs (as quoted in Shannon 1976).

There is general agreement that aquatic biota subjected to mirex-contaminated environments continue to accumulate mirex, and that equilibrium is rarely attained before death of the organism from mirex poisoning or from other causes. There is also general agreement that mirex resists metabolic and microbial degradation, exhibits considerable movement through food chains, and is potentially dangerous to consumers at the higher trophic levels (Hollister et al. 1975; NAS 1978; Mehrle et al. 1981; Eisler 1985). Marine algae, for example, showed a significant linear correlation between amounts accumulated and mirex concentrations in the medium. If a similar situation existed in nature, marine unicellular algae would accumulate mirex and, when grazed upon, act as passive transporters to higher trophic food chain compartments (Hollister et al. 1975). The evidence for elimination rates of mirex from aquatic biota on transfer to mirex-free media is not as clear. Biological half-times of mirex have been reported as 12 h for daphnids (Sanders et al. 1981), more than 28 days for fathead minnows (Huckins et al. 1982), about 70 days in Atlantic salmon (*Salmo salar*) (Zitko 1980), 130 days for mosquitofish (*Gambusia affinis*), and 250 days for pinfish (as quoted in Skea et al. 1981). However, Skea et al. (1981) averred that biological half-times may be much longer if organism growth is incorporated into rate elimination models. For example, brook trout (*Salvelinus fontinalis*) fed 29 mg mirex/kg ration for 104 days contained 6.3 mg/kg body weight or a total of 1.1 mg of mirex in whole fish. At day 385 postexposure, after the trout had tripled in body weight, these values were 2.1 mg/kg body weight, an apparent loss of 67%; however, on a whole-fish basis, trout contained 1.2 mg, thus showing essentially no elimination on a total-organism basis (Skea et al. 1981).

No mirex degradation products were detected in whole fathead minnow or in hydrosoils under aerobic or anaerobic conditions (Huckins et al. 1982). In contrast, three metabolites were detected in coastal marshes after mirex bait application, one of which, photomirex, was accumulated by fish and oysters (Cripe and Livingston 1977). The fate and effects of mirex photoproducts in the environment are unclear and merit additional research.

The significance of mirex residues in various tissues is unresolved, as is the exact mode of action of mirex and its metabolites. Minchew et al. (1980) and others indicated that mirex is a neurotoxic agent, with a mode of action similar to that of other chlorinated hydrocarbon insecticides, such as DDT. In studies with crayfish and radiolabeled mirex, mirex toxicosis was associated with neurotoxic effects that included hyperactivity, uncoordinated movements, loss of equilibrium, and

paralysis (Minchew et al. 1980). Before death, the most significant differences in mirex distributions in crayfish were the increases in concentrations in neural tissues, such as brain and nerve cord, by factors up to 14 (or 0.4 mg/kg) in low-dose groups held in solutions containing 7.4 µg mirex/L, and up to 300 (or 6.2 mg/kg) in high-dose groups held in solutions with 74.0 µg/L. With continued exposure, levels in the green gland and neural tissues approached the levels in the hepatopancreas and intestine (Table 21.3). Schoor (1979) also demonstrated that mirex accumulates in the crustacean hepatopancreas, but suggested that other tissues, such as muscle and exoskeleton, have specific binding sites that, once filled, shunt excess mirex to hepatopancreas storage sites.

21.5.2 Birds and Mammals

Like aquatic organisms, birds and mammals accumulated mirex in tissue lipids, and the greater accumulations were associated with the longer exposure intervals and higher dosages (Table 21.3). Sexual condition of the organism may modify bioconcentration potential. For example, in adipose fat of the bobwhite, males contained 10 times dietary levels and females only 5 times dietary levels; the difference was attributed to mirex loss through egg laying (Kendall et al. 1978).

Data on excretion kinetics of mirex are incomplete. Prairie voles fed mirex for 90 days contained detectable whole-body levels 4 months after being placed on a mirex-free diet (Shannon 1976). Levels of mirex in voles after 4 months on uncontaminated feed were still far above levels in their mirex diets. Humans living in areas where mirex has been used for ant control contained 0.16 to 5.94 mg/kg in adipose fat; 60% of the mirex was excreted and most of the rest was stored in body tissues, especially fat (28%), and in lesser amounts of 0.2 to 3% in muscle, liver, kidney, and intestines (Waters et al. 1977). Almost all excretion of mirex takes place through feces; less than 1% is excreted in urine and milk. The loss rate pattern is biphasic, the fast phase was estimated at 38 h and the slow phase at up to 100 days. Mirex binds firmly to soluble liver proteins and appears to be retained in fatty tissues, a property that may contribute to its long biological half-life. Chickens given single doses of mirex at 30 mg/kg intravenously or 300 mg/kg orally demonstrated a biphasic decline in blood concentrations (Ahrens et al. 1980). The fast component, constituting about 25% of the total, was lost during the first 24 h; the loss of the slow component was estimated to be at a constant rate of about 0.03% daily, suggesting a half-life of about 3 years. Growing chicks fed 1 or 10 mg/kg dietary mirex for 1 week lost the compound rather rapidly; disappearance half-times were 25 days for skin and 32 days for fat (Ahrens et al. 1980). It is clear that much additional research is warranted on loss rate kinetics of this persistent compound and its metabolites.

Table 21.3 Uptake of Mirex from Ambient Medium or Diet by Selected Species

Habitat, Organism, and Tissue	Mirex in Medium (M) (g/L) or in Diet (D) (mg/kg)	Exposure	Bioconcentration factor (BCF)	Reference ^a
AQUATIC, FRESHWATER				
Fish				
Fathead minnow, <i>Pimephales promelas</i>				
Whole	2.0 (M)	120 days	28,000	1
Whole	7.0 (M)	120 days	18,400	1
Whole	13.0 (M)	120 days	12,000	1
Whole	34.0 (M)	120 days	13,800	1
Whole	2.0 (M)	120 + 56 days	12,000	1
Whole	7.0 (M)	120 + 56 days	6860	1
Whole	13.0 (M)	120 + 56 days	5460	1
Whole	34.0 (M)	120 + 56 days	7880	1

Table 21.3 (continued) Uptake of Mirex from Ambient Medium or Diet by Selected Species

Habitat, Organism, and Tissue	Mirex in Medium (M) (g/L) or in Diet (D) (mg/kg)	Exposure	Bioconcentration factor (BCF)	Reference ^a
Bluegill, <i>Lepomis macrochirus</i>				
Whole	1.3 (M)	60 days	1540	2
Whole	1000.0 (M)	90 days	150	2
Goldfish, <i>Carassius auratus</i>				
Skin	100.0 (M)	224 days	1220	2
Muscle	100.0 (M)	224 days	460	2
Liver	100.0 (M)	224 days	370	2
Gut	100.0 (M)	224 days	1520	2
Atlantic salmon, <i>Salmo salar</i>				
Whole	0.6 (D)	15 days	0.06	3
Whole	0.6 (D)	42 days	0.13	3
Brook trout, <i>Salvelinus fontinalis</i>				
Whole	29.0 (D)	17 days	0.04	4
Whole	29.0 (D)	104 days	0.22	4
Whole	29.0 (D)	104 + 385 days	0.07	4
Crustaceans				
Crayfish, <i>Procambarus</i> sp.				
Muscle	7.4 (M)	10–21 days	81	5
Brain	7.4 (M)	(interval	54	5
Nerve cord	7.4 (M)	represents	54	5
Green gland	7.4 (M)	appearance of	243	5
Gill	7.4 (M)	late symptoms	108	5
Digestive gland	7.4 (M)	of mirex	622	5
Intestine	7.4 (M)	toxicity)	257	5
Muscle	74.0 (M)	7–14 days	8	5
Brain	74.0 (M)	(See above)	80	5
Nerve cord	74.0 (M)	(See above)	84	5
Green gland	74.0 (M)	(See above)	76	5
Gill	74.0 (M)	(See above)	23	5
Digestive gland	74.0 (M)	(See above)	105	5
Intestine	74.0 (M)	(See above)	43	5
AQUATIC, MARINE				
Fish				
Diamond killifish, <i>Adinia xenica</i> (exposed adults)				
Embryo	1.5 (D)	9 days	1.7	6
Embryo	6.0 (D)	9 days	1.3	6
Embryo	24.0 (D)	9 days	1.2	6
Embryo	96.0 (D)	9 days	0.9	6
Hogchoker, <i>Trinectes maculatus</i>				
Muscle	56.0–5000.0 (M)	4 weeks	3800–10,400	7
Striped mullet, <i>Mugil cephalus</i>				
Whole	10.0 (M)	4 days	17–38	8
Crustaceans				
Shrimp, <i>Palaemonetes vulgaris</i>				
Hepatopancreas	0.04 (M)	4 days	9250	9
Hepatopancreas	0.04 (M)	13 days	16,250	9
Muscle	0.04 (M)	4 days	2250	9
Muscle	0.04 (M)	13 days	2000	9
Whole	0.04 (M)	4 days	4000	9
Whole	0.04 (M)	13 days	3250	9
Algae				
Whole	0.04 (M)	13 days	375	9
Whole, 4 spp.	0.01 (M)	7 days	3200–7500	10

Table 21.3 (continued) Uptake of Mirex from Ambient Medium or Diet by Selected Species

Habitat, Organism, and Tissue	Mirex in Medium (M) (g/L) or in Diet (D) (mg/kg)	Exposure	Bioconcentration factor (BCF)	Reference ^a
BIRDS AND MAMMALS				
Birds				
Chicken, <i>Gallus</i> sp.				
Fat	1.06 (D)	39 weeks	24	11
Kidney	1.06 (D)	39 weeks	3	11
Liver	1.06 (D)	39 weeks	2	11
Muscle	1.06 (D)	39 weeks	0.3	11
Skin (chick)	1.0 (D)	2 weeks	37	12
Fat (chick)	1.0 (D)	2 weeks	586	12
Mallards, <i>Anas platyrhynchos</i> (exposed adults)				
Eggs	1 (D)	18 weeks	2.4	13
Eggs	100 (D)	18 weeks	28	13
Fat	100 (D)	18 weeks	29	13
American kestrels, <i>Falco sparverius</i> , yearling males				
Muscle lipids	8.0 (D)	69 days	7	14
Testes lipids	8.0 (D)	69 days	6	14
Liver lipids	8.0 (D)	69 days	3	14
Common bobwhite, <i>Colinus virginianus</i>				
Fat	1.0 (D)	36 weeks	20	15
Fat	20.0 (D)	36 weeks	10	15
Fat	40.0 (D)	36 weeks	9.5	15
Breast muscle	1.0 (D)	36 weeks	0.7	15
Breast muscle	20.0 (D)	36 weeks	0.6	15
Breast muscle	40.0 (D)	36 weeks	0.3	15
Mammals				
Rat, <i>Rattus</i> sp.				
Adipose fat	3.0 (D)	6 days	16	16
Adipose fat	12.5 (D)	6 days	23	16
Adipose fat	5.0 (D)	16 weeks	62	17
Adipose fat	10.0 (D)	16 weeks	42	17
Adipose fat	20.0 (D)	16 weeks	43	17
Adipose fat	40.0 (D)	16 weeks	18	17
Liver	5.0 (D)	16 weeks	1	17
Liver	10.0 (D)	16 weeks	1.4	17
Liver	20.0 (D)	16 weeks	1.6	17
Liver	40.0 (D)	16 weeks	3	17
Old-field mouse, <i>Peromyscus polionotus</i>				
Liver	1.8 (D)	24 weeks	3.3	18
Liver	17.8 (D)	24 weeks	3.6	18
Rhesus monkey, <i>Macaca mulatta</i>				
Fat	1.0 (D)	Single dose	1.7–5.8	16

^a 1, Buckler et al. 1981; 2, Van Valin et al. 1968; 3, Zitko 1980; 4, Skea et al. 1981; 5, Minchew et al. 1980; 6, Koenig 1977; 7, Kobylinski and Livingston 1975; 8, Lee et al. 1975; 9, Schoor 1979; 10, Hollister et al. 1975; 11, Waters et al. 1977; 12, Ahrens et al. 1980; 13, Hyde 1972; 14, Bird et al. 1983; 15, Kendall et al. 1978; 16, NAS 1978; 17, Chu et al. 1981; 18, Wolfe et al. 1979.

21.6 MIREX IN THE SOUTHEASTERN UNITED STATES

Between 1961 and 1975, about 400,000 kg mirex were used in pesticidal formulations, of which approximately 250,000 kg were sold in the southeastern United States for control of native and imported fire ants (*Solenopsis* spp.). Most of the rest was exported to Brazil for use in fire ant control in that country (NAS 1978). Mirex was also used to control big-headed ant populations in Hawaiian pineapple fields (Bell et al. 1978), Australian termites (Paton and Miller 1980), South American leaf cutter ants, South African harvester termites, and, in the United States, western harvester ants and yellow jackets (Shannon 1976). Chemical control measures for imported fire ants began in the southeastern United States during the 1950s with the use of heptachlor, chlordane, and dieldrin. The large mounds built by ants in cultivated fields were believed to interfere with mowing and harvesting operations; the “vicious sting” of the insects presented a hazard to workers harvesting the crops; and the species was considered to be a pest in school playgrounds and homes (Lowe 1982). In 1965, the use of organochlorine insecticides to control fire ants was discontinued, due partly to their high acute toxicity to nontarget biota and their persistence. Previously used compounds were replaced by mirex 4X bait formulations, consisting of 0.3% mirex by weight, dissolved in 14.7% soybean oil, and soaked into corncob grits (85%). Initially, the 4X baits were broadcast from low-flying airplanes at a total yearly rate of 1.4 kg bait/ha (1.25 lb total bait/acre) or 4.2 g mirex/ha. Usually, three applications were made yearly. More than 50 million ha in nine southeastern states were treated over a 10-year period. Later, dosages were modified downward, and mirex was applied to mounds directly. Ecologically sensitive areas, such as estuaries, prime wildlife habitats, heavily forested areas, and state and federal parks, were avoided. In 1977, for example, the formulation was changed to 0.1% mirex and the application rate lowered to 1.12 g/ha; about 8200 kg of the lower-concentration bait were manufactured in 1977 (Bell et al. 1978). Under ideal aerial application conditions, about 140 particles of mirex-impregnated bait were distributed per square meter. When an infested area is treated, the bait is rapidly scavenged by the oil-loving fire ant workers, placed in the mound, and distributed throughout the colony, including queen and brood, before any toxic effects become evident. Death occurs in several days to weeks. The exact mode of action is unknown, but is believed to be similar to that of other neurotoxic agents such as DDT (Waters et al. 1977; NAS 1978).

Widespread use of mirex may lead to altered population structure in terrestrial systems, with resurgence or escalation of nontarget pests due to selective mirex-induced mortality of predators (NAS 1978). For example, populations of immature horn flies and rove beetles, two species of arthropods normally preyed upon by fire ants, were higher in mirex-treated areas than in control areas (Howard and Oliver 1978). Conversely, other species, such as crickets, ground beetles, and various species of oil-loving ants, were directly affected and populations were still depressed or eliminated 14 months posttreatment (NAS 1978), whereas fire ants recovered to higher than pretreatment levels, as judged by mound numbers and mound size (Summerlin et al. 1977).

Field results from aquatic and terrestrial ecosystems receiving mirex bait formulations indicated, with minor exceptions, that mirex accumulates sequentially in food complexes and concentrates in animals at the higher trophic levels. In both ecosystems, omnivores and top carnivores contained the highest residues (Hyde 1972; Shannon 1976; Waters et al. 1977; de la Cruz and Lue 1978a; Hunter et al. 1980; Eisler 1985). In South Carolina, where the 4X formulation was used to control fire ants from 1969 to 1971, mirex was translocated from treated lands to nearby marshes and estuarine biota, including crustaceans, marsh birds, and raccoons (Lowe 1982). Juvenile marine crustaceans showed delayed toxic effects after ingesting mirex baits, or after being exposed to low concentrations in seawater. About 18 months posttreatment, mirex residues of 1.3 to 17.0 mg/kg were detected in shrimp, mammals, and birds (Table 21.4); however, 24 months after the last mirex treatment, less than 10% of all samples collected contained detectable residues (Lowe 1982). A similar study was conducted in pasturelands of bahia grass (*Paspalum notatum*) (Markin 1981). Within a month after application, the target fire ant colonies were dead. Of the 4.2 g mirex/ha

applied to the 164 ha block, 100% was accounted for on day 1, 63% at 1 month, and 3% at 1 year (Table 21.5). Unaccounted mirex residues could include loss through biodegradation; through movement out of the study area by migratory insects, birds, other fauna, and groundwater; and through photodecomposition and volatilization (Markin 1981).

Table 21.4 Mirex Residues in Water, Sediments, and Fauna in a South Carolina Coastal Marsh 18 months after Application of 4.2 g/ha

Sample	Maximum Mirex Residues (mg/kg)	Percent Samples with Mirex Residues
Water	<0.01	0
Sediments	0.7	1
Crabs	0.6	31
Fishes	0.8	15
Shrimps	1.3	10
Mammals	4.4	54
Birds	17.0	78

Modified from Lowe, J.I. 1982. Mirex, fire ants, and estuaries. Pages 63-70 in *Proceedings of the Workshop on Agrochemicals and Estuarine Productivity*. Duke Univ. Mar. Lab., Beaufort, NC. Sept. 18-19, 1980. U.S. Dep. Comm. NOAA/OMPA.

Table 21.5 Temporal Persistence of Residues for 1 Year after Applications of Mirex 4X Formulation to Bahia Grass Pastures (Values represent rounded percentages recovered of the original 4.2 g/ha applied.)

Sample	Time, postapplication						
	1 d	2 wk	1 mo	3 mo	6 mo	9 mo	12 mo
Imported fire ants	44	8	0	0	0	0	0
Grit from bait	40	35	^a	—	—	—	—
Soil from mound	0.3	2	4	3	2	^b	—
Pasture soil	18	18	52	26	24	5	3
Bahia grass	0.3	0.9	0.4	0.7	0.3	0.6	0.0
Invertebrates	0.3	0.2	0.3	0.2	0.0	0.1	0.1
Vertebrates	—	0.1	0.2	0.2	0.1	0.1	0.1
Not accounted for	0	35	43	69	74	94	97

^a Grit now included with pasture soil.

^b Mounds badly weathered, not possible to identify.

Modified from Markin, G.P. 1981. Translocation and fate of the insecticide mirex within a bahia grass pasture ecosystem. *Environ. Pollut.* 26A:227-241.

Mirex residues in bobwhites from a South Carolina game management area were documented after treatment with 4.2 g mirex/ha (Kendall et al. 1977). Pretreatment residues in bobwhites ranged from nondetectable to 0.17 mg mirex/kg breast muscle on a dry-weight basis, and 0.25 to 2.8 mg/kg in adipose tissues on a lipid-weight basis. Mirex residues in adipose tissue increased up to 5 times within 1 month posttreatment and declined thereafter; however, another residue peak was noted in the spring after mirex treatment and corresponded with insect emergence (Kendall et al. 1977).

Mirex concentrations in muscle and liver of mammalian wildlife in Alabama and Georgia during the period 1973 to 1976 from reference areas were always less than 0.04 mg mirex/kg FW in muscle and less than 0.07 mg/kg FW in liver (Hill and Dent 1985). In mirex-treated areas, conspecifics were collected up to 2 years posttreatment. Maximum concentrations of mirex in muscle and liver from mirex-treated areas were always less than 1.0 mg/kg FW in raccoons, bobcats (*Lynx rufus*), mink (*Mustela vison*), and foxes (*Urocyon* sp., *Vulpes* sp.). Higher concentrations of 3.7 mg/kg FW in muscle and 1.1 mg/kg FW in liver were measured in the river otter (*Lutra*

canadensis) 1 year posttreatment, 3.5 mg/kg FW in muscle of skunks (*Spilogale* sp., *Mephitis* sp.) 6 months posttreatment, and 1.1 to 1.5 mg/kg FW in embryos and muscle of the opossum (*Didelphis marsupialis*) 6 to 12 months after treatment (Hill and Dent 1985).

Heavily treated watershed areas in Mississippi were investigated by Wolfe and Norment (1973) and Holcombe and Parker (1979). After treatment, mirex residues were elevated in crayfish and stream fish. Among mammals, residues were highest in carnivores and insectivores, lower in omnivores, and lowest in herbivores (Wolfe and Norment 1973). Mirex residues in liver and eggs were substantially higher in the box turtle (*Terrapene carolina*), an omnivorous feeder, than in the herbivorous slider turtle (*Chrysemys scripta*); mirex did not accumulate for protracted periods in tissues of these comparatively long-lived reptiles (Holcombe and Parker 1979). Among migratory reptiles, mirex was detected in only 11% of the eggs of the loggerhead turtle (*Caretta caretta*) and not at all in eggs of the green turtle (*Chelonia mydas*) collected during summer 1976 in Florida (Clark and Kryniotsky 1980). However, DDT or its isomers were present in all eggs of both species, and PCBs were detected in all loggerhead turtle eggs. The low levels of mirex and other organochlorine contaminants suggest that these turtles, when not nesting, live and feed in areas remote from Florida lands treated with mirex and other insecticides (Clark and Kryniotsky 1980).

A 10-5 bait formulation containing 0.1% mirex was designed to make more of the toxicant available to the fire ant and less to nontarget biota. In one study, the 10-5 formulation was applied to a previously untreated 8000-ha area near Jacksonville, Florida, infested with fire ants (Wheeler et al. 1977). The bait was applied by airplane at 1.12 kg/ha, or 1.12 g mirex/ha. Insects accumulated mirex to the greatest extent during the first 6 months after application, and most of the mirex was lost by 12 months (Table 21.6). Other invertebrates accumulated only low levels during the first 9 months, and no residues were detected after 12 months. Fish also showed low concentrations for 9 months and no detectable residues afterward. Amphibians contained detectable residues after 12 months, but not at 24; and reptiles contained measurable, but low, residues for the entire 24-month study period. Mammals had higher residue levels than reptiles, particularly in fat, whereas birds contained low to moderate residues (Table 21.6). After 24 months, mirex was found infrequently and only at low concentrations in birds, mammals, reptiles, and insects. It was concluded that 10-5 mirex formulations were as effective in controlling fire ants as the 4X formulation and that residues in nontarget species were reduced from that following 4X treatment, or were lacking (Wheeler et al. 1977).

Eggs of the American crocodile (*Crocodylus acutus*) from the Florida Everglades contained up to 2.9 mg/kg fresh weight of DDE and 0.86 mg/kg of polychlorinated biphenyls, but less than 0.02 mg mirex/kg (Hall et al. 1979). Livers of the deep sea fish (*Antimora rostrata*) collected from 1971 to 1974 from a depth of 2500 m off the U.S. east coast, contained measurable concentrations of DDT and its degradation products, and dieldrin, but no mirex (Barber and Warlen 1979).

Table 21.6 Mirex Residues in Fauna near Jacksonville, Florida, at Various Intervals Posttreatment Following Single Application of 1.12 g mirex/ha

Taxonomic Group and Time (months posttreatment)	Maximum Residue (mg/kg wet weight whole organism)
INSECTS	
1	4.1
3	19.8
6	7.8
12	1.1
24	0.8
AMPHIBIANS	
1	0.78
24	ND ^a
REPTILES	
1–9	1.2
24	0.06

Table 21.6 (continued) Mirex Residues in Fauna near Jacksonville, Florida, at Various Intervals Posttreatment Following Single Application of 1.12 g mirex/ha

Taxonomic Group and Time (months posttreatment)	Maximum Residue (mg/kg wet weight whole organism)
FISH	
1	0.08
3–9	0.25
>9	ND
BIRDS	
1–12	10.00 (fat) ^b
9–24	
MAMMALS	
1–6	3.4 (fat)
12–18	0.7 (fat)
24	0.09 (fat)

^a ND = not detectable.

^b Pretreatment levels.

Modified from Wheeler, W.B., D.P. Jouvenay, D.P. Wojcik, W.A. Banks, C.H. Van Middelem, C.S. Lofgren, S. Nesbitt, L. Williams, and R. Brown. 1977. Mirex residues in nontarget organisms after application of 10-5 bait for fire ant control, Northeast Florida — 1972–74. *Pestic. Monitor. Jour.* 11:146–156.

21.7 MIREX IN THE GREAT LAKES

Between 1959 and 1975, 1.5 million kg mirex were sold, of which 74%, or more than 1.1 million kg, were predominantly Dechlorane, a compound used in flame-resistant polymer formulations of electronic components and fabrics (Bell et al., 1978; NAS 1978). The total amounts are only approximate because almost half the mirex sold from 1962 to 1973 could not be accounted for (NAS 1978). Mirex loadings to Lake Ontario were estimated at 200 kg per year in 1960 to 1962, which decreased to 28 kg in 1980 (Halfon 1987). Mirex entered Lake Ontario mainly from the Niagara and Oswego Rivers. About 700 kg mirex were present in the bottom sediments of Lake Ontario in 1968, 1600 kg in 1976, and 1784 kg in 1981 (Halfon 1984). Kaiser (1978) reported that all fish species in Lake Ontario were contaminated with mirex, and that concentrations in half the species exceeded the Food and Drug Administration guideline of 0.1 mg/kg; other aquatic species had mirex residues near this level. Reproduction of the herring gull (*Larus argentatus*) on Lake Ontario was poor; mirex levels were an order of magnitude higher in gull eggs from Lake Ontario than in eggs from other Great Lakes locations (Kaiser 1978). It was concluded that the probable source of contamination was a chemical manufacturer that used mirex (Dechlorane) as a flame retardant, and that only Lake Ontario was contaminated (Kaiser 1978; NAS 1978). Until 1988, mirex had been reported for only a few locations in the Great Lakes, primarily Lake Ontario and the St. Lawrence River. Since 1988, however, mirex in water and fish samples has been measured from the other Great Lakes (Sergeant et al. 1993).

Gilman et al. (1977, 1978) observed poor reproductive success and declines in colony size of the herring gull at Lake Ontario at a time when dramatic increases of this species were reported along the Atlantic seaboard. In 1975, herring gull reproduction in Lake Ontario colonies was about one tenth that of colonies on the other four Great Lakes. In addition, in Lake Ontario colonies, there were reductions in nest site defense, the number of eggs per clutch, hatchability of eggs, and chick survival. Hatching success of Lake Ontario gull eggs was 23 to 26%, compared with 53 to 79% for eggs from other areas. Analysis of herring gull eggs from all colonies for organochlorine compounds and mercury demonstrated that eggs from Lake Ontario colonies had mean mirex levels of 5.06 mg/kg fresh weight (range, 2.0 to 18.6), or about 10 times more mirex than any other colony. Mean PCB and mercury levels were up to 2.8 and 2.3 times higher, respectively, in gull eggs from Lake Ontario than in those from other colonies, but only mirex levels could account for

the colony declines (Gilman et al. 1977, 1978). Short-term deviations from long-term trends in mirex concentrations in eggs of herring gulls from Lake Ontario seem to be correlated with weather patterns (i.e., warm spring weather conducive to phytoplankton growth produces relatively uncontaminated plankton, which results in less contamination for gulls during the critical period of egg yolk formation — and the reverse for cold spring weather) (Smith 1995). As judged by log-linear regression models, the half-life for mirex in herring gull eggs was 1.9 to 2.1 years, or essentially none was lost during egg incubation (Weseloh et al. 1979). Reproductive success of the Lake Ontario herring gull colonies improved after the early 1970s, an improvement that was directly paralleled by a decline in mirex, other organochlorine pesticides, and PCBs (Weseloh et al. 1979).

Concentrations of mirex and other contaminants in eggs of the Caspian tern (*Sterna caspia*) from the Great Lakes are declining, and tern populations are increasing (Struger and Weseloh 1985; Ewins et al. 1994). In Lake Huron, mirex concentrations in Caspian tern eggs declined from 0.51 mg/kg FW in 1976 to 0.12 mg/kg FW in 1991, equivalent to a decline of 8.6% annually. In Lake Ontario, mirex concentrations in tern eggs declined from 1.6 mg/kg FW in 1981 to 0.77 mg/kg FW in 1991, a decline of 7.1% annually (Ewins et al. 1994). Similar trends are reported for eggs of herring gulls from Lakes Michigan, Huron, and Ontario (Ewins et al. 1992, 1994), whole lake trout (*Salvelinus namaycush*) from Lake Ontario (Borgmann and Whittle 1991), and whole young-of-the-year spottail shiners (*Notropis hudsonicus*) throughout the Great lakes (Suns et al. 1993).

The fate of mirex in the environment and the associated transfer mechanisms have not been well defined (NAS 1978). One of the more significant works on this subject area was that by Norstrom et al. (1978), who documented levels of mirex and its degradation products in herring gull eggs collected from Lake Ontario in 1977 (Table 21.7). They concluded that photodegradation was the only feasible mechanism for production of the degradation compounds, although mirex and its photoproducts rapidly become sequestered in the ecosystem and protected from further degradation. Norstrom et al. (1980) found mirex degradation products in herring gull eggs from all of the Great Lakes and suggested that a high proportion of mirex and related compounds in herring gull eggs from Lakes Erie and Huron originated from Lake Ontario fish, whereas lower levels in eggs from Lakes Superior and Michigan originated from other sources. Mirex in sediments was considered an unlikely source because it was not being recycled into the ecosystem at an appreciable rate (Norstrom et al. 1980). Migrating salmon (*Oncorhynchus* spp.) make a significant contribution to the upstream transport of mirex from Lake Ontario, estimated at 53 to 121 g mirex annually (Lewis and Makarewicz 1988; Scrudato and McDowell 1989). Ingestion of salmon eggs by brown trout, decomposition of salmon carcasses by blowfly larvae, and ingestion of carcasses by aquatic and terrestrial scavengers are all means by which mirex is introduced to upstream environments (Scrudato and McDowell 1989). A harvest rate of 50% by fisherman represents a removal of an additional 61 g mirex annually from Lake Ontario (Lewis and Makarewicz 1988).

Table 21.7 Mirex and Its Degradation Products in Herring Gull Eggs Collected from the Great Lakes in 1977

Compound	Mirex Concentration, (mg/kg fresh weight)	Percent of Samples Containing Compound
Mirex	2.58	66.7
8-Monohydro mirex (photomirex)	0.95	24.5
10-Monohydro mirex	0.199	5.1
C ₁₀ C ₁₁ H(III), possibly 9-monohydro mirex	0.077	2.0
C ₁₀ C ₁₂ (II)	0.039	1.0
2,8-Dihydromirex	0.016	0.4
C ₁₀ C ₁₀ H ₂ (II), possibly 3,8-dihydromirex	0.011	0.3
Total	3.872	100

Modified from Norstrom, R.J., D.J. Hallett, F.I. Onuska, and M.E. Comba. 1980. Mirex and its degradation products in Great Lakes herring gulls. *Environ. Sci. Technol.* 14:860-866.

Table 21.8 Biomagnification of Mirex in Great Lakes Food Chains

From	To	Bioconcentration Factor (BCF)
Water	Whole rainbow smelt (<i>Osmerus mordax</i>) or whole alewife (<i>Alosa pseudoharengus</i>)	500,000
Water	Muscle of coho salmon (<i>Oncorhynchus kisutch</i>)	1,500,000
Water	Egg of herring gull (<i>Larus argentatus</i>)	25,000,000
Alewife or rainbow smelt	Muscle of coho salmon	2.6
Alewife or rainbow smelt	Egg of herring gull	50.0

Modified from Norstrom, R.J., D.J. Hallett, and R.A. Sonstegard. 1978. Coho salmon (*Oncorhynchus kisutch*) and herring gulls (*Larus argentatus*) as indicators of organochlorine contamination in Lake Ontario. *Jour. Fish. Res. Board Canada* 35:1401-1409.

Biomagnification of mirex through food chains was investigated by Norstrom et al. (1978). Their basic assumption was that both herring gulls and coho salmon ate alewives (*Alosa pseudoharengus*) and rainbow smelt (*Osmerus mordax*). Mirex residues in these organisms, in mg/kg (parts per million) fresh weight, were 4.4 in gull eggs, 0.23 in salmon muscle, 0.10 in salmon liver, and 0.09 in whole alewives and smelt retrieved from stomachs of salmon. Bioconcentration factors (BCFs) from prey to predator ranged up to 50, and those from water to gull egg were estimated to be near 25 million (Table 21.8). Norstrom et al. (1978) indicated that salmon muscle and gull eggs are complementary indicators of organochlorine contamination in the Great Lakes.

Among Great Lakes fishes, the highest mirex value recorded was 1.39 mg/kg FW in whole American eels (*Anguilla rostrata*) collected from Lake Ontario and was substantially in excess of the tolerated limit of 0.3 mg/kg FW for human consumption at that time (NAS 1978). In the early 1980s, mirex was detected in 100% of the American eels sampled from Lake Ontario (Dutil et al. 1985). High mirex values were also reported in chinook salmon (*Oncorhynchus tshawytscha*) and coho salmon (*Oncorhynchus kisutch*) from South Sandy Creek, a tributary of Lake Ontario, during autumn 1976. As a consequence, possession of all fish from that area was prohibited by the State of New York (Farr and Blake 1979). Mirex concentrations in coho and chinook salmon tissues from Lake Ontario in 1977/78 ranged between 0.07 and 0.24 mg/kg FW tissue and increased with individual fish weight in direct relation to lipid content (Insalaco et al. 1982). The significance of mirex residues in salmonid fishes is unclear. Skea et al. (1981), in laboratory studies with brook trout, showed that whole-body residues of 6.3 mg/kg fish weight were not associated with adverse effects on growth or survival and speculated that long-lived species, such as the lake trout, would probably continue to accumulate mirex in Lake Ontario as long as they were exposed, and may continue to contain residues for most of their lives, even after the source has been eliminated.

There was no widespread mirex contamination of urban environments near Lake Ontario as a result of Dechlorane use, although local contamination of the Lake Ontario area was high when compared with other Great Lakes areas (NAS 1978). Among humans living in the Great Lakes area, there was great concern that mother's milk might be contaminated, owing to the high lipophilicity of mirex. Bush (1983) found mirex concentrations in mother's milk from residents of New York state to be 0.07 µg/L in Albany, 0.12 µg/L in Oswego, and 0.16 µg/L in Rochester, confirming that mirex was present in human milk but that concentrations were sufficiently low to be of little toxicological significance. It is noteworthy that none of the mothers had eaten Lake Ontario fish or any freshwater fish, and only a few had eaten marine fishes (Bush 1983). For a 5-kg infant consuming 500 g milk daily, this amount would approximate a daily dietary intake of 0.01 µg mirex/kg body weight (Bush 1983), or about 1/10,000 of the lowest recorded dietary value causing delayed maturation in prairie voles (Shannon 1976). It is not known if a safety factor of 10,000 is sufficient to protect human health against delayed toxic effects of mirex, but it now appears reasonable to believe that it is.

21.8 MIREX IN OTHER GEOGRAPHIC AREAS

Mirex residues were determined in birds collected nationwide or from large geographic areas of the United States; however, aside from the Southeast and the Great Lakes, concentrations were low, considered nonhazardous, and occurred in a relatively small proportion of the samples collected (Cain and Bunck 1983; Wood et al. 1996). Among wings of mallards and American black ducks (*Anas rubripes*) collected from the four major flyways during 1976/77, mirex concentrations were highest and percent occurrence greatest in samples from the Atlantic Flyway: mallards, 50% occurrence, 0.14 mg/kg fresh weight; black ducks, 19% and 0.04 mg/kg (White 1979). Data for mallards collected from other flyways follow: Mississippi, 29% and 0.03 mg/kg; Central, 14% and 0.06 mg/kg; and Pacific 4% and 0.03 mg/kg (White 1979). Carcasses of several species of herons found dead or moribund nationwide from 1966 to 1980 were analyzed for a variety of common organochlorine pesticides by Ohlendorf et al. (1981). They detected mirex in less than 15% of the carcasses, a comparatively low frequency, and only in nonhazardous concentrations. However, about 20% of all herons found dead or moribund had lethal or hazardous concentrations of dieldrin or DDT. In bald eagles (*Haliaeetus leucocephalus*) found dead nationwide, elevated mirex levels were recorded in carcass lipids (24.0 mg/kg) and in fresh brain tissues (0.22 mg/kg) (Barbehenn and Reichel 1981). Among endangered species such as the bald eagle, it was determined that the most reliable indicator for assessing risk of organochlorine compounds was the ratio of carcass to brain residues on a lipid weight basis (Barbehenn and Reichel 1981). Wings from American woodcocks (*Philohela minor*) collected from 11 states in 1970/71 and 14 states in 1971/72 were analyzed for mirex and other compounds by McLane et al. (1978). Mirex residues in the 1971/72 wings showed the same geographical pattern of recovery as those observed in 1970/71: residues were highest in the southern states and New Jersey, and lowest in the northern and midwestern states. Mirex residues were significantly lower in 1971/72 than in 1970/71. As judged by the analysis of wings of immature woodcocks in Louisiana, mirex residues were significantly lower in immatures than in adults: 2.48 mg/kg lipid weight vs. 6.20 mg/kg, respectively (McLane et al. 1978).

Mirex concentrations in bald eagle eggs collected nationwide between 1969 and 1979 ranged from 0.03 to 2.0 mg/kg FW, and were highest in Florida and the Chesapeake Bay region (Wiemeyer et al. 1984). Up to 87% of bald eagle eggs from Florida and the Chesapeake Bay had detectable mirex residues, whereas this value was as low as 17% in Alaska. Wiemeyer et al. (1984) note that eggs from successful bald eagle nests had 0.03 mg mirex/kg FW and lower, but eggs from unsuccessful nests had 0.05 mg/kg FW and higher. Eggs of Cooper's hawk, *Accipiter cooperi*, collected in 1980 from various locations, all contained more than 0.05 mg mirex/kg FW. Concentrations were highest in Pennsylvania (with 0.84 mg/kg FW) and Wisconsin (with 1.6 mg/kg FW) (Pattee et al. 1985). Eggs of the loggerhead shrike (*Lanius ludovicianus*) from the Shenandoah Valley region of Virginia in 1985/86 contained an average of 0.04 mg mirex/kg FW, with a 63% frequency of occurrence; loggerhead shrike populations in that region are declining but the cause of the decline is not known with certainty (Blumton et al. 1990). Eggs of the ring-necked grebe (*Podiceps grisigena*) from Manitoba, Canada, in 1980/81, had as much as 28.6 mg mirex/kg lipid weight, and this may account, in part, for the high nesting loss of 79% observed in grebes at that time (De Smet 1987). Mirex and other organochlorine compounds in eggs of anhingas (*Anhinga anhinga*) and 17 species of waders (including herons, egrets, bitterns, ibises, and storks) were measured in various locations throughout the eastern United States during 1972 and 1973 (Ohlendorf et al. 1979). The highest mean concentration of 0.74 mg mirex/kg, range 0.19 to 2.5 mg/kg, was found in eggs of the green heron (*Butorides striatus*) from the Savannah National Wildlife Refuge in South Carolina; a single egg of the cattle egret (*Bubulcus ibis*) analyzed from there contained 2.9 mg mirex/kg. However, the overall frequency of mirex occurrence was higher in eggs collected from the Great Lakes region (24%) than in those from the South Atlantic coast (15.6%),

inland areas (10.7%), Gulf Coast (4.4%), or North Atlantic region (3.2%). Measurable mirex residues were detected in migratory birds collected from a variety of locations, including areas far from known sources or applications of mirex. For example, 22% of all eggs from 19 species of Alaskan seabirds collected in 1973 to 1976 contained mirex. The highest concentration was 0.044 mg/kg in eggs of a fork-tailed storm petrel (*Oceanodroma furcata*) from the Barren Islands. Mirex residues were low compared with those of other organochlorine compounds (Ohlendorf et al. 1982). Eggs from the clapper rail (*Rallus longirostris*) collected in New Jersey from 1972 to 1974 contained 0.16 to 0.45 mg mirex/kg (Klaas et al. 1980). Eggs from the greater black-backed gull (*Larus marinus*) collected from Appledore Island, Maine, in 1977 contained up to 0.26 mg/kg, but no mirex was detected in eggs of common eider (*Somateria mollissima*) or herring gull from the same area (Szaro et al. 1977). The greater black-backed gull is an active carnivore; 36 to 52% of its diet consists of small birds and mammals, whereas these items compose less than 1% in eider and herring gull diets. The higher mirex levels in black-backed gulls are attributed to its predatory feeding habits (Szaro et al. 1979). In New England, eggs of the black-crowned night-heron (*Nycticorax nycticorax*) contained between 0.28 and 0.66 mg mirex/kg wet weight in 1973; in 1979, this range was 0.11 to 0.37 mg/kg (Custer et al. 1983). Falcon eggs contained detectable mirex; levels were highest in the pigeon hawk (*Falco columbarius*) (0.25 mg/kg) and in the peregrine falcon (*Falco peregrinus*) (0.43 mg/kg), two species that feed on migratory birds or migrate to mirex-impacted areas (Kaiser 1978). Active mirex was also found in eggs of a cormorant (*Phalacrocorax* sp.) from the Bay of Fundy on the Atlantic coast; the suspected source of contamination was the southern wintering range (Kaiser 1978).

Mirex residues in 20 great horned owls (*Bubo virginianus*) found dead or dying in New York state in 1980 to 1982 contained concentrations of mirex and PCBs higher than those reported for great horned owls elsewhere (Stone and Okoniewski 1983). Owls in "poor flesh" contained higher residues than those in "good flesh"; these values were 6.3 mg/kg FW vs. 0.07 mg/kg FW for brain, and 5.6 mg/kg FW vs. 0.1 mg/kg FW for liver (Stone and Okoniewski 1983). Waterfowl collected from upstate New York between 1979 and 1982 had about 0.07 mg mirex/kg FW breast muscle and 0.28 mg/kg FW subcutaneous fat (Kim et al. 1984, 1985).

Mink (*Mustela vison*) collected from the Northwest Territories of Canada between 1991 and 1995 had liver mirex concentrations between 0.08 and 0.39 µg/kg FW. These extremely low mirex concentrations were, nevertheless, higher than liver mirex concentrations in prey species (snowshoe hare, *Lepus americanus*, 0.08 to 0.13 µg/kg FW; northern red-backed vole, *Clethrionomys rutilus*, 0.32 µg/kg FW), suggesting that mirex biomagnification in mammalian wildlife food chains is possible (Poole et al. 1998).

21.9 RECOMMENDATIONS

Mirex is classified as a Group 2B carcinogen, indicating that it is a possible human carcinogen (USPHS 1995). For the protection of human health, oral intake should not exceed 0.0002 mg/kg BW daily, equivalent to 0.014 mg daily for a 70-kg person (USPHS 1995). At present, the recommended concentration of mirex in water should not exceed 0.001 µg/L in order to protect human health, freshwater and marine life, irrigated crops, and watered livestock (USPHS 1995). Fish in the human diet should not contain more than 0.1 mg mirex/kg fresh weight. Average acceptable ambient air concentrations recommended for the protection of human health range between 0.03 µg/m³ in New York to 0.88 µg/m³ in Pennsylvania. In Kentucky, air emission levels of mirex products should not exceed 232 µg per hour (USPHS 1995).

Before the banning of mirex for all uses in 1978, the tolerance limits in food for human consumption were 0.1 mg/kg for eggs, milk, and fat of meat from cattle, goats, hogs, horses, poultry, and sheep, and 0.01 mg/kg for all other raw agricultural commodities (Waters et al. 1977; Buckler

et al. 1981); higher limits of 0.3 mg mirex/kg in fish and shellfish and 0.4 mg/kg in crabs were tolerated (NAS 1978). The maximum recommended allowable concentration of mirex in edible portions of domestic fish for human consumption was 0.1 mg/kg FW at that time (Scrudato and McDowell 1989). Avoidance of larger and older fish to minimize ingestion of fat-soluble contaminants, including mirex, was recommended. Trimming the fatty tissues from muscle of salmon and trout from Lake Ontario prior to consumption resulted in a mirex reduction of at least 44% in the trimmed fillet — reflecting loss of fat content — and a product considered safe (i.e., <0.1 mg mirex/kg FW) by the U.S. Food and Drug Administration (Insalaco et al. 1982; Voiland et al. 1991). However, mirex concentrations as low as 0.1 mg/kg in diets of adult prairie voles were associated with delayed maturation of pups, and with significant delays in the attainment of various early development behaviors such as bar-holding ability, hind-limb placing, and negative geotaxis (Shannon 1976). It is not known whether or not prairie voles can serve as a model for protection of health of humans or various wildlife species. In the absence of supporting data, however, it seems prudent now to establish a dietary threshold of mirex at some level lower than 0.1 mg/kg. A maximum concentration of 0.01 mg/kg total dietary mirex, which is a recommended level for most raw agricultural commodities, appears reasonable and conservative for the protection of fish, wildlife, and human health. This value could be modified as new data become available.

Although mirex is extremely persistent in the environment, research findings suggest that some degradation occurs and that some of the degradation products, such as photomirex, are biologically active. Accordingly, additional research is warranted on the fate and effects of mirex degradation products, with special emphasis on biomagnification through aquatic and terrestrial food chains.

Alternate means of controlling imported fire ants are under consideration. One approach has been to reduce the concentrations of active mirex in bait formulations from 0.3% to some lower, but effective, level. Paton and Miller (1980) demonstrated that mirex baits containing 0.07% mirex were effective in controlling Australian termites, reporting a 90% kill in 9 days. Baits containing as little as 0.01% mirex were also reported effective, although termite mortality was delayed considerably. Waters et al. (1977) indicated that alternate chemical control agents, such as chlordpyrifos, diazinon, dimethoate, or methyl bromide may be suitable and that nonbiocidal chemicals, such as various pheromones and hormones, which are capable of disrupting reproductive behavior of fire ants, are also under active consideration. Another proposal was to chemically modify mirex to a more water-soluble and rapidly degradable product (Waters et al. 1977). The formulation Ferriamicide, which consisted of 0.05% mirex, ferrous chloride, and a small amount of long-chain alkyl amines, was formulated in baits during 1978/79 for ant control (Lowe 1982). Ferriamicide degraded within a few days after initial application; however, approval was revoked in 1980 when it was learned that the toxicity of various degradation products to mammals, especially that of photomirex, exceeded that of 4X bait formulations (Lowe 1982).

Mirex replacements should not manifest the properties that led to the discontinuance of mirex for all uses, namely:

- Delayed mortality in aquatic and terrestrial fauna
- Numerous birth defects
- Tumor formation
- Histopathology
- Adverse effects on reproduction, early growth, and development
- High biomagnification and persistence
- Disrupted energy metabolism
- Degradation into toxic metabolites
- Population alterations
- Movement through aquatic and terrestrial environmental compartments.

It is emphasized that mirex replacement compounds must be thoroughly tested before widespread application in the environment; if testing is incomplete, it is almost certain that the nation's fish

and wildlife resources will be adversely affected. In 1980, the use of Amdro (tetrahydro-5,5-dimethyl-2) (Lh)-pyrimidine) was conditionally approved by the U.S. Environmental Protection Agency (Lowe 1982). Amdro reportedly has good ant control properties, degrades rapidly in sunlight, has a biological half life of less than 24 h, is nonmutagenic, and is relatively nontoxic to other than targeted species, except fish. Amdro was more acutely toxic than mirex to fish.

21.10 SUMMARY

Mirex (dodecachlorooctahydro-1,3,4-metheno-2H-cyclobuta [*c,d*] pentalene) has been used extensively in pesticidal formulations to control the red imported fire ant (*Solenopsis invicta*), and as a flame retardant in electronic components, plastics, and fabrics. One environmental consequence of mirex was the severe damage recorded to fish and wildlife in nine southeastern states and the Great Lakes, especially Lake Ontario. In 1978, the U.S. Environmental Protection Agency banned all further use of mirex, partly because of the hazards it imposed on nontarget biota. These included:

- Delayed mortality and numerous birth defects in aquatic and terrestrial fauna
- Tumor formation
- Histopathology
- Wildlife population alterations
- Adverse effects on reproduction, early growth, and development
- High biomagnification and persistence
- Degradation into toxic metabolites
- Movement through aquatic and terrestrial environmental compartments
- Disrupted mammalian energy metabolism
- Detection of residues in human milk and adipose tissues

Among susceptible species of aquatic organisms, significant damage effects were recorded when concentrations of mirex in water ranged from 2 to 3 µg/L. The recommended concentration of 0.001 µg mirex/L affords an unusual degree of protection. Evidence suggests that sensitive species of wildlife are adversely affected at 0.1 mg/kg of dietary mirex. For comparison, tolerance limits for mirex in food for human consumption range from 0.01 mg/kg for raw agricultural commodities to 0.1 mg/kg for eggs, milk, animal fat, and various seafood products. Additional research is needed on the fate of mirex degradation products and their effects on natural resources. Further, it is strongly recommended that environmental use of all mirex replacement compounds be preceded by intensive ecological and toxicological evaluation.

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CHAPTER 22

Paraquat

22.1 INTRODUCTION

Paraquat (1,1'-dimethyl-4,4'-bipyridinium) is one of the most widely used herbicidal chemicals in the world and is now available in more than 130 countries (Kimbrough 1974; Calderbank 1975; Dasta 1978; Haley 1979; Hughes 1988; Smith 1988b; Eisler 1990). Its chemical structure was first described in 1882, its oxidizing and reducing properties in 1933, and its herbicidal properties in 1955. Paraquat was marketed commercially in the United Kingdom in 1962 and registered for use in the United States in 1964. As the dichloride salt, it has found wide use as a nonselective contact herbicide at application rates of 1.12 kg/ha (1 pound/acre) and lower. Paraquat kills plants by affecting the green parts, not the woody stems, and is usually completely and rapidly inactivated by contact with clay in the soil. In its bound form, paraquat is biologically inert and innocuous to plants and animals (Fletcher 1974). In 1977, the discovery by narcotics authorities that some marijuana imported from Mexico had been treated with paraquat as a control agent generated much interest in the media (Dasta 1978; Haley 1979). Up to 70% of the paraquat in paraquat-treated marijuana, on smoking, is converted to bipyridine, a respiratory irritant. Frequent consumption of heavily contaminated cigarettes may result in cyanosis and possibly death. The use of paraquat for this purpose has been largely discontinued.

Numerous human injuries and deaths have resulted from intentional ingestion of the concentrated commercial product (Fletcher 1974; Dasta 1978; Haley 1979; Crome 1986; Smith 1988a, 1988b). For example, in the first 10 years following paraquat commercial use, 232 human deaths from paraquat poisoning were reported, about half suicidal, and almost all were due to the drinking of concentrated material. Most poisonings resulted from the ingestion of the 21% cation concentrate, which had been decanted and stored in empty beer, soft drink, or lemonade bottles; paraquat is a reddish-brown liquid that resembles root beer or cola drinks. One individual sprinkled paraquat on French fried potatoes, thinking that it was vinegar. He died 25 days later. Another died after applying the concentrated solution to his beard and scalp to treat a lice infestation. In Japan, more than 1000 persons each year are reportedly poisoned by paraquat. Initially, paraquat may produce multiorgan toxicity of kidneys, liver, heart, central nervous system, adrenal glands, skeletal muscle, and spleen, but the ultimate target organ is the lung, in which progressive irreversible pulmonary fibrosis develops. This effect has been described in man, rats, mice, guinea pigs, and dogs (Kimbrough 1974; Giri et al. 1979; Hampson and Pond 1988; O'Sullivan 1989). At present, there is no specific antidote for paraquat poisoning. In normal use as a spray, minor reversible injuries are reported to abraded skin, eyes, nose, and fingernails; it is not absorbed through intact skin (Kimbrough 1974; Smith 1988a). Paraquat is fetotoxic as judged by deliberate ingestion of concentrated solutions by nine pregnant Taiwanese women. Paraquat crosses the placenta and concentrates there to levels 4 to 6 times that of maternal blood. All fetuses died whether or not an emergency cesarean operation was performed (Talbot and Fu 1988). Research has focused on the tendency of paraquat to accumulate

in neuromelanin of mammals and amphibians and to cause lesions in the pigmented nerve cells, leading to effects very similar to those of Parkinson's disease (De Gori et al. 1988; Lindquist et al. 1988). Reviews on ecological and toxicological aspects of paraquat include those by Kimbrough (1974), Smith and Heath (1976), Autor (1977), Dasta (1978), Haley (1979), Summers (1980), Bauer (1983), Onyeama and Oehme (1984), Smith (1985, 1988a, 1988b), and Eisler (1990).

22.2 USES

Paraquat is a broad-spectrum contact weed killer and herbage desiccant that is used widely in agriculture and horticulture. Paraquat was originally formulated in 1882, but its herbicidal properties were not discovered until 1955. Since its introduction in the early 1960s, paraquat has been used extensively in about 130 countries, including the United Kingdom, Canada, and the United States, on a wide variety of agricultural crops (Fletcher 1974; Haley 1979; Kelly et al. 1979; Anonymous 1988).

Primary uses of paraquat include: weed control in orchards, plantation crops, and forests; weed control before sowing or before crop emergence; pasture renovation; preharvest desiccation; and aquatic weed control, although use as an aquatic herbicide in the United States is not permitted (Anonymous 1963, 1974; Summers 1980; Dial and Bauer 1984). In New Zealand, use of paraquat for aquatic weed control (2 mg/L for 30 min) in 1966/67 on the Waimakariri River severely reduced amphipod populations; paraquat is no longer used for this purpose in that country (Burnet 1972). Paraquat is registered domestically for preplant or preemergence use for cotton, barley, corn, lettuce, melons, peppers, safflower, soybeans, sorghum, sugar beets, tomatoes, potatoes, and wheat. It is also registered for use on noncrop areas, such as roadsides, highway margins, rights-of-way, around commercial buildings, power plants, storage yards, fence lines, and parkways (Anonymous 1963, 1974). In Switzerland, it is used to control voles (*Arvicola terrestris*) in fruit orchards (Summers 1980). Paraquat application to corn using a manual knapsack sprayer is considered unsafe to the human operators if lances are less than 1.0 m. Lances >1.0 m in length are recommended, as well as additional protective garments for legs, feet, and hands and switching the paraquat spraying operation to the back of the worker's body (Machado-Neto et al. 1998).

Paraquat is available as the dichloride or dimethylsulfate salt; both compounds are extremely soluble in water (Kimbrough 1974). In the United States, paraquat dichloride is available as a 29% liquid concentrate containing 240 g/L (2 pounds/gallon) of paraquat cation, or as a 42% liquid concentrate. Elsewhere, it is sold as Gramoxone liquid containing 20 to 24% paraquat dichloride (Fletcher 1974; Bauer 1983; Dial and Dial 1987a). Paraquat dichloride concentrates usually contain various wetting agents (condensation products of ethylene oxide and alkyl phenols), spreaders, humectants to promote moisture retention (calcium chloride, glycerol, polyethylene glycol), plant adhesion materials (carboxymethylcellulose, polymethacrylates), and antifoaming agents (Summers 1980).

The recommended field application rates for terrestrial weed control usually range between 0.28 and 1.12 kg paraquat cation/ha (0.25 and 1.0 pounds/acre), between 0.56 and 2.24 kg paraquat dichloride/ha (0.5 and 2.0 pounds/acre) — both applied as an aerosol — and between 0.1 and 2.0 mg/L for aquatic weed control, although sensitive aquatic plants may be affected between 0.019 and 0.372 mg/L (Ross et al. 1979; Summers 1980; Bauer 1983; Dial and Bauer 1984). Paraquat is frequently used in combination with other herbicides (Fletcher 1974; Summers 1980). Water solutions of the dichloride salt, which usually contain 240 g/L, have been successfully mixed with 2,4-D, substituted ureas, dalapon, amitrol, and various triazines (Anonymous 1963, 1974).

22.3 CONCENTRATIONS IN FIELD COLLECTIONS

Data are scarce on ecosystems treated with paraquat. It is clear, however, that both terrestrial and aquatic plants accumulate paraquat, and that the compound disappears rapidly from the water column and tends to concentrate in surface muds (Table 22.1).

Table 22.1 Paraquat Concentrations in Field Collections of Selected Organisms and Nonbiological Materials

Sample and Other Variables	Concentration (mg/kg dry weight)	Reference ^a
TREATED FIELDS		
Alfalfa, <i>Medicago sativa</i>	Up to 30	1
Graminaceae, various species	Up to 60	1
MUD, SURFACE		
From British lake treated with 0.5 mg paraquat/L		
Days after treatment		
1	1.2	2
2	2.4	2
8	6.7	2
32	11.2	2
197	17.7	2
364	8.0	2
COLORADO FARM POND TREATED WITH 1.0 mg/L		
3 h after treatment		
Water	0.6	3
Mud	1.1	3
Submerged plant, <i>Chara</i> sp.	320	3
Algae, <i>Spirogyra</i> sp.	27	3
4 days after treatment		
Water	0.2	3
Mud	0.8	3
<i>Chara</i> sp.	840	3
<i>Spirogyra</i> sp.	1300	3
16 days after treatment		
Water	<0.1	3
Mud	16	3
<i>Chara</i> sp.	540	3
<i>Spirogyra</i> sp.	13	3

^a 1, Bauer 1983; 2, Way et al. 1971; 3, Earnest 1971.

Water from irrigation channels, rivers, and lagoons from Spanish marshes in 1996 bordering the Mediterranean Sea contained an average of 0.01 µg paraquat/L, with a maximum recorded value of 3.95 µg/L (Fernandez et al. 1998). Paraquat values were highest in the summer owing to high application rates, low rainfall, and high evaporation rates. At these comparatively low concentrations, paraquat is not easily degraded chemically or biologically and persists in river waters with more than 80% remaining after 56 days of incubation (Fernandez et al. 1998).

22.4 ENVIRONMENTAL CHEMISTRY

22.4.1 General

Paraquat is a nonvolatile, ionic compound that is almost completely soluble in organic solvents, which is typical of the bipyridyl group of chemicals. As discussed later, the biochemical mechanism of paraquat toxicity is due to the cyclic oxidation and reduction that occurs in various tissues, especially lung, leading to production of superoxide anion and other free radicals. These chemical species react with polyunsaturated free radicals, eventually forming the highly destructive hydrogen peroxide. Excretion of paraquat is rapid in living organisms, but delayed toxic effects, including

death, are not unusual. No treatment or chemical has proven completely successful in protecting against paraquat-induced lung toxicity.

Paraquat is strongly adsorbed to soils and sediments and is biologically unavailable in that form; however, it is not degraded significantly for many years, except in surface soils. In surface soils, paraquat loss through photodecomposition approaches 50% in 3 weeks. In freshwater ecosystems, loss from water column is rapid: about 50% in 36 h and 100% in 4 weeks. In marine ecosystems, 50 to 70% loss of paraquat from seawater was usually recorded within 24 h.

22.4.2 Chemical Properties

Paraquat is a nonvolatile, ionic compound that is almost completely insoluble in fat, and therefore not likely to be accumulated in food chains (Calderbank 1975). The compound belongs to the bipyridyl group of chemicals and is typical of the many hundreds that have been synthesized, variation usually being the result of introducing different quaternizing groups on the nitrogen atoms, which also shift (Fletcher 1974) (Table 22.2). Paraquat dichloride is produced from pyridine in the presence of sodium in anhydrous ammonia, then quaternizing the 4,4'-dipyridyl with methyl chloride (Haley 1979). The common paraquat salts are all fully ionized, and experiments have shown that the anions (e.g., chloride, sulfate, methyl sulfate) do not affect the toxicity of paraquat (Fletcher 1974). Chemical and other properties of paraquat are briefly summarized in Figure 22.1 and Table 22.2.

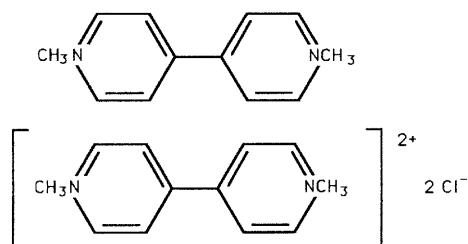


Figure 22.1 Structural formulas of paraquat cation (upper) and paraquat dichloride salt (lower).

22.4.3 Mode of Action

Paraquat is absorbed systematically in mammals, following different routes of exposure; absorption is greatest for the pulmonary route, followed by intragastric and dermal routes (Chui et al. 1988). Administration of paraquat by every route of entry tested frequently results in irreversible changes in lung (Boudreau and Nadeau 1987). In the intestinal tract, where some microbial degradation occurs, most paraquat (95 to 100%) is usually excreted unchanged in feces and urine within 2 days (Summers 1980). Absorption in the gastrointestinal tract ranges from 0.26% in cow, to 5% in man, 8% in guinea pig, 16% in cat, and up to 20% in rat. The half-time persistence (T_b 1/2) of paraquat in certain tissues ranges between 20 and 30 min, but up to 4 days in muscle and 2 days in plasma (Bauer 1983). Delayed toxic effects of paraquat occurring after the excretion of virtually all of the material have caused it to be classified as a “hit and run” compound, that is, a compound causing immediate damage, the consequences of which are not readily apparent (Conning et al. 1969).

Most authorities agree that free radical pathology is the most likely mechanism by which paraquat is cytotoxic (Bus et al. 1976; Frank et al. 1982; Patterson and Rhodes 1982; Combs and Peterson 1983; Onyeama and Oehme 1984; Gabryelak and Klekot 1985; Smith 1985; Wong and Stevens 1986; Seto and Shinohara 1987; Suleiman and Stevens 1987; Darr et al. 1988; Dunbar et al. 1988a; Wegener et al. 1988; Wenning et al. 1988; Arias et al. 1991; Babich et al. 1993). The biochemical mechanism of paraquat toxicity is related to the cyclic oxidation and reduction of paraquat that occurs in lung cells, which leads to continued production of high levels of superoxide

Table 22.2 Chemical and Other Properties of Paraquat

Variable	Datum
Chemical name	
Paraquat (cation)	1,1'-dimethyl-4,4'-bipyridinium
Paraquat dichloride (salt)	1,1'-dimethyl-4,4'-bipyridinium dichloride
Molecular weight	186.2 (cation), 257.2 (salt)
CAS Number	4685-14-17 (cation), 1910-42-5 (salt)
Empirical formula	C ₁₂ H ₁₄ N ₂ (cation), C ₁₂ H ₁₄ Cl ₂ N ₂ (salt)
Alternate names	Cekuquat, Crisquat, Dextrone, Dextrone X, Dexuron, Dual Paraquat, Esgram, Gramonol, Gramoxone, Gramuron, Herbaxon, Herboxone, Methyl Viologen, Ortho Paraquat, Orvar, Paracol, Paraquat CL, Pathclear, Pillarquat, Pillarxone, Preeglove, PP 148, PP 910, Sweep, Tenaklene, Totacol, Toxer Total, Weedol
Solubility at 20°C	
Water	561 g/L
Methanol	144 g/L
Ethanol	1.7 g/L
Acetone	200 mg/L
Most organic solvents	Insoluble or sparingly soluble
Physical state	White (pure), yellow (technical) solid
Main uses	Herbicide, desiccant
Specific gravity	1.24–1.26
Melting point	175–180°C, decomposes at 345°C
Stability	Stable on exposure to hot acids, unstable in alkalis at pH > 10
Flash point	Nonexplosive, nonflammable
Volatility	Nonvolatile

Data from Anonymous 1963, 1974, 1988; Haley 1979; Kelly et al. 1979; Johnson and Finley 1980; Hudson et al. 1984; Hill and Camardese 1986; Mayer 1987.

anion (O₂⁻) and other cytotoxic oxygen free radicals. Superoxide anion and other oxygen free radicals initiate the peroxidation of membrane lipids, causing tissue damage and death. Paraquat oxidation is coupled with the reduction of molecular oxygen, forming superoxide anion, singlet oxygen, and hydroxyl radicals. These molecular species react with polyunsaturated fatty acid free radicals and, on further oxidation, with lipid hydroperoxide radicals. The hydroperoxide radicals then maintain the formation of new fatty acid radicals while being converted to lipid peroxides in a chain reaction. Various enzymes in the cells catabolize the superoxide radical and reduce the lipid hydroperoxides to less-toxic lipid alcohols. The superoxide anions are converted to hydrogen peroxide and oxygen; hydrogen peroxide is further inactivated to water and oxygen by catalases and peroxidases. In the presence of reduced nicotinamide adenine dinucleotide phosphate (NADPH), paraquat is reduced by microsomal NADPH-cytochrome reductase. The reduction of lipid peroxides by glutathione peroxidase requires reduced glutathione. Because the reduction of oxidized glutathione is coupled with NADPH oxidation via glutathione reductase, it seems that the availability of NADPH is essential for paraquat detoxification, and that the critical depletion of NADPH may render the cell more susceptible to lipid peroxidation.

The lung is the organ most severely affected in paraquat poisoning (Campbell 1968; Conning et al. 1969; Haley 1979; Aldrich et al. 1983; Bauer 1983; Combs and Peterson 1983; Christian et al. 1985; Smith 1985; Wong and Stevens 1986; Boudreau and Nadeau 1987; Baud et al. 1988; Dunbar et al. 1988a; Wegener et al. 1988). Pulmonary injury is due largely to the preferential accumulation of paraquat in lung — mediated by an energy-dependent system for uptake of endogenous polyamines — and to the continuous exposure of lung to atmospheric oxygen. Characteristic signs of poisoning include severe anoxia, marked and widespread fibroblastic proliferation in the alveolar walls around the terminal bronchi and blood vessels, and frequently death. The specific toxicity to the lung can be explained by the accumulation of paraquat in the alveolar Type II cells. These cells are responsible for the synthesis of pulmonary surfactant, the surface-active material lining the alveolar epithelium. The pulmonary surfactant is secreted after storage in

cytoplasmic organelles known as lamellar bodies. Thus, any damage to the alveolar epithelium could alter synthesis and secretion of the pulmonary surfactant. The pulmonary effects of paraquat are probably related to the conversion of paraquat to a free radical, followed by conversion to a long-lived dihydroderivative, which causes transformation of normal alveolar epithelial cells to fibroblasts. The increase in toxicity of paraquat by oxygen supports the hydroperoxide theory, in which the reversible action of the free radical's oxidation-reduction gives rise to hydrogen peroxide. Paraquat also depletes NADPH in the isolated lung to the extent of mixed function oxidation impairment. Depletion of NADPH would impair fatty acid and lipoprotein synthesis and inhibit various detoxification and biosynthetic functions.

Other organs and systems affected by paraquat include the kidney (pathology of proximal tubules), liver (hepatocellular necrosis), spleen and thymus (pathology), circulatory system (irregular and feeble heart beat, myocardial congestion, increase in erythrocytes and leucocytes, external pericarditis, myocardium edema), brain (neuronal depletion, myelin destruction), gastrointestinal tract (esophagitis; ulceration of buccal cavity, pharynx, gastric mucosa; mucosal erosion), skin (erythema, hyperkeratosis), reproductive system (degeneration), nervous system (hyperexcitability, irritability, incoordination, convulsions), various enzyme systems, and the eye (Giri et al. 1979, 1982, 1983; Summers 1980; Bauer 1983; Seto and Shinohara 1987, 1988; Hughes 1988; Takegoshi et al. 1988).

Several early indicators of paraquat-induced stress have been proposed, including alkaline phosphatase activity, fibronectin levels, and intracellular calcium uptake. Alkaline phosphatase activity is associated with the lamellar body, and changes in this variable are suggested as indicative of toxicity to Type II alveolar epithelium cells (Boudreau and Nadeau 1987). Levels of fibronectin, an extracellular matrix glycoprotein, were elevated in patients with fibrotic lung diseases and in monkeys given multiple injections of paraquat (Dubaybo et al. 1987). Lung intracellular calcium uptake was significantly disrupted, even at doses that normally produce significant increases in lung water content (Agarwal and Coleman 1988). These subjects seem to merit additional research, as does the role of polyamines in mediating fibrotic changes in the lung (Dunbar et al. 1988b); paraquat-altered synthesis of proteins, DNA, collagen, and pentose phosphate metabolism (Simon et al. 1983); and hyperoxia, that is, increased oxygen-free radical generation (Frank et al. 1982).

Certain treatments or chemicals provide varying degrees of protection against paraquat-induced lung toxicity and lethality, although no treatment or chemical has proven completely successful. Present treatment of paraquat-poisoned animals and humans is directed to elimination of the material from the body using repeated doses of adsorbents such as Fuller's earth or bentonite, cathartics to reduce paraquat absorption, and hemodialysis, forced diuresis, and hemofiltration to enhance excretion (Fletcher 1974; Autor 1977; Haley 1979; Pond et al. 1987; Kitakouji et al. 1989). The use of 100% oxygen is contraindicated, as mortality is greatly increased (Fletcher 1974; Autor 1977; Wong and Stevens 1986). Toxicity mediated by free radicals can be moderated by several cellular defense mechanisms, including superoxide dismutase, catalase, glutathione peroxidase, Vitamin E, and reduced glutathione (Gabryelak and Klekot 1985; Wenning et al. 1988). A low-molecular-weight superoxide dismutase mimic, based on manganese, was found to protect mammalian cells against the cytotoxic effects of the superoxide radical produced by paraquat (Darr et al. 1988). Certain chemicals reportedly provide limited protection to small laboratory animals under carefully controlled conditions of administration: nicotinic acid (Shibata and Iwai 1988); niacin (Heitkamp and Brown 1982); cysteine (Szabo et al. 1986); *N*-acetylcysteine (Wegener et al. 1988); metallothionein — a metal-binding, low-molecular-weight, protein rich in cysteine (Sato et al. 1989); d-penicillamine (Szabo et al. 1986); clofibrate (Frank et al. 1982); lipid-soluble anti-oxidants (Kohen and Chevion 1988; Wegener et al. 1988); various amino acids (Heitkamp and Brown 1982); phenobarbital (Bus et al. 1976; Summers 1980); methyl prednisolone (Kitazawa et al. 1988); and certain anti-inflammatory drugs (Autor 1977). In bluegills, 1,10-phenanthroline, a chelator of ionic iron, reduced the toxicity of paraquat through the prevention of hydroxyl radical formation (Babich et al. 1993). In tilapia, the paraquat-induced increase in gill carbonic anhydrase activity was not observed when ionic lead was present at 47 mg/L (Arias et al. 1991). In plants,

the pea (*Pisum sativum*) is protected by cerium chloride, in part, through counteracting peroxide formation (Vaughn and Duke 1983).

Paraquat toxicity is increased and its effects otherwise exacerbated in organisms fed diets deficient in selenium or Vitamin E, although high levels of these substances in diets did not provide protection (Autor 1977; Haley 1979; Summers 1980); by methyl prostaglandins (Williams et al. 1988) or diethyl maleate (Summers 1980); and by increased iron and copper (Kohen and Chevion 1988; Ogino and Awai 1988). Dietary changes that do not result in nutrient deficiency or toxicity may affect the biocidal properties of paraquat and other compounds. In studies with rodents subjected to paraquat insult, survival was higher in those fed cereal-based diets vs. purified diets, and higher in egg-white (protein) purified diet vs. a casein diet (Tanaka et al. 1981; Evers et al. 1982), suggesting a need to use strictly defined diets in the study of paraquat toxicity to control for any paraquat-diet interactions.

Paraquat causes tissue damage and increased stress in the common carp (*Cyprinus carpio*), as judged by the increased enzyme activities of lactic dehydrogenase, glutamic oxaloacetic transaminase, and glutamate dehydrogenase, and by the elevated blood sugar levels. Paraquat and copper sulfate when administered together to carp were synergistic in terms of tissue damage and stress effects, especially liver damage (Asztalos et al. 1990).

Paraquat adhering to the plant surface is usually degraded photochemically (Haley 1979; Summers 1980). Paraquat is phytotoxic through inhibition of processes involving photosynthesis and respiration (Haley 1979; Christian et al. 1985; Anonymous 1988). Its mode of action in plants is similar to that in animals; that is, lipid peroxidation of membranes due to formation of the superoxide radical and related species (Summers 1980). Photosynthetic tissues reduce paraquat to stable free radicals that, upon reoxidation, produce hydrogen peroxide. Unsaturated lipids in the cells are oxidized by the peroxide, and damage is dependent largely on production of hydrogen peroxide (Haley 1979; Vaughn and Duke 1983). The reaction is light and oxygen dependent (Conning et al. 1969; Kelly et al. 1979).

In bacteria (*Escherichia coli*), paraquat is concentrated, reduced to the monocation radical, and combines with molecular oxygen to produce the superoxide radical within the cell. Copper and iron are essential mediators in bactericidal effects. The cytoplasmic membrane is the target organelle in paraquat toxicity to *E. coli*, and extent of damage correlates positively with levels of these metals (Kohen and Chevion 1988).

22.4.4 Fate in Soils and Water

In contact with soil, paraquat is rapidly adsorbed — usually in the clay mineral lattice sheets — and inactivated by base exchange. The process is facilitated by the flat and highly polarizable nature of the paraquat ion (Anonymous 1963; Conning et al. 1969; Calderbank 1975; Summers 1980; Kearney et al. 1985). The strong binding of paraquat to soil constituents reduces the mobility of the herbicide due to leaching, although paraquat is displaced from binding sites by low concentrations of ions of ammonium, potassium, sodium, and calcium (Smith and Mayfield 1978). Paraquat adsorption is not significantly affected by soil pH, but is modified by soil porosity, moisture content, residence time, and adsorption capacity (Smith and Mayfield 1978; Summers 1980). Paraquat applied to a sandy loam soil at field application rates between 0.56 and 2.24 kg/ha was adsorbed by organic matter and clays, usually in the top centimeter of soil (Smith and Mayfield 1978). Typical soils contain about 300 mg paraquat/kg after treatment at recommended applications; however, adsorption capacity varies among soils. Clay minerals, such as kaolinite, can adsorb 2500 to 3500 mg/kg, whereas others, such as montmorillonite, adsorb up to 85,000 mg/kg after paraquat treatment (Summers 1980).

Paraquat is not degraded significantly in soil during incubation periods up to 16 months at 25°C by chemical or microbiological vectors (Smith and Mayfield 1978). For example, paraquat dichloride applied once annually at 4.48 kg/ha, or 4 times annually at 1.12 kg/ha, remained essentially undegraded in the soil for 6 years (Fryer et al. 1975; Moyer and Lindwall 1985). Massive applications

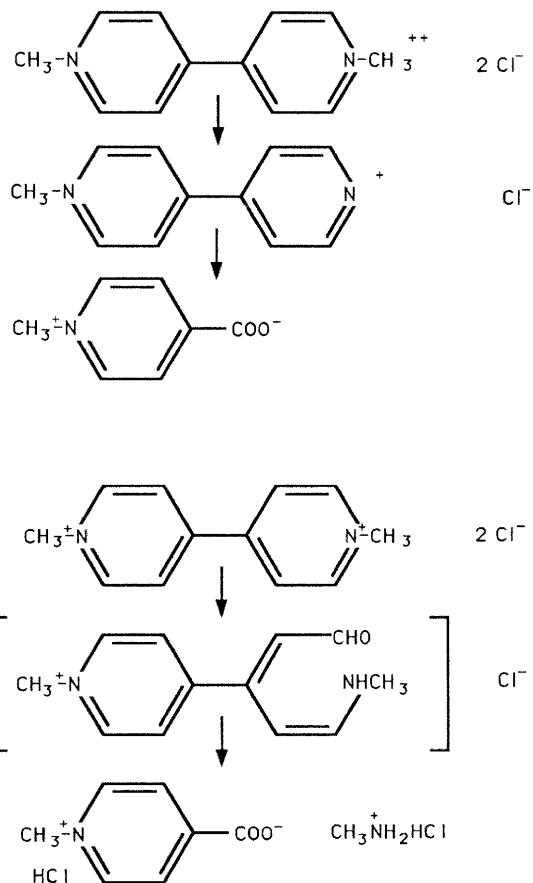


Figure 22.2 Proposed pathway of paraquat degradation by a bacterial isolate (*upper*) and by ultraviolet irradiation (*lower*). (Modified from Funderburk, H.H., Jr. and G.A. Bozarth. 1967. Review of the metabolism and decomposition of diquat and paraquat. *Jour. Agric. Food Chem.* 15:563-567.

to soils of 3000 kg/ha can persist for at least 6 months without significant degradation (Moyer and Lindwall 1985). Bacterial degradation — which occurs only slowly in soils — consists of demethylation, followed by ring cleavage to eventually form the carboxylated 1-methylpyridinium ion (Figure 22.2). Photochemical decomposition of paraquat is the predominant mechanism of paraquat degradation in soils (Smith and Mayfield 1978). In surface soils, paraquat loss through photodecomposition was 20 to 50% in 3 weeks (Christian et al. 1985). Photochemical degradation products of paraquat include 4-carboxy-1-methylpyridinium ion and methylamine hydrochloride (Figure 22.2). Laboratory studies have demonstrated that paraquat in soils slated for disposal can be degraded by ultraviolet (UV) irradiation in the presence of oxygen or ozone. Reaction products identified were 4-carboxy-1-methylpyridinium ion, 4-picolinic acid, hydroxy-4-picolinic acid, succinic acid, *N*-formylglycine, malic acid and oxalic acid (as trimethylsilicon derivatives), and 4,4'-bipyridyl (Kearney et al. 1985).

Paraquat is used to control aquatic weeds. It also passes into aquatic environments through rain, where it is rapidly accumulated by aquatic organisms, especially fish (Gabryelak and Klekot 1985). Paraquat applied to control aquatic weeds is accumulated by aquatic macrophytes and algae, and it is adsorbed to sediments and suspended materials. Initial applications of 1 to 5 mg/L in the water column are usually not detectable under field conditions after 8 to 27 days (Summers 1980). The half-time persistence of paraquat in water column at normal doses for weed control (i.e., 0.5 to 1.0 mg/L) was 36 h; less than 0.01 mg/L was detectable in 2 weeks (Calderbank 1975). In solution, paraquat was subject to photodecomposition and microbial metabolism, degrading to methylamine

and 4-carboxy-1-methylpyridium ion (Kearney et al. 1985). In freshwater, without sediment or plants, 100% of the initial concentration of 0.5 mg paraquat/L was degraded in 35 weeks. When sediments were present, 100% loss from the water column occurred in 6 to 8 weeks; and when both sediment and aquatic plants were present, paraquat was not detectable in the water column in 3 to 4 weeks (Summers 1980). Mud cores taken from a paraquat-treated lake had elevated paraquat residues, but showed no phytotoxic effects on barley seedlings germinated on them (Calderbank 1975).

Paraquat loss from seawater in 24 h was 70% at an initial concentration of 1 mg/L, 68% at 5 mg/L, and 76% at 10 mg/L; most of the loss occurred within the first 60 min (Fytizas 1980).

22.5 LETHAL AND SUBLETHAL EFFECTS

22.5.1 General

Adverse effects of paraquat in sensitive species of terrestrial plants and soil microflora have been documented at application rates of 0.28 to 0.6 kg/ha (death, inhibited germination of seeds, reduced growth), at soil concentrations of 10 to 25 mg/kg (growth inhibition), and at soil-water concentrations as low as 1.6 mg/L (reduced growth, inhibited synthesis of protein and RNA). Among terrestrial invertebrates, certain species of mites were sensitive to paraquat at recommended rates of application, and the sensitive honey bee died when its diet contained 100 mg/kg. However, paraquat in soils was not accumulated by earthworms and other species of soil invertebrates after applications up to 112 kg/ha. These points, and others listed in this section, are discussed in greater detail later.

Freshwater algae and macrophytes usually die at paraquat concentrations between 0.25 and 0.5 mg/L. Marine algae, however, are relatively resistant and usually require 5 mg/L or higher for significant inhibition in growth to occur in 10 days. Aquatic invertebrates, especially crustaceans, seem to be the most sensitive group, with effects most pronounced at elevated temperatures in early developmental stages. Adverse effects were noted in crab larvae at nominal water concentrations between 0.9 and 5.0 µg/L, although 1000 µg/L and higher were needed to produce similar effects in other species of aquatic invertebrates. Amphibians and fishes were usually unaffected at concentrations below 3000 µg/L, although sensitive species, such as frog tadpoles and northern carp (*Cyprinus carpio*), were impacted at 500 µg/L. There was little accumulation of paraquat from the medium by aquatic fauna.

Paraquat is embryotoxic to sensitive species of birds. Concentrations equivalent to 0.056 kg/ha applied in oil solution to the surface of eggs of the mallard (*Anas platyrhynchos*) inhibited development; when applied in aqueous solution, paraquat was toxic at a dose equivalent to 0.56 kg/ha. In each case, adverse effects occurred below the recommended field application rate of about 1.0 kg/ha. The lowest doses of paraquat that produced harmful effects in sensitive birds were 10 mg/kg body weight (BW) in nestlings of the American kestrel (*Falco sparverius*), 20 mg/kg in the diet of northern bobwhite (*Colinus virginianus*), 40 mg/L in the drinking water of domestic chickens (*Gallus* sp.), and 199 mg/kg BW in mallards (acute oral LD50).

Sensitivity of mammals to paraquat was variable, owing to inherent differences in interspecies resistance. Representative mammals were measurably affected at aerosol concentrations of 0.4 to 6.0 µg/L, acute oral doses of 22 to 35 mg/kg BW, dietary concentrations of 85 to 100 mg/kg ration, and drinking water levels of 100 mg/L.

22.5.2 Terrestrial Plants and Invertebrates

In terrestrial plants, paraquat's action is at the point of local absorption (Anonymous 1963). Characteristic damage signs to susceptible species include wilting and general collapse in herbaceous plants. Regrowth may occur in some perennial plants, but in resistant species temporary scorch may be the most marked effect (Anonymous 1963). In sugarcane (*Saccharum officinarum*), paraquat

application severely desiccated the plant within 72 h, and disrupted activity of leaf amylase and sucrose (Haley 1979). Paraquat, once absorbed in plants, is likely to persist (Bauer 1983). The addition of cationic or nonionic surface active agents increases the phytocidal effectiveness of paraquat (Anonymous 1963), but in combination with various herbicides paraquat was markedly less phytotoxic to certain cereal grains (O'Donovan and O'Sullivan 1986).

Paraquat adsorbed to soils is usually unavailable to crops. In the case of wheat (*Triticum aestivum*), effects from contaminated soils were negligible until soil residues surpassed 600 to 1000 kg/ha, causing growth reduction of 10%, or 1650 kg/ha, causing elevated residues in leaves but not in grain (Moyer and Lindwall 1985).

Three species of grains (barley, *Hordeum vulgare*; wheat; oat, *Avena sativa*) died (>95% kill) following application of 0.28 kg paraquat/ha (O'Donovan and O'Sullivan 1986). At 0.6 kg/ha, paraquat inhibited germination and growth in seeds of six species of grasses (Kentucky bluegrass, *Poa pratensis*; perennial ryegrass, *Lolium perenne*; bentgrass, *Agrostis tenuis*; tall fescue, *Festuca arundinacea*; red fescue, *Festuca rubra*; orchard grass, *Dactylis glomerata*), but two species of legumes (alfalfa, *Medicago sativa*; red clover, *Trifolium pratense*) were comparatively resistant (Salazar and Appleby 1982). Paraquat was phytotoxic to several species of terrestrial plants (rape, *Brassica rapa*; ryegrass; white clover, *Trifolium repens*) for several days following application of 1.1 to 2.2 kg/ha (Summers 1980). Transpiration rate of soybean (*Glycine max*) was lowered at 1 mg/kg (Haley 1979). Paraquat is not considered to be carcinogenic or teratogenic, but is weakly mutagenic to some plants (e.g., 4.1% chromosomal aberrations in seeds of wheat at 9.3 mg/kg; Haley 1979). Spray solutions containing 0.6 g paraquat/L applied to crowns of eastern red cedar (*Juniperus virginiana*) killed up to 90% of small trees and up to 30% of large trees; at 0.3 g/L, up to 60% of small trees were affected (Engle et al. 1988). Seedlings of corn (*Zea mays*) sprayed with 0.2% paraquat ion solution for 6 h had decreased rates of total protein synthesis and some polysome dissociation (Wu et al. 1988), suggesting that additional research is needed on mutagenicity of paraquat in plants.

Paraquat resistance has been documented in several genera of weeds. For example, paraquat-resistant strains of barley grass (*Hordeum glaucum*) were first noted in 1982 in Australia; resistant strains (based on chromosome counts and resistance to paraquat) were confined to a small number of lucerne fields where paraquat had been used consistently for at least 10 years. However, the potential exists for this biotype to be transferred and established in other areas by the movement of livestock, machinery, hay, and seeds (Islam and Powles 1988; Tucker and Powles 1988). Paraquat-resistant strains of weeds have been reported in England, Japan, Egypt, and Australia (Polos et al. 1988). Paraquat-resistant strains of bacteria, ferns, and other species of flora have been documented (Carroll et al. 1988). Paraquat-tolerant ferns (*Ceratopteris richardii*) were 10 to 20 times more resistant than sensitive wild-type strains (Carroll et al. 1988). Paraquat-resistant strains of perennial rye were up to 10 times more resistant than normal susceptible strains (Faulkner and Harvey 1981). In the case of barley grass, survival was reduced 50% at 0.025 kg/ha in normal susceptible biotypes; but in resistant biotypes, 3.2 kg/ha were required (Islam and Powles 1988; Tucker and Powles 1988). Paraquat-tolerant plants may enjoy certain advantages over nonresistant plants, including resistance to various air pollutants. For example, paraquat-tolerant tobacco plants (*Nicotiana tabacum*), which had higher superoxide dismutase activity than controls, were tolerant to aerosol sprays of 2 mg SO₂/L, while controls experienced severe damage (Tanaka et al. 1988).

In every case of resistance, paraquat had been applied 2 or 3 times annually during the preceding 5 to 11 years. In some cases, a cross-resistance to atrazine was also reported (Polos et al. 1988). Paraquat-resistance mechanisms in plants include increased epicuticular wax (preventing penetration), binding of paraquat to cell walls, restricted movement into chloroplasts, and altered redox potential (Polos et al. 1988). For example, sequestration of paraquat within the apoplast of the leaf seems to be inheritable and controlled by a single nuclear gene with incomplete dominance (Islam and Powles 1988). Studies with paraquat-tolerant strains of various plants, including perennial rye and tobacco, suggest that tolerance is related to their general ability to rapidly detoxify the generated

oxygen species through increased levels of superoxide dismutase, glutathione reductase, and other antioxidants (Shaaltiel et al. 1988).

At recommended field concentrations, paraquat had negligible effect on soil microflora or soil fertility, although it did cause a temporary suspension of soil nitrification (Haley 1979). A concentration as low as 1.0 mg/L completely inhibited ammonium and nitrite oxidation for 40 days in a mixed culture of nitrifying bacteria isolated from soil (Gadkari 1988). Paraquat at 1.6 mg/L adversely affected *Escherichia coli* in 6 h, as judged by diminished growth rate and inhibited synthesis of RNA and protein; at a higher concentration of 18.6 mg/L, interference with metabolism of glucose and DNA synthesis was observed (Davison and Papirmeister 1971). Four species of soil bacteria had 50% growth inhibition at paraquat concentrations between 93 and 18,600 mg/kg soil; moreover, the mode of action in some species of microorganisms may differ from the generally accepted mechanisms for paraquat toxicity in mammals (Carr et al. 1986). Sensitive species of soil fungi experienced marked growth inhibition between 10 and 25 mg paraquat/kg soil (Summers 1980). In various genera of soil fungi (*Rhizopus*, *Ophiobolus*, *Helminthosporium*, *Fusarium*, *Eurotium*), paraquat concentrations up to 100 mg/L could be tolerated. At higher concentrations, spore germination was suppressed, mycelial growth was inhibited, and spore development was abnormal (Haley 1979).

Terrestrial invertebrates show varying degrees of sensitivity to paraquat. In honey bees (*Apis mellifera*), 100 mg paraquat/kg syrup (diet) produced toxic signs, 4.4 kg/ha applied as a spray killed 90% in 3 days, and 1000 mg/L in drinking water killed most in a few days and 100% within 5 weeks (Summers 1980). In soils, adsorbed paraquat may be ingested by soil invertebrates, such as earthworms, but it was not absorbed from the gut into tissues and was rapidly lost when the earthworms were transferred to clean soil (Calderbank 1975). For example, earthworms (*Lumbricus terrestris*) fed soil treated with 112 kg paraquat/ha had 111 mg paraquat/kg in gut contents, but <0.3 mg/kg in the carcass without gut (Summers 1980). Two species of collembolid insects (*Folsomia candida*, *Tullbergia granulata*) fed diets containing 600 mg paraquat/kg for 22 weeks survived without measurable adverse effects, but higher dietary levels of 1000 and 5000 mg/kg were associated with decreased survival, lengthier instar development, decreased egg production, and decreased egg viability (Subagja and Snider 1981). Adults and larvae of the German cockroach (*Blattella germanica*) died after consuming diets containing 1000 mg paraquat/kg (Summers 1980). Also, paraquat was lethal to two species of mites (*Tetranychus urticae*, *Typhlodromus* sp.) at concentrations below recommended field application rates (Summers 1980).

22.5.3 Aquatic Organisms

In general, paraquat is more toxic to aquatic fauna in soft water than in hard water, more toxic to early developmental stages than to juveniles or adults, and more toxic in formulations containing wetting agents than in formulations without these agents (Summers 1980; Arunlertarce and Kawatsu 1992). In water, paraquat is taken up rapidly by plants or adsorbed to particulate matter in the water column; however, paraquat is not bioconcentrated by aquatic fauna (Calderbank 1975; Summers 1980). Paraquat effects on aquatic biota are summarized in [Table 22.3](#), and these data suggest several trends. Early developmental stages of certain species of crustaceans are extremely sensitive, and significant adverse effects occur in the range of 0.9 to 100 µg/L, although most species of crustaceans and all other species of invertebrates tested were relatively unaffected at concentrations below 1000 µg/L. Freshwater algae and macrophytes are eliminated after treatment with 250 to 500 µg/L, but marine algae are relatively resistant and require 5000 µg/L or higher to produce significant growth inhibition. Aquatic vertebrates usually are not adversely affected and show little accumulation at 1000 µg/L or lower; but at 500 µg/L, frog tadpoles have low survival and a high frequency of developmental abnormalities, and carp experience biochemical upset.

Paraquat controlled *Typha* and *Phragmites* weeds in Egyptian irrigation canals, drains, and marshes without apparent harm to fishes (Haley 1979). Paraquat residues in decomposed plants

become available for adsorption to sediments and bottom muds and are not readily available for microbial degradation (Summers 1980). Indirect fish kills may occur from anoxia due, in part, to consumption of dissolved oxygen by decaying weeds (Bauer 1983). Paradoxically, it has been suggested that paraquat may be helpful in improving the oxygen status of aquatic environments at a concentration of 1 mg/L by restricting nitrate production due to inhibition of bacterial nitrification (Chan and Leung 1986; Gadkari 1988). At effective herbicidal concentrations, paraquat was also toxic to eggs, but not adults, of three species of gastropod vectors of bilharzia (*Bulinus truncatas*, *Biomphalaria alexandrina*, *Lymnaea calliaudi*); newly hatched snails were the most sensitive (Haley 1979).

Changes in fauna of a reservoir following use of paraquat for weed control are likely to be indirect effects caused by decomposition of angiosperms (Brooker and Edwards 1974). Planktonic invertebrates closely associated with aquatic macrophytes were either eliminated by paraquat or survived at lower densities for at least a year posttreatment; analysis of fish stomachs showed dietary changes following weed control and reflected availability of many invertebrate species associated with aquatic plants (Brooker and Edwards 1974).

Paraquat can induce activities of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, and catalase in many species of plants, invertebrates, and vertebrates. Results of studies with ribbed mussels (*Geukensia demissa*) support the hypothesis that these bivalve molluscs can activate redox cycling compounds and demonstrate responses typical of oxidative stress observed in other species (Wenning et al. 1988). Paraquat also disrupts glucose metabolism and acetylcholinesterase activity and accumulates in melanin. Disrupted glucose metabolism in paraquat-stressed carp was attributed to a high level of circulating epinephrine (Simon et al. 1983). Paraquat-induced acetylcholinesterase inhibition in erythrocytes and electric organs of the electric eel (*Electrophorus electricus*) was reversible (Seto and Shinohara 1987, 1988). Paraquat tended to concentrate in melanin, as judged by accumulation in neuromelanin of frogs (*Rana temporaria*) after intraperitoneal injection (Lindquist et al. 1988), with important implications for research on Parkinson's disease. It seems that paraquat has a structural similarity to a metabolite of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), which may induce a Parkinson-like condition. MPTP and its metabolites, like paraquat, have melanin affinity (Lindquist et al. 1988).

Table 22.3 Effects of Paraquat on Selected Species of Aquatic Plants and Animals (Concentrations are in mg of paraquat cation per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (mg/L) and Effect	Reference ^a
ALGAE AND MACROPHYTES		
Lesser duckweed, <i>Lemna minor</i>	0.00074; lethal	1
Submerged weeds		
4 species	0.25–0.5; lethal	2
3 species	0.5–2.5; lethal	2
<i>Chara</i> sp., <i>Polygonum</i> sp.	0.5; no adverse effects in 32 days	3
Freshwater algae		
3 species	0.25–1.0; lethal	2
2 species	>5.0; lethal	2
Rooted emergents		
2 species	0.25–0.5; lethal	2
2 species	2.0–3.0; lethal	2
1 species	>5.0; lethal	2
Floating weeds		
Water weed, <i>Elodea canadensis</i>	0.5; eradicated from British lakes in 32 days for at least 2 years	3
4 species	0.5; herbicidal	2
Pondweed, <i>Potamogeton pusillus</i>	0.5; residues of 36 mg/kg dry weight (DW) in 14 days	4, 5

Table 22.3 (continued) Effects of Paraquat on Selected Species of Aquatic Plants and Animals
 (Concentrations are in mg of paraquat cation per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (mg/L) and Effect	Reference ^a
Eurasian watermilfoil, <i>Myriophyllum spicatum</i>	1.0; residues up to 112 mg/kg DW in 14 days	4, 5
Cattail, <i>Typha latifolia</i>	0.5; shoreline colonies severely affected after exposure for 32 days	3
Duckweed, <i>Spirodella oligorrhiza</i>	0.5; inhibits chlorosis in 48 h	3
Marine algae		
<i>Isochrysis galbana</i>	5; 50% growth inhibition in 10 days	6
<i>Phaeodactylum tricornutum</i>	10; 50% growth inhibition in 10 days	6
<i>Dunaliella tertiolecta</i>	20; 50% growth inhibition in 10 days	6
<i>Chlorococcum</i> sp.	50; 50% growth inhibition in 10 days	6
4 species	2500–>5000; respiration reduced 50% in 2 h	6
INVERTEBRATES		
Mud crab		
<i>Rithropanopeus harrisii</i> , larvae	0.00086; LC50 (19 days)	4
<i>R. harrisii</i> , larvae	0.001–0.005; 50% mortality prior to zoeal stage	4
Isopod, <i>Asellus meridianus</i>		
15°C	0.1; LC50 (14 days)	7
15°C	0.58; LC50 (8 days)	7
5°C	0.62; LC50 (14 days)	7
5°C	6.3; LC50 (8 days)	7
Freshwater invertebrates, 3 species (<i>Asellus</i> , <i>Lymnaea</i> , <i>Sialis</i>)	0.5; no deaths in 4 days following spray application to British lake	3
Gastropod		
<i>Murex brandaris</i>	1; LC50 (18 days)	8
<i>M. brandaris</i>	10; LC50 (24 h)	8
<i>M. brandaris</i>	1–10; residues, in mg/kg fresh weight (FW) soft parts, after exposure for 3 days ranged between 1.5 and 2.8, and were dose dependent	8
Hermit crab		
<i>Pagurus</i> sp.	1; LC50 (10 days)	8
<i>Pagurus</i> sp.	10; LC50 (36 h)	8
<i>Pagurus</i> sp.	1–5; residues, in mg/kg whole-body FW, after exposure for 3 days ranged between 3.2 and 15, and were dose dependent	8
Brown shrimp, <i>Penaeus aztecus</i>	>1.0; 50% immobilization in 48 h	6
American oyster, <i>Crassostrea virginica</i>	>1.0; 50% growth reduction in 96 h	6
Louisiana red crayfish, <i>Procambarus clarkii</i>		
Juvenile	1.4; LC50 (96 h)	9
Juvenile	2.4; LC50 (72 h)	9
Adult	17; LC50 (72 h)	9
All stages	Sublethal; Dose-dependent increase in hyperactivity and oxygen consumption	9
Daphnid		
<i>Daphnia hyalina</i>	2.5; LC50 (14 days)	7
<i>Daphnia pulex</i>	2.7; 50% immobilization in 48 h	10
<i>D. pulex</i>	4.0; LC50 (48 h)	11
Cladoceran		
<i>Simocephalus serrulatus</i>	2.8; 50% immobilization in 48 h	10
<i>S. serrulatus</i>	3.7; LC50 (48 h)	11
Liver fluke, <i>Fasciola hepatica</i>		
Egg through miracidium	5; LC50 (20 days); effects counteracted by dinoseb	12
Egg	6; delayed embryonic development; delayed hatch of miracidia	12
Egg	8; 26% hatch	12

Table 22.3 (continued) Effects of Paraquat on Selected Species of Aquatic Plants and Animals
 (Concentrations are in mg of paraquat cation per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (mg/L) and Effect	Reference ^a
Egg	10; 9% hatch	12
Egg	15; no hatch	12
Freshwater copepods, 2 species (<i>Eucyclops</i> , <i>Diaptomus</i>)	5; LC50 (48 h)	13
Freshwater copepods, 2 species	10; LC50 (24 h); effects counteracted by metribuzin, another herbicide	13
Aquatic insects, nymphs		
Coreiid, <i>Sigara</i> sp.	5; LC50 (14 days)	7
Baetid, <i>Cloeon dipterum</i>	29; LC50 (14 days)	7
Daphnid		
<i>Daphnia magna</i>	6; 24% immobilized in 26 h; all mobile daphnids transferred to paraquat-free medium died within 48 h	14
<i>D. magna</i>	11; 50% immobilized in 26 h	14
<i>D. magna</i>	14; 70% immobilized in 26 h; all mobile daphnids transferred to paraquat-free medium died within 24 h	14
Amphipod, <i>Gammarus fasciatus</i>	11; LC50 (96 h)	10, 11
Ribbed mussel, <i>Geukensia demissa</i>		
<i>G. demissa</i>	93; elevated catalase activity, lipid peroxidation rate, and total superoxide dismutase levels in 12–36 h	15
<i>G. demissa</i>	744; no deaths in 7 days	15
<i>G. demissa</i>	1190; LC100 (7 days)	15
Chironomid, 4th instar larvae, <i>Psectrocladius</i> sp.	>100; LC50 (14 days)	7
Stonefly, <i>Pteronarcys californica</i>	>100; LC50 (96 h)	10, 11
Mosquito larvae, 2 species	275–>1000; LC50	4
FISHES		
Characid, <i>Bryconamericus iheringii</i>	20.2; LC50 (96 h)	29
Common carp <i>Cyprinus carpio</i>	0.5; after 6 days, 300% increase in phosphorylase and 200% increase in glucose-6-phosphatase activities in liver; increase in sugar level and serum lactic dehydrogenase activity	18
<i>C. carpio</i>	5; increase in activities of various liver enzymes, and in blood sugar levels during exposure for 6 days; effects enhanced by the herbicide methidation	19
<i>C. carpio</i>	5; initial reduction by 50% of serum cholinesterase activity which gradually increased to 130% of control values during exposure for 2 weeks, suggesting that paraquat may influence resynthesis of acetylcholinesterase	28
<i>C. carpio</i>	10; during exposure for 96 h, significant alterations were recorded in lipid peroxidation rate, hemoglobin concentration, and erythrocyte antioxidant enzymes, that is, catalase, superoxide dismutase, and glutathione peroxidase activities	20
<i>C. carpio</i>	10; after 8 h, increased superoxide dismutase in gill, liver, and brain; effects exacerbated under conditions of hypoxia	32
<i>C. carpio</i>	11.3–33.3; LC50 (96 h) values for early and late embryo developmental stages, respectively	31
<i>C. carpio</i>	13–214; acetylcholinesterase activity reduced 50% after exposure for 2 h in serum (13 mg/L), heart (39 mg/L), muscle (102 mg/L), and brain (214 mg/L)	21

Table 22.3 (continued) Effects of Paraquat on Selected Species of Aquatic Plants and Animals
 (Concentrations are in mg of paraquat cation per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (mg/L) and Effect	Reference ^a
<i>C. carpio</i>	67.5–134.1; LC50 (96 h) values for fry and fingerlings, respectively	31
Plecostomid catfish		
<i>Plecostomus commersonii</i> , fry	0.6; decrease in cardiac contraction rate after exposure for 36–60 h	27
<i>P. commersonii</i> , fry	1.3; decrease in opercular ventilation rate after exposure for 60 h	27
<i>P. commersonii</i> , fry	2.5; decrease in cardiac contraction rate after exposure for 12 h	27
<i>P. commersonii</i> , fry	5.2 (3.9–6.4); LC50 (60 h)	27
<i>P. commersonii</i> , fry	10.0; all dead within 60 h	27
Freshwater fish		
4 species	1.0; maximum residues, in mg/kg whole-body FW, during exposure for 16 days ranged between 0.6 in green sunfish (<i>Lepomis cyanellus</i>) and 1.6 in bluegill (<i>Lepomis macrochirus</i>); intermediate values were recorded for rainbow trout (<i>Oncorhynchus mykiss</i>) and channel catfish (<i>Ictalurus punctatus</i>)	22
3 species	10; in exposures lasting up to 96 h, paraquat caused an exposure-dependent increase in lipid peroxidation rate and in activity enhancement of peroxide metabolism enzymes in erythrocytes	23
3 species	250; lesions in skin and gills of survivors and increasing susceptibility to secondary invaders	30
Smallmouth bass, <i>Micropterus dolomieu</i>	1.0; adverse sublethal effects	22
Striped mullet		
<i>Mugil cephalus</i>	1.0; LC50 (16 days); survivors had pronounced gill histopathology and residues, in mg/kg FW, of 0.2 in muscle, 0.2 in ovary, 4.7 in skin, and 6.1 in digestive tract	8
<i>M. cephalus</i>	10.0; LC50 (60 min)	8
Thai silverbarb		
<i>Puntius gonionotus</i>	1.0; no tissue histopathology after exposure for 12 days	24
<i>P. gonionotus</i>	4.0; gill histopathology evident after exposure for 12 days; gills normal during exposure for only 5 days	24
Longnose killifish, <i>Fundulus similis</i>	>1.0; LC50 (48 h)	6
Mosquitofish		
<i>Gambusia affinis</i>	3; adverse effects	22
<i>G. affinis</i>	604; LC50 (96 h)	5
Zebra danio, <i>Brachydanio rerio</i>	7.5–48.5; LC50 (96 h)	4
Poeciliid fish, <i>Cnesterodon decemmaculatus</i> ; fry	9.4 (6.8–11.8); LC50 (96 h)	26
Shortfin molly, <i>Poecilia mexicana</i>	12; LC50 (24 h)	5
Medaka, <i>Oryzias latipes</i>		
Egg	12; normal development	5
Egg	23; abnormal development	5
Embryo	>50; 100% lethal	5
Bluegill, <i>Lepomis macrochirus</i>	13; LC50 (96 h)	10, 11
Guppy, <i>Poecilia reticulata</i>	15–22; LC50 (96 h)	4
Rainbow trout		
<i>Oncorhynchus mykiss</i>	15–32; LC50 (96 h)	5, 10, 11
<i>O. mykiss</i>	>100; LC50 (24 h)	10
Brown trout, <i>Salmo trutta</i>	25; LC50 (96 h)	5
Tilapia, <i>Oreochromis hornorum</i>	31.5; LC50 (96 h)	25
Channel catfish, <i>Ictalurus punctatus</i>	>100; LC50 (96 h)	5, 10, 11

Table 22.3 (continued) Effects of Paraquat on Selected Species of Aquatic Plants and Animals
 (Concentrations are in mg of paraquat cation per liter of medium.)

Taxonomic Group, Organism, and Other Variables	Concentration (mg/L) and Effect	Reference ^a
AMPHIBIANS		
Leopard frog, <i>Rana pipiens</i>		
Early gastrula stage	0.1; normal growth, survival, development, and swimming behavior after 7 days of exposure	16
Early gastrula stage	0.5; high mortality, high number of tail abnormalities, reduced growth rate in survivors, and abnormal swimming behavior after exposure for 7 days (3 days posthatch) to 0.5 mg/L and higher	16
15-day-old tadpoles	0.5; 33% dead after exposure for 16 days	17
15-day-old tadpoles	2.0; 95% dead after exposure for 16 days; increase in growth retardation and in developmental abnormalities such as tail malformations and cranial defects	17
Fowler's toad		
<i>Bufo woodhousei fowleri</i> , tadpole	15; LC50 (96 h)	10
<i>B. w. fowleri</i>	56; LC50 (24 h)	10
Water frog		
<i>Scinax nasica</i> , tadpoles	6.5–18; dose-dependent increase in gill histopathology in 96 h	33
<i>S. nasica</i> , tadpoles	10.8; no deaths in 96 h	33
<i>S. nasica</i> , tadpoles	18; LC15 (96 h)	33
<i>S. nasica</i> , tadpoles	22; LC50 (96 h)	33
Western chorus frog		
<i>Pseudacris triseriata</i> , tadpole	28; LC50 (96 h)	10
<i>P. triseriata</i>	43; LC50 (24 h)	10
Frog, <i>Limnodynastes peroni</i> , adult	100; LC50 (96 h)	5
Frog, <i>Adelotus brevis</i> , adult	262; LC50 (96 h)	5

^a 1, Ross et al. 1979; 2, Anonymous 1963; 3, Way et al. 1971; 4, Summers 1980; 5, Bauer 1983; 6, Mayer 1987; 7, Brooker and Edwards 1974; 8, Fytizas 1980; 9, Leung et al. 1980; 10, Mayer and Ellersiek 1986; 11, Johnson and Finley 1980; 12, Christian et al. 1985; 13, Naqvi et al. 1981; 14, Crosby and Tucker 1966; 15, Wenning et al. 1988; 16, Dial and Bauer 1984; 17, Dial and Dial 1987; 18, Simon et al. 1983; 19, Asztalos et al. 1988; 20, Matkovics et al. 1987; 21, Nemcsok et al. 1984; 22, Earnest 1971; 23, Gabryelak and Klekot 1985; 24, Sinhaseni and Tesprateep 1987; 25, Arias et al. 1991; 26, Di Marzio and Tortorelli 1994; 27, Tortorelli et al. 1990; 28, Szabo et al. 1992; 29, Di Marzio and Tortorelli 1993; 30, Muscarella and Galofaro 1973; 31, Arunlertarce and Kawatsu 1992; 32, Vig and Nemcsok 1989; 33, Lajmanovich et al. 1998.

22.5.4 Birds

Signs of oral paraquat intoxication in birds include excessive drinking and regurgitation, usually within 10 min of exposure. Other signs appeared after 3 h: diarrhea, ruffled feathers, muscular incoordination, imbalance, wing drop, hyporeactivity, slowness, weakness, running and falling, constriction of the pupil, and terminal convulsions. Additional signs reported after dermal exposure include blistering and cracking of skin, lacrimation, wing spread, and wing shivers. Deaths usually occurred between 3 and 20 h postexposure; remission took up to 12 days (Smalley 1973; Haley 1979; Summers 1980; Hudson et al. 1984). The blood chemistry pattern of paraquat-intoxicated Japanese quail (*Coturnix japonica*) suggested adrenal gland impairment, although recovery from hematologic effects was rapid (Clark et al. 1988). Paraquat causes pseudofeminization of male chicken and quail embryos; testes showed intersexual phenomena and Mullerian duct abnormalities; and both sexes had a reduction in gonocyte number (Haley 1979; Bauer 1983).

The lowest doses of paraquat causing measurable adverse effects in sensitive species of birds (Table 22.4) were:

- 0.2 mg/kg BW administered by single intravenous injection to Japanese quail, causing anemia
- 0.25 mg/kg applied in oil solution to the surface of eggs of the mallard, producing reduced survival, reduced growth, and increased frequency of developmental abnormalities
- 10 mg/kg BW administered orally for 10 days to nestlings of the American kestrel, causing reduced growth
- 20 mg/kg in diet of the northern bobwhite, producing a reduction in egg deposition
- 40 mg/L in drinking water of the domestic chicken, causing elevated tissue residues and an increase in the number of abnormal eggs produced
- 199 mg/kg BW in mallards, producing an acute oral LD₅₀

Paraquat is highly toxic to avian embryos but is less toxic to adult birds (Bunck et al. 1986). It is toxic by several routes of administration, including injection and topical application (Hoffman et al. 1985). Paraquat was the most toxic to eggs of the mallard of 42 herbicides and insecticides tested. Paraquat applied to eggshell surfaces in nontoxic oil vehicles was significantly more embryo-toxic than were aqueous paraquat solutions, presumably owing to greater penetration of oil past the shell and membranes (Hoffman and Eastin 1982; Hoffman and Albers 1984) (Table 22.4). The LC₅₀ values for paraquat and mallard eggs were 1.68 kg/ha (1.5 pounds/acre) in aqueous emulsion and 0.11 kg/ha (0.1 pound/acre) in an oil vehicle (Hoffman and Eastin 1982). The computed LC₅₀ aqueous value was about 1.5 times higher than the recommended field application rate of about 1.0 kg/ha; however, paraquat in aqueous solution caused some deaths at only half the field level of application, and survivors showed impaired growth and some developmental abnormalities (Hoffman and Eastin 1982) (Table 22.4).

Nestlings of altricial species, such as the American kestrel, were more sensitive to paraquat exposure than were young or adults of precocial species (Hoffman et al. 1985). There are several food items of kestrels (e.g., grasshoppers, small rodents, passerine birds) that are readily contaminated by paraquat through direct contact during agricultural spraying or by ingestion of contaminated vegetation (Hoffman et al. 1985). From a comparative viewpoint, however, lungs of nestling kestrels were less sensitive to paraquat than were mammalian lungs (Hoffman et al. 1987).

Northern bobwhite hens immediately exposed to simulated field application rates of paraquat took longer to lay a clutch of eggs once laying had commenced; the completed clutch appeared 10 days later in the season than birds free from paraquat exposure. It is uncertain whether the paraquat-induced delay in sexual maturation produced experimentally will also be reflected in nonlaboratory situations (Bauer 1983, 1985). Turkeys (*Meleagris gallopavo*), for example, held in field plots sprayed 24 h earlier with paraquat at 100 times the recommended agricultural application rate (i.e., up to 200 ounces cation/acre or 14 kg/ha) showed no signs of toxicity for 30 days after spraying (Smalley 1973).

Acute toxicity of paraquat in the domestic chicken was highly responsive to nutritional selenium status and not to Vitamin E status. As little as 0.01 mg Se/kg ration protected 8-day-old chicks against acute paraquat poisoning (Combs and Peterson 1983). Paraquat administered to chickens by way of diet was less toxic than the same amount administered in drinking water (Fletcher 1967).

Table 22.4 Paraquat Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effects and Reference
MALLARD, <i>Anas platyrhynchos</i>	
Fertilized eggs exposed on day 3 of incubation for 0.5 min at room temperature	
Oil solutions	
0.25 mg/kg egg, equivalent to 0.056 kg/ha or 0.05 pounds/ acre	17% dead, reduced growth, 16% abnormal development (Hoffman and Eastin 1982)
0.5 mg/kg egg	50% dead, some abnormal survivors (Hoffman and Albers 1984)
2.5 mg/kg egg	83% dead, 60% abnormal (Hoffman and Eastin 1982)

Table 22.4 (continued) Paraquat Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effects and Reference
Aqueous solutions 2.8 mg/kg egg, equivalent to 0.56 kg/ha or 0.5 pounds/ acre 8.3 mg/kg egg	23% dead, survivors stunted, 9% abnormal (Hoffman and Eastin 1982) 50% dead. The computed LC50 concentration was about 1.5 times the recommended field application rate. At 1.5–3.0 times the field level, paraquat produced abnormal development, including edema, stunting, and brain malformations (Hoffman and Albers 1984) 73% dead, 63% of survivors abnormal (Hoffman and Eastin 1982)
27.7 mg/kg egg Adults and juveniles 199 mg/kg body weight (BW)	Acute oral LD50; deaths usually occurred between 3 and 20 h after treatment. Remission took up to 12 days (Hudson et al. 1984)
600 mg/kg BW	Percutaneous LD50 for 10- to 11-month-old drakes after a 24-h dermal foot exposure. Deaths occurred between 6 and 22 h after treatment; remission took up to 5 days (Hudson et al. 1984)
4048 mg/kg diet	Fatal to 50% after 5 days on treated diet plus 3 days on untreated ration (Heath et al. 1972)
NORTHERN BOBWHITE, <i>Colinus virginianus</i>	
Parent generation (P_1) fed diets containing 20, 60, 180, or 360 mg /kg ration for 6 weeks; in next generation (F_1), none was administered	360-mg/kg P_1 group had reduced fertility and hatchability, significant body weight loss, and reduction in ovary and oviduct weight; there was no increase in chick abnormalities or histopathology; the 180-mg/kg P_1 group laid significantly fewer eggs during treatment; all F_1 hens from the 20-, 60-, and 180-mg/kg groups started laying 1 week later than controls and produced fewer eggs; F_1 males experienced a delay in maturation; F_1 chicks from the 20-mg/kg group were significantly heavier than all other groups (Bauer 1983, 1985)
Fed diets containing 25 or 100 mg paraquat/kg food for 60 days	No signs of toxicity or impaired learning (Bunck et al. 1986)
981 mg/kg diet, 2- to 3-week-old birds	Fatal to 50% after 5 days on treated diet plus 3 days on untreated diet (Heath et al. 1972; Anonymous 1974)
JAPANESE QUAIL, <i>Coturnix japonica</i>	
Juveniles received a single intravenous injection of 0.2, 2, or 20 mg/kg BW	Some deaths in 20 mg/kg group. All survivors from all groups showed hemolytic anemia within 24 h postinjection, recovery beginning within 72 h; the 0.2-mg/kg birds also showed reductions in erythrocyte number, hematocrit, and hemoglobin within 24 h (Clark et al. 1988)
14-day-old chicks fed treated diets for 5 days followed by 3 days of untreated food	
500 mg/kg diet	Fatal to 20% (Hill and Camardese 1986)
948–970 mg/kg diet	Dietary LD50 (Heath et al. 1972; Hill and Camardese 1986)
1516 mg/kg diet	Fatal to 90% (Hill and Camardese 1986)
Eggs dusted with 0.4–0.8% paraquat powder	Hatching rate ranged between 58 and 79% (Bauer 1983)
100 mg/L in drinking water	Lethal within 7 days (Summers 1980)
AMERICAN KESTREL, <i>Falco sparverius</i>, nestlings	
Daily oral doses, for 10 days, of 10, 25, or 60 mg paraquat/kg BW	All groups exhibited reduced growth rate and elevated total sulphydryl and protein-bound sulphydryl levels in lung, when compared to controls. The 25-mg/kg group had reduced skeletal growth of humerus and femur. In the 60-mg/kg group, 44% died in 4 days; survivors showed abnormal blood chemistry, liver histopathology, kidney damage, and reduced skeletal growth of humerus, femur, radius-ulna, and tibiotarsus (Hoffman et al. 1985, 1987).
DOMESTIC CHICKEN, <i>Gallus</i> sp.	
Egg >0.1 mg/kg 0.5 mg	Hatching rate reduced after injection (Fletcher 1967; Bauer 1983) Injected eggs did not hatch (Haley 1979)

Table 22.4 (continued) Paraquat Effects on Selected Species of Birds

Species, Dose, and Other Variables	Effects and Reference
0.4–0.8% paraquat powder	Hatching rate of eggs dusted with powder ranged between 46 and 77% (Bauer 1983)
Adult	
Single intravenous injection of 25 mg paraquat dichloride/kg BW	60% reduction in urine flow within 50 min (Prashad et al. 1981)
40 mg/L in drinking water for 14 days followed by 14 days of paraquat-free water	No effect on egg production or hatchability, but 7% increase in number of abnormal eggs produced. Paraquat residues in eggs rose to about 0.1 mg/kg, but declined to below detection limits 6 days after treatment was halted. No effect on food and water consumption of hens or on number and type of abnormalities in chicks (Fletcher 1967)
131 mg/kg BW	Acute oral LD50, diet deficient in Vitamin E and selenium (Combs and Peterson 1983)
148 mg/kg BW	Acute oral LD50, diet deficient in selenium (Combs and Peterson 1983)
419 mg/kg BW	Acute oral LD50, diet deficient in Vitamin E (Combs and Peterson 1983)
Chicks, 8-days old, 200–380 mg/kg BW	Acute oral LD50 (Haley 1979; Summers 1980; Bauer 1983)
TURKEY, <i>Meleagris gallopavo</i>	
20 mg/kg BW	Lethal dose, intravenous injection route (Smalley 1973)
100 mg/kg BW	Lethal dose, intraperitoneal injection route (Smalley 1973)
290 mg/kg BW	Lethal dose, oral administration route (Smalley 1973)
500 mg/kg BW	Lethal dose, dermal route (Smalley 1973)
RING-NECKED PHEASANT, <i>Phasianus colchicus</i>	
1468 mg/kg diet	Fatal to 50% after 5 days on treated diet plus 3 days on untreated diet (Heath et al. 1972)

22.5.5 Mammals

Resistance to paraquat among mammals varied substantially owing to inherent differences in sensitivity between species, to route of administration, and to reproductive state (Table 22.5). The lowest recorded doses of paraquat causing measurable adverse effects on growth, survival, or reproduction were (Table 22.5):

- Aerosol concentrations of 0.4 to 6.0 µg/L (rat, guinea pig)
- 0.05 mg administered directly in lung (rat)
- Intravenous injection of 1 to 12 mg/kg BW (sheep, dog, rat)
- Subcutaneous injection of 2.4 to 28 mg/kg BW (rat, mouse, monkey)
- Intraperitoneal injection of 3 to 10 mg/kg BW (mouse, guinea pig, goat)
- Acute oral dose of 22 to 35 mg/kg BW (dog, cat, hare, guinea pig)
- Dermal application of 70 to 90 mg/kg BW (rat)
- Dietary levels of 85 to 100 mg/kg ration (dog, mouse, rat)
- Drinking water concentration of 100 mg/L (mouse)

In microtine rodents, feed aversion and toxicant avoidance were the most significant behaviors elicited by feed tainted with paraquat (Linder and Richmond 1990).

In general, intraperitoneal and intravenous injections were the most sensitive administration routes (Bauer 1983). LD50 dermal values, however, are often not true percutaneous values because of oral contamination from normal grooming (Summers 1980). Aerosol exposure to paraquat produced a concentration-dependent rapid, shallow breathing pattern in guinea pigs (*Cavia* sp.)

18 h after exposure (Burleigh-Flayer and Alarie 1988). Aerosol LC50 values in paraquat toxicity tests with mammals were directly related to the duration of exposure, paraquat concentration in spray, and particle size; particles of 3 µm diameter seemed most effective (Haley 1979).

Paraquat produces rapidly progressive, fatal, interstitial inflammation and fibrosis of the lung in humans following accidental ingestion, and this has been produced experimentally in several species of laboratory animals (Butler and Kleinerman 1971; Murray and Gibson 1972). Initial symptoms of paraquat poisoning include burning of the mouth and throat, followed by nausea and vomiting. After a latent period of up to several days, increasing respiratory distress develops; death is usually the result of a progressive fibrosis and epithelial proliferation that occurs in the lungs (Kimbrough 1974). Paraquat poisoning in humans has a mortality of 30 to 70%, depending largely on the dose ingested. It causes multiorgan failure, including the heart, lungs, kidney, liver, and brain. Although recovery may follow mild involvement of any of these organs, many patients die from progressive untreatable pulmonary fibrosis. This illness usually succeeds renal failure and relates in part to active pulmonary uptake of paraquat (Webb 1983). In one case, a 15-year-old boy accidentally ingested a mouthful of paraquat and developed severe respiratory distress, necessitating transplantation of one lung; paraquat-induced rejection of the graft resulted in death 2 weeks after the operation (Matthew et al. 1968). Paraquat cannot be absorbed significantly through intact human skin; but in the event of broken or abraded skin brief exposure to a concentration of 5 g paraquat/L may result in death (Smith 1988a).

Paraquat tends to rapidly localize in selected tissues of injected mice, including melanin, alveolar type cells of the lung, choroid plexus, muscle, proximal tubules of the kidney, liver, gallbladder, and intestinal contents (Waddell and Marlowe 1980). Half-time persistence of paraquat in rat tissues ranged from 20 to 30 min in plasma to about 5 days in muscle (Sharp et al. 1972).

Acute effects of paraquat poisoning in livestock and small laboratory animals are similar to those in humans (Conning et al. 1969; Murray and Gibson 1972; Rose et al. 1976; Smith and Heath 1976; Haley 1979; Kelly et al. 1979; Manzo et al. 1979; Summers 1980) (Table 22.5). Signs of acute paraquat toxicosis included hyperexcitability leading to convulsions or incoordination, inflammation of the mouth and throat, vomiting, reluctance to eat or drink, diarrhea, tachycardia, eye irritation of the conjunctiva, corneal lesions, skin reddening, skin ulceration, skin necrosis, histopathology of liver and kidney, and respiratory failure. Paraquat was selectively accumulated in lung of canines, primates, and rodents, regardless of route of administration. Lung pathology included congestion, hemorrhage, edema, and collapse. This was associated with degeneration of alveolar and bronchial cells. Death may occur within 10 days of acute exposure.

Chronic administration of small doses or repeated injections usually produce no clinical signs for several weeks. Signs develop suddenly, in general, and include weight loss, anorexia, and death — usually within 10 days of onset of signs (Smith and Heath 1976). Decreased food consumption and consequent loss of body weight are common in paraquat-poisoned rats and dogs. The area postrema of the hindbrain is an important neural site for detection of blood-borne chemicals and is speculated to control paraquat-induced taste aversion formation and weight loss (Dey et al. 1987).

Rabbits are comparatively resistant to paraquat-induced lung damage, regardless of the route of administration (Summers 1980; Dikshith et al. 1979; Bauer 1983), but the closely related hare (*Lepus europaeus*) is comparatively sensitive to paraquat. Hares placed on alfalfa plots within a few hours after the fields were treated with 0.6 kg paraquat/ha experienced 50% mortality in 120 h; survivors that were killed 2 weeks later showed lung damage and ulceration of the lingual mucous membrane. Plant residues were about 30 mg/kg fresh weight for alfalfa and 60 mg/kg for weeds; residues were negligible in tissues of the hare (Lavaur et al. 1973). In a similar incident in Italy, Stracciari et al. (1980) found that only 1 of 56 hares found dead had lung damage, although all had elevated urine paraquat levels of 0.5 mg/L. It was concluded that paraquat alone was not the causative agent of death, and that paraquat interactions with other chemicals applied at the same time on other crops in the same area may be responsible.

Paraquat applications to spruce plantations for grass control had no effect on the movement or density of field mice (*Microtus arvalis*) and voles (*Microtus agrestis*), but shrews (*Sorex* sp.) migrated from treated areas to untreated ones (Summers 1980).

Paraquat is poorly absorbed from the gut and readily excreted. Typical gut absorption rates (%) and peak concentrations in blood (mg/L) were 15 to 20% and 3 to 4 mg/L in rat, 5 to 10% and 1 mg/L in guinea pig, 16% and 13 mg/L in cat, 0.26% in cow, and 1 to 5% in humans (Conning et al. 1969). Paraquat is actively secreted by a renal mechanism that is vulnerable to paraquat toxicity; poisoning of the secretory component removed a large part of the excretory capacity for paraquat (Webb 1983). In rats, a single oral LD₅₀ dose produced a reduction in renal function within 24 h. This effect is probably secondary to a decrease in plasma volume with a consequent reduction in renal blood flow (Lock 1979). Paraquat caused mild renal tubular damage in the rat; within 24 h of injection of 20 mg/kg BW, there was marked diuresis, sugar and albumin in the urine, and increased plasma urea concentrations (Lock and Ishmael 1979). Paraquat-poisoned mice showed a decreased ability to excrete organic acids and bases, probably reflecting interference with proximal tubule function because no change in glomerular filtration rate was observed (Ecker et al. 1975).

Paraquat was not mutagenic, as judged by noninterference with DNA metabolism, and had no reverse mutation-inducing capability (Anonymous 1988). Paraquat had little or no teratogenicity to mammals (Bus et al. 1975). No teratogenic effects were observed in rats fed diets containing 400 mg paraquat/kg for three generations (Anonymous 1988). The most common malformations in paraquat-stressed rats were those involving costal cartilage (Bauer 1983). Studies demonstrated transplacental transfer of paraquat in pregnant rats and guinea pigs. High concentrations of radio-labeled paraquat were found in the placenta and throughout the fetuses within 30 min of intravenous administration. Concentrations in placenta, maternal blood, and fetal blood were in the ratio of 16 to 4 to 1 (Ingebrigtsen et al. 1984), suggesting that additional research is needed on paraquat embryotoxicity.

Table 22.5 Paraquat Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects and Reference
COW, CATTLE, <i>Bos</i> sp.	
Calves administered 5 mg/kg BW, iv injection	No effect on pulmonary function or blood gases after 7 days (Kiorpis et al. 1982)
20 mg/L drinking water, 1 month	No measurable effect (Calderbank 1975)
35–75 mg/kg BW	Acute oral LD ₅₀ (Fletcher 1974; Haley 1979; Summers 1980; Heitkamp and Brown 1982)
200–400 mg/kg diet for 30 days	No observable effect; no measurable residues in meat or milk (Calderbank 1975)
DOG, <i>Canis familiaris</i>	
25 µg/L air, 60 min exposure	No ill effects (Haley 1979)
Fed diets containing 7, 34, 85, or 170 mg paraquat/kg ration for 27 months	No significant abnormalities at 7 or 34 mg/kg; toxic effects noted at 85 and 170 mg/kg diet (Anonymous 1974)
12 mg/kg BW, single iv injection	Extensive lung damage after 7 days (Hampson and Pond 1988)
25 mg/kg BW, single iv injection	All dead within 36 h. Prior to death, plasma levels of glucose, cortisol, and catecholamines increased and glucose levels decreased. Increases in activity of plasma lactic dehydrogenase, creatinine phosphokinase, glutamic oxaloacetic transaminase, creatinine, and rennin. Residues in dead dogs, in µg/kg fresh weight (FW), were highest in bile (41), kidney (8), lung (5), liver (5), spleen (4), heart (3), adrenal (3), pancreas (1), thymus (1), and muscle (1) (Giri et al. 1982, 1983)
25–50 mg/kg BW	Acute oral LD ₅₀ (Heitkamp and Brown 1982; Anonymous 1988)
36 mg/kg diet for 2 years	No measurable effect (Haley 1979)

Table 22.5 (continued) Paraquat Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects and Reference
GOAT, <i>Capra</i> sp.	
10 mg/kg BW, ip injection	Mild paraquat-related lung tissue changes, but toxicosis was not clinically significant after 10 days (Kiorpis et al. 1982)
GUINEA PIG, <i>Cavia</i> sp.	
Aerosol exposure, in mg/m ³	
0.1, 0.4, or 0.8, 6 h daily, 5 days weekly, 3-week exposure	Rapid shallow dose-dependent breathing pattern, with return to control values during first 7 days of exposure, suggesting adaptation (Burleigh-Flayer and Alarie 1988)
0.7, 4-h exposure, 2-week observation	Decrease in lung volume and increase in respiratory frequency; maximum effects measured several days postexposure with return to control values (Burleigh-Flayer and Alarie 1988).
0.83–2.07, 4-h exposure, flow rate 21 L/min, particles usually <0.65 µ diameter	Concentration-related decrease in lung volume and 2-fold increase in respiratory frequency 18 days postexposure (Burleigh-Flayer and Alarie 1987)
3 mg/kg BW	Acute intraperitoneal LD50 (Haley 1979; Manzo et al. 1979)
22–80 mg/kg BW	Acute oral LD50 in 7 days (Murray and Gibson 1972; Haley 1979; Summers 1980; Heitkamp and Brown 1982; Bauer 1983)
CHINESE HAMSTER, <i>Cricetus</i> spp.	
Cultured cells subjected to 0.8 mg/L for 3 h, recovery for 21 days	50% frequency of chromosomal aberrations; higher frequency by pretreatment with diethyldithiocarbamate (an inhibitor of superoxide dismutase), or dimethyl maleate (a glutathione scavenger), or at high oxygen concentrations (Sofuni and Ishidate 1988)
CAT, <i>Felis domesticus</i>	
26–50 mg/kg BW	Acute oral LD50 (Fletcher 1974; Haley 1979; Summers 1980; Heitkamp and Brown 1982; Bauer 1983)
26–50 mg/kg BW	Peak concentration in blood of 13 mg/L (Conning et al. 1969)
HUMAN, <i>Homo sapiens</i>	
Child, 6-year-old, accidentally swallowed unknown amount of Gramoxone W (contains paraquat)	Residue in urine 6 days after exposure was 3.6 mg paraquat/L; death 7 days after onset of symptoms. Autopsy showed ulceration of buccal mucosa, emphysema, severe lung damage, jaundice, and renal failure (Campbell 1968)
Adult male. Died 30 h after swallowing paraquat solution	Histopathology of lung and adrenal gland. Residues, in mg/kg fresh weight, were highest in kidney (17), followed by lung (6), muscle (4.4), liver (3.8), blood (1.4), skin (0.9), and brain (0.4) (Spector et al. 1978)
Ingestion — but not necessarily swallowing — of about 15 mL ("mouthful") of a 20% solution	Fatal dose (Kimbrough 1974)
4–>40 mg/kg BW	Acute oral LD50 (Manzo et al. 1979; Summers 1980)
Ingestion of 30 mg/kg BW	Associated with hepatic, cardiac, or renal failure, and sometimes death (Dasta 1978)
Total ingested dose of 3–6 g	Fatal dose (Haley 1979)
HARE, <i>Lepus</i> sp.	
35 mg/kg BW	Acute oral LD50 (Fletcher 1974)
JAPANESE MONKEY, <i>Macaca fuscata</i>	
Adults, >3.5 year of age, 2 mg/kg BW every 2 days for 8 or 10 days, sc injection	After 4 injections (8 days), 63% died; after 5 injections, 75% died; all deaths occurred between days 11 and 35. At day 66, survivors had elevated lung collagen and increased ceruloplasmin (Masaoka et al. 1987)

Table 22.5 (continued) Paraquat Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects and Reference
MONKEY, <i>Macaca</i> sp.	
50–75 mg/kg BW	Acute oral LD50 in 7 days (Fletcher 1974; Smith and Heath 1976; Heitkamp and Brown 1982; Bauer 1983).
>63 mg/kg BW, oral route	All dead within 2 days; death preceded by convulsions (Murray and Gibson 1972)
PRAIRIE VOLE, <i>Microtus ochrogaster</i>	
56 mg/kg BW; single oral dose	50% dead in 10 days (Linder and Richmond 1990)
60 mg/kg ration	Feed aversion and reduced dietary intake (Linder and Richmond 1990)
MOUSE, <i>Mus musculus</i>	
Fed diets containing 45, 90, or 125 mg/kg ration for two generations	At 45 mg/kg and 90 mg/kg, there was no significant difference from controls in reproductive organ development, fertility, mating behavior, embryotoxicity, or developmental abnormalities; at 125 mg/kg diet, survival was significantly lower, fewer pairs reproduced, and females matured later; second generation mice were more resistant than the first generation (Dial and Dial 1987a)
DOMESTIC MOUSE, <i>Mus</i> spp.	
1.65 or 3.35 mg/kg BW ip injection, or 20 mg/kg BW orally, daily on days 8–16 of gestation	No significant teratogenic effects; low accumulations in embryos (Bus et al. 1975)
Fed diets containing 2, 10, 30, or 100 mg/kg ration for 2 years	Maximum no-effect level was 30 mg/kg diet, equivalent to 3.92 mg/kg BW daily for males and 3.82 mg/kg BW daily for females (Anonymous 1988)
Single ip injection of 8 mg/kg BW on day 9 of pregnancy, or 2 mg/kg BW on day 9, 10, 11, or 12 of pregnancy	No measurable effect on survival, reproduction, birth weight, or chromosomal aberrations; no evidence of mutagenicity to mice liver cells (Selypes et al. 1980)
16–30 mg ion/kg BW	LD50, intraperitoneal injection (Manzo et al. 1979; Selypes et al. 1980; Anonymous 1988)
28 mg ion/kg BW	LD50, subcutaneous injection (Anonymous 1988)
38–120 mg/kg BW	Acute oral LD50 (Fletcher 1974; Haley 1979)
50 or 100 mg/L in drinking water	Low dose had no effect on growth or survival; high-dose group showed increased postnatal mortality after 2 generations (Bauer 1983)
RABBIT, <i>Oryctolagus</i> sp.	
Single iv injection of 0.05 mg/kg BW	Plasma paraquat concentrations, in mg/L, were 0.6 within 2 h, 0.01 at 8 h, and <0.002 at 24 h; estimated half-life (T _b 1/2) of 24.5 h (Yonemitsu 1986)
Single iv injection of 5 mg/kg BW	Plasma paraquat concentrations, in mg/L, were about 30 in 2 h, 1 in 8 h, 0.1 in 24 h, and <0.01 in 48 h; estimated T _b 1/2 of 12.8 h; kidney histopathology evident 7 days after injection but lung damage negligible (Yonemitsu 1986)
Oral administration of 11 mg/kg BW daily for 30 days	No significant toxic signs (Dikshith et al. 1979)
5 ip injected doses totaling 2–100 mg/kg BW	At doses of 25 mg/kg BW and higher, rabbits usually died within 4 days after treatment. No delayed pulmonary changes in rabbit typical of those induced in man and other animals observed in survivors up to 1 month after treatment (Butler and Kleinerman 1971)
20 mg/kg BW, iv injection	Paraquat tended to concentrate in lung; lung histopathology and biochemical upset (Ilett et al. 1974)
24 mg/kg BW, 20 dermal applications	No effect (Anonymous 1974)
49–150 mg/kg BW	Acute oral LD50 (Fletcher 1974; Haley 1979)
Total aerosol dose of 250 mg delivered in 60 min	Significantly increased levels in serum of phospholipids, cholesterol, and triglycerides; reduced growth rate; no evidence of liver or lung damage (Seidenfeld et al. 1984)
346–480 mg/kg BW	Acute dermal LD50 (Anonymous 1974; Haley 1979)

Table 22.5 (continued) Paraquat Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects and Reference
SHEEP, <i>Ovis aries</i>	
Single iv injection of 1, 2, 4, or 8 mg/kg BW	Paraquat was nephrotoxic, producing glomerular and tubular defects in a dose-dependent manner, including inhibited glomerular filtration rates and inhibited paraquat secretion. LD50 (6 weeks) about 1 mg/kg BW. Serum levels 60 min postexposure, in mg paraquat/L, were 0.07 for the 1-mg/kg group, 0.25 for the 2-mg/kg group, 1.23 for the 4-mg/kg group, and 2.05 for the 8-mg/kg group (Webb 1983, 1983a)
50–75 mg/kg BW	Acute oral LD50 (Fletcher 1974; Summers 1980; Heitkamp and Brown 1982)
RAT, <i>Rattus sp.</i>	
0.000116 or 0.000232 µg/kg BW hourly for 7 days, iv infusion, equivalent to a total dose of 0.0465 mg (low dose) or 0.093 mg (high dose)	No adverse effects evident at low dose. At high dose, survivors showed weight loss, histopathology, increased lung glutathione and glucose-6-phosphate dehydrogenase activity — reflecting paraquat-induced oxidant stress and an increased demand on lung NADPH (Dunbar et al. 1988a).
0.0001 or 0.0004 mg/L air, 6-h exposure daily for 3 weeks	No effect at 0.0001 mg/L; pulmonary irritation at 0.0004 mg/L (Haley 1979)
0.001–1.0 mg/kg BW, entire dose in right lung	Dose-dependent lung injury and fibrosis; tissue fibronectin levels remained elevated for at least 14 days after administration (Dubaybo et al. 1987)
0.006 mg/L air for 60 min	LC50; 3-µm particle size most effective (Haley 1979)
0.01 or 0.05 mg, brain injection	Intense pattern of behavioral stimulation, including increased locomotor activity, especially circling, and convulsions; abnormal brain wave patterns (De Gori et al. 1988)
0.0116 mg/kg BW, single dose, various routes	Dose administered by intravenous and intragastric routes cleared rapidly; urine and feces were major excretion routes; Tb 1/2 in blood about 68 min. Dose administered by dermal and pulmonary routes tended to remain at site of injection (Chui et al. 1988)
0.05 mg/kg BW, entire dose in lung	Pulmonary lesions, lung congestion and collapse, edema, hemorrhage, degenerate changes, proliferative fibrosis in lung tissue (Kimbrough and Gaines 1970; Summers 1980).
0.09–9 mg/kg BW, single sc injection	At doses >0.5 mg/kg BW, paraquat produced a dose-dependent avoidance of foods; the ED50 for conditioned taste aversion was 2.4 mg/kg BW (minimum effective dose was 0.78 mg/kg BW); none of these doses produced overt clinical or histological signs of toxicity (Dey et al. 1987)
0.125 or 0.25 mg/kg BW hourly, continuous iv infusion	After 7 days, lungs of high-dose group had elevated putrescine, spermidine, and ornithine decarboxylase activity, reflecting changes in polyamine metabolism; no measurable effects in low-dose group (Dunbar et al. 1988b)
Pregnant dams given 1.5, 4.5, or 13.5 mg/kg BW daily from day 7 to day 17 of gestation	No fetal toxicity or teratogenicity in any group, although maternal survival was low in the 13.5-mg/kg group (Anonymous 1988)
6 mg/kg BW, iv injection	Lung fibrosis (Summers 1980)
Fed diets containing 10, 30, 100, or 300 mg/kg for 2 years	No adverse effects in males at 30 mg/kg diet (1.06 mg/kg BW daily) and lower, or in females at 100 mg/kg diet (4.3 mg/kg BW daily) and lower. Lung histopathology observed in males at 100 mg/kg diet, and in both sexes at 300 mg/kg. At 300 mg/kg diet, clinical signs included reduced growth, reduced food and water intake, abnormal blood chemistry, and increased frequency of cataracts. No conclusive evidence of carcinogenicity (Anonymous 1988)
10 or 30 mg/kg BW, ip injection	At both doses, there was a decrease in calcium uptake by lung microsomes for 3–4 days after injection, followed by recovery during the next 4 days (Agarwal and Coleman 1988)
14–34 mg/kg BW	LD50, ip injection (Haley 1979; Manzo et al. 1979; Anonymous 1988)
16–18 mg/kg BW	LD50, iv injection (Sharp et al. 1972)

Table 22.5 (continued) Paraquat Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects and Reference
18 mg/kg BW, single ip injection	Significant increases in enzymes and compounds responsible for protecting against lipid peroxidation, including catalase, glucose-6 phosphate dehydrogenase, and nonprotein sulfhydryl (Omaye and Reddy 1980)
19–26 mg/kg BW	LD50, sc injection (Haley 1979; Lock 1979; Anonymous 1988)
20 mg/kg BW, iv injection	
Time, after injection	
5 min	Residues were 90 mg/kg in kidney, 30 in plasma, and 10–20 in lung, liver, and muscle (Summers 1980)
4 h	Residues (in mg/kg) were 8 in lung, 6 in kidney, 2 in liver, 0.8 in muscle, and 0.3 in plasma (Summers 1980)
3 days	Lung contained 3 mg/kg, kidney 0.7, muscle 0.5, liver 0.3, and plasma 0.04 (Summers 1980)
10 days	In survivors, muscle contained 0.25 mg/kg, lung 0.1, kidney 0.06, liver 0.03, and plasma 0.01 (Summers 1980)
Fed diets containing 20, 100, or 200 mg/kg ration for 2 generations	Maternal and fetal toxicity in the 200 mg/kg diet group (Anonymous 1988)
21 mg/kg BW	90-dose oral LD50 in females (Kimbrough and Gaines 1970)
27 mg/kg BW, single iv injection	Within 24 h, lung surfactant decreased 32%, suggesting a loss in alveolar stability (Haley 1979)
Adult males	
30 mg/kg BW, single ip injection	No deaths in 72 h; marked reduction of acid and alkaline phosphatase activity in alveolar epithelium of lung (Boudreau and Nadeau 1987)
45 mg/kg BW, ip injection	After 48 h, marked increase in blood glucose, depressed plasma insulin level, marked depletion of liver glycogen, significant increase in plasma creatinine phosphokinase and glutamic oxaloacetic transaminase activity (Giri et al. 1979)
Fed diets containing 50, 120, or 250 mg/kg ration for 8 weeks	No progressive accumulations in tissues. No pulmonary lesions at 50 or 120 mg/kg diet; however, 100% of the 250 mg/kg group had pulmonary lesions (Summers 1980)
Fed 2-year diet containing 70 mg/kg ration	No significant toxicity (Anonymous 1974)
70–90 mg/kg BW	LD50, dermal exposure (Kimbrough and Gaines 1970; Kimbrough 1974; Haley 1979; Anonymous 1988)
95–174 mg/kg BW	Acute oral LD50 (Kimbrough and Gaines 1970; Murray and Gibson 1972; Anonymous 1974, 1988; Kimbrough 1974; Manzo et al. 1979; Heitkamp and Brown 1982; Bauer 1983)
125 mg/kg BW, oral dose	Survivors had decreased kidney glomerular filtration rate within 24 h (Lock 1979)
170 mg/kg diet for 2 years	No measurable adverse effect (Haley 1979)

22.6 RECOMMENDATIONS

Criteria have not yet been promulgated by regulatory agencies for the protection of sensitive species of fish and wildlife against paraquat.

The degradation rate of paraquat in certain soils can be slow, and the compound can persist for years — reportedly in a form that is biologically unavailable. But data are missing or incomplete on flux rates of paraquat from soil into food webs and on interaction dynamics of paraquat with other herbicides frequently applied at the same time. It seems prudent at this time to keep under close surveillance the residues of paraquat in soils in situations where repeated applications have been made over long periods of time (Summers 1980).

In Argentina, paraquat concentrations used to control aquatic weeds is set at 0.1 to 0.2 mg/L, with no more than four applications each year (Tortorelli et al. 1990). However, some aquatic

invertebrates, especially early developmental stages of crustaceans, are unusually sensitive to paraquat. Adverse effects to aquatic invertebrates are documented in the range of 1.0 to 100 µg/L ([Table 22.6](#)). For this reason, paraquat should be used with caution in estuarine and marshy areas (Summers 1980). Fish seem to be “safe” against aquatic weed control concentrations of <1.0 mg paraquat/L (Summers 1980). But aquatic plants tend to accumulate paraquat from the medium; accordingly, more research is needed on the effects of ingestion of contaminated plants and plant detritus by amphibians, reptiles, and other aquatic fauna (Dial and Dial 1987).

Eggs of migratory waterfowl seem to be especially sensitive to paraquat at recommended application rates in an oil vehicle, but were significantly more resistant to the same dose applied in water ([Table 22.6](#)). Application of paraquat in oil solution appears contraindicated in areas containing nesting waterfowl.

Among mammals, one of the most sensitive species is man, and permissible residues in his diet are low when compared to no-observed-effect levels in other warm-blooded species ([Table 22.6](#)). An air concentration of 0.4 mg/m³ may exceed a safe level for certain mammals, particularly if the size of the aerosol particle is submicroscopic and capable of penetrating the lung (Burleigh-Flayer and Alarie 1988). Accordingly, the proposed paraquat aerosol standard — set at 0.5 mg/m³ — may have to be modified downward. Misuse of paraquat has raised the question of cancellation of its registration, cancellation of its use in homes and recreational areas, or changing its packaging to prevent individuals from drinking it (Haley 1979). In almost all cases of fatal human poisonings, death was due to the ingestion of a concentrated (20%) solution. More dilute formulations (5% paraquat) are usually not fatal if swallowed accidentally, suggesting that a dilute form of paraquat should be the only formulation permitted commercially (Kimbrough 1974).

Table 22.6 Proposed Paraquat Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
AQUATIC ORGANISMS		
Adverse effects level, in mg/L		
Algae and Macrophytes		
Freshwater	0.25	1
Marine	5.0	2
Invertebrates		
Most species	0.1	3
Sensitive species	0.001	4
Vertebrates		
Most species	1.0	5, 6
Sensitive species	0.5	7–9
BIRDS		
Adverse effects level		
Egg surface, in mg/kg egg		
Oil solution	0.25	10
Aqueous solution	2.8	10
Oral administration, in mg/kg body weight (BW) daily	10	11, 12
Diet, in mg/kg ration	20	13, 14
Drinking water, in mg/L	40	15
Acute oral dose, in mg/kg BW	199	16
MAMMALS		
No-observable-effect level		
Livestock		
Forage (alfalfa, clover, pasture, and range grasses), in mg/kg	5	17

Table 22.6 (continued) Proposed Paraquat Criteria for the Protection of Natural Resources and Human

Resource, Criterion, and Other Variables	Concentration	Reference ^a
Laboratory rodents		
Diets, in mg/kg ration		
Males	30	18
Females	100	18
Diet, in mg/kg BW daily		
Males	1.1–6.6	18
Females	4.3–7.1	18
Air, in µg/L	0.1	19
Adverse effects level		
Blood, in mg/L		
Guinea pig	5	20
Rat	22	20
Cat	70	20
Lung, in µg directly into lung	6	17
Lung, in mg/kg BW	0.05	4, 21
Diet, in mg/kg ration	85–100	22
Air, in µg/L, particle size range of 2.5–5 microns	0.4–6	17, 23
Drinking water, in mg/L	100	13
Acute oral dose, in mg/kg BW, sensitive species	25–35	4, 13, 15, 17, 18, 24, 25

HUMAN HEALTH

Permissible residues in food items, in mg/kg fresh weight

Eggs, milk, meat, meat by-products of domestic animals	0.01	17
Most fruits and vegetables	0.05	17
Fresh hops	0.1	17
Passion fruit	0.2	17
Almond hulls, cotton seed, beans, hop vines, potatoes, sugar beets, sugarcane	0.5	17
Sunflower seeds	2.0	17
Aerosol standard, in mg/m ³	0.5	26
Acute poisoning level, blood, in mg/L	7.4	20

TERRESTRIAL PLANTS

Safe, Argentina, in L/ha	<4; not to exceed two applications annually	27
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^a 1, Anonymous 1963; 2, Mayer 1987; 3, Brooker and Edwards 1974; 4, Summers 1980; 5, Earnest 1971; 6, Fytizas 1980; 7, Dial and Bauer 1984; 8, Dial and Dial 1987; 9, Simon et al. 1983; 10, Hoffman and Eastin 1982; 11, Hoffman et al. 1985; 12, Hoffman et al. 1987; 13, Bauer 1983; 14, Bauer 1985; 15, Fletcher 1967; 16, Hudson et al. 1984; 17, Haley 1979; 18, Anonymous 1988; 19, Kimbrough 1974; 20, Seto and Shinohara 1987; 21, Kimbrough and Gaines 1970; 22, Anonymous 1974; 23, Conning et al. 1969; 24, Murray and Gibson 1972; 25, Heitkamp and Brown 1982; 26, Burleigh-Flayer and Alarie 1988; 27, Tortorelli et al. 1990.

22.7 SUMMARY

Paraquat (1,1'-dimethyl-4,4'-bipyridinium) and its dichloride salt (1,1'-dimethyl-4,4'-bipyridinium dichloride) are broad-spectrum contact plant killers and herbage desiccants that were introduced commercially during the past 35 years. Today, they rank among the most widely used herbicides globally and are frequently used in combination with other herbicides. The recommended field application rates for terrestrial weed control usually range between 0.28 and 1.12 kg paraquat/ha (0.25 and 1.0 pounds/acre); for aquatic weed control, it is 0.1 to 2.0 mg/L. Target plant species are unable to metabolize paraquat and tend to contain elevated residues; paraquat-resistant

strains of terrestrial flora, whose numbers are increasing, require greater concentrations for control and may contain proportionately greater residues. Paraquat from decayed flora is usually adsorbed to soils and sediments. Paraquat in surface soils generally photodecomposes in several weeks, but paraquat in subsurface soils and sediments may remain bound, and biologically unavailable, for many years without significant degradation.

Paraquat is not significantly accumulated by earthworms and other species of soil invertebrates, and is usually excreted rapidly by higher animals. However, delayed toxic effects — including death of birds and mammals — are common. At concentrations below the recommended application rate, paraquat is embryotoxic to developing eggs of migratory waterfowl (0.056 kg/ha), and adversely affects sensitive species of freshwater algae and macrophytes (250 µg/L), larvae of crustaceans (0.9 to 5.0 µg/L), and frog tadpoles and carp (500 µg/L). Sensitive species of birds are negatively affected at dose rates of 10 mg paraquat/kg body weight daily, or when fed diets containing 20 mg/kg ration, or drinking water containing 40 mg/L. Adverse effects in sensitive mammals were observed at dietary levels of 85 to 100 mg/kg ration and higher, or 100 mg/L in drinking water. Acute oral LD₅₀ values for sensitive species of birds were near 200 mg/kg body weight, and for mammals 22 to 35 mg/kg body weight. Man is one of the more sensitive species, and numerous human poisonings have resulted from accidental or intentional ingestion of a concentrated paraquat formulation.

The biochemical mechanism of paraquat toxicity is due to the cyclic oxidation and reduction in tissues, leading to production of superoxide anion and other free radicals, and eventually the highly destructive hydrogen peroxide. The lung is the organ most severely affected in paraquat poisoning, due largely to the preferential accumulation of paraquat in lung alveolar cells. Although many organs are affected by paraquat, death is usually due to progressive pulmonary fibrosis. At present, there is no completely successful treatment for paraquat-induced lung toxicity.

More information is needed in several areas in order to establish effective criteria for the protection of sensitive species of fish and wildlife against paraquat. These include:

- Flux rates of paraquat from soil into terrestrial food chains
- Biomagnification potential of paraquat in aquatic food chains, with special reference to plants, plant detritus, amphibians, and reptiles
- Toxicokinetics of mixtures of paraquat and other herbicides applied concomitantly
- The implications of the high sensitivities of crustacean larvae and waterfowl embryos to paraquat

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CHAPTER 23

Pentachlorophenol

23.1 INTRODUCTION

Pentachlorophenol (PCP) and its water-soluble salt, sodium pentachlorophenate, are commercially produced organochlorine compounds used primarily as preservatives of wood and wood products, and secondarily as herbicides, insecticides, fungicides, molluscicides, and bactericides (U.S. Environmental Protection Agency [USEPA] 1980; Prescott et al. 1982; U.S. Public Health Service [USPHS] 1994). Both compounds have been sold for these purposes since 1936 under a variety of trade names (Knudson et al. 1974). Because of its widespread use, animals and humans are exposed to significant amounts of PCP. Detectable PCP levels are found in most people living in industrialized societies, probably as a result of food chain exposure to PCP-treated wood products (Dougherty 1978; McConnell et al. 1980; Prescott et al. 1982). In Japan, PCP has been widely used as an herbicide in rice fields; but owing to its high toxicity to fishes, its use was limited (beginning in 1971) to upland fields (Nishimura 1984; Mikesell and Boyd 1986). The use of PCP in Japan has resulted in the contamination of all surface water in that country to concentrations of 0.01 to 0.1 µg/L (Lu et al. 1978). The chemical and its degradation products bioconcentrate in fish and are among the phenolic compounds known to taint fish flesh (Boyle et al. 1980). It has been detected in the atmosphere over industrial as well as remote areas, lake sediments, aquatic biota, drinking water, and human blood and urine (Schimmel et al. 1978; Klemmer et al. 1980; Trujillo et al. 1982; Larsson et al. 1993). All samples of human milk from nursing mothers tested in Bavaria from 1979 to 1981 contained PCP (Gebefugi and Korte 1983). In the United States between 1976 and 1980, PCP was present in the urine of 71.6% of the general population, suggesting that almost 112 million individuals age 12 to 74 years had been exposed to PCP (Kutz et al. 1992).

In humans, illnesses and deaths have been reported after exposure to PCP through diet or by direct contact with PCP-treated products (Prescott et al. 1982). For example, 20 of 80 infants who wore, for 8 days, diapers rinsed in an antimicrobial laundry neutralizer containing sodium pentachlorophenate developed enlarged livers and spleens, had high fevers, and sweated profusely. Although most recovered spontaneously, seven died (Knudsen et al. 1974; USEPA 1980). At least 24 industrial PCP fatalities have been reported. The first deaths occurred at a wood preservative plant in France in 1952. Others were recorded at a chemical factory in Japan in 1953, during herbicide spraying in Australia in 1956, at a sawmill in Indonesia in 1958, in South Africa in 1961, and in Canada and the United States in 1965 (Wood et al. 1983). The acute toxic action of PCP in humans and experimental animals is caused by the uncoupling of oxidative phosphorylation mechanisms, resulting in marked increases in metabolism (Murphy 1986).

Data are scarce on PCP effects on wildlife, although it is speculated that no wildlife losses should occur under normal PCP application conditions and that chronic toxicity would not be serious because PCP is rapidly excreted (Bevenue and Beckman 1967). However, mortality was

heavy in two species of bats that came into contact with PCP-treated timbers up to 14 months after treatment (Leeuwangh and Voute 1985; Racey and Swift 1986). Wood preservatives, including PCP, are implicated in the decline of the bat population in the United Kingdom (Chadwick and Reston 1993). Furthermore, evidence accumulating on the harmful effects of PCP to domestic animals suggests that the chemical may have considerable adverse effects on other species of wildlife. In the poultry industry, for example, PCP has been implicated in the cause of musty taint in chicken meat and eggs and in increased morbidity in chickens housed on PCP-contaminated wood shavings or given PCP-contaminated food (Prescott et al. 1982).

Pentachlorophenol is repellent to animals. Diets containing PCP have been rejected by rats, cats, and cattle (Bevenue and Beckman 1967). In farm animals, PCP intoxication has increased as a result of confinement in buildings recently treated with a PCP wood preservative, and through dermal contact with PCP-treated fences and feed bunks (Osweiler et al. 1984). Dairy cattle contaminated by PCP produced less milk, grew poorly, and developed skin lesions (Firestone et al. 1979; Greichus et al. 1979; Parker et al. 1980). The issue is confounded by the presence of various amounts of toxic impurities — primarily dioxins and dibenzofurans — in technical and commercial preparations of PCP. These contaminants are mainly responsible for its observed toxicity in rabbits, rats, pigs, cattle, and chickens (Dougherty 1978; McConnell et al. 1980; Prescott et al. 1982). In one example in 1957, millions of chickens died in the southeastern United States after eating poultry feeds containing fat from hides preserved with PCP. Nine dioxins were detected in the toxic animal fat, including the potent 1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin isomer (Parker et al. 1980; Stedman et al. 1980; Prescott et al. 1982).

Useful reviews on the ecological and toxicological aspects of PCP have been published by Bevenue and Beckman (1967), Cote (1972), Rao (1978), USEPA (1980, 1986), Williams (1982), Choudhury et al. (1986), World Health Organization [WHO] (1987), Eisler (1989), and USPHS (1992, 1994).

23.2 ENVIRONMENTAL CHEMISTRY

23.2.1 General

Pentachlorophenol and its water-soluble salt, sodium pentachlorophenate, are used extensively in agriculture and industry. Most — about 80% — of the 50 million kg PCP manufactured each year is used in the protection and preservation of wood products. Commercial samples of technical-grade PCP are heavily contaminated with many compounds, including chlorophenols, dioxins, dibenzofurans, hexachlorobenzene, and phenoxyphenols. The relative toxicities and accumulation potentials of some of these contaminants may exceed those of PCP by several orders of magnitude. Pentachlorophenol interferes with the production of high-energy phosphate compounds essential for cell respiration. In general, it readily degrades in the environment by photochemical, chemical, and microbiological processes.

23.2.2 Sources and Uses

In the United States, PCP is one of the most heavily used compounds and is found in all environmental media as a result of its past widespread use. In addition, a number of other chemicals are known to be metabolized to PCP, including hexachlorobenzene, pentachlorobenzene, and benzenehexachloride isomers (Rugman and Cosstick 1990; van Raaij et al. 1991b; USPHS 1994). Although PCP was first synthesized in 1841, it was not produced commercially until 1936 (Wood et al. 1983; Menzer and Nelson 1986). It has since been registered for use as an insecticide, fungicide, herbicide, algicide, and disinfectant, and as an ingredient in antifouling paint; at least

578 products contain PCP (Cote 1972; Cirelli 1978; Choudhury et al. 1986; Murphy 1986). By 1967, PCP and its sodium salt, sodium pentachlorophenate (Na-PCP), were used extensively in industry and agriculture, due in large part to the solubility of PCP in organic solvents and of Na-PCP in water (Bevenue and Beckman 1967; Cirelli 1978). The major commercial application of technical-grade preparations of PCP is in wood preservation formulations, where its fungicidal and bactericidal actions inhibit the growth of wood-destroying organisms (Kinzell et al. 1981; USPHS 1994).

In the United States, about 80% of the 23 million kg of technical PCP produced annually — or about 46% of worldwide production — is used mainly for wood preservation, especially utility poles (Pignatello et al. 1983; Kinzell et al. 1985; Zischke et al. 1985; Choudhury et al. 1986; Mikesell and Boyd 1986; USPHS 1994). It is the third most heavily used pesticide, preceded only by the herbicides atrazine and alachlor (Kinzell et al. 1981). Pentachlorophenol is a restricted-use pesticide and is no longer available for home use (USPHS 1994). Before it became a restricted-use pesticide, annual environmental releases of PCP from production and use were 0.6 million kg to the atmosphere from wood preservation plants and cooling towers, 0.9 million kg to land from wood preservation use, and 17,000 kg to aquatic ecosystems in runoff waters of wood treatment plants (USPHS 1994). There are about 470 wood preservative facilities in the United States, scattered among 45 states. They are concentrated in the South, Southeast, and Northwest — presumably due to the availability of preferred timber species in those regions (Cirelli 1978). Livestock facilities are often constructed of wood treated with technical PCP; about 50% of all dairy farms in Michigan used PCP-treated wood in the construction of various components of livestock facilities (Kinzell et al. 1985). The chemical is usually applied to wood products after dilution to 5% with solvents such as mineral spirits, No. 2 fuel oil, or kerosene. More than 98% of all wood processed is treated with preservative under pressure; about 0.23 kg of PCP is needed to preserve 1 cubic foot of wood (Cirelli 1978). Lumber treated with PCP retains its natural appearance, has little or no odor, and can be painted as readily as natural wood (Wood et al. 1983).

In addition to its extensive use by the construction and lumber industries to control damage by mold, termites, powder post beetles, and wood-boring insects (Bevenue and Beckman 1967), PCP has been used as a bactericide and fungicide to protect many products, such as adhesives, paper and paperboard, cable coverings, leather, paints, textiles, rope, ink, rubber, and petroleum drilling muds (Bevenue and Beckman 1967; Firestone et al. 1979; Williams 1982). It has been used to control algae and fungi in cooling towers at electric plants (Williams 1982). It has also been added to fabrics for moth-proofing, although derivatives such as pentachlorophenol laurate are more widely used for this purpose because their resistance to dry cleaning and washing exceeds that of PCP, and their toxicity to mammals is lower (Bevenue and Beckman 1967). It has been applied in agriculture and around industrial sites as an herbicide and preharvest desiccant, on pastureland, and in pineapple, rice, and sugarcane fields (Bevenue and Beckman 1967). A Japanese manufacturer added PCP to soy sauce — in violation of the law — as a preservative (Bevenue and Beckman 1967). It has also been used as a bird repellent: PCP discourages woodpeckers when it is mixed as a pellet and plugged into holes drilled by the bird (Cirelli 1978).

In Canada, the main use of PCP is in the protection and preservation of wood, and secondarily as an herbicide and insecticide for agricultural purposes. A total of 50 wood preserving plants — mostly in British Columbia, Alberta, and Ontario — used about 2.7 million kg PCP in 1978 (Hoos 1978). Treatment with PCP significantly increased the life of timbers, construction lumber, telephone poles, and railway ties. For example, jackpine poles treated with PCP lasted at least 35 years, compared to 7 years for untreated poles (Hoos 1978). Sodium pentachlorophenate has been used to control schistosomiasis by eliminating snails that are intermediate hosts of human schistosomes (Bevenue and Beckman 1967). It is also used as a fungicide, bactericide, and algicide in construction materials, emulsion polymers, paints, textiles, and finished paper products; as a preservative for ammonium alginate; and at concentrations of 15 to 40 mg/L, to control microbial growth in secondary oil recovery (Bevenue and Beckman 1967; Cirelli 1978).

23.2.3 Properties

Pentachlorophenol is readily soluble in most organic solvents, oils, and highly aromatic and olefinic petroleum hydrocarbons — a property that makes it compatible for inclusion in many pesticide formulations (Table 23.1; Figure 23.1). Purified PCP, however, is practically insoluble in water; therefore, the readily water-soluble sodium pentachlorophenate salt is substituted in many industrial applications (Table 23.1) (Beveneu and Beckman 1967; USPHS 1994).

The solubility of sodium and potassium pentachlorophenolate in water is pH dependent; it increases from 79 mg/L at pH 5.0 to >4 g/L at pH 8.0 (Beveneu and Beckman 1967). But the differential toxicity of PCP in solution is primarily attributable to variations in uptake as a function

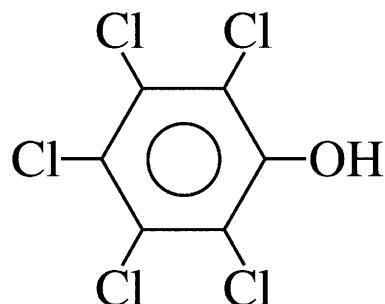


Figure 23.1 Structural formula of pentachlorophenol.

Table 23.1 Chemical and Other Properties of Pentachlorophenol

Variable	Datum
Chemical name	Pentachlorophenol
CAS Number	87-86-5
Alternate names	Chem-Penta, Chemtrol, Chlorophen, Dow Pentachlorophenol, Dowicide 7, Dowicide EC-7, Dowicide G, DP-2, Durotox, Lauxtol A, Ontrack WE-1, PCP, Penchlorol, Penta, 2,3,4,5,6-pentachlorophenol, Penta General Weed Killer, Petacon, Penta-kil, Pentanol, Pentasol, Penwar, Permacide, Permaguard, Permasem, Permatox, Prilox, Santobrite, Santophen, Sinituho, Term-I-trol, Weed-Beads, Weedone
Primary uses	Wood preservative, preharvest defoliant, herbicide, molluscicide, insecticide, fungicide
Producers	Dow Chemical Company, Monsanto Company, Reichold Chemical Company, Vulcan Materials Company
Empirical formula	C_6Cl_5OH
Physical state	White solid with needle-like crystals. Produced by chlorination of molten phenol. Technical-grade material is dark gray to brown
Molecular weight	266.35
Melting point	190–191°C
Boiling point	309–310°C (decomposes)
Specific gravity	1.978 g/mL at 22°C
Vapor pressure	
25°C	0.0016 mmHg
100°C	0.02 mmHg
211°C	40.0 mmHg
Solubility	
Water	
0°C	5 mg/L
20°C	14 mg/L
30°C	20 mg/L
50°C	35 mg/L
Carbon tetrachloride	20–30 g/L
Benzene	110–140 g/L
Ethanol	470–520 g/L
Methanol	570–650 g/L
Solubility of sodium salt (sodium pentachlorophenate, CAS 131–52-2) in water at 25°C	330 g/L
Log K_{ow} (octanol/water partition coefficient)	5.01–5.12

Data from Beveneu and Beckman 1967; Cote 1972; Cirelli 1978; USEPA 1980; Williams 1982; Hudson et al. 1984; Choudhury et al. 1986; Hill and Camardese 1986; Mayer 1987; USPHS 1994.

of pH (Jayaweera et al. 1982; Kaiser and Valdmanis 1982; Fisher and Wadleigh 1986; Smith et al. 1987), and not to water solubility. At pH 4.0, for example, PCP is fully protonated and therefore highly lipophilic, and has its greatest accumulation potential. Conversely, PCP is completely ionized at pH 9.0; lipophilicity is markedly reduced, as is its toxicity to the alga *Selenastrum capricornutum* (Jayaweera et al. 1982; Smith et al. 1987) and the midge *Chironomus riparius* (Fisher and Wadleigh 1986).

In recent years, it has become clear that many commercial samples of technical-grade PCP are heavily contaminated with a large number of potentially toxic compounds and materials (Figure 23.2) (Table 23.2). These contaminants include, in part, various isomers of chlorophenols, dibenzofurans, dioxins, hexachlorobenzene, and phenoxyphenols (Table 23.2), as well as various chlorinated diphenyl ethers, dihydroxybiphenyls, anisoles, catechols, guaiacols, and other chlorinated dibenzodioxin and dibenzofuran isomers (Kaufman 1978; Nilsson et al. 1978; Firestone et al. 1979; USEPA 1980; Singh et al. 1985; Menzer and Nelson 1986; Mikesell and Boyd 1986; Murphy 1986; Holsapple et al. 1987). In relative toxicity and accumulation potential, some contaminants in technical-grade PCP may exceed the parent compound by several orders of magnitude (Huckins and Petty 1981). For example, some isomers of hexachlorodibenzodioxin, which are present in technical-grade PCP at concentrations of 1000 to 17,300 µg/kg (Table 23.2), produce LD₅₀ values in guinea pigs of 60 to 100 µg/kg body weight — thus ranking them as extremely toxic chemicals (Eisler 1986; Murphy 1986).

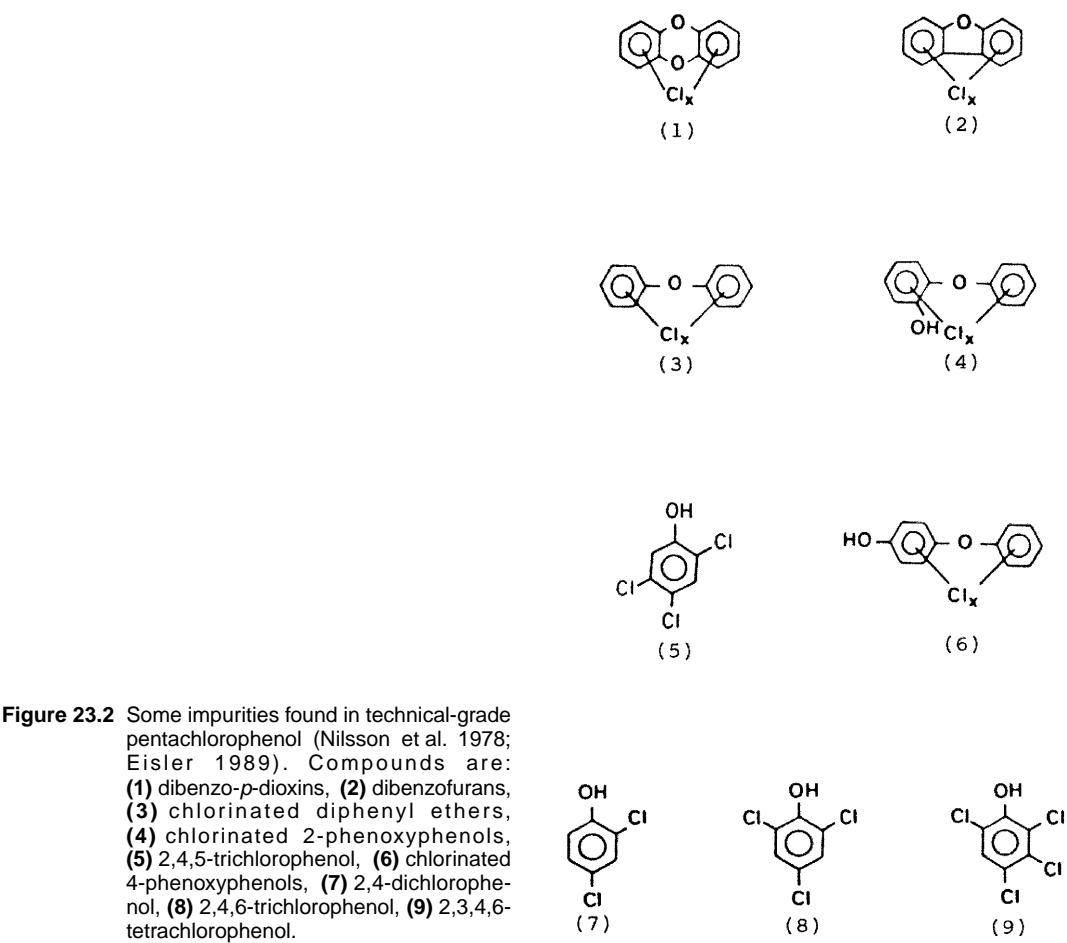


Table 23.2 Partial List of Contaminants Detected in Technical-Grade and Purified Pentachlorophenol (All values are in mg contaminant/kg product [ppm].)

Contaminant	Grade and Concentration (% PCP)			Reference
	Technical 85–90%	Purified >99%		
CHLOROPHENOLS				
Trichlorophenols ^b	1000	—	—	1
Tetrachlorophenols				
2,3,4,6-tetrachlorophenol	49,000	0.25	—	2, 3
2,3,4,5-tetrachlorophenol	9000	0.073	—	2, 3
Total	40,000–80,000	500	—	1, 4
Other chlorophenols ^b	20,000–60,000	—	—	1, 4
DIBENZOFURANS				
Pentachlorodibenzofurans ^b	40	—	—	5
Hexachlorodibenzofurans ^b	90	—	—	5
Heptachlorodibenzofurans ^b	400	—	—	5
Octachlorodibenzofurans ^b	29–260	—	—	5, 6
DIOXINS				
Total	1900–2625	<7	—	7
Tetrachlorodioxins ^b	0.035–0.12	—	—	1, 5
Pentachlorodioxins ^b	0.03	—	—	5
Hexachlorodioxins ^b	1–173	0.00001	—	1–5, 8
Heptachlordioxins ^b	119–1000	1.8	—	1, 5, 6, 8
Octachlorodioxins ^b	40–4700	0.0002–3.0	—	1–6, 8
HEXAChLOROBENZENE	56–270	0.0014	—	2, 3, 6
PHENOXYPHENOLS				
Heptachlorophenoxyphenols ^b	1200	4.8	—	6
Octachlorophenoxyphenols ^b	28,000	300	—	6
Nonachlorophenoxyphenols ^b	15,000	500	—	6

^a 1, Shull et al. 1986; 2, Zischke et al. 1985; 3, Pignatello et al. 1983; 4, Lamparski et al. 1980; 5, Williams 1982; 6, Cleveland et al. 1982; 7, Eisler 1986; 8, Singh et al. 1985.

^b Total, when not indicated otherwise.

23.2.4 Fate

Pentachlorophenol can be absorbed into the body through inhalation, diet, or skin contact (Bevenue and Beckman 1967; Williams 1982; Gray et al. 1985). PCP residues in blood serum, adipose tissue, and urine are useful biomarkers of PCP exposure (USPHS 1994). Its acute toxicity results from its ability to interfere with the production of high-energy phosphate compounds essential for cell respiration. This interference, or uncoupling, causes stimulation of the cell's metabolism to the toxic stage, which is accompanied by fever and other signs of stress (Bevenue and Beckman 1967; Hodson and Blunt 1981; Williams 1982; USPHS 1994). The metabolic consequences resemble those of vigorous exercise in some species (Hodson and Blunt 1981). In addition to the proven uncoupling effects on oxidative phosphorylation, the overall inhibitory effects on a variety of enzymes, metabolism of lipids and carbohydrates, ion transport, and protein synthesis may account for the broad-spectrum biocidal effects of PCP and its salts (Rao et al. 1979; Gray et al. 1985; Smith et al. 1987; Renner and Hopfer 1991).

Pentachlorophenol is fetotoxic and teratogenic during early gestation; however, evidence of its mutagenic or carcinogenic properties is incomplete (Williams 1982). PCP is not mutagenic in bacteria or *Drosophila*, but positive mutagenicity was reported in yeast and in mice, indicating a need for additional research (USPHS 1994). Tetrachlorohydroquinone (TCHQ), a major metabolite of PCP, can induce mutations in Chinese hamster cells through formation of reactive oxygen species (Jansson and Jansson 1991). PCP was carcinogenic in the B6C3F1 mouse strain (Reigner et al. 1992b). Purified PCP fed to mice in chronic dietary studies was carcinogenic (USPHS 1994). Human case histories suggest a possible association with occupational exposure to technical PCP and cancer — including Hodgkin's disease, soft tissue sarcoma, acute leukemia — but no convincing epidemiological evidence exists to indicate that inhalation of PCP in any form produces cancer in humans. Nevertheless, the International Agency for Research on Cancer has assigned pentachlorophenol a Group 2B classification, indicating that PCP is possibly carcinogenic in humans (USPHS 1994).

Pentachlorophenol readily degrades in the environment by chemical, microbiological, and photochemical processes (Kaufman 1978; Choudhury et al. 1986; Seech et al. 1991; Rutgers et al. 1998). Its suggested metabolic fates include oxidation and dechlorination to tri- and tetrachloro-*p*-hydroquinones, and glucuronide conjugation to PCP- and tetrachloro-*p*-hydroquinone conjugates (Williams 1982; Stehly and Hayton 1988; Renner and Hopfer 1990; Reigner et al. 1991, 1992a). In soils, reductive dehalogenation appears to be the most significant PCP degradation pathway, producing mono-, di-, tri-, and tetrachlorophenols, as well as various tetrachlorocatechols and tetrachlorohydroquinones. Further degradation results in ring cleavage, liberation of chloride, and carbon dioxide evolution; degradation is more rapid in flooded or anaerobic soils than in aerobic moist soils (Kaufman 1978). Irradiation of PCP solutions with sunlight or ultraviolet light produces photodegradation products that include chlorinated phenols, tetrachlorodihydroxyl benzenes, and nonaromatic fragments such as dichloromaleic acid (Wong and Crosby 1978; USEPA 1980). Subsequent irradiation of the tetrachlorodiols produces hydroxylated trichlorobenzoquinones, trichlorodiols, dichloromaleic acid, and nonaromatic fragments (Wong and Crosby 1978; Boyle et al. 1980). Prolonged irradiation of PCP or its degradation products yielded colorless solutions containing no ether-extractable volatile materials; evaporation of the aqueous layer left no observable polymeric residue (Wong and Crosby 1978). Photolytic condensation of PCP to form octachlorodioxins was observed on a wood substrate. Octachlorodioxin residues ranged from 4 mg/kg for purified PCP, to about 1500 mg/kg for technical-grade PCP (Lamparski et al. 1980).

Pentachlorophenol can be degraded by microbial flora, both aerobically and anaerobically. Degradation is more rapid under aerobic conditions but slows significantly at temperatures <19°C (Pignatello et al. 1985, 1986). Several strains of aerobic bacteria can metabolize and degrade PCP: *Flavobacterium* sp., a pseudomonad, a coryneform bacterium, and a strain of *Arthrobacter* (Pignatello et al. 1983; Mikesell and Boyd 1986; Steiert and Crawford 1986; Steiert et al. 1987; Seech et al. 1991; Rutgers et al. 1998). Microbial degradation under aerobic or anaerobic conditions was the major process by which PCP was degraded in estuarine sediments; tidal transport and photodegradation played minor roles (DeLaune et al. 1983). The biotic process requires a moderately long adaptive response by the aquatic microflora, but eventually becomes the predominant mechanism of PCP removal (Pignatello et al. 1983, 1985). Several significant observations were recorded when the degradation and transformation of PCP were documented in freshwater streams continuously dosed with PCP for 16 weeks (Pignatello et al. 1983):

- Photolysis accounted for a 5 to 28% decline in initial PCP concentrations and was most rapid at the water surface under conditions of bright sunlight
- Adsorption to sediments and uptake by biota accounted for less than 5% loss in acclimated waters and probably less than 15% in unacclimatized waters
- Microbial degradation of PCP became significant about 3 weeks after dosing and eventually became the primary mechanism of PCP removal, accounting for up to a 46% decline in initial PCP.

A Gram-negative bacterium, *Pseudomonas* sp. strain SR3, can degrade PCP from 39 to 40 mg PCP/L (a concentration lethal to many species of aquatic organisms) to a nonlethal 0.0006 mg PCP/L within 5 days (Middaugh et al. 1993). However, biodegraded PCP may still be environmentally hazardous. Bioassays with embryonic inland silversides (*Menidia beryllina*) showed that the bio-degraded PCP samples were embryotoxic or teratogenic, suggesting that toxic intermediate metabolites were present (Middaugh et al. 1993).

The half-life (T_b 1/2) of PCP in water ranged from 0.15 to 1.5 days; degradation was most rapid under conditions of high incident radiation, high dissolved oxygen, and elevated pH (Bevene and Beckman 1967; Wong and Crosby 1978; Boyle et al. 1980; Niimi and Cho 1983; Crossland and Wolff 1985; Smith et al. 1987). The T_b 1/2 in the water column controlled by microbial degradation alone is usually 5 to 12 h (Pignatello et al. 1986). Pentachlorophenol solutions in water at the appropriate pH and dissolved oxygen content decompose in sunlight, and this makes a strong case for the likelihood of essentially total PCP destruction in aquatic environments (Wong and Crosby 1978). The short residence time of PCP in an aquatic system before degradation further suggests that biological effects would be most pronounced in localized areas that continuously receive PCP from a point source (Niimi and Cho 1983). Technical-grade PCP was initially degraded at the same rate as reagent-grade PCP by anaerobic microorganisms in municipal sewage sludge, but was later degraded more slowly. Dechlorination and mineralization (to carbon dioxide and methane) of the reagent-grade PCP was complete in 7 to 9 days, but only half the technical-grade PCP had been transformed in 6 to 10 days (Mikesell and Boyd 1986). At nontoxic concentrations, PCP was readily biodegradable in activated sludge after an adaptation period of 10 to 20 days. Preexposure of activated sludge to PCP drastically eliminated the acclimatization period and increased the tolerance of the sludge to PCP toxicity (Ingerslev et al. 1998).

In soils, PCP persisted for 15 to more than 60 days, depending on soil conditions and application rate. At initial concentrations of 100 mg PCP/kg soil, the T_b 1/2 was 10 to 40 days at 30°C under flooded conditions. However, in aerobic soils there was virtually no degradation after 2 months (Kaufman 1978). In rice paddy soils, initial concentrations of 4 mg PCP/kg fell to 2 mg/kg in 7 days (Bevene and Beckman 1967). Pentachlorophenol was still measurable after 12 months in warm, moist soils (Cote 1972; USEPA 1980). In estuarine sediments, degradation was most rapid under conditions of increased oxygen and a pH of 8.0 (DeLaune et al. 1983).

A variety of analytical techniques are used to measure PCP, including gas chromatography–mass spectrometry (GC–MS), which has a detection limit of 7.6 µg/kg honey (Muino and Luzano 1991), liquid chromatography with fluorescence detection (de Ruiter et al. 1990), and liquid chromatography–electrochemistry (LC–ED) procedures (Butler and Pont 1992). At present, GC–MS is the most accurate, but LC–ED is used most frequently (Butler and Pont 1992).

23.3 CONCENTRATIONS IN FIELD COLLECTIONS

23.3.1 General

Measurable PCP concentrations in field collections of living and nonliving materials over widespread geographic areas are almost certainly due to anthropogenic activities, especially to the use of the chemical as a wood preservative.

23.3.2 Biological and Nonbiological Samples

Pentachlorophenol-contaminated air, rain, snow, surface waters, drinking waters, groundwaters, and aquatic biota are common in the United States (Table 23.3) (Pignatello et al. 1983; Choudhury et al. 1986). Residues of PCP in food, water, and mammalian tissues may result from the direct use of PCP as a wood preservative and pesticide, or as a result of the use of other chemicals that

form PCP as degradation products (i.e., hexachlorobenzene and lindane) (USEPA 1980; Choudhury et al. 1986). To confound matters, PCP was judged to be the source of dioxin and dibenzofuran contamination in chickens in Canada (Ryan et al. 1985). More than 50% of all chickens sampled contained hexachlorinated dibenzo-*p*-dioxins (hexa-CDDs) at concentrations of 27 ng/kg fat and higher; 62% contained hepta-CDDs at more than 52 ng/kg, and 46% contained octa-CDDs at more than 90 ng/kg; concentrations of hexa- and heptachlorinated dibenzofurans were similar.

Pentachlorophenol was found at high concentrations in all samples of sediments, waters, and biota collected near industrial facilities that used PCP as a wood preservative (Niimi and Cho 1983; Oikari and Kukkonen 1988) (Table 23.3). Fish can bioconcentrate PCP from water up to 10,000 times (Fox and Joshi 1984). However, similar concentrations were measured in blue mussel, *Mytilus edulis* (Folke and Birklund 1986), and softshell clam, *Mya arenaria* (Butte et al. 1985), from the vicinity of PCP-contaminated wastewater discharges as well as from more distant collection sites. Thus, PCP bioaccumulation in marine bivalve molluscs does not appear to be dose related.

Pentachlorophenol in terrestrial ecosystems clears rapidly (Haque et al. 1988). In one case, a terrestrial ecosystem was given a single surface application of radiolabeled PCP equivalent to 5 kg sodium pentachlorophenate/ha. PCP residues on foliage decreased rapidly, with 50% metabolized within 15 days. After 131 days (autumn), most of the remaining PCP was in the topsoil and plant litter. After 222 days (winter), 39% of the radiocarbon remained. There was little bioconcentration in the resident fauna, due to rapid metabolism and excretion (Haque et al. 1988).

There are differences between the United States, Germany, and the United Kingdom in human intake and absorption of PCP. In the United Kingdom, the typical nonoccupationally exposed individual has a total daily intake of 5.7 µg PCP, of which 4.5 µg is absorbed (Wild and Jones 1992). Most of the PCP (92%) comes from the diet, 1% via inhalation, and the rest from drinking water. Occupationally-exposed individuals in the U.K. absorb 21.2 µg daily from an intake of 39 µg daily; most of the PCP (78.8%) in this group is via inhalation and only 19.6% from the diet (Wild and Jones 1992). In Germany, the main route of PCP uptake by nonoccupationally exposed humans is by ingestion of contaminated food, including drinking water, fish, sugar, pork, chicken, and other foodstuffs (Geyer et al. 1987). The chickens and pigs were contaminated by PCP because they were reared on PCP-treated wooden floors. The average German diet contains 13.9 (2.7 to 27.6) µg PCP/kg ration. The total amount of PCP in an average nonoccupationally exposed German citizen (weight 65 kg, age 45 years) is about 532 µg: 204 µg in body fat, 143 µg in liver, 103 µg in blood, 63 µg in brain, 14 µg in kidneys, 4 µg in spleen, and about 1.6 µg in urine in bladder (Geyer et al. 1987). In the United States, it was estimated that the long-term average daily intake of PCP by humans is 16 µg (Hattemer-Frey and Travis 1989), and this is in good agreement with the value of Geyer (1987). However, the source of PCP in that study was attributed almost exclusively (99.9%) to fruits, vegetables, grains, and other crops grown in PCP-contaminated soils. PCP concentrations in U.S. citizens were usually higher in adipose tissues than in nonfatty tissues, and between the ages of 22 and 75 will increase by a factor of at least 2 (Wagner et al. 1991).

Table 23.3 Pentachlorophenol Concentrations in Nonbiological and Living Materials

Compartment and Units	Concentration	Reference ^a
NONBIOLOGICAL		
Aquatic (µg/L)		
Rivers, Southwest Japan	1–10	1
Willamette River, Oregon	0.1–0.7	1
Waters of British Columbia	Up to 7.3	1
Drinking water	0.06	2, 3
Northern California		
Moss Landing, seawater	<1	4
Sacramento, sewage discharge	<1	4

Table 23.3 (continued) Pentachlorophenol Concentrations in Nonbiological and Living Materials

Compartment and Units	Concentration	Reference^a
Oroville		
Drainage water	20	4
Drinking water	227 (1–800)	4
Surface water	0.7	3
Near wood preserving facility, Bay of Quinte, Lake Ontario, 1978		
Surface film	5.8	5
Water column	5.7	5
Air (ng/m ³)		
Uninhabited mountainous area	~0.25	6
Rooms containing PCP-treated wood or paint	Up to 160	6
Near PCP wood preservative facility	Usually 263–1188; Max. 297,000	2
PCP pressure treating room	Max. 15,000	2
PCP storage areas	9–9000	2
Sediments (µg/kg dry weight)		
Bay of Quinte, Lake Ontario, 1978	60	5
BIOLOGICAL		
Freshwater organisms (µg/kg fresh weight)		
Lake Ontario, western basin		
Fish, whole less intestine		
Rainbow trout, <i>Oncorhynchus mykiss</i>	24 (10–39)	7
Lake trout, <i>Salvelinus namaycush</i>	Max. 11	7
Coho salmon, <i>Oncorhynchus kisutch</i>	Max. 21	7
Brown trout, <i>Salmo trutta</i>	6, Max. 11	7
Rainbow smelt, <i>Osmerus mordax</i>	Max. 0.5	7
Alewife, <i>Alosa pseudoharengus</i>	Max. 0.3	7
Bay of Quinte, Lake Ontario, 1978		
Fish, whole		
Brown bullhead, <i>Ictalurus nebulosus</i>	260	5
Yellow perch, <i>Perca flavescens</i>	155	5
Invertebrates		
Annelids	Max. 85	5
Chironomids	Max. 1	5
Alga		
<i>Cladophora</i> sp.	7	5
Sweden, 1990; northern pike, <i>Esox lucius</i> ; whole		
Acidified lake (pH 5.2–6.3)		
Fresh weight	3.9 (2.1–8.7)	13
Lipid weight	201–799	13
Nonacidified lake (pH 8.1)		
Fresh weight	2.2 (1.5–3.2)	13
Lipid weight	114–346	13
Marine organisms (µg/kg)		
Blue mussel, <i>Mytilus edulis</i> , Denmark, 1985, soft parts		
Fresh weight	5–33	8
Dry weight	32–244	8
Lipid weight	398–3473	8
Wildlife (mg/kg whole mummified body)		
Dutch pond bat, <i>Myotis dasycneme</i> , Netherlands, found dead		
Berlikum roost (treated with PCP)		
1974	8–36	9
1977	410–795	9
1978	746–1105	9
1979	10–283	9
Tjerkwerd roost (Control site)		
1978	<7	9
1979	<4	9

Table 23.3 (continued) Pentachlorophenol Concentrations in Nonbiological and Living Materials

Compartment and Units	Concentration	Reference^a
Livestock, Canada ($\mu\text{g}/\text{kg}$)		
Fat, chicken and pork		
Lipid weight	Usually (60% frequency) >10	10
Liver, pig		
Fresh weight	Always >50	10
Human, <i>Homo sapiens</i>		
Net daily intake; μg ; 8 countries		
Nonexposed individuals	5–37	20
Residents of homes made of PCP-treated logs	51–157	20
Occupationally exposed to PCP	35–24,000	20
Barcelona, Spain; 1985–86; $\mu\text{g}/\text{L}$; 100% frequency of detection		
Serum	21.9 (2.5–116.5)	18
Urine	25.0 (4–136)	18
Western Oregon; autopsied males; mg/kg lipid weight		
Liver	0.59; Max. 1.5	15
Prostate gland	0.84; Max. 1.6	15
Kidney	0.95; Max. 3.3	15
Testes	1.1; Max. 4.2	15
Germany, $\mu\text{g}/\text{kg}$ fresh weight		
Liver	79	15
Kidney, Brain	45	15
Blood, Spleen	19	15
Adipose tissue	14	15
Unexposed ($\mu\text{g}/\text{kg}$ fresh weight)		
Urine	2–11	2, 11, 14
Blood serum	4–10	2, 11
Adipose tissue	12–52	11
Milk, nursing mothers, Bavaria, 1979–81	0.67 (0.03–2.8)	10
Exposed ($\mu\text{g}/\text{kg}$ fresh weight)		
Urine	80–300	2
Blood serum	1000–2000; Max. 3900	2
Suicide victim; mg/kg FW		
Blood	173	19
Kidney	116	19
Liver	225	19
Urine	75	19
Daily diet (mg)	1–6	12
Neurological patients, $\mu\text{g}/\text{L}$		
Serum	22 (4–60)	17
Cerebrospinal fluid	0.75 (0.24–2.03)	17

^a 1, Dominguez and Chapman 1984; 2, USEPA 1980; 3, Menzer and Nelson 1986; 4, Wong and Crosby 1978; 5, Fox and Joshi 1984; 6, Pignatello et al. 1983; 7, Niimi and Cho 1983; 8, Folke and Birklund 1986; 9, Leeuwangh and Voute 1985; 10, Ryan et al. 1985; 11, Gebefugi and Korte 1983; 12, Choudhury et al. 1986; 13, Larsson et al. 1993; 14, Kutz et al. 1992; 15, Wagner et al. 1991; 16, Geyer et al. 1987; 17, Jorens et al. 1991; 18, Gomez-Catalan et al. 1987; 19, Haley 1977; 20, Reigner et al. 1992a.

23.4 EFFECTS

23.4.1 General

The toxicity of commercial or technical grades of PCP significantly exceeds that of analytical or purified PCP. Some of this added toxicity is attributed to impurities such as dioxins, dibenzofurans, chlorophenols, and hexachlorobenzene. Pentachlorophenol is rapidly accumulated and rapidly excreted, and has little tendency to persist in living organisms. It acts by uncoupling oxidative

phosphorylation. Terrestrial plants and soil invertebrates were adversely affected at 0.3 mg PCP/L (root growth), and at 1 to 5 g PCP/m² soil (reduction in soil biota populations).

Pentachlorophenol was most toxic and most rapidly metabolized in aquatic environments at elevated temperatures and reduced pH. Adverse effects on growth, survival, and reproduction of representative sensitive species of aquatic organisms occurred at PCP concentrations of about 8 to 80 µg/L for algae and macrophytes, about 3 to 100 µg/L for invertebrates (especially molluscs), and <1 to 68 µg/L for fishes, especially salmonids. Fatal PCP doses for birds were 380 to 504 mg/kg BW (acute oral), >3850 mg/kg in diets, and >285 mg/kg in nesting materials. Adverse sublethal effects were noted at dietary levels as low as 1.0 mg/kg ration. Residues (mg/kg fresh weight) in birds found dead from PCP poisoning were >11 in brain, >20 in kidney, >46 in liver, and 50 to 100 in egg.

Data are scarce on the toxicity of PCP to mammalian wildlife, but studies with livestock and small laboratory animals show that the chemical is rapidly excreted. However, there is great variability between species in their ability to depurate PCP, as well as in their overall sensitivity. Acute oral LD₅₀ values in laboratory animals were 27 to 300 mg/kg BW. Tissue residues were elevated at dietary levels as low as 0.05 mg/kg feed and at air levels >0.1 mg/m³. Histopathology, reproductive impairment, and retarded growth were evident at doses of 0.2 to 1.25 mg/kg BW, and when the diets fed contained >30 mg PCP/kg.

23.4.2 Terrestrial Plants and Invertebrates

Pentachlorophenol is toxic to plant mitochondria; the mode of action is similar to that in other organisms (i.e., uncoupling of oxidative phosphorylation). At 267 µg PCP/L, 50% uncoupling was noted in isolated mitochondria of potato, *Solanum tuberosum*, and mung bean, *Phaseolus aureus* (Ravanel and Tissut 1986). Both PCP and its metabolite tetrachlorohydroquinone adversely affect cell growth and synthesis of RNA and ribosome in yeast, *Saccharomyces* sp., in a dose-related manner (Ehrlich et al. 1987). Uptake of PCP by rice (*Oryza sativa*) grown over a 2-year period under flooded conditions was studied after a single application of radiolabeled PCP was applied to the soil at 23 kg/ha (Weiss et al. 1982). During the first year, PCP uptake was 12.9% of the application. Roots contained about 5 mg PCP/kg, distributed as follows (mg/kg): 3.95 as unextractable residues, 0.48 as polar nonhydrolyzable substances, 0.43 as free and conjugated lower chlorinated phenols, 0.14 as free PCP, 0.07 as anisoles, 0.06 as conjugated PCP, 0.03 as hydroxymonomethoxytetrachlorobenzenes, and 0.01 as dimethoxytetrachlorobenzenes. In the second year, PCP uptake was reduced to 2.5%, and soil residues corresponded to 8.4 kg/ha; the amounts of unextractable residues in plants increased, and lower chlorinated conjugated phenols were identified (Weiss et al. 1982). Root growth in rice seedlings was inhibited 50% at 0.3 mg PCP/L (Nagasawa et al. 1981).

Laboratory studies with adult earthworms (*Lumbricus terrestris*) exposed for 96 h to filter paper containing 5 to 50 µg PCP/cm² were conducted by Giggelman et al. (1998). The LC₅₀ (96 h) concentration was 25 µg PCP/cm² filter paper; the LD₅₀ (96 h) value was 878 mg PCP/kg DW whole worm. At 10 µg PCP/cm², all worms survived for 96 h with an average whole-body concentration of 501 mg PCP/kg DW. At 20 µg PCP/cm², 20% died and survivors had 804 mg/kg DW. At 35 µg PCP/cm², none survived 96 h; dead worms had approximately 1060 mg PCP/kg DW.

Pentachlorophenol applied to beech forest soils every 2 months for 2 years at the rate of 1.0 g/m² markedly reduced populations of soil organisms. At 5.0 g/m², it drastically reduced most of the soil animal species and also the microflora (Zietz et al. 1987). Reduction of the soil metabolism by PCP retards decomposition and affects the overall nutrient balance of forest ecosystems (Zietz et al. 1987). Pentachlorophenol is more toxic to earthworms in soils with comparatively low levels of organic materials. The LC₅₀ (14-day) value for *Lumbricus rubellus* was 1094 mg PCP/kg DW soils with 6.1% organic matter, and 883 mg/kg DW soils with 3.7% organic matter (Van Gestel and Ma 1988). The earthworm *Eisenia fetida andrei* is more sensitive than *Lumbricus rubellus*;

the LC50 (14-day) values were 143 mg/kg DW for soils containing 6.1% organic matter, and 94 mg/kg DW for soils of 3.7% organic matter. Both species accumulated similar concentrations of PCP (Van Gestel and Ma 1988). Other studies with earthworms (*Allolobophora caliginosa*, *Lumbricus terrestris*) demonstrated differences between species in sensitivity to PCP, differences in PCP accumulation rates, and rapid metabolism of sodium-PCP when compared to PCP (Haque and Ebing 1988).

23.4.3 Aquatic Biota

In general, the most sensitive stages are embryo and larval stages of invertebrates and the late larval premetamorphosis stage of fish; fish are more sensitive to PCP than invertebrates (USEPA 1986). Pentachlorophenol affects energy metabolism by partly uncoupling oxidative phosphorylation and increasing oxygen consumption, by altering the activities of several glycolytic enzymes and the citric acid cycle enzymes, and by increasing the consumption rate of stored lipid (Johansen et al. 1985; Brown et al. 1987; McKim et al. 1987). Collectively, these events could reduce the availability of energy for maintenance and growth and thereby reduce the survival of larval fish and the ability of prey to escape from a predator (Brown et al. 1985, 1987; Hodson et al. 1991; Samis et al. 1993, 1994). Pentachlorophenol has a dose-dependent inhibitory effect on chemiluminescence activity of isolated phagocyte cells of the Japanese medaka (*Oryzias latipes*) (Anderson and Brubacher 1992), and the mummichog (*Fundulus heteroclitus*) (Roszell and Anderson 1993). Since chemiluminescence is due to the production of reactive oxygen intermediates (ROIs), such as superoxide anion (O_2^-) and H_2O_2 , suppression of ROI may adversely affect the teleost immune system (Roszell and Anderson 1993).

The accumulation of PCP in fishes is rapid, and primarily by direct uptake from water rather than through the food chain or diet (Niimi and Cho 1983). Signs of PCP intoxication in fish include rapid swimming at the surface and increased opercular movements, followed by loss of balance, settling to the bottom, and death (Holmberg et al. 1972; Gupta 1983). PCP is rapidly excreted by fishes after conjugates of PCP-glucuronide and PCP-sulfate are formed; half-lives in tissues are less than 24 h (USEPA 1980; Makela et al. 1991; Cravedi et al. 1995). Major roles were played by gall bladder and bile in PCP-glucuronide depuration kinetics, and by gill in PCP-sulfate depuration (Kobayashi 1978; Lech et al. 1978; McKim et al. 1986). It has been suggested that the efficient elimination of PCP should allow vertebrates to tolerate periodic low doses of PCP without toxic effects (McKim et al. 1986).

Many species of aquatic organisms were found dead in rice fields of Surinam, South America, after they were sprayed with PCP to control populations of snails (Vermeer et al. 1974). Residues of PCP in dead organisms (mg PCP/kg fresh body weight) were 8.1 in frogs (*Pseudis paradoxa*); 36.8 in snails (*Pomacea* spp.); and, in three species of fish, 31.2 in krobia (*Cichlasoma bimaculatum*), 41.6 in kwi kwi (*Hoplosternum littorale*), and 59.4 in srieba (*Astyanax bimaculatus*). Pentachlorophenol was also implicated in fish kills in Europe and North America, all of which were associated with the pulpwood industry (Schimmel et al. 1978). In December 1974, near Hattiesburg, Mississippi, water containing PCP in fuel oil that overflowed the banks of a holding pond of a wood-treatment wastewater facility killed all fish in a 24-ha lake. Concentrations of PCP in water and fish returned to background concentrations 10 months after the spill. However, the chemical persisted in leaf litter and sediments for at least 17 months after the spill (Pierce and Victor 1978). In December 1976, another fish kill was observed near the same facility. Residues of PCP in surviving fish — including bluegills (*Lepomis macrochirus*), largemouth bass (*Micropterus salmoides*), and channel catfish (*Ictalurus punctatus*) — were greatly elevated 1 month later: 8 to 19 mg PCP/kg fresh weight in muscle, 42 to 48 mg/kg in gill, and 130 to 221 mg/kg in liver (Pierce and Victor 1978). Pentachlorophenol persisted in fish for 6 to 10 months before reaching background concentrations.

Studies with experimental ecosystems have indicated that the effects of PCP on community structure and activity are profound. These included a reduction in the number of individuals and species of estuarine macrobenthos after exposure to 55 to 76 µg PCP/L for 5 to 9 weeks (Tagatz et al. 1977, 1983) or 15.8 µg/L for 13 weeks (Tagatz et al. 1978); a decrease in periphyton biomass, fish growth, and larval drift, and a suppression of community metabolism at 48 µg PCP/L after 3-months' exposure (Hedtke and Arthur 1985; Zischke et al. 1985; Yount and Richter 1986); elevated levels of PCP in postlarval shrimp, *Penaeus vannamei*, after chronic exposure to 10 µg PCP/L (Seidler et al. 1986); and bioconcentration factors after exposure to radiolabeled PCP of 5 for an alga (*Oedogonium cardiacum*), 21 for a snail (*Physa* sp.), 26 for a mosquito larva (*Culex pipiens quinquefasciatus*), 132 for mosquitofish (*Gambusia affinis*), and 205 for *Daphnia magna* (Lu et al. 1978). In laboratory studies, increased accumulation and adverse effects on growth, survival, and reproduction were seen in sensitive species of aquatic organisms: in algae and macrophytes at water concentrations (µg PCP/L) of 7.5 to 80; in a wide variety of invertebrates, especially molluscs, at 2.5 to 100; and in fishes, especially salmonids, at less than 1.0 to 68 (Table 23.4).

Biocidal properties of PCP were significantly modified by water pH, dissolved oxygen, salinity, and temperature, and by the purity of PCP compounds tested. In general, PCP was most toxic and was metabolized most rapidly at elevated water temperatures (USEPA 1980, 1986; Hodson and Blunt 1981; Niimi and Palazzo 1985; Fisher 1986), reduced pH (Bevenue and Beckman 1967; USEPA 1980, 1986; Dave 1984; Choudhury et al. 1986; Fisher 1986; Seidler et al. 1986; Larsson et al. 1993), and decreased dissolved oxygen (USEPA 1986). Increasing the pH of the water column decreases the hazard of PCP to aquatic biota: at pH values above 4.8, for example, hydroxyl proton is dissociated and penetration in aquatic organisms is reduced (Fisher 1986; Rutgers et al. 1998). In studies with goldfish (*Carassius auratus*) exposed to 5 µg PCP/L for 96 h, a pH increase from 7 to 9 resulted in lesser amounts of PCP in the fish, fewer metabolites formed, and a decreased ability to deplete the PCP from the exposure water; the uptake of PCP at pH 7, 8, and 9 seemed to be controlled by its K_{ow} at these pH values (Stehly and Hayton 1990). Water salinity affects PCP accumulations in euryhaline teleosts. In the Japanese medaka (*Oryzias latipes*), for example, increasing salinity was associated with decreased PCP uptake rates and increased clearance rates; the greater excretion of PCP-glucuronide by seawater-adapted medakas may be responsible for the rapid elimination of PCP (Tachikawa et al. 1991; Tachikawa and Sawamura 1994). All authorities agree that commercial or technical grades of PCP are significantly more toxic to aquatic organisms than is purified PCP (USEPA 1980; Cleveland et al. 1982; Huckins and Petty 1983; Dominguez and Chapman 1984; Stuart and Robinson 1985; Hamilton et al. 1986; Nagler et al. 1986). The sublethal effects of low concentrations of commercial PCP to aquatic biota are due primarily to impurities, composed mostly of octa- and nonachlorophenoxyphenols (Hamilton et al. 1986), and also to relatively large quantities of hexachlorobenzene, dioxins, and dibenzofurans (Cleveland et al. 1982).

Salicylamide and PCP dose are important. Salicylamide is an inhibitor of PCP metabolism in fry of rainbow trout, producing elevated BCF values. Fry exposed to 5 µg PCP/L for 96 h in the presence of 25 mg salicylamide/L had higher concentrations of PCP than did fry exposed without salicylamide (Stehly and Hayton 1989). Bluegills exposed to PCP at continuous low-level sublethal concentrations were at greater risk for decreased growth than were bluegills exposed to a more concentrated short-term pulse of PCP resulting in some deaths (Samis et al. 1991). Fat content of diets of juvenile rainbow trout, however, were relatively unimportant in PCP acute toxicity bioassays. Rainbow trout juveniles fed high-fat (21%) or low-fat (13%) diets for 11 weeks had similar LC50 (144 h) values (109 µg/L vs. 108 µg/L), although the high-fat group had 3% more body lipids than the low-fat group (van den Heuvel et al. 1991).

Table 23.4 Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
ALGAE AND MACROPHYTES			
Alga			
<i>Chlorella pyrenoidosa</i>	7.5	Total chlorosis inhibition in 72 h	1
<i>Skeletonema costatum</i>	17–20	50% reduction in cell numbers at 96 h	1
Filamentous algae (<i>Chara</i> sp., <i>Enteromorpha</i> sp.)	50–100	Lethal in 30 days in outdoor ponds; decay was responsible for depression of dissolved oxygen and later fish deaths	2
Alga, <i>Scenedesmus costatum</i>	80	50% growth inhibition in 96 h	2
<i>Selenastrum capricornutum</i>	110–150	50% growth reduction in 96 h in soft water	3
<i>S. capricornutum</i>	290	50% growth inhibition in 96 h	2
<i>S. capricornutum</i>	760	50% growth reduction in 96 h in hard water	3
<i>Dunaliella tertiolecta</i>	170–206	50% reduction in cell numbers in 96 h	1
<i>Thalassiosira pseudonana</i>	179–189	50% reduction in cell numbers in 96 h	1
Giant kelp, <i>Macrocystis pyrifera</i>	277	50% inhibition of photosynthetic activity in 4 days	70
Duckweed			
<i>Lemna minor</i>	800	50% inhibition of chlorosis in 48 h	1
<i>L. minor</i>	1000	Inhibition of photosynthetic oxygen production	5
<i>L. minor</i>	1400	No measurable effect after exposure for 21 days	4
INVERTEBRATES			
Duck mussel			
<i>Anodonta anatina</i>	0.5–1.0	Bioconcentration factor (ratio PCP in mg/kg FW soft tissues: PCP medium in mg/L) during 3-h exposure ranged between 81 and 162 and was independent of water temperature or PCP concentration	59
<i>A. anatina</i>	0.6–5.2	BCF values after 8 days at 13°C ranged between 263 and 461	59
American oyster			
<i>Crassostrea virginica</i>	2.5	Bioconcentration factor (BCF) of 78 in 28 days; 100% depuration within 4 days postexposure	6
<i>C. virginica</i>	25	BCF of 41 between days 4 and 28 of exposure; 100% depuration within 4 days postexposure	6
<i>C. virginica</i>	34	50% reduction in shell deposition in 8 days	1
<i>C. virginica</i>	40	50% abnormal development of larvae in 48 h	7
<i>C. virginica</i>	77	LC50 (96 h)	1
Cladoceran			
<i>Ceriodaphnia reticulata</i>	4.1	Reduction in number of young/female in lifetime exposure	4
<i>C. reticulata</i>	164	LC50 (48 h)	8
Polychaete worm			
<i>Ophryotrocha diadema</i>	10–13	No effect on reproduction in 41 days	8
<i>O. diadema</i>	23–75	50% inhibition in reproduction in 41 days	8
Clam, <i>Mulinia lateralis</i>	15.8	Populations reduced after 7 days	9
Razor clam, <i>Ensis minor</i>	15.8	Populations reduced after 7 days	9
Hydra, <i>Hydra littoralis</i>	19	Threshold for reproduction inhibition	8

Table 23.4 (continued) Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
Snail			
<i>Physa gyrina</i>	26	Reduction in number of egg masses produced and in egg survival during lifetime exposure	4, 10, 70
<i>P. gyrina</i>	220	LC50 (96 h) at 24°C	4
<i>P. gyrina</i>	730	LC50 (96 h) at 8.6°C	11
<i>P. gyrina</i>	1380	LC50 (96 h) at 3.2°C	4
Pacific oyster, <i>Crassostrea gigas</i>	55	62% of exposed embryos developed abnormally in 48 h	1
Midge			
<i>Chironomus riparius</i> , 4th instar	84	LC50 (24 h) at pH 4	12
<i>C. riparius</i>	465	LC50 (24 h) at pH 6	12
<i>C. riparius</i>	631	50% locomotion inhibition at 35°C	13
<i>C. riparius</i>	1176	50% locomotion inhibition at 15°C	13
<i>C. riparius</i>	1948	LC50 (24 h) at pH 9	12
Snail			
<i>Lymnaea acuminata</i>	100	LC16 (96 h)	14
<i>L. acuminata</i>	160	LC50 (96 h)	14
<i>L. acuminata</i>	210	LC84 (96 h)	14
Snail, <i>Australorbis glabratus</i>	100	Reduction in egg production and viability after exposure for 7–8 days	2
Sea urchin			
<i>Paracentrotus lividus</i> , embryos	100	Reductions in various amino acid activity levels during exposure for 40 h	15
<i>P. lividus</i>	200	Number and size of swimming blastulae, gastrulae, and plutei reduced in 40-h exposure	15
Short-necked clam, <i>Tapes philippinarum</i>	100	Lethal in 120 h	16
Snail, <i>Lymnaea luteola</i>	112	LC50 (96 h)	17
Flatworm, <i>Dugesia lugubris</i>	130	LC50 (48 h)	8
Snail, <i>Lymnaea stagnalis</i>	180	LC50 (16 days)	2
Cladoceran			
<i>Daphnia magna</i>	180	No observable effect level in lifetime exposure	1
<i>D. magna</i>	320	Some adverse effects observed in lifetime exposure	1
<i>D. magna</i>	370–440	50% immobilization in 48 h	18
<i>D. magna</i>	475	LC50 (96 h)	1
Cladoceran			
<i>Simocephalus vetulus</i>	204	LC50 (96 h) at 24°C	4
<i>S. vetulus</i>	670	LC50 (96 h) at 18°C	11
Tubificid worm			
<i>Tubifex tubifex</i>	286	LC50 (24 h) at pH 7.5	1
<i>T. tubifex</i>	619	LC50 (24 h) at pH 8.5	1
<i>T. tubifex</i>	1294	LC50 (24 h) at pH 9.5	1
Snail			
<i>Gillia altilis</i>	300	LC50 (96 h) in flow-through test	19
<i>G. altilis</i>	810	LC50 (96 h) in static test	19
Mysid, <i>Mysidopsis bahia</i>	320	LC50 (96 h)	20
Grass shrimp			
<i>Paleomonetes pugio</i>	400–440	LC50 (96 h) during molting	20, 21
<i>P. pugio</i>	473–637	Adversely affects initiation and progress of limb regeneration without altering duration of molt cycle	22

Table 23.4 (continued) Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
<i>P. pugio</i>	649–1200	LC50 (96 h)	1, 7
<i>P. pugio</i>	1000	Histopathology of gill, hepatopancreas, and midgut epithelial cells after exposure for 12 days in shrimp that molted; normal tissues in shrimp that had not yet molted	21
<i>P. pugio</i>	2500	LC50 (96 h) during intermolt	20, 21
Polychaete worm, <i>Neanthes arenaceodentata</i>	435	LC50 (96 h)	1
Amphipod			
<i>Gammarus pseudolimnaeus</i>	770	Significant decreases in free amino acids after 5 days; in whole-body glycogen, protein, and caloric content after 15 days; and in lipid content after 30 days	23
<i>G. pseudolimnaeus</i>	860	LC50 (30 days)	23
<i>G. pseudolimnaeus</i>	1150	LC50 (96 h)	24
<i>G. pseudolimnaeus</i>	1680	At 48 h, significant decrease in total free amino acid levels	24
Pond snail, <i>Viviparus bengalensis</i>	840	LC50 (96 h)	25
Caddisfly, <i>Philarctus quaeris</i>	1200	LC50 (96 h)	11
Mayfly, <i>Callibaetis skokianus</i>	1700	LC50 (96 h)	11
Amphipod, <i>Crangonyx pseudogracilis</i>	1900	LC50 (96 h)	11
Isopod			
<i>Asellus racovitzai</i>	2300	LC50 (96 h) at 8.6°C	11
<i>A. racovitzai</i>	4320	LC50 (96 h) at 4.2°C	4
<i>A. racovitzai</i>	>7770	LC50 (96 h) at 3.2°C	4
Crayfish			
<i>Astacus fluviatilis</i>	9000	LC50 (8 days) at pH 6.5	26
<i>A. fluviatilis</i>	53,000	LC50 (8 days) at pH 7.5	26
VERTEBRATES			
Rainbow trout			
<i>Oncorhynchus mykiss</i>	0.035	After 115 days, whole fish BCF of 286–572; half eliminated in 7 days	8, 57
<i>O. mykiss</i>	0.7	After 115 days, BCF of 160 in whole fish; Tb 1/2 elimination time of 7 days	8, 57
<i>O. mykiss</i>	1.0	Whole-body BCF of 221 in 18 h and 466 in 11.7 days; Tb 1/2 of 65 h and 95% depuration in 12 days. Highest PCP tissue residues were bile > liver > blood > kidney > spleen > skin-bone-gill-gonad > muscle	27
<i>O. mykiss</i>	7.4	27% inhibition of growth in 28 days	1
<i>O. mykiss</i>	10–20	Some deaths during exposure from fertilization to yolk-sac absorption; 100% dead at 5 mg dissolved oxygen (DO)/L and 20 µg PCP/L; 100% dead at 3 mg DO/L and 10 µg PCP/L	28
<i>O. mykiss</i>	11	No adverse effects observed during exposure from fertilization through day 72	29, 70

Table 23.4 (continued) Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
<i>O. mykiss</i>	19	Embryo mortality negligible during exposure from fertilization through day 72 but alevin mortality was 3 times that of controls. Growth in length and weight reduced. Fin erosion, mild cranial malformations, and lethargy reported	29
<i>O. mykiss</i>	22	48% reduction in viable oocytes after exposure for 18 days	30
<i>O. mykiss</i>	25	After 24 h, BCF of 40 in muscle, 240 in fat, 260 in blood, and 640 in liver. Tb 1/2 values ranged from 7 h in muscle to 23 h in fat	31, 58
<i>O. mykiss</i>	28	11–19% inhibition in growth in 20–38 days	1
<i>O. mykiss</i>	34–121	LC50 (96 h)	1, 29, 32–34
<i>O. mykiss</i>	40	100% mortality during exposure from fertilization to yolk-sac absorption (72 days)	28
<i>O. mykiss</i>	46	LC100 (41 days)	1
<i>O. mykiss</i>	49	81% reduction in oocytes available to complete oogenesis after exposure for 18 days	30
<i>O. mykiss</i>	60	Eye abnormalities noted in developing embryos after exposure for 17 days; all dead at day 72 of exposure	29
<i>O. mykiss</i>	122	LC50 (17 h)	68
<i>O. mykiss</i>	271	LC50 (5 h)	68
<i>O. mykiss</i>	10,000	LC50 (3.5 h)	35
Sockeye salmon			
<i>Oncorhynchus nerka</i>	3.2	10% growth inhibition in 6 weeks	1
<i>O. nerka</i>	46–120	LC50 (96 h)	1, 56, 70
American flagfish, <i>Jordanella floridae</i>	5	BCF after 28 days was 216 for whole fish on fresh-weight basis and 1633 on lipid-weight basis; 90% steady state attained in 54 h; 50% cleared in 16.3 h in uncontaminated media	63
Common carp			
<i>Cyprinus carpio</i>	9.5	LC50 (96 h), larvae	8
<i>C. carpio</i>	266	Reduction in liver glucose and glycogen release after 3 days; high accumulations in liver	36
<i>C. carpio</i>	1500	LC50 (3 h)	37
Largemouth bass			
<i>Micropterus salmoides</i>	10	Food conversion efficiency reduced in a concentration-dependent fashion at concentrations >10 µg/L	38
<i>M. salmoides</i>	25.2	Growth reduction after exposure for 52 days	38
<i>M. salmoides</i>	45	Decline in feeding activity after 8 weeks	38
<i>M. salmoides</i>	50	After 14 days, food conversion efficiency reduced 30%, reduction in ability to capture prey and in food consumed	39
<i>M. salmoides</i>	54	LC50 (120 days)	38

Table 23.4 (continued) Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
<i>M. salmoides</i>	67	Exposure for 8 weeks produced hyperactivity and reductions in feeding rate and in prey capture	40
<i>M. salmoides</i>	136–287	LC50 (96 h)	38, 39, 41
Rasbora			
<i>Rasbora daniconius neilgeriensis</i>	10	LC0 (96 h)	42
<i>R.d. neilgeriensis</i>	67	LC16 (96 h)	42
<i>R.d. neilgeriensis</i>	148	LC50 (96 h)	42
<i>R.d. neilgeriensis</i>	330	LC84 (96 h)	42
Fathead minnow			
<i>Pimephales promelas</i>	16.5–34.6	No adverse effect-adverse effect values in lifetime exposure at pH 6.5	70
<i>P. promelas</i>	27.6–58.2	As above at pH 7.5	70
<i>P. promelas</i>	32–75	As above at pH 8.0	70
<i>P. promelas</i>	64–125	As above at pH 8.5	70
<i>P. promelas</i>	45	No-observable-effect level in lifetime exposure	1, 54
<i>P. promelas</i>	48	Growth and larval drift reduced after exposure for 12 weeks	10
<i>P. promelas</i>	50	Whole-body BCF of 174 after 14 days; nondetectable residues after 14 days in clean water	45
<i>P. promelas</i>	73	Some adverse effects in lifetime exposure	1, 54
<i>P. promelas</i>	85	Growth reduction after 90 days exposure	46
<i>P. promelas</i>	120	LC50 (96 h) at 16.6°C	4
<i>P. promelas</i>	170	LC50 (96 h) at 10.1°C	4
<i>P. promelas</i>	200–350	LC50 (96 h)	2, 11, 35
<i>P. promelas</i>	300	LC50 (96 h) at 3.4°C	4
Japanese medaka			
<i>Oryzias latipes</i>	20–100	Freshwater-adapted fish had BCF of 1680 (vs. 370 for saltwater-adapted group) after 10 days	66
<i>O. latipes</i>	60–200	Time for 50% depuration was 71–108 h for freshwater medakas (vs. 31 h for marine group)	66
Pinfish, <i>Lagodon rhomboides</i>	31–53	LC50 (96 h)	1, 7, 20
Coho salmon, <i>Oncorhynchus kisutch</i>	32–60	LC50 (96 h), juveniles	70
Bluegill			
<i>Lepomis macrochirus</i>	32–215	LC50 (96 h)	1, 11, 32, 33
<i>L. macrochirus</i>	48	Food intake normal but growth rate declined 26%; food conversion normal after 22 days in untreated water	61, 62, 69
<i>L. macrochirus</i>	100	After exposure for 8 days, BCF 13 in muscle, 60 in gill, 210 in gastrointestinal tract, and 350 in liver. Rapid elimination, but some residues in muscle and liver were detectable 16 days postapplication	43
<i>L. macrochirus</i>	100	Liver histopathology after 32 days; degenerative changes detectable after 2 days	44

Table 23.4 (continued) Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
<i>L. macrochirus</i>	173	No deaths. Food intake declined 29% and growth rate declined 75%	61, 62, 69
<i>L. macrochirus</i>	240	22% dead in 3 days; survivors had normal food conversion efficiency	69
<i>L. macrochirus</i>	240	LC50 (96 h)	69
<i>L. macrochirus</i>	432	LC100 (8 days)	10
Freshwater fishes, Scandinavia, 5 species	38–66	LC50 (96 h) range for newly hatched larvae and juveniles	60
Atlantic salmon			
<i>Salmo salar</i>	46	Altered temperature preference in 24 h	1
<i>S. salar</i>	59–140	LC50 (96 h), juveniles	64
<i>S. salar</i>	500	LC50 (96 h)	35
<i>S. salar</i>	2000	LC50 (10.5 h)	35
<i>S. salar</i>	10,000	LC50 (2.7 h)	35
Sheepshead minnow			
<i>Cyprinodon variegatus</i>	47	No-observable-effect level in lifetime exposure	1
<i>C. variegatus</i>	88	12% mortality in lifetime exposure	47
<i>C. variegatus</i>	195	Life cycle exposure resulted in reduced hatch and survival of second-generation fish	47
<i>C. variegatus</i>	223–392	LC50 (96 h) for fry age 1 day to 6 weeks	7
<i>C. variegatus</i>	389	LC100 (60 days)	47
<i>C. variegatus</i>	442	LC50 (96 h)	1, 47
Plaice (flounder)			
<i>Pleuronectes platessa</i>	50	LC50 (8 weeks), eggs	8
<i>P. platessa</i>	60–140	LC50 (96 h), larvae	8
<i>P. platessa</i>	100–130	LC50 (96 h), juveniles	8
Channel catfish, <i>Ictalurus punctatus</i>	54–68	LC50 (96 h)	8, 32, 33
Coho salmon, <i>Oncorhynchus kisutch</i>	55	LC50 (96 h)	1
White crappie, <i>Pomoxis annularis</i>	56–75	LC50 (96 h)	35
Longnose killifish, <i>Fundulus similis</i>	57–610	Whole-body BCF of 53 after 168 h; Tb 1/2 of 4.7 days. Whole-body residues up to 33 mg/kg FW	48
Chinook salmon, <i>Oncorhynchus tshawytscha</i>	68–78	LC50 (96 h)	1, 32, 55
White sucker, <i>Catostomus commersoni</i>	85	LC50 (96 h)	4
Eel, <i>Anguilla anguilla</i>	100	Seawater-exposed eels, after exposure for 8 days, had 33 mg PCP/kg FW in liver, 9 in muscle, and 4 in blood; after depuration for 8 days, values were 12 in liver, 4 in muscle, and 2 in blood. Eels exposed in freshwater for 4 days had 2–9 mg PCP/kg tissue, and <1.2 mg/kg 38 days postexposure	49
Goldfish			
<i>Carassius auratus</i>	100	BCF of 1000 after 12 h. Residues in dead fish were 82–116 mg PCP/kg BW; no surviving fish contained more than 114 mg/kg	16, 48
<i>C. auratus</i>	200	Whole-body residue of 116 mg/kg after exposure for 120 h	48

Table 23.4 (continued) Lethal and Sublethal Effects of Pentachlorophenol on Selected Species of Aquatic Organisms

Species and Other Variables	Concentration (g PCP/L medium)	Effect	Reference ^a
Tilapia, <i>Tilapia nilotica</i>	100	In 24-h tests, fish acclimatized to seawater were twice as resistant as freshwater-acclimatized fish to biocidal PCP properties, and contained lower residues	50
Mullet			
<i>Rhinomugil corsula</i>	100	Metabolic rate elevated after 3 h	37
<i>R. corsula</i>	1000	LC50 (3 h)	37
Striped mullet, <i>Mugil cephalus</i>	112	LC50 (96 h), whole-body BCF of 38	1, 6
Brook trout, <i>Salvelinus fontinalis</i>	128	LC50 (96 h)	1
Salamander			
<i>Ambystoma mexicanus</i>	130	LC0 (48 h)	8
<i>A. mexicanus</i>	300	LC50 (48 h)	8
Common shiner			
<i>Notropis cornutus</i>	180	25% growth reduction after exposure for 7 days	51
<i>N. cornutus</i>	320	LC100 (7 days)	51
Fish, 19 species	200–600	LC50 (96 h)	35
Frog			
<i>Xenopus laevis</i>	210	LC0 (48 h)	8
<i>X. laevis</i>	260	LC50 (48 h)	8
Arctic charr, <i>Salvelinus alpinus</i>	500	LC50 (96 h), larvae	65
Guppy			
<i>Poecilia reticulata</i>	500–700	Reduction in ability to escape from piscine predators	52
<i>P. reticulata</i>	700	LC21 (30 days)	52
<i>P. reticulata</i>	1000	LC0 (12 days); possible acclimatization	53
<i>P. reticulata</i>	1020	LC50 (96 h)	52
Sea lamprey, <i>Petromyzon marinus</i>	924	LC100 (4 h)	1
Mummichog, <i>Fundulus heteroclitus</i>	1000–20,000	Dose-dependent inhibition of peak chemiluminescence in phagocytes after incubation for 20 h	67

^a 1, USEPA 1980; 2, Crossland and Wolff 1985; 3, Smith et al. 1987; 4, Hedtke et al. 1986; 5, Huber et al. 1982; 6, Schimmel et al. 1978; 7, Borthwick and Schimmel 1978; 8, Choudhury et al. 1986; 9, Tagatz et al. 1981; 10, Zischke et al. 1985; 11, Hedtke and Arthur 1985; 12, Fisher and Wadleigh 1986; 13, Fisher 1986; 14, Gupta and Rao 1982; 15, Ozretic and Krajnovic-Ozretic 1985; 16, Kobayashi 1978; 17, Gupta et al. 1984; 18, Berglind and Dave 1984; 19, Stuart and Robinson 1985; 20, Mayer 1987; 21, Rao and Doughtie 1984; 22, Rao et al. 1978; 23, Graney and Giesy 1987; 24, Graney and Giesy 1987; 25, Gupta and Durve 1984; 26, Kaila and Saarikoski 1977; 27, McKim et al. 1986; 28, Chapman and Shumway 1978; 29, Dominguez and Chapman 1984; 30, Nagler et al. 1986; 31, Lech et al. 1978; 32, Johnson and Finley 1980; 33, Mayer and Ellersiek 1986; 34, McKim et al. 1987; 35, Cote 1972; 36, Yousri and Hanke 1985; 37, Peer et al. 1983; 38, Johansen et al. 1987; 39, Mathers et al. 1985; 40, Brown et al. 1987; 41, Johansen et al. 1985; 42, Gupta 1983; 43, Pruitt et al. 1977; 44, Owen and Rosso 1981; 45, Huckins and Petty 1983; 46, Cleveland et al. 1982; 47, Parrish et al. 1978; 48, Trujillo et al. 1982; 49, Holmberg et al. 1972; 50, Tachikawa et al. 1987; 51, Borgmann and Ralph 1986; 52, Brown et al. 1985; 53, Norup 1972; 54, Holcombe et al. 1982; 55, Iwama and Greer 1979; 56, Webb and Brett 1973; 57, Niimi and McFadden 1982; 58, Glickman et al. 1977; 59, Makela et al. 1991; 60, Oikari 1987; 61, Samis et al. 1994; 62, Samis et al. 1993; 63, Smith et al. 1990; 64, Burridge and Haya 1990; 65, Cravedi et al. 1995; 66, Tachikawa et al. 1991.; 67, Roszell and Anderson 1993; 68, van den Heuvel et al. 1991; 69, Samis et al. 1991; 70, USEPA 1986.

23.4.4 Birds

Signs of PCP intoxication in birds include excessive drinking and regurgitation, rapid breathing, wing shivers or twitching, jerkiness, shakiness, ataxia, tremors, and spasms (Hudson et al. 1984). Signs

sometimes appear within 10 min. Mallards usually die 2 to 24 h posttreatment, and ring-necked pheasants 3 to 5 days posttreatment; remission in pheasants requires up to 2 weeks (Hudson et al. 1984).

Pentachlorophenol killed various species of birds at single oral doses of 380 to 504 mg/kg BW, at dietary concentrations of 3850 mg/kg ration fed over a 5-day period, and when nesting materials contained >285 mg/kg. Residues (mg/kg fresh weight tissue) in birds found dead from PCP poisoning were 11 in brain, 20 in kidney, 46 in liver, and 50 to 100 in egg (Table 23.5). Sublethal effects, including liver histopathology and diarrhea, were reported in domestic chickens at dietary levels as low as 1 mg PCP/kg feed over an 8-week period; significant accumulations in tissues were measured after consumption for 14 days of diets containing 10 mg PCP/kg (Table 23.5). Residues in chickens fed PCP-containing diets for 8 weeks were dose related and highest in kidney and liver and lower in other tissues; the high residues may reflect the principal routes of metabolism and excretion (Stedman et al. 1980). The loss of body fat in chickens, accomplished by feeding bile acid-binding resins, hastens PCP excretion (Table 23.5) (Polin et al. 1986).

Spraying of PCP to control populations of water snails in rice fields of Surinam resulted in the death of fish and birds, including snail kites (*Rostrhamus sociabilis*), certain egrets and herons, and wattled jacanas (*Jacana jacana*). Levels of PCP in these birds and their food items suggested that PCP-contaminated food probably caused the deaths (Vermeer et al. 1974) (Table 23.5).

Pentachlorophenol is widely used as a wood preservative, which often results in residues in wood shavings used as poultry litter. A moldy smell and taste in chicken tissue has been traced to the presence of chloroanisoles formed from PCP and tetrachlorophenol in the bedding. Several dioxins, diphenyl ethers, dibenzofurans, and 2-phenoxyphenols have also been identified (Newsome et al. 1984). For example, PCP-contaminated (134 mg/kg) commercial wood shavings used as chicken litter contained detectable levels of heptachlorinated diphenyl ethers (18 µg/kg), octachlorinated diphenyl ethers (12 µg/kg) nonachlorinated diphenyl ethers (6 µg/kg), octachlorinated 2-phenoxyphenols (299 µg/kg), nonachlorinated 2-phenoxyphenols (50 µg/kg), heptachlorinated dibenzodioxins (19 µg/kg), and octachlorinated dibenzodioxins (143 µg/kg). After 9 weeks, PCP was detectable in liver, fat, and muscle; chlorinated diphenyl ethers were detectable in fat, but not in muscle or liver; octa- and nonachlorinated 2-phenoxyphenols were found in all three tissues; and dioxins only in liver and fat (Newsome et al. 1984). Exposure of domestic chickens to litter contaminated with PCP enhanced susceptibility to common poultry pathogens, perhaps due to immunosuppression by the chemical (Prescott et al. 1982).

Table 23.5 Effects of Pentachlorophenol on Selected Species of Birds

Species and Other Variables	Effect and Reference
MALLARD, <i>Anas Platyrhynchos</i>	Acute oral LD50 of 380 mg/kg body weight (BW); 95% confidence interval 205–704 mg/kg BW (Hudson et al. 1984)
JAPANESE QUAIL, <i>Coturnix japonica</i>, Birds age 14 days were fed treated diets for 5 days, then untreated feed for 3 days	No deaths at 3100 mg/kg diet, 35% dead at 3850, 50% at 5139 (4149–6365), and 69% dead at 6000 mg PCP/kg diet (Hill and Camardese 1986)
DOMESTIC CHICKEN, <i>Gallus gallus</i> Fed diets containing 1, 10, 100, or 1000 mg PCP/kg for 8 weeks	Liver histopathology and diarrhea recorded in all treated groups vs. none in controls. The 1000 mg/kg diet was the only ration to adversely affect the weight of all organs analyzed. After 5 weeks on PCP-free diet, residues were still measurable in adipose tissues of all treated birds (Stedman et al. 1980) No deaths in any group. Residues (mg/kg fresh weight) in 600 mg/kg group at 8 weeks were 2 in muscle, 10 in fat, 25 in liver and 80 in kidney vs. <0.02 in controls; no significant difference from controls in growth, blood chemistry, histopathology, or immune response. In the 1200- and 2400-mg/kg groups body weight decreased and liver weight increased; tissue residues were dose related (Prescott et al. 1982)
Fed dietary levels of 600, 1200, or 2400 mg/kg for 8 weeks	The PCP residues (mg/kg FW) were 3.7 in liver, 0.4 in muscle, and 0.3 in fat, vs. <0.08 in controls (Newsome et al. 1984)
Raised over wood shavings containing 134 mg PCP/kg for 9 weeks	

Table 23.5 (continued) Effects of Pentachlorophenol on Selected Species of Birds

Species and Other Variables	Effect and Reference
Fed diets containing 10 mg PCP/kg for 14 days, then 21 days on PCP-free diets containing either no additives, 5% mineral oil, or 5% colestipol hydrochloride Eggs received single injected dose	Body burden at 14 days was 362 µg/bird or 1.1 µg/kg BW. After 21 days, body burdens were 255 µg/bird in no-additive diet and nondetectable levels of <0.7 µg/bird in mineral oil and colestipol additive diets (Polin et al. 1986)
RING-NECKED PHEASANT, <i>Phasianus colchicus</i>	Hatching reduced 50% at a dose of 50 mg PCP/kg egg and 100% at 100 mg/kg (none hatched) (Stedman et al. 1980)
SNAIL KITE, <i>Rostrhamus sociabilis</i>. Found dead in rice fields after spraying to control snails (<i>Pomacea glauca</i> , <i>P. lineata</i>) — the exclusive food of snail kites. Residues in soft parts of snails found dead after spraying were about 37 mg PCP/kg fresh weight	Acute oral LD ₅₀ of 504 mg/kg BW; 95% confidence interval of 343–743 mg/kg BW (Hudson et al. 1984)
CANARY, <i>Serinus canarius</i>. Nesting on straw containing 285 mg PCP/kg	Residues in dead snail kites, in mg PCP/kg FW, were 46 in liver, 20 in kidney, and 11 in brain vs. <0.2 in controls, and 2–17 in birds surviving exposure (Vermeer et al. 1974)
	Reduced hatch, high mortality of young during the first week posthatch, and none surviving to age 3 months. Prior to death, young showed inhibited growth and feather development. Adult birds appeared normal (Dorrestein and Zella 1979)

23.4.5 Mammals

Data are scarce on the biological effects of PCP on mammalian wildlife, although evidence continues to accumulate on this subject for humans, livestock, and small laboratory animals (Table 23.6). Available data on PCP and domestic mammals are briefly summarized, but it is not clear if these findings are applicable to representative species of sensitive mammalian wildlife. PCP tends to accumulate in mammalian tissues unless it is efficiently conjugated into a readily excreted form (Kinzell et al. 1985). The ability to conjugate PCP varies widely among species (Braun and Sauerhoff 1976; USEPA 1980). For example, both laboratory rats (*Rattus* sp.) and humans eliminate about 75% of all PCP in the urine in an unconjugated form, but rhesus monkeys (*Macaca mulatta*) are unable to excrete PCP efficiently, whereas mice were the most efficient. As one result, Tb 1/2 values were low (about 24 h) for mice, high (up to 360 h) for rhesus monkeys, and intermediate for rats and humans (USEPA 1980; van Raaij et al. 1991a). In humans, however, the observed elimination half-life indicates that steady-state body burdens are 10 to 20 times higher than values extrapolated from animal pharmacokinetic data (Uhl et al. 1986).

Biotransformation of PCP in mammals occurs via conjugation, reductive dechlorination, hydrolytic dechlorination, and oxidation. In the process, a number of metabolites are formed, some of which are demonstrably toxic (Renner and Hopfer 1990; Jansson and Jansson 1991; Reigner et al. 1991). Metabolites of PCP found in rat urine and identified (acute oral LD₅₀ to mice, in mg/kg BW) include (Renner and Hopfer 1990):

- PCP (74)
- 2,3,5,6-Tetrachlorophenol (109)
- 2,3,4,6-Tetrachlorophenol (131)
- Tetrachlorocatechol (325–612)
- Trichlorohydroquinone and tetrachlorohydroquinone (376–500)
- 2,3,4,5-tetrachlorophenol (400)
- Tetrachlororesorcinol (752)
- Traces of trichloro-1,4-benzoquinone and tetrachloro-1,4-benzoquinone

Pentachlorophenol is not a carcinogen, and the evidence for mutagenicity is mixed. No carcinomas were produced in rodents, regardless of the composition of the PCP solution tested or route of exposure (USEPA 1980; Choudhury et al. 1986). Some studies suggested that PCP may be

mutagenic in the bacterium *Bacillus subtilis*, the yeast *Saccharomyces cerevisiae*, and in laboratory mice (*Mus* sp.), but not in two other species of bacteria tested — *Salmonella typhimurium* and *Escherichia coli* (Choudhury et al. 1986). The PCP metabolite tetrachlorohydroquinone — found in urine of occupationally exposed humans and experimentally dosed rodents — is twice as toxic to cultured Chinese hamster ovary cells as PCP (based on growth), and induced significant dose-related increases in micronuclei and DNA single-strand breaks (Ehrlich 1990; Jansson and Jansson 1992). But tetrachlorohydroquinone was 5 times less toxic than PCP to mice *in vivo*, with no evidence of mutagenicity (Ehrlich 1990).

The primary sources of PCP in humans include direct intake by way of diet, air, or water and through contact with PCP-contaminated materials (Uhl et al. 1986). It is now established that PCP is taken up by female rhesus monkeys via the skin from PCP-contaminated soils. Monkeys accumulated up to 24% of the PCP in contaminated California soils over a 24-h period (Wester et al. 1993). In humans, the chief routes of exposure in an industrial setting are by way of inhalation and skin contact. Percutaneous absorption is significantly enhanced when PCP is dissolved in organic solvents, such as fuel oil, or when PCP comes in contact with open cuts and scratches (Wood et al. 1983). PCP has resulted in death of humans through suicide and occupational and accidental exposures (USEPA 1980; Rozman et al. 1982; Lambert et al. 1986). Cases of PCP intoxication in humans, including fatalities, have been described in farmers, handlers of preserved wood, and industrial workers. Symptoms always included high fever, renal insufficiency, profuse perspiration, rapid heart beat and breathing, abdominal pain, dizziness, nausea, spasms, and sometimes death 3 to 25 h after onset of symptoms (Knudsen et al. 1974; Haley 1977; USEPA 1980; Wood et al. 1983). Postmortem examination showed kidney degeneration, inflamed gastric mucosa, edematous lungs, and centrilobular degeneration of liver (USEPA 1980; St. Omer and Gadusek 1987). Symptoms of nonfatal PCP intoxication in man include conjunctivitis, chronic sinusitis, nasal irritation, upper respiratory complaints, sneezing, coughing, recurring headache, neurological complaints, weakness, several types of skin lesions (Knudsen et al. 1974; USEPA 1980; Rozman et al. 1982), chloracne (O'Malley et al. 1990), aplastic anemia, leukemia, and other hematologic disorders (Roberts 1990). All symptoms were related to proximity to PCP-treated wood, and sometimes to elevated PCP residues in serum and urine (Lambert et al. 1986). Chloracne and hematologic disorders may be associated with various contaminants in the PCP, including various chlorophenols, phenoxy acids, dioxins, and dibenzofurans (O'Malley et al. 1990; Roberts 1990). At the cellular level, PCP — like other halogenated phenols — uncouples oxidative phosphorylation. A possible antidote to PCP poisoning is the administration of cholestyramine, a compound that interferes with the enterohepatic cycle of PCP, and also increases its elimination directly across the intestinal wall (Rozman et al. 1982). Cholestyramine is known to bind phenols and to enhance fecal elimination of PCP in rats, humans, and rhesus monkeys (USPHS 1994). Phenobarbital increases the biotransformation of PCP, and its action is enhanced in combination with cholestyramine. Substances to be avoided in suspected cases of PCP poisoning include atropine and salicylates, such as aspirin, because they exacerbate the toxicity of phenolic substances (USPHS 1994).

The exposure of livestock to PCP can result from ingestion of feeds stored or fed in PCP-treated wooden structures, licking of treated wood, cutaneous absorption by direct contact with treated wood, and inhalation of air containing preservative chemicals — particularly volatile chlorophenols (Forsell et al. 1981). Acute signs of PCP intoxication in various domestic and laboratory animals include elevated blood sugar, vomiting, elevated blood pressure, increased respiration rate, tachycardia, motor weakness, weakened eye reflex, frequent defecation, high fever, collapse, asphyxial convulsions, and death followed by rapid rigor mortis (Knudsen et al. 1974; Nishimura 1984; St. Omer and Gadusek 1987). In domestic cattle (*Bos* sp.), PCP has also been associated with decreased milk production, skin lesions, increased mastitis, persistent infections, reduced survival (Forsell et al. 1981), and in sheep, disrupted reproductive and metabolic hormones, and oviductal cysts (Rawlings et al. 1998).

Among sensitive species of mammals tested against PCP (Table 23.6), acute oral LD₅₀ values ranged from 27 to 300 mg/kg BW, but most values were between 55 and 150 mg/kg BW. Sublethal effects were noted at much lower concentrations than those causing death. They included elevated tissue residues at dietary intake equivalent to 0.05 mg/kg BW, or atmospheric concentrations >0.1 mg/m³; organ damage at 0.2 to 2.0 mg/kg BW; reproductive impairment at >1.25 mg/kg BW; and retarded growth and reproduction in animals fed rations containing >30 mg/kg (Table 23.6). PCP was responsible for the deaths of pipistrelle bats (*Pipistrellus pipistrellus*) roosting on PCP-treated wooden surfaces; PCP concentrations on the roosting structures were similar to those applied in remedial timber treatment (Shore et al. 1991).

Many commercial lots of technical PCP are known to contain small — but possibly biologically significant — amounts of highly toxic dioxins, dibenzofurans, and hexachlorobenzene. These contaminants may be responsible for most of the toxicity of technical PCP preparations (McConnell et al. 1980; Parker et al. 1980; Wollesen et al. 1986; Holsapple et al. 1987). However, both technical- and analytical-grade PCP can induce hepatic mixed-function oxidases in intoxicated rats and cattle. In cattle, this effect was observed in both calves and adults, and in hepatic as well as pulmonary microsomes, and seemed to be dose related (Shull et al. 1986).

Table 23.6 Effects of Pentachlorophenol on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
DOMESTIC CATTLE, <i>Bos taurus</i>	
Oral dose of 0.05 or 0.5 mg/kg BW	Maximal plasma values of 1.5 and 9.6 mg/L, respectively. Calves fed grain and hay from a PCP-treated feeder for 10 days contained plasma PCP levels of 1.1 mg/L, but levels returned to normal after access to feeder was denied (Osweiler et al. 1984)
Fed equivalent of 0.2 mg/kg BW daily for 75–84 days, then 2.0 mg/kg BW daily for 50 to 62 days	No effect on milk production, feed intake, body weight, lymphocyte function, or histopathology of spleen, thymus, or lymph nodes. Postmortem examination showed enlarged liver, lungs, kidneys, and adrenals; significant loss of renal function (Forsell et al. 1981; Kinzell et al. 1981)
Fed 0.2 mg/kg BW daily for 95 days, then given single oral dose of uniformly ring-labeled C ¹⁴ -PCP; analyzed 4 days postadministration	Highest residues were in liver, kidney, and lungs; in milk, fat fraction contained the greatest amount. Tb 1/2 for absorption was 4.3 h, and for elimination 43 h. Most excretion was by way of urine (76%), then milk and feces (5% each). In urine, PCP was present in the conjugated form (Kinzell et al. 1985)
Fed 20 mg technical-grade PCP/kg BW daily for 10 days, then 10 mg/kg BW for an additional 60 days	No clinical effects noted during the 70-day treatment or during a 165-day posttreatment period. Contaminants in PCP — including several dioxins and hexachlorobenzene — were found in milk, fat, and blood. PCP residues in whole milk rose to 4 mg/kg, but declined to <0.1 mg/kg within a few days after PCP cessation (Firestone et al. 1979)
Female yearling Holsteins fed technical- or analytical-grade PCP in diets at 20 mg/kg BW daily for 42 days (647 mg/kg diet), then 15 mg/kg BW daily for 118 days (491 mg/kg diet) 140 mg/kg BW	Technical-grade PCP was related to decreased body weight and feed conversion efficiency, anemia, enlarged liver and lungs, decreased thymus weight, and lesions in urinary bladder mucosa. Holsteins exposed to analytical grade PCP were comparable to controls. The toxicity of PCP in cattle seems to be due to its contamination with toxic impurities, especially dioxins (McConnell et al. 1980; Parker et al. 1980) Acute oral LD ₅₀ (Knudsen et al. 1974)
DOMESTIC DOG, <i>Canis familiaris</i>	
150–200 mg/kg BW	Acute oral LD ₅₀ (Knudsen et al. 1974)
GUINEA PIG, <i>Cavia porcellus</i>	
100 mg/kg BW	Acute oral LD ₅₀ (Choudhury et al. 1986)
HAMSTER, <i>Cricetus spp.</i>	
1.25–20 mg/kg BW	Fetal deaths and resorption (USEPA 1980)

Table 23.6 (continued) Effects of Pentachlorophenol on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
DOMESTIC CAT, <i>Felis domesticus</i>	
Pine wood shavings used as litter, containing 470 mg PCP/kg	Of 14 cats in contact with litter, 3 died and 8 became ill but recovered. Maximum PCP residues (mg/kg) in the dead cats were 20 in liver, 24 in kidney, and 10 in stomach contents (Peet et al. 1977)
HUMAN, <i>Homo sapiens</i>	
Humans exposed occupationally for 6.5 (0.3–26.3) years vs. reference population	No adverse health effects, although daily urinary PCP levels were increased in occupationally exposed population: 174 µg/L vs. 35 µg/L (USPHS 1994)
Average concentrations of 0.0012–0.18 mg/m ³ air for 3–34 years among occupationally exposed workers	PCP concentrations in blood of 20 workers ranged between 0.023 and 0.775 mg/L and were below the "biological tolerance value" of 1.0 mg/L; no effect on sister chromatid exchange or chromosomal aberrations (Ziemsen et al. 1987)
<0.02–>0.1 mg/L urine in occupationally exposed woodworkers	During a 16-day vacation and plant shutdown, urinary excretion accounted for 90% elimination in those with high initial PCP levels (i.e., >0.1 mg/L) to 67% elimination in those with initial urinary levels of 0.02–0.1 mg PCP/L, and to 34% reduction in workers with <0.02 mg/L; Tb 1/2 was estimated at 33 h in urine and 30 h in plasma (Kalmann and Horstman 1983)
Single oral dose of 0.1 mg/kg BW	In urine of four subjects, 74% was eliminated unchanged and 12% as PCP-glucuronide; 4% was eliminated in feces as PCP and PCP-glucuronide. A peak blood level of 0.25 µg/L was reached 4 h after dosing (USEPA 1980; USPHS 1994)
>1.0 mg/m ³ air	Painful irritation in upper respiratory tract, sneezing, and coughing in persons newly exposed to PCP; up to 2.4 mg/m ³ can be tolerated by conditioned individuals (USEPA 1980)
Total dose of 3.9–18.0 mg	Steady state attained in about 3 months; Tb 1/2 values of 20 days in whole body and about 17 days in urine and blood (Uhl et al. 1986)
Blood concentrations of chronically exposed workers	
>25 µg PCP/L	Increased frequency of female reproductive disorders (USPHS 1994)
>42 µg PCP/L	Increased frequency of menstrual dysfunction (USPHS 1994)
>73 µg PCP/L	Increased frequency of female infertility (USPHS 1994)
8–1130 mg/kg fresh weight tissue	Residues in tissues of 33-year-old male who died after working in chemical plant for 3 weeks; job involved breaking up large blocks of PCP with jackhammer. Before death, high body temperature and coma. After death, rigor mortis was profound and immediate. Postmortem examination showed cerebral edema, fatty degeneration of viscera, and PCP levels (mg/kg) of 8 in stomach contents, 29 in urine, 52 in liver, 116 in lung, 162 in blood, 639 in kidney, and 1130 in bile (Wood et al. 1983; Gray et al. 1985)
28–225 mg/kg fresh weight tissue	Residues associated with acute toxicosis and death were 28–123 in kidney, 50–176 in blood, and 62–225 in liver (USEPA 1980)
75–225 mg/kg fresh	Residues in tissues of PCP suicide victim were 75 in urine, 116 weight tissue in kidney, 173 in blood, and 225 in liver (USEPA 1980)
4000 mg/L solution	Immersion of hands for 10 min produced skin irritation (USEPA 1980)
RHESUS MONKEY, <i>Macaca mulatta</i>	
Radiolabeled [¹⁴ C]PCP given intravenously or dermally	Half-time persistence of 4.5 days regardless of route (Wester et al. 1993)
10 mg/kg BW, single oral dose	Residues highest in liver and GI tract; all other tissues contributed <4% of total body burden (USEPA 1980)
10 mg/kg BW, single oral dose	Tb 1/2 values in blood and urine were 41–72 h in males and 84–92 h in females (Braun and Sauerhoff 1976)
50 mg/kg BW, repeated 4 weeks later	During the first day after each dose, 20% was excreted into urine, 0.5% into feces, and 20% into bile. The addition of 4% cholestyramine to diets for 6 days resulted in increased fecal excretion by a factor of 18 and increased total body burden excretion by 1.4 times (Rozman et al. 1982)

Table 23.6 (continued) Effects of Pentachlorophenol on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
DOMESTIC MOUSE, <i>Mus</i> sp.	
Fed diet equivalent to 0.5 mg/kg BW daily for 6 weeks	Decreased antibody response (USPHS 1994)
Fed diets equivalent to 3 mg/kg BW daily for 24 months	No measurable effect in females, based on clinical chemistry, hematology, routine histopathology, and organ weight changes (USEPA 1980)
Fed diet equivalent to 6.5 mg/kg BW daily for 12 weeks	Hepatocellular swelling; enhanced susceptibility to tumor growth (USPHS 1994)
Fed diets equivalent to 10 mg/kg BW daily for 22 months	No measurable effect in males, based on clinical chemistry, hematology, routine histopathology, and organ weight changes (USEPA 1980)
15–37 mg/kg BW through ip or sc route	T _b 1/2 of about 24 h through urinary excretion (USEPA 1980)
Fed diet equivalent to 17.5 mg/kg BW daily for 2 years	Increased frequency of hepatocellular carcinoma (USPHS 1994)
Single oral dose of 15 mg/kg BW by iv injection or orally	Peak PCP concentration of 28 mg/L was measured in plasma 1.5 h after administration; half-time persistence of PCP was 5.2 h for iv injection and 5.8 h for oral route. PCP was primarily recovered in urine as conjugates, including the mutagen tetrahydroquinone (5%) and its conjugates (15%); sulfates accounted for >90% of the total conjugates (glucuronides and sulfates); only 8% of the PCP administered was excreted unchanged (Reigner et al. 1992b)
Fed diets containing 50 mg pure (99%) PCP/kg or technical grade (86%) for 10–12 weeks	Mice exposed to technical-grade PCP had enhanced tumor susceptibility (1.9 times) from transplanted tumors; mortality increased 2.4 times over controls after sarcoma virus inoculation. Mice exposed to pure PCP showed no enhanced growth of reduced tumors, but developed splenic tumors; 22% vs. none in controls (Kerkvliet et al. 1982)
Single ip injection of 59 mg/kg BW	LD50 (Reigner et al. 1992b)
Single dose of 65–252 mg/kg BW	Acute oral LD50; females more sensitive than males (Knudsen et al. 1974; Borzelleca et al. 1985; Choudhury et al. 1986; USPHS 1994)
Single oral dose of 15 mg/kg BW	Peak plasma concentration of 28 mg/L reached 1.5–2 h after administration (USPHS 1994)
WHITE RABBIT, <i>Oryctolagus cuniculus</i>	
1–3 mg/kg BW daily for 90 days administered orally	No signs of intoxication (USEPA 1980)
39 mg/kg BW	Lethal cutaneous dose administered in pine oil (Cote 1972)
60–200 mg/kg BW	Acute dermal lethal dose (USEPA 1980)
100–130 mg/kg BW	Acute oral LD50 (Knudsen et al. 1974; Choudhury et al. 1986)
350 mg/kg BW	Lethal cutaneous dose administered in olive oil (Cote 1972)
DOMESTIC SHEEP, <i>Ovis aries</i>	
Ewes given 2 mg/kg BW twice weekly for 43 days via oral route	By day 36, serum had significantly less thyroxine than controls and more insulin; significant increase in severity of oviductal epithelial cysts (Rawlings et al. 1998)
120 mg/kg BW	Acute oral LD50 (Knudsen et al. 1974)
PIPISTRELLE BAT, <i>Pipistrellus pipistrellus</i>	
Females roosting in contact with timbers treated with 5% PCP solutions	All bats introduced 6 weeks postapplication died in 3–7 days; those introduced 8 weeks postapplication died in 1–2 days; bats in contact with timbers 14 months postapplication died in 5–23 days (Racey and Swift 1986)
Adult females and weaned juveniles of both sexes held in outdoor flight enclosures; roost boxes treated with 69,300 mg PCP/kg and wood shavings contained 65,000 mg/kg FW	All dead within 24 h (90% survival in controls after 32 days). Carcasses of dead bats had 13.1 mg PCP/kg FW. Total PCP burden, in µg, ranged from 17–152 in whole body and 29–181 in fur. Maximum tissue concentrations, in µg/kg FW, were 99 in fat, 65 in liver, 25 in kidney, and 30 in remainder (Shore et al. 1991)

Table 23.6 (continued) Effects of Pentachlorophenol on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
LABORATORY WHITE RAT, <i>Rattus</i> sp.	
Dietary levels of 20, 100, and 500 mg/kg feed equivalent to 1.2, 6, and 30 mg/kg BW daily, respectively	No effect after exposure for 8 months to pure-grade PCP at doses of 20 and 100 mg/kg. Technical-grade PCP produced disruptions in liver enzyme activity in females at 20 and 100 mg/kg. At 500 mg/kg, body weight gain was reduced in both sexes and by both grades of PCP (USEPA 1980)
Diets containing 25, 50, or 200 mg PCP/kg, equivalent to 1.5, 3, and 12 mg/kg BW daily, respectively	After 12 weeks, no observable effect at 25 mg/kg diet; dose-related adverse effects on liver, kidney calcium deposits, and chemistry at higher dietary levels (Knudsen et al. 1974)
Single dose of 2.5 mg PCP/kg BW given orally or by iv injection	PCP clearance was essentially metabolic, with only 5.3% unchanged by the kidney. About 60% of the dose was recovered in urine mainly as conjugated PCP and conjugated tetrachlorohydroquinone. For both routes of administration, about 10% of the dose was recovered in feces as PCP and its metabolites, which indicates that biliary excretion contributes to total elimination (Reigner et al. 1991)
Dietary level of 50 mg/kg, equivalent to about 3 mg/kg BW daily	After 62 days, no observable effect on reproduction, neonatal growth, survival, or development. After 12 weeks, males had decreased hemoglobin and erythrocytes. After 2 years, no significant adverse effects on growth, survival, reproduction, or development (Schwetz et al. 1978; USEPA 1980; McConnell et al. 1980)
Single oral dose of 2.5 mg PCP/kg BW	Peak plasma concentration of 7.3 mg/L reached 1.5–2 h after administration (USPHS 1994)
5.0–5.8 mg/kg BW on days 6 to 15 of gestation	Delayed ossification of skull (USEPA 1980)
10 mg/kg BW	
10 or 100 mg/kg BW	After a single oral dose, 0.44% remained after 9 days; 82% of total residue was in kidney and liver, and lowest residues were in brain, spleen, and fat. A maximum residue of 45 mg/L was attained in blood plasma; the Tb 1/2 in plasma was 13–121 h (USEPA 1980)
Pregnant females given 75 mg PCP/kg BW daily by gavage on days 7–18 of gestation	After a single dose, elimination occurred by way of several routes: catabolism to tetrachlorohydroquinone; excretion of unchanged PCP and its glucuronide conjugate in urine; excretion of PCP or its metabolites into bile. More than 90% was eliminated during the rapid phase, the Tb 1/2 being 13–17 h (Braun et al. 1977)
Dietary levels of 200 mg/kg, equivalent to about 13 mg/kg BW daily	Decrease in mean fetal weight (USPHS 1994)
14 mg/m ³ air for 45 min	
15 mg/kg BW daily of purified PCP on days 6–15 of gestation	After 181 days, reduction in crown-rump length and increase in fetal skeletal variations (Welsh et al. 1987)
27–300 mg/kg BW	LC50 for sodium pentachlorophenate aerosols (USPHS 1994) No measurable effect on development (USEPA 1980)
Dietary levels equivalent to 25 mg/kg BW daily for 2 generations	Acute oral LD50 range. Lower values in tests when PCP dissolved in fuel oil, in weanling rats, and in adult rats; higher values in tests with juveniles and when immersion vehicle is peanut oil (Knudsen et al. 1974; McConnell et al. 1980; Borzelleca et al. 1985; Choudhury et al. 1986; St. Omer and Gadusek 1987; USPHS 1994)
Dietary levels equivalent to 30 mg/kg BW daily	Decrease in size of litter (USPHS 1994)
Dietary levels equivalent to 43 mg PCP/kg BW daily for 181 days	
50 mg/kg BW on days 6 to 15 of gestation	Decrease in neonatal survival and growth after 62 days. After 2 years, no evidence of carcinogenicity, but adverse effects on adult growth and serum enzyme activity levels (Schwetz et al. 1978)
60 mg/kg BW	Embryo deaths (USPHS 1994) 100% fetal resorption (USEPA 1980) Single dose on day 9 or 10 of gestation produced reduction in fetal weight; no effect when given on days 11, 12, or 13 (USEPA 1980)

Table 23.6 (continued) Effects of Pentachlorophenol on Selected Mammals

Organism, Dose, and Other Variables	Effects and Reference
120 mg/kg BW	Single dose results in early hepatic glycogen depletion and elevation in blood glucose (Nishimura 1984)
DOMESTIC PIG, <i>Sus</i> spp.	
5, 10, or 15 mg purified PCP/kg BW daily for 30 days	No effect on weight gain, food consumption, or kidney weight. Significantly enlarged liver in 10- and 15-mg/kg groups. Elevated PCP residues in all groups. Residues in 5-mg/kg group vs. controls, in mg/kg fresh weight, were: 78.1 vs. 0.7 for blood, 6.7 vs. 0.2 for muscle, 22.0 vs. 0.2 for kidney, and 28.9 vs. 0.5 for liver (Grechus et al. 1979)
27–55 mg/kg BW	Fatal chronic dose (Schipper 1961)
30 mg/kg BW daily for 7 days	Acute toxicosis (Grechus et al. 1979)
Pregnant swine in direct contact with lumber freshly treated with PCP	Extensive mortality in newborn swine (Schipper 1961)
EASTERN CHIPMUNK, <i>Tamias striatus</i>	
138 mg/kg BW	Acute oral LD50 (Ege 1985)
200 mg/kg BW	Acute oral LD100 (Ege 1985)
Fed diets containing 250 or 500 mg PCP/kg for 2 weeks	No increase in metabolic activity. Some weight loss due to food avoidance; enlarged livers (Ege 1985)

23.5 RECOMMENDATIONS

Commercial PCP preparations often contain variable amounts of chlorophenols, hexachlorobenzene, phenoxyphenols, dioxins, dibenzofurans, chlorinated diphenyl ethers, dihydroxybiphenyls, anisoles, catechols, and other chlorinated dibenzodioxin and dibenzofuran isomers. These contaminants contribute to the toxicity of PCP — sometimes significantly — although the full extent of their interactions with PCP and with each other in PCP formulations are unknown. Unless these contaminants are removed or sharply reduced in existing technical- and commercial-grade PCP formulations, efforts to establish sound PCP criteria for protection of natural resources may be hindered.

Proposed PCP ambient water quality criteria to protect freshwater and marine life range from 48 to 55 µg/L for acute effects, 3.2 to 34 µg/L for chronic effects, and daily mean concentrations of 6.2 µg/L, not to exceed 140 µg/L (Table 23.7). Available data, however, suggest that significant adverse effects occur at much lower PCP concentrations (i.e., between 0.035 and 19 µg/L). In rainbow trout (*Oncorhynchus mykiss*), for example, concentrations of 0.035 to 1.0 µg/L produced elevated tissue residues (Choudhury et al. 1986; McKim et al. 1986); 7.4 µg/L caused growth inhibition in 28 days (USEPA 1980), and 10 to 19 µg/L produced adverse effects and some deaths (Chapman and Shumway 1978; Dominguez and Chapman 1984). Other sensitive fish species include sockeye salmon (*Oncorhynchus nerka*), showing growth inhibition after prolonged exposure to 1.8 µg PCP/L (USEPA 1980; Choudhury et al. 1986); larvae of common carp (*Cyprinus carpio*), having an 96-h LC50 of 9.5 µg/L (Choudhury et al. 1986); and largemouth bass (*Micropterus salmoides*), exhibiting reduced food conversion efficiency at 10 µg/L (Johansen et al. 1987). Among sensitive species of plants and invertebrates, American oysters (*Crassostrea virginica*) have elevated tissue residues after exposure for 28 days to 2.5 µg/L (Schimmel et al. 1978); cladocerans have impaired reproduction at 4.1 µg/L (Hedtke et al. 1986); alga show chlorosis inhibition in 72 h at 7.5 µg/L (USEPA 1980); and estuarine macrobenthos populations decreased in abundance and species after exposure for 13 weeks to 15.8 µg/L (Tagatz et al. 1981). Also, an air concentration of 0.2 mg/m³ — a tolerable level to humans (Table 23.7) — interfered with photosynthesis in

duckweed, *Lemna minor* (Huber et al. 1982). As judged by these studies, it seems appropriate to suggest modification of certain aquatic PCP criteria. A maximum PCP concentration of 3.2 µg/L is indicated, and this level would probably protect most aquatic species, although it would not prevent accumulations and growth inhibition in salmonids or accumulations in oysters. Some downward modifications have been proposed (see [Table 23.7](#)). However, additional research is needed to establish sound water quality criteria for PCP, and also to interpret the significance of its residues and their metabolites in tissues of representative species.

Microorganisms and other bioremediation processes followed by hyperfiltration may be useful in removing PCP from groundwater and yielding a final effluent acceptable for discharge into the environment or into a municipal sewage treatment facility (Wall and Stratton 1991; Middaugh et al. 1994a). At present, diluted PCP-contaminated groundwater may be discharged into the sewerage collection system of Escambia County, Florida, provided that 1% solutions were not teratogenic or embryotoxic to embryos of the inland silverside (*Menidia beryllina*) or lethal to the daphnid (*Ceriodaphnia dubia*) (Middaugh et al. 1994b). More research is encouraged on the use of sentinel organisms to assess PCP water quality (Middaugh et al. 1994b).

Dietary concentrations of 1.0 mg/kg and higher produced diarrhea and liver histopathology in chickens (*Gallus* spp.) after 8 weeks (Stedman et al. 1980), and deaths occurred at relatively high dietary concentrations (i.e., 3850 mg/kg, in Japanese quail [*Coturnix japonica*] after 5 days) (Hill and Camardese 1986). Wood shavings contaminated with PCP produced elevated residues when used as litter for domestic chickens (Newsome et al. 1984), and death in canaries (*Serinus canarius*), when used as nesting materials (Dorresteijn and Zelle 1979). Tissue residues >2 mg/kg fresh weight are considered to be indicative of significant environmental PCP contamination, and those >11 mg/kg fresh weight were associated with birds that died or were recovering from PCP exposure ([Table 23.7](#)) (Vermeer et al. 1974). No data are currently available on avian wildlife and PCP contamination in their diets, residues in their tissues, or frequency of use of PCP-contaminated wood shavings for nesting materials and other purposes.

As judged by studies with domestic and small laboratory mammals, no observable adverse effects have been noted at dietary levels equivalent to 3 to 10 mg PCP/kg BW ([Table 23.7](#)). Variability is great among species, however, and adverse effects have been documented in some species ([Table 23.7](#)) at doses as low as 0.05 to 0.2 mg/kg BW (elevated tissue residues), 0.2 to 2.0 mg/kg BW or 50 mg/kg diet (histopathology, reproductive impairment, increased tumor frequency), and 55 to 60 mg/kg BW (death). Based on guidelines for carcinogen risk assessment and inadequate evidence for animal carcinogenicity or absence of human cancer data, PCP is classified as group D, meaning that it is *not* classified as a human carcinogen (Choudhury et al. 1986). More research is recommended on the genotoxic and carcinogenic potential of PCP and its metabolites, with special reference to tetrachlorohydroquinone (WHO 1987; Jansson and Jansson 1992; USPHS 1994).

Data for humans show that adverse effects occur at concentrations in air >1.0 mg PCP/m³ and in tissues at more than 8 mg/kg fresh weight ([Table 23.7](#)). No adverse effects were noted at daily intakes of 2.1 mg per 70-kg adult or 30 µg/kg BW, up to 1.01 mg/L in drinking water, <0.5 mg/m³ in air, <0.5 mg/L in blood plasma, and <1.0 mg/L in blood ([Table 23.7](#)). It is noteworthy that the recommended PCP air concentration of 0.5 mg/m³ results in a daily intake of 2.5 to 3.8 mg (based on 15 to 23 m³ of air inhaled daily, 8-h exposure), equivalent to 42 to 63 µg/kg BW for a 60-kg female. These levels are higher than the currently recommended no-adverse-effect level of 30 µg/kg BW daily ([Table 23.7](#)), and overlap or exceed the 58 to 74 µg/kg BW daily range — a level recommended by Williams (1982). Air concentrations >1.0 mg PCP/m³ can produce respiratory irritation in unacclimatized individuals, but concentrations as high as 2.4 mg/m³ can be tolerated by conditioned individuals (USEPA 1980). The biological tolerance value of <1000 µg PCP/L in blood, recommended by Ziems et al. (1987), is based on occupational air exposure studies: exposure to maximum average air concentrations of 0.18 mg PCP/m³ for up to 34 years produced blood PCP residues of 23 to 775 µg/L, with no measurable adverse effects. The authors concluded

that PCP and its impurities in occupationally relevant concentrations below the maximum concentration in the workplace and below the biological tolerance value do not produce genotoxic damage that can be detected on the chromosomal level, either *in vivo* or *in vitro*.

The human taste threshold for PCP in drinking water is about 30 µg/L (USEPA 1980), a level far below the upper safe limit of 1.01 mg/L and near the no-observable-effect level of 21 µg/L (Table 23.7). Odor detection is not as sensitive as taste: the odor threshold for PCP ranges from about 857 µg/L at 30°C, to 1600 µg/L at 20 to 22°C, to 12,000 µg/L at 60°C (USEPA 1980). It is not clear whether the determined organoleptic threshold values made the water undesirable or unfit for consumption (USEPA 1980). If fish and wildlife species of concern have PCP organoleptic thresholds that are similar to those of humans, or lower, will they too avoid contaminated habitats or diets?

Data for PCP and terrestrial wildlife are incomplete and — in view of the large interspecies variations in sensitivity — need to be collected. Research is needed on reproductive effects in animals following inhalation exposure to PCP; additional acute and intermediate toxicity testing; chronic duration exposure studies on cancer induction, genotoxicity, and immunotoxicity; and the development of alternate biomarkers of PCP exposure and antidotes (WHO 1987; USPHS 1994). Until the results of these studies become available, it seems reasonable to apply to wildlife the same levels recommended for human health protection.

Table 23.7 Proposed Pentachlorophenol Criteria for the Protection of Natural Resources and Human Health

Resource and Criterion	Concentration or Dose	Reference ^a
AQUATIC BIOTA		
Freshwater life		
Acute (former)	48 to <55 µg/L	1–3
Chronic (former)	<3.2 µg/L	1
24-h mean (former)	<6.2 µg/L	2
Current		
pH 6.5	4-day mean concentration not to exceed 3.5 µg/L more than once every 3 years and 1-h mean concentration does not exceed 5.5 µg/L ^e	28
pH 7.8	4-day mean concentration not to exceed 13.0 µg/L more than once every 3 years and 1-h mean concentration does not exceed 20 µg/L ^e	28
pH 9.0	4-day mean concentration not to exceed 43.0 µg/L more than once every 3 years and 1-h mean concentration does not exceed 68 µg/L	28
Maximum concentration		
Fish	<140 µg/L	2
Warmwater species	10 to <15 µg/L	4
Coldwater species	20 to <40 µg/L	4
Saltwater life		
Acute (former)	<53 µg/L	1
Chronic (former)	<34 µg/L	1, 5
Current	4-day mean concentration not to exceed 7.9 µg PCP/L more than once every 3 years, and 1-h concentration does not exceed 13.0 µg/L more than once every 3 years	28
BIRDS		
Tissue residues		
Contaminated	>2 mg/kg fresh weight	6
Life-threatening	>11 mg/kg fresh weight	6
Diets		
Adverse effects	>1.0 mg/kg diet	7
Fatal	>3850 mg/kg diet	8

Table 23.7 (continued) Proposed Pentachlorophenol Criteria for the Protection of Natural Resources and Human Health

Resource and Criterion	Concentration or Dose	Reference ^a
Wood shavings		
Litter	<134 mg/kg	9
Nesting materials	<285 mg/kg	10
LIVESTOCK AND LABORATORY MAMMALS		
No measurable adverse effects		
Rat		
Females	3 mg/kg BW daily for 24 months	1, 11
Males	10 mg/kg BW daily for 22 months	1, 11
Rabbit	3 mg/kg BW daily for 90 days	1
Adverse effects		
Elevated tissue residues, cattle		
Blood plasma	0.05 mg/kg BW, single dose	12
Internal organs	0.2 mg/kg BW for 95 days	13
Histopathology, cattle		
Internal organs	0.2 mg/kg BW daily for about 80 days, then 2.0 mg/kg BW daily for about 59 days	14, 15
Internal organs	50 mg/kg diet for 12 weeks, equivalent to 3 mg/kg BW daily	16
Reproductive impairment		
Hamster	1.25–20 mg/kg BW, single dose	1
Rat	5 mg/kg BW daily or 50 mg/kg diet daily, chronic	5
Rat	5–5.8 mg/kg BW daily	1, 17
Increased tumor frequency		
Mice	50 mg/kg diet, chronic	18
Death, various species		
Acute oral LD50	55–200 mg/kg BW	5, 16, 19, 20
Acute dermal LD50	60–200 mg/kg BW	1
Contaminated wood shavings, dermal contact	470 mg/kg	21
HUMAN HEALTH		
Current exposure levels, 70-kg adult		
Food	15 µg daily, or 0.21 µg/kg BW daily	1
Water	0.12 µg daily, or 1.7 µg/kg BW daily	1
No-adverse-effect levels		
Food, upper safe limit, 70-kg adult	30 µg/kg BW, or 2.1 mg per person	1
Wood, in contact with food	Up to 50 mg/kg	1
Drinking water		
Recommended	<0.021 mg/L ^b	1, 5, 22
Global proposed	<0.01 mg/L	27, 29
Upper safe limit	1.01 mg/L	1
Arizona	<0.2 mg/L	27
California	<0.03 mg/L	27
Kansas, Montana	<0.22 mg/L	27
Maine	<0.006 mg/L	27
New York	<0.021 mg/L	27
Air, 8 h exposure daily, 5 days weekly	<0.5 mg/m ³	1, 5, 23, 24, 27
Blood	<1.0 mg/L	25
Blood, normal	<0.1 mg/L	27
Blood plasma	<0.5 mg/L	24, 27
Total intake	<3 µg/kg BW daily ^c	22
Total intake, 70-kg adult	<30 µg/kg BW daily or 2.1 mg daily ^d	5
Expectant mothers	No safe level established to guard against fetal toxicity	17

Table 23.7 (continued) Proposed Pentachlorophenol Criteria for the Protection of Natural Resources and Human Health

Resource and Criterion	Concentration or Dose	Reference ^a
Adverse effect levels		
Air	>1.0 mg/m ³	1
Dermal solutions	4000 mg/L	1
Tissue residues associated with acute toxicosis		
Kidney	>28 mg/kg FW	1
Blood	>40–80 mg/L	1, 23
Liver	>62 mg/kg FW	1
Tissue residues associated with death		
Stomach contents	8 mg/kg FW	24, 26
Urine	29–75 mg/L	1, 24, 26
Liver	52–225 mg/kg FW	1, 24, 26
Lung	116 mg/kg FW	24, 26
Blood	162–176 mg/L	1, 24, 26
Kidney	116–639 mg/kg FW	1, 24, 26
Bile	1130 mg/kg FW	24, 26
Effluent discharges to water		
New York	<0.021 mg/L	27
Wisconsin	<0.000001 mg/L	27

^a 1, USEPA 1980; 2, Zischke et al. 1985; 3, Johansen et al. 1987; 4, Hodson and Blunt 1981; 5, Choudhury et al. 1986; 6, Vermeer et al. 1974; 7, Stedman et al. 1980; 8, Hill and Camardese 1986; 9, Newsome et al. 1974; 10, Dorrestein and Zelle 1979; 11, Schwetz et al. 1978; 12, Osweiler et al. 1984; 13, Kinzell et al. 1985; 14, Forsell et al. 1981; 15, Kinzell et al. 1981; 16, Knudsen et al. 1974; 17, Williams 1982; 18, Kerkvliet et al. 1982; 19, Schlipper 1961; 20, Ege 1985; 21, Peet et al. 1977; 22, Lu et al. 1978; 23, Cote 1972; 24, Wood et al. 1983; 25, Ziemsen et al. 1987; 26, Gray et al. 1985; 27, USPHS 1994; 28, USEPA 1986; 29, WHO 1987.

^b Based on no-observable-adverse-effect level of 3 mg/kg BW daily in rat study, uncertainty factor of 1000 and water consumption of 2 L daily.

^c Based on animal data and uncertainty factor of 1000.

^d Based on rat chronic oral no-observable-effect level of 3 mg/kg BW daily and uncertainty factor of 100.

^e At pH 6.6, a water concentration of 1.74 µg PCP/L caused a 50% reduction in growth of yearling sockeye salmon in an 8-week test (USEPA 1986).

23.6 SUMMARY

Pentachlorophenol (PCP) is a synthetic organochlorine compound that was first manufactured commercially in 1936 and is now used primarily as a wood preservative and secondarily as an herbicide, insecticide, fungicide, molluscicide, and bactericide. Current global production of PCP is estimated to be 50 million kg annually. Widespread use of PCP has resulted in the detection of residues in air, rain, snow, groundwater, surface water, drinking water, fish, and aquatic invertebrates, as well as in human urine, blood, and milk. Pentachlorophenol may be incorporated into animal tissues through inhalation, diet, or contact; its toxic action results from its ability to interfere with the production of high-energy phosphate compounds essential for cell respiration. Pentachlorophenol has caused numerous occupational illnesses and deaths, and has had significant adverse effects on domestic animals. It is fetotoxic and teratogenic, but evidence for mutagenicity and carcinogenicity is incomplete or negative. Commercial PCP preparations often contain variable amounts of toxic impurities — including chlorophenols, hexachlorobenzene, phenoxyphenols, dioxins, and dibenzofurans — that contribute to its toxicity. Pentachlorophenol is rapidly accumulated and rapidly excreted, and has little tendency to persist in living organisms; it is readily degraded in the environment by chemical, microbiological, and photochemical processes.

In sensitive aquatic species, PCP adversely affected growth, survival, and reproduction at media concentrations of 8 to 80 µg PCP/L in algae and higher plants, at 3 to 100 µg/L in invertebrates,

and <1 to 68 µg/L in fish. In birds, PCP was fatal at 380 to 580 mg/kg body weight (BW) in oral doses, >3580 mg/kg in the diet, and >285 mg/kg in contaminated nesting materials (i.e., wood shavings). Residues >11 mg PCP/kg fresh weight in bird tissues were associated with acute toxicosis. Adverse sublethal effects in birds were noted at dietary levels as low as 1 mg/kg ration. In small laboratory mammals and domestic livestock, acute oral LD₅₀ values ranged from 27 to 300 mg/kg BW. Tissue residues in mammals were elevated at PCP doses as low as 0.05 mg/kg BW, and at air levels >0.1 mg/m³. Histopathology, reproductive impairment, growth retardation, and other effects were evident in sensitive mammals at PCP concentrations of 0.2 to 1.25 mg/kg BW, and at dietary levels >30 mg/kg ration.

Pentachlorophenol is an undesirable pollutant whose use patterns should be carefully regulated to avoid contamination of soil, water, and food. Recommendations for protection of sensitive fishery and wildlife resources follow; however, it is emphasized that some of these recommendations are markedly lower than those proposed by regulatory agencies. For protection of aquatic life, it is recommended that the PCP water concentration not exceed 3.2 µg/L; but even at this level, certain species of fishes and oysters accumulate enough of the toxicant to retard their growth. In birds, dietary concentrations greater than 1.0 mg/kg feed and tissue residues greater than 2.0 mg/kg fresh weight should be viewed as presumptive evidence of significant environmental PCP contamination. Data are scarce for PCP and mammalian wildlife; until more data are collected, PCP levels recommended for human health protection (i.e., “no adverse effects” levels) are suggested as reasonable substitutes. In humans, no adverse effects were noted at daily PCP intakes equivalent to 39 µg/kg BW in food, or at concentrations of 21 µg/L in drinking water, 0.5 mg/m³ in air, 0.5 mg/L in blood plasma, and 1.0 mg/L in blood.

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CHAPTER 24

Polychlorinated Biphenyls

24.1 INTRODUCTION

Polychlorinated biphenyls (PCBs), a group of 209 synthetic halogenated aromatic hydrocarbons, are used extensively in the electricity generating industry as insulating or cooling agents in transformers and capacitors. Because of human activities and the chemical characteristics of the products, PCBs are now distributed worldwide, and measurable concentrations occur in aquatic organisms and wildlife from North America, Europe, the United Kingdom, and the Atlantic and Pacific Oceans. PCBs elicit a variety of effects, including death, birth defects, reproductive failure, liver damage, tumors, and a wasting syndrome. They bioaccumulate and biomagnify in the food chain. Legislation has prohibited virtually all uses of PCBs and their manufacture in the United States since 1979; the ban has been accompanied by declines in PCB residues in fishes and wildlife. But the current environmental burden of PCBs in water, sediments, disposal sites, deployed transformers, and other PCB containers — now estimated at more than 374 million kg, much of it localized — continues to represent a potential hazard to associated natural resources (Pal et al. 1980; Eisler 1986; Hansen 1987; Parkinson and Safe 1987; Safe 1987a, 1990, 1994; Huckins et al. 1988; Tanabe 1988; Skaare et al. 1991; U.S. Public Health Service [USPHS] 1995; Eisler and Belisle 1996; Hoffman et al. 1996a; Niimi 1996).

24.2 SOURCES AND USES

The Monsanto Industrial Chemical Company, the principal domestic manufacturer of PCBs, began PCB production in 1929; commercial mixtures of PCBs were also produced in Western Europe and Japan. PCBs have been used in dielectric fluids; in waxes for metal castings; as heat transfer agents; as plasticizers in paints, coatings, and carbonless copy paper; in cutting oils; in sealants and caulking compounds; and as pesticide extenders (Eisler 1986). The use of PCBs was curtailed in the United States in 1971, and sales were limited to manufacturers of capacitors and transformers; all new uses were banned in 1976 (U.S. National Oceanic and Atmospheric Administration [NOAA] 1991). In 1977, all production of PCBs was halted, and no shipments were made after October. Direct and indirect sources of PCB contamination may include aerial transport of combustion products, vaporization from continental and marine areas, current and historic industrial and municipal waste discharges, precipitation, land runoff, concealed dumping, transformer fires, and accidental spills (NOAA 1991; U.S. Environmental Protection Agency [USEPA] 1992a).

The ubiquity of PCBs is indicated by their presence in environmental samples from the polar regions of air, snow, ice, water, and in living organisms (Norstrom et al. 1988; Hargrave et al. 1989; Larsson et al. 1992; Tanabe et al. 1993). The presence of PCBs in such remote areas suggests the importance of atmospheric transport. The Committee on the Assessment of Polychlorinated Biphenyls

in the Environment estimated that 50 to 80% of the PCBs derived from the United States were now in sediments and waters of the north Atlantic Ocean (National Academy of Sciences [NAS] 1979). Of the estimated total world PCB production of 1.2 million tons to date, about 374,000 tons are now in various portions of the terrestrial, coastal, and open ocean ecospheres (Table 24.1). Another 783,000 tons are still in use in electrical equipment and other products or deposited in landfills and dumps (Tanabe 1988) and represent a potential source of environmental contamination. An additional 43,000 tons have been degraded or incinerated (Tanabe 1988). Long-range atmospheric and oceanic transport seem to be the primary mechanisms of global PCB dispersal (Kannan et al. 1989).

Table 24.1 Estimated PCB Loads in the Global Environment

Ecosystem	PCB Loads (metric tons)
TERRESTRIAL AND COASTAL	
Air	500
River and lakewater	3500
Seawater	2400
Soil	2400
Sediment	130,000
Biota	4300
OPEN OCEAN	
Air	790
Seawater	230,000
Sediment	110
Biota	270
TOTAL	374,000

Data from Tanabe, S. 1988. PCB problems in the future: foresight from current knowledge. *Environ. Pollut.* 50:5-28.

24.3 CHEMICAL AND BIOCHEMICAL PROPERTIES

24.3.1 General

Polychlorinated biphenyls, a highly lipophilic group of global pollutants, consist of 209 congeners (Figure 24.1) with widely different toxicity and other biological effects (Kannan et al. 1989). In vertebrates, toxicological effects of PCBs have been related to their ability to induce the cytochrome P-450-dependent monooxygenase system (P-450). This varies with the degree of chlorination and the arrangement of chlorine atoms on the biphenyl molecule (Skaare et al. 1991). Transformation of PCBs to hydroxylated metabolites by the cytochrome P-450 system is the major pathway of PCB metabolism (Sipes and Schnellmann 1987) and occurs mainly in the liver. The rate of cytochrome P-450-catalyzed hydroxylation of PCBs decreases as the number of chlorine atoms increases and as the number of unsubstituted adjacent carbon atoms decreases. Some animals metabolize PCBs at different rates, and this is related in part to differences in the basal level of particular isozymes of cytochrome P-450 present in liver. For example, the dog eliminates PCBs more rapidly than other species because it has higher levels of a constitutive isozyme of cytochrome P-450 with activity toward the slowly metabolized, bioaccumulated 2,2',4,4',5,4'-hexachlorobi-

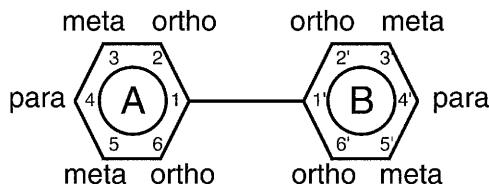


Figure 24.1 Structure of biphenyl. (Modified from National Academy of Sciences 1979; USEPA 1980; Safe 1984, 1994; Eisler 1986.) Polychlorinated biphenyls (PCBs) are commercially produced by chlorination of a biphenyl with anhydrous chlorine in the presence of iron filings or ferric chloride as the catalyst. Depending on the conditions under which chlorination occurred, the purified product is a complex mixture of chlorobiphenyls containing 18 to 79% chlorine. Ten possible degrees of chlorination of the biphenyl group produce 10 PCB congener groups: mono-, di-, tri-, tetra-, penta-, hexa-, hepta-, octa-, nona-, and decachlorobiphenyl. Within any congener group, a number of positional isomers are possible. For example, the tetrachlorobiphenyl group consists of 30 possible isomers, and the pentachlorobiphenyl congener group contains 46 possible isomers. Not all of the 209 possible isomers are likely to be formed during the manufacturing process. In general, the most common PCB isomers formed have either an equal number of chlorine atoms on both rings, or a difference of one chlorine atom between rings. Chlorine substitution is favored at the *ortho*- and *para*-positions; however, commercial products are complex mixtures of isomers and congeners with no apparent positional preference for halogen substitution.

phenyl (Hansen 1987; Sipes and Schnellmann 1987). The reactive arene oxides formed during biotransformation can bind covalently to tissue macromolecules or conjugate with glutathione. Derivatives of glutathione conjugates and glucuronides of the hydroxylated products are major PCB metabolites. Biotransformation of xenobiotics by cytochrome P-450 is not always beneficial to the organism because metabolites can be more toxic or biologically active than the parent compound (Parkinson and Safe 1987). The carcinogenic effect of certain xenobiotics depends on the conversion by cytochrome P-450 to a reactive carcinogenic metabolite (Parkinson and Safe 1987). In general, PCB metabolites are less toxic than their parent compounds, although hydroxylated metabolites of 3,3',4,4'-tetrachlorobiphenyl can disrupt thyroxine levels and serum transport of Vitamin A in rodents (Klasson-Wehler et al. 1998). Hydroxylated metabolites and methylsulfonyl metabolites of PCBs were found in plasma and liver of the Laysan albatross (*Diomedea immutabilis*) and the black-footed albatross (*Diomedea nigripes*). Total concentrations of hydroxylated metabolites accounted for 20 to 100% of the total PCBs, but methylsulfonyl metabolites accounted for only 0.004% of the total PCBs (Klasson-Wehler et al. 1998). Metabolites and possible degradation pathways of selected PCBs in mammals are presented in detail by Sipes and Schnellmann (1987).

Sedimentation and volatilization are the dominant processes that determine the fate of PCBs in lakes. Both processes remove PCBs from the water, but the relative importance of the transferred amount is influenced by particulate dissolved-phase partitioning that determines the relative size of the particulate pool for sedimentation and the soluble pool for volatilization of PCBs (Millard et al. 1993). PCB-contaminated sediments from the St. Lawrence River (300 mg total PCBs/kg DW sediment) dechlorinated rapidly (36% loss during the first 4 months) under laboratory incubations over a 39-month period, and more slowly afterwards (Sokol et al. 1998). High productivity of algae increased the proportion of added PCBs that is absorbed to particulate matter and sedimented. In general, PCB volatilization losses increase under conditions of high mixing and low productivity (Millard et al. 1993). Volatilization of mono-, di-, and trichlorobiphenyls from Aroclor 1248-contaminated sediments occurs at ambient environmental conditions with volatilization enhanced by microbial reductive dechlorination (Bushart et al. 1998). Aroclor 1242 and 1254 were anaerobically dechlorinated by microorganisms eluted from PCB-contaminated sediments. Dechlorination occurred mainly from the *meta*-position and suggests that dioxin-like toxicities of PCB mixtures are markedly reduced by microbial reductive dechlorination (Quensen et al. 1998).

24.3.2 Physical Properties

Mullin et al. (1984) synthesized and determined the retention times and response factors relative to a reference standard (octachloronaphthalene) of all 209 congeners (Table 24.2) by using temperature-programmed, high-resolution gas chromatography, and electron-capture detection methods (HRGC/ECD). The relative retention times (the ratio of congener retention time/reference standard retention time) of 187 of the 209 congeners differed and permitted HRGC column identification contingent on full or partial separation. Eleven congener pairs had the same retention times and coeluted: 60/56, 70/76, 94/61, 95/80, 133/122, 140/139, 144/135, 145/81, 163/160, 202/171, and 203/196. Of the 209 congeners, 20 can assume a planar configuration (Creaser and Al-Haddad 1989) because of the absence of chlorine substitution in the *ortho*-positions (Hong et al. 1992) (Figure 24.1). Approximately 1% of the non-*ortho*-substituted biphenyl molecules adopt the planar configuration (Safe 1987a). Among the isomers of each homolog, the planar PCBs had the longest retention times. The presence of *ortho*-chloro-substituents reduces planarity of the rings. However, congeners with 1 or 2 *ortho*-chlorines can also assume a planar ring position (Safe 1990). Although peak resolution is greatly improved by substitution of high-resolution capillary columns for packed columns, more than one candidate congener may occur at many GC peaks. Using a narrow bore column, Duinker et al. (1988a) found only 17 PCB congeners that were fully separated without potential interference from coeluting congeners.

The transport and fate of PCBs in aquatic systems and their partitioning between sediment, water, and organisms depends largely on sorption reactions. In soils, the sorption and retention of PCB congeners is influenced by the number of chlorine atoms in the molecule, and the more highly chlorinated PCBs tend to be more strongly bound. Relative sorption capacity and other properties of congeners also depend on PCB configuration. The soil sorption capacities of PCB congeners and their bioconcentration factors were related to octanol/water partition coefficients (Connor 1984) as follows:

$$K_{ow} = C_{ow}/C_{wo}$$

where K_{ow} is the octanol/water partition coefficient, C_{ow} the concentration of the solute in octanol saturated with water, and C_{wo} the concentration of the solute in water saturated with octanol.

K_{ow} values are used to estimate bioconcentration factors (bioaccumulation after uptake from water), soil and sediment organic carbon/water partition coefficients, toxicities, and aqueous solubilities (Woodburn et al. 1987; Hawker and Connell 1988). Techniques for measuring the K_{ow} values include the shake-flask method (Shiu and Mackay 1986), the reverse-phase thin-layer chromatography (Bruggeman et al. 1982), reverse-phase high-performance liquid chromatography (Rapaport and Eisenreich 1984), and the generator column technique (Woodburn et al. 1987; Hawker and Connell 1988), or it can be calculated by an estimation technique based on correlation with properties of compounds with known K_{ow} values. From a strong linear relation calculated between known log K_{ow} values and calculated total surface areas (TSA; correlation coefficient of 0.951 for 30 congeners), Hawker and Connell (1988) estimated K_{ow} values of individual congeners from the calculated TSA. Estimated K_{ow} values (Table 24.2) were previously unavailable for many PCB congeners, including toxic non-*ortho*-substituted congeners found only in relatively small amounts in commercial Aroclors. Reported K_{ow} values of some congeners vary in the literature and may not be comparable when different measuring techniques are used. Reverse-phase thin-layer chromatography (RP-TLC) and high-performance liquid chromatography (RP-HPLC) require empirical correction factors. Discrepancies in K_{ow} values between the generator column and RP-HPLC techniques for *ortho*-PCBs relative to the other PCBs were resolved with an *ortho*-correction factor (Woodburn et al. 1987). Nonplanarity of the *ortho*-substituted PCBs may reduce the ability of the solute to interact with the stationary phase in RP-TLC (Bruggeman et al. 1982). Despite these uncertainties, the K_{ow} is routinely used in hazard evaluation and risk assessment of most organic chemicals.

Table 24.2 Polychlorinated Biphenyls: Structure, Retention Times, Response Factors, and Octanol/Water Partition Coefficients ($\log K_{ow}$)

Isomeric Group and PCB Number	Structure (chlorine-filled)	Relative Retention Time ^a	Relative Response Factor ^b	Log K_{ow}^c
MONOCHLOROBIPHENYLS				
1	2	0.0997	0.0251	4.601
2	3	0.1544	0.0393	4.421
3	4	0.1937	0.04	4.401
DICHLOROBIPHENYLS				
4	2,2'	0.2245	0.0374	5.023
5	2,3	0.2785	0.119	— ^d
6	2,3'	0.2709	0.38	5.021
7	2,4	0.2566	0.69	5.15
8	2,4'	0.2783	0.206	5.301
9	2,5	0.257	0.388	5.18
10	2,6	0.2243	0.262	5.311
11	3,3'	0.3238	0.0449	5.343
12	3,4	0.3298	0.179	5.295
13	3,4'	0.3315	0.2	— ^d
14	3,5	0.2373	0.3047	5.404
15	4,4'	0.3387	0.107	5.335
TRICHLOROBIPHENYLS				
16	2,2',3	0.3625	0.447	5.311
17	2,2',4	0.3398	0.412	5.761
18	2,2',5	0.3378	0.313	5.551
19	2,2',6	0.3045	0.3037	5.481
20	2,3,3'	0.417	0.7238	5.577
21	2,3,4	0.4135	1.0598	5.517
22	2,3,4'	0.4267	1.0935	5.421
23	2,3,5	0.377	0.5	5.577
24	2,3,6	0.3508	0.793	5.671
25	2,3',4	0.3937	0.5	5.677
26	2,3',5	0.3911	0.603	5.667
27	2,3',6	0.3521	0.495	5.447
28	2,4,4'	0.4031	0.854	5.691
29	2,4,5	0.382	0.6339	5.743
30	2,4,6	0.3165	0.8202	5.504
31	2,4',5	0.4094	0.562	5.677
32	2,4',6	0.3636	0.278	5.751
33	2',3,4	0.4163	0.447	5.572
34	2',3,5	0.3782	0.6092	5.667
35	3,3',4	0.4738	0.3746	5.827
36	3,3',5	0.4375	0.2948	4.151
37	3,4,4'	0.4858	0.58	4.941
38	3,4,5	0.5102	0.722	5.767
39	3,4',5	0.4488	0.347	5.897
TETRACHLOROBIPHENYLS				
40	2,2',3,3'	0.5102	0.722	5.561
41	2,2',3,4	0.499	0.5469	6.111
42	2,2',3,4'	0.487	0.792	5.767
43	2,2',3,5	0.4587	0.503	5.757
44	2,2',3,5'	0.4832	0.524	5.811
45	2,2',3,6	0.4334	0.54	5.537
46	2,2',3,6'	0.445	0.468	5.537

Table 24.2 (continued) Polychlorinated Biphenyls: Structure, Retention Times, Response Factors, and Octanol/Water Partition Coefficients ($\log K_{ow}$)

Isomeric Group and PCB Number	Structure (chlorine-filled)	Relative Retention Time ^a	Relative Response Factor ^b	$\log K_{ow}^c$
47	2,2',4,4'	0.4639	0.848	6.291
48	2,2'4,5	0.4651	0.556	5.787
49	2,2',4,5'	0.461	0.648	6.221
50	2,2',4,6	0.4007	0.6817	5.637
51	2,2',4,6'	0.4242	0.6	5.637
52	2,2',5,5'	0.4557	0.418	6.091
53	2,2',5,6'	0.4187	0.3606	5.627
54	2,2',6,6'	0.38	0.3643	5.904
55	2,3,3',4	0.5562	0.829	6.117
56	2,3,3',4'	0.5676	0.829	6.117
57	2,3,3',5	0.5515	0.6	6.177
58	2,3,3',5'	0.5267	0.609	6.177
59	2,3,3',6	0.486	0.6	5.957
60	2,3,4,4'	0.5676	1.0164	5.452
61	2,3,4,5	0.5331	1.2227	5.943
62	2,3,4,6	0.4685	1.1478	5.897
63	2,3,4',5	0.529	0.728	6.177
64	2,3,4',6	0.4999	0.607	5.957
65	2,3,5,6	0.4671	0.8408	5.867
66	2,3',4,4'	0.5447	0.646	5.452
67	2,3',4,5	0.5214	0.6	6.207
68	2,3',4,5'	0.504	0.726	6.267
69	2,3',4,6	0.451	0.8024	6.047
70	2,3',4',5	0.5407	0.658	6.231
71	2,3',4',6	0.4989	0.468	5.987
72	2,3',5,5'	0.4984	0.5515	6.267
73	2,3',5',6	0.4554	0.5805	6.047
74	2,4,4',5	0.5341	0.671	6.671
75	2,4,4',6	0.4643	0.6461	6.057
76	2',3,4,5	0.5408	0.5795	6.137
77	3,3',4,4'	0.6295	0.3812	6.523
78	3,3',4,5	0.6024	1.1151	6.357
79	3,3',4,5'	0.5894	0.881	6.427
80	3,3',5,5'	0.5464	0.7278	6.583
81	3,4,4',5	0.6149	0.7159	6.367

PENTACHLOROBIPHENYLS

82	2,2',3,3',4	0.6453	0.773	6.142
83	2,2',3,3',5	0.6029	0.6339	6.267
84	2,2',3,3',6	0.5744	0.386	6.041
85	2,2',3,4,4'	0.6224	0.7396	6.611
86	2,2',3,4,5	0.6105	0.7968	6.204
87	2,2',3,4,5'	0.6175	1.021	6.371
88	2,2',3,4,6	0.5486	0.6892	7.516
89	2,2',3,4,6'	0.5779	0.561	6.077
90	2,2',3,4',5	0.5814	0.611	6.367
91	2,2',3,4',6	0.5549	0.571	6.137
92	2,2',3,5,5'	0.5742	0.5375	6.357
93	2,2',3,5,6	0.5437	0.6676	6.047
94	2,2',3,5,6'	0.5331	0.4514	6.137
95	2,2',3,5',6	0.5464	0.443	6.137
96	2,2',3,6,6	0.5057	0.4308	5.717
97	2,2',3,4,5	0.61	0.631	6.671

Table 24.2 (continued) Polychlorinated Biphenyls: Structure, Retention Times, Response Factors, and Octanol/Water Partition Coefficients ($\log K_{ow}$)

Isomeric Group and PCB Number	Structure (chlorine-filled)	Relative Retention Time ^a	Relative Response Factor ^b	$\log K_{ow}^c$
98	2,2',3',4,6	0.5415	0.6246	6.137
99	2,2',4,4',5	0.588	0.613	7.211
100	2,2',4,4',6	0.5212	0.5871	6.237
101	2,2',4,5,5'	0.5816	0.668	7.071
102	2,2',4,5,6'	0.5431	0.4561	6.167
103	2,2',4,5',6	0.5142	0.6068	6.227
104	2,2',4,6,6	0.4757	0.4561	5.817
105	2,3,3',4,4'	0.7049	0.94	6.657
106	2,3,3',4,5	0.668	1.0046	6.647
107	2,3,3',4',5	0.6628	0.8183	6.717
108	2,3,3',4,5'	0.6626	1.0654	6.717
109	2,3,3',4,6	0.6016	0.9625	6.487
110	2,3,3',4',6	0.6314	0.65	6.532
111	2,3,3',5,5'	0.6183	0.6601	6.767
112	2,3,3',5,6	0.5986	0.8286	6.457
113	2,3,3',5',6	0.5862	0.604	6.547
114	2,3,4,4',5	0.6828	1.0261	6.657
115	2,3,4,4',6	0.6171	1.1328	6.497
116	2,3,4,5,6	0.6132	1.3987	6.304
117	2,3,4',5,6	0.615	0.8895	6.467
118	2,3',4,4',5	0.6693	0.87	7.121
119	2,3',4,4',6	0.5968	0.8239	6.587
120	2,3',4,5,5'	0.6256	0.7444	6.797
121	2,3',4,5',6	0.5518	0.7659	6.647
122	2',3,3',4,5	0.6871	0.7247	6.647
123	2',3,4,4',5	0.6658	0.6645	6.747
124	2',3,4,5,5'	0.6584	0.848	6.737
125	2',3,4,5,6'	0.6142	0.556	6.517
126	3,3',4,4'5	0.7512	0.4757	6.897
127	3,3',4,5,5'	0.7078	0.5834	6.957

HEXACHLOROBIPHENYLS

128	2,2',3,3',4,4'	0.7761	1.188	6.961
129	2,2',3,3',4,5	0.7501	0.997	7.321
130	2,2',3,3',4,5'	0.7184	0.952	7.391
131	2,2',3,3',4,6	0.6853	0.8492	6.587
132	2,2',3,3',4,6'	0.7035	0.7303	6.587
133	2,2',3,3',5,5'	0.6871	1.148	6.867
134	2,2',3,3',5,6	0.6796	0.7331	7.304
135	2,2',3,3',5,6'	0.6563	0.7031	7.151
136	2,2',3,3',6,6'	0.6257	0.444	6.511
137	2,2',3,4,4',5	0.7329	1.112	>7.711
138	2,2',3,4,4',5'	0.7403	0.827	7.441
139	2,2',3,4,4',6	0.6707	0.7219	6.677
140	2,2',3,4,4',6'	0.6707	0.6732	6.677
141	2,2',3,4,5,5'	0.720	1.352	7.592
142	2,2',3,4,5,6	0.6848	1.218	6.517
143	2,2',3,4,5,6'	0.6789	0.7088	6.607
144	2,2',3,4,5',6	0.6563	0.8764	6.677
145	2,2',3,4,6,6'	0.6149	0.6789	6.257
146	2,2',3,4',5,5'	0.6955	0.728	6.897
147	2,2',3,4',5,6	0.6608	0.6	6.647
148	2,2',3,4',5,6'	0.6243	0.554	6.737

Table 24.2 (continued) Polychlorinated Biphenyls: Structure, Retention Times, Response Factors, and Octanol/Water Partition Coefficients ($\log K_{ow}$)

Isomeric Group and PCB Number	Structure (chlorine-filled)	Relative Retention Time ^a	Relative Response Factor ^b	$\log K_{ow}^c$
149	2,2',3,4',5',6	0.6672	0.572	7.281
150	2,2',3,4',6,6'	0.5969	0.5676	6.327
151	2,2',3,5,5',6	0.6499	0.785	6.647
152	2,2',3,5,6,6'	0.6062	0.5235	6.227
153	2,2',4,4',5,5'	0.7036	0.688	7.751
154	2,2',4,4',5,6'	0.6349	0.57	6.767
155	2,2',4,4',6,6'	0.5666	0.586	7.123
156	2,3,3',4,4',5	0.8105	1.389	7.187
157	2,3,3',4,4',5'	0.8184	1.1965	7.187
158	2,3,3',4,4',6	0.7429	1.132	7.027
159	2,3,3',4,5,5'	0.7655	0.9934	7.247
160	2,3,3',4,5,6	0.7396	1.1914	6.937
161	2,3,3',4,5,6'	0.6968	0.9672	7.087
162	2,3,3',4',5,5'	0.7737	1.0322	7.247
163	2,3,3',4',5,6	0.7396	0.9976	6.997
164	2,3,3',4',5,6'	0.7399	0.9848	7.027
165	2,3,3',5,5',6	0.692	1.0777	7.057
166	2,3,4,4',5,6	0.7572	1.0421	6.937
167	2,3',4,4',5,5'	0.7814	1.0658	7.277
168	2,3',4,4',5',6	0.7068	0.8375	7.117
169	3,3',4,4',5,5'	0.8625	0.8355	7.427

HEPTACHLOROBIPHENYLS

170	2,2',3,3',4,4',5	0.874	0.75	7.277
171	2,2',3,3',4,4',6	0.8089	1.1712	6.704
172	2,2',3,3',4,5,5'	0.8278	1.172	7.337
173	2,2',3,3',4,5,6	0.8152	2.044	7.027
174	2,2',3,3',4,5,6'	0.7965	0.806	7.117
175	2,2',3,3',4,5',6	0.7611	0.381	7.177
176	2,2',3,3',4,6,6'	0.7305	1.0589	6.767
177	2,2',3,3',4',5,6	0.8031	1.0009	7.087
178	2,2',3,3',5,5',6	0.7537	0.621	7.147
179	2,2',3,3',5,6,6'	0.7205	0.8237	6.737
180	2,2',3,4,4',5,5'	0.8362	1.295	7.367
181	2,2',3,4,4',5,6	0.7968	1.6046	7.117
182	2,2',3,4,4',5,6'	0.7653	1.1272	7.207
183	2,2',3,4,4',5',6	0.772	0.976	7.207
184	2,2',3,4,4',6,6'	0.7016	1.0046	6.857
185	2,2',3,4,5,5',6	0.7848	1.437	7.933
186	2,2',3,4,5,6,6'	0.7416	1.2236	6.697
187	2,2',3,4',5,5',6	0.7654	1.122	7.177
188	2,2',3,4',5,6,6'	0.692	0.7337	6.827
189	2,3,3',4,4',5,5'	0.9142	1.5091	7.717
190	2,3,3',4,4',5,6	0.874	1.31	7.467
191	2,3,3',4,4',5',6	0.8447	1.4741	7.557
192	2,3,3',4,5,5',6	0.8269	1.599	7.527
193	2,3,3',4',5,5',6	0.8397	1.4167	7.527

OCTACHLOROBIPHENYLS

194	2,2',3,3',4,4',5,5'	0.962	1.868	8.683
195	2,2',3,3',4,4',5,6	0.9321	0.415	7.567
196	2,2',3,3',4,4',5',6	0.8938	1.2321	7.657
197	2,2',3,3',4,4',6,6'	0.8293	0.9522	7.307

Table 24.2 (continued) Polychlorinated Biphenyls: Structure, Retention Times, Response Factors, and Octanol/Water Partition Coefficients ($\log K_{ow}$)

Isomeric Group and PCB Number	Structure (chlorine-filled)	Relative Retention Time ^a	Relative Response Factor ^b	Log K_{ow}^c
198	2,2',3,3',4,5,5',6	0.8845	1.07	7.627
199	2,2',3,3',4,5,6,6'	0.8494	1.1508	7.207
200	2,2',3,3',4,5',6,6'	0.8197	0.369	7.277
201	2,2',3,3',4',5,5',6	0.8875	0.803	7.627
202	2,2',3,3',5,5',6,6'	0.8089	1.165	8.423
203	2,2',3,4,4',5,5',6	0.8938	1.629	7.657
204	2,2',3,4,4',5,6,6'	0.8217	0.8034	7.307
205	2,3,3',4,4',5,5',6	0.9678	1.406	8.007
NONACHLOROBIPHENYLS				
206	2,2',3,3',4,4',5,5',6	1.0103	1.673	9.143
207	2,2',3,3',4,4',5,6,6'	0.9423	1.3257	7.747
208	2,2',3,3',4,5,5',6,6'	0.932	1.1756	8.164
DECACHLOROBIPHENYL				
209	2,2',3,3',4,4',5,5',6,6'	1.0496	1.139	9.603

^a Gas chromatography retention time of PCB congener relative to the retention time of the reference standard octachloronaphthalene on a capillary column of SE-54.

^b Gas chromatography peak area response of PCB relative to peak area of 1 ng octachloronaphthalene.

^c K_{ow} (octanol/water partition coefficient) = C_{ow}/C_{wo} , where C_{ow} is the concentration of the solute in octanol saturated with water, and C_{wo} is the concentration of the solute in water saturated with octanol.

^d — = no data.

Data from Ballschmiter and Zell 1980; McDuffie 1981; Bruggeman et al. 1982; Yalkowsky et al. 1983; Mullin et al. 1984; Rapaport and Eisenreich 1984; Shiu and Mackay 1986; Woodburn et al. 1987; Hawker and Connell 1988.

24.3.3 Toxic Equivalency Factors

A significant part of the toxicity associated with commercial PCB mixtures is related to the presence of the small number of planar congeners. These compounds induce several similar toxic effects in mammals and birds, such as hepatotoxicity, immunotoxicity, and reproductive toxicity (Janz and Metcalfe 1991b; Brunstrom et al. 1995). Planar halogenated aromatic compounds act, in part, by a common mechanism initiated by binding to a cytosolic aryl hydrocarbon receptor. The relative toxicities of planar halogenated hydrocarbons are calculated by expressing their toxicity in relation to 2,3,7,8-TCDD, the most potent compound in this class of chemicals. Toxic equivalency factors (TEFs) are fractional potencies that relate a compound's potency to that of 2,3,7,8-TCDD. The 2,3,7,8-TCDD TEF has been used to estimate the relative toxic potencies of individual planar halogenated hydrocarbons (Safe 1987b; 1990, 1994; Janz and Metcalfe 1991b; Johansen et al. 1993). According to Safe (1990), TEF values should be derived from data on the following effects in descending order of priority:

1. Long-term carcinogenicity studies
2. Reproductive studies
3. Subchronic studies that measure Ah receptor-mediated responses, such as thymic atrophy, loss in body weight, and immunotoxicity
4. Acute toxicity studies
5. *In vivo* or *in vitro* biochemical responses such as enzyme induction and receptor binding.

Relative toxic potencies are modified by many variables, including age, sex, species, and strain of the animal; the efficiency of the chemical to induce cytochrome P-450 and associated monooxygenase enzyme activities, glucuronosyl and glutathione transferases, and other drug-metabolizing enzymes; and the efficiency of the organism to modulate steroid-metabolizing enzymes, induce delta-aminolevulinic acid synthetase, inhibit porphyrinogen decarboxylase, decrease Ah receptor binding activity, and alter Vitamin A and thyroid hormone levels (Safe 1990, 1994).

The *in vitro* induction of the cytochrome P-450c-dependent monooxygenases, AHH, or EROD by 2,3,7,8-TCDD and related halogenated aryl hydrocarbons in rat liver cells was developed as a short-term quantitative bioassay for these chemicals. Aromatics that do not fit this correlation are considered as congeners that are readily metabolized *in vivo* (Safe 1987b). Induction of either AHH or EROD activity in the H4IE rat hepatoma cell line by PCB, PCDF, and PCDD congeners, either singly or in combination, correlates well with the *in vivo* toxicity of these compounds to rats (as quoted in Ankley et al. 1991). The proposed mean TEF values range from 0.01 to 0.1 in non-*ortho*-substituted planar PCBs, to 0.001 in mono-*ortho*-substituted planar PCBs, to 0.00002 in di-*ortho*-substituted planar PCBs (Table 24.3). Although the concentration of non- and mono-*ortho*-substituted PCBs in animal tissues ranges from about 0.01 µg/kg to several micrograms per kg (about 1000 to 100,000 times lower than the sum of total PCBs), it is significantly higher than the concentration of the highly toxic 2,3,7,8-TCDD and 2,3,4,7,8-pentachlorodibenzofuran. Accordingly, the non- and mono-*ortho*-PCBs — despite their lower toxic potency — often contribute as much or more to the 2,3,7,8-TCDD-like activity than either dioxins or furans (Johansen et al. 1993). However, the overall importance of mono-*ortho*-PCBs to the TEF is questioned by Ahlborg et al. (1994), and this must be considered in future risk assessment evaluations.

Table 24.3 Proposed Toxicity Equivalency Values (TEF) Relative to 2,3,7,8-TCDD of non-*ortho*, mono-*ortho*, and di-*ortho* Planar PCBs

PCB congener	TEF
NON-<i>ORTHO</i> PLANAR PCBs	
PCB 77	0.0005
PCB 126	0.1
PCB 169	0.01
MONO-<i>ORTHO</i> PLANAR PCBs	
PCB 105	0.0001
PCB 114	0.0005
PCB 118	0.0001
PCB 123	0.0001
PCB 156	0.0005
PCB 157	0.0005
PCB 167	0.00001
PCB 189	0.0001
DI-<i>ORTHO</i> PLANAR PCBs	
PCB 170	0.0001
PCB 180	0.00001

Data from Safe 1990, 1994; Ahlborg et al. 1994.

Mammal-derived TEFs underestimate the potency of planar PCB mixtures in fish (Newsted et al. 1995). TEF values of non-*ortho*-PCB congeners based on mortality of rainbow trout in early life stages are as much as 1000 times lower than TEFs proposed for human risk assessment (Walker

and Peterson 1991, 1994). Clemons et al. (1996) compared TEFs for PCBs using cytochrome P-4501A1 induction measured as EROD activity in a rainbow trout liver cell line and in a rat hepatoma cell line. EROD activity in trout liver cells was induced only by PCBs 77, 81, 118, and 126 under normal growth conditions, and in some cultures with PCBs 105, 156, and 169. The trout TEFs were 0.023 for PCB 126, 0.064 for PCB 81, 0.0034 for PCB 77, 0.00016 for PCB 169, and 0.000017 for PCB 118; TEFs for PCBs 105 and 156 were <0.00003. In rat cells, however, all seven PCBs clearly induced EROD activity. Clemons et al. (1996) concluded that the toxic impact of PCBs on rainbow trout is overestimated by risk assessment TEFs based on rat cells and assessed more appropriately with TEFs derived from rainbow trout cells.

24.3.4 Structure—Function Relations

Safe (1984, 1990) described three classes of PCB congeners on the basis of their ability to induce benzo[*a*]pyrene hydroxylase (also known as aryl hydrocarbon hydroxylase or AHH) and ethoxyresorufin *O*-deethylase (EROD) activities:

1. Planar PCBs
2. Mono-*ortho*-analogs of the planar PCBs
3. Di-*ortho*-analogs of the planar PCBs

Among the 20 possible planar PCB congeners and their analogs (Figure 24.2), the most toxic in rats were PCBs 77, 126, and 169; these three congeners are approximate isostereomers of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) and have similar toxic effects, including induction of 3-methylcholanthrene-type drug-metabolizing enzymes, body weight loss, thymic atrophy, dermal disorders, hepatic damage, high binding affinity to hepatic cytosolic receptor proteins, immunotoxicity, reproductive impairment, and teratogenicity (Massee et al. 1986; Parkinson and Safe 1987; Tanabe et al. 1987; Gooch et al. 1989; Kannan et al. 1989; Janz et al. 1992; Himberg 1993; Giesy et al. 1994a). PCBs 77, 126, and 169 have been detected in eggs of terns from Lake Michigan, in marine mammals and humans, and in fish from the Hudson and Ohio Rivers (Huckins et al. 1988). However, they are difficult to detect without proper methods (Tanabe 1988; Schwartz et al. 1993).

The structural characteristics of individual PCB congeners influence their induction of various P-450 activities. In mammals, PCB congeners have been characterized as 3-methylcholanthrene-type inducers, phenobarbital-type inducers, or mixed-type inducers of both. AHH and EROD activities (which are preferentially catalyzed by the P-4501A gene subfamily) have been induced by planar PCBs in fish and mammals and by some mono- and di-*ortho*-analogs of planar PCBs in mammals (Skaare et al. 1991). The mechanism of toxic action of planar and mono-*ortho* planar PCBs is linked to an interaction with the 2,3,7,8-TCDD (or Ah) receptor protein. But this mechanism does not account for all observed PCB toxicities (Hansen 1987; Safe 1994). Toxic responses unrelated to Ah receptor effects have been reported of PCBs 4, 28, 31, 49, 52, 84, 95, 110, 136, and 153. For example, PCB 153 is less cytotoxic than PCB 169 but is a more effective inhibitor of intercellular communication. PCB 52 caused moderate chick embryotoxicity; however, PCBs 18 and 153 were inactive, and PCBs 84 and 118 were severely toxic but by different mechanisms (Hansen 1987). The induction of cytochrome P-4501A activity in the presence of both an inducer (PCB 126) and low concentrations of an inhibitor (tributyltin = TBT) indicates that TBT does not interfere with the Ah receptor binding (Kannan et al. 1998). Potentiation of EROD activity and cytotoxicity as a result of coexposure to PCB 126 and TBT is significant because they both accumulate in a variety of marine organisms (Kannan et al. 1998).

Group I planar PCBs are 10 times more toxic and 100 times more effective as inducers of cytochrome P-450c-dependent monooxygenase and 70 times more effective in competitively displacing 2,3,7,8-TCDD from a rat cytosol receptor protein than Group II planar PCBs (Table 24.4;

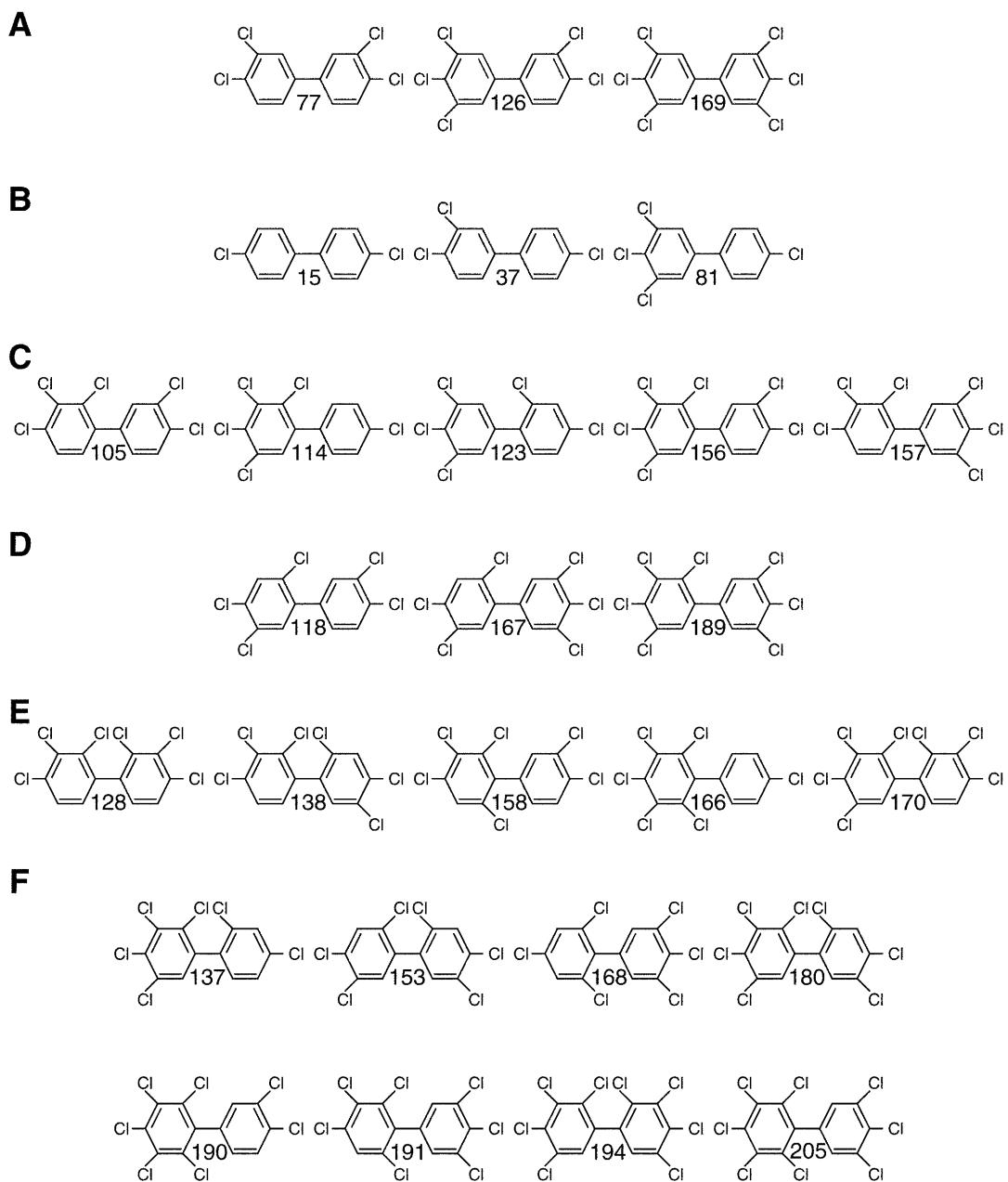


Figure 24.2 (See caption on facing page.)

Safe 1990; [Figure 24.2](#)). Mono-*ortho*-analogs of the planar PCBs have one substituent in the *ortho* (2 or 2') position; these compounds possess diminished yet significant EROD- or AHH-inducing capacity and also induce P-450 forms that are induced by the phenobarbital class of compounds (Gooch et al. 1989). Mono-*ortho*-derivatives (PCBs 105, 118, 156, and 189) may be more important in terms of 2,3,7,8-TCDD-like activity and in occurrence (Hansen 1987). Di-*ortho*-analogs of the planar PCBs, that is, those with *ortho*-, *meta*-, and *para*-substituents, possess still weaker but significant AHH-inducing activity (Gooch et al. 1989). Certain di-*ortho*-derivatives of the 3,3',4,4' pattern (PCBs 128, 138, 153, 170, 180) are significant components of PCB residues; however, PCBs 128, 138, and 170 have reduced 2,3,7,8-TCDD-like effects (Hansen 1987). In rats, several

Table 24.4 Interactive Effects of PCBs on the Induction of Rat (*Rattus* sp.) Liver Microsomal Cytochrome P-450c

PCB Congener and Dose (mole/kg body weight)	Microsomal Enzyme Activity (nmoles product/mg protein/min)		
	Benzo[a]pyrene Hydroxylase	Ethoxresorufin-O-deethylase	
Control, corn oil	0.088	0.277	
PCB 153 (300)	0.121	0.530	
PCB 126 (0.01)	0.486	3.60	
PCB 126 (0.01) plus PCB 153 (300) ^a	0.887	6.03	
PCB 169 (125)	0.676	6.89	
PCB 169 (125) plus PCB 153 (300) ^b	1.06	10.5	

^a Administered 7 days prior to treatment with PCB 126.

^b Administered 7 days prior to treatment with PCB 169.

Data from Parkinson, A. and S. Safe. 1987. Mammalian biologic and toxic effects of PCBs. Pages 49-75 in S. Safe (ed.). *Polychlorinated Biphenyls (PCBs): Mammalian and Environmental Toxicology*. Environ. Toxin Ser. 1. Springer-Verlag, New York.

PCBs (105, 114, 118, 123, 126, 156, 157, 169) produced a linear correlation between the EC50 response (*in vitro*) of AHH induction against the ED50 (*in vivo*) of body weight loss, thymic atrophy, hepatic AHH, and EROD induction (Safe 1987b). The planar mono- and di-*ortho*-derivatives (PCBs 105, 118, 156, 189, 128, 138, 153, 170, 180) are referred to as mixed inducers because they elicit effects similar to coadministration of phenobarbital plus methylcholanthrene (Hansen 1987).

PCB 156, a mixed inducer of microsomal enzymes, significantly increases the incidences of cleft palates by 2,3,7,8-TCDD in rodents (Birnbaum et al. 1985). Interactions among polychlorinated congeners may range from antagonism to additivity to synergism (Safe 1990), and the toxicity of individual PCBs can be raised by interaction with other PCBs (Table 24.5).

Figure 24.2 Planar polychlorinated biphenyls and their derivatives. (Data from Hansen 1987; Parkinson and Safe 1987; Safe 1987b, 1994; Tanabe et al. 1987; Kannan et al. 1989; de Voogt et al. 1990; Ankley et al. 1991; Sonzogni et al. 1991; Hong et al. 1992; Johansen et al. 1993.) The general order of biological activity is: Group I non-*ortho* planar PCBs > Group II non-*ortho* planar PCBs > mono-*ortho* planar PCBs > di-*ortho* planar PCBs. **A.** Group I: potent non-*ortho* planar PCBs. This group contains no *ortho*-, 2 *para*-, and at least 2 *meta*-chlorines (PCBs 77, 126, and 169), and are approximate stereoisomers of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD). They are less potent than 2,3,7,8-TCDD but elicit similar biological responses, including induction of cytochrome P-450 and aryl hydrocarbon hydroxylase (AHH). This group is the most biologically active of all planar PCBs and their derivatives. **B.** Group II: less-potent non-*ortho* planar PCBs (PCBs 15, 37, and 81). Group II non-*ortho* planar PCBs, when compared to Group I, were only 0.1 times as toxic, 0.01 times as effective in inducing cytochrome P-450c-dependent monooxygenase, and about 0.015 times as effective in competitively displacing 2,3,7,8-TCDD from a cytosol-receptor protein in rat liver. **C.** Potent mono-*ortho* planar PCBs. The addition of a single *ortho*-chlorine substituent to non-*ortho* planar PCBs 77, 81, 126, and 169 yields eight derivatives, of which five (PCBs 105, 114, 123, 156, 157) were more potent when the *ortho*-chlorine was adjacent to a *meta*-hydrogen. **D.** Less-potent mono-*ortho* planar PCBs. The toxicity of non-*ortho* planar PCBs is reduced by the introduction of an *ortho*-chloro substituent, especially when it is adjacent to a *meta*-chlorine (PCBs 118, 167, 189). **E.** Potent di-*ortho* planar PCBs. The di-*ortho* planar PCBs are less toxic than the mono-*ortho* planar PCBs. At least five di-*ortho* derivatives (PCBs 128, 138, 158, 166, 170) compete with 2,3,7,8-TCDD for receptor binding sites in rat liver cytosol to induce cytochrome P-450c. **F.** Less-potent di-*ortho* planar PCBs. These eight di-*ortho* derivatives (PCBs 137, 153, 168, 180, 190, 191, 194, 205) are less potent than those figured in E.

Table 24.5 Summary of PCB Structure—Function Relations in Rats (*Rattus* sp.)

PCB Structure	Cytochrome P-450 Induction (% of controls)		Relative Activity (% of controls)		Receptor Binding
	P-450c + P-450d	P-450b + P-450e	In vivo	In vitro	
Planar PCBs: Group I	1800–4100	None	+++	1–100	35–100
Planar PCBs: Group II	1100–1500	600–1400	++	0.03	0.5
Mono-ortho planars	750–2400	2600–4700	++	0.00002–0.3	1.5–6
Di-ortho planars	250–900	1000–6300	+	Inactive	<0.3
PCB 153	None	7300	Inactive	Inactive	<0.3
2,3,7,8-TCDD	3500	None	+++++	400	2500

Data from Parkinson, A. and S. Safe. 1987. Mammalian biologic and toxic effects of PCBs. Pages 49–75 in S. Safe (ed.). *Polychlorinated Biphenyls (PCBs): Mammalian and Environmental Toxicology*. Environ. Toxin Ser. 1. Springer-Verlag, New York.

24.3.5 Quantitation

PCBs are chemically inert, nonpolar compounds and relatively stable during collection and storage. However, PCB concentrations in environmental samples vary with different measurement techniques (Kratochvil et al. 1984; Huckins et al. 1990b; Lebo et al. 1992; Prest et al. 1992; Bidleman et al. 1993; Litten et al. 1993), with types of Aroclor standards used for calibration (Table 24.6), and with oven-drying techniques (Table 24.7). Reports of interlaboratory comparison studies for PCB analysis show wide variations and strongly indicate a need for more rigorous quality control and assurance. In one multilaboratory study (Alford-Stevens 1988) — wherein PCBs were determined in water, soil, and sediments — percent recoveries from analysis of fortified waters averaged 60% in the high concentration sample containing 148 µg/L total PCBs and 55% in the low concentration sample of 37 µg/L. No single combination of extraction and cleanup was best for all solid samples. An analytical intercomparison exercise (International Council for the Exploration of the Sea [ICES] 1992) was conducted on solutions containing 10 PCB congeners. Of the 61 evaluated laboratories, a group of 47 laboratories produced between-group standard deviations of 1.10 to 1.13 by all PCB congeners except PCB 52; a group of 11 laboratories was identified as an outlier group. Only three laboratories were able to quantify PCBs 110 and 77, which coelute in most GC columns. Peak height measurements gave better reproducibility than peak area methods. In another intercomparison study, the analysis by 11 laboratories of a solution containing 12 pure congeners resulted in a variation of as much as 20% for analysis of a single congener. For the analysis of the same congeners in a fish oil, the coefficient of variation ranged from 17.4 to 132% (66.2% without outliers) and had a median of 47.1% (ICES 1992).

PCBs in biological samples are usually extracted by a Soxhlet column and with a nonpolar solvent such as hexane. The sample is first mixed with sodium sulfate to remove moisture. The extraction of PCBs from sediments was tested with sonication, with two sonications interspersed at a 24-h quiescent interval, with steam distillation, or with Soxhlet extraction (Dunnivant and Elzerman 1988). Comparison of the recoveries of various PCB mixtures from dry and wet sediments by the four techniques and the extraction efficiency of four solvents showed that the best overall recoveries were obtained by Soxhlet extraction and the two sonication procedures. In comparisons of solvent systems of acetone, acetonitrile, acetone–hexane (1+1), and water–acetone–isoctane (5+1.5+1), recoveries of lower chlorinated congeners (dichloro- to tetrachloro-) were usually higher with acetonitrile and recoveries of higher chlorinated congeners (tetrachloro- to heptachloro-) extracted with acetone were superior (Dunnivant and Elzerman 1988). The completeness of extraction from a sample matrix does not seem to discriminate against specific isomers; however, discrimination in the cleanup and fractionation process may occur and must be tested (Duinker et al. 1988b).

With most analytical techniques for the quantification of PCB residue levels, chromatographic separations were used, most frequently electron-capture gas chromatography (GC/ECD). With early methods, selected peaks were used to estimate total PCBs. Low-resolution separations were satisfactory when packed columns that produced a pattern of peaks with measured areas were used. The patterns were compared with known amounts of Aroclor mixtures. If the Aroclor peaks in a sample closely resembled a particular Aroclor reference mixture of known weight, the total area or peak height of the sample PCBs was compared to those of the reference mixture and the weight of calculated sample PCBs (Kaiser et al. 1980). Other investigators used selected peaks to report Aroclor equivalents (Draper et al. 1991; Turle et al. 1991), but these methods are not useful when samples and Aroclor standards are dissimilar. For another procedure, response factors were used for individual Aroclor peaks as determined by GC and GC-MS procedures (Webb and McCall 1973). The sample peaks were compared with peaks from common Aroclors obtained on packed columns; retention time windows for the early-, middle-, and late-eluting peaks were assigned to three Aroclors (1242, 1254, 1260), based on the presence or absence of specific peaks. The weight of PCB in the sample peak was calculated by multiplying its peak area by the appropriate response factor; all peaks were added to obtain a total weight of PCB. However, packed columns failed to separate and to identify many congeners because several congeners usually eluted under a single peak of identical retention time. These methods do not account for changes in composition from interfering compounds; congener changes from hydrolysis, photodegradation, and biodegradation; selective evaporation and adsorption of certain isomers; or solubility differences resulting in different partitioning ratios among the various environmental compartments. Some researchers, who used capillary columns, estimated PCB residues on the basis of a relatively simple cleanup and analysis by high-resolution GC/ECD (Duinker et al. 1988b; Maack and Sonzogni 1988; Sericano et al. 1990; Draper et al. 1991) or by HRGC-MS (Porte et al. 1988; Niimi and Oliver 1989; Harrad et al. 1992). Others emphasized total PCBs, homologue subgroups, or individual congeners present in substantial amounts in the sample or in commercial mixtures (Maack and Sonzogni 1988; Niimi and Oliver 1989). And still others used total PCBs derived from the sum of homologue subgroup concentrations (Gebhart et al. 1985; Sericano et al. 1990), concentrations of individual subgroups (Gebhart et al. 1985), or the contribution of all congeners in each subgroup (Niimi and Oliver 1989).

Gas chromatography/mass spectrometry in the electron ionization mode (GC-MS/EI) has been used to a more limited extent for routine analysis of PCBs (Alford-Stevens et al. 1985; Kuehl et al. 1991). Some interference with quantification ions can occur with EI when compounds such as PCBs 77 and 110 coelute. GC-MS has also been operated in the negative chemical ionization mode (NCI) for PCB determinations (Guevremont et al. 1987; Swackhammer et al. 1987; Erhardt-Zwabik et al. 1990). Increased selectivity is observed in the NCI mode, although interference from other compounds that readily form stable negative ions may be observed. Improvements have also been made in capillary column separations. However, the application of single long, narrow bore capillary columns does not enable investigators to attain full separation of PCB congeners (Ballschmiter and Zell 1980; Bush et al. 1983; Mullin et al. 1984; Duinker et al. 1988b). Multidimensional GC (MDGC) analysis of PCBs drastically improved congener separations and the analysis of all sample constituents. Schomburg et al. (1985) connected two capillary columns of different polarities in a double-oven instrument. The first column was temperature programmed, the second was operated isothermally. Congeners of Clophen A 50 were separated by valveless flow switching. Using MDGC techniques, Duinker et al. (1988a, 1988b) analyzed PCBs 28, 52, 101, 138, 153, and 180, and positively identified PCBs 52, 101, and 180 as well as coeluting peaks of PCBs 24, 26, 29, 44, 49, 81, 84, 114, 128, 151, 169, 177, 183, 187, 189 and 194. In a following paper, Schultz et al. (1989) used the same MDGC technique to fully resolve all congeners in commercial PCB mixtures of Clophen A30, A40, A50, A60 and in Aroclors 1221, 1016, 1242, 1254, and 1260. A column of SE-54 with ECD was used to monitor the eluate, and a second, more polar column (usually OV-210) with ECD was used to obtain fully resolved single peaks. The procedure required exact timing of cuts based on retention time but fully separated the PCB congeners by gas chromatography for the

first time. A total of 132 congeners at concentrations above 0.05% (w/w) were eluted as fully resolved single peaks and measured (Schultz et al. 1989).

Pattern recognition techniques that incorporate statistical methods have been used to determine spatial and temporal patterns in PCB residue data. Stalling et al. (1980, 1987), for example, characterized sample PCB profiles from 105 individual congeners, measured parameters of similarity between sample and standard mixtures, and determined whether the sample residue pattern corresponded to an Aroclor mixture. Modeling environmental samples with the individual congener concentrations provided more accurate estimations of Aroclor profiles than homologue concentrations. Intact commercial Aroclors have been characterized by automated mass spectrometric determination of weight percent distribution by homologue groups (Alford-Stevens 1986). One isomer from each level of chlorination was normally used to calibrate the MS response to all measurable isomers in that group. In another example, Macdonald et al. (1992) applied pattern recognition techniques to assess biomagnification and to characterize source patterns of multicomponent pollutants such as PCBs, PCDDs, and PCDFs in eggs of the herring gull (*Larus argentatus*) from the Great Lakes between 1983 and 1990. Turle et al. (1991) fitted a linear regression to PCB concentrations in herring gull eggs from the Great Lakes during 1970 to 1985 and from more recent measurements. Aroclor equivalents in eggs were determined with PCB 138 as a single peak estimate for the older data and more recent PCB data as the sum of 41 congeners. The earlier choice of PCB 138 for quantitation seemed fortunate; uptake of heptachloro isomers maintained a stable percentage of total PCB egg residues over time, whereas less chlorinated congeners generally declined and more chlorinated congeners increased over time (Turle et al. 1991).

Table 24.6 PCB Congeners in Aroclor 1254 and 1260

PCB Number	Average Percent in Aroclor		PCB Number	Average Percent in Aroclor	
	1254	1260		1254	1260
16	— ^a	0.04	74	0.78	0.03
17	0.19	0.05	82	0.95	0.112
18	0.41	0.12	83	0.45	0.04
21	—	0.01	84	1.95	0.45
22	—	0.01	85	1.66	0.09
24	—	0.01	87	3.78	0.61
26	—	0.02	90	0.93	0.56
28	0.25	0.045	91	0.83	0.07
29	—	0.02	92	1.58	0.59
31	0.22	0.05	95	6.02	2.87
33	0.14	0.09	96	0.08	—
37	—	0.04	97	2.55	0.34
40	0.20	0.03	99	3.60	0.12
41	0.64	0.20	100	0.10	0.02
42	—	0.04	101	7.94	3.82
43	—	0.02	105	3.83	0.07
44	2.03	0.11	107	0.72	0.03
45	—	0.07	110	5.85	1.80
46	—	0.02	115	0.30	0.05
47	0.17	0.11	118	6.39	0.53
48	0.14	0.19	119	0.14	—
49	1.64	0.06	122	0.50	0.21
52	5.18	0.41	123	0.81	—
53	0.09	0.04	128	2.07	0.76
56/60	0.56	0.14	129	0.23	0.66
63	0.05	—	130	0.63	0.08
64	0.45	—	131	0.16	0.16
66	0.59	—	132	1.98	3.69
67	0.09	—	134	0.49	0.35
70	3.21	0.12	135	1.62	2.56

Table 24.6 (continued) PCB Congeners in Aroclor 1254 and 1260

PCB Number	Average Percent in Aroclor		PCB Number	Average Percent in Aroclor	
	1254	1260		1254	1260
136	1.12	1.82	180	0.38	8.11
137	0.25	0.14	183	0.17	2.03
138	3.20	6.31	185	—	2.72
141	1.04	2.53	187	0.32	4.24
144/135	— ^a	1.5	189	—	0.13
146	0.83	1.39	190	0.08	0.79
149	2.21	7.61	191	—	0.18
151	1.17	3.08	193	—	0.57
153	4.26	10.20	194	—	1.50
156	1.62	0.66	195	—	0.38
157	—	0.14	196	—	1.90
158	0.77	0.70	197	—	0.12
160	—	0.05	198	—	0.09
167	0.21	0.21	199	—	0.82
169	—	0.05	200	—	0.62
170	0.31	5.36	201	0.68	1.95
171/202	0.05	1.65	203	—	2.05
172	0.05	0.78	205	—	0.13
173	0.09	0.21	206	—	0.65
174	0.34	4.68	207	—	0.07
175	0.05	0.36	208	—	0.17
176	0.32	0.64	209	—	0.05
177	0.21	2.06			
178	1.35	1.41	Total (%)	96.25	105.55

^a — = no data.

Data from Bush et al. 1985; Safe et al. 1985; Schulz et al. 1989; Smith et al. 1990.

Table 24.7 Effect of Oven Drying of Sediments on Percent Loss of Selected PCB Congeners Present at >0.1 mg/kg Fresh Weight

PCB Number	Percent Loss	PCB Number	Percent Loss
1	65	40/41	50
4	61	42	0
6	50	44	0
8	50	46	46
9	50	47	43
10	62	49	47
15	100	51	53
16	43	52	44
17	43	59	50
18	57	60	33
19	53	64	45
22	50	66	50
25	40	70	32
26	50	82	40
28	43	84	50
31	33	94	34
		136	0
		151	0

Note: Mean loss of these congeners is 56%.

Data from Bush, B., L.A. Shane, and M. Wahlen. 1987. Sedimentation of 74 PCB congeners in the upper Hudson River. *Chemosphere* 16:733-744.

Methods were developed for routine analysis of AHH-inducing and other PCB congeners in fish using a comparatively simple gel permeation chromatography (GPC) cleanup and GC-MS/NCI (Schmidt and Hesselberg 1992). Methane was used as the reagent gas for NCI, source temperature and pressure were optimized (1100°C and 0.9 Torr), and fragmentation of the major ions was reduced as much as 10%. A peak area correction factor for interfering ion fragmentation was obtained by instrument calibration with standards and manually applied to coeluting ions as needed (Schmidt and Hesselberg 1992). Additional methods were developed for the analysis of planar congeners. Using a carbon foam adsorbent, Huckins et al. (1978, 1980, 1988) devised procedures for the analysis of toxic non-*ortho*-chloro-substituted PCB congeners and trace planar impurities in Aroclors. With carbon-foam chromatography (carbon particles suspended on a polyurethane substrate), concentrations of planar PCB congeners in Aroclors 1016, 1242, 1248, 1254, and 1260 were detected by high-resolution electron capture gas chromatography (HRGC/ECD). With current chemical methods for analysis of non-*ortho*-chloro-substituted planar PCBs, extraction and a preliminary cleanup, carbon chromatography, and HRGC/ECD or HRGC-MS are generally used (Feltz et al. 1995). The brands of carbon available for isolating planar PCBs include Amoco AX-21 (PX-21), Alltech SK-4, Serva SP-1, and Wako active carbon (Storr-Hansen and Cederberg 1992). All methods shared at least three characteristics:

1. They require some form of adsorption chromatography (usually with carbon) to isolate planar compounds.
2. They include several cleanup steps.
3. They are complicated.

A semipermeable membrane device (SPMD) with a nonpolar, low-density polymeric film is used to separate PCBs from large amounts (20 to >50 g) of lipids by dialysis in an organic solvent prior to chemical analysis (Huckins et al. 1990a; Meadows et al. 1993). Liquid–liquid phase partitioning of extracts in organic solvent with sulfuric acid has been used to convert fats and pigments into water-soluble compounds that can be separated and removed from the target analytes with water rinses. Fats may be removed by refluxing or partitioning extracts with alcoholic potassium hydroxide to form water-soluble hydrolysis products. For example, Tanabe et al. (1987) and Kannan et al. (1987b) combined alkali digestion, active carbon column chromatography, fuming sulfuric acid cleanup, HRGC/ECD, and HRGC-MS confirmation for the analysis of PCBs 77, 126, and 169 in porpoise blubber. Measurement of these three highly toxic PCBs in Aroclor and Kanechlor mixtures is reported by Kannan et al. 1987a). Creaser and Al-Haddad (1989) separated five non-*ortho*-substituted PCBs from a synthetic mixture containing Aroclors, organochlorine and organophosphorus pesticides, dioxins, and dibenzofurans on an HPLC column packing of porous graphite carbon (PGC). Soil samples required prior cleanup to remove coextracted organics, and elution from a multilayered column containing acid, base, and silica was followed by elution from Florisil. Procedures are available for separating mono- and non-*ortho*-chloro PCBs. Hong and Bush (1990) used sulfuric acid cleanup, low-pressure liquid chromatography with activated carbon/silica gel, and HRGC/ECD to analyze four non-*ortho*- and eight mono-*ortho*-substituted PCBs. Haglund et al. (1990) used a non-carbon HPLC column of 2-(1-pyrenyl)ethylidimethylsilylated silica (PYE) column to isolate mono- and non-*ortho*-chloro PCBs from tissue samples. Isolation with this column required almost complete prior removal of lipids by sulfuric acid partitioning and subsequent gel permeation chromatography (GPC) with Bio-Beads S-X3 to remove remaining lipids. Ford et al. (1993) adapted an automated dioxin analysis system with programmable pump and valve setup for the sequential processing of non-*ortho*-substituted PCBs in five blubber samples. The procedure included ball/mill tissue extraction, preliminary GPC separation and cleanup, silica gel chromatography, and automated separation of non-*ortho*-substituted PCBs on AX21 activated carbon/glass fiber with three solvent systems and was followed by GC/ECD and GC-MS/EI analysis with selected ion monitoring (SIM). The application of high-resolution capillary column techniques combined

with the development of carbon adsorbents for the separation of planar aromatics has become a powerful tool for the identification and measurement of single congeners in complex PCB mixtures and has facilitated the resolution and more accurate quantification of individual congeners and the correction of the presence of non-PCB interferences. But the introduction of such methods in long-term monitoring programs, where one, several, or all peaks in Aroclor standard mixtures were used to estimate total PCBs, raises the problem of comparing results among the data sets. For such purposes, a value for total Aroclor can also be reported (Porte et al. 1988; Turle et al. 1991).

24.4 CONCENTRATIONS IN FIELD COLLECTIONS

24.4.1 General

An increasing number of reports indicate the widespread presence of toxic planar PCB congeners such as the non-*ortho*-substituted planar PCBs 77, 126, and 169. These PCB congeners were detectable in all Finnish food commodities of animal origin sold in Helsinki (Himberg 1993); in all samples of salmon muscle, cod liver, and seal blubber from the Baltic Sea and environs in the 1980s (Koistinen 1990); and at concentrations between 0.03 and 30 µg/kg fat fresh weight (FW) in a wide variety of vertebrates, including fish, marine mammals, dogs, cats, and humans (Tanabe et al. 1987). These and other planar congeners contribute the majority of the toxic potency to PCB mixtures, as judged by their ability to induce AHH and EROD (Kannan et al. 1989; Ankley et al. 1991; Sonzogni et al. 1991). Detection of these toxic residues in field collections from remote areas suggests that planar PCBs are now as widely distributed as other PCB isomers (Tanabe et al. 1987). The clear positive correlation between concentrations of total PCBs and PCBs 77, 126, and 169 in all analyzed mammals suggests that the sources of planar PCB contamination to the environment are mainly commercial PCB formulations (Tanabe et al. 1987).

24.4.2 Nonbiological Materials

Relatively little contamination from PCBs was found in sediments from riverine and pothole wetlands at national wildlife refuges and waterfowl production areas (WPA) in the north central United States in 1980 to 1982. PCBs were above detection levels (20 µg/kg) in less than 4% of the sediments; a similar case was recorded in fish from WPAs (Martin and Hartman 1985). Maximum total PCB concentrations in field collections of nonbiological materials were 0.000028 µg/kg in ice, 0.000125 µg/kg in snow, 12.3 µg/m³ in air, 233 µg/L in seawater, 3860 µg/L in sediment interstitial waters, and 1800 mg/kg in sediments. Concentrations were comparatively elevated in urban areas, near anthropogenic activities, and at known sites of PCB contamination (Table 24.8).

Atmospheric transport is a major route in PCB distribution (Swackhamer et al. 1988). Deposition and evaporation studies of 17 PCB congeners in Siskiwit Lake on Isle Royale, Michigan, showed that PCB input fluxes to the lake from rain, snow, and aerosol equalled output fluxes from sedimentation and evaporation. The magnitude of the net vapor flux, calculated by difference and with the assumption that inputs equal outputs, was large and positive for almost all 17 congeners (Swackhamer et al. 1988). Low but measurable PCB concentrations (measured as Aroclor 1254) were found in air, snow, ice, seawater, and sediment in the Arctic Ocean north of Axel Heiberg Island off Canada's northern outer coast (Hargrave et al. 1989). PCB residues were relatively high in melted snow (8 to 125 pg/L), indicating efficient scavenging from air. The ice island area from which surface seawater samples were collected was well removed from any direct influence of river drainage, and PCB concentrations probably reflect those over much of the Arctic Ocean (Hargrave et al. 1989). PCBs were also monitored in the atmosphere of Ross Island, Antarctica, from March 1988 to January 1990 (Larsson et al. 1992). The geometric mean of total PCBs in air during this

period was 15.2 pg/m³, and the maximum concentration was 12,300 pg/m³. The geometric mean during the Antarctic summers of 1988/89 and 1989/90 was 21 pg/m³. During one sampling period (December 16 to 28, 1988), PCB levels were about 100 times higher than during any other period, suggesting either irregular, long-range transport of atmospheric pollutants or volatilization of PCBs from a local dumpsite at McMurdo Base on Ross Island. PCB levels did not correlate with seasonal temperature changes, although changes in atmospheric levels were recorded. The absence of seasonal differences may be due to the cold climate and the low vapor pressure of PCBs (Bidleman et al. 1983).

PCB concentrations in sediment cores from Lake Ontario were similar to production and sales data of PCBs in the United States (Eisenreich et al. 1989). Annual PCB accumulation rates in the sediments rose from about 2 ng/cm² in 1950 to about 40 ng/cm² in the 1966 to 1969 peak years and declined in 1980 to 10 to 20 ng/cm²; about 50% of the 1966 to 1969 load was attributed to the upward mixing by oligochaete worms (Eisenreich et al. 1989). Each of several PCB congeners in Lake Ontario sediments contributed 5.7 to 7.9% of the total PCBs (PCBs 66, 110, and 56/60) and others (including PCBs 44, 52, 70/76, 101, and 153) contributed 4.0 to 4.7% (Oliver and Niimi 1988; Oliver et al. 1989). Surficial sediments of Lake Ontario in 1981 to 1986 contained elevated concentrations of organochlorine compounds, including mirex, chlorobenzenes, octachlorostyrenes, DDT, 2,3,7,8-TCDD, fluorinated aromatic compounds, and PCBs (Oliver et al. 1989). Among the identified congeners, PCBs 60 (5.7%) and 118 (2.6%) are AHH-active (Smith et al. 1990). The frequency of isomers of low chlorination decreased with core depth in sediments, remained fairly stable of hexa-isomers, and increased with core depth of the more highly chlorinated congeners. This pattern with depth reflects the change in use pattern over time to less highly chlorinated PCBs such as Aroclor 1016. The more highly chlorinated congeners that are disproportionately present in deeper sediments may be due to stronger partitioning to sediment and higher hydrophobicity than those of less chlorinated congeners and to the positive correlation with their high octanol/water partition coefficients (Karickhoff 1981). Anaerobic dechlorination was not evident in these sediments. This contradicts the findings of others who maintain that relatively high levels of less chlorinated PCBs in the bottom (anaerobic) core sections of Hudson River sediments were due to anaerobic dechlorination (Brown et al. 1985). Oliver et al. (1989) concluded that the total mass of PCBs in Lake Ontario sediments was about 50 tons and sufficient to impact Lake Ontario for many years. Lake Michigan sediments, analyzed for 18 planar AHH-active PCBs, total PCBs, 2,3,7,8-TCDD, and 2,3,7,8-tetrachloro-*p*-dibenzofuran (2,3,7,8-TCDF), had elevated levels of PCBs 77, 126, and 169 (Smith et al. 1990). Results suggest that the contribution of toxic equivalents — that is, the sums of congeners after the raw congener concentrations were normalized by the TEF — was greater from PCBs 77, 126, and 169 than from 2,3,7,8-TCDD and 2,3,7,8-TCDF, even in environments with significant concentrations of dioxins and dibenzofurans (Smith et al. 1990). Sediments from the Waukegan Harbor, Illinois, in 1978 contained weathered mixtures of Aroclors 1242, 1248, and 1254. Total PCB concentrations were variable between stations and ranged from 10.6 mg/kg to 13,360 mg/kg DW; 3,3',4,4'-TCB residues ranged from 5 to 27,500 µg/kg DW, or about 0.16% of the total PCBs; concentrations were higher of 2,3,3',4,4'-TCB (102 to 131,000 µg/kg DW, or 0.66%) (Huckins et al. 1988).

PCB homologues and total PCBs in water, sediments, and biota were measured in Hamilton Harbour on Lake Ontario and Wheatley Harbour on Lake Erie. Hamilton Harbour receives inputs from steel mills and an incinerator plant; Wheatley Harbour receives fish-processing plant wastes. Total PCBs in sediments ranged from 608 to 14,185 µg/kg DW in Hamilton Harbour and from 166 to 1177 µg/kg DW in Wheatley Harbour (Mudroch et al. 1989). The high PCB value in Hamilton Harbour is similar to values reported earlier in Lake Erie sediments (Frank et al. 1977). Concentrations of lower chlorinated homologues were greater in water than in sediment in both harbors (Mudroch et al. 1989). Homologue patterns in biota (oligochaetes, snails, isopods, and fish) reflected patterns in sediments but not in water. Concentrations of penta- and hexachlorobiphenyls were dominant in the oligochaetes and sediment samples from Wheatley Harbour; concentrations

of these homologues also predominated in Hamilton Harbour, but the differences were less pronounced. Particle size distribution of 82 to 98% silt and clay (63 µm) was similar in both harbors. The concentrations of several metals (Zn, Pb, Cu, and Cr) were much higher in Hamilton Harbour, but their effect on PCB bioaccumulation is unknown (Mudroch et al. 1989).

Contaminated sediments are a major source of PCBs in aquatic environments (Dillon and Burton 1992). PCB discharges prior to 1977 from capacitor-manufacturing plants on the Hudson River at Ft. Edward and Harbor Falls, New York (14 kg PCBs daily for 30 years, mostly Aroclors 1242 and 1016), contaminated 306 km of riverbed between Hudson Falls and New York Harbor. By 1978, an estimated 63,500 kg PCBs were in the riverbank deposits, 134,000 kg in the upper river, and 91,000 kg in the lower river (Brown et al. 1985; Eisler 1986; Bush et al. 1987; Kennish 1992). PCB concentrations in biota and the water column are largely controlled by PCB concentrations in surficial sediments. Declines in PCB levels in Hudson River sediments corresponded to decreased use of PCBs at local capacitor-manufacturing plants (Brown et al. 1985; Kennish 1992). The stabilization of highly contaminated upper stream banks and reduced PCB releases from bed sediments contributed to lower concentrations in the water column. A model of the fate and accumulation of seven PCB homologues in the Hudson River estuary showed that 66% of the 270,454 kg total PCBs discharged into the estuary between 1947 and 1987 had volatilized, 6% was stored in sediments, and the rest was either dredged or lost by boundary transport to the New York Bight and Long Island Sound (Thomann et al. 1991). Total PCBs peaked in the mid-1970s and upstream loading now has a relatively small effect. The upstream PCB load above Troy, New York, accounts for about 20% of the PCB concentrations in striped bass. A steady decline of Aroclors 1016 and 1254 in upstream contribution was projected to the year 2005 and suggests that 95% of 3- to 6-year-old striped bass in the lower Hudson would have residues below the USFDA action level of 2 mg/kg FW by the year 2004 (Thomann et al. 1991). PCB congener patterns in Hudson River sediments differed from the Aroclors discharged into the river. Sediments had comparatively enriched concentrations of certain lower-chlorinated congeners, especially *ortho*-substituted congeners, and some congeners not usually detected in commercial Aroclor mixtures. Changes in PCB composition of sediments were greater in lower portions of sediment cores than in surficial sediments (Brown et al. 1987). Two dechlorination mechanisms seemed to be operating: *meta*-, *para*-dechlorinations with stepwise, selective dechlorination at the *meta*- and *para*-positions of certain *ortho*-substituted di- through tetra-*ortho*-chlorinated biphenyls; and *ortho*-, *meta*-, *para*-dechlorinations, in which the dechlorinations occur at *ortho*-, *meta*-, or *para*-positions and reactivity is favored by increasing electron affinity and relatively positive reduction potential. Both mechanisms preferentially removed toxic congeners (Brown et al. 1987). Residues of individual PCB congeners in the upstream water were similar to residues in caddisfly larvae from that system (Bush et al. 1985), although residues in the larvae were enriched with lower-chlorinated congeners. Because of their relatively high water solubility and low affinity for sediment, higher concentrations of lower-chlorine homologues were expected to preferentially dissolve in water. But PCB profiles of dissolved residues transported downstream in the water samples during low-flow season were dominated by only three low-chlorinated PCBs; more than half of the residues consisted of 2-chlorobiphenyl and 2,2'- and 2,6'-dichlorobiphenyl congeners (Bush et al. 1985).

Anoxic Hudson River sediments contaminated with PCBs and dredged sediments in clay encapsulation were treated to induce or raise anaerobic biodegradation of PCBs (Rhee et al. 1989). Variations in sediment type, bacterial flora, and treatment influenced dechlorination. The addition of biphenyl under anoxic nitrogen was the most effective treatment for raising biodegradation. Unlike the findings of Brown et al. (1987), no evidence was found of accumulation of less-chlorinated PCBs from biodegradation of more highly chlorinated congeners, although a faster degradation rate of less-chlorinated congeners than the more highly substituted PCBs would have allowed this phenomena to occur unobserved. Hudson River sediments incubated at room temperature (25°C) under a nitrogen atmosphere or incubated with biphenyl enrichment under nitrogen for 7 months decreased significantly in chlorobiphenyl compounds of 33 to 65%. In general, mono- and

dichlorobiphenyl congeners from Hudson River sediments were not significantly degraded by the biphenyl, but biphenyl addition significantly decreased the higher chlorinated congeners (Rhee et al. 1989). In earlier studies with the same mixed bacterial culture without biphenyl addition, significant reductions were evident in Hudson River sediments of PCB congeners with as many as three chlorines (Chen et al. 1988).

Sediments in oceans, estuaries, rivers, and lakes concentrate PCBs. Organisms accumulate PCBs by way of the water column, from interstitial sediment waters, and from consumption of contaminated prey by predator species. Coastal sediments with the highest total PCB concentrations between 1984 and 1989 are usually within 20 km of population centers of more than 100,000 people (NOAA 1991) and directly correlate with sediment content of total organic carbon (Karickhoff 1981). Variability in PCB content of sediments is great, and large differences between adjacent stations is not uncommon (NOAA 1988). The approximate percent PCB distribution in sediments by level of chlorination was di- 3.9%, tri- 11%, tetra- 20%, penta- 24%, hexa- 21%, hepta- 12%, octa- 3.9%, and nona- 1.3%. The mean PCB concentration in sediments at 233 sites was 39 µg/kg, and concentrations greater than 200,000 µg/kg were considered elevated (NOAA 1988) ([Table 24.8](#)). In most regions of New Jersey, for example, PCB contamination of sediments and water column was negligible (Kennish 1992). But PCBs in estuarine and coastal locations of New Jersey showed elevated sediment contamination in the northeastern region — an area that included the Hudson–Raritan estuary and adjacent ocean waters of the New York Bight — where direct discharges from capacitor-manufacturing plants on the upper Hudson River, dredged material, and sewage-sludge dumping were the principal sources of PCB contamination. PCB levels in teleosts from the northeastern region in 1986/87 exceeded the USFDA action level of 2000 µg/kg and were consistent with data from previous years. Action levels were also exceeded in fishes from Camden and from the northern coastal regions (Kennish 1992). PCB sediment residues in Raritan Bay in the 1970s averaged 100 µg/kg DW in a range of 3.4 to 2035 µg/kg (Stainken and Rollwagen 1979). Water column concentrations were usually not detectable but approached 0.04 µg/L in parts of the New York Bight after sewage sludge and dredged material were deposited in the 1970s and early 1980s (Boehm 1981). Sediments near dumpsites in the New York Bight contained as many as 15,000 µg/kg PCBs (MacLeod et al. 1981), and bottom sediments in the upper Hudson River had localized contaminated areas containing more than 50,000 µg/kg (Brown et al. 1985). Nationwide, PCB loadings in surficial sediments and mussels (*Mytilus edulis*) in the Long Island Sound were greater than in other sites (Robertson et al. 1991).

Surficial stream sediments in the San Francisco estuarine system during 1972 had high residues (350 to 1400 µg/kg DW) at several locations (Phillips and Spies 1988). However, residues were highly variable between sites (Law and Goerlitz 1974). In 1984, low to intermediate concentrations of PCBs (9 to 60 µg/kg DW) were measured at four locations in the San Francisco Bay. Overall, congener profiles resembled Aroclor 1254 and were dominated by pentachlorobiphenyl isomers (NOAA 1987). The patterns of the 11 reported congeners were variable between areas, indicating many sources of different PCB mixtures.

Lake Hartwell in South Carolina received Aroclor 1016 and 1254 discharges for 21 years from a capacitor-manufacturing plant (Elzerman et al. 1991). Analysis of sediment cores collected between 1984 and 1987 showed that samples nearest the source were relatively high in lower-chlorinated PCB congeners, and downstream samples were enriched with the higher congeners; in all samples, total PCB concentrations decreased with increasing distance from the point source. The estimated total remaining PCBs was 41,000 kg (Elzerman et al. 1991). The highest PCB concentrations were in subsurface sediments, although PCB levels in surficial sediments were also elevated (Dunnivant et al. 1989). A survey of total PCBs in sediments and invertebrates in major estuaries of South Carolina showed no significant contamination. PCBs were found only in sediments (622 µg/kg) and in oysters (87 µg/kg) from the Wando River near a large ship repair and retrofitting facility; PCB residues in crabs, when present, ranged from 95 to 375 µg/kg (Marcus and Renfrow 1990).

**Table 24.8 PCB Concentrations in Field Collections of Selected Nonbiological Materials
(Concentrations are in g/kg fresh weight [FW] or dry weight [DW] unless indicated otherwise.)**

Material	Concentration ^a	Reference ^b
AIR (g/m³)		
Antarctica, Ross Island; 1988–90		
PCB 95	Max. 0.000415 FW	1
PCB 101	Max. 0.000574 FW	1
PCB 110	Max. 0.000444 FW	1
PCB 138	Max. 0.00181 FW	1
PCB 149	Max. 0.00161 FW	1
PCB 153	Max. 0.00128 FW	1
Total PCBs	0.015 FW; Max. 12.3 FW	1
Arctic Ocean; 1986–87; total PCBs	<0.00001 FW	2
ICE		
Arctic Ocean; 1986–87; total PCBs	Max. 0.000028 FW	2
SEAWATER		
Arctic Ocean; 1986–87; total PCBs; water column vs. particulates under ice	Max. 0.00001 FW vs. 2–99 DW	2, 3
Massachusetts; New Bedford Harbor (PCB-contaminated); 1986; total PCBs; bedded phase vs. suspended phase	15 FW vs. 233 FW	4
New York Bight dumpsite; 1970s–1980s; total PCBs	Max. 0.04 FW	5
SEDIMENT INTERSTITIAL WATERS		
New Bedford Harbor; 1986; total PCBs	3860 FW	4
SEDIMENTS		
Arctic Ocean; 1986–87; total PCBs	<0.05 DW	2
Canada, Lake Ontario		
Cores; total PCBs		
1940	0–10 FW	6
1966–69	470–880 FW	6
1980	250–290 FW	6
Surficial sediments; 1981		
Total PCBs	(71–1200) FW	7
Tri-CBs	(11–22) FW	7
Tetra-CBs	(77–200) FW	7
Penta-CBs	(76–180) FW	7
Hexa-CBs	(41–93) FW	7
Hepta-CBs	(20–48) FW	7
Octa-CBs	(11–22) FW	7
Nona-CBs	(2.4–5.7) FW	7
Deca-CB	(5.3–9.4) FW	7
Settling sediments; total PCBs		
1982–83	1300–1900 FW	7
1983–84	350–500 FW	7
1984–85	410–680 FW	7
1985–86	80–290 FW	7
Sweden, Eman River; near paper recycling plant		
PCB 77	30.0 DW	8
PCBs 126, 169	Nondetectable	8
Switzerland, Lake Zurich; total PCBs		
1929–34	<0.5 DW	9
1960–65	210 DW	9

Table 24.8 (continued) PCB Concentrations in Field Collections of Selected Nonbiological Materials (Concentrations are in g/kg fresh weight [FW] or dry weight [DW] unless indicated otherwise.)

Material	Concentration ^a	Reference ^b
1975–80	70 DW	9
United States		
California; total PCBs		
Hunter's Point	40 DW	10
Islais Creek	164 (57–255) DW	11
Long Beach; 1984–89	>200,000 DW	12
Oakland Bay	30–61 DW	10, 11
Palos Verdes; 1984–89	>200,000 DW	12
San Diego Bay; 1984–89	>200,000 DW	12
San Francisco Bay	Max. 1400 DW	13
San Pablo Bay	11.4 (5.7–17.5) DW	10, 11
San Pedro Bay; 1984–89	>200,000 DW	12
Santa Monica Bay; 1984–89	>200,000 DW	12
Southampton Shoal	12 DW	10
Connecticut; 1984–89; total PCBs		
Connecticut River	>200,000 DW	12
Long Island Sound	>200,000 DW	12
Florida; 1984–89; total PCBs		
Choctawhatchee Bay	>200,000 DW	12
St. Andrews Bay	>200,000 DW	12
Tampa Bay	>200,000 DW	12
Illinois, Waukegan Harbor; 1978		
PCB 77	1.05 (0.005–27.5) DW	14
PCB 105	0.86 (0.10–131.0) DW	14
Total PCBs	515 (11–13,360) DW	14
Maryland; 1984–89; total PCBs		
Baltimore Harbor	>200,000 DW	12
Upper Chesapeake Bay	>200,000 DW	12
Michigan		
Raisin River; 1983		
PCB 77	0.6 DW	15
PCB 126	0.28 DW	15
PCB 169	0.07 DW	15
Total PCBs	40,000 DW	15
Saginaw River; 1984		
PCB 77	0.017 DW	15
PCB 126	<0.015 DW	15
PCB 169	ND	15
Massachusetts; total PCBs		
Boston Harbor and Buzzards Bay; 1984–89	>200,000 DW	12
New Bedford Harbor; 1986	1,800,000 FW	4
Salem Harbor; 1984–89	>200,000 DW	12
Nebraska; waterfowl production areas; 1980–82; total PCBs	ND	16
New Jersey; Raritan Bay; total PCBs		
1970s	(3–2035) DW	17
1984–89	>200,000 DW	12
New York		
Hudson-Raritan estuary and Long Island Sound; 1984–89; total PCBs	>200,000 DW	12
Upper Hudson River; anoxic sediments		
PCB 1	200,000 DW	18
PCB 4	160,000 DW	18
PCBs 6/19	40,000 DW	18
PCB 8	33,000 DW	18

Table 24.8 (continued) PCB Concentrations in Field Collections of Selected Nonbiological Materials (Concentrations are in g/kg fresh weight [FW] or dry weight [DW] unless indicated otherwise.)

Material	Concentration ^a	Reference ^b
PCB 10	75,000 DW	18
PCB 18	7800 DW	18
PCB 31	12,000 DW	18
PCB 32	12,000 DW	18
PCB 47	12,000 DW	18
PCB 49	21,000 DW	18
PCB 50	9200 DW	18
PCB 52	30,000 DW	18
PCB 64	11,000 DW	18
PCBs 82/85/110	12,000 DW	18
PCB 92	5500 DW	18
Others	52,000 DW	18
Ohio, Cuyahoga River; 1984		
PCB 77	0.09 DW	15
PCB 126	0.011 DW	15
PCB 169	<0.01 DW	15
Rhode Island, Narragansett Bay; 1984–89; total PCBs	>200,000 DW	12
South Carolina, Lake Hartwell; total PCBs		
Cores; 1984–87	Max. 153,840 DW	19
Cores; distance from source, in km		
33.2	40,500 DW; Max. 88,500 DW	20
78.2	380 DW; Max. 1100 DW	20
South Dakota; waterfowl production areas; 1980–82; total PCBs	ND	16
U.S. National Wildlife Refuges; North Central area; 1980–82; total PCBs	ND–1 DW	16
Virginia; Elizabeth River; 1984–89; total PCBs	>200,000 DW	12
Washington; total PCBs		
Elliot Bay; 1984–89	>200,000 DW	12
Puget Sound; 1980s		
Main basin	93 DW	21
Nonurban bays	15–34 DW	21
Urban bays	750 DW	21
Wisconsin		
Fox River; 1984		
PCB 77	1.4 DW	15
PCBs 126, 169	ND	15
Fox River; 1988		
Total PCBs	22,000–41,450 DW	15, 22
Total AHH-active PCBs	710 DW	15
PCB 77	8.5 DW	15
PCB 105	6 DW	15
PCB 118	17 DW	15
PCB 128	13 DW	15
PCB 138	87 DW	15
PCB 156	2 DW	15
PCB 158	1.5 DW	15
PCB 170	31 DW	15
Green Bay; 1984		
PCB 77	0.94 DW	15
PCB 126	0.024 DW	15
PCB 169	<0.005 DW	15
Lake Pepin; 1983		
PCBs 77, 126, 169	<0.002–0.002 DW	15

Table 24.8 (continued) PCB Concentrations in Field Collections of Selected Nonbiological Materials (Concentrations are in g/kg fresh weight [FW] or dry weight [DW] unless indicated otherwise.)

Material	Concentration ^a	Reference ^b
Total PCBs	56 DW	15
Menominee River; 1984		
PCB 77	0.1 DW	15
PCB 126	0.04 DW	15
PCB 169	0.003 DW	15

SNOW

Arctic Ocean; 1986–87; total PCBs	Max. 0.000125 FW	2
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^a Concentrations are shown as mean, range (in parentheses), maximum (Max.), and nondetectable (ND).

^b 1, Larsson et al. 1992; 2, Hargrave et al. 1989; 3, Hargrave et al. 1992; 4, Burgess et al. 1993; 5, Boehm 1981; 6, Eisenreich et al. 1989; 7, Oliver et al. 1989; 8, Asplund et al. 1990; 9, Buser and Muller 1986; 10, NOAA 1987; 11, Chapman et al. 1986; 12, NOAA 1991; 13, Law and Goerlitz 1974; 14, Huckins et al. 1988; 15, Smith et al. 1990; 16, Martin and Hartman 1985; 17, Stainken and Rollwagen 1979; 18, Rhee et al. 1989; 19, Elzerman et al. 1991; 20, Dunnivant et al. 1989; 21, Ginn and Pastorok 1992; 22, Ankley et al. 1992.

24.4.3 Marine Mammals

Marine mammals are the most vulnerable to and most probable target organisms of PCBs (Tanabe 1988). The metabolic potential to degrade organochlorine contaminants and therefore accumulate relatively high concentrations of persistent PCBs is lower in marine mammals, particularly in cetaceans, than in terrestrial mammals (Tanabe et al. 1987; Kannan et al. 1989, 1993). Dead harbor porpoises (*Phocoena phocoena*) along the Dutch coast contained 51,350 to 139,790 µg total PCBs/kg blubber; 35 to 50% of the total PCBs were PCBs 138 and 153 (Duinker et al. 1988a). A similar pattern was noted in harbor porpoises from Scandinavia in 1987 to 1991 (Kleivane et al. 1995), and harbor seals from the northern hemisphere in 1988 to 1995 (Vetter et al. 1996). The intrinsic toxicity of PCBs mainly resulted from the planar PCB congeners that imposed a greater toxic threat to marine mammals than chlorinated dioxins and furans (Tanabe 1988; Tanabe et al. 1989; Daelemans et al. 1993; Falandysz et al. 1994b). The toxic threat of planar PCBs to higher aquatic predators was primarily assessed by 2,3,7,8-tetracholoridibenzo-*p*-dioxin toxic equivalent analysis, which is based on the induction of arylhydrocarbon hydroxylase (AHH) and ethoxyresorufin *O*-deethylase (EROD) (Kannan et al. 1989). The concentrations of planar PCBs in marine mammals were higher (in the order of di-*ortho* > mono-*ortho* > non-*ortho* congeners) and significantly higher than the levels of toxic dioxins and furans (Tanabe 1988; Tanabe et al. 1989; Kannan et al. 1989). In particular, the accumulation of PCBs 105 and 126 in carnivorous aquatic mammals is cause for considerable concern (Tanabe et al. 1987, 1989; Kannan et al. 1989; Daelamans et al. 1993; Storr-Hansen and Spliid 1993). TCDD-like toxicity is relatively serious in Baikal seals (*Phoca sibirica*) because of the enrichment of toxic PCB congeners in tissues (Nakata et al. 1997).

Declines in total PCB levels in blubber of marine mammals between the late 1960s and 1990 to 1992 have been noted worldwide (Muir et al. 1988; Lake et al. 1995a), possibly because of the PCB ban in the mid-1970s. PCB levels in animal tissues will probably not decline in the near future because of the greater quantities of PCBs still in use than the quantity that already escaped into the open environment (Tanabe 1988). Temporal changes of PCBs in remote marine waters are slow and could be attributable to the large PCB load in the marine environment (Loganathan et al. 1990). The geographical distribution of planar PCBs with reference to total PCBs did not vary in terrestrial, coastal, and open ocean mammals, whereas those of dioxins and furans decreased from land to ocean (Tanabe et al. 1989). PCB concentrations — including planar PCBs — in blubber of striped

dolphins (*Stenella coeruleoalba*) from the Mediterranean Sea in 1990 to 1992 are among the highest reported in the literature (Table 24.9) (Kannan et al. 1993; Borrell et al. 1996). Striped dolphins affected by the western Mediterranean morbillivirus epizootic also contained extremely high concentrations of PCBs (including non- and mono-*ortho* planar congeners) and low immune suppression, suggesting that PCBs were a major factor in this epizootic; however, this needs verification. Planar PCBs in blubber of striped dolphins accounted for about 53% of total PCBs and for virtually all of the potential toxicity. Di-*ortho* planar PCBs accounted for 93.7% of all planar PCB residues (especially PCB 170) in striped dolphins and for 21% of the potential toxicity, mono-*ortho* planars for 6.3% of the residues and 70.8% of the potential toxicity, and non-*ortho* planars (especially PCB 126) for 0.03% of the residues and 8.2% of the potential toxicity (Kannan et al. 1993; Borrell et al. 1996). Concentrations of PCBs in tissues of adult male striped dolphins of the same age from the Pacific coast of Japan did not change between 1979 and 1986 (Loganathan et al. 1990). However, PCB concentrations in blubber of male striped dolphins were about twofold higher than in females, and this is attributed to PCB transfer to offspring by females (Borrell et al. 1996).

Beluga whales (*Delphinapterus leucas*) of the St. Lawrence River estuary were severely contaminated by DDT metabolites and PCBs; the highest residues were in blubber (Masse et al. 1986). High concentrations of PCBs and other organochlorines may impair the immune function in these animals (De Guise et al. 1998). Several PCB congeners known to be AHH inducers — including PCBs 138 and 153 — were among the major PCB congeners detected in tissues of beluga whales (Masse et al. 1986). Because these compounds are not metabolized and persist indefinitely in tissues of the beluga whale, the integrated total exposure to these AAH inducers may be significant. Considerable variations by sex, age, and lipid content of the tissues in PCB concentrations were observed in beluga whales. Qualitative and quantitative differences in the PCB profiles of beluga whales were not solely related to the respective lipid content of the tissues, but also to the specific nature of the lipids, which varied from one tissue to the other. The major PCB components in various tissues of beluga whales were PCBs 52, 99, 129, 137, 141, 153, 165, 180, and 185. Organ-specific retention of some PCB congeners occurs in beluga whales. PCBs 165 and 179, which were minor in blubber, were more abundant in kidney, liver, and lung. PCB 129 was more abundant in kidney and liver than in lung. Atlantic cod (*Gadus morhua*) composed a minor part of the beluga whale diet. However, PCB patterns in cod positively correlated with those in beluga whale tissues, suggesting a common source of intake. PCB congeners 52, 91, 99, 108, 118, 128, 138, 144, 149, 153, 163, and 180 were among the most abundant chlorinated biphenyls in cod liver oil and in the beluga whale blubber, liver, lung, kidney, and milk (Masse et al. 1986). Beluga whales from the St. Lawrence River estuary had elevated levels of PCBs in blubber in 1987 to 1990 due to elevated levels in diet, as judged by bioaccumulation ratios. PCB 126 was the most prominent planar PCB in blubber; other biologically active congeners found were PCBs 105 and 118 (Muir et al. 1996a). Significant declines in concentrations of Aroclor PCBs were measured in blubber of male — but not female — beluga whales from the St. Lawrence estuary between the 1982 to 1985 and 1993/94 collection periods; these declines were also evident in eels, harp seals, and seabirds (Muir et al. 1996b).

When compared to other cetaceans, PCB residues in blubber of harbor porpoises (*Phocoena phocoena*) from the Black Sea showed a measurable sexual difference. PCB concentrations were lower in older female porpoises possibly due to lactational transfer to their calves, while in males the PCB concentrations were positively correlated with increasing age (Tanabe et al. 1997). In stellar sea lions (*Eumetopias jubatus*), the transfer rate of PCBs through lactation was estimated at 80% of the total body PCB burden of adult females (Lee et al. 1996). PCB concentrations in liver of the stellar sea lion from the Bering Sea increased with increasing age and correlated positively with those of blubber (Lee et al. 1996). In ringed seals (*Phoca hispida*) from the Russian Arctic, lactational transfer of PCBs was estimated at 25% of whole-body burden in the mature female (Nakata et al. 1998), or about one third that of stellar sea lions. In grey seals (*Halichoerus*

grypus), PCBs were transferred from blubber to milk by way of the circulatory system. Of the total concentration of PCBs in various tissues of maternal grey seals, PCB 153 accounted for about 30% in blubber, 20% in serum, and 30% in milk; PCB 180 accounted for 20% in blubber, 20% in serum, and 10% in milk; and PCB 77 accounted for 20% in serum (Addison and Brodie 1987). Most of the toxicity in grey seal milk was attributed to PCB 126; the mono-*ortho*-chlorinated PCBs 105, 118, 156 and *ortho*-chlorinated PCBs 170 and 180 — especially PCB 170 — were responsible for 47% of the toxicity (Green et al. 1996). In whales (*Ziphius* sp.), the dominant PCB congeners in blubber had 5 to 8 chlorines; PCBs 138, 153, 149, 180, and 201 accounted for about 70% of the total PCBs (Duinker et al. 1988b). In the Canadian Arctic food chain of Arctic cod (*Boreogadus saida*) to ringed seal (*Phoca hispida*) to polar bear (*Ursus maritimus*), the total PCB concentrations, in µg/kg FW, ranged from 4 in cod muscle to 680 in seal blubber to 4500 in bear fat. The hexachlorobiphenyl PCB 153 accounted for 42% of the total PCBs in bear fat and for only 20% in seal blubber and 7% in cod muscle. Tri- and tetrachlorobiphenyl homologues predominated in cod, penta- and hexachlorobiphenyl congeners predominated in seal blubber, and hexa- and heptachlorobiphenyl congeners in fat of polar bears (Muir et al. 1988).

Table 24.9 PCB Concentrations in Field Collections of Selected Aquatic Organisms (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
INVERTEBRATES		
Bivalve molluscs, (<i>Mytilus</i> , <i>Tapes</i> , <i>Ostrea</i> , <i>Crassostrea</i> ; Catalonia, Spain, 1989–90; soft parts		
Sum of PCBs 28, 52, 101, 118, 138, 153, 180	1.4–596.0 DW	1
Crabs; southern Norway, 1990–92; hepatopancreas		
PCBs 28, 52, 66, 74, 99, 101, 110, 157	ND	2
PCB 77	Max. 3.4 LW	2
PCB 126	Max. 2.5 LW	2
PCB 169	Max. 1.1 LW	2
PCB 209	Max. 2600 LW	2
Total of PCBs 105, 118, 128, 138, 149, 153, 156, 170, 180, 187, 194, 206	600–2050 LW	2
American oyster, <i>Crassostrea virginica</i> ; soft parts; 1990–1991; Galveston Bay, TX vs. Tampa Bay, FL; maximum values		
PCB 77	2.0 DW vs. 1.5 DW	45
PCB 105	39.0 DW vs. 7.6 DW	45
PCB 118	48.0 DW vs. 36.0 DW	45
PCB 126	2.2 DW vs. 0.3 DW	45
PCB 128	4.4 DW vs. 2.0 DW	45
PCB 138	50.0 DW vs. 8.9 DW	45
PCB 169	0.79 DW vs. 0.28 DW	45
Freshwater crab, <i>Eriocheir japonicus</i> ; hepatopancreas; Tone River, Japan; August–September		
PCB 77	2.5 LW	64
PCB 126	0.45 LW	64
PCB 169	0.08 LW	64
Mayfly, <i>Hexagenia bilineata</i> ; upper Mississippi River, summer 1988; total PCBs (sum of 125 congeners)	210–4100 DW; 1200–29,000 LW	46
Mayfly, <i>Hexagenia limbata</i> ; Lake St. Clair, July 1987, sediments vs. whole adults		
PCB 87	1.2 DW vs. 0.7 FW	34
PCB 101	2.9 DW vs. 1.7 FW	34
PCB 118	2.1 DW vs. 0.9 FW	34
PCB 138	2.4 DW vs. ND	34
PCB 153	1.8 DW vs. 0.9 FW	34
PCB 180	0.8 DW vs. 0.6 FW	34

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Burrowing mayfly, <i>Hexagenia</i> sp., adults; summer 1987; contaminated sites on Detroit and St. Clair Rivers		
PCB 18	Max. 7.6 DW	35
PCB 31	Max. 2.8 DW	35
PCB 52	Max. 10.9 DW	35
PCB 66	Max. 4.6 DW	35
PCB 87	Max. 6.5 DW	35
PCB 97	Max. 3.5 DW	35
PCB 101	Max. 16.6 DW	35
PCB 110	Max. 6.0 DW	35
PCB 118	Max. 13.6 DW	35
PCB 138	Max. 18.1 DW	35
PCB 141	Max. 6.1 DW	35
PCB 153	Max. 23.2 DW	35
PCB 170	Max. 4.8 DW	35
PCB 180	Max. 10.4 DW	35
PCB 182	Max. 7.3 DW	35
PCB 194	Max. 4.7 DW	35
Squid, <i>Ilex illecebrosus argentinus</i> ; near Falkland Islands, March 1988; muscle		
PCBs 28, 31, 44, 47 49, 52, 66, 87, 97, 101, 105, 110, 118, 128, 138, 141, 149, 151, 153, 170, 180, 184, 187, 206	ND	3
Common mussel, <i>Mytilus edulis</i>		
German Bight, 6 locations; 1993; extractable organic matter; spring vs. autumn		
PCB 77	33–50 DW vs. 4–8 DW	49
PCB 81	5–7 DW vs. 2–4 DW	49
PCB 105	45–60 DW vs. 37–130 DW	49
PCB 114	Max. 1.1 DW vs. Max. 0.5 DW	49
PCB 118	75–97 DW vs. 65–520 DW	49
PCB 123	9–150 DW vs. 0.2–4 DW	49
PCB 126	4–15 DW vs. 6–12 DW	49
PCB 138	280–420 DW vs. 83–210 DW	49
PCB 156	Max. 3.9 DW vs. Max. 1.4 DW	49
PCB 169	0.0–2.1 DW vs. 0.4–4.1 DW	49
PCB 170	0.0–7.9 DW vs. 2.2–4.1 DW	49
PCB 180	18–43 DW vs. 9–23 DW	49
PCB 189	0.5–1.7 DW vs. 0.1–0.4 DW	49
Long Island Sound, New York vs. freshwater mussels (species unknown) from a contaminated site near Troy, New York; soft parts		
Total PCBs	247 DW vs. 2734 DW	4
Total planar PCBs	11.9 DW vs. 112.9 DW	4
PCB 77	0.4 DW vs. 6.9 DW	4
PCB 81	ND vs. 0.9 DW	4
PCB 105	3.3 DW vs. 27.0 DW	4
PCB 114	ND vs. 4.0 DW	4
PCB 118	8 DW vs. 53 DW	4
PCB 123	ND vs. ND	4
PCB 126	ND vs. 0.6 DW	4
PCB 156	ND vs. 1.8 DW	4
PCB 157	ND vs. 0.6 DW	4
PCB 167	0.2 DW vs. 18.6 DW	4
PCB 169	ND vs. 0.1 DW	4
PCB 189	ND vs. 0.1 DW	4

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
FISHES		
Bloater, <i>Coregonus hoyi</i> ; Lake Michigan		
Whole; total PCBs		
1972 vs. 1975	5700 FW vs. 4500 FW	5
1978 vs. 1982	3100 FW vs. 2100 FW	5
1986	1600 FW	5
Diet; invertebrate prey		
1970	350–650 FW	59
1975	170–250 FW	59
1980	120–210 FW	59
1990	50–100 FW	59
Margined flyingfish, <i>Cypselurus cyanopterus</i> ; near Falkland Islands, March 1988; muscle		
PCBs 28, 31, 44, 47, 49, 52, 66, 87, 97, 101, 105, 110, 128, 141, 151, 170, 194, 206	0.01–0.1 FW	3
PCBs 118, 138, 180, 187	0.14–0.31 FW	3
PCB 153	0.45 FW	3
Fish liver oil; various species; Finland		
PCB 77	2.7 LW	6
PCB 105	30.0 LW	6
PCB 126	0.62 LW	6
PCB 169	0.13 LW	6
Fish muscle; various species sold for human consumption; Finland		
PCB 77	0.006–0.153 FW	6
PCB 105	0.113–2.7 FW	6
PCB 126	0.002–0.035 FW	6
PCB 169	ND–0.012 FW	6
Fish, 14 species, muscle; Wisconsin, 1986–87; total PCBs	1300 (700–7000) FW	7
Freshwater fishes; U.S.; nationwide; whole; adults; total PCBs measured as Aroclors 1248, 1254, and 1260; noncontaminated sites		
1976–77	Max. 70.6 FW	48
1978–79	Max. 92.8 FW	48
1980–81	Max. 11.3 FW	48
1984	Max. 6.7 FW	48
Freshwater fishes; U.S.; nationwide; whole; 1986–87; mostly contaminated sites		
Median	209 FW	52
Mean	1890 FW	52
Maximum	124,000 FW	52
Atlantic cod, <i>Gadus morhua</i>		
Liver; Norway, 1988		
PCB 28	19 (0.5–64) FW	8
PCB 52	31 (0.5–144) FW	8
PCB 101	78 (0.5–533) FW	8
PCB 118	170 (1.1–653) FW	8
PCB 138	283 (1.4–918) FW	8
PCB 153	363 (1.3–1175) FW	8
PCB 170	28 (0.4–163) FW	8
PCB 180	68 (1.1–391) FW	8
PCB 209	7 (0.3–35) FW	8

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Liver; Norway 1989		
PCB 77	Max. 4.8 LW	9
PCB 105	Max. 39.0 LW	9
PCB 126	Max. 1.0 LW	9
PCB 169	Max. 0.3 LW	9
Muscle; Baltic Sea, 1988		
PCB 77	Max. 4.2 LW	9
PCB 105	Max. 36.0 LW	9
PCBs 126, 169	ND	9
Ictalurids, 4 species (blue catfish, <i>Ictalurus furcatus</i> ; black bullhead, <i>Ameiurus melas</i> ; channel catfish, <i>Ictalurus punctatus</i> ; flathead catfish, <i>Pylodictis olivaris</i>); whole; 1944-km stretch of Mississippi River; July–August 1987		
Total PCBs	Max. 138 FW; Max. 2910 LW	10
Tetrachlorobiphenyls	Max. 21 FW; Max. 671 LW	10
Pentachlorobiphenyls	Max. 56 FW; Max. 1230 LW	10
Hexachlorobiphenyls	Max. 67 FW; Max. 870 LW	10
Heptachlorobiphenyls	Max. 12 FW; Max. 140 LW	10
Dab, <i>Limanda limanda</i>		
German Bight; December 1988–May 1989; total of 35 PCB congeners		
Females		
Liver (mostly PCBs 77, 138, and 153)	1200–16,200 LW	36
Ovaries (mostly PCBs 77, 138, and 153)	2600–4300 LW	36
Males		
Liver	900–24,400 LW	36
Testes (mostly PCBs 15, 13, 52)	1900–11,800	36
North Sea; January–March 1987; total PCBs		
Liver, Females	1450 FW	11
Liver, Males	2000 FW	11
Ovaries	2600 FW	11
Tilefish, <i>Lopholatilus chamaeleonticeps</i> ; 1981–1982; New Jersey vs. Georges Bank		
Total PCBs		
Gonad	3373 DW vs. 1004 DW	12
Liver	4693 DW vs. 1002 DW	12
Muscle	435 DW vs. 190 DW	12
Dichlorobiphenyls		
Gonad	196 DW vs. 15 DW	12
Liver	258 DW vs. 42 DW	12
Muscle	9 DW vs. 5 DW	12
Trichlorobiphenyls		
Gonad	164 DW vs. 11 DW	12
Liver	278 DW vs. 35 DW	12
Muscle	11 DW vs. 7 DW	12
Tetrachlorobiphenyls		
Gonad	1176 DW vs. 192 DW	12
Liver	789 DW vs. 151 DW	12
Muscle	62 DW vs. 25 DW	12
Pentachlorobiphenyls		
Gonad	806 DW vs. 463 DW	12
Liver	1273 DW vs. 358 DW	12

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Hexachlorobiphenyls		
Gonad	664 DW vs. 191 DW	12
Liver	1290 DW vs. 221 DW	12
Muscle	112 DW vs. 46 DW	12
Heptachlorobiphenyls		
Gonad	158 DW vs. 27 DW	12
Liver	109 DW vs. 27 DW	12
Muscle	14 DW vs. 3 DW	12
Nonochlorobiphenyls		
Gonad	62 DW vs. 6 DW	12
Liver	22 DW vs. 13 DW	12
Muscle	3 DW vs. 0.5 DW	12
Decachlorobiphenyl		
Gonad	45 DW vs. 6 DW	12
Liver	24 DW vs. 16 DW	12
Muscle	2 DW vs. 0.7 DW	12
PCB 77		
Gonad	48 DW vs. 19 DW	12
Liver	86 DW vs. 45 DW	12
Muscle	62 DW vs. ND	12
PCB 126		
Gonad	ND vs. 27 DW	12
Liver	214 DW vs. 33 DW	12
Muscle	19 DW vs. 4 DW	12
Argentinian hake, <i>Merluccius merluccius hubbsi</i> ; near Falkland Islands, March 1988; muscle		
PCBs 28, 31, 44, 47, 49, 87, 97, 105, 128, 141, 151, 194, 206	0.01–0.04 FW	3
PCBs 52, 66, 101, 110, 170	0.05–0.1 FW	3
PCBs 118, 138, 149, 153, 180, 187	0.11–0.28 FW	3
Striped bass, <i>Morone saxatilis</i> ; muscle		
New York, Long Island Sound, 1985		
Total PCBs	5500 FW; Max. 15,000 FW	13
PCBs 48, 52, 82, 101, 118, 138, 153	Contributed at least 28% of total PCB concentration	13
New York, various locations		
Total PCBs	1100–24,100 FW	4
Total planar PCBs	100–2020 FW	4
PCB 77	Max. 37 FW	4
PCB 81	Max. 5 FW	4
PCB 105	Max. 562 FW	4
PCB 114	Max. 112 FW	4
PCB 118	Max. 779 FW	4
PCB 126	Max. 8 FW	4
PCB 156	Max. 202 FW	4
PCB 157	Max. 68 FW	4
PCB 167	Max. 232 FW	4
PCB 169	Max. <0.1 FW	4
PCB 189	Max. 19 FW	4
Striped mullet, <i>Mugil cephalus</i> ; Japan, May 1976; muscle		
Total PCBs	1200 (220–3200) FW	14
PCB 77	2.1 (0.6–4.8) FW	14
PCB 126	0.1 (0.03–0.23) FW	14
PCB 169	0.002 (0.001–0.004) FW	14

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Rainbow trout, <i>Oncorhynchus mykiss</i> ; Lake Ontario, 1989; liver vs. muscle		
PCB 77	2.9 FW, 78 LW vs. 3.3 FW, 85 LW	31
PCB 126	0.7 FW, 18 LW vs. 0.9 FW, 22 LW	31
PCB 169	0.3 FW, 8 LW vs. 0.3 FW, 9 LW	31
Red mullet, <i>Mullus barbatus</i> ; Spain, Mediterranean coast, summers 1989, 1990; muscle		
Sum of PCBs 28, 52, 101, 118, 138, 153, 180	21.2 (7.4–33.2) FW	33
Sum of PCBs 18, 31, 44, 97, 99, 105, 110, 128, 134, 146, 149, 151, 170, 174, 177, 183, 187, 194, 201	38.4 (15.5–61.4) FW	33
Chinook salmon, <i>Oncorhynchus tshawytscha</i> ; Lake Michigan, 1986; eggs		
Total PCBs	7020 FW	32
PCBs 77, 105, 118, 126	0.2–12 FW	32
Fathead minnow, <i>Pimephales promelas</i> ; upper Hudson River, 1985; caged juveniles exposed for 3–42 days during the year; whole fish	Regardless of exposure duration or season, the consistently most abundant congeners in caged fish were PCBs 37, 42, 44, 47, 48, 49, 52, 59, 61, 66, 70, 73, 75, 76, 93, 95, and 104	15
European flounder, <i>Platichthys flesus</i> ; Norway, 1988; liver		
PCB 28	7 (0.3–68) FW	8
PCB 52	21 (0.7–609) FW	8
PCB 101	44 (1.1–1452) FW	8
PCB 118	77 (3.2–1693) FW	8
PCB 138	90 (1.1–1960) FW	8
PCB 153	95 (5.7–2088) FW	8
PCB 170	7 (0.4–158) FW	8
PCB 180	16 (1.2–296) FW	8
PCB 209	4 (0.4–88) FW	8
Paddlefish, <i>Polyodon spathula</i> ; Ohio River, Kentucky; 1988–89; total PCBs; males vs. females		
Gonads	16,200 (5600–23,000) FW vs. 7300 (50–18,700) FW	16
Red muscle (females only)	4200 (2000–6300) FW	16
White muscle	700 (50–3300) FW vs. 400 (50–1000) FW	16
Winter flounder, <i>Pleuronectes americanus</i>		
Long Island Sound, New York, 1984–86; total PCBs		
Liver	420–2400 FW	17
Ovaries	30–730 FW	17
Testes	50–190 FW	17
New Bedford Harbor, Massachusetts vs. two control sites in Rhode Island; spring, 1988; liver		
Planar PCBs		
PCB 77	391 DW vs. 4.6 DW	38
PCB 126	49 DW vs. 1.8 DW	38
PCB 169	3.7 DW vs. 0.4 DW	38
Nonplanar PCBs		
PCB 47	2530 DW vs. 14 DW	38
PCB 52	1100 DW vs. 6.5 DW	38
PCB 101	2450 DW vs. 49 DW	38
PCB 105	2200 DW vs. 92 DW	38
PCB 118	12,800 DW vs. 239 DW	38
PCB 128	1370 DW vs. 47 DW	38
PCB 138	7070 DW vs. 286 DW	38

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 151	422 DW vs. 19 DW	38
PCB 153	11,000 DW vs. 441 DW	38
PCB 180	1010 DW vs. 141 DW	38
PCB 194	79 DW vs. 23 DW	38
PCB 195	32 DW vs. 1.4 DW	38
PCB 206	33 DW vs. 33 DW	38
PCB 209	3.1 DW vs. 20.5 DW	38
Total PCBs		
Gravid females	333,000 DW vs. 3900 DW	38
Spent females	132,000 DW vs. 4000 DW	38
Ripe males	124,000 DW vs. 13,300 DW	38
Sediments	8000 DW vs. 500 DW	38
Atlantic salmon, <i>Salmo salar</i> , Baltic Sea and environs		
Eggs, 1988		
PCB 77	Max. 28 LW	9
PCB 105	Max. 90 LW	9
PCB 126	Max. 2.4 LW	9
PCB 169	Max. 0.6 LW	9
Muscle, 1985		
Total PCBs	Max. 332 FW	18
PCB 77	Max. 1.1 FW	18
PCBs 126, 169	ND	18
Muscle, 1988		
PCB 77	Max. 34 LW	9
PCB 105	Max. 170 LW	9
PCB 126	Max. 3.8 LW	9
PCB 169	Max. 0.8 LW	9
Brown trout, <i>Salmo trutta</i> ; Catalonia, Spain; isolated mountain lakes; summers 1989, 1990; muscle		
Sum of PCBs 28, 52, 101, 118, 138, 153, 180	2.5 (1.3–3.8) FW	33
Sum of PCBs 18, 31, 44, 97, 99, 105, 110, 128, 134, 146, 149, 151, 170, 174, 177, 183, 187, 194, 201	4.8 (2.7–7.5) FW	33
Lake trout, <i>Salvelinus namaycush</i>		
Lake Ontario; total PCBs; whole fish		
1977 vs. 1978	6800 FW vs. 8000 FW	19
1979 vs. 1980	3700 FW vs. 3900 FW	19
1981 vs. 1982	2900 FW vs. 5300 FW	19
1983 vs. 1984	4500 FW vs. 4800 FW	19
1985 vs. 1986	2500 FW vs. 3100 FW	19
1987 vs. 1988	3400 FW vs. 2500 FW	19
Lake Michigan		
Adult females; whole; total PCBs		
1985	4900–10,100 FW	47
1986	6100–6800 FW	47
1987	3500–13,900 FW	47
Adult females; 1987; whole fish vs. eggs		
PCB 77	9.7 FW vs. 2.1 FW	47
PCB 126	4.0 FW vs. 0.65 FW	47
PCB 169	<0.4 FW vs. <0.4 FW	47
Great Lakes; adults; liver; 1993		
PCB 77	0.07–92.9 FW	63
PCB 81	<0.00009–0.3 FW	63
PCB 126	0.01–0.58 FW	63
PCB 169	0.0001–0.26 FW	63

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
MARINE MAMMALS		
Giant bottlenosed whale, <i>Berardius bairdii</i> ; blubber Japan, July 1985		
Total PCBs	2300 (1800–2800) FW	20, 21
Di-ortho planars		
PCB 128	54 (36–70) FW	20, 21
PCB 138	460 (260–810) FW	20, 21
Mono-ortho planars		
PCB 105	5 (2–8) FW	20, 21
PCB 118	47 (15–94) FW	20, 21
PCB 156	23 (6–50) FW	20, 21
Non-ortho planars		
PCB 77	1.3 (0.7–1.9) FW	20, 21
PCB 126	0.35 (0.1–0.57) FW	20, 21
PCB 169	0.24 (0.09–0.45) FW	20, 21
Northern north Pacific, July 1985		
Total PCBs	2600 (2400–2800) FW	14
PCB 77	1.6 (1.3–1.9) FW	14
PCB 126	0.48 (0.39–0.57) FW	14
PCB 169	0.31 (0.17–0.45) FW	14
Beluga whale, <i>Delphinapterus leucas</i>		
St. Lawrence estuary; found dead; 1987–90; blubber; females vs. males		
Total PCBs	29,600 (8820–83,300) LW vs. 78,900 (7930–451,000) LW	53
TrichloroBPs	30 LW vs. 37 LW	53
TetrachloroBPs	2470 LW vs. 10,200 LW	53
PentachloroBPs	6360 LW vs. 17,600 LW	53
HexachloroBPs	11,300 LW vs. 32,900 LW	53
HeptachloroBPs	6920 LW vs. 14,300 LW	53
Nonachloro and decachloroBPs	121 LW vs. 58 LW	53
St. Lawrence River estuary; found dead; 1993–94; blubber; females vs. males		
Total PCBs	61,100 (15,300–181,000) LW vs. 79,200 (49,300–135,000) LW	54
TrichloroBPs	188 LW vs. 305 LW	54
TetrachloroBPs	4900 LW vs. 7290 LW	54
PentachloroBPs	12,300 LW vs. 16,100 LW	54
HexachloroBPs	26,700 LW vs. 36,200 LW	54
HeptachloroBPs	13,800 LW vs. 15,500 LW	54
OctachloroBPs	2378 LW vs. 3030 LW	54
Nonachloro and decachloroBPs	172 LW vs. 230 LW	54
Canada, St. Lawrence estuary; 1983–84; beach-stranded whales; total PCBs		
Blubber	Max. 72,200 FW	22
Kidney	Max. 10,000 FW	22
Liver	Max. 2500 FW	22
Lung	Max. 560 FW	22
Milk	Max. 1720 FW	22
Dolphins and toothed whales; blubber; total PCBs		
Atlantic Ocean, 1980–88; 15 species	130–190,000 FW	23
Indian Ocean, 1980–91; 5 species	520–7900 FW	23
Pacific Ocean, 1980–86; 7 species	190–40,000 FW	23

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Stellar sea lion, <i>Eumetopias jubatus</i> ; Alaska and Russian portion of Bering Sea; blubber; 1976–81; males vs. females	17,000 (5700–41,000) LW vs. 5300 (600–16,000) LW	55
Gray seal, <i>Halichoerus grypus</i> Baltic Sea and environs; 1981–87; blubber		
PCB 77	Max. 10 LW	9
PCB 105	Max. 180 LW	9
PCB 126	Max. 3 LW	9
PCB 169	Max. 2 LW	9
Nova Scotia, 1984–85; total PCBs; mother vs. pups		
Blood	6080 LW vs. 6240 LW	24
Blubber	16,200–30,300 LW vs. 8800–10,400 LW	24
Milk (mother)	7480–10,120 LW	24
Serum	10,210 LW vs. 11,840 LW	24
Scotland; Isle of May; 1990–93; maternal milk		
PCB 77	20–66 LW	60
PCB 126	81–434 LW	60
PCB 169	11–352 LW	60
Pacific white-sided dolphin, <i>Lagenorhynchus obliquidens</i> ; Japan, 1981; blubber		
Total PCBs	53.00 (40,000–71,000) FW	14
PCB 77	27 (14–38) FW	14
PCB 126	3.8 (3.2–4.4) FW	14
PCB 169	1.2 (0.9–1.4) FW	14
Finless porpoise, <i>Neophocaena phocaenoides</i> ; Japan, July 1985; blubber		
Total PCBs	320,000 FW	20, 21
Di-ortho planars		
PCB 128	3500 FW	20, 21
PCB 138	35,000 FW	20, 21
Mono-ortho planars		
PCB 105	1200 FW	20, 21
PCB 118	11,000 FW	20, 21
PCB 156	160 FW	20, 21
Non-ortho planars		
PCB 77	14 FW	14, 20, 21
PCB 126	0.9 FW	14, 20, 21
PCB 169	0.6 FW	14, 20, 21
Killer whale, <i>Orcinus orca</i> ; blubber		
Died after 2 years in captivity		
Total PCBs	160,000 FW	14
PCB 77	42.0 FW	14
PCB 126	4.0 FW	14
PCB 169	3.6 FW	14
Pacific coast of Japan; July 1985		
Total PCBs	370,000 (350,000–410,000) FW	20, 21
Di-ortho planars		
PCB 128	8000 (3200–12,000) FW	20, 21
PCB 138	65,000 (24,000–85,000) FW	20, 21
Mono-ortho planars		
PCB 105	3000 (2300–3600) FW	20, 21
PCB 118	11,000 (6700–14,000) FW	20, 21
PCB 156	1900 (950–3100) FW	20, 21

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Non-ortho planars		
PCB 77	48 (39–55) FW	14, 20, 21
PCB 126	3.7 (2.4–4.4) FW	14, 20, 21
PCB 169	7.7 (2.3–12.0) FW	14, 20, 21
Ringed seal, <i>Phoca hispida</i> ; Kera Sea; Russian Arctic; 1995; blubber		
Total PCBs	7100 LW	62
Non-ortho congeners		
PCB 77	0.99 LW	62
PCB 126	0.57 LW	62
PCB 169	<0.003 LW	62
Mono-ortho congeners		
PCB 105	230 LW	62
PCB 118	450 LW	62
PCB 156	61 LW	62
Di-ortho congener		
PCB 180	270 LW	62
Baikal seal, <i>Phoca sibirica</i> ; Lake Baikal, Siberia; blubber; May–June 1992		
Males; immature vs. mature		
Total PCBs	5000 FW vs. 26,000 FW	56
PCB 77	6.3 FW vs. 23.0 FW	56
PCB 126	2.4 FW vs. 3.5 FW	56
PCB 169	0.2 FW vs. 0.4 FW	56
PCB 105	250 FW vs. 1200 FW	56
PCB 118	650 FW vs. 2800 FW	56
PCB 156	87 FW vs. 260 FW	56
PCB 137	180 FW vs. 1300 FW	56
PCB 138	650 FW vs. 3800 FW	56
PCB 153	990 FW vs. 6700 FW	56
PCB 180	250 FW vs. 1700 FW	56
Females; immature vs. mature		
Total PCBs	5000 FW vs. 10,000 FW	56
PCB 77	8.8 FW vs. 14.0 FW	56
PCB 126	2.5 FW vs. 3.4 FW	56
PCB 169	0.3 FW vs. 0.3 FW	56
PCB 105	260 FW vs. 360 FW	56
PCB 118	740 FW vs. 960 FW	56
PCB 156	74 FW vs. 150 FW	56
PCB 137	160 FW vs. 370 FW	56
PCB 138	650 FW vs. 1400 FW	56
PCB 153	990 FW vs. 2400 FW	56
PCB 180	190 FW vs. 710 FW	56
Harbor porpoise, <i>Phocoena phocoena</i>		
Black Sea, Turkey; 1993; blubber; accidentally drowned in sturgeon trammel nets; males vs. females; total PCBs	16,000 FW vs. 12,000 FW; Max. 39,000 FW	57
Dutch coast; 1990–93; found stranded		
Blubber		
PCB 77	0.3–3.2 FW	58
PCB 126	0.2–1.1 FW	58
PCB 169	0.2–1.2 FW	58
Maximum values		
PCBs 31, 50, 207, and 209	34–78 FW	58

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCBs 18, 28, 44, 97, 156, 195, and 202	143–464 FW	58
PCBs 105, 143, 194	538–658 FW	58
PCBs 52, 101, 118, 151, 170, 183	1405–2899 FW	58
PCB 138	12,256 FW	58
PCB 149	6395 FW	58
PCB 153	15,676 FW	58
PCB 180	4065 FW	58
PCB 187	4089 FW	58
PCB 153 vs. total PCBs		
Blubber	600–19,200 FW vs. 1900–61,200 FW	58
Liver	30–2400 FW vs. 100–7300 FW	58
Kidney	300–1200 FW vs. 100–3600 FW	58
Ringed seal, <i>Pusa hispida</i> ; Norway, March–April, 1990		
Blubber		
PCBs 77, 126, 169	ND–0.19 LW	25
PCBs 66, 110, 149	20–22 LW	25
PCBs 52, 61, 105, 180	40–52 LW	25
PCBs 101, 118, 138	108–188 LW	25
PCBs 153	280 LW	25
Kidney		
PCBs 77, 126, 169	ND	25
PCBs 66, 110, 149 180	12–14 LW	25
PCBs 52, 61, 105	21–28 LW	25
PCBs 101, 118, 138	49–67 LW	25
PCB 153	95 LW	25
Liver		
PCBs 77, 126, 169	ND–0.78 LW	25
PCBs 61, 66, 105, 110, 149, 180	18–43 LW	25
PCBs 52, 101, 118	57–71 LW	25
PCBs 138, 153	115–188 LW	25
Harbor seal, <i>Phoca vitulina</i> ; northeast coast of U.S.; 1980–92		
Blubber; 1980 vs. 1990–92		
Total PCBs	12,000 (7300–24,300) FW vs. 6660 (2610–11,300) FW	51
PCB 8	ND vs. 0.9 FW	51
PCB 18	26 FW vs. 2 FW	51
PCB 28	99 FW vs. 16 FW	51
PCB 44	105 FW vs. 17 FW	51
PCB 52	661 FW vs. 213 FW	51
PCBs 66 + 95	192 FW vs. 29 FW	51
PCB 77	0.36 FW vs. 0.07 FW	51
PCB 101	897 FW vs. 500 FW	51
PCB 105	205 FW vs. 82 FW	51
PCBs 118 + 149	615 FW vs. 279 FW	51
PCB 126	1.45 FW vs. 0.53 FW	51
PCB 128	459 FW vs. 244 FW	51
PCB 138	2990 FW vs. 1650 FW	51
PCB 153	3040 FW vs. 1880 FW	51
PCB 169	0.019 FW vs. 0.013 FW	51
PCBs 170 + 190	458 FW vs. 266 FW	51
PCB 180	1210 FW vs. 713 FW	51
PCB 187	865 FW vs. 601 FW	51
PCB 195	67 FW vs. 56 FW	51

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 206	72 FW vs. 79 FW	51
PCB 209	22 FW vs. 34 FW	51
Liver; 1980 vs. 1990–92		
Total PCBs	9860 (6290–16,000) FW vs. 6260 (528–25,300) FW	51
PCB 8	ND vs. 1.2 FW	51
PCB 18	8.2 FW vs. 0.5 FW	51
PCB 28	27 FW vs. 10 FW	51
PCB 44	42 FW vs. 8 FW	51
PCB 52	343 FW vs. 145 FW	51
PCBs 66 + 95	127 FW vs. 9 FW	51
PCB 101	523 FW vs. 371 FW	51
PCB 105	345 FW vs. 26 FW	51
PCBs 118 + 149	470 FW vs. 196 FW	51
PCB 128	385 FW vs. 232 FW	51
PCB 138	2250 FW vs. 1550 FW	51
PCB 153	2040 FW vs. 1690 FW	51
PCBs 170 + 190	476 FW vs. 253 FW	51
PCB 180	1160 FW vs. 696 FW	51
PCB 187	1450 FW vs. 904 FW	51
PCB 195	85 FW vs. 60 FW	51
PCB 206	97 FW vs. 80 FW	51
PCB 209	41 FW vs. 36 FW	51
Common porpoise, <i>Phocoena phocoena</i>		
Found dead along Dutch coast, 1971–81		
Blubber vs. liver		
PCB 44	530 FW vs. 1 FW	26
PCB 49	900 FW vs. 5 FW	26
PCB 52	10,000 FW vs. 80 FW	26
PCB 101	3200 FW vs. 20 FW	26
PCB 118	8200 FW vs. 35 FW	26
PCB 138	28,900 FW vs. 280 FW	26
PCB 149	16,700 FW vs. 140 FW	26
PCB 153	32,600 FW vs. 340 FW	26
PCB 172	530 FW vs. 5 FW	26
PCB 174	3700 FW vs. 40 FW	26
PCB 177	6200 FW vs. 60 FW	26
PCB 180	4000 FW vs. 80 FW	26
PCB 183	3700 FW vs. 50 FW	26
PCB 194	700 FW vs. 10 FW	26
PCB 201	1200 FW vs. 20 FW	26
PCB 206	360 FW vs. 7 FW	26
PCB 209	40 FW vs. 10 FW	26
Total PCBs (from above congeners)		
Blubber	51,350–139,790 FW	26
Heart	1410–4900 FW	26
Kidney	860–3970 FW	26
Liver	1190–17,400 FW	26
Muscle	960–3990 FW	26
Three females found dead in fishing nets; Baltic Sea, 1989–90		
Blubber, maximum concentrations		
PCB 77	3.6 FW	37
PCB 126	1.4 FW	37

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 169	2.1 FW	37
PCB 60	15 FW	37
PCB 105	150 FW	37
PCB 118	1100 FW	37
PCB 156	ND	37
PCB 137	730 FW	37
PCB 138	7700 FW	37
PCB 153	9600 FW	37
PCB 170	380 FW	37
PCB 180	1500 FW	37
PCB 194	84 FW	37
Liver vs. muscle		
PCB 77	0.2 FW vs. ND	37
PCB 126	0.05 FW vs. ND	37
PCB 169	0.02 FW vs. ND	37
PCB 118	63 FW vs. 120 FW	37
PCB 138	250 FW vs. 350 FW	37
PCB 153	320 FW vs. 500 FW	37
PCB 170	33 FW vs. 64 FW	37
PCB 180	110 FW vs. 220 FW	37
Scandinavia; 1987–91; blubber; males; total of 47 detected PCB congeners	23,300 (3710–65,260) LW	50
Dall's porpoise, <i>Phocoenoides dalli dalli</i> ; northern North Pacific, 1980–85; blubber		
Total PCBs		
Females	1500 (1000–2000) FW	14
Males	12,000 (7100–18,000) FW	14
All samples	8600 (1000–18,000) FW	20, 21
Di-ortho planars		
PCB 128	480 (110–1100) FW	20, 21
PCB 138	970 (160–2000) FW	20, 21
Mono-ortho planars		
PCB 105	100 (30–200) FW	20, 21
PCB 118	280 (90–450) FW	20, 21
PCB 156	11 (5–15) FW	20, 21
Non-ortho planars		
PCB 77	2.3 (0.4–3.5) FW	14, 20, 21
PCB 126	0.16 (0.08–0.25) FW	14, 20, 21
PCB 169	0.11 (0.04–0.2) FW	14, 20, 21
Ringed seal, <i>Pusa hispida</i> ; Baltic Sea and environs, 1981–87; blubber		
PCB 77	Max. 9 LW	9
PCB 105	Max. 1100 LW	9
PCB 126	Max. 4 LW	9
PCB 169	Max. 0.3 LW	9
Striped dolphin, <i>Stenella coeruleoalba</i> ; blubber		
Japan; 1978–79 vs. 1986; adult males; total PCBs	29,000 (15,000–46,000) FW vs. 28,000 (17,000–38,000) FW	27
Mediterranean Sea; 1990–92; 30 dead animals killed by morbillivirus epizootic		
Total PCBs	855,000 LW	61
PCB 77	122 LW	61
PCB 105	8000 LW	61

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 118	19,000 LW	61
PCB 126	43 LW	61
PCB 156	4000 LW	61
PCB 169	21 LW	61
PCB 179	47,000 LW	61
PCB 180	63,000 LW	61
Mediterranean Sea; 1990		
Total PCBs		
Alive vs. dead	480,000 FW vs. 340,000 FW	28
Males vs. females	430,000 FW vs. 94,000 FW	28
Matures vs. immatures	430,000 FW vs. 380,000 FW	28
Healthy vs. emaciated	480,000 FW vs. 340,000 FW	28
Di-ortho planars		
PCB 137	5500 FW	28
PCB 138	60,000 FW	28
PCB 153	73,000 FW	28
PCB 170	12,000 FW	28
PCB 180	39,000 FW	28
PCB 194	4000 FW	28
Mono-ortho planars		
PCB 60	160 FW	28
PCB 105	2000 FW	28
PCB 118	7900 FW	28
PCB 156	3000 FW	28
Non-ortho planars		
PCB 77	43 (16–85) FW	28
PCB 126	6.8 (2.4–13.0) FW	28
PCB 169	7.8 (1.9–15.0) FW	28
Goosebeaked whale, <i>Ziphius cavirostris</i> ; Bermuda, 1981; beached		
Blubber vs. liver		
PCB 44	5 FW vs. 0.4 FW	26
PCB 49	6 FW vs. 0.4 FW	26
PCB 52	36 FW vs. 4 FW	26
PCB 101	47 FW vs. 6 FW	26
PCB 118	74 FW vs. 13 FW	26
PCB 138	153 FW vs. 19 FW	26
PCB 149	73 FW vs. 15 FW	26
PCB 153	186 FW vs. 21 FW	26
PCB 172	14 FW vs. 2 FW	26
PCB 174	32 FW vs. 6 FW	26
PCB 177	24 FW vs. 5 FW	26
PCB 180	92 FW vs. 11 FW	26
PCB 183	37 FW vs. 6 FW	26
PCB 194	20 FW vs. 3 FW	26
PCB 201	64 FW vs. 10 FW	26
PCB 206	26 FW vs. 5 FW	26
PCB 209	6 FW vs. 0.5 FW	26
Total PCBs (from above congeners)		
Blubber	720–1450 FW	26
Heart	18 FW	26
Kidney	26–78 FW	26

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Liver	98–127 FW	26
Muscle	6–138 FW	26
INTEGRATED STUDIES		
Freshwater lake near Amsterdam, the Netherlands; near dredged materials discharge site		
Sediments		
PCB 28	1.4 DW	29
PCB 52	2.3 DW	29
PCB 101	4.1 DW	29
PCB 138	13.7 DW	29
PCB 153	7.2 DW	29
PCB 180	3.4 DW	29
Plankton, 2 species (whole) vs. zebra mussel, <i>Dreissena polymorpha</i> (soft parts)		
PCB 28	0.2 FW, 68 LW vs. 0.5 FW, 36 LW	29
PCB 52	0.3 FW, 102 LW vs. 0.9 FW, 57 LW	29
PCB 101	0.5 FW, 206 LW vs. 3.8 FW, 220 LW	29
PCB 138	0.7 FW, 259 LW vs. 4.5 FW, 258 LW	29
PCB 153	0.5 FW, 209 LW vs. 5.8 FW, 322 LW	29
PCB 180	0.2 FW, 60 LW vs. 1.2 FW, 75 LW	29
Crustaceans, 3 species (whole) vs. European eel, <i>Anguilla</i> sp. (whole)		
PCB 28	3 FW, 362 LW vs. 4 FW, 21 LW	29
PCB 52	3 FW, 400 LW vs. 15 FW, 83 LW	29
PCB 101	4 FW, 532 LW vs. 28 FW, 186 LW	29
PCB 138	4 FW, 529 LW vs. 97 FW, 986 LW	29
PCB 153	4 FW, 505 LW vs. 89 FW, 932 LW	29
PCB 180	0.8 FW, 107 LW vs. 41 FW, 436 LW	29
Gulf of Mexico; 1986–87; coastal sediments vs. oyster soft parts		
Di-CBs	0.08–0.6 DW vs. 0.4–1.6 DW	39
Tri-CBs	0.6–2.6 DW vs. 7.6–8.3 DW	39
Tetra-CBs	1.8–11.0 DW vs. 26–38 DW	39
Penta-CBs	3.1–13.4 DW vs. 66–78 DW	39
Hexa-CBs	2.7–15.6 DW vs. 26–42 DW	39
Hepta-CBs	1.3–9.5 DW vs. 5–6 DW	39
Octa-CBs	0.3–2.6 DW vs. 0.4–1.0 DW	39
Nona-CBs	0.06–0.4 DW vs. 0.3–0.4 DW	39
Total PCBs	9.8–55.7 DW vs. 134–1734 DW	39
Hudson River (upper), New York; 1983; total PCBs; water column vs. fish muscle	0.14 FW vs. 3800 FW	40
Lake Clear (PCB-contaminated), Canada; 1986–87; vs. Lake Scugog (noncontaminated); total of 19 PCB congeners		
Sediments	571 DW vs. 22 DW	41
Crayfish	73 FW vs. 9 FW	41
Plankton	59 FW vs. ND	41
Fish	90–153 FW vs. 6–27 FW	41
Lake Erie, Hamilton Harbour; 1984		
Water column vs. sediments		
Tri-CBs	0.04 FW vs. 244 FW	42
Tetra-CBs	0.07 FW vs. 405 FW	42
Penta-CBs	0.07 FW vs. 1025 FW	42
Hexa-CBs	0.02 FW vs. 982 FW	42
Hepta-CBs	0.01 FW vs. 983 FW	42

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Octa-CBs	0.002 FW vs. 246 FW	42
Total PCBs	0.22 FW vs. 3927 FW; Max. 14,185 FW	42
Oligochaetes		
Tri-CBs	33 FW	42
Tetra-CBs	39 FW	42
Penta-CBs	54 FW	42
Hexa-CBs	45 FW	42
Hepta-CBs	31 FW	42
Octa-CBs	5 FW	42
Total PCBs	207 FW	42
Lake Ontario, Wheatley Harbour; 1984; sediments vs. oligochaetes		
Tri-CBs	14 FW vs. 22 FW	42
Tetra-CBs	53 FW vs. 40 FW	42
Penta-CBs	133 FW vs. 102 FW	42
Hexa-CBs	141 FW vs. 72 FW	42
Hepta-CBs	69 FW vs. 23 FW	42
Octa-CBs	6 FW vs. 3 FW	42
Puget Sound, Washington; total PCBs		
Sediments	270–380 DW	43
Crab hepatopancreas	32,000 DW	43
English sole (<i>Pleuronectes vetulus</i>); liver	35,000 DW	43
Rainy River, Ontario; 1988; total PCBs		
Mill effluent, water vs. suspended solids	86–334 FW vs. 131–414 FW	44
Fish, two species; upstream vs. downstream	ND vs. 149–229 FW	44
Marine mammals (4 species; blubber) vs. terrestrial mammals (human, dog, cat; adipose or intestinal fat)		
Total PCBs	2300–370,000 FW vs. 100–2000 FW	20
Di-ortho planars		
PCB 128	54–8000 FW vs. 1.2–72 FW	20
PCB 138	460–65,000 FW vs. 6.2–360 FW	20
Mono-ortho planars		
PCB 105	5–3000 FW vs. 0.6–46 FW	20
PCB 118	47–11,000 FW vs. 2–160 FW	20
PCB 156	11–1900 FW vs. 1–22 FW	20
Non-ortho planars		
PCB 77	1.3–48.0 FW vs. 0.03–0.37 FW	20
PCB 126	0.16–3.7 FW vs. 0.007–0.33 FW	20
PCB 169	0.11–7.7 FW vs. 0.03–0.09 FW	20
Waukegan Harbor, Illinois, Lake Michigan; August 1978; heavily contaminated by PCBs		
Sediments, samples from 5 locations		
Total PCBs	10,600–6,996,000 DW	30
PCB 77	10–390 DW	30
PCB 105	70–43,400 DW	30
PCBs 126, 169	ND	30
Fish		
White sucker, <i>Catostomus commersoni</i> ; whole		
Total PCBs	41,400 FW	30
PCB 77	50 FW	30
PCB 105	483 FW	30
PCBs 126, 169	ND	30
Black bullhead, <i>Ameiurus melas</i> ; whole		
Total PCBs	49,400 FW	30
PCB 77	89 FW	30

Table 24.9 (continued) PCB Concentrations in Field Collections of Selected Aquatic Organisms
 (Concentrations are in micrograms PCBs per kilogram [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Organism, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 105	352 FW	30
PCBs 126, 169	ND	30
Largemouth bass, <i>Micropterus salmoides</i> ; offal		
Total PCBs	56,600 FW	30
PCB 77	86 FW	30
PCB 105	290 FW	30
PCBs 126, 169	ND	30
Coho salmon, <i>Oncorhynchus kisutch</i> ; whole		
Total PCBs	2400 FW	30
PCB 77	2 FW	30
PCB 105	45 FW	30
Yellow perch, <i>Perca flavescens</i> ; whole		
Total PCBs	11,200 FW	30
PCB 77	23 FW	30
PCB 105	80 FW	30
White crappie, <i>Pomoxis annularis</i> ; whole		
Total PCBs	40,300 FW	30
PCB 77	24 FW	30
PCB 105	242 FW	30
Black crappie, <i>Pomoxis nigromaculatus</i> ; whole		
Total PCBs	32,200 FW	30
PCB 77	43 FW	30
PCB 105	114 FW	30

^a Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

^b 1, Galceran et al. 1993; 2, Johansen et al. 1993; 3, de Boer and Wester 1991; 4, Hong et al. 1992; 5, Hesselberg et al. 1990; 6, Himberg 1993; 7, Maack and Sonzogni 1988; 8, Marthinsen et al. 1991; 9, Koistinen 1990; 10, Leiker et al. 1991; 11, Knickmeyer and Steinhart 1989; 12, Steimle et al. 1990; 13, Bush et al. 1990; 14, Tanabe et al. 1987; 15, Jones et al. 1989; 16, Gundersen and Pearson 1992; 17, Greig and Sennefelder 1987; 18, Tarhanen et al. 1989; 19, Borgmann and Whittle 1991; 20, Kannan et al. 1989; 21, Tanabe et al. 1989; 22, Masse et al. 1986; 23, Tanabe et al. 1993; 24, Addison and Brodie 1987; 25, Daelemans et al. 1993; 26, Duinker et al. 1988b; 27, Loganathan et al. 1990; 28, Kannan et al. 1993; 29, Van der Oost et al. 1988; 30, Huckins et al. 1988; 31, Janz et al. 1992; 32, Williams and Giesy 1992; 33, Sanchez et al. 1993; 34, Gobas et al. 1989; 35, Kovats and Ciborowski 1989; 36, Kammann et al. 1993; 37, Falandysz et al. 1994b; 38, Elskus et al. 1994; 39, Sericano et al. 1990; 40, Brown et al. 1985; 41, Macdonald and Metcalfe 1989; 42, Mudroch et al. 1989; 43, Long 1982; 44, Merriman et al. 1991; 45, Sericano et al. 1994; 46, Steingraeber et al. 1994; 47, Mac et al. 1993; 48, Schmitt et al. 1990; 49, Huhnerfuss et al. 1995; 50, Kleivane et al. 1995; 51, Lake et al. 1995a; 52, USEPA 1992a; 53, Muir et al. 1996a; 54, Muir et al. 1996b; 55, Lee et al. 1996; 56, Nakata et al. 1997; 57, Tanabe et al. 1997; 58, van Scheppingen et al. 1996; 59, Eby et al. 1997; 60, Green et al. 1996; 61, Borrell et al. 1996; 62, Nakata et al. 1998; 63, Whyte et al. 1998; 64, Ishizuka et al. 1998.

24.4.4 Other Aquatic Organisms

In comparison to conspecifics from noncontaminated sites, aquatic invertebrates from PCB-contaminated sites contained elevated concentrations of PCBs in tissues (Table 24.9). Adult aquatic insects are one of the groups considered useful and reliable indicators of PCB contamination (Wood et al. 1987; Kovats and Ciborowski 1989). Mayflies (*Hexagenia* spp.) from Lake St. Clair had PCB concentrations that reflected sediment PCB concentrations (Table 24.9). Observed mayfly sediment concentration ratios from PCBs linearly correlated with K_{ow} when expressed on a logarithmic basis (Gobas et al. 1989). PCB congener distributions in lake biota showed that no particular trophic level consistently accumulated the highest PCB concentrations and suggest that accumulations were associated with the organism's lipid concentrations (Table 24.9). A relation was consistent between the concentration of dissolved PCBs and tissue concentrations in mussels from PCB-contaminated sites, such as New Bedford Harbor, Massachusetts. Uptake of PCB congeners in blue mussels

(*Mytilus edulis*) from the dissolved phase of seawater was predictable from the log of the bioconcentration factor and the log K_{ow} of the congeners (Bergen et al. 1993). American oysters (*Crassostrea virginica*) from Galveston Bay, Texas, contained as much as 1100 µg/kg total PCBs DW soft parts, whereas conspecifics from Tampa Bay, Florida, contained only 580 µg/kg DW soft parts; most (54 to 94%) of the relative toxicity in both groups was due to PCBs 77, 126, and 169 (Sericano et al. 1994).

The partitioning of individual, highly chlorinated PCB congeners with small differences in K_{ow} values may not adequately explain the accumulations in aquatic organisms (van der Oost et al. 1988). Hydrophobic chemicals, such as PCBs, are accumulated as a consequence of chemical partitioning between the water column, the organic phase of sediment, and biotic lipids, or from biomagnification, a process reflecting the ratio between uptake rate from food and elimination rate from the organism. Accumulations of six PCB congeners (PCBs 28, 52, 101, 138, 153, 180) in surficial sediments (0 to 20 cm) and in an aquatic food chain in Lake Nieuwe Meer — a freshwater lake near Amsterdam containing contaminated dredged materials discharged over 30 years — were low in sediments; elevated in carnivores, plankton, molluscs, crustaceans, and eels; and independent of fat content (van der Oost et al. 1988). With concentrations in organisms expressed on the basis of lipid content (C_{org}) and concentrations in sediments expressed on the basis of organic carbon (C_{sed}) the median C_{org}/C_{sed} PCB accumulation patterns in aquatic organisms showed significant differences and indicated that mechanisms other than partitioning were operating. In plankton and molluscs, C_{org}/C_{sed} ratios seemed to be independent of hydrophobicity of PCB congeners. But with ascending trophic level from plankton to molluscs to crustaceans to eels, the median C_{org}/C_{sed} ratios of higher chlorinated congeners (PCBs 138, 153, 180) increased. Differences in accumulations of individual congeners were attributed to:

1. Increased biomagnification of higher chlorinated congeners because increasing hydrophobicity decreased elimination rates but not uptake efficiency
2. Greater mobility of eels and different feeding habits of eels and crustaceans that impact accumulation patterns because of biomagnification and partitioning
3. Variability in the time period (limited by lifespan) available in a particular trophic level for equilibration between uptake and clearance
4. The tendency of equilibrium to be established at faster rates in less chlorinated congeners.

In crustaceans, C_{org}/C_{sed} ratios decreased with decreasing hydrophobicity; the opposite occurred in eels and is attributed to differences in uptake efficiencies and low elimination rates of lower-chlorinated congeners in crustaceans (van der Oost et al. 1988).

A correlation exists between the concentration of lipophilic, hydrophobic, chlorinated hydrocarbons in benthic fishes and the concentration of these compounds in sediments. The correlation is affected by the solubility of the contaminants, as reflected by the octanol/water partition coefficient K_{ow} and the carbon content of the sediment (Connor 1984; Breck 1985). Connor (1984) suggested that surface sediments, which change more slowly than the water column, are useful for averaging spatial and temporal contaminant inputs. However, correlations between PCB concentrations in sediment and those in nonbenthic carnivores with limited home ranges are extremely variable. PCBs in a tidal creek in Georgia were traced to Aroclor 1268 used at a former chloralkali plant near the creek. Sediment-ingesting forage fishes, such as the striped mullet (*Mugil cephalus*), efficiently accumulate PCBs and are an important link in the food web transfer of sediment-associated contaminants (Maruya and Lee 1998).

Concentrations of total PCBs — measured as Aroclors 1248, 1254, and 1260 — in adult freshwater fishes in the United States from noncontaminated sites declined between 1976 and 1984 (Table 24.9), and more than 90% of all analyzed samples contained measurable quantities of PCBs during this period (Schmitt et al. 1990). Total PCB concentrations in domestic freshwater fishes in 1986/87 from contaminated sites were as high as 124,000 µg/kg FW (USEPA 1992a). In general, total PCB concentrations in domestic freshwater fishes sampled between 1976 and 1984 were

highest in the industrialized regions of the Northeast, the Great Lakes, the upper Mississippi River, and the Ohio River (Schmitt et al. 1990). Phillips and Birchard (1990) reviewed PCB concentrations (as judged by residues of Aroclors 1016, 1221, 1232, 1242, 1248, 1254, and 1260) in sediments and fish tissues in the United States during 1978 to 1987. During 1978 to 1981, total PCB concentration rankings in sediments were highest in the lower Mississippi, Tennessee, South Atlantic–Gulf of Mexico, and lower Colorado regions and lowest in the Great Lakes, Arkansas, mid-Atlantic, Pacific Northwest, and Rio Grande regions. During this same period, PCB concentrations in fish tissues were highest in the Missouri, upper Colorado, California, and the Great Lakes regions and lowest in the upper Mississippi, New England, Ohio, Pacific Northwest, Tennessee, lower Mississippi, and Rio Grande regions. Sediment PCB rankings during 1982 to 1987 were highest in the Arkansas, California, Ohio, and Missouri regions and lowest in the south Atlantic–Gulf and Colorado regions. Total PCBs were highest in fish tissues in the upper Mississippi region during 1982 to 1987. The fish tissue rankings in descending order assigned to 12 regions with sufficient total PCB data were the upper Mississippi and Missouri regions, Ohio, south Atlantic–Gulf, Arkansas, Great Basin, lower Colorado, California, Pacific Northwest, Ohio, upper Colorado, and lower Mississippi. PCB rankings between fish tissues and sediments were not necessarily comparable because high levels in sediment do not necessarily result in high levels in fishes if bioconversion was significant (Phillips and Birchard 1990). Total PCB concentrations in coastal sediments and fish liver in the United States were highest in the Boston Harbor (17.1 mg/kg DW sediment, 10.5 mg/kg in liver of winter flounder, *Pleuronectes americanus*), San Diego Harbor (0.42 mg/kg DW sediment, 19.7 mg/kg in barred sand bass, *Paralbrax nebulifer*), and Elliot Bay, Washington (0.33 mg/kg sediment, 14.7 mg/kg in flathead sole, *Hippoglossoides elassodon*). Trichloro-PCBs were in sediments at many sites but did not accumulate in fish livers except in the Boston Harbor. Sediments in the Boston Harbor, western Long Island Sound, and Raritan Bay were contaminated with PCB mixtures that were relatively high in tri- and tetrachlorobiphenyl isomers, although penta- and particularly hexachlorobiphenyls were the dominant isomers at most sediment sites. As expected, levels of hexachlorobiphenyls in fish livers were dominant because of the more persistent and lipophilic characteristics of increasingly chlorinated PCBs (NOAA 1987).

Variations in PCB concentrations in sediment and water in the Great Lakes can largely account for the variability in fish PCB residues between different bodies of water. Other variables include fish lipid content, position of the fish species in the food web, and trophic structure of the food chain. Collectively, these variables explain 72% of the variation in PCB concentrations of 25 species of Great Lakes fishes (Rowan and Rasmussen 1992). There is a strong linear correlation between total PCB concentration and percent lipid in five species of Lake Michigan salmonids between 1984 and 1994; however, there is considerable variability among individuals, especially among nonspawning individuals (Stow et al. 1997). Tissue concentrations of PCBs in benthic and lower trophic organisms in lakes can be estimated by assuming equal lipid-normalized concentrations in biota and sediment; however, food chain transport had a greater effect on PCB concentrations in higher trophic levels (Macdonald et al. 1993). Total PCB concentrations in whole body of lake fishes were higher among older piscivores and higher with increasing lipid concentration and seemed to reflect exposure conditions at the capture site (Southworth 1990).

Eggs of chinook salmon (*Oncorhynchus tshawytscha*) from Lake Michigan in 1986 contained AHH-active PCB congeners — including PCBs 77, 105, 118, and 126 — at concentrations from 0.9 to 262 µg/kg FW. Concentrations of these congeners did not correlate with survival (Williams and Giesy 1992). Mortality of chinook salmon eggs was not related to total PCB concentrations as high as 7020 µg/kg FW (Williams and Giesy 1992). In Lake Ontario, the overall trend in total PCB concentrations in whole lake trout (*Salvelinus namaycush*) between 1977 and 1988 was a gradual decline with a half-time persistence of about 10 years (Borgmann and Whittle 1991). In Lake Superior, the PCB congener fingerprint in eggs of the lake trout differed from that of lake trout eggs of other Great Lakes (Mac et al. 1993). A difference between residue patterns was also identified between eggs and the parent fish, suggesting preferential deposition of congeners other

than AHH-active congeners. Concentrations of individual congeners in lake trout have been declining at similar rates in the Great Lakes during a 10-year period (Mac et al. 1993). In Lake Michigan, total PCB concentrations declined 64% in bloaters (*Coregonus hoyi*) from 5700 mg/kg FW in 1972 to 1600 µg/kg FW in 1986 (Hesselberg et al. 1990); however, PCB concentration trends may have been influenced by sampling methodology. During this period, the bloater population increased 40-fold, resulting in a diet shift and a density-dependent decline in growth (Eby et al. 1997). The lower growth rates during the 1980s placed older, more contaminated bloaters in the size range most vulnerable to predators and also in the size range sampled by PCB monitoring programs. Future sampling should include a representative sample of bloaters of known age from the population (Eby et al. 1997).

Distribution patterns of PCB congeners in water, sediment, and four groups of biota from two lakes in Ontario contaminated by known point sources of PCBs (Lake Clear, Rice Lake) were compared with the congener distribution in Lake Scugog, a relatively clean control lake exposed only to atmospheric inputs of PCBs (Macdonald and Metcalfe 1989). Samples were analyzed for 19 PCBs. Those from Lake Clear had a distribution pattern similar to Aroclor 1254 and dominant concentrations of congeners 87, 101, and 118; this lake was contaminated with a PCB mixture similar to Aroclor 1254 in the mid- to late 1970s. The sources to Rice Lake were less clear. Lake Scugog contained a higher proportion of less chlorinated PCBs, in agreement with another study of atmospheric deposition to isolated lakes (Swackhammer et al. 1988). Because the sediments contained elevated levels of organic carbon, the sediments were expected to also hold relatively large concentrations of the higher, more hydrophobic PCBs, in accord with previous reports (Karickhoff 1981; Formica et al. 1988). But this was not the case; subsequent deposition of total and higher chlorinated congeners into the bottom sediments (organic carbon basis) was unexpectedly low. The proportion of higher chlorinated congeners in sediments was also lower than in biota (lipid weight basis) in all three lakes. Because dissolved organic carbon (DOC) increases the solubility of PCBs in water (Gschwend and Wu 1985), the high DOC levels may have caused partitioning of more PCBs into the water and less sorbed onto sediments. The sediments were not efficient at accumulating PCBs, although bottom sediment concentrations were higher in contaminated lakes. Adsorption of PCBs on suspended particles occurred, as anticipated; PCBs on total suspended solids were higher in contaminated lakes (978 µg/kg) than in the control lake (49 µg/kg) and reflected lake concentrations (Gschwend and Wu 1985). In a related study, Macdonald and Metcalfe (1991) analyzed the concentration and distribution of 19 PCB congeners in biota, sediments, water, and suspended solids of isolated oligotrophic lakes in central Ontario that were contaminated by atmospheric deposition. The range of the total congener concentrations was 1 to 2 ng/L dissolved in water, 10 to 50 µg/kg DW in sediment, 5 to 10 µg/kg FW in lower trophic levels, and 10 to 30 µg/kg in fishes from upper trophic levels. The high proportion of trichlorobiphenyls previously reported in vapor (Duinker and Bouchertall 1989; Baker and Eisenreich 1990) and hexachlorobiphenyl congeners 153 and 138 in particulate-bound PCBs (Swackhammer et al. 1988; Duinker and Bouchertall 1989; Baker and Eisenreich 1990) were reflected in the four study lakes. PCB concentrations (lipid basis) were higher in teleosts than in invertebrate prey organisms.

Winter flounder from the PCB-contaminated harbor in New Bedford, Massachusetts, had grossly elevated concentrations of PCBs in their livers (as high as 333,000 µg/kg DW); concentrations were about 5 times higher than in any other fish sample collected worldwide (Table 24.9) (Elskus et al. 1994). PCB patterns in the New Bedford Harbor showed high agreement between the exposure environment (water and sediments) and ribbed mussels (*Geukensia demissa*) and mummichogs (*Fundulus heteroclitus*). However, agreements with American eels (*Anguilla rostrata*) or grass shrimp (*Palaemonetes pugio*) were poor because, in part, of differential metabolism of PCBs by these species (Lake et al. 1995b). PCB concentrations in four species of catfishes from the Mississippi River and its tributaries in summer 1987 were highest from the Illinois River; the Ohio River at Olmsted; and the Mississippi River at Helena, Arkansas, and Arkansas City, Arkansas. These sites seem to be point sources of PCB pollution because PCB residues in catfishes above and below these sites were lower. Although PCBs were banned in 1978, the elevated levels in catfishes suggests

PCB leakage from hazardous waste sites with transformer and hydraulic fluids and flame-resistant plasticizers (Leiker et al. 1991). Findings of high (greater than 4000 µg/kg FW) total PCB levels in mature roe samples of the paddlefish (*Polyodon spathula*) from the Ohio River warranted warnings of the general public about consuming this domestic caviar (Gundersen and Pearson 1992).

The upper Hudson River was massively contaminated with PCBs from an industrial plant for several decades prior to 1975. All fishing in this section in 1976 was banned because of PCB contamination. The prohibition is still in effect because, in part, of measurable PCB residues in caged fishes from this area (Table 24.9) (Jones et al. 1989). Striped bass (*Morone saxatilis*) collected near Troy and Albany, New York, contained higher concentrations in muscle of PCB 77 (37 µg/kg FW) and PCB 126 (8 µg/kg FW) than conspecifics from other locations in New York (Hong et al. 1992). Almost all (99%) the PCB toxicity in muscle of striped bass was attributed to PCBs 77, 105 (62 µg/kg FW), and 126 (Hong et al. 1992).

The most prominent PCB congeners in muscle from 14 species of Wisconsin fishes in 1986/87 were PCBs 28/31, 66/95, 70/76, 101, 105, 110, 118, 138, 146, 149, and 180 (Maack and Sonzogni 1988). Congeners 105 and 118 were found in the greatest amount in fishes at 1 to 5% of the total PCB concentration of each. Congeners with responses similar to 2,3,7,8-TCDD — that is, the planar PCBs — were seldom present above detection levels. The sum of the individual congeners measured in Wisconsin fish muscle were similar to total recorded PCB values (Maack and Sonzogni 1988). Increased fish consumption by Wisconsin anglers in 1985 positively correlated with increased human serum PCB concentrations (Sonzogni et al. 1991). Human consumers of Wisconsin game fishes (chinook salmon, *Oncorhynchus tshawytscha*; yellow perch, *Perca flavescens*; walleye, *Stizostedion vitreum*) in 1986 contained various PCB congeners in their sera. PCB 153 (78% frequency of occurrence) was present at 1.46 (0.6 to 7.3) µg/L human serum; PCB 138 (56%) at 1.32 (0.6 to 6.0) µg/L; PCB 180 (42%) at 1.06 (0.6 to 3.5) µg/L; PCB 118 (34%) at 1.12 (0.6 to 5.7) µg/L; PCB 187 (11%) at 0.98 (0.6 to 2.2) µg/L; PCB 170 (5.8%) at 0.86 (0.6 to 1.4) µg/L; PCB 28 (1.2%) at 0.8 µg/L; PCB 101 (0.58%) at 0.8 µg/L; PCB 70 (0.58%) at 0.7 µg/L; and a single planar PCB — PCB 77 — (0.58% frequency of occurrence) at 1.3 µg/L. PCBs 118, 138, and 180 are potentially most toxic to human consumers, as judged by the concentrations of these congeners in human sera (Sonzogni et al. 1991).

Concentrations of PCBs in female northern pike (*Esox lucius*) from a Scandinavian lake decreased with increasing age, weight, or body length (Larsson et al. 1993). Seasonal elimination of the lipophilic contaminants in roe — which contained as much as 10 times more fat than muscle and more than 10 times the amount of pollutants than muscle — is the major route of PCB loss. Male northern pikes contained higher concentrations of PCBs than females because of the lower elimination by way of gonadal products; males showed no significant relation between age and PCB burdens in tissues (Larsson et al. 1993). Total PCB levels of 7700 to 34,000 µg/kg LW in eggs of the Arctic char (*Salvelinus alpinus*) from Lake Geneva, Switzerland, correlated with a mortality rate of 29 to 100% (Gundersen and Pearson 1992).

On the Pacific coast and in adjacent areas of Mexico, data from more than 150 survey and monitoring programs were summarized on contamination of sediments, invertebrates, and fishes (Mearns 1992). PCBs in sediments seem to be reflected in mussels, and PCB residues from mussels collected at harbor entrances remained unchanged or were increasing. The harbors in Los Angeles–Long Beach and San Diego remained contaminated with PCBs, and PCB concentrations in sediments were reflected in fish livers. Waste management seems to have been effective in the Palos Verdes outfall area. Sediments and mussel samples in Palos Verdes from 1974 to 1988 showed decreasing PCB levels that reflected a 100-fold reduction in PCB wastewater emissions during that period. Contamination of the coastal zone declined to levels found 30 and 40 years ago. PCB levels had declined at least one order of magnitude in teleosts and shellfish at offshore sites since the 1970s. Bays and harbors were more contaminated than the open coastal zone and must be monitored more closely; lower detection levels (0.001 to 0.01 mg/kg FW vs. the current analytical limits of 0.02 mg/kg FW) were proposed to monitor the effectiveness of current source control programs (Mearns 1992).

PCBs in Puget Sound, Washington, were measured in sediments, fish livers, and benthic invertebrates. Maximum total PCB concentrations were 2100 µg/kg DW in sediments near Tacoma, and 32,000 µg/kg DW in crab hepatopancreas and 35,000 µg/kg DW in fish liver near Seattle (Long 1981). PCB concentrations in sediments of the Puget Sound in May 1988 positively correlated with PCB concentrations in livers of several species of flatfishes in these sediments (Stein et al. 1992). Increased sediment PCB concentrations also correlated well with increased hepatic AHH and EROD activities and with increases in total hepatic GSH, all of which are acknowledged early indicators of chemical contamination by PCBs and other organic contaminants (Gooch et al. 1989; Stein et al. 1992).

PCB residues in liver of the European flounder (*Platichthys flesus*) were extremely variable, but residues of individual congeners were usually higher in fall, higher in females, and higher in flounders captured inland near a PCB point source (Marthinsen et al. 1991). A similar pattern was documented in the Atlantic cod (*Gadus morhua*) (Marthinsen et al. 1991). In the dab (*Limanda limanda*), a marine flatfish, the accumulation of PCBs 128, 138, and 163 differs significantly by sex (Knickmeyer and Steinhart 1989). Depletion of lipids from the liver of female dabs during ovary maturation is an important excretory pathway for PCBs during spawning (Knickmeyer and Steinhart 1989). PCB levels in liver of dabs were higher in spring than in winter; livers and ovaries were dominated by penta- and hexachlorobiphenyls, but the dominant PCBs in testes were tri- and tetrachlorobiphenyls (Kammann et al. 1993).

The most prominent PCB congeners at 280 to 323 µg/kg DW in the tilefish (*Lopholatilus chamaeleonticeps*) from Georges Bank in 1981 to 1992 were PCBs 138 and 153 in gonad and liver. At 69 to 82 µg/kg DW, the most prominent PCB congeners in the tilefish from New Jersey during this same period were PCBs 138 and 153 in liver (Steimle et al. 1990). Total PCB concentrations in marine coastal fishes were dominated by the hexachlorobiphenyls (Knickmeyer and Steinhart 1989), but trout from isolated mountain lakes had tri-, tetra-, and pentachlorobiphenyls as the major components of total PCBs (Sanchez et al. 1993).

24.4.5 Reptiles

PCBs accumulate in the fat, testes, and brain of snapping turtles (*Chelydra serpentina*), and concentrations seem to reflect the lipoprotein solubility of individual congeners (Bryan et al. 1987a) (Table 24.10). With increasing hydrophobicity (increasing K_{ow}) of PCB congeners, accumulations increased in livers of snapping turtles; and total liver PCB concentrations in adults increased with increasing age, length, and weight (Hebert et al. 1993). PCB loadings in snapping turtle eggs were not related to the body size of females or to the number of eggs in the clutch (Bishop et al. 1994). However, a positive relation between PCB loadings in liver of adult female snapping turtles and their eggs was significant (Hebert et al. 1993).

PCB 105 may be an important contributor to the toxic burden of snapping turtle populations (Hebert et al. 1993). Eggs of snapping turtles from the Great Lakes had a lower hatch rate and a significantly increased frequency of deformed hatchlings than eggs from a control site, and this seemed to be strongly associated with total PCB concentrations and PCB 105 (Bishop et al. 1991). Of the five toxic PCB congeners measured in the yolks, egg whites, and shells of snapping turtle eggs, PCBs 105 and 167 accounted for more than 99% of the total toxicity — as measured by 2,3,7,8-TCDD TEF equivalents — and 95% of the total toxicity resided in the yolk (Bryan et al. 1987b). Large reserves of fat in eggs of the snapping turtle do not seem to protect against toxic PCB congeners from being dispersed into egg components low in fat (Bryan et al. 1987b).

In loggerhead turtles (*Caretta caretta*), PCB concentrations in the chorioallantoic membrane correlate closely with whole-egg PCB concentrations (Cobb and Wood 1997). The authors recommend the use of chorioallantoic membrane tissues as a nonlethal methodology for predicting PCB concentrations in sea turtle hatchlings.

Table 24.10 PCB Concentrations in Field Collections of Selected Reptiles
 (Concentrations are in g/kg [ppb] fresh weight [FW] or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
AMERICAN ALLIGATOR, <i>Alligator mississippiensis</i>		
Total PCBs; Florida		
Eggs, 1984	80–170 FW; Max. 670 FW	1
Muscle, 1985	100–2100 LW	2
LOGGERHEAD TURTLE, <i>Caretta caretta</i>		
September 1993; South Carolina; chorioallantoic membrane vs. egg contents		
Total PCBs	10,100 LW vs. 1188 LW	8
DichloroBPs	236 LW vs. 9 LW	8
TrichloroBPs	889 LW vs. 9 LW	8
TetrachloroBPs	2406 LW vs. 120 LW	8
PentachloroBPs	2998 LW vs. 446 LW	8
HexachloroBPs	2707 vs. 427 LW	8
HeptachloroBPs	763 LW vs. 173 LW	8
OctachloroBPs	197 LW vs. 30 LW	8
NonachloroBPs	37 LW vs. 4 LW	8
DecachloroBPs	55 LW vs. 5 LW	8
SNAPPING TURTLE, <i>Chelydra serpentina</i>		
Canada		
Great Lakes (Ontario and Erie) vs. control site in central Ontario; eggs; sum of PCB congeners 105, 118, 138, 153, 170, and 180		
1986–87	2600–2700 FW vs. 80 FW	3
1988–89	300–3300 FW vs. 30 FW	3
Hamilton Harbour; adults; found dead; 1986–87; fat; sum of PCBs 105, 118, 138, 153, 170, and 180	57,700–72,200 LW	3
Lake Ontario; eggs; 1990		
PCB 52	20 (10–40) LW	4
PCB 105	1700 (500–2900) LW	4
PCB 118	7300 (2100–11,700) LW	4
PCB 138	9300 (2000–16,200) LW	4
PCB 153	9300 (2500–16,200) LW	4
PCB 180	6400 LW	4
PCB 194	600 LW	4
Total PCBs	54,300 (13,300–96,400) LW	4
Southern Ontario; adults; 1988–89; muscle; sum of Aroclors 1254 and 1260	7–660 FW; Max. 2120 FW	5
United States		
Contaminated site (South Glen Falls, New York) vs. noncontaminated site (Columbus, New York); adults; total PCBs		
Brain	82,000 LW vs. 1000 LW	6
Heart	49,000 LW vs. 600 LW	6
Kidney	48,000 LW vs. 1200 LW	6
Liver	72,000 LW vs. 1000 LW	6
Lungs	13,000 LW vs. 400 LW	6
Pancreas	48,000 LW vs. 1200 LW	6
Testes	100,000 LW vs. 1600 LW	6
Fat	1,600,000 LW vs. 4200 LW	6

Table 24.10 (continued) PCB Concentrations in Field Collections of Selected Reptiles (Concentrations are in g/kg [ppb] fresh weight [FW] or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 66	272,000 LW vs. 200 LW	6
PCB 82	100,000 LW vs. 90 LW	6
PCB 99	166,000 LW vs. 50 LW	6
PCB 105	171,000 LW vs. 160 LW	6
PCB 136	297,000 LW vs. 200 LW	6
PCB 176	152,000 LW vs. 300 LW	6
Upper Hudson River, New York; egg yolk		
PCB 105	700–1890 FW	7
PCB 118	16–32 FW	7
PCB 120	120–280 FW	7
PCB 167	200–560 FW	7
PCB 189	60–120 FW	7

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).

^b 1, Heinz et al. 1991; 2, Delaney et al. 1988; 3, Bishop et al. 1991; 4, Bishop et al. 1994; 5, Hebert et al. 1993; 6, Bryan et al. 1987a; 7, Bryan et al. 1987b; 8, Cobb and Wood 1997.

24.4.6 Birds

Embryos of the double-crested cormorant (*Phalacrocorax auritus*) exposed *in ovo* to elevated mixtures of PCBs in the environment were 25 times more likely to hatch with asymmetric brains than were those from reference sites (Henshel et al. 1997). A high frequency of dead and deformed embryos of double-crested cormorants and Caspian terns was documented in the upper Great Lakes in 1986 to 1991 (Ludwig et al. 1996). Half the embryos found dead in eggs were deformed. Only one of ten cross-billed cormorant embryos survived to hatch and no bill-deformed terns hatched, although tern embryos had a higher frequency of crossed bills than did cormorants. Planar PCB congeners were present at sufficient concentrations to cause the observed effects (Ludwig et al. 1996). A severely deformed bill of the type associated with high environmental levels of PCBs was observed in a newly hatched chick of the shag (*Phalacrocorax aristotelis*); the two dominant congeners in the chick, accounting for about 57% of the total PCB body burden, were PCBs 153 (35%) and 138 (22%), both of which are known to show selective biomagnification (Allen and Thompson 1996).

In general, total PCB concentrations in birds were usually higher in males and in eggs than in livers, in adipose tissues, in fish-eating species, and at PCB-contaminated sites; PCBs 138 and 153 tended to predominate in all samples (Table 24.11). The change in PCB content in livers of Norwegian raptors between 1965 and 1983 was not significant despite a marked reduction in the use of these compounds (Froslie et al. 1986). When total PCB concentrations declined, for example, in eggs of red-breasted mergansers (*Mergus serrator*) between 1977 and 1990, the relative potency of the mixture of PCBs — as measured by 2,3,7,8-TCDD equivalents — was unchanged (Williams et al. 1995).

Commercial PCB mixtures frequently contain impurities that may contribute to the 2,3,7,8-TCDD toxic equivalency factor. These impurities may include other PCBs, dioxins, dibenzofurans, naphthalenes, diphenyl ethers and toluenes, phenoxy and biphenyl anisoles, xanthenes, xanthones, anthracenes, and fluorenes (Jones et al. 1993). PCB concentrations in avian tissues sometimes correlate positively with DDE concentrations (Mora et al. 1993). Eggs of peregrine falcons (*Falco peregrinus*) from California, for example, contained measurable quantities of various organochlorine compounds, including dioxins, dibenzofurans, mirex, hexachlorobenzene, and *p,p'*-DDE at 7.1 to 26.0 mg/kg FW; PCB 126 accounted for 83% of the 2,3,7,8-TCDD equivalents, but its interaction with other detectable organochlorine compounds is largely unknown (Jarman et al. 1993).

There is a relation between PCB uptake and the position of the species in the food chain. In a three-step, central European oak forest food chain involving the great tit (*Parus major*), caterpillars (*Tortrix viridana*, *Operophtera brumata*, *Erannis defoliaria*), and leaves of the red oak (*Quercus* sp.), mean concentrations of PCB 153 — the most abundant measured congener — rose from about 1 µg/kg DW in leaves to 10 in caterpillars to 170 in bird eggs (Winter and Streit 1992). Older juvenile tits contained 307 µg PCB 153/kg whole-body DW; these birds received PCBs from the mother during egg transfer and from the caterpillar food source during the nesting period. PCBs 101, 138, and 180 were also present in most samples but at lower concentrations than PCB 153. Populations of *Parus major* in this area have declined in recent years, and the influence of anthropogenic contaminants may be a factor (Winter and Streit 1992). Fish-eating waterfowl and seabirds had comparatively high total PCB and high planar PCB concentrations in eggs and tissues; waterfowl and seabirds that feed mainly on invertebrates had lower PCB concentrations (Focardi et al. 1988b; Borlakoglu et al. 1990; Gonzalez et al. 1991; Jones et al. 1993). PCB concentrations were higher in adipose tissues of the Arctic tern (*Sterna paradisaea*) than in those of their fish and invertebrate food items (Scharenberg 1991a). PCB concentrations in adipose tissues of cormorants, when compared to their diet of fishes, were 10 to 100 times higher than marine fishes, and 100 to 1000 times higher than freshwater fishes (Scharenberg 1991b). Double-crested cormorants (*Phalacrocorax auritus*) biomagnify total PCBs from their fish diet to their eggs — based on 2,3,7,8-TCDD equivalents — by a factor of 31.3 (Jones et al. 1994). Higher-chlorinated PCBs accumulated in tissues of the herring gull (*Larus argentatus*) to a greater extent than were present in the alewife (*Alosa pseudoharengus*), a primary food item; lower-chlorinated biphenyls, including the tetra- and penta-CBs, did not biomagnify (Braune and Norstrom 1989).

PCBs can move from local sediments into the avian food web, as judged by PCB accumulation rates of tree swallows (*Tachycineta bicolor*) from contaminated and reference sites (Custer et al. 1998). Patterns of relative concentrations of PCB congeners change from sediment to invertebrates, and from tree swallow eggs to nestlings (Froese et al. 1998). Dioxin-like activity (TEF) measured in tree swallow tissues could predict TEF in sediments and the reverse. Models of dioxin-like activity in the sediments of Saginaw Bay, Michigan, predicted that sediments were not harmful to tree swallows from that area (Froese et al. 1998).

Declining populations of Caspian terns (*Sterna caspia*) — especially populations nesting in Green Bay and Saginaw Bay between 1986 and 1990 — were associated with elevated PCB concentrations in blood. The frequency of developmental abnormalities and deformities in Caspian tern populations at Saginaw Bay was almost 100 times above that recorded in the same area between 1962 and 1972 (Table 24.11) (Mora et al. 1993). High concentrations of PCB 126 found in eggs of the bald eagle (*Haliaeetus leucocephalus*) are nearly 20-fold higher than the lowest toxic concentration tested in American kestrels (*Falco sparverius*) and may be a factor in the decline of some eagle populations (Hoffman et al. 1998). High PCB concentrations in tissues of white-tailed eagles (*Haliaeetus albicilla*) are directly connected to high concentrations in eggs and associated with eggshell thinning and low reproductive success (Falandyisz et al. 1994a). A total lack of reproduction among white-tailed sea eagles in the coastal area of the southwestern Baltic Sea in the 1960s and 1970s may be related, in part, to high concentrations of PCBs 105, 118, 126, and 156 in tissues of adult eagles. It is noteworthy that concentrations of planar PCBs in adult white-tailed sea eagles were among the highest reported in wildlife and that total PCB concentrations in this species were similar to those reported in dead eagles from Sweden and Finland in the 1960s and 1970s (Falandyisz et al. 1994a).

PCB 153 is the most widespread PCB in the environment because it is easily stored and retained in adipose tissue. PCB 153 was the main PCB congener in eggs of eight examined species of Italian waterfowl and accounted for 11.4 to 21.2% of the total PCB concentration (Focardi et al. 1988b). Infertile eggs of the endangered imperial eagle (*Aquila heliaca adalberti*) contained as much as 28.9 mg total PCBs/kg FW; PCB 153 constituted 13.5% of the total PCB loading, PCB 180 13%,

PCB 138 3.2%, PCB 101 3.2%, and PCB 118 0.7% (Hernandez et al. 1989). In the endangered Audouin's gull (*Larus audouinii*), most (62%) of the total PCB burden consisted of PCBs 138, 153, 170, and 180. Other important congeners were PCBs 118, 194, and 203, and each contributed about 5% (Leonozio et al. 1989). PCBs 138, 153, and 180 comprised more than 50% of the total PCB burden in eggs of the yellow-legged herring gull (*Larus cachinnans*); a similar case is made for eggs of other species of marine birds (Focardi et al. 1988a). PCBs 138, 153, and 180 were also dominant in tissues of most birds collected in Great Britain between 1988 and 1990, although total PCB concentrations ranged from 0.02 to 105 mg/kg FW and also differed considerably in different tissues from individual birds (Boumphrey et al. 1993). PCBs 138 and 153 were the most prominent congeners in eggs of three species of gulls collected in Spain during 1988, accounting for 10.5% and 8.7%, respectively, of the total PCB burden. Other important congeners were PCBs 180 (7.5%), 170 (3.2%), 101 (1.9%), 151 (1.1%), and 194 (0.9%) (Gonzalez et al. 1991).

PCB signatures in bird eggs are not constant. Eggs of the dipper (*Cinclus cinclus*) from Wales and Ireland were dominated by PCB 118 in 1990, PCB 170 in 1991, and PCB 153 in 1992; six congeners accounted for 26 to 35% of the total PCBs in Welsh eggs and for 10 to 26% of the total in eggs from Ireland (Ormerod and Tyler 1992, 1994). In tissues of birds in Great Britain, the mono-*ortho*-congeners — PCBs 105 and 118 — made a high contribution (70%) to the TEF, whereas the non-*ortho*-congeners (PCBs 77, 126, 169) contributed 20% and the di-*ortho*-congeners (PCBs 138, 153, 180) contributed 10% (Boumphrey et al. 1993). Young of all avian species sampled in Wisconsin accumulated PCBs 77, 105, 126, and 169. Chicks of Forster's terns (*Sterna forsteri*) had daily uptakes of 15 µg total PCBs, 0.07 µg PCB 77, 0.2 µg PCB 105, 0.006 µg PCB 126, and 0.00014 µg PCB 169 (Ankley et al. 1993).

Concentrations of mono-*ortho*-PCBs in yolk sac of cormorants ranged from 10 to 250 mg/kg LW; high PCB residues in yolk were associated with increased cytochrome P-450 and EROD activities and decreased thyroid hormone activity (van den Berg et al. 1992). Embryos of the black-crowned night heron (*Nycticorax nycticorax*) with the greatest burdens of total PCBs had increased cytochrome P-450-associated monooxygenase activities and cytochrome P-450 proteins, which suggests that cytochrome P-450 may be a useful biomarker of exposure to some PCB mixtures (Rattner et al. 1993, 1997). The absence of established thresholds for P-450 induction indicates that more research is needed (Rattner et al. 1994) to make this a useful technique for evaluating PCB exposure.

Table 24.11 PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Northern goshawk, <i>Accipiter gentilis</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	2000 (<100–1,260,000) FW vs. 12,300 (2600–53,000 FW	1
Northern sparrow hawk, <i>Accipiter nisus</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	1100 (<100–107,000) FW vs. 5900 (<100–39,000) FW	1
Sharp-shinned hawk, <i>Accipiter striatus</i> ; blood plasma; total PCBs (as Aroclors 1254 and 1260); Great Lakes, 1985–89	80 (10–190) FW	2
Tengmalm's owl, <i>Aegolius funereus</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	1000 (<100–9400) FW vs. 400 (<100–1300) FW	1
Red-winged blackbird, <i>Agelaius phoeniceus</i> ; eggs (less shell) and chicks (less feathers, feet, beaks, stomach contents, and wings); total PCBs; Green Bay, Wisconsin, 1989	5400–8900 FW	9
Razorbill, <i>Alca torda</i> ; adipose tissue; males vs. females; England, 1988		
PCBs 3, 8, 18	ND vs. ND	3
PCB 28	110 FW vs. ND	3

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 52	140 FW vs. ND	3
PCB 101	310 FW vs. 32 FW	3
PCB 118	2500 FW vs. 500 FW	3
PCB 138	6500 FW vs. 1600 FW	3
PCB 153	4400 FW vs. 1100 FW	3
PCB 180	2600 FW vs. 600 FW	3
Total PCBs	16,500 FW vs. 4100 FW	3
Mallard, <i>Anas platyrhynchos</i>		
Age 12 months; confined to enclosures in lagoon of sewage treatment plant for 100 days then killed; whole duck analyzed less feathers, bill, feet, wings, and gizzard contents; non-detectable PCB concentrations at start		
Total PCBs	16,600 FW	30
PCB 28	6800 FW	30
PCB 49	1300 FW	30
PCB 56	820 FW	30
PCB 74	2800 FW	30
PCB 77	230 FW	30
PCB 105	380 FW	30
PCB 118	790 FW	30
PCB 126	5 FW	30
PCB 128	50 FW	30
PCB 138	250 FW	30
PCB 170	40 FW	30
Wisconsin; 1984–89; muscle; all seasons; total PCBs	200–700 FW, Max. 21,000 FW; 2000–10,000 LW, Max. 1,313,000 LW	31
Blue-winged teal, <i>Anas discors</i> ; breast muscle with associated skin and fat		
Colombia, South America; 1987–88; all seasons	ND	31
Wisconsin; 1984–89		
Spring	100 FW; 1700 LW	31
Summer	Max. 500 FW, 12,500 LW	31
Fall	100 FW; 900 LW, Max. 6300 LW	31
Imperial eagle, <i>Aquila heliaca adalberti</i> ; infertile eggs; Spain, 1986–87		
PCB 101	9–16 FW; Max. 440 FW	4
PCB 118	1–4 FW; Max. 66 FW	4
PCB 138	7–30 FW; Max. 620 FW	4
PCB 153	37–115 FW; Max. 5300 FW	4
PCB 180	30–110 FW; Max. 4800 FW	4
Total PCBs	280–820 FW; Max. 28,900 FW	4
Golden eagle, <i>Aquila chrysaetos</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	2000 (<100–250,000) FW vs. 1000 (400–5700) FW	1
Grey heron, <i>Ardea cinerea</i>		
England; 1988–90; total PCBs (35 congeners)		
Fat	198,000 FW; 226,000 LW	5
Kidney	3600 FW; 135,000 LW	5
Liver	2800 FW; 936,000 LW	5
Muscle	8100 FW; 139,000 LW	5
France; Lac de Grandlieu; May 1991; eggs; total PCBs	1280 (236–2731) FW	37
Great blue heron, <i>Ardea herodias</i> ; eggs; British Columbia		
PCB 77	0.05–0.2 LW	6
PCB 105	17–31 LW	6

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 118	63–116 LW	6
PCB 126	0.1–0.2 LW	6
PCB 169	0.02–0.04 LW	6
Short-eared owl, <i>Asio flammeus</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	300 (<100–46,000) FW vs. 2100 (2000–22,000) FW	1
Greater scaup, <i>Aythya marila</i> ; total PCBs; carcass; Detroit River, 1981	11,000 FW	25
Eagle owl, <i>Bubo bubo</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	3000 (100–550,000) FW vs. 4000 (2200–29,000) FW	1
Common buzzard, <i>Buteo buteo</i> ; infertile eggs; total PCBs; Spain, 1985–86	1650 (1600–1700) FW	7
Rough-legged buzzard, <i>Buteo lagopus</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	200 (<100–15,000) FW vs. 800 (200–9300) FW	1
White stork, <i>Ciconia ciconia</i> ; infertile eggs; total PCBs; Spain, 1985–86	800 (200–2700) FW	7
Dipper, <i>Cinclus cinclus</i> ; addled eggs; Wales vs. Ireland, 1990–92		
PCB 101	10–20 LW vs. <10 LW	8
PCB 118	10–70 LW vs. 10–1280 LW	8
PCB 138	10–380 LW vs. 10–80 LW	8
PCB 153	20–530 LW vs. 10–160 LW	8
PCB 170	10–190 LW vs. 10–30 LW	8
PCB 180	10–20 LW vs. 10–40 LW	8
Merlin, <i>Falco columbarius</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	400(<100–41,000) FW vs. 4500 (2400–11,000) FW	1
Peregrine, <i>Falco peregrinus</i>		
Liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	120,000 FW vs. 43,000 FW	1
Eggs; California, 1983–88		
PCB 37	0.18 FW	10
PCB 77	0.93 FW	10
PCB 126	1.0 FW	10
PCB 138	750 FW; Max. 2440 FW	10
PCB 153	1200 FW; Max. 4400 FW	10
PCB 169	0.14 FW	10
Total PCBs	4800 (1400–13,000) FW	10
Tundra peregrine, <i>Falco peregrinus tundrus</i> ; Canadian Arctic; total PCBs		
Addled eggs; 1982–86 vs. 1991–94	8700 (2000–47,800) FW vs. 8300 (1700–45,600) FW	32
Blood plasma; 1982–86 vs. 1991–94		
Males	470 FW vs. 750 FW	32
Females	750 FW vs. 950 FW	32
Chicks; found dead; 1991–94; age 22 days vs. age 29 days		
Breast muscle	400 FW vs. 7400 FW	32
Liver	1600 FW vs. 27,100 FW	32
Adult diet; whole organism		
Long-tailed duck, <i>Clangula hyemalis</i>	6900 (2900–18,900) FW	32
Birds, 8 species	ND–400 FW; Max. 5400 FW	32
Mammals	Usually <3 FW; Max. 4200 FW	32
Gyr falcon, <i>Falco rusticolus</i> ; liver vs. eggs; total PCBs; Norway 1965–83; dead on collection	5000 (300–42,000) FW vs. 12,000 FW	1
Kestrel, <i>Falco tinnunculus</i> ; liver vs. eggs; total PCBs; Norway 1965–83	500 (<100–45,000) FW vs. 600 (<100–1000) FW	1

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Southern fulmar, <i>Fulmarus glacialisoides</i> ; Antarctica; 1993–95; total PCBs in blood of breeding adult female at moment of egg hatching	572 FW	41
Chicken, <i>Gallus</i> sp.; fat vs. feather; total of PCBs 118, 138, 153, and 156; PCB-contaminated area	12,800 LW vs. 200 LW	11
Gull-billed tern, <i> Gelochelidon nilotica</i> ; infertile eggs; Spain, 1988		
PCB 138	Max. 220 FW	12
PCB 153	Max. 90 FW	12
PCB 180	Max. 190 FW	12
White-tailed sea eagle, <i>Haliaeetus albicilla</i>		
Liver vs. eggs; total PCBs; Norway 1965–83	5000 (100–180,000) FW vs. 13,900 (4200–31,000) FW	1
Breast muscle; Poland, 1982–90		
Non-ortho planars		
PCB 77	3–140 FW	13
PCB 126	1–160 FW	13
PCB 169	2–380 FW	13
Mono-ortho planars		
PCB 60	5–760 FW	13
PCB 105	110–9200 FW	13
PCB 118	290–28,000 FW	13
PCB 156	53–9200 FW	13
Di-ortho planars		
PCB 128	ND–600 FW	13
PCB 137	50–6800 FW	13
PCB 138	930–65,000 FW	13
PCB 153	1100–92,000 FW	13
PCB 170	100–22,000 FW	13
PCB 180	330–61,000 FW	13
PCB 194	20–8900 FW	13
Booted eagle, <i>Hieraetus pennatus</i> ; infertile eggs; total PCBs; Spain, 1985–86	1500 (500–8400) FW	7
Loggerhead shrike, <i>Lanius ludovicianus</i> ; eggs vs. carcasses; total PCBs; Virginia, 1985–88	940 FW; Max. 1300 FW vs. <5 FW	14
Herring gull, <i>Larus argentatus</i>		
Eggs; Great Lakes; total PCBs		
Lake Erie		
1972–74 vs. 1977–80	34,700–130,700 FW vs. 14,600–33,100 FW	26
1983 vs. 1987–88	11,800–14,100 FW vs. 5600–21,900 FW	26
Lake Huron		
1971–77 vs. 1980–83	43,000–59,500 FW vs. 8800–10,900 FW	26
1987–88	4500–11,300 FW	26
Lake Ontario		
1971–72 vs. 1974–77	58,800–143,900 FW vs. 36,200–96,600 FW	26
1980–83 vs. 1987	15,900–27,500 FW vs. 14,400–15,800 FW	26
Lake Superior; 1973–77 vs. 1980–87	37,100–46,400 FW vs. 5500–11,400 FW	26
Eggs; Great Lakes		
PCB 77	0.6–3.0 LW	6
PCB 105	50–860 LW	6

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 118	180–2550 LW	6
PCB 126	2–10 LW	6
PCB 169	0.2–9.0 LW	6
Infertile eggs; Spain, 1988		
PCB 138	Max. 450 FW	12
PCB 153	Max. 400 FW	12
PCB 180	Max. 280 FW	12
Total PCBs	2000 (1100–3600) FW	12
Lake Ontario, 1985		
Adults		
Total PCBs		
Carcass	47,000 FW	15
Diet (fish)	510 FW	15
Liver	12,000 FW	15
Total tetrachlorobiphenyls (PCBs 56, 60, 66, and 74); carcass vs. liver	1490 FW vs. 450 FW	15
Total penta-CBs (PCBs 99, 101, 105, 110, and 118); carcass vs. liver	7440 FW vs. 2050 FW	15
Total hexa-CBs (PCBs 128, 132, 137, 138, 141, 146, 149, 153); carcass vs. liver	19,900 FW vs. 5100 FW	15
Total hepta-CBs (PCBs 170, 171, 172, 174, 177, 178, 180, 182, 183, 187, 190, 197); carcass vs. liver	14,400 FW vs. 3700 FW	15
Total octa-CBs, carcass vs. liver	3400 FW vs. 860 FW	15
Eggs		
Total PCBs	16,000 FW	15
Total tetra-CBs	560 FW	15
Total penta-CBs	2880 FW	15
Total hexa-CBs	7250 FW	15
Total hepta-CBs	4340 FW	15
Total octa-CBs	860 FW	15
Yellow-legged herring gull, <i>Larus cachinnans</i> ; eggs; Italy, 1981–86		
Total PCBs (30 congeners)	30,400–56,100 DW	16, 17
PCB 138	4600–6800 DW	16
PCB 153	7800–14,100 DW	16
PCB 180	3900–7000 DW	16
Audouin's gull, <i>Larus audouinii</i> ; eggs		
Italy, 1981–86; total PCBs	28,600–45,900 DW	17
Spain, 1988		
Total PCBs	9000 (4700–20,500) FW	12
PCB 138	Max. 1800 FW	12
PCB 153	Max. 1600 FW	12
PCB 180	Max. 1300 FW	12
Red-breasted merganser, <i>Mergus serrator</i> , eggs; Michigan; 1977–78 vs. 1990		
Total PCBs	23,000 FW vs. 11,100 FW	28
PCB 77	24 FW vs. 20 FW	28
PCB 81	5 FW vs. 3 FW	28
PCB 126	13 FW vs. 6 FW	28
PCB 169	1.6 FW vs. 0.9 FW	28
PCB 105	454 FW vs. 205 FW	28
PCB 118	847 FW vs. 415 FW	28
PCB 101	246 FW vs. 115 FW	28
PCB 138	1417 FW vs. 659 FW	28
PCB 153	2313 FW vs. 1221 FW	28
PCB 180	641 FW vs. 327 FW	28

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Black kite, <i>Milvus migrans</i> ; infertile eggs; total PCBs; Spain, 1985–86	2900 (500–18,700) FW	7
Black-crowned night heron, <i>Nycticorax nycticorax</i>		
Pipping embryos; whole less liver; lipid extracts; 1991; Chincoteague Bay, VA (reference site) vs. Baltimore Harbor, MD (contaminated site)		
PCB 66	3 FW vs. 58 FW	29
PCB 77	508 FW vs. 4982 FW	29
PCB 81	0.04 FW vs. 1.2 FW	29
PCB 105	6 FW vs. 146 FW	29
PCB 114	0.5 FW vs. 5.2 FW	29
PCB 118	10 FW vs. 288 FW	29
PCB 123	0.4 FW vs. 1.3 FW	29
PCB 126	(ND–750) FW vs. 4527 (ND–39,640) FW	29
PCB 156	1.2 FW vs. 15.2 FW	29
PCB 157	2 FW vs. 62 FW	29
PCB 167	3 FW vs. 26 FW	29
PCB 169	32 (ND–190) FW vs. (ND–2210) FW	29
PCB 189	0.4 FW vs. 5.6 FW	29
Embryos; total PCBs		
Control site, Virginia	1130 (240–4000) FW	18
Cat Island, Green Bay, Wisconsin	9300 (2400–53,000) FW	18
San Francisco Bay	900–2600 (ND–12,000) FW	18
Osprey, <i>Pandion haliaetus</i> ; liver vs. eggs; Norway, 1965–83; dead on collection	5000 (<100–26,000) FW vs. 3200 (700–8300) FW	1
Shag, <i>Phalacrocorax aristotelis</i> ; Isle of Man; Irish Sea; 1994; eggs; total PCBs	1100 FW; 6600 (4100–13,400) DW	33
Double-crested cormorant, <i>Phalacrocorax auritus</i>		
Eggs; Great Lakes; total PCBs	900–7300 FW; reduced hatch at >6500 FW	27
Eggs; upper Great Lakes; 1986–91; total PCBs	8200 (5600–10,700) FW	34
Eggs; 1990–91; near Lake Ontario (contaminated site) vs. reference site		
PCB 77	0.3 FW vs. 0.08 FW	35
PCB 105	173 FW vs. 18 FW	35
PCB 118	173 FW vs. 133 FW	35
PCB 126	3.7 FW vs. 0.5 FW	35
PCB 169	0.4 FW vs. 0.09 FW	35
Great cormorant, <i>Phalacrocorax carbo</i>		
Netherlands; yolk sac		
PCB 105	Max. 25,000 LW	19
PCB 118	Max. 75,000 LW	19
PCB 156	Max. 20,000 LW	19
PCB 157	Max. 10,000 LW	19
PCB 167	Max. 15,000 LW	19
England; 1992–93; expanding colony; whole late embryo stage vs. chick liver		
Total PCBs	811 (145–1754) FW vs. 2271 FW	38
PCB 99	15 FW vs. 30 FW	38
PCB 105	21 FW vs. 38 FW	38
PCB 118	72 FW vs. 139 FW	38
PCB 128	18 FW vs. 33 FW	38
PCB 138	118 (24–254) FW vs. 292 FW	38
PCB 153	236 (41–512) FW vs. 763 FW	38

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 156	25 FW vs. 42 FW	38
PCB 163	34 FW vs. 111 FW	38
PCB 170	40 FW vs. 127 FW	38
PCB 177	11 FW vs. 25 FW	38
PCB 180	95 FW vs. 314 FW	38
PCB 183	16 FW vs. 33 FW	38
PCB 187	47 FW vs. 143 FW	38
PCB 189	2 FW vs. 5 FW	38
PCB 194	19 FW vs. 66 FW	38
PCB 195	5 FW vs. 14 FW	38
PCB 196	17 FW vs. 41 FW	38
PCB 201	23 FW vs. 64 FW	38
PCB 206	4 FW vs. 10 FW	38
Great cormorant, <i>Phalacrocorax carbo sinensis</i> ; age <2 years vs. age >2 years; Germany, 1985–86		
Brain		
PCB 28	100 FW vs. 50 FW	20
PCB 52	100 FW vs. 100 FW	20
PCB 101	20 FW vs. 10 FW	20
PCB 138	300 FW vs. 900 FW	20
PCB 153	200 FW vs. 1500 FW	20
PCB 180	100 FW vs. 600 FW	20
Liver		
PCB 28	200 FW vs. 100 FW	20
PCB 52	80 FW vs. 100 FW	20
PCB 101	100 FW vs. 50 FW	20
PCB 138	800 FW vs. 2400 FW	20
PCB 153	800 FW vs. 3700 FW	20
PCB 180	300 FW vs. 1000 FW	20
Subcutaneous fat		
PCB 28	1000 FW vs. 1400 FW	20
PCB 52	400 FW vs. 1200 FW	20
PCB 101	800 FW vs. 6100 FW	20
PCB 138	13,000 FW vs. 85,000 FW	20
PCB 153	20,000 FW vs. 93,000 FW	20
PCB 180	5800 FW vs. 53,000 FW	20
White spoonbill, <i>Platalea leucorodia</i> ; infertile eggs; total PCBs; Spain, 1985–86	600 (400–1300) FW	7
Adelie penguin, <i>Pygoscelis adeliae</i> ; Antarctica; Hop Island; 1993–94; total PCBs		
Fat		
Juveniles	4.8 LW	41
Nonbreeders	5.1 LW	41
Breeders	5.6 LW	41
Blood; breeding adult female at moment of egg hatching	286.0 FW	41
Gentoo penguin, <i>Pygoscelis papua</i> ; Antarctica; 1991–93; maximum concentrations		
Total PCBs		
Brain	7.8 FW	39
Liver	1.1 FW	39
Muscle	ND	39
Blood	4.8 FW	39
Bone	32.1	39
Uropygeal gland	1047 FW	39
Fat	1583 FW	39

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 18 vs. PCB 52		
Brain	0.4 FW vs. 0.9 FW	39
Liver	0.9 FW vs. 0.7 FW	39
Muscle	0.8 FW vs. 0.3 FW	39
Blood	4.5 FW vs. 1.8 FW	39
Bone	0.2 FW vs. 0.6 FW	39
Uropygeal gland	13.7 FW vs. 3.2 FW	39
Fat	28.2 FW vs. 8.2 FW	39
PCB 44 vs. PCB 101		
Brain	1.3 FW vs. 0.6 FW	39
Liver	0.3 FW vs. 0.6 FW	39
Muscle	0.2 FW vs. 0.1 FW	39
Blood	1.5 FW vs. 0.1 FW	39
Bone	0.4 FW vs. 0.4 FW	39
Uropygial gland	10.2 FW vs. 22.7 FW	39
Fat	10.7 FW vs. 9.5 FW	39
PCB 118 vs. PCB 153		
Brain	0.3 FW vs. 2.7 FW	39
Liver	0.2 FW vs. 0.7 FW	39
Muscle	0.2 FW vs. 0.2 FW	39
Blood	ND vs. 1.1 FW	39
Bone	0.4 FW vs. 2.9 FW	39
Uropygial gland	24.1 FW vs. 47.4 FW	39
Fat	10.1 FW vs. 17.4 FW	39
PCB 128 vs. PCB 138		
Brain	ND vs. 2.2 FW	39
Liver	0.3 FW vs. 0.8 FW	39
Muscle	0.1 FW vs. 0.3 FW	39
Blood	ND vs. 2.2 FW	39
Bone	0.4 FW vs. 1.0 FW	39
Uropygial gland	3.8 FW vs. 32.4 FW	39
Fat	7.2 FW vs. 11.6 FW	39
PCB 180 vs. PCB 187		
Brain	0.1 FW vs. 0.6 FW	39
Liver	0.2 FW vs. 0.1 FW	39
Muscle	0.2 FW vs. 0.1 FW	39
Blood	0.8 FW vs. ND	39
Bone	0.3 FW vs. 0.6 FW	39
Uropygial gland	27.3 FW vs. 94.0 FW	39
Fat	10.0 FW vs. 32.3 FW	39
Caspian tern, <i>Sterna caspia</i>		
Egg; Washington State; 1991		
Total PCBs	616 FW	40
PCB 77	0.10 FW	40
PCB 126	0.34 FW	40
PCB 169	0.21 FW	40
PCB 153	161.0 FW	40
PCB 180	87.9 FW	40
Blood plasma; total PCBs (Aroclors 1242, 1248, 1254, 1260); Great Lakes, 1990		
Green Bay	3500 (900–13,800) FW	21
Saginaw Bay	2500 (1600–3800) FW	21
Other locations	900–2100 (400–3600) FW	21
Forster's tern, <i>Sterna forsteri</i>		
Eggs; Washington State; 1991; total PCBs	720 (580–940) FW	40

Table 24.11 (continued) PCB Concentrations in Field Collections of Selected Birds (Concentrations are in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Whole eggs and chicks; total PCBs; Green Bay, Wisconsin; 1988 vs. 1989	Max. 5100–9500 FW vs. Max. 3800–8500 FW	9, 22
Common tern, <i>Sterna hirundo</i> ; eggs and chicks; total PCBs; Green Bay, Wisconsin, 1989	5000–14,100 FW	9
Arctic tern, <i>Sterna paradisaea</i> ; prefledgling carcass; German Wadden Sea, 1988; found dead; age 2–14 days vs. age 15–27 days		
PCB 26	2800 LW vs. 500 LW	23
PCB 44	200 LW vs. 40 LW	23
PCB 49	200 LW vs. 40 LW	23
PCB 128	2200 LW vs. 400 LW	23
PCB 138	15,800 LW vs. 4000 LW	23
PCB 153	25,700 LW vs. 5000 LW	23
PCB 180	8600 LW vs. 1700 LW	23
PCB 183	2200 LW vs. 300 LW	23
PCB 187	3300 LW vs. 600 LW	23
PCB 194	700 LW vs. 20 LW	23
Tawny owl, <i>Strix aluco</i> ; liver vs. eggs; total PCBs; Norway, 1965–83; dead on collection	700 (<100–70,000) FW vs. 1100 (300–6600) FW	1
Northern gannet, <i>Morus bassanus</i> ; total PCBs (35 congeners); England, 1988–90		
Fat	14,600 FW; 18,000 LW	5
Liver	700 FW; 184,000 LW	5
Muscle	2900 FW; 20,000 LW	5
Tree swallow, <i>Tachycineta bicolor</i>		
Eggs and chicks; total PCBs; Green Bay, Wisconsin, 1989	10,800–13,100 FW	9
Wisconsin; 1994–95; contaminated sites vs. reference sites; total PCBs		
Eggs and newly hatched young	3010 FW vs. 260 FW	42
12-day-old nestlings	2300 FW vs. 10 FW	42
Guillemot, <i>Uria aalge</i> ; total PCBs (35 congeners); England, 1988–90		
Brain	Max. 3200 FW; Max. 56,000 LW	5
Fat	Max. 450,000 FW; Max. 659,000 LW	5
Gizzard and contents	Max. 137,000 FW; Max. 563,000 LW	5
Kidney	Max. 5900 FW; Max. 321,000 LW	5
Liver	Max. 1500 FW; Max. 354,000 LW	5
Muscle	Max. 1100 FW; Max. 67,000 LW	5
Waterbirds; Laguna Madre, Texas; 1993–94; eggs; total PCBs		
Great blue heron, <i>Ardea herodias</i>	400 (60–2000) FW	36
Snowy egret, <i>Egretta thula</i>	80 (30–100) FW	36
Tricolored heron, <i>Egretta tricolor</i>	70 (40–100) FW	36
Caspian tern	560 (300–2800) FW	36
Waterfowl, 8 species; eggs; total PCBs; Italy	500–24,000 DW	24

^a Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

^b 1, Froslie et al. 1986; 2, Elliott and Shutt 1993; 3, Borlakoglu et al. 1991b; 4, Hernandez et al. 1989; 5, Boumphrey et al. 1993; 6, Kennedy et al. 1992; 7, Hernandez et al. 1988; 8, Ormerod and Tyler 1994; 9, Jones et al. 1993; 10, Jarman et al. 1993; 11, Zupancic-Kralj et al. 1992; 12, Gonzalez et al. 1991; 13, Falandysz et al. 1994a; 14, Blumton et al. 1990; 15, Braune and Norstrom 1989; 16, Focardi et al. 1988a; 17, Leonzio et al. 1989; 18, Rattner et al. 1993; 19, van den Berg et al. 1992; 20, Scharenberg 1991b; 21, Mora et al. 1993; 22, Ankley et al. 1993; 23, Scharenberg 1991a; 24, Focardi et al. 1988b; 25, Smith et al. 1985; 26, Turle et al. 1991; 27, Jones et al. 1994; 28, Williams et al. 1995; 29, Rattner et al. 1997; 30, Custer et al. 1996; 31, Botero et al. 1996; 32, Johnstone et al. 1996; 33, Allen and Thompson 1996; 34, Ludwig et al. 1996; 35, Henshel et al. 1997; 36, Mora 1996; 37, de Cruz et al. 1997; 38, Mason et al. 1997; 39, Inomata et al. 1996; 40, Blus et al. 1998; 41, van den Brink et al. 1998; 42, Custer et al. 1998.

24.4.7 Terrestrial Mammals

The highest total PCB concentrations recorded in terrestrial mammalian wildlife occurred in fat and liver tissues of species collected near urban areas; di-*ortho*-congeners were the major contributors to PCB tissue burdens (Table 24.12). Atmospheric transport of PCBs governed uptake in terrestrial mammalian herbivores and predators. For example, PCB residues in tissues of voles and shrews in the Scandinavian peninsula directly correlated with fallout loadings (Larsson et al. 1990). An increase in atmospheric deposition of PCBs increased PCB burdens in plants, herbivores, and predators of the herbivores. But herbivores and predators differentially metabolized PCBs, raising concentrations of highly chlorinated congeners in predators and concentrations of the more easily metabolized low-chlorinated PCBs in herbivores (Larsson et al. 1990).

Populations of mink (*Mustela vison*) declined in many areas of the world, and the declines were linked to exposures to synthetic halogenated hydrocarbons (Giesy et al. 1994b). In the Great Lakes region, mink density is lower along the shores of the Great Lakes and their tributaries where mink have access to fishes from the Great Lakes. Tissue PCB concentrations and their dioxin TEFs were considered critical in the hazard assessment of PCBs. Mink that consumed fishes below dams in Michigan were 10 to 20 times more likely to suffer PCB damage than mink consuming fishes from above the dams, as judged by the elevated concentrations of total PCBs and dioxin TEFs in fishes from below the dams (Giesy et al. 1994b). European polecats (*Mustela putorius*) collected in the Netherlands between 1985 and 1990 had PCB patterns that were independent of diet and seemed to be controlled by anal gland secretions containing elevated PCB residues (Leonards et al. 1994). Juvenile polecats contained higher PCB concentrations than adult males and females, and this is attributed to an increased elimination of PCBs by adults through anal gland secretions. In all examined polecat tissues, PCB 126 accounted for 63 to 98% of the 2,3,7,8-TCDD toxic equivalents (Leonards et al. 1994). Polecats — unlike weasels (*Mustela nivalis*), stoats (*Mustela erminea*), and otters (*Lutra lutra*) — can readily metabolize PCBs 126 and 169 (Leonards et al. 1998). As a consequence, PCBs 126 and 169 are selectively retained in the livers of weasels, stoats, and otters, when compared to polecats. Polecats are less sensitive to PCBs than other mustelids when dietary PCB intakes are similar. However, otters are exposed to high dietary concentrations of PCBs when compared to other species of mustelids and are considered the most vulnerable of all mustelids to PCBs (Leonards et al. 1998).

The use of PCBs in Germany was prohibited in 1989. From 1983 to 1991, the body fat of red foxes (*Vulpes vulpes*) in Germany showed a reduction in the mean concentration of highly chlorinated PCBs (PCBs 138, 153, and 180) but an increase in the lower-chlorinated congeners (PCBs 24, 49, and 52). These findings suggest a trend toward a reduction of environmental contamination with highly chlorinated biphenyls since 1983, perhaps as a consequence of metabolic degradation, whereas contamination with lower-chlorinated biphenyls from diverse sources is increasing (Georgii et al. 1994). Low-chlorinated congeners that are metabolized via reactive intermediates must be evaluated because they show weak tumor-initiating properties (Georgii et al. 1994). At present, PCB congeners considered as indicators of contamination in Germany include PCBs 28, 31, 52, 101, 138, 153, and 180 (Bachour et al. 1998).

Populations of bats in Europe have been declining, and PCBs together with pesticides and wood preservatives are the suspected main causes of the decline (Fernandez et al. 1993). Three species of bats collected in Spain in 1988 to 1990 contained only a few dominant PCB congeners; PCBs 138, 153, and 180 accounted for about 80% of the total PCB burden in whole bats (Fernandez et al. 1993). But the most abundant PCB congeners in brain and liver of European otters (*Lutra*) were in the descending order of PCBs 163, 153, 138, and 170, each constituting at least 10% of the total PCB burden (Mason and Ratford 1994).

Total PCBs in adipose tissue of polar bears (*Ursus maritimus*) throughout their known range, and collected between 1989 and 1993, are as high as 24.3 mg/kg on a lipid weight basis and are dominated by PCBs 153 (46% of total PCBs), 180 (18.5%), 170/190 (8.6%), and 99 (8.3%)

(Norstrom et al. 1998). Total PCBs were higher in adult males than females, and there was no significant trend with age. PCB content was higher in bears from Svalbard, East Greenland, and the Arctic Ocean near Prince Patrick Island than most other areas. Atmospheric, oceanic, and ice transport may contribute to the high concentrations of total PCBs (Norstrom et al. 1998). The PCB composition in tissues of polar bears suggests that polar bears — unlike other mammals — can readily metabolize PCB congeners with unsubstituted *para*-positions and unsubstituted adjacent *ortho-meta*-positions (Norheim et al. 1992). Six PCB congeners (PCBs 99, 138, 153, 170, 180, 194) — all with a minimum 2,2',4,4'-chlorine substitution — accounted for about 99% of the total PCB content in liver and 87% in fat; PCB 153 accounted for 37% of the total PCB loading in liver. The PCB congener pattern in polar bear liver and adipose tissue is similar and seems to be independent of sex, age, nutritional status, collection locale, and PCB body burden (Norheim et al. 1992).

In humans, total PCB concentrations in maternal milk were elevated (>1.1 mg/kg milk fat) in 4 of 122 cases in the New Bedford Harbor vicinity, Massachusetts (Korrick and Altshul 1998). At least one female was occupationally exposed, as judged by the congener profile and history. PCB exposures from fish consumption were likely, but not from residence adjacent to a PCB-contaminated site. In all four cases, their newborns were full-term and healthy (Korrick and Altshul 1998).

Table 24.12 PCB Concentrations in Field Collections of Selected Mammals (Concentrations are in g/kg [ppb] fresh weight [FW] or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
Bats; whole body less wings, feet, and head; total PCBs; Spain, 1988–90		
Schreiber's bat, <i>Miniopterus schreibersi</i>	760 LW	1
Common pipistrelle, <i>Pipistrellus pipistrellus</i>	1290 LW	1
Greater horseshoe bat, <i>Rhinolophus ferrumequinum</i>	480 LW	1
All species		
Madrid vs. other locations	2980 LW vs. <560 LW	1
Immatures vs. adults	1940 LW vs. 800 LW	1
Domestic dog, <i>Canis familiaris</i> ; muscle fat; Germany, 1987		
PCB 28	<1 LW	2
PCB 49	5 (6–8) LW	2
PCB 52	<1 LW	2
PCB 101	3 (ND–9) LW	2
PCB 138	11 (3–25) LW	2
PCB 153	22 (7–58) LW	2
PCB 180	47 (6–153) LW	2
Human, <i>Homo sapiens</i>		
Adipose tissue; United States; 1982 vs. 1986		
Tetra-CBs	16 FW vs. 56 FW	7
Penta-CBs	78 FW vs. 135 FW	7
Hexa-CBs	176 FW vs. 314 FW	7
Hepta-CBs	85 FW vs. 125 FW	7
Total PCBs	407 FW vs. 672 FW	7
Maternal milk; New York State, 1988–90; maximum values		
PCB 77	1.3 LW	3
PCB 81	1.1 LW	3
PCB 105	6.7 LW	3
PCB 114	1.3 LW	3
PCB 118	8.7 LW	3
PCB 123	6.2 LW	3
PCB 126	3.6 LW	3
PCB 156	3.2 LW	3
PCB 157	9.4 LW	3
PCB 167	8.8 LW	3
PCB 169	ND	3

Table 24.12 (continued) PCB Concentrations in Field Collections of Selected Mammals
 (Concentrations are in g/kg [ppb] fresh weight [FW] or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
PCB 189	4.7 LW	3
Total PCBs	52.9 (3.4–179) LW; 1.5 FW	3
Maternal milk; New Bedford Harbor and environs; 1993; milk fat basis		
Total PCBs		
118 of 122 samples	320 FW	8
4 of 122 samples	1107–2379 FW	8
PCB 28	14–380 FW	8
PCB 74	52–510 FW	8
PCB 105	26–81 FW	8
PCB 118	202–360 FW	8
PCB 138	112–245 FW	8
PCB 153	202–292 FW	8
PCB 156	23–56 FW	8
PCB 180	74–99 FW	8
European otter, <i>Lutra lutra</i>		
Ireland; brain vs. liver; total PCBs	4700 (1200–14,400) LW vs. 42,800 (18,500–92,100) LW	4
Denmark; liver; total PCBs	58,000 (22,000–104,000) LW	4
England; liver; total PCBs	51,000 (2000–190,000) LW	4
Northeastern Spain; 1988–93; found dead; Aroclor 1260 (18 congeners)		
Liver	20,000 (7200–64,300) LW	9
Diet (fish muscle)	6100 (1400–58,700) LW	9
European polecat, <i>Mustela putorius</i> ; the Netherlands, 1985–90		
Anal gland		
Total PCBs	32,000 (5000–104,000) LW	5
Non-ortho PCBs	6.9 LW	5
Di-ortho PCBs	28,000 (4000–88,000) LW	5
Mono-ortho PCBs	3700 (700–13,000) LW	5
Fat (mesenteric)		
Total PCBs	51,000 (1000–370,000) LW	5
Non-ortho PCBs	2.7 LW	5
Di-ortho PCBs	49,000 (2000–350,000) LW	5
Mono-ortho PCBs	1800 (100–11,000) LW	5
Kidney		
Total PCBs	22,000 (2000–114,000) LW	5
Non-ortho PCBs	7.6 LW	5
Di-ortho PCBs	20,000 (1000–107,000) LW	5
Mono-ortho PCBs	1100 (200–4200) LW	5
Liver		
Total PCBs	48,000 (4000–260,000) LW	5
Non-ortho PCBs	5.5 LW	5
Di-ortho PCBs	45,000 (4000–248,000) LW	5
Mono-ortho PCBs	1200 (300–3400) LW	5
Muscle		
Total PCBs	28,000 (3000–150,000) LW	5
Non-ortho PCBs	2.8 LW	5
Di-ortho PCBs	26,000 (3000–140,000) LW	5
Mono-ortho PCBs	1300 (200–5700) LW	5
Mink, <i>Mustela vison</i> ; Northwest Territories, Canada; 1991–95		
Liver, total PCBs	7.0–73.1 FW	10
Prey species, liver		
Northern red-backed vole, <i>Clethrionomys rutilus</i>	0.5–4.7 FW	10
Snowshoe hare, <i>Lepus americanus</i>	1.2–8.8 FW	10

Table 24.12 (continued) PCB Concentrations in Field Collections of Selected Mammals
 (Concentrations are in g/kg [ppb] fresh weight [FW] or lipid weight [LW].)

Species, Tissue, PCB Congener, and Other Variables	Concentration ^a (g/kg)	Reference ^b
The Netherlands; 4 species of mustelids; 1985–93		
European otter, <i>Lutra lutra</i> ; total PCBs; liver vs. diet	34,750 (4430–222,180) LW vs. 2560 LW	11
Stoat, <i>Mustela erminea</i> ; total PCBs; liver	1093–16,510 LW	11
Weasel, <i>Mustela nivalis</i> ; liver		
Total PCBs	880 (530–2365) LW	11
PCB 77	<0.2–1.1 LW	11
PCB 105	9–32 LW	11
PCB 118	37–105 LW	11
PCB 126	1.5–14 LW	11
PCB 153	82–363 LW	11
PCB 156	12–34 LW	11
PCB 169	0.005–0.92 LW	11
Polecat, <i>Mustela putorius</i> ; liver		
Total PCBs	18,730 (4815–260,115) LW	11
PCB 77	0.05–2.3 LW	11
PCB 105	16–262 LW	11
PCB 118	77–1513 LW	11
PCB 126	2.3–8.7 LW	11
PCB 153	1569–112,535 LW	11
PCB 156	75–465 LW	11
PCB 169	0.15–0.53 LW	11
Prey organisms of weasel, stoat and polecat; liver; total PCBs	30–813 LW	11
Polar bear, <i>Ursus maritimus</i>		
Adults; known range; adipose tissue; 1989–93; total PCBs	5940 (2760–24,320) LW	12
Total PCBs; Norway, 1978–89; liver vs. fat		
Adults	13,000 FW vs. 31,000 FW	6
Juveniles	12,000 FW vs. 15,000 FW	6
Red fox, <i>Vulpes vulpes</i> ; muscle fat; Germany, 1983 vs. 1991; maximum values		
PCB 28	160 LW vs. 50 LW	2
PCB 49	<1 LW vs. 30 LW	2
PCB 52	130 LW vs. 50 LW	2
PCB 101	240 LW vs. 90 LW	2
PCB 138	2720 LW vs. 310 LW	2
PCB 153	4300 LW vs. 1000 LW	2
PCB 180	7890 LW vs. 2080 LW	2

^a Concentrations are shown as means, range (in parentheses), maximum (Max.), and nondetectable (ND).

^b 1, Fernandez et al. 1993; 2, Georgii et al. 1994; 3, Hong et al. 1994; 4, Mason and Ratford 1994; 5, Leonards et al. 1994; 6, Norheim et al. 1992; 7, USEPA 1994; 8, Korrick and Altshul 1998; 9, Lopez-Martin and Ruiz-Olmo 1996; 10, Poole et al. 1998; 11, Leonards et al. 1998; 12, Norstrom et al. 1998.

24.5 LETHAL AND SUBLETHAL EFFECTS

24.5.1 General

In all tested organisms, PCBs — especially PCBs with 2,3,7,8-TCDD-like activity — adversely affected patterns of survival, reproduction, growth, metabolism, and accumulation. Common manifestations of PCB exposure in animals include hepatotoxicity (hepatomegaly, necrosis), immunotoxicity (atrophy of lymphoid tissues, suppressed antibody responses), neurotoxicity (impaired behavior and development, catecholamine alterations), increased abortion, low birth weight, embryolethality, teratogenicity, gastrointestinal ulceration and necrosis, bronchitis, dermal toxicity (chloracne, edema,

hyperplasia), weak mutagenicity at high doses, and preneoplastic changes at low doses (Hansen 1987). PCBs can mimic female hormones in human cell lines and other mammalian systems and may be associated with learning deficiencies and lowered IQs in children (Bushart et al. 1998). At concentrations above a threshold, PCBs are potent promoters of hepatic carcinogenesis in laboratory rodents. However, there is no clear evidence of carcinogenicity of PCBs to human and animal populations from natural exposure (Hayes 1987). Induction of hepatic microsomal enzymes is one of the earliest and most sensitive responses to PCBs (Hansen 1987).

PCB-induced toxicity patterns are highly variable. Variability, as discussed later, is attributed in part to differences between species and strains in ability to metabolize PCBs and in primary sites of action; in the age, growth rate, biomass, and lipid content of the species; in dose rate, duration of exposure, route of administration, and tested congeners; in physicochemical characteristics of the habitat during exposure; and in PCB interactions with other PCBs, other organochlorine compounds, and heavy metals. Chinook salmon (*Oncorhynchus tshawytscha*) had decreased hatch when eggs contained the equivalent of 0.1 µg 2,3,7,8-TCDD/kg fresh weight (FW); domestic chickens (*Gallus* sp.) had decreased survival and increased developmental abnormalities when embryos had 20 µg PCB 77/kg FW; mink (*Mustela vison*) had reduced growth when fed 100 µg Aroclor 1254/kg BW daily and reduced survival at 50 µg PCB 169/kg diet; rhesus macaques (*Macaca mulatta*) had reproductive impairment when fed more than 8 µg Aroclor 1016/kg BW daily; and rats (*Rattus* sp.) had reduced litter sizes and survival when given 10 µg PCB 126/kg BW daily during gestation.

24.5.2 Aquatic Organisms

PCBs influence patterns of survival, reproduction, growth, enzyme activities, and accumulation in representative aquatic organisms (Table 24.13). Some PCB congeners at laboratory concentrations that were several orders of magnitude higher than those encountered under field conditions killed 47 to 83% of tested freshwater fishes and invertebrates in 24 to 48 h. However, most PCB congeners tested produced negligible mortality under these conditions (Dillon and Burton 1992) (Table 24.13). Mortality increased when PCB 133 or PCB 177 concentrations in whole guppies (*Poecilia reticulata*) exceeded 1 µmole/g, equivalent to more than 200 mg PCB/kg whole-body FW or about 4000 mg PCB/kg on a lipid weight basis (Opperhuizen and Schrap 1988). PCBs — especially those with TCDD-type activity — adversely affect reproductive success of spawning female chinook salmon. Chinook salmon eggs that contained total PCB concentrations equivalent to 0.1 µg 2,3,7,8-TCDD equivalents/kg eggs and higher had a dose-dependent decrease in hatching success (Ankley et al. 1991). PCBs also impair the reproductive capacities of marine mammals (Kannan et al. 1993).

The relation between PCB accumulation by the freshwater alga *Scenedesmus* sp. and the compound's octanol/water partition coefficient (K_{ow}) was measured with 40 PCB compounds in a log K_{ow} range of 4.46 to 8.18, PCB concentrations between 0.03 and 1.1 µg/L, and exposures between 20 and 30 days (Swackhammer and Skoglund 1993). The accumulation process was consistent with partitioning from water into cell lipids but was slower than the growth of *Scenedesmus* (i.e., no significant uptake of PCBs from congeners with $\log K_{ow} > 5.0$ under conditions of rapid growth or $>\log 7.0$ under conditions of slow growth). Thus, under nonwinter field conditions, many PCB congeners never reached equilibrium concentrations (Swackhammer and Skoglund 1993). Similar results are reported of other species of freshwater algae, including *Selenastrum capricornutum*, *Anabaena* sp., and *Synedra* sp. (Stange and Swackhammer 1994). High algal densities alter bioconcentration factors of PCBs. Bioconcentration factors for PCBs 15, 52, and 153 by the alga *Chlorella pyrenoidosa* were higher at comparatively low algal densities (Sijm et al. 1998), suggesting that BCF values determined at high algal densities should be applied with caution to field situations.

Zebra mussels (*Dreissena polymorpha*) accumulated PCB 77 from their diet and from the surrounding lake sediments (Brieger and Hunter 1993). An uptake rate of PCB 77 by zebra mussels followed the descending order of sediment, food, and water. Tissue concentrations in mussels peaked after 10 to 14 days at 3.4 to 3.7 mg PCB 77/kg FW soft parts; equilibrium levels of PCB 77 were near 1.0 mg/kg FW. Zebra mussels are more efficient accumulators of PCBs than other bivalve molluscs to which they are attached; accordingly, high densities of zebra mussels probably influence contaminant dynamics (Brieger and Hunter 1993). A freshwater crustacean (*Mysis relicta*) plays an important role in the transfer of PCBs from sediments into the Lake Champlain food web (Lester and McIntosh 1994), and freshwater grazing and shredding benthic invertebrates promote downstream transport of PCB 153 (Sallenave et al. 1994). Marine invertebrates accumulated PCBs 52, 101, 128, 138, 151, 153, 180, 194, 206, and 209 from PCB-contaminated sediments (Pruell et al. 1993). Clams (*Macoma nasuta*) reached a steady-state equilibrium in 10 days, but sandworms (*Nereis virens*) took 70 to 120 days. Clams showed preferential accumulation of lower-molecular-weight PCB congeners, and this may be due to the comparatively low lipid content in this species. Sandworms and grass shrimp (*Palaemonetes pugio*) metabolized PCBs 52, 101, and 151 (Pruell et al. 1993).

Golden shiners (*Notemigonus crysoleucas*) rapidly accumulated radiolabeled PCBs from water during 96-h exposure (Karara and McFarland 1992). The uptake rate of PCBs from water was controlled by gill blood-flow rate. About 50% of the accumulated PCBs in shiners was eliminated in 4.9 days, and this is similar to PCB elimination rates in striped bass (*Morone saxatilis*) and channel catfish (*Ictalurus punctatus*) (Karara and McFarland 1992). In guppies, residual PCB concentrations increased with increasing duration of exposure. However, steady-state concentrations did not occur during dietary exposure for 65 days (Schrap and Opperhuizen 1988). PCB congeners with *ortho*-chlorine substitutions (PCBs 77, 105, 118, 128, 138) were effective inducers of EROD (7-ethoxyresorufin O-deethylase) and AHH (aryl hydrocarbon hydroxylase) activities in marine mammals (Gooch et al. 1989) and freshwater fishes (Janz and Metcalfe 1991a; Skaare et al. 1992), but were ineffective at doses as high as 10 mg/kg BW in scup (*Stenotomus chrysops*), a marine teleost (Gooch et al. 1989). Industrial mixtures containing both planar and nonplanar PCBs induced AHH in fishes (Skaare et al. 1991). Mixtures of planar PCBs and dioxins, however, produced synergism of AHH activity in fish liver at low doses and antagonism at high doses; the possible antagonistic effects of nonplanar halogenated compounds may further complicate these interactions (Janz and Metcalfe 1991b). Liver is the primary target organ for the induction of cytochrome P-450-dependent monooxygenases by PCBs in fishes, and the most frequently examined organ. However, in salmonids, muscle tissue is also suitable for evaluation of hepatic monooxygenase induction, as judged by PCB concentrations in muscle (Janz et al. 1992).

Table 24.13 Effects of PCBs on Representative Aquatic Organisms

Taxonomic Group, Organism, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
INVERTEBRATES		
Daphnid, <i>Daphnia magna</i> ; early life stages		
PCB 1; 710 µg/L	LC50 (24h)	1
PCB 2; 430 µg/L	LC50 (24h)	1
PCB 3; 420 µg/L	LC50 (24h)	1
PCB 18; 86 µg/L	47% dead in 48 h	1
PCBs 28 (1.5 µg/L), 52 (74 µg/L), 77 (0.3 µg/L), 101 (1.2 µg/L), 116 (2.8 µg/L), 128 (0.4 µg/L), 153 (1.3 µg/L), 171 (1.7 µg/L), 194 (3.0 µg/L)	Negligible mortality; 87–100% survival in 48 h	1
PCB 47; 30 µg/L	LC50 (24h)	1

Table 24.13 (continued) Effects of PCBs on Representative Aquatic Organisms

Taxonomic Group, Organism, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
Zebra mussel, <i>Dreissena polymorpha</i> Fed alga (<i>Chlorella</i> sp.) containing 500 mg PCB 77/kg for 32 days	Maximum tissue concentration of 3.4 mg PCB 77/kg FW soft parts reached in about 14 days; concentration dropped to about 2 mg/kg after 32 days	2
Fed <i>Chlorella</i> containing 500 mg PCB 169/kg for 50 days, then clean <i>Chlorella</i> diet for 45 days	Maximum tissue concentration of 3.7 mg PCB 169/kg soft parts reached in 10 days, then declined during exposure to equilibrium level of about 1 mg/kg soft parts. After 25 days of clearance, soft parts contained 0.1 mg/kg FW	2
Amphipod, <i>Gammarus pseudolimnaeus</i> PCBs 8, 15, 32, 155, 101; initial water concentrations of 70–210 µg/L	LC50 (96 h)	1
Mysid, <i>Mysis relicta</i> ; exposed to radiolabeled PCB 153 for 6 h at 4°C, then transferred to clean water for 26 days	BCF from water of 442,230; calculated half-time persistence of 220 days	10
Amphipod, <i>Pontoporeia hoyi</i> ; exposed to radiolabeled PCB 153 for 6 h at 4°C, then transferred to clean water for 26 days	BCF from water of 101, 660; calculated half-time persistence of 50 days	10
VERTEBRATES		
Zebrafish, <i>Brachydanio rerio</i> Females given diets containing 8, 80, or 400 µg/kg diet containing 20 PCBs for 30 weeks (equal amounts of PCBs 41, 51, 58, 60, 68, 78, 91, 99, 104, 109, 112, 115, 126, 143, 153, 173, 184, 188, 190, and 193) Treatment as above. After 9 weeks, exposed females and normal males were mated	PCBs accumulated in dose-dependent relation. Treated groups had significantly lower whole-body, liver, and ovary weight and increased hepatic EROD Egg production reduced in all treated groups; females in the 8 and 400 µg/kg groups had a reduced number of mature oocytes. Median survival time of larvae in high-dose group was 7.7 days vs. 14 days in controls	21
Beluga whale, <i>Delphinapterus leucas</i> ; isolated blood leukocytes and splenocytes; exposure to various concentrations of PCBs 138, 153, 169, or 180 for 48 h	No marked effect on phagocytosis at 25 mg/kg medium; significant inhibition of proliferative response of splenocytes at 20–25 mg/kg PCB 138, but no inhibition at this concentration by other PCBs; no measurable effect at 5 mg/kg medium for any PCB tested	23
Mummichog, <i>Fundulus heteroclitus</i> Adult females given single ip injection of a mixture of 9 PCBs equivalent to 0.76, 3.8, or 19 mg/kg BW on a fresh weight basis, and observed for about 2 months	High-dose fish had 58% dead; survivors had egg production reduced 77% and their livers had 33 mg total PCBs/kg DW. The two lower dose groups had 60 and 62% reduction in egg production and liver residues of 3 and 12 mg total PCBs/kg DW, respectively. Food consumption declined with increasing dose. Egg production was related to pituitary gonadotropin content and food consumption	15
Adults collected from 4 sites in PCB-contaminated New Bedford Harbor, Massachusetts, in 1993, during their natural spawning season. Transported to laboratory and bred	After 5 weeks, fish from the most heavily contaminated site (2100 mg total PCBs/kg DW sediment) had liver concentrations of non-ortho (PCBs 77, 126, 169) plus mono-ortho PCBs of 29.3 mg/kg DW, reduced growth, and 30% mortality. Progeny of fish from this group had significantly reduced survival and a greater incidence of spinal abnormalities when compared to fish from a reference site	22

Table 24.13 (continued) Effects of PCBs on Representative Aquatic Organisms

Taxonomic Group, Organism, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
Channel catfish, <i>Ictalurus punctatus</i> ; juveniles; exposed to PCB 126, tributyltin, or both.		
Single injected dose of 0.01, 0.1, or 1 mg/kg BW of each, or both in combination	PCB alone, but not TBT alone, induced cytosolic aryl hydrocarbon receptor and cytochrome P-4501A activities	16
Six injections of 0.017, 1.7, or 17 µg/kg BW of each given every 3 days over a 16-day period to yield a cumulative dose of 0.01, 0.1, or 1.0 mg/kg BW. Examined 7 days after final injection for hepatic EROD activity and CYP1A protein	TBT potentiates PCB 126-induced CYP1A at environmentally relevant doses. Low and middle doses of TBT (0.01 and 0.1 mg/kg BW), but not the high dose, potentiated PCB 126-induced activity at these same doses	16
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Eggs injected 24–50 h after fertilization with graded doses of various PCBs		
PCB 4; >24,200 µg/kg egg fresh weight (FW)	LD50, embryos	13
PCB 28; >24,300 µg/kg egg FW	LD50, embryos	13
PCB 52; >30,400 µg/kg egg FW	LD50, embryos	13
PCB 77 0.578 µg/kg egg FW	At age 35 days, sac-fry contained 78% of original dose	13
1348 (1064–1621) µg/kg egg FW	LD50, embryos; blue-sac syndrome	13, 14
PCB 81; 549 µg/kg egg FW	LD50, embryos; blue-sac-syndrome	13
PCB 105 67 µg/kg egg FW >6970 µg/kg egg FW	At sac-fry stage, 78% of original dose remained	13
PCB 118 1330 µg/kg egg FW >6970–>57,400 µg/kg egg FW	LD50, embryos	14
PCB 126 74 (44–83) µg/kg egg FW 1203 µg/kg egg FW	About 81% of original dose present in sac-fry	13
PCBs 128, 138, and 156; >115,000 µg/kg egg FW	LD50, embryos	13, 14
PCB 153; >6200 µg/kg FW	LD50, embryos	14
PCB 169; 7110 (5630–8090) µg/kg egg FW	LD50, embryos; blue-sac syndrome	13
PCB 170; >41,100 µg/kg egg FW	LD50, embryos	13
Larvae; age 3 days posthatch; exposed to 1, 5, or 20 mg Aroclor 1260/L for 3 h and examined 6 months later	All treatment groups accumulated 2.1–2.5 mg Aroclor 1260/kg BW after 3 h. Survival normal for all groups. Altered sex ratios and gonadal abnormalities in juvenile females: reduction in number of females produced in groups that accumulated 2.5 mg/kg BW; about 18% of females that initially contained 2.1 mg/kg BW had abnormal gonads vs. 2.7% in controls	18
Single ip injection; 134 µg/kg BW of PCB 77; or 5.8 µg/kg BW of PCB 126; or 93.7 µg/kg BW of PCB 169; subadults	50% increase in liver EROD activity	12
Single ip injection of 1.0 mg PCB 77/kg BW; livers analyzed 13 days postinjection; subadults	Compared to controls, livers were elevated in levels of cytochrome P-450 (2X), ethoxocoumarin-O-deethylase (10X), and ethoxresorufin-O-deethylase (50X)	11
Injected ip with 2,3,7,8-TCDD at 0.00037, 0.0022 or 0.0045 µmol/kg BW, or with PCB 77 at 0.2, 1.1, or 2.2 µmol/kg BW; subadults	50% induction of AHH (arylhydrocarbon hydroxylase) activity in liver microsomes of sexually immature trout at 0.002 µmol/kg for TCDD and 0.37 µmol/kg for PCB 77	3

Table 24.13 (continued) Effects of PCBs on Representative Aquatic Organisms

Taxonomic Group, Organism, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
Single ip injection of mixture of 0.00018 µmol TCDD/kg BW plus 0.1 µmol/kg PCB 77; or mixture of 0.0011 µmol TCDD/kg BW plus 0.6 µmol PCB 77/kg BW; subadults	Mixtures of TCDD and PCB 77 produced greater than additive AHH responses	3
Single ip injection of mixture of 0.0022 µmol TCDD/kg BW plus 1.1 µmol PCB 77/kg BW; subadults	AHH induction response was less than additive	3
Single ip injection of PCB 77, PCB 126, or 2,3,7,8-TCDD. Liver AHH activity measured 3 days later; subadults	50% AHH induction occurred at 0.005 µmol/kg BW for TCDD, 1.0 for PCB 77 and 2.2 for PCB 126. PCB 77 was 1/200 as effective in inducing AHH activity in liver as TCDD, and PCB 126 was 1/500 as effective	4
Single ip injection of 30 mg PCB 118/kg BW to immatures. Fish killed 4 days later and liver analyzed	Liver EROD (7-ethoxyresorufin O-deethylase) activity was 5.6 times higher than controls; AHH activity was 2.7 times higher than controls	5
Single ip injection of 50 or 250 mg PCB 153/kg BW of juveniles 20–60 g BW; livers examined after 4 weeks	Dose-dependent induction of hepatic EROD activity, CYP1A protein, and CYP1A1 mRNA content	17
Fingerlings were injected ip with ¹⁴ C-labeled PCB mixture at 0.3, 1, 3, 10, and 30 mg PCB/kg BW; tissues sampled up to 70 days postinjection	At 3 days postinjection high doses of 10 and 30 mg PCB/kg BW caused elevation of liver microsomal monooxygenase activity when maximum tissue concentrations, in mg total PCB/kg FW, were 55 in bile, 12 in blood, 8 in muscle, and 8 in liver. Elevated hepatic microsomal monooxygenase activity with muscle and liver PCB concentrations of >0.3 mg/kg FW, but not 0.25 mg/kg FW	6
Juveniles fed diets containing 16 PCBs for 30 days; individual PCBs had high accumulation potential and high persistence in tissues	Half-time persistence of individual PCBs ranged between 24 and 224 days. Increasing persistence was positively related to increasing Log K _{ow} in the range 5–8, with a peak at 7	19
Fathead minnow, <i>Pimephales promelas</i> ; fry PCB 18; 86 µg/L	83% dead in 48h	1
PCBs 28 (1.5 µg/L), 52 (74 µg/L), 77 (0.3 µg/L), 101 (1.2 µg/L), 116 (2.8 µg/L), 128 (0.4 µg/L), 153 (1.3 µg/L), 171 (1.7 µg/L), 194 (3.0 µg/L)	Negligible mortality; 97–100% survival in 48h	1
Guppy, <i>Poecilia reticulata</i> ; adult males Fed diets containing 6–150 mg PCB 133 or PCB 197/kg diet for 191–247 days, or 550–1400 mg/kg diet for 65 days	At 6–150 mg/kg diet, uptake efficiency was near 50%; at higher dietary loadings, uptake efficiency decreased to 25%. No deaths in controls or at low dietary dosages; 13–25% mortality at 550–1400 mg/kg diet. Prior to death, guppies were sluggish, uncoordinated, and darkly colored; fish that died during exposure contained >0.7 µmol PCB/g FW	7
Fed PCB 133 at 550 mg/kg diet FW or PCB 197 at 530 mg/kg diet FW for 65 days, followed by a clean diet for 89 days, then reexposure to the contaminated diet for another 37 days	No PCB clearance during initial exposure; significant elimination of both PCBs when fed a clean diet. During reexposure, uptake efficiency for both PCBs was significantly higher than during the initial exposure	8
Leopard frog, <i>Rana pipiens</i> ; adults; single ip injection of PCB 126 at 0.0, 0.2, 0.7, 2.3, or 7.8 mg/kg BW. Four hepatic monooxygenases were examined	After 1 week, specific activities were not affected at 0.7 mg/kg BW and lower, but were 3–6.4 times higher than controls at 2.3 mg/kg BW and higher — and remained elevated for at least 4 weeks	20

Table 24.13 (continued) Effects of PCBs on Representative Aquatic Organisms

Taxonomic Group, Organism, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
Scup, <i>Stenotomus chrysops</i> ; injected intraperitoneally with 1, 5, or 10 mg/kg BW of PCBs 77, 105, 118, 128, or 138 and examined for increases in ethoxyresorufin O-deethylase (EROD) activity, immunodetectable cytochrome P-450E (the EROD catalyst in scup) and <i>in vitro</i> translatable mRNA for P-450E	Monooxygenase parameters were significantly induced only by PCB 77; translatable mRNA for P-450E was induced at all doses; EROD activity and P-450E were decreased at the 5 and 10 mg/kg BW doses; a positive correlation was established between PCB 77 residues in liver and decreased EROD activity at the higher doses	9

^a 1, Dillon and Burton 1992; 2, Brieger and Hunter 1993; 3, Janz and Metcalfe 1991b; 4, Janz and Metcalfe 1991a; 5, Skaare et al. 1991; 6, Melancon et al. 1989; 7, Schrap and Opperhuizen 1988; 8, Opperhuizen and Schrap 1988; 9, Gooch et al. 1989; 10, Evans and Landrum 1989; 11, Tyle et al. 1991; 12, Newsted et al. 1995; 13, Zabel et al. 1995; 14, Walker and Peterson 1991; 15, Black et al. 1998a; 16, Rice and Roszell 1998; 17, Foster et al. 1998; 18, Matta et al. 1998; 19, Fisk et al. 1998; 20, Huang et al. 1998; 21, Orn et al. 1998; 22, Black et al. 1998b; 23, De Guise et al. 1998.

24.5.3 Birds

PCB 126 is among the most toxic of all PCB congeners to birds, and the domestic chicken is the most sensitive tested species (Table 24.14) (Hoffman et al. 1996a, 1998). However, adverse effects of PCBs in birds vary markedly between species and tissues. And birds react differently to different PCB congeners and to PCB–metal mixtures. American kestrels (*Falco sparverius*) differ from Japanese quail (*Coturnix japonica*) after exposure to PCBs 105, 126, and 153; quail accumulated porphyrins in liver, but kestrels did not (Elliott et al. 1991). Japanese quail dosed with PCB 47 or 77 showed marked differences between the abilities of the small intestines and liver to metabolize porphyrin and the induction of cytochrome P-450 isozymes and associated monooxygenases (Miranda et al. 1987). Japanese quail fed different dietary concentrations of Aroclor 1260 for 25 days had a significant dose-dependent correlation between liver monooxygenase activity and PCB levels in blood (Marsili et al. 1996). EROD and porphyrin-induction responses of primary hepatocytes to various PCBs in newly hatched chickens, gulls, terns, and cormorants followed a concentration-dependent increase with significant variability in response between species (Sanderson et al. 1998). Pure hexachlorobiphenyls (HCBs) caused uroporphyrin accumulations and increased delta-aminolevulinic acid synthetase activity in chicken livers, and some HCBs significantly increased cytochrome P-450 and *p*-nitrophenol glucuronyl transferase when given in the feed for 3 weeks at 400 mg/kg ration. However, PCBs 128 and 169 caused greater accumulations of hepatic porphyrins than PCBs 138, 155, and 156 (Goldstein et al. 1976, 1977). PCBs 77, 136, 153, and 159 produced acute histopathological changes in chick embryo livers and selectively induced cytochrome P-448-mediated mixed-function oxidases; the degree of histopathologic change produced by each of the tested PCBs positively correlated with the degree of P-448 inhibition (Rifkind et al. 1984). Interactions of metals with PCBs are not well documented, although some studies with Japanese quail showed that cadmium raises PCB uptake from the diet. In one study, cadmium fed at high dietary levels of 100 mg/kg ration interfered with high levels of dietary PCBs (100 mg/kg ration). In that study, muscle of treated quails had increased loadings of congeners chlorinated in the 2,4,5-positions (such as PCBs 138, 153, 170, and 180), and these are comparatively toxic and resistant to metabolic degradation (Leoncio et al. 1992). More research is needed on variables known to modify PCB uptake, retention, translocation, and toxicity.

Embryos of the domestic chicken (*Gallus* sp.) are unusually sensitive to PCB 77. Mortality and a high incidence of developmental abnormalities — including microphthalmia, beak deformities,

edema, and retarded growth — were recorded in chicks at 0.02 mg PCB 77/kg egg FW, but no deaths or abnormalities were recorded in embryos of ducks, pheasants, and gulls at 0.1 to 1.0 mg PCB 77/kg egg FW (Table 24.14) (Brunstrom and Lund 1988). Chicken embryos were 20 to 100 times more sensitive to PCB 77 than embryos of the wild turkey (*Meleagris gallopavo*), and this sensitivity emphasizes the uncertainties of applying toxicity data from one species of bird to predict toxic effects in other avian species (Brunstrom 1988; Brunstrom and Lund 1988). Differences in sensitivity of birds to PCB 77 may be related to differences in metabolism and in the formation of toxic metabolites and to the increased availability of Ah receptors in chicks (Brunstrom and Reutergardh 1986). For example, Ah receptors were detected in livers of 7-day-old chicken embryos but not in livers of 9-day-old turkey embryos (Brunstrom and Lund 1988). Chicken embryos were extremely sensitive to PCB 126 when compared to embryos of the American kestrel and common tern. LD₅₀ values, in µg/kg FW egg, were 0.4 in chickens, 65.0 in kestrels, and 104.0 in terns; EROD induction in chicken embryo liver by PCB 126 was about 800 times more responsive than in tern and at least 1000 times more responsive than in kestrels (Hoffman et al. 1998).

Birds and mammals exposed to PCB mixtures frequently react differently. PCBs generally elicit large-colloid goiters in birds. These goiters are inherently different from hyperplastic goiters produced in mammals exposed to PCBs (Spear and Moon 1985). Fish-eating seabirds, such as the razorbill (*Alca torda*), can rapidly metabolize PCB congeners that have at least one pair of adjacent unsubstituted *meta-para* combinations in the biphenyl moiety (Borlakoglu et al. 1991b). Razorbills metabolized 4-chlorobiphenyl to 4-chloro-4'-hydroxybiphenyl. However, mice (*Mus sp.*) metabolized the same compound 15 times faster. PCB-exposed razorbills and rock doves (*Columba livia*) had similar concentrations of cytochrome P-450 and glutathione-S-transferase enzymes, but concentrations were significantly higher in rats (*Rattus sp.*) than either avian species (Borlakoglu et al. 1991b). The relative potency of tested PCBs — as measured by EROD activity of microsomal liver enzymes — in fertile eggs of the domestic chicken were 0.02 for PCB 77, and less than 0.001 for PCB 169 (Bosveld et al. 1992); these values differ somewhat from those proposed for mammals of 0.0005 for PCB 77, and 0.01 for PCB 169 (Safe 1990). Lymphoid development in the bursa of Fabricius of the avian embryo is inhibited by TCDD-like congeners. PCB 77, for example, affects the immune system by interacting with the Ah receptor, causing inhibition of lymphoid development in the mammalian thymus and in the avian bursa of Fabricius (Nikolaides et al. 1988). More research seems needed on the relation of avian Ah receptors to natural physiological processes.

Table 24.14 Effects of PCBs on Selected Birds

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
MALLARD, <i>Anas platyrhynchos</i>		
PCB 77; single injection into egg yolk on day 5 of incubation	No effect on hatching rate; chicks normal	1
0.1 mg/kg egg fresh weight (FW)	No effect on embryo survival and no gross abnormalities	2
5.0 mg/kg egg FW	PCB concentrations increased linearly with time of exposure and at day 100 exceeded 16 mg/kg FW in carcass and 3.9 mg/kg FW in breast muscle (26–523 mg/kg LW muscle); these values were 50–1000 times greater than human consumption guidelines for edible poultry in Canada (0.5 mg/kg LW), and 9–176 times greater than consumption guidelines for edible poultry in the U.S. (3.0 mg/kg LW)	18
GREYLAG GOOSE, <i>Anser anser</i>		
PCB 77; single injection into egg yolk on day 5 of incubation; 1.0 mg/kg egg FW	No effect on survival or development	2
GOLDFENEYE, <i>Bucephala clangula</i>		
PCB 77; single injection into egg yolk; 1.0 mg/kg egg FW	33% hatch vs. 52% hatch in controls; chicks normal	1

Table 24.14 (continued) Effects of PCBs on Selected Birds

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
NORTHERN BOBWHITE, <i>Colinus virginianus</i>		
PCB 126; single injection of egg with 0.04–0.07 mg/kg FW	LD50 through hatching	16
JAPANESE QUAIL, <i>Coturnix japonica</i>		
Adults given a single oral dose of either PCB 47 at 87.6 mg/kg body weight (BW), PCB 77 at 87.6 mg/kg BW, or Aroclor 1242 at 100–500 mg/kg BW. Quail were killed 48 h postdosing and liver and intestine analyzed for porphyrins and cytochrome P-450 monooxygenases	All compounds caused a significant increase in EROD activity and porphyrin content in small intestine and liver, and a significant increase in hepatic P-450 content	3
Adults fed diets for 30 days containing 100 mg cadmium/kg diet, 100 mg Aroclor 1260/kg diet, or mixture of 100 mg cadmium plus 100 mg Aroclor 1260/kg	Quail fed the mixture diet had 3 times more PCBs in muscle than the Aroclor group alone, and 70 times more PCBs than controls. The most dominant PCB congeners were 138, 153, 170, and 180	4
Fed in diet for 25 days at 5, 50, or 500 mg Aroclor 1260/kg diet	A dose-response relation was found between dietary PCB concentrations and porphyrins in liver and excreta. PCB concentrations in the 500 mg/kg group were about 900 mg/kg DW liver and 78 mg/kg DW excreta; in the 50 mg/kg group, liver had about 150 mg/kg DW	20
AMERICAN KESTREL, <i>Falco sparverius</i>		
Aroclor 1248; fed diets containing 3 mg/kg ration for 6 months; carcasses and eggs analyzed for total PCBs (Aroclors 1248, 1254, and 1260)	Carcasses of adults had 18.5 mg total PCBs/kg FW (vs. 3.3 in controls); eggs had 5.6 mg/kg FW vs. 1.5 in controls; shell thickness of eggs reduced 5%	5
Fed diets for 4 weeks containing daily doses equivalent to 3 mg PCB 105/kg BW, 0.05 mg PCB 126/kg BW, or 4.0 mg PCB 153/kg BW. Birds were killed 3 days after final treatment and livers analyzed for porphyrins, PCB residues, and activities of ethoxyresorufin O-deethylase-(EROD), aminopyrine-N-demethylase (APND), and aldrin epoxidase (AE)	PCB 105 caused significant APND induction; liver had 182.0 mg PCB 105/kg FW vs. 2.4 in corn oil controls. PCB 126 induced hepatic EROD and AE; liver had 3.3 mg PCB 126/kg FW. PCB 153 induced APND and AE; liver contained 119.0 mg PCB 153/kg FW. For all dose groups, liver weights and liver porphyrin levels were normal	6
Nestlings given daily oral doses of PCBs 77, 105, or 126 for 10 days		
PCB 77; 1.0 mg/kg BW daily	Liver contained 892 µg PCB 77/kg FW; onset of liver necrosis	16
PCB 105; 4.0 mg/kg BW daily	Liver contained 1677 µg PCB 105/kg FW; liver necrosis	16
PCB 126 50 µg/kg BW daily	Liver contained 156 (68–563) µg PCB 126/kg FW; pronounced liver enlargement; lymphoid depletion of spleen; 10-fold increase in hepatic microsomal EROD and benzyloxyresorufin-O-dealkylase; 5-fold increase in methoxyresorufin-O-dealkylase	16, 19
250 µg/kg BW daily	Liver had 380 µg PCB 126/kg FW with increasing necrosis; above effects plus decreased bone growth, decreased spleen weight, and degenerative lesions of thyroid	16, 19
1.0 mg/kg BW daily	Liver had 1.1 (0.6–4.5) mg PCB 126/kg FW; above effects plus decreased body weight, decreased hepatic thiol concentrations, and increased plasma enzyme activities	16, 19

Table 24.14 (continued) Effects of PCBs on Selected Birds

Species, PCB Congener, Dose, and Other Variables	Effect	Reference^a
Eggs injected with PCB 126 through air cell on days 3–4 of incubation 2.3–23 µg/kg FW 65.0 µg/kg egg FW	Malformations and edema at hatching LD50 at hatching	17 16, 17
Eggs injected with 316.0 µg PCB 77/kg FW on day 4 of incubation through air sac	LD50	17
DOMESTIC CHICKEN, <i>Gallus</i> sp.		
PCB 77; single dose injected into egg yolk on day 4 of fertilization 0.0006 mg/kg egg FW 0.004 mg/kg egg FW 0.010 mg/kg egg FW 0.020 mg/kg egg FW	50% increase in AHH activity after 48 h 60% hatch vs. 88% in controls 17% dead in 18 days; reduced thymus weight 70–100% dead by day 18; treated embryos had increased frequency of liver lesions, subcutaneous edema, shortened beaks, and microphthalmia	7 1, 8 7 1, 2, 8
0.050 mg/kg egg FW 0.100 mg/kg egg FW	All dead within 18 days Zero hatch; all dead	7 8
PCB 77; single dose injected into air sac on day 3 of incubation; 0.005 mg/kg egg FW	Whole liver homogenates had increases of 300-fold in 7-ethoxycoumarin O-deethylase and 75-fold in AHH activities between days 5 and 10	15
PCB 77; single dose of 0.0026 mg/kg egg FW injected into air sac on day 4 of incubation	LD50 by time of hatch	17
PCB 77; single dose injected into air sac on day 13 of incubation 0.045 mg/kg egg FW 0.20–0.30 mg/kg egg FW	Reduction by 50% in lymphoid cells in bursa of Fabricius 30-fold increase in AHH activity; bursa almost devoid of lymphoid cells	9 9
PCBs 77, 136, 153, 169; 17-day-old embryos; single injection at 0.5–30,000 nmol/egg; examined for liver histopathology and induction of mixed function oxidases after 24 h	Significant alterations occurred at 0.5 nmol PCB 77/egg (about 0.003 mg/kg egg), at 5 nmol PCB 169/egg, and between 500 and 5000 nmol PCB 153/egg. PCB 136 had no effect on liver pathology at the highest dose tested of 30,000 nmol/egg	10
Single injection of eggs of PCBs 105 (2.2 mg/kg FW), 126 (0.0006–0.0031 mg/kg FW), 157 (1.5–2.0 mg/kg FW), or 169 (0.17 mg/kg FW)	LD50 through hatching	16
PCB 126; single air sac injection on day 4 of egg incubation 0.0003 mg/kg egg FW and higher 0.0004 mg/kg	Malformations and edema noted at hatching LD50 at hatching	17 17
PCBs 128, 136, 153, 155, and 169; each was fed in diets to 1-day-old chicks for 21 days at 400 mg/kg ration PCB 128	Decrease in weight gain; moderate liver pathology; gross accumulations of hepatic porphyrins and increased delta-aminolevulinic acid synthetase activity	11, 12
PCB 136	Decrease in weight gain; comparatively small increase in liver weight	11
PCB 153	Decrease in weight gain; mild liver pathology	11
PCB 155	Largest increase in liver weight; significant liver pathology	11
PCB 169	All dead in 11 days; thymic involution and edema; gross accumulations of uroporphyrins in liver	11, 12

Table 24.14 (continued) Effects of PCBs on Selected Birds

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
HERRING GULL, <i>Larus argentatus</i> PCB 77; single injection into egg yolk on day 5 of incubation; 1.0 mg/kg egg FW	No effect on survival or development	2
BLACK-HEADED GULL, <i>Larus ridibundus</i> PCB 77; single injection into egg yolk of 1.0 mg/kg egg FW	No effect on hatching rate; chicks normal	1
WILD TURKEY, <i>Meleagris gallopavo</i> PCB 77; single injection into air sac of 5-day-old embryos 0.006 mg/kg egg FW 1.0 mg/kg egg FW	50% increase in AHH activity after 48 h 60% dead in 24 days	7 7
DOUBLE-CRESTED CORMORANT, <i>Phalacrocorax auritus</i> PCB 126; yolks of fertilized eggs injected with 70–698 µg PCB 126/kg FW egg prior to incubation	LD50 at hatch was 177 µg/kg. No increase in developmental abnormalities in any treatment group. Hepatic EROD activities higher in all treatment groups when compared to controls	22
RING-NECKED PHEASANT, <i>Phasianus colchicus</i> PCB 77; single injection into egg yolk 0.1 mg/kg egg FW 1.0 mg/kg egg FW	No decrease in hatching rate; chicks normal All embryos died	1 1
PCB 105; adult hens orally dosed with 0, 0.06, 0.6, or 6 mg PCB 105/kg BW weekly for 10 weeks to achieve cumulative doses of 0, 0.6, 6, or 60 mg PCB 105/kg BW after which hens were bred with untreated roosters once a week for 8 weeks	Production of fertilized eggs and survival of embryos and chicks in PCB 105 groups were not different from controls. Hepatic microsomal monooxygenase activities were significantly elevated in chicks at day 1 posthatch from hens given a cumulative dose of 6 mg/kg BW and in chicks at day 21 posthatch from hens given a total dose of 60 mg/kg BW	21
COMMON EIDER, <i>Somateria mollissima</i> Single injection into yolk on day 5 of incubation PCB 77; 1.0 mg/kg egg FW PCB 126; 0.1 mg/kg egg FW	No effect on survival 35% dead on day 24 of incubation vs. 20% dead in controls	13 13
COMMON TERN, <i>Sterna hirundo</i> PCB 126 Single egg injection with 0.045 mg/kg FW Single egg injection of 0.104 mg/kg egg FW via air sac on day 4 of incubation	35% embryo mortality through hatching LD50 at hatch; beak defects in survivors, especially crossed beaks	16 17
RINGED-TURTLE DOVE, <i>Streptopelia risoria</i> Fed iodine-deficient diet PCB 77; given 20 mg/kg BW 3 times over a 28-day period PCB 77; single dose of 60 mg/kg BW	Thyroid hyperplasia caused by low iodine diet was not enhanced by PCB 77 Thyroid hyperplasia reversed within 7 days	14 14

^a 1, Brunstrom and Reutergardh 1986; 2, Brunstrom 1988; 3, Miranda et al. 1987; 4, Leonzio et al. 1992; 5, Lowe and Stendell 1991; 6, Elliott et al. 1991; 7, Brunstrom and Lund 1988; 8, Brunstrom and Darnerud 1983; 9, Nikolaides et al. 1988; 10, Rifkind et al. 1984; 11, McKinney et al. 1976; 12, Goldstein et al. 1976; 13, Brunstrom et al. 1990; 14, Spear and Moon 1985; 15, Brunstrom 1986; 16, Hoffman et al. 1996a; 17, Hoffman et al. 1998; 18, Custer et al. 1996; 19, Hoffman et al. 1996b; 20, Fossi et al. 1996; 21, Hornung et al. 1998; 22, Powell et al. 1998.

24.5.4 Mammals

Deleterious effects were significant on growth, survival, reproduction, or metabolism from chronic exposures of sensitive species of tested rodents, primates, and mustelids to daily concentrations as low as 0.008 mg/kg BW of Aroclor 1016, 0.01 to 0.02 mg/kg BW of PCB 126, 0.01 to 0.05 mg/kg diet or 0.1 mg/kg BW of PCB 169, 0.09 mg/kg BW of Aroclor 1246, 0.1 mg/kg BW of Aroclor 1254, and 0.3 to 1.0 mg/kg diet or 0.6 mg/kg BW of PCB 77 (Table 24.15). Several PCBs had negligible adverse effects on tested mammals during chronic daily exposures to doses of at least 5 mg/kg ration or 5 mg/kg BW — specifically, PCBs 4, 15, 47, 52, 80, 136, 153, 155, and 167 (Table 24.15). Although subhuman primates seem to be more sensitive to reproductive and other adverse effects of PCBs than humans, no clear and convincing evidence associated PCB exposures with human cancers and reproductive problems (Kimbrough 1995). At present, no meaningful reproductive problems have been identified in female capacitor workers, and no carcinogenicity was evident in humans having more than 1.0 mg total PCBs/L serum or more than 400 mg total PCBs/kg adipose fat (Kimbrough 1995).

The mink (*Mustela vison*) is among the most sensitive mammals to PCB toxicity (Aulerich et al. 1987; Edqvist et al. 1992) (Table 24.15). Reproductive failure, especially fetal death and resorption, of PCB-fed mink is well documented (Backlin and Bergman 1992; Bergman et al. 1992b; Edqvist et al. 1992; Madej et al. 1992). The mechanisms of intrauterine death of mink fetuses after PCB exposure are not fully understood (Backlin and Bergman 1992), although planar PCB congeners seem to be implicated (Hakansson et al. 1992). Studies showed that EROD and AHH activities were maximally induced in adult mink by PCB fractions containing non-*ortho*- or mono-*ortho*-chlorobiphenyls and that mink kits are about 10 times more sensitive to P-450-inducers than adults (Brunstrom 1992; Kihlstrom et al. 1992). PCB-dosed mink also show altered blood chemistry (Edqvist et al. 1992), abnormal liver metabolism and histology (Edqvist et al. 1992; Bergman et al. 1992b), raised cortisol excretion (Madej et al. 1992), enhanced EROD activity (Brunstrom 1992), and altered metabolism of Vitamin A (Hakansson et al. 1992). Selective retention of certain PCBs and their hydroxylated metabolites occurred in mink muscle after 3 months of a diet containing a PCB mixture (Bergman et al. 1992a). Retention of PCBs 99, 105, 118, 138, 153, 156, and 180 was high in muscle of mink on the diet. Not retained and presumably metabolized were PCBs 44, 49, 52, 91, 92, 95, 97, 107, 132, 149, and 174 (Bergman et al. 1992a).

Estrogen receptors bind to many compounds other than natural estrogen. Several organochlorine compounds, including certain PCBs, reportedly act as estrogen mimics (Hileman 1994). Many estrogen mimics are persistent, lipid-soluble compounds defined by their ability to stimulate the proliferation of cells in the uterus of the mouse (*Mus spp.*). In males, these mimics may also inhibit sperm production and testes growth. PCBs and their metabolites may be estrogenic to wildlife, although the evidence is not conclusive (Hileman 1994). PCB mixtures and pure individual chlorobiphenyls with a significant degree of *ortho*-substitution have elevated estrogenic activity; Aroclor 1221, for example, rich in *ortho*-chlorobiphenyl, has estrogenic activity in female rats (Korach et al. 1988). Hydroxylated metabolites of PCBs also show estrogenic hormonal activity (Korach et al. 1988; Li et al. 1994). Hydroxylation of PCBs occurs in amphibians and teleosts but at a much slower rate than that of mammals (Safe et al. 1976). Hydroxylated metabolites of PCB 3 include 4'-chloro-4-biphenylol, 4'-chloro-3,4-biphenyldiol, and 4'-chloro-3-methoxy-4-biphenylol; PCB 15 gave 4,4'-dichloro-3-biphenylol; and Aroclor 1254 yielded mono-, di-, and tri-chlorophenylols (Safe et al. 1976). PCB 77 is detoxified by metabolic hydroxylation to hydroxybiphenyl metabolites (Borlakoglu et al. 1991a). Hydroxylated PCB metabolites may be more toxic than the parent product because of their (1) estrogenic properties (Yoshimura et al. 1987); (2) tendency to accumulate in the fetus (Darnerud et al. 1986), and (3) interference with thyroxine metabolism (Brouwer et al. 1990). The ability of hydroxylated PCB metabolites to bind to the uterine estrogen receptor in rats was, in increasing order of effectiveness, 4-hydroxy-3,5,4'-trichlorobiphenyl, 4,4'-dihydroxy-3,5,3',5'-tetrachlorobiphenyl, 4-hydroxy-2-chlorobiphenyl, 4-hydroxy-4'-chlorobiphenyl,

4,4'-dihydroxy-2',3',5',6'-tetrachlorobiphenyl, 4,4'-dihydroxybiphenyl, 4-hydroxybiphenyl. PCB compounds that demonstrated appreciable receptor binding activity were also active in stimulating uterine weight increases (Korach et al. 1988). More research seems needed on the estrogenic properties of hydroxylated PCB metabolites.

Long-term neurobehavioral changes were reported in children, monkeys, and rodents exposed to commercial PCB mixtures during fetal and neonatal development (Schantz et al. 1995). Perinatal exposure of rats (*Rattus* sp.) to *ortho*-substituted PCBs (PCBs 28, 118, 153) can cause long-lasting learning deficits in females; males were not affected (Table 24.15). The PCB-induced deficit in spatial learning did not appear to be mediated by decreased thyroid hormone levels; however, neonatal hyperthyroid rats exposed to low concentrations of PCBs 77 and 126 *in utero* and during lactation had enhanced spatial learning (Schantz et al. 1997).

In comparison to primates and mustelids, rodents are only moderately sensitive to intoxication by most PCBs (Abdel-Hamid et al. 1981). In rodents, PCBs 77 and 169 cause effects that are characteristic of the dioxins and furans, including P-450 induction, porphyrin accumulations, and atrophy of the lymphatic organs (Abdel-Hamid et al. 1981), as well as teratogenicity in mice (Darnerud et al. 1986). Exposure of rats to PCB 126 *in utero* and through lactation produced fetotoxic effects, delayed physical maturation, and induced liver xenobiotic metabolizing enzymes without causing neurobehavioral effects (Bernhoft et al. 1994). In mice, PCBs 77, 126, and 169 were teratogenic in a high percentage of the fetuses from treated dams but without apparent effect on the dams (Marks et al. 1981). PCB 77, for example, was toxic to the conceptus at dose levels below those toxic to the dam when administered to pregnant CD-1 mice on days 6 to 15 of gestation (Marks et al. 1989). The predominant PCB-induced fetal malformations in mice were cleft palate and hydronephrosis (Marks et al. 1981). PCB 77 also interferes with retinyl ester hydrolase (REH), the enzyme responsible for the hydrolysis of Vitamin A into free retinol, lowering levels of Vitamin A in liver and decreasing serum concentrations of REH and retinol (Mercier et al. 1990).

Toxicokinetics of PCBs in rodents were altered when administered in mixtures (de Jongh et al. 1992). PCBs 153, 156, and 169 produced biphasic elimination patterns in mice when administered in combinations, but single-phase elimination when administered alone. Elimination of all PCBs was more rapid after coadministration. Mixtures of PCBs 153 and 156 raised EROD activity and lengthened retention of each congener in liver; however, a mixture of PCB 153 and 169 lowered EROD activity (de Jongh et al. 1992). Selected PCBs of low acute toxicity may increase the toxicity of compounds such as 2,3,7,8-TCDD (Birnbaum et al. 1985). Thus, PCB 153 or 157 at sublethal dosages (20 to 80 mg/kg BW) did not produce cleft palate deformities in mouse embryos. But a mixture of PCB 157 and 2,3,7,8-TCDD produced a tenfold increase in the incidence of palate deformities that were expected of 2,3,7,8-TCDD alone; palate deformities did not increase with a mixture of PCB 153 and 2,3,7,8-TCDD. The widespread environmental occurrence of PCB-PCDD and PCB-PCDF combinations suggests a need for further evaluation of the mechanism of this interaction (Birnbaum et al. 1985).

Intraspecific variability to PCBs was high in fish-eating mammals (Boon et al. 1997), and genetically inbred AHH-responsive and AHH-nonresponsive strains of mice (Robertson et al. 1984). In fish-eating mammals, the ability to metabolize PCB congeners with H-atoms only in the *ortho*- and *meta*-positions and with one *ortho*-chlorine substituent generally increased in the order phocid seals > cetaceans > otters. But the metabolism of PCB congeners with H-atoms in the *meta*- and *para*-positions and with two *ortho*-chlorines increased in the order otter > seals > cetaceans. Both categories of congeners were probably metabolized by different families of cytochrome P-4501A and P-4502B, of which levels were different between the cetaceans, pinnipeds, and otters. Within-species PCB patterns differed in a concentration-dependent manner; the induction of cytochrome P-450 enzymes is the most likely explanation for this phenomenon, although starvation could have a similar effect (Boon et al. 1997). In mice, PCB 77 was metabolized and excreted more rapidly than 2,3,7,8-TCDD (d'Argy et al. 1987). In rats, PCB 77 was excreted more rapidly than PCB 47 (Shimada and Sawabe 1984). PCBs that lack adjacent hydrogen atoms in at least one of the rings

are enriched in rat tissues, indicating that accumulation exceeds elimination by metabolism and excretion. PCBs with a tendency to accumulate were non-*ortho*- and mono-*ortho*-substituted congeners; however, PCBs with *meta*-*para*-unsubstituted carbon atoms in at least one ring were not enriched in tissues (Borlakoglu et al. 1991a). Uptake and retention of individual PCB congeners in rats are related to properties associated with K_{ow} and high chlorination, especially in the tetra- and penta-chlorobiphenyls (Shain et al. 1986). The highly chlorinated hexa- and octa-chlorobiphenyls produced morphological changes in rats comparable to those produced by DDT, Aroclor 1254, and Aroclor 1260 (Hansell and Ecobichon 1974).

Table 24.15 Effects of PCBs on Selected Mammals

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
COTTON TOP MARMOSET MONKEY, <i>Callithrix jacchus</i>		
PCB 77; adult females orally dosed with 0.1, 1.0, or 3.0 mg/kg body weight (BW) twice weekly for 18–28 weeks	Severe toxicity in the 3.0 mg/kg group that included body weight loss, hair loss, abnormal nail growth, scaly skin, anemia, elevated blood triglyceride and cholesterol levels, and tissue histopathology. Toxicity was less severe in the 1.0 mg/kg group and minor in the low-dose group	1
RHESUS MACAQUE, <i>Macaca mulatta</i>		
Aroclor 1016		
>0.008 mg/kg BW daily via the diet	Adverse effects on reproduction	2
>0.028 mg/kg BW daily	Adverse effects on growth	2
Aroclor 1248; >0.09 mg/kg BW daily	Adverse effects on growth	2
Aroclor 1254; females were fed 0, 5, 20, 40, or 80 µg/kg BW daily for 6 years. During this time, females were bred with non-dosed males. Resultant offspring were nursed for 22 weeks and fed no additional PCBs until they were necropsied at age 120 weeks	Total PCB concentrations in all tissues of adult females increased with increasing dosage; highest levels were in adipose tissue (Max. 141 mg/kg fresh weight [FW]; Max. 171 mg/kg lipid weight [LW]) and lowest in brain (1.1 mg/kg FW; 12.9 mg/kg LW). PCB concentrations were higher in infants from dosed dams than those nursed by controls; higher in females having a stillborn infant than those with a viable infant; and higher in those in poor health. The PCB distribution pattern in tissues from a dosed mother/infant pair was different; more hepta-chlorobiphenyls were found in the infant than in the dam	28
PCB 52	No clinical effects or pathologic lesions	3, 4
Fed diets containing 3.0–5.0 mg/kg for 180–200 days		
PCB 77		
Fed diets containing 0.3–3.0 mg/kg ration for 1–6 months	Dose-and time-dependent increase in chloracne; weight loss; death; and histopathology of sebaceous glands, thymus, and gastric mucosa	3
Fed diet containing 1.0 mg/kg ration for 38 days	Adverse effects on survival	4
Immature males fed diets containing 1.0 or 3.0 mg/kg ration	All were moribund in 7–14 weeks; abnormal gastric histology	5
Adult females received a total of 9 intragastric doses 20–40 days postconception; total doses were 0.6 or 3.15 mg/kg BW	All animals in both dose groups survived, but all aborted	4
Adult females given a single intravenous injection of 0.6 mg/kg BW; blood measured 1 h to 42 days postinjection	As a percentage of the total dose administered, PCB 77 concentrations in blood fell from 4.4% at 1 h to 0.14% at 42 days. About 60% of the total dose was excreted in feces, and 10% in urine	18
PCBs 136, 153, or 155; each fed in diet at 15–65 mg/kg ration for 63–122 days	No discernible deleterious effects	4

Table 24.15 (continued) Effects of PCBs on Selected Mammals

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
PCB 169; fed diet containing 400.0 mg/kg ration for 40 days	Concentrations in body fat increased steadily during exposure; recovery was protracted and incomplete during a 6-month observation period	4
MOUSE, <i>Mus</i> sp.		
Aroclor 1254	Adverse effects on reproduction	2
>1.3 mg/kg BW daily via diet	In carcass fat, net PCB loss was attributed to metabolic loss of PCBs 105 and 138. In lung, all congeners except 153 were retained and decreased only as a function of dilution due to growth. In liver, all congeners were retained and PCB 105 was enriched. Total PCBs in carcass averaged 80.8 mg/kg BW 24 h after treatment and about 10 mg/kg BW after 16 weeks; similar trends occurred in liver and lung. Tb 1/2 for PCB 153 was 81–101 days	6
Single ip injection of 500 mg/kg BW (a dose that promoted nitrosamine-initiated lung and liver tumors). The amounts of the 9 congeners that made up >90% of the PCBs present 1 day after treatment (PCBs 99, 105, 118, 128, 138, 153, 156, 170, 180) were quantified in liver, lung, and whole body for 112 days after dosing	Toxic to dams at 64 mg/kg BW daily, but no embryotoxicity	7
PCB 15; pregnant mice given daily doses of 16, 32, or 64 mg/kg BW on days 6–15 of gestation and killed on day 18	Dose-dependent increase in incidence of malformed fetuses — especially cleft palate and hydronephrosis — at 4 mg/kg BW daily and higher. At 16 mg/kg BW and higher, dams had dose-dependent increase in weight loss, frequency of vaginal bleeding, and other evidence of abortion	7
PCB 77	Radioactivity levels were elevated in uterine fluid and in fetuses in late gestation. No unmetabolized PCB 77 was detected in fetuses, but PCB 77 metabolites (including 3,3',4,4'-tetrachloro-2-biphenylol, and methylsulphonyl-tetrachloro-biphenyl) were found in fetuses in late gestation	8
Pregnant mice given single iv injection of 3.5 mg/kg BW of ¹⁴ C-labeled PCB 77 on days 4–17 of gestation and killed 4–96 h later	30–40% reduction of retinol and retinyl palmitate concentrations in liver within 2–4 days	9
Strain C57BL/R _j given single ip injection 15 mg/kg BW	50% reduction in hepatic retinyl palmitate	9
17 mg/kg BW	50% reduction in hepatic retinol	9
32 mg/kg BW	No reduction in hepatic retinoids	9
Strain DBA/2; single ip injection of 729 mg/kg BW	Dose-dependent increase in embryo deaths, resorption of the conceptus, and frequency of developmental abnormalities (cleft palate, dilated kidney pelvis, thymus hypoplasia). ED ₅₀ for cleft palate was about 100 mg PCB 77/kg BW	10
Single oral dose of 25, 50, or 100 mg/kg BW given to Ah-responsive pregnant mice on gestation day 11, 12, or 13; mice killed on day 18 of gestation	Permanent motor dysfunction in weaning mice characterized by swift circling movements, restlessness, and hyperkinesia; spinal and cranial nerve roots abnormal	11
Dams received oral dose of 32 mg/kg BW daily on days 10–16 of gestation	Both groups had increased body weight, increased blood EROD activity, decreased plasma retinol levels, and increased plasma total thyroid hormone levels. The Ah-responsive group also had increased hepatic pentoxyresorufin-O-deethylase activity, increased liver cytochrome P-450 activity, and increased liver weight	12
Ah-responsive and Ah-nonresponsive strains; females, age 10 weeks; given single ip injection of 50 mg/kg BW; killed after 7 days		

Table 24.15 (continued) Effects of PCBs on Selected Mammals

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
PCB 80; pregnant mice given 64 mg/kg BW daily on days 6–15 of gestation and killed on day 18	No effect on maternal or developmental toxicity	7
PCB 169; pregnant mice given daily doses of 0.1, 1, 2, 4, 8, or 16 mg/kg BW by gavage on days 6–15 of gestation; mice killed on day 18 and dams evaluated for reproductive health and fetuses for malformations	All dams survived all treatments; some lost weight during pregnancy at 8 mg/kg BW and higher. Incidence of malformed fetuses increased from 0.9% in controls, to 3.6–4.3% in the 0.1–1.0 mg/kg groups, to 37% in the 4 mg/kg group to 61–66% in the 8–16 mg/kg groups. Fetal deaths increased at daily doses of 4 mg/kg BW and higher, and abortions increased in the 8 and 16 mg/kg groups. Fetal liver discolored at 1 mg/kg BW daily	13
MINK, <i>Mustela vison</i>		
Aroclor 1254		
0.1 mg/kg BW daily	Adverse effects on growth	2
0.115 mg/kg BW daily (1.64 mg daily)	Adverse effects on reproduction	2, 16
PCB 47; subadult females given daily ip injections of 50 mg/kg BW for 3 days and killed 7 days after last dose	No evidence of illness or pathology. PCB 47 residues, in mg/kg FW, were 389 in fat and 38 in liver	14, 15
PCB 77; subadult females given daily ip injections of 50 mg/kg BW for 3 days and killed 7 days after last dose	Severe anorexia, diarrhea, and melena. Significant histopathology of mucosa of the small intestine. PCB residues, in mg/kg FW, were 139 in fat and 16 in liver	14, 15
PCBs 136 and 167; each fed to adult females in the diet at 5 mg/kg ration for 3 months	No adverse effects on reproduction	16
PCB 169; fed in diet at concentrations of 0.01–0.5 mg/kg ration for 135 days		
0.01 mg/kg diet	No deaths; some weight loss and liver enlargement	17
0.05 mg/kg diet	50% mortality in 135 days	17
0.1 mg/kg diet	50% dead in 75 days	17
0.5 mg/kg diet	All dead within 73 days	17
Fed PCB-contaminated common carp (<i>Cyprinus carpio</i>) from Saginaw Bay, Lake Huron. Total PCBs in diet was 8.4 mg/kg FW ration (including, in µg/kg FW, 0.3 of PCB 81, 1.5 of 77, 0.6 of 126, 0.07 of 169, 6.9 of 123, 262 of 118, 9.1 of 114, 87 of 105, 8.5 of 167, 9.6 of 156, 1.9 of 157, and 1.3 of 189); also 15 µg total dioxins/kg FW ration and 1 µg total dibenzofurans/kg. A multigenerational study on reproduction and health. Mink were fed diets containing 0, 0.25, 0.5, or 1.0 mg total PCBs/kg ration through substitution of carp for ocean fish in the diets. Half the P ₁ animals were switched from respective diets to control diets after whelping the first of two F ₁ generations; half the first-year F ₁ offspring (kits) were switched to the control diet at weaning, while the other continued on the parental diet	Continuous exposure to 0.25 mg total PCBs/kg ration and higher delayed the onset of estrus and lessened the whelping rate. Litters whelped by females continually exposed to 0.5 mg/kg and higher had lower survival and reduced body weights. Those continually exposed to 1.0 mg total PCBs/kg ration had altered weights of kidney, brain, liver, spleen, heart, and thyroid. Plasma and liver PCB concentrations of adults and kits reflected dietary concentrations of PCBs and duration and time of exposure. Short-term parental exposure to PCBs had adverse effects on survival of subsequent generations of mink conceived months after the parents were placed on uncontaminated food	32
Exposure as above	Continuous exposure to diets containing PCBs from Saginaw Bay carp induced cytochrome P-450 activity in a dose-dependent manner. Cytochrome P-450 activity in animals switched to the control diet from the PCB-containing diet was the same as controls. EROD hepatic activity is a potential biomarker for current exposure to PCBs and other similar cytochrome P-450 inducers	33

Table 24.15 (continued) Effects of PCBs on Selected Mammals

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
Exposure as above	PCB diets were associated with reproductive impairment including anovulation, fetal resorption, delayed ovulation, increased gestation, and decreased litter size. Hepatic estrogen binding site concentrations decreased with increasing dietary PCB concentrations but not uterine estrogen receptor sites	34
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Aroclor 1254		
Dams and resultant pups fed diets containing 0, 3, 30, or 300 mg Aroclor 1254/kg ration from conception to weaning	Most congeners that accumulated in pup tissues were concentrated in the dam's milk when compared to the feed. PCB uptake by pups was greater during lactation than during gestation. Congeners that accounted for 46% of the brain PCB content and also accumulated in a dose-dependent manner were PCBs 105, 138, 141, 153, 168, 178, 179, and 186	19
0.25 mg/kg BW daily via the diet	Adverse effects on reproduction	2
Males held on soil containing 207 mg Aroclor 1254/kg soil for 3 days. Soils also contained 2.7 mg total PAHs/kg, 1200 mg Pb/kg, and 2270 mg Zn/kg	PCB concentrations, in µg Aroclor 1254/kg, were 1845 in liver and 241 in lung; EROD activity was induced in both tissues. When soils were diluted with uncontaminated soils, a dose-response relation was found between PCBs in litter and EROD activity, suggesting that EROD activity and tissue residues can be used to assess bioavailability of PCBs from soils to mammals	30
PCB 4; young males given ip injections of 50 mg/kg BW daily for 3 days and killed 4 days after last injection	Negligible morphological effects on liver when compared to PCBs 15, 52, and 77 groups dosed at same regimens	20
PCB 28; dams dosed on days 10–16 of gestation by gavage with 8 or 32 mg/kg BW daily; offspring tested in mazes at age 12–16 weeks	Birth weight lower in high-dose group; female pups — but not males — in the high-dose group had learning deficits	27, 29
PCB 47; subadult females given 3 daily injections of 50 mg/kg BW and killed 7 days after last injection	No clinical signs of illness and no significant gross or microscopic lesions. PCB 47 residues, in mg/kg FW, were 747 in fat and 28 in liver	14, 15
PCB 77	In males (females), adipose tissue 4 h postinjection contained 23% (12%) of the total dose administered, skin 14% (16%), liver 6.8% (8.8%), muscle 6.7% (16.2%), and blood 4.1% (4.0%); after 7 days, adipose tissue contained 2.7% (7.4%) and other tissues 0.5–2.2% (1.0–3.4%)	18
Pregnant rats dosed orally on days 6–18 of gestation with 1, 3, or 10 mg/kg BW daily; fetuses were examined on day 19 for developmental abnormalities	A dose-dependent increase in mortality, intestinal histopathology, and external malformations, and decrease in fetal size and length of tibias. A daily dose of 3 mg/kg BW significantly affected fetus growth, bone development, and survival	21
Single ip injection of 15 mg/kg BW	Significant reduction in liver and heart retinol and in liver retinylester concentrations	22
Single ip injection of 50 mg/kg BW	Metabolites in feces included 5-hydroxy-3,4,3',4'-tetrachlorobiphenyl, 4-hydroxy-3,5,3',4'-tetrachlorobiphenyl, and a dihydroxy- and monohydroxy trichlorophenyl. After 5 days, unchanged PCB 77 in feces accounted for 0.8% of the initial dose, but hydroxylated metabolites constituted about 32%	23

Table 24.15 (continued) Effects of PCBs on Selected Mammals

Species, PCB Congener, Dose, and Other Variables	Effect	Reference ^a
Subadult females given 3 daily ip injections of 50 mg/kg BW and killed 7 days after last injection	No signs of illness or histopathology. PCB 77 residues, in mg/kg FW, were 148 in fat and 138 in liver	14, 15
Adults injected ip for 3 days at 80 mg/kg BW daily then killed 24 h after last injection	Heme destruction in the P-448-containing reconstituted monooxygenase system; reactive epoxide, or possibly nonepoxyde, intermediate metabolites may participate in cytochrome P-448 destruction	24
PCB 118; dams dosed on days 10–16 of gestation by gavage with 4 or 16 mg/kg BW daily; offspring tested in mazes at age 12–16 weeks	Birth weight lower in high-dose group; female offspring, but not males, in high-dose group had learning deficits	27, 29
PCB 126; dams given 0.01 or 0.02 mg/kg BW by gavage every second day from days 9–19 of gestation	Reduction in litter size, body weight, and survival of sucklings; delayed spontaneous movement and neuromuscular maturation. Dams and pups had reduced body weight, and increased cytochrome P-4501A1 activity	25
PCB 126; isolated rat hepatoma cells; 49–3140 pM	EROD activity increases in dose-dependent manner; potentiated by coexposure to low noncytotoxic concentrations of tributyltin	31
PCB 153	Female offspring from high-dose group had learning deficits; males were not affected	27, 29
Dams dosed on days 10–16 by gavage with 16 or 64 mg/kg BW daily; offspring tested in mazes at age 12–16 weeks	Increased uterine weight at 25 and 51 mg/kg BW, but not in other groups	26
Immature female pups given 8, 11, 25, 51, or 59 mg/kg BW on days 20 and 21; killed on day 22		

^a 1, van den Berg et al. 1988; 2, Golub et al. 1991; 3, McNulty et al. 1980; 4, McNulty 1985; 5, Becker and McNulty 1984; 6, Anderson et al. 1993; 7, Marks et al. 1989; 8, Darnerud et al. 1986; 9, Brouwer et al. 1985; 10, d'Argy et al. 1987; 11, Chou et al. 1979; 12, Murk et al. 1991; 13, Marks et al. 1981; 14, Gillette et al. 1987a; 15, Gillette et al. 1987b; 16, Kihlstrom et al. 1992; 17, Aulerich et al. 1987; 18, Abdel-Hamid et al. 1981; 19, Shain et al. 1986; 20, Hansell and Ecobichon 1974; 21, Wardell et al. 1982; 22, Brouwer et al. 1988; 23, Yoshimura et al. 1987; 24, Shimada and Sawabe 1983; 25, Bernhoff et al. 1994; 26, Li et al. 1994; 27, Schantz et al. 1995; 28, Mes et al. 1995; 29, Schantz et al. 1997; 30, Fouchecourt et al. 1998; 31, Kannan et al. 1998; 32, Restum et al. 1998; 33, Shipp et al. 1998a; 34, Shipp et al. 1998b.

24.6 RECOMMENDATIONS

Proposed PCB criteria for the protection of natural resources are predicated on total PCBs and selected Aroclor compounds (Table 24.16) and offer minimal insight into PCB toxicokinetics. Most authorities now agree that future PCB risk assessments require (Eisler 1986; Maack and Sonzogni 1988; Tanabe 1988; Gooch et al. 1989; Hernandez et al. 1989; Kannan et al. 1989; Tanabe et al. 1989; Borlakoglu et al. 1990; Hebert et al. 1993; Giesy et al. 1994a; Safe 1994; Walker and Peterson 1994; Eisler and Belisle 1996; Weihe et al. 1996; Gribaldo et al. 1998):

1. Analysis of non-*ortho*-PCBs and selected mono-*ortho*-PCBs
2. Exposure studies of individual species to specific congeners alone or in combination with other compounds, including other PCB congeners, dioxins, and dibenzofurans
3. Clarification of existing structure-induction relations
4. More refined analytical techniques

Because component-based analysis of PCBs has limited the usefulness of the historical database for current environmental research and in formulation of regulatory criteria, procedures were

developed to accurately detect, speciate, and quantify mixtures of multiple Aroclors (Newman et al. 1998). Aroclor conversion factors have been calculated for 14 PCB congeners (PCBs 18, 28, 31, 99, 118, 128, 138, 149, 153, 180, 194, 195, 201, and 203), allowing quantification of PCB profiles as Aroclors 1248, 1254, and 1260 using measurements of these congeners (Newman et al. 1998).

Marked differences between species in their abilities to metabolize specific PCB congeners must be considered in toxicity testing. Foxes and dogs, for example — in contrast to monkeys and rats — can degrade the otherwise highly persistent PCB 153 because they possess an unusual cytochrome P-450 isoenzyme that metabolizes PCB 153 (Georgii et al. 1994). Also, low-chlorinated congeners that are metabolized via reactive intermediates must be critically evaluated because they show weak tumor-initiating properties (Georgii et al. 1994). Intraspecies differences are also documented. Three populations of the harbor porpoise (*Phocoena phocoena*) from Newfoundland, St. Lawrence River, and the Gulf of Maine are distinguishable based on PCB levels in blubber (Westgate and Tolley 1999).

To complement PCB chemical residue analyses, the rat hepatoma cell bioassay was useful for assessing the toxic potency of PCBs in extracts from environmental samples (Tillitt et al. 1991). This *in vitro* bioassay of cytochrome P-450IA1 catalytic activity in the H4IIE cells in response to planar halogenated hydrocarbons was considered accurate and precise. Comparison of the responses of the H4IIE cells was calibrated against their responses to 2,3,7,8-TCDD (Tillitt et al. 1991). EROD (ethoxyresorufin-*O*-deethylase) and porphyria induction measurements also potentially complement PCB chemical residue analyses and have been used to determine the toxic potencies of complex mixtures of PCBs and other halogenated aromatic hydrocarbons extracted from wildlife tissues (Kennedy et al. 1992). In one case, extracts of PCB-contaminated eggs of herring gulls (*Larus argentatus*) from the Great Lakes and of great blue herons (*Ardea herodias*) from British Columbia induced EROD and porphyria in primary cultures of chicken embryo hepatocytes (Kennedy et al. 1992). Porphyrins in feces as a nondestructive biomarker is recommended as an alternative to the traditional liver porphyrins in the hazard assessment of birds contaminated with PCBs (Fossi et al. 1996). Hepatic cytochrome P-450-associated monooxygenases and cytochrome P-450 proteins in embryos of the black-crowned night-heron (*Nycticorax nycticorax*) were associated with concentrations of total PCBs and 11 PCB congeners that express toxicity through the Ah receptor, and also should be considered as biomarkers for assessing PCB contamination of wetlands (Rattner et al. 1994). Hepatic cytochromes P-450, P-420 (degraded P-450), and mixed-function oxidases are recommended as biomarkers of PCB exposure in harbor seals (*Phoca vitulina*); total PCB burdens in both blubber and liver had positive correlations with P-450, P-420, and MFO activity levels (Troisi and Mason 1997).

The interpretation of PCB residue data is challenging from several perspectives, as judged by analysis of eggs of Forster's terns (*Sterna forsteri*) from Wisconsin (Schwartz and Stalling 1991):

1. Data from a single analysis frequently contained measurable concentrations of 100 to 150 PCB congeners.
2. A single sample was not sufficient to understand the environmental distribution of PCBs.
3. Source profiles of PCB inputs into the environment were poorly characterized.
4. PCB congeners in the original polluting material often merged with congeners from other sources.
5. The contaminant mixture may have been altered by metabolism and subsequent partition into multiple environmental compartments that may be further changed by weathering or degradation.

To understand these processes and correlate residue profiles with specific toxic responses required congener-specific methods of analysis and complex statistical techniques (principal component analysis). Using these techniques, it was established that eggs of Forster's terns of two colonies differed significantly in PCB composition (Schwartz and Stalling 1991). Similar techniques were used to identify various PCB-contaminated populations of harbor seals (*Phoca vitulina*) in Denmark (Storr-Hansen and Spliid 1993).

Selected congeners should be quantified in human foodstuffs and tissues, as determined from a survey of PCB congener frequency in commercial formulations, environmental and biological samples and human tissues, and a consideration of the relative toxicity and persistence of the congeners (Jones 1988). PCBs 28, 74, 77, 99, 105, 118, 126, 128, 138, 153, 156, 169, 170, 179, and 180 reportedly account for more than 70% of the total PCB burden in any sample and should be quantified. Additionally, PCBs 8, 37, 44, 49, 52, 60, 66, 70, 82, 87, 101, 114, 158, 166, 183, 187, and 189 should be considered for quantification because of their reported occurrence or toxicity. Some PCBs are particularly prevalent in aquatic animals, especially PCBs 95, 101, 110, 118, 138, 149, 153, 180, and 187. Also detected in aquatic biota and reported as important components were PCBs 26, 52, 66, 70, 99, 105, 132, 151, 170, 177, 201, and 206. In the Netherlands, maximum PCB limits in fishes as dietary items for human health protection are now derived from the sum of PCBs 28, 95, 101, 138, 149, 153, and 180. From a toxicological viewpoint, other congeners may be more important. These have been identified (on the basis of ability to induce AHH) as the most toxic planars (PCBs 15, 37, 77, 81, 126, and 169), the mono-*ortho*-analogues of the planar PCBs (PCBs 105, 114, 123, 156, and 189), and the di-*ortho*-analogues (PCBs 128, 138, 158, 166, and 170). Of these compounds, PCBs 37, 105, 114, 128, 138, 156, and 158 occur in human tissues, and PCBs 15, 77, 81, 123, 126, 166, and 169 do not occur (Jones 1988). In Germany, PCB congeners 49, 118, 156, and 170 are considered carcinogen initiators; these four congeners and PCBs 28, 31, 52, 101, 138, 153, and 180, are proposed as indicators of PCB contamination in that country (Bachour et al. 1998). *In vitro* studies with PCBs 138 and 169 indicate a relation between PCB structure, bioavailability, and the capacity to stimulate oncogene expression, strongly indicating the need for more research in this subject area (Gribaldo et al. 1998).

Ecological considerations in setting limits in foods for human consumption are complex. In Lake Ontario, for example, stocking rates of the alewife (*Alosa pseudoharengus*) — the main food of all Great Lakes sportfishes — necessary to achieve PCB consumption advisories of <0.5 mg total PCBs/kg FW fish muscle, carry about a 90% probability of an alewife population crash (Jackson 1977). It is postulated that increases of 25% in current stocking rates of chinook salmon would decrease PCB concentrations of chinook salmon without a large increase in the probability that the alewife population would crash. These scenarios are applicable to species of salmonids in the Great Lakes because they, too, exhibit size-selective predation and their recruitment is largely determined by stocking (Jackson 1997).

Table 24.16 Proposed PCB Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Concentration	Reference ^a
AQUATIC LIFE PROTECTION		
Fish, total PCBs		
Diet	<500 µg/kg fresh weight (FW)	1
Eggs	<300 µg/kg FW	1
Whole body	<400 µg/kg FW	1
Adverse effects, total PCBs		
Invertebrates, whole	>25 mg/kg FW	8
Fish, whole	>50 mg/kg FW	8
Marine mammals		
Blubber		
Total PCBs	<70 mg/kg FW	2, 7
PCB 101	<0.6 mg/kg FW	7
PCB 138	<7 mg/kg FW	7
PCB 153	<10 mg/kg FW	7
PCB 180	<3 mg/kg FW	7
Blood lipid, total PCBs	<25 mg/kg FW	7

Table 24.16 (continued) Proposed PCB Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Concentration	Reference ^a
Medium, total PCBs		
Freshwater		
Acute	<2.0 µg/L	6, 10
Chronic	<0.014 µg/L	1, 6, 10
Saltwater		
Acute, most species	<10.0 µg/L	6, 10
Chronic, sensitive species	<0.03 µg/L	6, 10
Filter-feeding shellfish	<0.006 µg/L	1
BIRDS		
Total PCBs		
Brain	<300 mg/kg FW	3
MAMMALS		
Aroclor 1016		
Rhesus macaque	<0.008–<0.028 mg/kg body weight (BW) daily	4
Aroclor 1248		
Rhesus macaque	<0.009 mg/kg BW daily	4
Aroclor 1254		
Mink	<0.1–<0.115 mg/kg BW daily	4
Mouse	<1.3 mg/kg BW daily	4
Rat	<0.25 mg/kg BW daily	4
Total PCBs		
Fat	<10 mg/kg FW	7
Liver	<4 mg/kg FW	7
HUMAN HEALTH PROTECTION		
Air		
Aroclor 1242, acceptable vs. hazardous	<0.001 mg/m ³ vs. 10 mg/m ³	10
Aroclor 1254, acceptable vs. hazardous	<0.001 mg/m ³ vs. 5 mg/m ³	10
Arizona; total PCBs, acceptable	<0.3 µg/m ³ for 1 h; <0.079 µg/m ³ for 24 h; 0.0061 µg/m ³ annually	10
Florida; acceptable		
Aroclor 1254	5 µg/m ³ for 8 h; 1.2 µg/m ³ for 24 h; 0.00083 µg/m ³ annually	10
Aroclor 1242	10 µg/m ³ for 8 h; 2.4 µg/m ³ for 24 h	10
South Carolina; total PCBs	<2.5 µg/m ³ for 24 h	10
Virginia, 24-h exposure; acceptable		
Total PCBs	<8 µg/m ³	10
Aroclor 1242	<17 µg/m ³	10
Aroclor 1254	<8.3 µg/m ³	10
Diet		
Acceptable daily intake, total PCBs, Scandinavia	<0.2 mg, equivalent to about 2.8 µg/kg BW daily for a 70-kg person	13
Drinking water, total PCBs		
Acceptable, AZ, KS, ME, NH, VT	0.008–0.05 µg/L	10
Acceptable, CT, MA, NJ, NY, RI	0.5–1.0 µg/L	10
Connecticut		
Action level	>1.0 µg/L	10
Hazardous	>2.0 µg/L	10
U.S.		
Child	<1.0 µg/L	6
Adult	<4 µg/L	6
Public water supplies, Wisconsin, total PCBs		
Warm water sport fish communities	0.49 ng/L	10
Cold water communities	0.15 ng/L	10
Great Lakes communities	0.15 ng/L	10

Table 24.16 (continued) Proposed PCB Criteria for the Protection of Natural Resources and Human Health

Resource, Criterion, and Other Variables	Effective Concentration	Reference ^a
Land disposal restriction, U.S.; wastewater vs. nonwastewater		
Aroclors 1016, 1232, or 1248	0.013 mg/L vs. 0.92 mg/kg	10
Aroclor 1221	0.014 mg/L vs. 0.92 mg/kg	10
Aroclor 1242	0.017 mg/L vs. 0.92 mg/kg	10
Aroclor 1254	0.014 mg/L vs. 1.8 mg/kg	10
Reduced risk from cancer, total PCBs	<7.7 mg/kg BW daily	6
Commercial milk, total PCBs	<1.5 mg/kg, fat basis	9
Edible poultry, total PCBs		
Canada	<0.5 mg/kg LW	11
U.S.	<3.0 mg/kg LW	11
Fish, edible portion, total PCBs		
Canada	<2 mg/kg FW	5
Great Lakes, gamefish	<1.9 mg/kg FW	11
United States	<2 mg/kg FW	6
Great Lakes	<0.5 mg/kg FW	12
New York State	<2 µg/kg FW	5

^a 1, Eisler 1986; 2, Norheim et al. 1992; 3, Bryan et al. 1987a; 4, Golub et al. 1991; 5, Hebert et al. 1993; 6, USEPA 1992b; 7, Kamrin and Ringer 1996; 8, Niimi 1996; 9, Korick and Altshul 1998; 10, USPHS 1995; 11, Custer et al. 1996; 12, Jackson 1977; 13, Weihe et al. 1996.

24.7 SUMMARY

Ecological and toxicological aspects of polychlorinated biphenyls (PCBs) in the environment are reviewed, with emphasis on biologically active congeners and fish and wildlife. Subtopics include sources and uses, chemical and biochemical properties, concentrations in field collections, lethal and sublethal effects, and recommendations for the protection of sensitive resources. All production of PCBs in the United States ceased in 1977. Of the 1.2 million tons of PCBs manufactured to date, about 65% are still in use in electrical equipment and 31% in various environmental compartments, and 4% were degraded or incinerated. The 209 PCB congeners and their metabolites show wide differences in biological effects. A significant part of the toxicity associated with commercial PCB mixtures is related to the presence of about 20 planar congeners (i.e., congeners without chlorine substitution in the *ortho*-positions). Toxic planar congeners, like other PCB congeners, have been detected in virtually all analyzed samples, regardless of collection locale. Planar PCB concentrations were usually highest in samples from near urban areas and in fat and liver tissues, filter-feeding bivalve molluscs, fish-eating birds, and carnivorous marine mammals. Adverse effects of planar PCBs on growth, survival, and reproduction are highly variable because of numerous biotic and abiotic modifiers, including interaction with other chemicals. In general, embryos and juveniles were the most sensitive stages tested to planar PCBs, and the chinook salmon (*Oncorhynchus tshawytscha*), domestic chicken (*Gallus* sp.), mink (*Mustela vison*), rhesus macaque (*Macaca mulatta*), and laboratory white rat (*Rattus* sp.) were among the most sensitive species. For protection of natural resources, most authorities now recommend:

1. Analysis of environmental samples for planar and other potentially hazardous congeners
2. Exposure studies with representative species and specific congeners, alone and in combination with other environmental contaminants
3. Clarification of existing structure-induction-metabolism relations
4. More research on physiological and biochemical indicators of PCB-stress

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CHAPTER 25

Polycyclic Aromatic Hydrocarbons

25.1 INTRODUCTION

Several polycyclic aromatic hydrocarbons (PAHs) are among the most potent carcinogens known to exist, producing tumors in some organisms through single exposures to microgram quantities. PAHs act at both the site of application and at organs distant to the site of absorption. Their effects have been demonstrated in nearly every tissue and species tested, regardless of the route of administration (Lee and Grant 1981; Schnitz and O'Connor 1992). The evidence implicating PAHs as an inducer of cancerous and precancerous lesions is overwhelming, and this class of substances is probably a major contributor to the increase in cancer rates reported for industrialized nations (Cooke and Dennis 1984). PAHs were the first compounds known to be associated with carcinogenesis (Lee and Grant 1981). Occupational skin cancer was first documented in London chimney sweeps in 1775 and in German coal tar workers in the late 1800s. By the early 1900s, soot, coal tar, and pitch were all found to be carcinogenic to humans. By 1918, it was shown that topical applications of coal tar produced skin tumors in mice and rabbits; benzo[*a*]pyrene, a PAH, was identified as one of the most carcinogenic compounds in coal tar (Dipple 1985). The carcinogenic activity to humans of soots, tars, and oils is beyond dispute. In addition to the skin cancers noted initially, higher incidences of respiratory tract and upper gastrointestinal tract tumors were associated with occupational exposures to these carcinogens (Dipple 1985). PAH-induced cancers in laboratory animals are well documented. Benzo[*a*]pyrene, for example, has produced tumors in mice, rats, hamsters, guinea pigs, rabbits, ducks, and monkeys following administration by oral, dermal, and intraperitoneal routes (Pucknat 1981). Teratogenic or carcinogenic responses have been induced in sponges, planarians, echinoderm larvae, teleosts, amphibians, and plants by exposure to carcinogenic PAHs (Neff 1979, 1982b; Michel et al. 1992). An unusually high prevalence of oral, dermal, and hepatic neoplasms has been observed in bottom-dwelling fish from polluted sediments containing grossly elevated PAH levels (Balch et al. 1985; Couch and Harshbarger 1985; Fabacher et al. 1991; Baumann and Harshbarger 1995). Hepatic disorders, including adenomas and carcinomas, were found in common carp (*Cyprinus carpio*) from West Point Lake in Georgia in 1991 and are linked to elevated concentrations in lake sediments (Pritchard et al. 1996). PAH compounds have damaged chromosomes in cytogenetic tests, have produced mutations in mammalian cell culture systems, and have induced DNA repair synthesis in human fibroblast cultures (U.S. Environmental Protection Agency [USEPA] 1980). While some PAHs are potent mutagens and carcinogens, others are less active or suspected carcinogens. Some, especially those of biological origin, are probably not carcinogens (Jackim and Lake 1978). Certain lower-molecular-weight, noncarcinogenic PAHs, at environmentally realistic levels, were acutely toxic to aquatic organisms, or produced deleterious sublethal responses (Neff 1985). However, few generalizations can be made about the class of PAH compounds because of the extreme variability in toxicity and physicochemical properties of PAHs and their various effects on individual species (Lee and Grant 1981).

PAHs are widely distributed in the environment and have been detected in animal and plant tissues, sediments, soils, air, surface water, drinking water, industrial effluents, ambient river water, well water, and groundwater (USEPA 1980; Schnitz and O'Connor 1992). Humans have probably always been exposed to PAHs from the natural background level in soils and plants (Harrison et al. 1975). Avoiding exposure to nanogram quantities of these substances on a daily basis is now considered essentially impossible for all living resources (Dipple 1985). Ever since benzo[a]pyrene was recognized as a carcinogen at the beginning of this century, the presence of it and of other PAHs in the environment has received continuous attention. As one consequence, many reviews have been published on ecological and toxicological aspects of PAHs in the environment, with special reference to their carcinogenic properties (Harrison et al. 1975; Barnett 1976; Suess 1976; Gelboin and Ts'o 1978a, 1978b, 1981; Jackim and Lake 1978; Jones and Freudenthal 1978; Lo and Sandi 1978; Jones and Leber 1979; Neff 1979, 1982a, 1982b, 1985; Tsang and Griffin 1979; Bjorseth and Dennis 1980; USEPA 1980; Cooke and Dennis 1981, 1983, 1984; Futoma et al. 1981; Lee and Grant 1981; Pucknat 1981; Sims and Grover 1981; Stegeman 1981; Cooke et al. 1982; Richards and Jackson 1982; Couch et al. 1983; Edwards 1983; Grimmer 1983; Quaghebeur et al. 1983; Sims and Overcash 1983; Couch and Harshbarger 1985; Harvey 1985; Johnson et al. 1985; Sugimura 1986; Eisler 1987; U.S. Public Health Service [USPHS] 1995; Hellou 1996).

25.2 ENVIRONMENTAL CHEMISTRY, SOURCES, AND FATE

25.2.1 Properties

Polycyclic aromatic hydrocarbons (PAHs), also known as polynuclear aromatic hydrocarbons (PNAs) and polycyclic organic matter (POM), are composed of hydrogen and carbon arranged in the form of two or more fused benzene rings in linear, angular, or cluster arrangements, which may or may not have substituted groups attached to one or more rings (Sims and Overcash 1983). In some cases, the newly defined substituted PAH has strikingly greater toxicological effects than does the parent compound (Cooke and Dennis 1984). The nomenclature of PAH compounds has been ambiguous in the past due to different peripheral numbering systems. The currently accepted nomenclature is shown in [Figure 25.1](#).

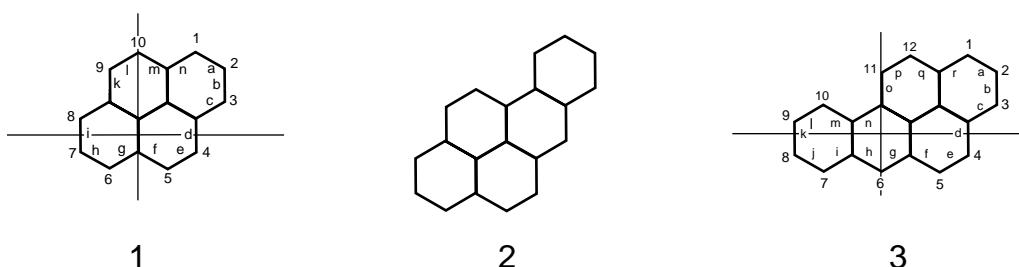


Figure 25.1 Nomenclature of PAHs. (Modified from Lee and Grant 1981; Grimmer 1983.) The PAH formula is oriented so that the greatest number of rings are in a horizontal row and a maximum number of rings are above and to the right of the horizontal row. The first carbon atom that belongs to the uppermost ring and is not engaged in ring fusion with another ring is given the number C-1; numbering continues in a clockwise direction, omitting those carbon atoms that do not carry a hydrogen atom. The bond between C-1 and C-2 is designated as side "a"; other peripheral sides continue in clockwise direction in alphabetical order. Examples are: (1) pyrene (correctly oriented, numbered, and lettered), (2) benzo[a]pyrene (not oriented correctly), and (3) benzo[a]pyrene (correctly oriented, numbered, and lettered).

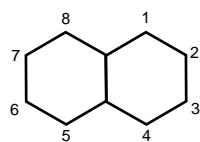
Of major environmental concern are mobile PAHs that vary in molecular weight from 128.16 (naphthalene, C₁₀H₈) to 300.36 (coronene, C₂₄H₁₂). Higher-molecular-weight PAHs are relatively immobile because of their large molecular volumes and their extremely low volatility and solubility. Among the mobile forms are thousands of compounds that differ in the number and position of aromatic rings, and in the position of substituents on the basic ring system. The lower-molecular-weight, unsubstituted PAH compounds, containing two to three rings, such as naphthalenes, fluorenes, phenanthrenes, and anthracenes ([Figure 25.2](#)), have significant acute toxicity to some organisms, whereas the higher-molecular-weight, four- to seven-ring aromatics do not. However, all known PAH carcinogens, cocarcinogens, and tumor producers are in the high-molecular-weight PAH group ([Figure 25.3](#)).

Physical and chemical characteristics of PAHs generally vary with molecular weight. With increasing molecular weight, aqueous solubility decreases, and melting point, boiling point, and the log K_{ow} (octanol/water partition coefficient) increase ([Table 25.1](#)), suggesting increased solubility in fats, a decrease in resistance to oxidation and reduction, and a decrease in vapor pressure. Accordingly, PAHs of different molecular weight vary substantially in their behavior and distribution in the environment and in their biological effects. Additional and more comprehensive data on the physical and chemical properties of PAHs are given in Barnett (1976), Lo and Sandi (1978), Neff (1979, 1985), USEPA (1980), Futoma et al. (1981), Lee and Grant (1981), Pucknat (1981), Edwards (1983), Grimmer (1983), Sims and Overcash (1983), Whitehouse (1985), and de Maagd et al. (1998). Measurements of various PAH metabolites, especially naphthalene and benzo[*a*]pyrene-type metabolites, in bile and other tissues are now conducted routinely using high-performance liquid chromatography with fixed-wavelength fluorescence (Lin et al. 1996).

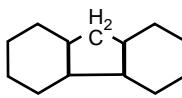
25.2.2 Sources

About 43,000 metric tons of PAHs are discharged into the atmosphere each year, and another 230,000 tons enter aquatic environments ([Table 25.2](#)). PAHs are ubiquitous in nature as a consequence of synthesis in terrestrial vegetation, microbial synthesis, and volcanic activity, but quantities formed by these natural processes are small in comparison with those produced from forest and prairie fires and anthropogenic sources (Barnett 1976; Suess 1976; Lo and Sandi 1978; Neff 1979, 1985; USEPA 1980; Lee and Grant 1981; Pucknat 1981; Edwards 1983; Grimmer 1983; Sims and Overcash 1983). Anthropogenic activities associated with significant production of PAHs include: coke production in the iron and steel industry; catalytic cracking in the petroleum industry; the manufacture of carbon black, coal tar pitch, and asphalt; heating and power generation; controlled refuse incineration; open burning; and emissions from internal combustion engines used in transportation. Thus, the formation of PAHs in the environment is due to an endogenous synthesis by microorganisms, algae, and macrophytes that provide natural background, and to a second process that is connected to human-controlled, high-temperature (>700°C) pyrolysis of organic materials, to open burning, and to natural volcanic activities. The discovery in fossil fuels of complex mixtures of PAHs spanning a wide range of molecular weights has led to the conclusion that, given sufficient time (i.e., millions of years), pyrolysis of organic materials at temperatures as low as 100 to 150°C can also lead to production of PAHs (Neff 1985).

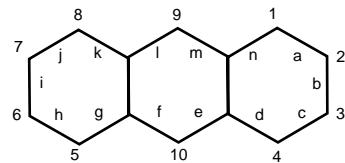
Forest and prairie fires release much greater amounts of PAHs to the atmosphere than does fossil fuel burning. Nearly all of the airborne PAHs produced by flame pyrolysis are associated with the particulate fraction produced during combustion, and these are significantly modified by the chemical composition of the fuel, the pyrolysis temperature, the duration of exposure to elevated temperature, and to other factors (Neff 1979; Edwards 1983). In one study, a PAH profile was established for a series of laboratory fires simulating the prescribed burning of pine needle litter (McMahon and Tsoukalas 1978). Heading fires (moving with wind) produced more total particulate matter than backing fires (moving against wind), but backing fires produced significantly higher amounts of PAHs, with the actual amounts formed dependent on fuel loading and the residence



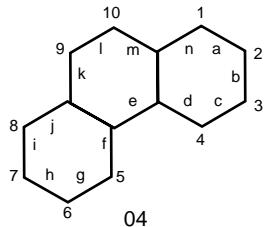
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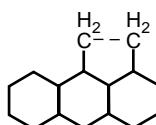
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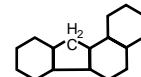
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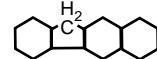
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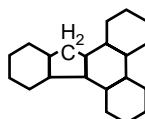
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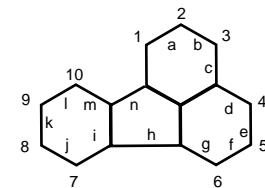
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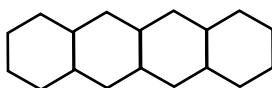
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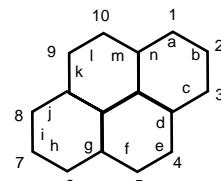
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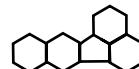
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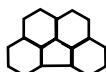
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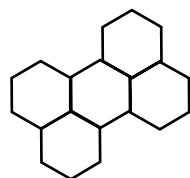
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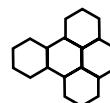
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Figure 25.2 Ring structures of representative noncarcinogenic PAHs. (Modified from Lee and Grant 1981; Neff 1985.) The numbering and lettering system for several PAHs is also given. Compounds are: (1) naphthalene, (2) fluorene, (3) anthracene, (4) phenanthrene, (5) aceanthrylene, (6) benzo[a]-fluorene, (7) benzo[a]-phenanthrene, (8) benzo[a]-anthracene, (9) fluoranthene, (10) naphthacene, (11) pyrene, (12) benzo[a]-naphthacene, (13) benzo[g,h,i]fluoranthene, (14) perylene, (15) benzo[e]pyrene, (16) benzo[g,h,i]perylene, (17) anthanthrene, and (18) coronene.

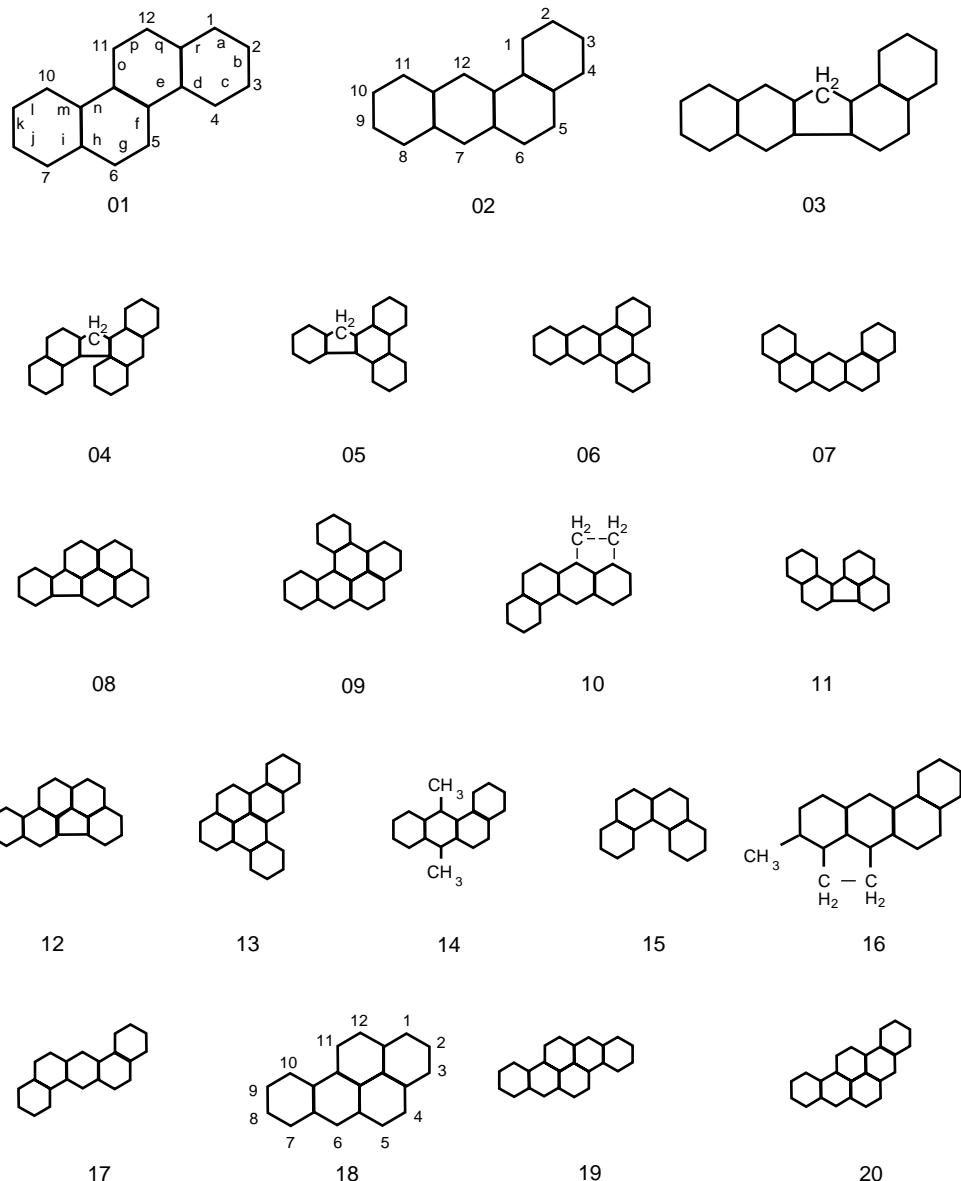


Figure 25.3 Ring structures of representative tumorigenic, cocarcinogenic, and carcinogenic PAHs. (Modified from Lee and Grant 1981.) The numbering and lettering system for several PAHs is also given. Compounds are: (1) chrysene, (2) benz[a]anthracene, (3) dibenz[a,h]fluorene, (4) dibenz[a,g]fluorene, (5) dibenzo[a,c]fluorene, (6) dibenzo[a,j]anthracene, (7) dibenzo[a,j]anthracene, (8) indeno [1,2,3-cd] pyrene, (9) dibenzo[a,1]pyrene, (10) cholanthrene, (11) benzo[j]fluoranthene, (12) benzo[b]fluoranthene, (13) dibenzo[a,e]pyrene, (14) dimethylbenz[a]anthracene, (15) benzo[c]phenanthrene, (16) 3-methylcholanthrene, (17) dibenz[a,h]anthracene, (18) benzo[a]pyrene, (19) dibenzo[a,h]pyrene, (20) dibenzo[a,i]pyrene. Compounds 1 to 9 are weakly carcinogenic, cocarcinogenic, or tumorigenic; compounds 10 to 13 are carcinogenic; and compounds 14 to 20 are strongly carcinogenic.

time of combustible gases in the burning zone. Emission factors for benzo[a]pyrene varied from 238 to 3454 µg/kg in backing fires and 38 to 97 µg/kg in heading fires.

PAHs present in the atmosphere enter rain as a result of in-cloud and below-cloud scavenging (van Noort and Wondergem 1985). Total PAHs deposited on land and water are almost equivalent

Table 25.1 Some Physical and Chemical Properties of Selected PAHs

Compound	Number of Rings	Approximate Molecular Weight	Melting Point (°C)	Solubility in Water (mg/L)	Log K _{ow}
Naphthalene	2	128	80	30.0	3.37
Anthracene	3	178	216	0.07	4.45
Benz[a]anthracene	4	228	158	0.014	5.61
Benz[a]pyrene	5	252	179	0.0038	6.04
Benz[g,h,i]perylene	6	276	222	0.00026	7.23

to PAH content in rainfall. Significant quantities of PAHs are found in presumed pollution-free areas, indicating the importance of rain in transport and distribution of PAHs (Quaghebeur et al. 1983).

PAHs may reach aquatic environments in domestic and industrial sewage effluents, in surface runoff from land, from deposition of airborne particulates, and especially from spillage of petroleum and petroleum products into water bodies (Jackim and Lake 1978; Lake et al. 1979; Neff 1979; USEPA 1980; Martens 1982; Boehm and Farrington 1984; Hoffman et al. 1984; Prahl et al. 1984; von Hofe and Puffer 1986). The majority of PAHs entering aquatic environments remains close to sites of deposition, suggesting that lakes, rivers, estuaries, and coastal marine environments near centers of human populations are the primary repositories of aquatic PAHs (Neff 1979). Large variations in aquatic PAH contents were evident due to localized source inputs and physicochemical conditions. For example, urban runoff from stormwater and highways to Narragansett Bay, Rhode Island, accounted for 71% of the total inputs for higher-molecular-weight PAHs, and 36% of the total PAHs (Hoffman et al. 1984). More than 30% of all combustion-derived PAHs in coastal sediments of Washington state is supplied by riverine transport of suspended particulate materials, while direct atmospheric input accounts for a maximum of 10% (Prahl et al. 1984). In contrast, concentrations of PAHs in sediments from the vicinity of Georges Bank, off the U.S. northeastern coast, varied from 1 to 100 µg/kg dry weight, and were directly related to total organic carbon, silt, and clay contents in sediments. Combustion-derived PAHs dominated at the higher concentrations, while lower levels were often associated with a fossil fuel origin (Boehm and Farrington 1984).

Human activities have resulted in exposure of Antarctic fishes to petroleum-derived PAHs (McDonald et al. 1992). Fish captured near Palmer station on the Antarctic peninsula had induced EROD activities and elevated concentrations of biliary PAH metabolites of phenanthrene and naphthalene when compared to conspecifics from reference sites (McDonald et al. 1995). Artificial reefs consisting of oil and coal flyash stabilized with cement and lime in Florida waters near Vero Beach contained elevated PAH levels ranging from as high as 1.2 mg fluoranthene/kg and 0.25 mg naphthalene/kg. But there is negligible leaching because seawater is not an effective medium for removing PAHs from reef bricks or the ash (Frease and Windsor 1991).

Discharge water from hydrostatic testing of natural gas pipelines is a significant source of PAH loading into aquatic environments, contributing as much as 32,000 µg PAHs/L of discharge water, mostly as naphthalenes (Eiceman et al. 1984). More than 25 PAHs, primarily anthracenes and pyrenes, were detected in pipeline residues on inner walls of natural gas pipelines at concentrations up to 2400 µg/m² of inner surface; the same compounds may be reasonably expected in aqueous waste from pipeline maintenance (Eiceman et al. 1985). Release of these, or similar, discharge waters directly into aquatic environments will result in contamination similar to that caused by oil spills. However, these sites for pollution may occur in locations far distant from oil production and refinery activities (Eiceman et al. 1984). PAHs are also present in tap water at concentrations of 0.1 to 1.0 ng/L, primarily as mono- and di-chlorinated derivatives of naphthalene, phenanthrene, fluorene, and fluoranthene (Shiraishi et al. 1985). The presence of PAHs and chlorinated PAHs in tap water indicates the reaction of PAHs with chlorine; however, their significance to human health and to aquatic biota is unknown.

Creosote (about 85% PAHs) has been used extensively as a long-term wood preservative for marine and freshwater support structures such as pilings, railway ties, and utility poles (Bestari et al. 1998b). About 75% of the creosote applied to marine pilings will remain in the wood after 40 years of service. Most of the PAHs leached into water from creosote-treated pilings is rapidly lost owing to volatility, photodegradation, and microbial degradation pathways (Bestari et al. 1998b).

Table 25.2 Major Sources of PAHs in Atmospheric and Aquatic Environments

Ecosystem and Sources	Annual Input (metric tons)
ATMOSPHERE	
Total PAHs	
Forest and prairie fires	19,513
Agricultural burning	13,009
Refuse burning	4769
Enclosed incineration	3902
Heating and power	2168
Benzo[a]pyrene	
Heating and power	
Worldwide	2604
U.S. only	475
Industrial processes (mostly coke production)	
Worldwide	1045
U.S. only	198
Refuse and open burning	
Worldwide	1350
U.S. only	588
Motor vehicles	
Worldwide	45
U.S. only	22
AQUATIC ENVIRONMENTS	
Total PAHs	
Petroleum spillage	170,000
Atmospheric deposition	50,000
Wastewaters	4400
Surface land runoff	2940
Biosynthesis	2700
Total benzo[a]pyrene	700

Modified from Lo and Sandi; Neff 1979; Edwards 1983; and Sims and Overcash 1983.

25.2.3 Fate

Concern about PAHs in the environment is due to their persistence and to the fact that some are known to be potent mammalian carcinogens, although environmental effects of most noncarcinogenic PAHs are poorly understood (Neff 1985). Prior to 1900, a natural balance existed between the production and degradation of PAHs. Synthesis of PAHs by microorganisms and volcanic activity and production by man-made, high-temperature pyrolytic reactions and open burning seemed to be balanced by PAH destruction via photodegradation and microbial transformation. With increased industrial development and increased emphasis of fossil fuels as energy sources, the balance has been disturbed to the extent that PAH production and introduction into the environment greatly exceeds known PAH removal processes (Suess 1976; Sims and Overcash 1983). Mass balance models that quantitatively estimate PAH cycling in various aquatic systems seem

promising. In one case, a steady-state model for naphthalene, phenanthrene, and benzo[*a*]pyrene in Saguenay Fjord, in Quebec, has been constructed incorporating atmospheric and industrial sources, and transport and transformation rates (Lun et al. 1998). More research on mass balance models is needed.

When released into the atmosphere, PAH compounds will become associated with particulate materials. Their residence time in the atmosphere and transport to different geographic locations are governed by particle size, meteorological conditions, and atmospheric physics. The highly reactive PAHs photodecompose readily in the atmosphere by reaction with ozone and various oxidants; degradation times range from several days to 6 weeks for PAHs adsorbed onto particulates <1 µm in diameter (in the absence of rainfall), to <1 day to several days for those adsorbed to larger particles (Suess 1976). Smaller atmospheric particulates containing PAHs are easily inhaled (Lee and Grant 1981), and may pose special problems, as yet unevaluated, for airborne organisms such as birds, insects, and bats. Photooxidation, one of the most important processes in the removal of PAHs from the atmosphere, can also produce reaction products that are carcinogenic or mutagenic, although little is known of their persistence (Edwards 1983). One of the more common photooxidation reactions of PAHs is the formation of endoperoxides that ultimately undergo a series of reactions to form quinones (Edwards 1983). Various parameters may modify chemical and photochemical transformation of PAHs in the atmosphere, including light intensity, concentration of gaseous pollutants (O_3 , NO_x , SO_x), and chemicophysical characteristics of particulates or substrates into which the PAHs are adsorbed. Depending on these variables, the half-life of benzo[*a*]pyrene in the atmosphere varies from 10 min to 72 days (Valerio et al. 1984). Atmospheric PAHs are transported over relatively long distances from industrial areas and from natural forest and prairie fires (Edwards 1983). However, sites nearer urban centers have much higher PAH deposition rates than more rural areas (Hites and Gschwend 1982).

Much of the PAHs released into the atmosphere eventually reaches the soil by direct deposition or by deposition on vegetation (Edwards 1983). In soils, adsorption of naphthalene mainly occurs on the organic matter and is not related to the size of the soil particles (Bayard et al. 1998). The PAHs may be adsorbed or assimilated by plant leaves before entering the animal food chain, although some adsorbed PAHs may be washed off by rain, chemically oxidized to other products, or returned to the soil as the plants decay (Edwards 1983). PAHs assimilated by vegetation may be translocated, metabolized, and possibly photodegraded within the plant. In some plants growing in highly contaminated areas, assimilation may exceed metabolism and degradation, resulting in an accumulation in plant tissues (Edwards 1983).

In water, PAHs may either evaporate, disperse into the water column, become incorporated into bottom sediments, concentrate in aquatic biota, or experience chemical oxidation and biodegradation (Suess 1976). The most important degradation processes for PAHs in aquatic systems are photooxidation, chemical oxidation, and biological transformation by bacteria and animals (Neff 1979). Most PAHs in aquatic environments are associated with particulate materials; only about 33% are present in dissolved form (Lee and Grant 1981). PAHs dissolved in the water column will probably degrade rapidly through photooxidation (USEPA 1980) and degrade most rapidly at higher concentrations, at elevated temperatures, at elevated oxygen levels, and at higher incidences of solar radiation (McGinnes and Snoeyink 1974; Suess 1976; Bauer and Capone 1985). Microcosm studies with creosote-associated PAHs showed that initial concentrations of 7 µg total PAHs/L degraded to 0.8 µg/L in 84 days, and 5803 µg/L to 14 µg/L in the same time frame (Bestari et al. 1998a). Low- and high-molecular-weight PAHs were lost first from the water column followed by PAHs of intermediate molecular weight (i.e., those with four to five aromatic rings). The half-time persistence in water of most PAHs in that study was about 1 week. In sediments, PAHs peaked at about 8 weeks, with little degradation during the next 6 weeks (Bestari et al. 1998a).

The ultimate fate of those PAHs that accumulate in sediments is believed to be biotransformation and biodegradation by benthic organisms (USEPA 1980). PAHs in aquatic sediments, however, degrade very slowly in the absence of penetrating radiation and oxygen (Suess 1976), and may

persist indefinitely in oxygen-poor basins or in anoxic sediments (Neff 1979). Persistence of phenanthrene and naphthalene is high in Cook Inlet, Alaska, where the sediments are organic rich and contain low numbers of microbial degraders (Braddock and Richter 1998). Carroquino and Alexander (1998) aver that the presence of microorganisms accelerates degradation of phenanthrene and other PAHs and is a better predictor of maximum biodegradation rate than media without microorganisms. PAH degradation in aquatic environments occurs at a slower rate than that in the atmosphere (Suess 1976), and the cycling of PAHs in aquatic environments, as is true for other ecological systems, is poorly understood (Neff 1979). Degradation rates of fluoranthene and other PAHs are dependent on the presence of sediments and other PAHs (Beckles et al. 1998). In sediment-free systems, fluoranthene biodegradation did not occur when it was present alone or in combination with acenaphthene, but was degraded when combined with naphthalene. Naphthalene and acenaphthene degradations were not influenced by fluoranthene. In sediment-containing systems, fluoranthene degradation occurred only in the presence of naphthalene. After complete degradation of naphthalene, fluoranthene degradation ceased (Beckles et al. 1998).

Animals and microorganisms can metabolize PAHs to products that may ultimately experience complete degradation. The degradation of most PAHs is not completely understood. Those in the soil may be assimilated by plants, degraded by soil microorganisms, or accumulated to relatively high levels in the soil. High PAH concentrations in soil can lead to increased populations of microorganisms capable of degrading the compounds. Of equal importance to PAH cycling dynamics is the physical state of the PAH (i.e., whether in vapor phase or associated with particles such as flyash). Particles may increase or decrease the susceptibility of PAHs to degradation, depending on the PAH and particles involved (Edwards 1983).

PAHs can be taken into the mammalian body by inhalation, skin contact, or ingestion, although they are poorly absorbed from the gastrointestinal tract. The main routes of elimination of PAHs and their metabolites include the hepatobiliary system and the gastrointestinal tract (Sims and Overcash 1983; Batel et al. 1985). In mammals, an enzyme system variously known as the cytochrome P-450-dependent mixed-function oxidase, mixed-function oxidase, mixed-function oxygenase, aryl hydrocarbon hydroxylase, or drug metabolizing system is responsible for initiating the metabolism of various lipophilic organic compounds, including PAHs. The primary function of this system is to render poorly water-soluble lipophilic materials more water soluble, and therefore more available for excretion. Some PAHs are transformed to intermediates, which are highly toxic, mutagenic, or carcinogenic to the host. Oxidative metabolism of PAHs in this system proceeds via high electrophilic intermediate arene oxides, some of which bind covalently to cellular macromolecules such as DNA, RNA, and protein. Most authorities agree that metabolic activation by the mixed-function oxidase system is a necessary prerequisite for PAH-induced carcinogenesis and mutagenesis (Neff 1979; Johnson 1993). This enzyme system is known to be present in rodent tissues, and human liver, skin, placenta, fetal liver, macrophages, lymphocytes, and monocytes (Lo and Sandi 1978; Yu et al. 1995). Studies with rodents have shown that the mixed-function oxidase system can convert PAHs to various hydroxylated derivatives, including phenols, quinones, and epoxides, and can also activate PAHs to produce carcinogenic metabolites (Lo and Sandi 1978). Oxygenated groups of xenobiotics are then conjugated with glutathione-S-transferase and other transferase enzymes. The resulting polar and water-soluble end product is excreted via the bile or urine (Arinc and Sen 1994). Fish and most crustaceans tested to date possess the enzymes necessary for activation (Statham et al. 1976; Varanasi et al. 1980; Fabacher and Baumann 1985), but some molluscs and other invertebrates are unable to efficiently metabolize PAHs (Jackim and Lake 1978; Varanasi et al. 1985). Although many aquatic organisms possess the requisite enzyme systems for metabolic activation of PAHs, it is not certain in many cases whether these enzymes produce the same metabolites as those produced by mammalian enzymes (Neff 1979).

Virtually all organisms possess biotransformation or detoxification enzymes that convert lipophilic xenobiotics to water-soluble and excretable metabolites (Yu et al. 1995). In the metabolic process, PAHs are altered by Phase I metabolism into various products such as epoxides, phenols,

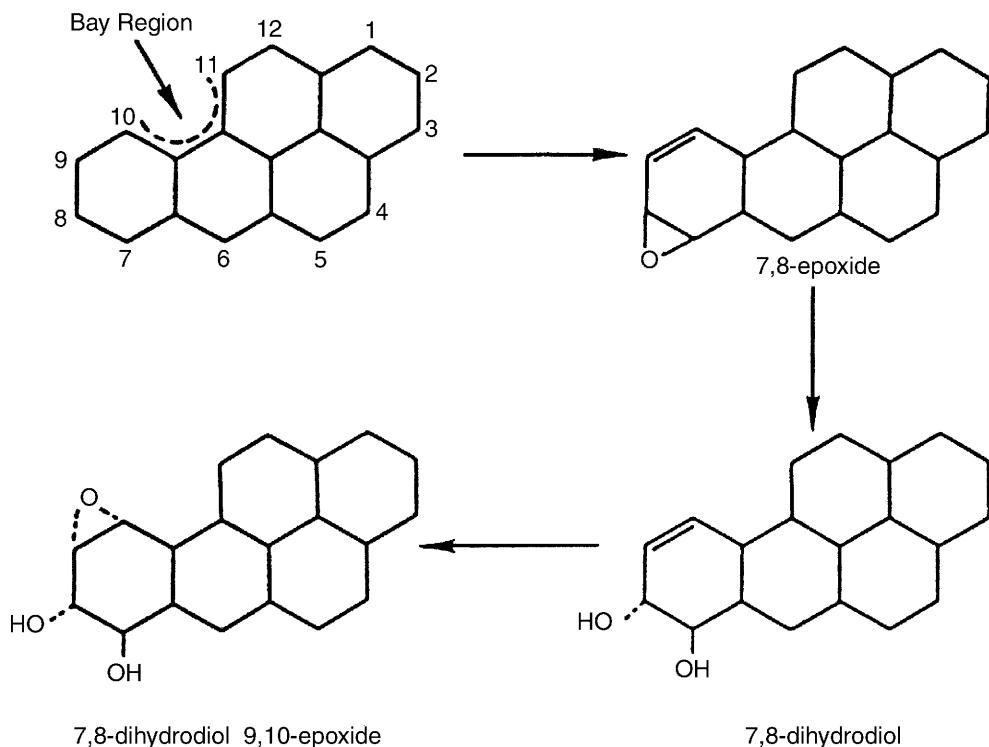


Figure 25.4 The bay region dihydrodiol epoxide route of benzo[a]pyrene. (Modified from Dipple, A. 1985. Polycyclic aromatic hydrocarbon carcinogenesis: an introduction. Pages 1-17 in R.D. Harvey (ed.), *Polycyclic Hydrocarbons and Carcinogenesis*. ACS Symp. Ser. 283. Amer. Chem. Soc., Washington, D.C.)

quinones, dihydrodiols, dihydrodiol epoxides, tetrahydrotriols, and tetrahydrotetrols. The intermediate metabolites have been identified as the mutagenic, carcinogenic, and teratogenic agents (Sims and Overcash 1983). The activation mechanisms occur by hydroxylation or production of unstable epoxides of PAHs which damage DNA, initiating the carcinogenic process (Jackim and Lake 1978; Schnitz and O'Connor 1992). Metabolic formation of bay region diol epoxides represents an important pathway by which PAHs are activated to carcinogens (Figure 25.4). Such metabolic activation proceeds via initial formation of the dihydrodiol with the bay region double bond, followed by subsequent oxidation of the dihydrodiol to the bay region diol epoxide (Sims and Overcash 1983). Active epoxides may be converted to less toxic products by various enzymatic and other reactions (Neff 1979). In the case of benzo[a]pyrene, the “ultimate carcinogen” (7-beta,8-alpha-dihydroxy-7,8,9,10-tetrahydrobenzo[a]pyrene-9-alpha,10-alpha-epoxide) reacts with the guanine of RNA and DNA, the linkage taking place between the C-10 atom of benzo[a]pyrene and the C-2 amino group of guanine (Grimmer 1983; Dipple 1985; Fernandez and L'Haridon 1994) (Figure 25.4). Additional information on actual and theoretical mechanisms involved in the metabolic activation of PAHs is given in Cavalieri et al. (1978, 1980), Bjorseth and Dennis (1980), Herd and Greene (1980), Cooke and Dennis (1981), Sims and Grover (1981), Grimmer (1983), Szentpaly (1984), Harvey (1985), Yan (1985), Steward et al. (1990, 1991), Collier and Varanasi (1991), McElroy et al. (1991), Sikka et al. (1991), Michel et al. (1992), Schnitz and O'Connor (1992), Lemaire et al. (1994), and Ueng et al. (1994). In Phase II metabolism, these products are converted into highly water-soluble conjugates with a large water-soluble moiety, such as the tripeptide glutathione or sugar derivative glucuronic acid (Kennedy 1990; Yu et al. 1995).

There is considerable variability between species in their ability to metabolize benzo[a]pyrene (BaP). For example, two bottom-dwelling species of fish (common carp, *Cyprinus carpio*; brown bullhead, *Ictalurus nebulosus*) differ by a factor of about 12 in the rate at which liver microsomes degrade BaP to metabolites, with carp degrading BaP more rapidly (Sikka et al. 1990). Major BaP metabolites from both species included BaP-7,8-diol, BaP-8,9-diol, 3-hydroxy-BaP, 9-hydroxy-BaP, BaP-1,6-quinone, BaP-3,6-quinone, and BaP-6,12-quinone. Carp liver microsomes converted a much greater proportion of BaP to benzo-ring dihydriodols than did bullhead liver microsome; bullhead liver microsomes formed a significantly higher percentage of BaP-quinones (Sikka et al. 1990). In other species, glutathione conjugation represented the major hepatic detoxification pathway of benzo[a]pyrene, as was the case for white suckers (*Catostomus commersonii*) (Kirby et al. 1990).

25.3 CONCENTRATIONS IN FIELD COLLECTIONS

25.3.1 General

PAHs are ubiquitous in the environment. In nonbiological materials, concentrations are elevated in the vicinity of urban industrialized locales, and from areas of significant wood-burning activities such as forest fires and residential home heating. Terrestrial vegetation and aquatic invertebrates can accumulate significant concentrations of PAHs, possibly due to inefficient or missing mixed-function oxidase systems. Fish do not appear to contain grossly elevated PAH residues. This may be related to their efficient degradation system. At present, data are scarce on PAH background concentrations in natural populations of birds and other wildlife — although it seems unlikely that significant accumulations will occur. Some investigators have shown that aquatic invertebrates, fish, and amphibians collected from areas of high sediment PAH content show elevated frequencies of hyperplasia and neoplasia (Rose 1977; Mix 1982; Black 1983; Malins et al. 1984, 1985a, 1985b; Black et al. 1985; Baumann et al. 1987; Baumann and Whittle 1988), and that hepatic carcinoma has been induced in rainbow trout (*Oncorhynchus mykiss*) by benzo[a]pyrene through dietary and intraperitoneal injection routes (Hendricks et al. 1985).

More comprehensive information on PAH background levels in various biological and nonbiological compartments is given in Lo and Sandi (1978), Neff (1979, 1985), Pucknat (1981), Edwards (1983), Grimmer (1983), and Sims and Overcash (1983).

25.3.2 Nonbiological Samples

Total PAH levels in air are usually much higher in winter than in summer, higher in urban communities than in rural areas (Table 25.3) (Grimmer 1983), and appear to be related primarily to the weight of total suspended particulates in the atmosphere (Hites and Gschwend 1982; Greenberg et al. 1985; Srivastava et al. 1985; Ang et al. 1986). PAH levels in precipitation are significantly higher in winter than in summer, primarily due to emissions from household heating (Quaghebeur et al. 1983; van Noort and Wondergem 1985). Among industrial sources, the production of metallurgical coke is the single most significant source of atmospheric PAHs in Ontario, Canada. Coke production in 1977 represented about 52% of all PAH emissions from Ontario sources versus about 46% formed as a result of forest fires (Potvin et al. 1981). Beyond 2 km distant from the coke point source, PAH concentrations in air were typical of those measured in major urban nonindustrialized areas (Table 25.3) (Potvin et al. 1981). A variety of PAHs have been detected in ambient air in the United States and elsewhere. Benzo[a]pyrene (BaP), because of its carcinogenic properties, has been monitored extensively, and has frequently been used as an indicator of PAHs (USEPA 1980). In general, total PAHs in air are about 10 times higher than BaP levels, although this relation is extremely variable (Lee and Grant 1981). BaP levels, like total PAHs, were higher in winter than

summer, probably due to residential and industrial heating; air levels in urban areas with coke ovens were 40 to 70% higher than in cities without coke ovens, but this may be related to higher industrial emissions in those cities (Lee and Grant 1981). In one case, BaP levels in air from the center of a remote mountain community in Colorado were several times higher than those usually found in U.S. metropolitan areas and was attributed to extensive residential wood burning (Murphy et al. 1982). Average concentrations of BaP in urban air nationwide declined from 3.2 ng/m³ in 1966 to 0.5 ng/m³ in 1978, an 80% decrease (Lee and Grant 1981). These decreases are believed to be due primarily to decreases in coal consumption for commercial and residential heating, improved disposal of solid wastes, and restrictions on open burning (USEPA 1980).

A major source of PAHs in soils and soil litter is from emissions and deposition from forest fires. In a controlled burn study, Sullivan and Mix (1985) showed that lower-molecular-weight PAHs, such as phenanthrene and fluorene, which had been deposited in soil litter, degraded to nondetectable levels within 2 years after burning. Higher-molecular-weight PAHs, such as benzo[k]fluorene, benzo[a]pyrene, benzo[g,h,i]perylene, perylene, and indeno[1,2,3-cd]pyrene, were more persistent in litter, decreasing after 5 years to about 20% of initial deposition. Although movement into the top 2 cm of the soil profile was initially more pronounced for lower-molecular-weight PAHs, all compounds appeared to reach equilibrium between litter and soil on the basis of organic content within 1 year postburn. Differential persistence and fate of PAHs on slash burn sites is explained by solubility, K_{ow}, and other physicochemical properties (Sullivan and Mix 1985). PAHs from vehicle emissions constitute a minor, but measurable, source of soil PAHs (Table 25.3). The majority of highway-derived PAHs appears to be deposited within 3.8 m of the road, but the influence of the highway may extend to nearly 70 m (Johnston and Harrison 1984). The use of composted municipal wastes for conditioning agricultural soils is not recommended, as these contain at least nine identified carcinogenic PAHs (Martens 1982).

PAH-contaminated sediments are involved in epizootics of neoplasms in native fishes at contaminated sites (Fabacher et al. 1991), and other adverse biological effects. In the Detroit River, Michigan, brown bullheads (*Ameiurus nebulosus*) from sediments with the highest PAH concentration of 346 mg/kg DW had the highest prevalence of external abnormalities (lip and skin lesions, truncated barbels) and liver lesions, and these were positively correlated with concentrations of total PAHs in the sediments (Leadley et al. 1998). In the Black River, Ohio, between 1980 and 1982, PAH concentrations declined by 65% and in tissues of brown bullheads by 93%. By 1987, sediment PAHs declined an additional 99%, coincident with closure of a coking facility in 1983. Liver cancer frequency in 3- to 4-year-old bullheads declined to 10% frequency in 1987 vs. 39% frequency in 1982; livers without lesions increased from 20% frequency in 1982 to 42% in 1987 (Baumann and Harshbarger 1995). Sediments and sediment extracts from the Buffalo River, New York, contained elevated levels of carcinogenic PAHs (1000 to 16,000 µg/kg). Brown bullheads, in response to repeated applications of Buffalo River sediment extracts, showed epidermal hyperplasia and neoplasia when compared to controls (Black 1983). Extraction of PAHs from industrially contaminated sediments of Lake Erie and its tributaries (27,000 to 363,000 mg/kg dry weight total PAHs) established the presence of chemical mutagens that could be correlated with neoplasms in fish from many of the sites (Fabacher et al. 1988). In the Netherlands, high-molecular-weight PAHs dominated in the sediments, fluoranthene and pyrene in freshwater isopods, and naphthalene in water. Lipid-based bioconcentration factors increased with increasing hydrophobicity, that is, with increasing K_{ow} (van Hottum et al. 1998). Elevated PAH concentrations in sediments from the North Sea were positively correlated with increasing DNA breaks in the pyloric caeca of resident starfish (*Asterias rubens*) (Everaarts et al. 1994). PAH concentrations in sediments from the Great Barrier Reef, Australia, were always <0.8 µg/kg dry weight, except in small areas close to sites frequently visited by power boats. In those instances, total PAH levels exceeded 13,400 µg/kg (Smith et al. 1985). Highest PAH levels measured in sediments of Cayuga Lake, New York, were found in

marinas or areas of the lake receiving urban runoff, and were apparently not related to stack emissions from a nearby coal-fired power plant; Heit (1985) believed that stack emissions were either masked by other sources or were atmospherically transported and deposited elsewhere. Coastal and offshore sediments are subject to highly elevated PAH levels from a variety of sources, mostly unknown, relative to preindustrial times (Johnson et al. 1985). For example, PAH levels in sediments of Penobscot Bay, Maine, fell within the range found in sediments near industrialized regions and were significantly higher than expected for an area previously considered to be uncontaminated (Table 25.3) (Johnson et al. 1985).

Sewage effluents usually contained measurable levels of PAHs, although extreme variability between and among sites is common. During a heavy storm, individual PAH levels in a sewage works may increase more than 100 times over a dry weather period (Harrison et al. 1975). Conventional sewage treatment plant processes remove up to 90% of carcinogenic PAHs, and this may be increased to 99% using percolating filters and activated sludge processes (Harrison et al. 1975). Tiger salamanders (*Ambystoma tigrinum*), collected in 1975 from a 13-ha sewage effluent lagoon at Reese Air Force Base, Texas, showed a remarkably high incidence (53%) of neoplastic and other lesions (Rose 1977). Analysis of sludge composites showed elevated PAH levels, especially perylene; levels of organochlorine and organophosphorus pesticides, nitrosamines, and heavy metals were judged to be nonelevated (Rose 1977). Careful disposal of used motor oils is warranted, as these contain high quantities of mutagenic and carcinogenic PAHs (Table 25.3) (Pasquini and Monarca 1983).

All but the most heavily contaminated fresh and marine waters contain total PAH concentrations in the part-per-trillion or low part-per-billion range (Table 25.3) (Neff 1982b). A large proportion of the PAH content in water is probably adsorbed onto suspended solids (Harrison et al. 1975). In Lake Michigan, concentrations of total PAHs in the surface microlayer varied from 0.15 to 0.45 µg/L, representing on a relative scale, 106 times the concentration in air, suggesting that aerosols are a major source of these compounds and that the microlayer is a repository until the PAHs are removed by adsorption and sedimentation (Strand and Andren 1980).

Table 25.3 PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference ^a
AIR (ng/m³)		
U.S. cities, 1959, total PAHs		
Detroit	95.1	1
Birmingham	63.4	1
Nashville	60.6	1
New Orleans	33.6	1
Los Angeles	31.8	1
Atlanta	26.3	1
San Francisco	13.7	1
Sydney, Australia		
Winter	8.2	2
Summer	0.6	2
U.S. cities, 1971–77		
Benzo[a]perylene = BaPER	0.2–9.2	1
Benzo[e]pyrene = BeP	0.9–4.6	1
Benzo[k]fluoranthene = BkFL	0.03–1.3	1
Pyrene = PYR	0.18–5.2	1
Coronene = COR	0.2–6.4	1
Perylene = PER	0.01–1.2	1
Anthracene = A	0.07–0.3	1
Naphthalene = NA	Max. 0.4	1
Benz[a]anthracene = BaA	Max. 4.6	1
Indeno[1,2,3-cd]pyrene = IP	Max. 1.3	1

Table 25.3 (continued) PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference^a
Steel mill, Ontario, Canada, 1971–79		
Station 0.8 km distant		
Benzo[a]pyrene = BaP	9.4 (Max. 110.0)	3
BkFL	8.9 (Max. 142.0)	3
Fluoranthene = FL	7.0 (Max. 43.3)	3
PER	9.1 (Max. 106.0)	3
Benzo[g,h,i]perylene = BghiPER	13.7 (Max. 90.0)	3
Station 2.8 km distant		
BaP	0.4 (Max. 7.9)	3
BkFL	0.7 (Max. 5.1)	3
FL	1.1 (Max. 4.8)	3
PER	0.7 (Max. 9.1)	3
BghiPER	1.4 (Max. 8.5)	3
Benzo[a]pyrene = BaP		
Urban areas	0.1–61.0	4
Downwind from coal gasification plant, Yugoslavia	Max. 80.0	4
Urban areas		
1966	3.2	1
1970	2.1	1
1976	0.5	1
Rural areas	0.01–1.9	4
Rural areas		
1966	0.4	1
1976	0.1	1
Mississippi Sandhill Crane, National Wildlife Refuge, Jackson County, MS; May–September 1991		
Total PAHs	2.55 (Max. 3.03)	17
Naphthalene = NA	0.13 (Max. 0.24)	17
2-Methylnaphthalene = 2MNA	0.04 (Max. 0.06)	17
Fluorene	0.01	17
Phenanthrene = PHEN	0.84 (Max. 1.0)	17
Anthracene = A	0.10 (Max. 0.14)	17
FL	0.62	17
PYR	0.6 (Max. 0.7)	17
BaA	0.01	17
Chrysene = CHRY	0.03	17
Benzo[b]fluoranthene = BbFL	0.03	17
BkFL	0.007	17
BeP	0.01	17
BaP	0.007 (Max. 0.008)	17
IP	0.008	17
BghiPER	0.015	17

SOILSNear M6 Motorway, Lancaster, U.K. (maximum deposition rate, ng/m²/week)

Distance from roadway

3.8 meters

A	2300	5
FL	15,200	5
BaA	5800	5
BbFL	7300	5
BkFL	2800	5
BaP	4900	5

9.0–47 meters

A	420	5
FL	1700	5

Table 25.3 (continued) PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference ^a
BaA	260	5
BbFL	690	5
BkFL	470	5
BaP	290	5
Vicinity slash burn site, Oregon (g/ha)		
0–2 cm depth		
Preburn		
PHEN	0.5	6
FL	0.6	6
103 days postburn		
PHEN	9.8	6
FL	3.6	6
365 days postburn		
PHEN	ND	6
FL	0.8	6
2–5 cm depth		
105 days postburn		
PHEN	1.3	6
FL	0.3	6
365 days postburn		
PHEN	ND	6
FL	ND	6
BaP (mg/kg)		
Rural areas	0.4	6
Industrial areas	400.0	6
Nonpolluted areas	Up to 1000	4
Near known sources	>100,000	4
Near coal-tar pitch disposal site, Germany	650,000	7
Near recreation area, U.S.S.R.	0.4	8
Forest soil	1.5–4.0	8
Near Lyon, France, contaminated site, mg/kg		
Total PAHs	88.7	18
A	0.7	18
CHRY	22.7	18
FL	12.6	18
BbkFL	16.8	18
PYR	13.2	18
BaP	4.4	18
IP	5.5	18
BgHiPER	4.9	18
NA	0.3	18
PHEN	8.6	18
PER	2.4	18
Fluorene	0.4	18
LITTER		
Forest, Oregon (g/ha)		
3 Days postburn		
PHEN	603	6
FL	245	6
32 days postburn		
PHEN	ND	6
FL	ND	6
Coniferous trees (mg/kg)		
BgHiPER	42	9
BaP	51	9
IP	47	9
FL	164	9

Table 25.3 (continued) PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference^a
SEDIMENTS (mg/kg dry weight)		
Black River, Lake Erie tributary; sediment extracts; heavily contaminated by wastes from steel mills and coking complex		
Total PAHs vs. reference site	344 vs. <1	16
A	12–15	16, 25
Acenaphthylene	17	16
BaA	11	16, 25
Benzofluoranthenes	1.5	16, 25
CHRY	10	25
FL	33	16, 25
Fluorene	16	16
NA	14	16
PHEN	52	16, 25
PYR	24	16, 25
1980 vs. 1987		
PYR	140 vs. 0.9	24
BaP	43 vs. 0.2	24
BghiPER	24 vs. 0.3	24
IP	26 vs. 0.01	24
Total PAHs	1096 vs. 4	24
Buffalo River, near Buffalo, NY; sediments vs. sediment extracts		
BaA	7 vs. 16	10
CHRY	4 vs. 14	10
BbFL	4 vs. 14	10
BaP	5 vs. 15	10
Dibenz[a,h]anthracene = DBA	1 vs. 3	10
IP	4 vs. 12	10
Cayuga Lake, Ithaca, NY, 1978		
Total PAHs		
Within marinas	4.6–13.9	11
Deepwater	1.3–2.5	11
Near power plant	0.1–6.8	11
FL		
Within marinas	1.7	11
Deepwater	0.3	11
Near power plant	0.01–1.0	11
Hamilton Harbour, Ontario, Canada; October 1987; contaminated site		
NA	0.8	21
Acenaphthylene	0.8	21
Acenaphthene	1.8	21
Fluorene	2.9	21
PHEN	22.3	21
A	9.6	21
FL	30.1	21
PYR	22.8	21
BaA	7.1	21
CHRY	6.8	21
BbFL	15.6	21
BkFL	ND	21
BaP	7.5	21
Niagara River; 1991; contaminated sites (Buffalo River, Love Canal) vs. reference site		
Total PAHs	3.3–5.4 vs. 0.4	26
PHEN	0.4 vs. 0.01	26
A	0.2 vs. ND	26

Table 25.3 (continued) PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference ^a
FL	0.9 vs. 0.04	26
PYR	0.7 vs. 0.03	26
BaA	0.45 vs. 0.01	26
CHRY	0.5 vs. 0.02	26
BbFL	0.4 vs. 0.02	26
BeP	0.2 vs. 0.02	26
BaP	0.3 vs. 0.01	26
IP	0.24 vs. 0.01	26
DBA	0.06 vs. ND	26
BghiPER	0.25 vs. 0.02	26
Penobscot Bay, Maine		
Total PAHs	0.3–8.8	12
PHEN	0.02–0.2	12
A	ND–0.05	12
FL	0.2–3.7	12
PYR	0.01–0.5	12
BaA	0.01–0.5	12
CHRY	0.01–0.6	12
BbFL	0.02–1.0	12
BkFL	0.01–0.7	12
BaP	0.01–0.5	12
DBA	0.002–0.1	12
BghiPER	0.02–0.6	12
IP	0.01–0.2	12
Total PAHs		
Casco Bay, ME	0.2–14.4	12
Charles River, MA	87–120	12
Chesapeake Bay	0.01–96	22
Boston Harbor, MA	8.5	12
New Bedford Harbor, MA	63	12
Lake Erie	0.5–3.8	12
Adirondack lakes	4–13	12
Alaska	0.01–0.1	12
Tamar estuary, U.K.	5	12
Southampton estuary, U.K.	91–1791	12
Severn estuary, U.K.	1.6–25.7	12
Monaco	5.2–12.1	12
Gulf of Finland	0.4	12
Norway	0.3–99.4	12
Walvis Bay, Africa	0.07	12
Amazon River system	ND–0.5	12
Iraq	<0.5	23
SEWAGE		
Waters, worldwide, total PAHs (mg/L)	100–500	7
Sludge, total PAHs, United Kingdom, 12 sites (mg/kg)		
Fresh weight	80–1760	13
Dry weight	200–50,300	13
Sludge, Texas, Reese Air Force Base, effluent lagoon (mg/kg FW)		
PER	300.0	14
PYR	5.8	14
FL	5.7	14
BaA	1.4	14
CHRY	1.3	14
BaP	0.5	14
BeP	0.2	14
A	0.2	14

Table 25.3 (continued) PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference ^a
MOTOR OILS (g/L)		
Unused		
BaP	115	15
CHRY	56	15
PER	11	15
Used		
BaP	1382	15
CHRY	10,170	15
PER	1024	15
DIESEL FUEL ARCTIC (g/kg)		
BaA	0.1–1.0	19
FL, CHRY	1.1–10	19
A, PYR	11–20	19
C ₄ PHEN and A	31–100	19
C ₃ PHEN and A	101–300	19
Fluorene	301–500	19
PHEN, NA, C ₄ NA, C ₁₊₂ fluorenes, C ₁₊₂ PHEN/A	500–1000	19
1-MNA, 2-MNA, C ₂₊₃ NA	1001–5000	19
GROUNDWATER (g/L)		
Worldwide		
Total PAHs	0.01–0.05	7
Total PAHs	0.045–0.51	8
Carcinogenic PAHs	0.00–0.081	8
Germany		
Total PAHs	0.04	1
Carcinogenic PAHs	0.003	1
Champaign, Illinois		
Total PAHs	0.007	1
Carcinogenic PAHs	0.003	1
Elkhart, Indiana		
Total PAHs	0.02	1
Carcinogenic PAHs	0.004	1
DRINKING WATER (g/L)		
U.S., total PAHs	0.015	7
Europe, total PAHs	0.04–0.06	7
Monongahela River, Pittsburgh, PA		
Untreated		
Total PAHs	0.6	1
Carcinogenic PAHs	0.14	1
Treated		
Total PAHs	0.003	1
Carcinogenic PAHs	0.002	1
Ohio River, Wheeling, WV		
Untreated		
Total PAHs	1.59	1
Carcinogenic PAHs	0.57	1
Treated		
Total PAHs	0.14	1
Carcinogenic PAHs	0.011	1
Lake Winnebago, Appleton, WI		
Untreated		
Total PAHs	0.007	1
Carcinogenic PAHs	0.002	1

Table 25.3 (continued) PAH Concentrations in Selected Nonbiological Materials

Material (units) and Other Variables	Concentration	Reference ^a
Treated		
Total PAHs	0.006	1
Carcinogenic PAHs	0.002	1
SURFACE WATER (g/L)		
Worldwide		
Low-level contamination	0.05–0.25	7
Medium polluted	0.2–1.0	7
Germany, Rhine River		
Total PAHs	1.12	1
Carcinogenic PAHs	0.49	1
Thames River, U.K.		
Total PAHs	0.5–1.33	1
Carcinogenic PAHs	0.18–0.56	1
ARTIFICIAL REEF COMPONENTS (mg/kg FW)		
Bricks made from oil ash vs. bricks made of flyash		
NA	0.3 vs. 0.3	20
FL	1.2 vs. 0.7	20
PYR	1.1 vs. 0.5	20
CHRY	0.5 vs. 0.3	20
BaP	0.4 vs. 0.3	20
PER	0.3 vs. 0.2	20
Total PAHs	3.8 vs. 2.2	20

^a 1, USEPA 1980; 2, Barnett 1976; 3, Potvin et al. 1981; 4, Edwards 1983; 5, Johnston and Harrison 1984; 6, Sullivan and Mix 1985; 7, Lee and Grant 1981; 8, Harrison et al. 1975; 9, Thomas et al. 1984; 10, Black 1983; 11, Heit 1985; 12, Johnson et al. 1985; 13, McIntyre et al. 1981; 14, Rose 1977; 15, Pasquini and Monarca 1983; 16, Fabacher et al. 1988; 17, White and Hardy 1994; 18, Fouche court and Riviere 1995; 19, Yu et al. 1995; 20, Frease and Windsor 1991; 21, Balch et al. 1995; 22, Van Veld et al. 1990; 23, Al-Saad and Al-Timari 1989; 24, Baumann and Harshbarger 1995; 25, Lin et al. 1994; 26, Eufemia et al. 1997.

25.3.3 Biological Samples

Carcinogenic PAHs have been extracted from a large variety of fresh plants, including root and leaf vegetables, fruits, grains, and edible mushrooms, as well as from various marine bacteria and phytoplankton under circumstances suggesting that PAHs were present due to local biosynthesis (Suess 1976). PAH concentrations in terrestrial vegetation were lower at higher altitudes and higher near highways when compared to conspecifics from lower altitudes and further from the highway (Lodovici and Akpan 1997). Vegetation and soil near known PAH sources are more highly contaminated with PAHs than those collected at greater distances (Edwards 1983). PAH levels in lettuce (*Lactuca sativa*) grown in Sweden seemed to be directly related to its proximity to local recognized point sources of PAH emitters (Table 25.4; Larsson and Sahlberg 1982). Washing lettuce with water had little effect on phenanthrene levels, but significantly reduced other PAHs, such as benzo[*a*]pyrene, benz[*a*]anthracene, and benzo[*g,h,i*]perylene by 68 to 87% (Larsson and Sahlberg 1982). Fruits and vegetables grown in polluted atmospheres may contain up to 100-fold higher levels of total PAHs than those grown in unpolluted environments (USEPA 1980; Lee and Grant 1981). PAH concentrations for plants are generally greater on plant surfaces than in internal tissues, greater in above-ground plant parts than those below ground, and greater in plants with broad leaves (greater surface area) than those with narrow leaves (Edwards 1983). Plants can become contaminated with PAHs through environmental pollution, particularly through deposition from the atmosphere, and also through food processing. For example, the bran portion of milled wheat, as well

as finished bran cereal, had a considerably higher PAH content than other fractions or finished products (Lawrence and Weber 1984b). Enrichment of PAHs in plants is associated with deposition of atmospheric particulate matter with relatively small particle sizes; thus, PAH content is usually in the order of humus > mosses > lichens (Thomas et al. 1984). Mosses appear to be good indicators of regional PAH air pollution and have been recommended for this purpose (Herrmann and Hubner 1984). Concentrations of total PAHs in soils, usually the sum of 5 to 20 PAHs, typically exceeded benzo[a]pyrene levels by at least one order of magnitude; however, concentrations of benzo[a]pyrene in vegetation were generally less than those in soil where plants were growing (Edwards 1983).

PAH accumulations in marine molluscs have been reported (Table 25.4). However, some of these data may be misleadingly low. For example, lengthy cold storage of 10 months can result in loss of volatile PAHs, such as anthracene, in tissues of mussels (Smith et al. 1984); accordingly, background concentrations in these organisms may be underreported. Bivalve molluscs tend to accumulate high PAH levels due to their inability to metabolize and excrete them (Lawrence and Weber 1984a), presumably due to inefficient or missing mixed-function oxidase systems (Sirota and Uthe 1981). Cellular proliferative disorders, resembling neoplastic conditions in vertebrates, were found in mussels with the greatest PAH concentrations: 9.5% vs. 0.7% in control site (Mix 1982). Baseline levels of PAHs in indigenous bivalve molluscs reflected the degree of human onshore activity at the various sample sites, and presumably the level of water contamination; however, little relation was evident between accumulated levels of individual PAHs and total PAHs (Mix 1982). Elevated PAH concentrations, especially benz[a]anthracene, chrysene, fluorene, phenanthrene, and pyrene in oyster tissues and sediments were measured in samples from the vicinity of marinas and were higher in oysters in cooler months when lipids and glycogen were being stored preparatory to spawning (Marcus and Stokes 1985). In general, PAH concentrations in marine clams and mussels were highest in areas adjacent to industrialized bayfronts and lowest in more remote areas; higher in larger animals and in those with higher lipid concentrations; and lowest in autumn–winter, and highest during spring–summer (Mix and Schaffer 1983a; Hellou 1996). A similar pattern was observed in mussels, *Mytilus edulis*, with the more water-soluble, lower-molecular-weight PAHs bioconcentrated 10 to 100 times above that of the higher-molecular-weight, less water-soluble PAHs (Mix and Schaffer 1983b; Baumard et al. 1998). PAH levels in mussels seemed to be independent of water salinity (Mix and Schaffer 1979). Clams contaminated with PAHs and removed to clean seawater for 24 h showed significant depuration of unsubstituted 3- and 4-ring PAHs. In contrast, concentrations of all 5-, 6-, and 7-ring compounds, which includes most of the carcinogenic PAHs, were not significantly depurated (Mix 1982). A positive relation exists between PAH isomers in sediments, soft tissues of the mussel *Mytilus edulis*, and a seaweed (*Fucus* sp.) collected at Vancouver, British Columbia (Dunn 1980). For mussels, the general trend toward lower levels of higher-molecular-weight PAHs relative to levels in sediments suggests an uptake mechanism that involves the solution of PAHs in water; superimposed on this pattern is the more rapid turnover and shorter half-life of lower-molecular-weight PAHs in mussels (Dunn 1980; Baumard et al. 1998).

PAH residues were higher than expected in American lobsters (*Homarus americanus*) collected offshore (mean weight 3.6 kg) when compared to smaller (0.6 kg) lobsters collected inshore (Sirota and Uthe 1981), suggesting that age or body size are important modifiers in PAH accumulation dynamics. PAH concentrations in sediments collected near a coking facility in Nova Scotia in 1980 contained up to 2830 mg/kg dry weight, or more than 20 times the levels recorded in Boston (MA) Harbor; concentrations in excess of 100 mg/kg dry weight sediment were recorded for phenanthrene, fluorene, pyrene, benz[a]anthracene, chrysene, benzo[e]pyrene, benzo[b]fluoranthene, and benzo[a]pyrene, and these seemed to reflect the elevated tissue levels in American lobsters collected from that locale (Sirota et al. 1983). PAH residues in digestive glands of American lobsters collected in 1979 in Nova Scotia from the vicinity of a major oil spill were higher than those from coastal

control sites; however, PAH contents of edible muscle from control and oiled lobsters were similar (Sirota and Uthe 1981).

PAH levels in fish are usually low because this group rapidly metabolizes PAHs (Lawrence and Weber 1984a; Lemaire et al. 1990, 1992b; van der Weiden et al. 1994). Furthermore, higher-molecular-weight PAHs, which include the largest class of chemical carcinogens, do not seem to accumulate in fish (West et al. 1984). Tissue lipid concentration was the primary factor in determining PAH concentrations in fishes (Kayal and Connell 1995). Raw fish from unpolluted waters usually do not contain detectable amounts of PAHs, but smoked fish contain elevated concentrations of PAHs (Akpan et al. 1994) (Table 25.4). The concentration of benzo[a]pyrene in skin of cooked fish was much higher than in other tissues, suggesting that skin may serve as a barrier to the migration of PAHs in body tissues (USEPA 1980).

In many cases, aquatic organisms from PAH-contaminated environments have a higher incidence of tumors and hyperplastic diseases than those from nonpolluted environments. Carcinogenic PAHs have not been unequivocally identified as the causative agent for an increased incidence of cancer in any natural population of aquatic organisms, according to Neff (1982b). However, a growing body of evidence links PAHs to cancer in feral fish populations, especially bottom-dwelling fish from areas with sediments heavily contaminated with PAHs (Baumann and Whittle 1988; Black et al. 1988; Baumann 1989).

Sediments and biota collected from the Hersey River, Michigan, in 1978, were heavily contaminated with phenanthrene, benz[a]anthracene, and benzo[a]pyrene when compared to a control site. Elevated PAH concentrations were recorded in sediments, whole insect larvae, crayfish muscle, and flesh of lampreys (family Petromyzontidae), brown trout (*Salmo trutta*), and white suckers (*Catostomus commersoni*), in that general order (Black et al. 1981). The polluted collection locale was the former site of a creosote wood preservation facility between 1902 and 1949, and, at the time of the study, received Reed City wastewater treatment plant effluent, described as an oily material with a naphthalene-like odor (Black et al. 1981). In San Francisco Bay, elevated PAH concentrations in fish livers reflected elevated sediment PAH concentrations (Stehr et al. 1997). In Chesapeake Bay, spot (*Leiostomus xanthurus*) collected from a PAH-contaminated tributary (up to 96 mg PAHs/kg DW sediment) had elevated cytochrome P-450 and EROD activity in liver and intestine microsomes (Van Veld et al. 1990). Intestinal P-450 activity was 80 to 100 times higher in fish from highly contaminated sites than in conspecifics from reference sites; intestinal EROD activity had a similar trend. Liver P-450 and EROD activity was about 8 times higher in spot from the contaminated sites when compared to the reference sites. Liver P-450 activity correlated positively with sediment PAH, but intestinal P-450 activity seemed to reflect dietary exposure (Van Veld et al. 1990). The poor correlation between hepatic concentrations of PAHs and P-4501A is attributed to the rapid metabolism of these compounds (van der Weiden et al. 1994).

Embryos of the common tern (*Sterna hirundo*) from eight colonies in the Netherlands and Belgium were analyzed for PAHs in May–July 1991. In general, eggs containing embryos with elevated PAH concentrations in the yolk sac and with elevated hepatic EROD activity levels were laid later, had a more prolonged incubation period, were of smaller volume, and produced smaller chicks (Murk et al. 1996).

Norway rats (*Rattus norvegicus*) from a PAH-contaminated site near Lyon, France, when compared to conspecifics from a reference site, had altered liver and lung monooxygenases and altered antioxidant enzyme activities in liver, lungs, and erythrocytes (Fouchecourt and Riviere 1995). PAH concentrations in muscle tissues of 10 species of marine mammals from Newfoundland–Labrador waters in 1988/89 were highest in harbor porpoise (*Phocoena phocoena*) and lowest in large whales and hooded seals (*Cystophora cristata*; Hellou et al. 1990). Benzo[a]pyrene was specifically related to the presence of tumors in beluga whales (*Delphinapterus leucas*) from the Gulf of St. Lawrence in Canada (Hellou et al. 1990).

Table 25.4 PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
ALGAE AND OTHER PLANTS		
Marine algae, Greenland		
Total PAHs	60 FW	1
Marine algae, Benzo[a]pyrene = BaP	Up to 60 DW	2
Freshwater alga, <i>Chlorella vulgaris</i> , BaP	10–50 DW	3
Bacteria, BaP	2–6 DW	3
Moss, <i>Hypnum cupressiforme</i> , southern Finland, 1982, near center of industrial town		
BaP	110 DW	4
Fluoranthene = FL	250 DW	4
Benzo[g,h,i]perylene = BghiPER	90 DW	4
Indeno[1,2,3cd]pyrene = IP	41 DW	4
Vegetation		
Total PAHs		
Nonpolluted areas	20–1000 DW	5
Near known source	25,000 DW	5
BaP	0.1–150.0 DW	5
Lettuce, <i>Lactuca sativa</i> , total PAHs; Sweden, summer 1980		
Grown near highway		
8–15 m distant	50 FW	6
15–50 m distant	26 FW	6
Near airport, 150–800 m	24 FW	6
Aluminum smelter		
0.5–1.5 km distant	654 FW	6
2.0–6.5 km	128 FW	6
Industrial areas	13 FW	6
Residential areas		
Urban	13 FW	6
Rural	12 FW	6
Olive, <i>Olea</i> spp; fruits; Florence, Italy; 1991		
Total PAHs	1.7–14.3 DW	22
BaP	0.03–0.5 DW	22
Laurel evergreen, <i>Laurus nobilis</i> ; leaves; Florence, Italy; 1994		
Total PAHs	87–880 DW	22
Benzo[a]anthracene = BaA	0.8–13.2 DW	22
BaP	3.4–22.5 DW	22
Benzo(b)fluoranthene = BbFL	Max. 42.0 DW	22
BkFL	Max. 1.0 DW	22
BghiPER	Max. 90.0 DW	22
Chrysene = CHRY	Max. 416.0 DW	22
Dibenz[a,h]anthracene = DBA	Max. 8.0 DW	22
Phenanthrene = PHEN	Max. 35.0 DW	22
Pyrene = PYR	Max. 424.0 DW	22
Fluoranthene = FL	Max. 82.0 DW	22
Seedlings, wheat and rye, BaP	10–20 DW	3
INVERTEBRATES		
Rock crab, <i>Cancer irroratus</i> , edible portions, 1980		
New York Bight		
Total PAHs	1600 FW	7
BaP	1 FW	7
Long Island Sound		
Total PAHs	1290 FW	7
BaP	ND	7

Table 25.4 (continued) PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
American oyster, <i>Crassostrea virginica</i> , soft parts, South Carolina, 1983, residential resorts, total PAHs		
Spring months		
Palmetto Bay	520 FW	8
Outdoor resorts	247 FW	8
Fripp Island	55 FW	8
Summer months		
Palmetto Bay	269 FW	8
Outdoor resorts	134 FW	8
Fripp Island	21 FW	8
Zebra mussel, <i>Dreissena polymorpha</i> ; Netherlands; 1994; soft parts; Meuse River vs. reference site		
Acenaphthene	2500 FW vs. 2 FW	37
A	21 FW vs. 0.4 FW	37
BaA	250 FW vs. 0.7 FW	37
BaP	15 FW vs. 2 FW	37
BbFL	63 FW vs. 6 FW	37
BeP	55 FW vs. 3 FW	37
BkFL	16 FW vs. 2 FW	37
CHRY	65 FW vs. 4 FW	37
FL	270 FW vs. 8 FW	37
Fluorene	250 FW vs. 0.4 FW	37
IP	2.1 FW vs. 0.5 FW	37
PHEN	120 FW vs. 2 FW	37
PYR	120 FW vs. 3 FW	37
American lobster, <i>Homarus americanus</i> , Edible portions, 1980		
New York Bight		
Total PAHs	367 FW	7
BaP	15 FW	7
Long Island Sound		
Total PAHs	328 FW	7
BaP	15 FW	7
Softshell clam, <i>Mya arenaria</i> , soft parts, Coos Bay, Oregon		
1976–78, BaP		
Near industrialized areas	6–20 FW	14
Remote areas	1–2 FW	14
1978/79, BaP		
Near industrialized areas	9 FW	14
Remote areas	4 FW	14
1978–79		
Contaminated site		
Total PAHs	555 FW	9
Phenanthrene = PHEN	155 FW	9
FL	111 FW	9
Pyrene = PYR	62 FW	9
BaP	55 FW	9
Benz[a]anthracene = BaA	42 FW	9
Chrysene = CHRY	27 FW	9
Benzo(b)fluoranthene = BbFL	12 FW	9
Others	<10 FW	9
Uncontaminated site		
Total PAHs	76 FW	9
PHEN	12 FW	9
FL	10 FW	9
Others	<10 FW	9

Table 25.4 (continued) PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
Bay mussel, <i>Mytilus edulis</i> , Oregon, 1979/80, soft parts, total PAHs		
Near industrialized area	106–986 FW	10
Remote site	27–274 FW	10
Sea scallop, <i>Placopecten magellanicus</i>		
Baltimore Canyon, east coast U.S.		
Muscle		
BaA	1 FW	11
BaP	<1 FW	11
PYR	4 FW	11
New York Bight, 1980		
Edible portions		
Total PAHs	127 FW	7
BaP	3 FW	7
Clam, <i>Tridacna maxima</i> , Australia, 1980–82, Great Barrier Reef, soft parts, total PAHs		
Pristine areas	<0.07 FW	12
Power boat areas	Up to 5 FW	12
Benzo[a]pyrene		
Marine plankton		
Greenland	5 FW	1
Italy	6–21 FW	1
France	400 FW	1
Worldwide	Up to 400 DW	2
Mussel, <i>Mytilus</i> sp.		
Greenland		
Shell	60 FW	1
Soft parts	18 FW	1
Italy		
Shell	11 FW	1
Soft parts	130–540 FW	1
Bivalve molluscs, 5 spp.		
Edible portions	6 (Max. 36) FW	13
Decapod crustaceans, 4 spp.		
Edible portions	2 (Max. 8) FW	13
FISHES		
Fish, muscle		
Lake Ontario, 6 spp., total PAHs	3–8 FW	15
Baltimore Canyon; east coast, U.S., 5 spp.		
BaA	Max. 0.3 FW	11
BaP	Max. <5 FW	11
PYR	Max. <5 FW	11
Smoked		
FL	3 FW	16
PYR	2 FW	16
Non-smoked		
FL	Max. 1.8 FW	16
Freshwater fishes; Nigeria; 3 cities; various species; muscle; non-smoked vs. smoked; maximum values recorded		
Acenaphthene	ND vs. 4372 DW	21
Fluorene	1526 DW vs. 2102 DW	21
PHEN	55 DW vs. 114 DW	21
FL	61 DW vs. 352 DW	21
PYR	239 DW vs. 285 DW	21
BaA	28 DW vs. 51 DW	21
CHRY	263 DW vs. 525 DW	21
BbFL	12 DW vs. 88 DW	21

Table 25.4 (continued) PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
BkFL	0.3 DW vs. 3 DW	21
BaP	44 DW vs. 139 DW	21
Dibenz[a,h]anthracene = DBA	5 DW vs. 35 DW	21
BghiPER	150 DW vs. 206 DW	21
Marine fishes; muscle; Arabian Gulf; 1992; exposed to 6–10 million barrels of crude oil during Arabian war of 1991 plus unknown airborne products from ignition of 500 million barrels of oil-well fires		
Naphthalene = NA	11 DW; Max. 67 DW	25
Acenaphthene	5 DW; Max. 8 DW	25
Fluorene	6 DW; Max. 18 DW	25
PHEN	19 DW; Max. 100 DW	25
Anthracene = A	68 DW; Max. 78 DW	25
FL	21 DW; Max. 123 DW	25
PYR	79 DW; Max. 341 DW	25
BaA	Max. 0.3 DW	25
CHRY	Max. 0.05 DW	25
BaP	2.7 DW; Max. 7.6 DW	25
Cod, <i>Gadus morhua</i>		
Northwest Atlantic Ocean; November 1990; muscle, liver, ovaries; max. concentrations measured		
Acenaphthene	9.2 FW (liver)	23
CHRY	11.0 FW (liver)	23
Fluorene	18.0 FW (ovary)	23
13 other PAHs	ND	23
Newfoundland coast (pristine) vs. Gulf of St. Lawrence (contaminated); 1990/91; muscle	Max. 10.0 DW vs. Max. 200 DW	34
Brown bullhead, <i>Ictalurus nebulosus</i> ; Black River, OH; whole body; 3-year-old fish; 1980 vs. 1982		
Total PAHs	6515 FW vs. 478 FW	33
PHEN	3930 FW vs. 161 FW	33
FL	1260 FW vs. 129 FW	33
CHRY	61 FW vs. 13 FW	33
Antarctic fish, <i>Notothenia coriiceps neglecta</i>		
Arthur Harbor, Antarctica; 1991; total PAHs		
Liver	Max. 1884 FW	24
Muscle	Max. 154 FW	24
Stomach contents	Max. 17,000 FW	24
Antarctica; March–April 1991–93		
Bile		
NA	33,000–77,000 FW	27
PHEN	5100–11,000 FW	27
Liver, total PAH	268–569 FW	27
Sand flathead, <i>Platycephalus bassensis</i> ; Victoria, Australia; 1990; total PAHs		
Liver lipids	Max. 93 FW	26
Muscle lipids	Max. 17 FW	26
Winter flounder, <i>Pleuronectes americanus</i> ; edible portions; 1980		
New York Bight		
Total PAHs	315 FW	7
BaP	21 FW	7
Long Island Sound		
Total PAHs	103 FW	7
BaP	ND	7
Windowpane, <i>Scophthalmus aquosus</i> ; edible portions, 1980		
New York Bight		
Total PAHs	536 FW	7
BaP	4 FW	7

Table 25.4 (continued) PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
Long Island Sound		
Total PAHs	86 FW	7
BaP	ND	7
Red hake, <i>Urophycis chuss</i> ; edible portions; 1980		
New York Bight		
Total PAHs	412 FW	7
BaP	22 FW	7
Long Island Sound		
Total PAHs	124 FW	7
BaP	5 FW	7
Marine fishes; edible portions, BaP, 9 spp.	Max. 3 FW	13
Greenland	15 FW	1
Italy	65 FW	1
REPTILES		
Leatherback turtle, <i>Dermochelys coriacea</i> ; adult male found drowned in fishing net; west coast of Britain; adipose tissue vs. liver		
Total PAHs	12.0 FW vs. 5.5 FW	36
NA	1.2 FW vs. 1.5 FW	36
PHEN	1.5 FW vs. 0.6 FW	36
FL	1.4 FW vs. 0.4 FW	36
PYR	1.8 FW vs. 0.6 FW	36
BIRDS		
Canvasback, <i>Aythya valisineria</i> ; San Francisco Bay, CA; winter 1988; skin and fat		
Fluorene	Max. 20 FW	29
NA	Max. 40 FW	29
PHEN	Max. 90 FW	29
PYR	Max. 10 FW	29
MAMMALS		
Cow, <i>Bos</i> sp., BaP		
Steak, charcoal broiled	5–8 DW	17
Ribs, barbecued	11 DW	17
From Newfoundland-Labrador waters; 1988/89; muscle; 10 species of marine mammals; total PAHs	100–1200 FW	30
Harbor porpoise, <i>Phocoena phocoena</i> ; muscle; UK waters; 1988–91		
Total PAHs	110–560 FW	31
NA	4.4 FW; Max. 16.0 FW	31
PHEN	Max. 5 FW	31
A	0.6 FW; Max. 3.6 FW	31
FL	Max. 6.0 FW	31
PYR	1.9 FW; Max. 7.2 FW	31
Harbor seal, <i>Phoca vitulina</i> ; northeast coast U.S.; 1990–92; blubber and liver		
PHEN, A	Less than 30 FW	32
Other PAHs	Below detection limits of 15 FW	32
INTEGRATED STUDIES		
Australia; Brisbane estuary; 1987/88; total of 12 PAHs; 5 locations		
Mud crab, <i>Scylla serrata</i> ; soft parts	56–123 FW; 2203 LW	35

Table 25.4 (continued) PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
Fishes, muscle		
Blue catfish, <i>Arius graffei</i>	43–156 FW; 1844 LW	35
Striped mullet, <i>Mugil cephalus</i>	54–195 FW; 3004 LW	35
Bony bream, <i>Nematalosa comi</i>	65–177 FW; 2504 LW	35
Birds, muscle		
Silver gull, <i>Larus novaehollandiae</i>	53–109 FW; 1062 LW	35
Pelican, <i>Pelecanus conspicillatus</i>	54–93 FW; 982 LW	35
All species		
NA	Max. 733 LW	35
PYR	Max. 180 LW	35
Acenaphthene	Max. 182 LW	35
Mediterranean Sea (western portion); October 1995; maximum concentrations; sediments vs. soft parts of mussel, <i>Mytilus galloprovincialis</i>		
Total PAHs	20,500 DW vs. 390 DW	38
PYR	1869 DW vs. 86 DW	38
A	446 DW vs. 8 DW	38
FL	3183 DW vs. 44 DW	38
PYR	2804 DW vs. 134 DW	38
BaA	1598 DW vs. 16 DW	38
CHRY	1756 DW vs. 142 DW	38
BbFL	2769 DW vs. 93 DW	38
BaFL	300 DW vs. 5 DW	38
BeP	1093 DW vs. 64 DW	38
BaP	1607 DW vs. 8 DW	38
Perylene	445 DW vs. 3 DW	38
IP	1296 DW vs. 16 DW	38
B(ghi)PER	1028 DW vs. 18 DW	38
DBA	247 DW vs. 3 DW	38
Michigan, 1978, Hersey River, near wastewater treatment plant		
PHEN		
Sediments	4097 FW	18
Insects, whole	5488 FW	18
Crustaceans, muscle	447 FW	18
Fish, muscle	28–15,313 FW	18
BaA		
Sediments	3504 FW	18
Insects	2893 FW	18
Crustaceans	40 FW	18
Fish	0.2–19 FW	18
BaP		
Sediments	1194 FW	18
Insects	725 FW	18
Crustaceans	8 FW	18
Fish	0.07–1 FW	18
Control location		
Sediments and biota		
PHEN	2–42 FW	18
BaA	ND–6.7 FW	18
BaP	0.04–1.2 FW	18
Netherlands, Amsterdam		
Sediments		
Total PAHs	Max. 141,000 FW	28
PYR	Max. 19,000 FW	28

Table 25.4 (continued) PAH Concentrations in Field Collections of Selected Biota (Values are shown in g/kg [ppb] fresh weight [FW], dry weight [DW], or lipid weight [LW].)

Taxonomic Group, Compound, and Other Variables	Concentration	Reference ^a
European eel, <i>Anguilla anguilla</i> ; muscle lipids		
Total PAHs	Max. 39,000 FW	28
PYR	Max. 600 FW	28
Nova Scotia, 1980, total PAHs		
Near coking facility		
Sediments	2,830,000 DW	19
American lobster, <i>Homarus americanus</i>		
Hepatopancreas	57,300–88,100 FW	19
Tail muscle	1910–2670 FW	19
Control area		
Sediments	<8220 DW	19
American lobster		
Hepatopancreas	1185 FW	19
Tail muscle	216 FW	19
Black River, Ohio, contaminated area, total PAHs		
Sediments	6700 DW	20
Brown bullhead, <i>Ictalurus nebulosus</i>		
Water	660 FW	20
	153 FW	20

^a 1, Harrison et al. 1975; 2, Lee and Grant 1981; 3, Suess 1976; 4, Herrmann and Hubner 1984; 5, Edwards 1983; 6, Larsson and Sahlberg 1982; 7, Humason and Gadbois 1982; 8, Marcus and Stokes 1985; 9, Mix 1982; 10, Mix and Schaffer 1983b; 11, Brown and Pancirov 1979; 12, Smith et al. 1984; 13, Stegeman 1981; 14, Mix and Schaffer 1983a; 15, Lawrence and Weber 1984a; 16, USEPA 1980; 17, Barnett 1976; 18, Black et al. 1981; 19, Sirota et al. 1983; 20, West et al. 1984; 21, Akpan et al. 1994; 22, Lodovici and Akpan 1997; 23, Hellou et al. 1994a; 24, McDonald et al. 1992; 25, Al-Yakoob et al. 1994; 26, Nicholson et al. 1994; 27, McDonald et al. 1995; 28, van der Oost et al. 1994; 29, Miles and Ohlendorf 1993; 30, Hellou et al. 1990; 31, Law and Whinnett 1992; 32, Lake et al. 1995; 33, Baumann and Harshbarger 1995; 34, Hellou et al. 1994c; 35, Kayal and Connell 1995; 36, Godley et al. 1998; 37, Hendricks et al. 1998; 38, Baumard et al. 1998.

25.4 LETHAL AND SUBLETHAL EFFECTS

25.4.1 General

A wide variety of PAH-caused adverse biological effects have been reported in numerous species of organisms under laboratory conditions, including effects on survival, growth, reproduction, metabolism, and especially tumor formation. Inter- and intraspecies responses to carcinogenic PAHs were quite variable, and were significantly modified by many chemicals, including other PAHs, that are weakly carcinogenic or noncarcinogenic. Until these interaction effects are clarified, the results of single-substance laboratory tests may be extremely difficult to apply to field situations of suspected PAH contamination.

25.4.2 Fungi

Fungal degradation of PAHs may be important in the detoxification and elimination of PAHs in the environment. The fungus *Cunninghamella elegans*, for example, inhibited the mutagenic activity of benzo[*a*]pyrene, 3-ethylcholanthrene, benz[*a*]anthracene, and 7,12-dimethylbenz[*a*]anthracene, as judged by results of the Ames test using *Salmonella typhimurium* (Cerniglia et al. 1985). The rate of decrease in mutagenic activity in bacterial cultures incubated with PAHs was coincident with the rate of increase in fungal metabolism. *C. elegans* metabolized PAHs to dihydrodiols, phenols, quinones, and dihydrodiol epoxides, and to sulfate, glucuronide, and glucoside conjugates of these primary metabolites in a manner similar to that reported for mammalian enzyme systems, suggesting

that this organism (and perhaps other fungi) is important in PAH metabolism and inactivation (Cerniglia et al. 1985).

25.4.3 Terrestrial Plants

Biological effects of PAHs on terrestrial vegetation have been reviewed by the USEPA (1980), Lee and Grant (1981), Wang and Meresz (1982), Edwards (1983), and Sims and Overcash (1983). In general, these authorities agreed on several points. First, plants and vegetables can absorb PAHs from soils through their roots and translocate them to other plant parts such as developing shoots. Uptake rates were governed, in part, by PAH concentration, PAH water solubility, soil type, and PAH physicochemical state (vapor or particulate). Lower-molecular-weight PAHs were absorbed by plants more readily than higher-molecular-weight PAHs. Under laboratory conditions, some plants concentrated selected PAHs above that of their immediate geophysical surroundings, but this has not been conclusively demonstrated in field-grown cultivated crops or other vegetation. Second, above-ground parts of vegetables, especially the outer shell or skin, contained more PAHs than underground parts, and this was attributed to airborne deposition and subsequent adsorption. Externally deposited PAHs in vegetables were difficult to remove with cold-water washings; not more than 25% were removed from lettuce, kale, spinach, leeks, and tomatoes using these procedures. Third, PAH-induced phytotoxic effects were rare; however, the database on this subject is small. Fourth, most higher plants can catabolize benzo[a]pyrene, and possibly other PAHs, but metabolic pathways have not been clearly defined. Finally, the biomagnification potential of vegetation in terrestrial and aquatic food chains needs to be measured; this work should be conducted with a variety of PAHs in both field and laboratory experiments.

Some plants contain chemicals known to protect against PAH effects. Certain green plants contain ellagic acid, a substance that can destroy the diol epoxide form of benzo[a]pyrene, inactivating its carcinogenic and mutagenic potential (Edwards 1983). PAHs synthesized by plants may act as plant growth hormones (Edwards 1983). Some vegetables, such as cabbage, brussels sprouts, and cauliflower, contain naturally occurring antineoplastic compounds, including benzyl isothiocyanate and phenethyl isothiocyanate. These compounds are known to inhibit mammary cancers, stomach tumors, and pulmonary edemas induced in rats by benzo[a]pyrene and 7,12-dimethylbenz[a]anthracene (USEPA 1980). Decreased activation of carcinogens has also been demonstrated in animals fed diets that were high in protein, low in carbohydrate, and containing adequate choline; the reverse was observed in diets high in carbohydrate, low in protein, or containing certain organophosphorus insecticides, piperonyl butoxide, carbon tetrachloride, nickel carbonyl, or tin (USEPA 1980). In cases where dietary constituents can alter the metabolism of foreign agents, such as PAHs, the anticarcinogenic effect may result from an alteration of steady-state levels of activated vs. detoxified metabolites (USEPA 1980). The implications of these observations to herbivorous wildlife are unknown at present.

25.4.4 Aquatic Biota

PAHs vary substantially in their toxicity to aquatic organisms ([Table 25.5](#)). In general, toxicity increases as molecular weight increases (although high-molecular-weight PAHs have low acute toxicity, perhaps due to their low solubility in water) and with increasing alkyl substitution on the aromatic ring. Toxicity is most pronounced among crustaceans and least among teleosts (Neff 1979) ([Table 25.5](#)). In all but a few cases, PAH concentrations that are acutely toxic to aquatic organisms are several orders of magnitude higher than concentrations found in even the most heavily polluted waters (Neff 1979). Sediments from polluted regions, however, may contain PAH concentrations similar to those that are acutely toxic, but their limited bioavailability would probably render them substantially less toxic than PAHs in solution (Neff 1979).

Several PAHs accumulated by aquatic organisms during exposure are severely toxic when the contaminated organisms were exposed to sunlight or ultraviolet radiation (Nagpal 1994). PAHs that have exhibited photoinduced toxicity in fishes, daphnids, frogs, or algae and macrophytes at PAH concentrations well below their aqueous solubility due to simultaneous UV radiation exposure include fluoranthene, pyrene, benzo[a]pyrene, benz[a]anthracene, acridine, and benz[a]fluorene (Gala and Giesy 1994; Hatch and Burton 1998; Walker et al. 1998). Anthracene, for example, is not acutely toxic to fish and algae within its aqueous solubility range (about 35 µg/L at 25°C) unless the exposure is performed in the presence of ultraviolet radiation from simulated or natural sunlight. Anthracene is phototoxic in this concentration range to mosquito larvae, bluegills, and leopard frog embryos (McCloskey and Oris 1991, 1993). Anthracene is phototoxic to alga (*Selenastrum capricornutum*), with growth inhibition of 50% at 16.1 µg/L in 28 h and 10% inhibition at 8.3 µg/L (Gala and Giesy 1994). PAH phototoxicity is due to PAH concentrations in tissues, length of exposure to radiation and absorption, efficiency of the photoconversion process, and the probability of the excited intermediary reacting with a target molecule (Nagpal 1994). Studies with larvae of the bullfrog (*Rana catesbeiana*) and phototoxic effects of fluoranthene suggest that behavioral and histopathological endpoints — especially skin histology — are more sensitive than survival (Walker et al. 1998). Sediments contaminated with complex mixtures of PAHs also show enhanced toxicity to aquatic species under conditions of ultraviolet light representative of sunlight. In one case, interstitial sediment pore water from sediments near an oil refinery discharge was toxic to a freshwater oligochaete worm (*Lumbriculus variegatus*) following exposure to UV light, but worms exposed to the same pore water without UV treatment were unaffected (Kosian et al. 1998). Electron density shape features have been used to model photoinduced toxicity of 16 PAHs to duckweed (*Lemna gibba*), with good correlation between detailed molecular shape features and toxicity (Mezey et al. 1998).

Table 25.5 Toxicity of Selected PAHs to Aquatic Organisms

PAH Compound, Organism, and Other Variables	Concentration in Medium (g/L)	Effect ^a	Reference ^b
ACENAPHTHENE			
Algae, <i>Selenastrum capricornutum</i>	520	LC50 (96 h)	6
Brown trout, <i>Salmo trutta</i>	580	LC50 (96 h)	6
Fathead minnow, <i>Pimephales promelas</i>	610	LC50 (96 h)	6
ANTHRACENE			
Bluegill, <i>Lepomis macrochirus</i>			
Dissolved oxygen (DO) of 6.9 mg/L and 20°C	1.3	LC50 (96 h)	7
DO 6.9 mg/L, 30°C	3.7	LC50 (96 h)	7
DO 5 mg/L, 30°C	6.8	LC50 (96 h)	7
DO 5 mg/L, 20°C	7.5	LC50 (96 h)	7
DO 8.1 mg/L, 20°C	8.0	LC50 (96 h)	7
DO 8.1 mg/L, 30°C	8.3	LC50 (96 h)	7
Daphnid, <i>Daphnia pulex</i>	750	50% immobilized in 48 h	6
BENZ[a]ANTHRACENE			
Bluegill, <i>Lepomis macrochirus</i>	1000	LC87 (6 m)	1
7,12-DIMETHYLBENZ[a]ANTHRACENE			
Rainbow trout, <i>Oncorhynchus mykiss</i> ; juveniles; exposed for 20 h and examined for tumors 33 weeks later	1000	Stomach tumor frequency of 42–66% vs. none in controls. Liver tumor frequency was 50% vs. <0.1% in controls	10

Table 25.5 (continued) Toxicity of Selected PAHs to Aquatic Organisms

PAH Compound, Organism, and Other Variables	Concentration in Medium (g/L)	Effect ^a	Reference ^b
Minnows, <i>Poeciliopsis</i> spp.			
Juveniles	250	LC0 (20 h)	3
Juveniles	500	LC100 (20 h)	3
DIBENZ[a,h]ANTHRACENE			
Sandworm	>1000	LC50 (96 h)	2
METHYLANTHRACENE			
Daphnid, <i>Daphnia pulex</i>	96	50% immobilized in 48 h	6
9-METHOXYANTHRACENE			
Daphnid, <i>Daphnia pulex</i>	400	50% immobilized in 48 h	6
BENZO[a]PYRENE			
Sandworm, <i>Neanthes arenaceodentata</i>	>1000	LC50 (96 h)	2
CHRYSENE			
Sandworm	>1000	LC50 (96 h)	2
FLUORANTHENE			
Amphibians; embryos and larvae; embryos exposed from early development through hatching under artificial ultraviolet light; newly hatched larvae were exposed outdoors in varying sunlight intensity levels			
Spotted salamander, <i>Ambystoma maculatum</i>	247	LC50 (288 h), embryos	8
Northern leopard frog, <i>Rana pipiens R. pipiens</i>	366	LC50 (96 h), embryos	8
	25	50% dead in 1.4 h in full sun vs. 50% dead in controls in 15.7 h	8
South African clawed frog, <i>Xenopus laevis</i>	193	LC50 (96 h), embryos	8
<i>X. laevis</i>	5	LC50 in 6.7 h in full sun vs. 50% dead in controls in 19 h	8
Bullfrog, <i>Rana catesbeiana</i> ; larvae; sublethal concentration	10	Skin necrosis in 96 h	9
<i>R. catesbeiana</i> , as above	40	Hyperactivity after 96 h under simulated UV radiation	9
<i>R. catesbeiana</i> , as above	60	Adverse effect on locomotion after 48 h under simulated UV radiation	9
Sandworm	500	LC50 (96 h)	2
FLUORENE			
Grass shrimp, <i>Palaemonetes pugio</i>	320	LC50 (96 h)	2
Bluegill	500	LC12 (30 d)	4
Amphipod, <i>Gammarus pseudolimnaeus</i>	600	LC50 (96 h)	4
Rainbow trout, <i>Oncorhynchus mykiss</i>	820	LC50 (96 h)	4
Bluegill	910	LC50 (96 h)	4

Table 25.5 (continued) Toxicity of Selected PAHs to Aquatic Organisms

PAH Compound, Organism, and Other Variables	Concentration in Medium (g/L)	Effect ^a	Reference ^b
Sandworm	1000	LC50 (96 h)	2
Sheepshead minnow, <i>Cyprinodon variegatus</i>	1680	LC50 (96 h)	2
Snail, <i>Mudalia potosensis</i>	5600	LC50 (96 h)	4
Mayfly, <i>Hexagenia bilineata</i>	5800	LC50 (120 h)	4
Fathead minnow, <i>Pimephales promelas</i>	>100,000	LC0 (96 h)	4
NAPHTHALENE			
Copepod, <i>Eurytemora affinis</i>	50	LC30 (10 d)	2
Pink salmon, <i>Oncorhynchus gorbuscha</i> , fry	920	LC50 (24 h)	2
Dungeness crab, <i>Cancer magister</i>	2000	LC50 (96 h)	5
Grass shrimp	2400	LC50 (96 h)	2
Sheepshead minnow	2400	LC50 (24 h)	2
Brown shrimp, <i>Penaeus aztecus</i>	2500	LC50 (24 h)	2
Amphipod, <i>Elasmopus pectenircus</i>	2680	LC50 (96 h)	2
Coho salmon, <i>Oncorhynchus kisutch</i> , fry	3200	LC50 (96 h)	5
Sandworm	3800	LC50 (96 h)	2
Mosquitofish, <i>Gambusia affinis</i>	150,000	LC50 (96 h)	2
1-METHYLNAPHTHALENE			
Dungeness crab, <i>Cancer magister</i>	1900	LC50 (96 h)	2
Sheepshead minnow	3400	LC50 (24 h)	2
2-METHYLNAPHTHALENE			
Grass shrimp	1100	LC50 (96 h)	5
Dungeness crab	1300	LC50 (96 h)	5
Sheepshead minnow	2000	LC50 (24 h)	2
TRIMETHYLNAPHTHALENES			
Copepod, <i>Eurytemora affinis</i>	320	LC50 (24 h)	2
Sandworm	2000	LC50 (96 h)	2
PHENANTHRENE			
Rainbow trout	30	LC50 (96 h)	6
Grass shrimp	370	LC50 (24 h)	2
Sandworm	600	LC50 (96 h)	1
1-METHYLPHENANTHRENE			
Sandworm	300	LC50 (96 h)	1

^a m = months, d = days, h = hours.^b 1, USEPA 1980; 2, Neff 1979; 3, Schultz and Schultz 1982; 4, Finger et al. 1985; 5, Neff 1985; 6, Nagpal 1994; 7, McCloskey and Oris 1991; 8, Hatch and Burton 1998; 9, Walker et al. 1998; 10, Donohoe et al. 1998.

A growing literature exists on uptake, retention, and translocation of PAHs by aquatic plants and animals. Authorities generally agree that most species of aquatic organisms studied to date rapidly accumulate (i.e., bioconcentrate) PAHs from low concentrations in the ambient medium. Uptake of PAHs is highly species specific, being higher in algae, molluscs, and other species that are incapable of metabolizing PAHs. Bioconcentration factors (BCF) tend to increase as the molecular weight of the PAH increases, with increasing octanol/water partition coefficient values, with time until approaching an apparent equilibrium level (sometimes within 24 h), and with

increases in dissolved organic matter in the medium, lipid content of organism, and a variety of endogenous and exogenous factors (Jackim and Lake 1978; Southworth et al. 1978; Lee and Grant 1981; Neff 1982a; Ma et al. 1998). BCF values have been determined for selected PAHs and aquatic organisms (Table 25.6). Additional BCF data for aquatic biota are available for plants (Dobroski

Table 25.6 PAH Bioconcentration Factors (BCF) for Selected Species of Aquatic Organisms

PAH Compound, Whole Organism, and Other Variables	Exposure Period ^a	BCF	Reference ^b
ANTHRACENE			
Cladoceran, <i>Daphnia magna</i>	60 m	200	1
Fathead minnow, <i>Pimephales promelas</i>	2–3 d	485	2
Cladoceran, <i>Daphnia pulex</i>	24 h	760–1200	1–4
Mayfly, <i>Hexagenia</i> sp.	28 h	3500	1
Rainbow trout, <i>Oncorhynchus mykiss</i>	72 h	4400–9200	5
Guppy, <i>Poecilia reticulata</i> , kidney and GI tract	7 d	4550	18
9-METHYLANTHRACENE			
Cladoceran, <i>Daphnia pulex</i>	24 h	4583	4
BENZ[a]ANTHRACENE			
Cladoceran, <i>Daphnia pulex</i>	24 h	10,109	3
BENZO[a]PYRENE			
Teleosts, 3 spp., muscle	1–96 h	0.02–0.1	1
Clam, <i>Rangia cuneata</i>	24 h	9–236	1, 6
Bluegill, <i>Lepomis macrochirus</i>	4 h	12	7
Atlantic salmon, <i>Salmo salar</i> , egg	168 h	71	8
Midge, <i>Chironomus riparius</i> , larvae	8 h	166	7
Rainbow trout, liver	10 d	182–920	9
American oyster, <i>Crassostrea virginica</i>	14 d	242	1
Northern pike, <i>Esox lucius</i>			
Bile and gallbladder	3.3 h	3974	10
"	19.2 h	36,656	10
"	8.5 d	82,916	10
"	23 d	53,014	10
Liver	3.3 h	259	10
"	19.2 h	578	10
"	8.5 d	1376	10
"	23 d	619	10
Gills	3.3 h	283	10
"	19.2 h	382	10
"	8.5 d	372	10
"	23 d	213	10
Kidney	3.3 h	192	10
"	19.2 h	872	10
"	8.5 d	1603	10
Other tissues	3.3 h–23 d	<55	10
Grunion, <i>Leuresthes tenuis</i> ; newly fertilized eggs	15 d	249–466	17
Mosquitofish, <i>Gambusia affinis</i>	3 d	930	11
Bluegill			
No dissolved humic material (DHM)	48 h	2657	12
20 mg DHM/L	48 h	225	12
Cladoceran, <i>Daphnia magna</i>	6 h	2837	7
Alga, <i>Oedogonium cardicacum</i>	3 d	5258	11
Periphyton, mostly diatoms	24 h	9600	7
Mosquito, <i>Culex pipiens quinquefasciatus</i>	3 d	11,536	11

Table 25.6 (continued) PAH Bioconcentration Factors (BCF) for Selected Species of Aquatic Organisms

PAH Compound, Whole Organism, and Other Variables	Exposure Period ^a	BCF	Reference ^b
Sand sole, <i>Psettichthys melanostictus</i> , egg	6 d	21,000	13
Snail, <i>Physa</i> sp.	3 d	82,231	11
Cladoceran, <i>Daphnia pulex</i>	3 d	134,248	11
CHRYSENE			
Clam, <i>Rangia cuneata</i>	24 h	8	6
Mangrove snapper, <i>Lutjanus griseus</i>			
Liver	4 d	83–104	14
Liver	20 d	258–367	14
Pink shrimp, <i>Penaeus duorarum</i>			
Cephalothorax	28 d	248–361	14
Cephalothorax	28 d+28 d after exposure	21–48	14
Abdomen	28 d	84–199	14
Abdomen	28 d+28 d after exposure	22–91	14
FLUORANTHENE			
Rainbow trout, liver	21 d	379	9
FLUORENE			
Bluegill	30 d	20–1800	15
Guppy, embryos	7 d	1050	18
NAPHTHALENE			
Clam, <i>Rangia cuneata</i>	24 h	6	6
Sandworm, <i>Neanthes arenaceodentata</i>	3–24 h	40	16
Sandworm	24 h+300 h posttreatment	ND	16
Atlantic salmon, egg	168 h	44–83	8
Cladoceran, <i>Daphnia pulex</i>	24 h	131	4
Crustaceans, 3 spp.	72 h	195–404	6
Bluegill	24 h	310	12
DIMETHYLNAPHTHALEMES			
Crustaceans, 3 spp.	72 h	967–1625	6
PERYLENE			
Cladoceran, <i>Daphnia pulex</i>	24 h	7191	4
PHENANTHRENE			
Clam, <i>Rangia cuneata</i>	24 h	32	6
Cladoceran, <i>Daphnia pulex</i>	24 h	325	4
PYRENE			
Rainbow trout, liver	21 d	69	9
Cladoceran, <i>Daphnia pulex</i>	24 h	2702	4
Guppy, liver	7 d	11,300	18

^a m = minutes, h = hours, d = days.

^b 1, USEPA 1980; 2, Southworth 1979; 3, Southworth et al. 1978; 4, Neff 1985; 5, Linder et al. 1985; 6, Neff 1979; 7, Leversee et al. 1981; 8, Kuhnhold and Busch 1978; 9, Gerhart and Carlson 1978; 10, Balk et al. 1984; 11, Lu et al. 1977; 12, McCarthy and Jimenez 1985; 13, Hose et al. 1982; 14, Miller et al. 1982; 15, Finger et al. 1985; 16, Neff 1982a; 17, Hose and Puffer 1984; 18, de Voogt et al. 1991.

and Epifanio 1980; Boyle et al. 1984), crustaceans (Southworth 1979; Sirota and Uthe 1981; Fox and Rao 1982; Neff 1982a; Williams et al. 1985), tunicates (Baird et al. 1982), molluscs (Jackim and Wilson 1979; Dobroski and Epifanio 1980; Neff 1982a), annelids (Ma et al. 1998; Penry and Weston 1998), and fishes (Southworth 1979; Neff 1982a; Stoker et al. 1984). Algal accumulation of benzo[a]pyrene increased linearly in a 24-h exposure period, and correlated positively with surface area (Leversee et al. 1981), suggesting adsorption rather than absorption. Algae readily transform benzo[a]pyrene to oxides, peroxides (Kirso et al. 1983), and dihydrodiols (Warshawsky et al. 1983). Photosynthetic rates of algae, and presumably PAH accumulations, were significantly modified by light regimens. For reasons still unexplained, algae grown in "white" light (major energy in blue-green portion of the spectrum) were more sensitive to benzo[a]pyrene than were cultures grown in "gold" light (Warshawsky et al. 1983; Schoeny et al. 1984).

Accumulation by American oysters (*Crassostrea virginica*) and clams (*Rangia cuneata*) of naphthalene, phenanthrene, fluorene, and their methylated derivatives increased with increasing methylation and PAH molecular weight; uptake was more rapid under conditions of continuous flow than in static tests (Neff et al. 1976). When returned to PAH-free seawater, molluscs released PAHs to nondetectable levels in about 60 days, with high-molecular-weight PAHs depurated more slowly than low-molecular-weight compounds. Brown shrimp (*Penaeus aztecus*) and longnose killifish (*Fundulus similis*), which can metabolize PAHs, lost PAHs more quickly than clams and oysters, which apparently lack the detoxifying enzymes (Neff et al. 1976). Pink shrimp (*Penaeus duorarum*) exposed to 1.0 µg chrysene/L for 2 days and then transferred to unpolluted seawater for an additional 28 days contained concentrations of chrysene (91 µg/kg fresh weight in abdomen, 48 µg/kg in cephalothorax) that were considered potentially hazardous to human consumers over extended periods (Miller et al. 1982). Eggs of the sand sole (*Psettidichthys melanostictus*) exposed to 0.1 µg benzo[a]pyrene/L for 5 days showed reduced and delayed hatch and, when compared to controls, produced larvae with high accumulations (2.1 mg/kg fresh weight) and gross abnormalities, such as twinning and tissue overgrowths, in 50% of the test larvae (Hose et al. 1982). Naphthalene and benzo[a]pyrene were rapidly accumulated from the medium by three species of California marine teleosts; loss was rapid, being >90% for naphthalene in 24 h, and 20% (muscle), to 90% (gill) for benzo[a]pyrene in a similar period (Lee et al. 1972). Phenanthrene is metabolized by many species of aquatic organisms, including fish. A marine flounder *Platichthys flesus*, given a single oral dose of 0.7 mg phenanthrene/kg body weight, contained elevated phenanthrene concentrations in lipids, melanin-rich tissues (such as skin), and the eye lens; most was eliminated within 2 weeks (Solbakken et al. 1984). Studies on uptake rates of radiolabeled phenanthrene by marine polychaetes (*Aberenicola pacifica*) from PAH-contaminated sediments of high or low organic content showed that rates increased when worms were acclimatized for 48 h to sediments of low organic content (Penry and Weston 1998). Different rates of accumulation and depuration of benzo[a]pyrene and naphthalene in bluegill (*Lepomis macrochirus*) and *Daphnia magna* have been documented by McCarthy and Jimenez (1985) and McCarthy et al. (1985). Benzo[a]pyrene accumulations in bluegill, for example, were 10 times greater than naphthalene, but benzo[a]pyrene is extensively metabolized, whereas naphthalene is not. Consequently, postexposure accumulations of naphthalene greatly exceeded that of the parent benzo[a]pyrene. Because the more hydrophobic PAHs, such as benzo[a]pyrene, show a high affinity for binding to dissolved humic materials and have comparatively rapid biotransformation rates, these interactions may lessen or negate bioaccumulation and food chain transfer of hydrophobic PAHs (McCarthy and Jimenez 1985; McCarthy et al. 1985).

Time to depurate or biotransform 50% of accumulated PAHs (T_b 1/2) varied widely. T_b 1/2 values for *Daphnia pulex* and all PAH compounds studied ranged between 0.4 and 0.5 h (Southworth et al. 1978). In rainbow trout given an intraarterial injection of 10 mg/kg BW of 2-methylnaphthalene, fluorene, or pyrene, the T_b 1/2 values ranged between 9.6 and 12.8 h; when route of exposure was intragastric and doses were 50 mg/kg BW, there was negligible uptake (Kennedy and Law 1990). For marine copepods and naphthalene, a T_b 1/2 of about 36 h was recorded (Neff 1982a).

For most marine bivalve molluscs, Tb 1/2 values ranged from 2 to 16 days. Some species, such as the hardshell clam (*Mercenaria mercenaria*), showed little or no depuration, while others, such as oysters, eliminated up to 90% of accumulated PAHs in 2 weeks — although the remaining 10% was released slowly and traces may remain indefinitely (Jackim and Lake 1978). Percent loss of various PAHs in American oysters (*Crassostrea virginica*), 7 days postexposure, ranged from no loss for benzo[a]pyrene to 98% for methylnaphthalene; intermediate were benz[a]anthracene (32%), fluoranthene (66%), anthracene (79%), dimethylnaphthalene (90%), and naphthalene (97%) (Neff 1982a). Teleosts and arthropods usually had low Tb 1/2 values. In bluegill, 89% loss of benzo[a]pyrene was recorded 4 h postexposure. For midge larvae, it was 72% in 8 h; and for daphnids, it was 21% in 18 h (Leversee et al. 1981).

The role of sediments in PAH uptake kinetics should not be discounted (Hontela et al. 1992; van der Weiden et al. 1993; Hellou et al. 1994b). Yellow perch (*Perca flavescens*) and northern pike (*Esox lucius*) exposed to sediments contaminated with up to 3.7 mg PAHs/kg had pituitary damage and were unable to increase serum cortisol in response to the acute stress of capture when compared to conspecifics from uncontaminated sites, suggesting that life-long exposure to PAHs will destabilize the cortisol-producing endocrine system (Hontela et al. 1992). Male winter flounders (*Pleuronectes americanus*) exposed to PAH-contaminated sediments at concentrations as low as 1 mg/kg for 4 months had altered mixed-function oxygenase levels and fat content of liver (Payne et al. 1988). Sediment-associated anthracene contributed about 77% of the steady-state body burden of this compound in the amphipod *Hyalella azteca* (Landrum and Scavia 1983). For benzo[a]pyrene and the amphipod *Pontoporeia hoyi*, the sediment source (including interstitial water) accounted for 53% in amphipods collected at 60 m, but only 9% at 23 to 45 m (Landrum et al. 1984). Benthos from the Great Lakes, such as oligochaete worms (*Limnodrilus* sp., *Stylodrilus* sp.) and amphipods (*Pontoporeia hoyi*), obtain a substantial fraction of their PAH body content from the water when sediment PAH concentrations are low. However, when sediment PAH concentrations are elevated, benthos obtain a majority of their PAHs from that source through their ability to mobilize PAHs from the sediment/pore water matrix; the high concentrations of phenanthrene, fluorene, benzo[a]pyrene, and other PAHs measured in these organisms could provide a significant source of PAHs to predator fish (Eadie et al. 1983). Great Lakes benthos appear to contain as much PAHs as the fine-grain fraction of the sediment that serves as their food, although overlying water or pore water appears to contribute a larger proportion of PAHs to the organism's body burden than do sediments (Eadie et al. 1984). Marine mussels (*Mytilus edulis*) and polychaete annelid worms (*Nereis virens*) exposed for 28 days to sediments heavily contaminated with various PAH compounds accumulated significant concentrations (up to 1000 times control levels) during the first 14 days of exposure, and little thereafter; during a 5-week postexposure period, depuration was rapid, with the more water-soluble PAHs excreted most rapidly; PAH levels usually remained above control values to the end of the postexposure period (Lake et al. 1985). English sole (*Pleuronectes vetulus*), during exposure for 11 to 51 days to PAH-contaminated sediments, showed significant accumulations of naphthalenes in liver (up to 3.1 mg/kg dry weight) after 11 days, with concentrations declining markedly thereafter; uptake of phenanthrene, chrysene, and benzo[a]pyrene was negligible during the first 7 days (Neff 1982a).

Selected studies on effects of benzo[a]pyrene to aquatic vertebrates are summarized in [Table 25.7](#) and demonstrate dose-dependent increases in death, enzyme disruption, liver and intestinal histopathology, carcinogenic and mutagenic effects, and behavioral deficits. In general, effects of benzo[a]pyrene were exacerbated by poor health, and by interactions with radiation or cadmium; effects were modified by route of exposure, diet, and organism age ([Table 25.7](#)). Exposure of fishes to BaP at early life stages has potential life-long significance. Embryonic sublethal doses of BaP are capable of inducing sublethal changes in behavior weeks or even months following hatching of salmon and trout (Ostrander et al. 1988, 1990).

Fluorene effects in freshwater pond ecosystems have been evaluated (Boyle et al. 1984, 1985; Finger et al. 1985). In ponds exposed to initial fluorene concentrations of 0.12 to 2.0 mg/L, Tb 1/2

Table 25.7 Benzo[a]pyrene Effects on Selected Aquatic Vertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
EUROPEAN EEL, <i>Anguilla anguilla</i>		
Seawater-adapted eels were exposed for 24 days to 0 or 5 µg cadmium/L, then given a single intraperitoneal (ip) injection of 20 mg BaP/kg BW and killed 24 h later	BaP alone produced glycogen depletion in liver; cadmium alone caused hepatic perivasicular fibrosis. Mixture produced complete disorganization of the hepatic parenchyma, including nuclear degeneration; higher increase in EROD activity (by 19-fold), BaP hydroxylase activity (by 71-fold), and cytochrome P-450 microsomal content by 2-fold	1
WHITE SUCKER, <i>Catostomus commersonii</i>		
Suckers with diseased bile ducts were given a single oral dose of BaP	Bile duct disease does not appear to restrict the metabolism and excretion of BaP. However, BaP metabolite levels were 57% higher in livers of affected suckers than controls, and may be due to bile retention within the diseased bile ducts	2
COMMON CARP, <i>Cyprinus carpio</i>		
Single ip injection of radiolabeled BaP	After 72 h, bile contained 25% of the total radioactivity; major BaP metabolites were glucuronides (54%), sulfates (12%), and unmetabolized BaP(14%). The potentially genotoxic metabolite BaP-7,8-dihydrodiol and its glucuronide represented 0.7 and 2.0%, respectively, of the bile radioactivity	3
Single ip injection of 99.5 µmol/kg BW of BaP, chrysene, fluoranthene, pyrene, or benzo[ghi]perylene	BaP and chrysene were most efficient in elevating EROD activities, cytochrome P-4501A protein levels, and total cytochrome P-450 content 1–14 days postinjection. Less pronounced increases were caused by fluoranthene and pyrene; B[ghi]PER did not affect these parameters	4
EUROPEAN SEA BASS, <i>Dicentrarchus labrax</i>		
Single ip injection of radiolabeled BaP	Half-time persistence (T _b 1/2) ranged from 2.2–2.4 days for liver, gills, gonads, and whole body; 2.9–5.1 days for muscle, spleen, gall bladder, and intestine; 6.5 days for kidney; and 12.4 days for fat	5
Immatures given single ip injection of 20 mg/kg BW, or by force feeding 20 mg/kg BW. Liver and intestine examined for pathology 17 days after treatment	Injection route of intoxication produced severe liver histopathology when compared to dietary route; intestinal histopathology observed with dietary route but not with injection route	6
Force feeding radiolabeled BaP to immatures; single administration	Gallbladder had 85% of radioactivity. T _b 1/2 values were 0.8 days for liver, 3.3 days for intestine, 3.5 days for gallbladder, and 8.2 days for liver	7
Fed diets containing fish oil vs. no fish oil diet for 5 months, then given single ip injection of BaP. Hepatic transformation enzymes measured 14 days postinjection	Diets rich in fish oils produced marked increases in activities of P-450 cytochromes, 7-EROD, and other enzyme activities; bass fed diets devoid of fish oil had lower microsomal enzyme activities	8
GIZZARD SHAD, <i>Dorosoma cepedianum</i>		
Single ip injection equivalent to 0, 0.1, 1, 10, or 50 mg BaP/kg BW and killed 72 h later	Maximum EROD activity was reached in the 10 and 50 mg/kg groups; no effect on EROD activity at 1 mg/kg BW and lower	9
Held for 10–20 days in water containing 0, 0.14, 0.24, 0.44, or 0.76 µg BaP/L	After 10 days, no effect on EROD enzyme activity at 0.24 µg/L and lower; EROD activity significantly elevated at 0.44 µg/L and higher. Concentration of parent BaP in whole fish after 20 days ranged from 20 µg/kg FW in the 0.14 µg/L group to 26.5 µg/kg FW in the 0.76 µg/L group	9

Table 25.7 (continued) Benzo[a]pyrene Effects on Selected Aquatic Vertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
MOSQUITOFISH, <i>Gambusia affinis</i>		
Exposed for 48 h in water containing 1–100 µg BaP/L	Dose-dependent increase in liver BaP monooxygenase activity; adverse effect on liver DNA at high dose	10
BROWN BULLHEAD, <i>Ictalurus nebulosus</i>		
Subadults given single ip injection of radiolabeled BaP and killed 72 h later	Biliary radioactivity accounted for 16% of the radioactivity; the potentially genotoxic metabolite BaP-7,8-dihydrodiol accounted for 3% of the bile radioactivity. Other accumulation sites were muscle, liver, and kidney	11
Adults given single ip injection of 0, 5, 25, or 125 mg BaP/kg BW and observed for 18 months	At 18 months, dose-dependent changes in liver pigmentation; no evidence of long-term DNA alterations; no neoplasms detected	12
BLUEGILL, <i>Lepomis macrochirus</i>		
Held for 40 days in 1 µg BaP/L, then for 45 days in uncontaminated media	Hypomethylation, as judged by loss of 5-methyl deoxycytidine content from DNA, occurred shortly after BaP exposure and continued upon termination of exposure conditions. Onset and persistence of hypomethylation were correlated with other types of DNA-damaging events, including strand breaks and DNA adduct formation	13
Chironomids (<i>Chironomus riparius</i>) held for 72 h on sediments with 47–4040 µg BaP/kg contained a maximum of 6030 µg BaP/kg DW; chironomids were fed to bluegills for 96 h	BaP was not detectable in muscle and gut, indicating that BaP on sediments may be mobilized and made available to benthic invertebrates and fish but that the process was highly inefficient with minor biomagnification; a similar case is made for fluoranthene	14
SUNFISH, <i>Lepomis</i> spp. hybrids		
Single ip injection of 8 mg BaP/kg BW and killed 4–5 days later	Hepatotoxicity. Decreased glutathione S-transferase activity in liver	15
RAINBOW TROUT, <i>Oncorhynchus mykiss</i>		
Juveniles given single intramuscular (im) injection of radiolabeled BaP	After 48 h, liver DNA and RNA contained 1–2.4% of administered dose; a similar case is made for 7,12-dimethylbenz[a]anthracene	16
Two days prior to hatch fertilized eggs were given a single transchorionic injection of 0.09–18.0 µg BaP/egg, equivalent to 1.2–197.8 mg BaP/kg FW egg. Mortality and neoplasms documented over the next 12 months	Control mortality ranged between 6.5 and 10%; mortality in BaP-treated fish ranged between 40 and 78% in a dose-dependent manner. Liver neoplasm frequency in controls at age 1 year was 1.8%; for the 4.5–9.0-µg groups (49.5–91.0 mg/kg), these values ranged between 5 and 6%; for the 18-µg group (197.8 mg/kg FW), the liver neoplasm frequency was 16% at age 12 months after a single-dose exposure as embryos	17
Newly fertilized embryos were incubated in water containing 0, 0.08, 0.2, 0.4, 1.5, 2.4, or 3.0 µg BaP/L. Alevins examined	Histologic and skeletal abnormalities in all BaP-exposed groups; depressed mitotic rates in retina and brain in groups exposed to 0.08 µg/L and higher; muscle necrosis in all groups exposed to 0.2 µg/L and higher; microphthalmia was observed in 17% of BaP-treated trout	18
Subadults exposed to 0.4 or 1.2 µg BaP/L for 30 days	No DNA adducts detected in liver	19
Subadults exposed to 0.5 µg BaP/L for 15 days then a pulse of 60 µg/L which naturally declined to 2.0 µg/L for another 15 days	Liver DNA adducts detected	19

Table 25.7 (continued) Benzo[a]pyrene Effects on Selected Aquatic Vertebrates

Organism, Dose, and Other Variables	Effect	Reference^a
Subadults given single ip injection of 20 mg/kg BW and killed after 7 days	No DNA adducts found in liver	19
Subadults given two ip injections of 25 mg/kg BW separated by 7 days and killed 14 days after the second injection	DNA adducts found in liver	19
Subadults fed diets for 6 days containing either 58 or 288 µg BaP daily, equivalent to 43 mg/kg BW or 216 mg/kg BW	Liver DNA adducts detected in both cases	19
Embryos exposed for 24 h to 25 mg BaP/L, one week prior to hatch	No effect on hatch, but alevins showed decreased tendency to orient upstream	20
COHO SALMON, <i>Oncorhynchus kisutch</i>		
Fertilized eggs exposed to 7, 10, or 25 mg BaP/L for 24 h at 1 week prior to hatch or 24 h after fertilization	BaP was easily accumulated and rapidly lost. Altered hatching rate and reduced survival at higher concentrations. Significant behavioral alterations in the months following hatching, including difficulty in upstream orientation, swimming, and foraging ability; fry were the most sensitive stage	21, 22
GULF TOADFISH, <i>Opsanus tau</i>		
Isolated hepatocytes acclimatized to 18 or 28°C, then exposed to BaP at 18, 23, or 28°C for about 2 h	Dose-dependent increase in metabolite production. Rapid metabolism of BaP independent of temperature	23
Isolated gill cells acclimatized to either 18 or 28°C for 3 weeks and exposed for 8 h to 1–100 mg BaP/L at incubation temperatures of 18, 23, and 28°C	Accumulation followed a dose-concentration gradient; uptake rate was higher for cells acclimatized to 18°C than those acclimatized to 28°C at all incubation temperatures. When cells were exposed to BaP at the respective acclimatization temperatures, uptake rates were similar	24
NILE TILAPIA, <i>Oreochromis niloticus</i>		
Single ip injection, various doses	Dose-dependent reduction in pronephros cell counts	25
MEDAKA, <i>Oryzias latipes</i>		
Exposed to approximately 5, 40, or 200 µg BaP/L for 6 h, once weekly, for up to 4 weeks; 6–10-day-old fish	Liver neoplasms at intermediate and high concentration exposures	26
NEWT, <i>Pleurodeles waltli</i>		
Embryos and larvae exposed to visible light alone, ultraviolet radiation alone, BaP alone at 12.5–500 µg/L, or combinations	Visible light alone, UV radiation alone, or BaP alone had no toxic effects. Genotoxic effects were observed at 500 µg BaP/L plus visible light, or 25 µg BaP/L plus UV radiation	27
WINTER FLOUNDER, <i>Pleuronectes americanus</i>		
Single oral dose of radiolabeled BaP and killed 8–96 h after dosing	After 8 h, 8.1% of the original dose administered was in intestine, 3.9% in blood, 1.6% in liver, 0.6% in bile, and <0.01% in urine. After 96 h, these values were 5.1% in bile, 1.1% in liver, 1.2% in intestine, and lesser amounts in blood, urine, and other tissues	28
ENGLISH SOLE, <i>Pleuronectes vetulus</i>		
Single ip injection of 5 mg/kg BW	Rapid increase in certain liver xenobiotic metabolizing enzymes (AHH), but no increase in GSH and epoxide hydrolase — even up to 42 days after exposure	29

Table 25.7 (continued) Benzo[a]pyrene Effects on Selected Aquatic Vertebrates

Organism, Dose, and Other Variables	Effect	Reference ^a
GUPPY, <i>Poecilia reticulata</i> Exposed to approximately 4, 47, or 270 µg BaP/L for 6 h, once weekly for 2–4 weeks	Hepatic neoplasms at intermediate and high concentration exposures; 7,12-dimethylbenz[a]-anthracene was more potent than BaP, and medakas were more sensitive than guppies	26
TOPMINNOW, <i>Poeciliopsis</i> spp. 1 mg BaP/L for 48 or 90 h	Induction of P-4501A proteins in multiple cell types in many organs with some sites of induction (olfactory epithelium) related to exposure route	30
GILTHEAD SEABREAM, <i>Sparus aurata</i> 25 mg BaP/kg BW by ip injection daily for 5 consecutive days	A 2- to 3-fold increase in 7-EROD activity of liver microsomes	31

^a 1, Lemaire-Gony and Lemaire 1992; 2, Smith et al. 1992; 3, Steward et al. 1991; 4, van der Weiden et al. 1994; 5, Lemaire et al. 1990; 6, Lemaire et al. 1992a; 7, Lemaire et al. 1992b; 8, Lemaire et al. 1992c; 9, Levine et al. 1994; 10, Batel et al. 1985; 11, Steward et al. 1990; 12, Grady et al. 1992; 13, Shugart 1990; 14, Clements et al. 1994; 15, Oikari and Jimenez 1992; 16, Schnitz and O'Connor 1992; 17, Black et al. 1988; 18, Hose et al. 1984; 19, Potter et al. 1994; 20, Ostrander et al. 1990; 21, Ostrander et al. 1989; 22, Ostrander et al. 1988; 23, Gill and Walsh 1990; 24, Kennedy and Walsh 1994; 25, Holladay et al. 1996; 26, Hawkins et al. 1990; 27, Fernandez and L'Haridon 1994; 28, McElroy and Colarusso 1988; 29, Collier and Varanasi 1991; 30, Smolowitz et al. 1992; 31, Arinc and Sen 1994.

values in water ranged from 6 to 11 days. Ten weeks after fluorene introduction, little degradation had occurred in the organic bottom sediments; fluorene residues were present in fish, invertebrates, and rooted submerged macrophytes. Studies with fingerling bluegills showed that 0.062 mg fluorene/L adversely affected their ability to capture chironomid prey, 0.12 mg/L reduced growth, and 1.0 mg fluorene/L increased their vulnerability to predation by largemouth bass (*Micropterus salmoides*). The authors concluded that fluorene, at concentrations well below its solubility and at levels that could realistically occur in the environment, represents a potential hazard to aquatic organisms.

Large interspecies differences in ability to absorb and assimilate PAHs from food have been reported. For example, crustaceans (Neff 1982a; McElroy and Colarusso 1988) and fish (Maccubbin et al. 1985; Malins et al. 1985a, 1985b; McElroy and Colarusso 1988) readily assimilated PAHs from contaminated food, whereas molluscs and polychaete annelids were limited (Neff 1982a). In all cases where assimilation of ingested PAHs was demonstrated, metabolism and excretion of PAHs were rapid (Neff 1982a). Thus, little potential exists for food chain biomagnification of PAHs (Southworth 1979; Dobroski and Epifanio 1980; Neff 1982a; Kayal and Connell 1995). In laboratory aquatic ecosystem studies, Lu et al. (1977) found that benzo[a]pyrene can be accumulated to high, and potentially hazardous, levels in fish and invertebrates. In the case of mosquitofish (*Gambusia affinis*), almost all of the accumulated benzo[a]pyrene was from its diet, with negligible accumulations from the medium. However, mosquitofish degraded benzo[a]pyrene about as rapidly as it was absorbed, in contrast to organisms such as snails (*Physa* sp.) which retained most (88%) of the accumulated benzo[a]pyrene for at least 3 days postexposure, presumably due to deficiencies in their mixed-function oxidase detoxication system (Lu et al. 1977). Benzo[a]pyrene, when administered to northern pike (*Esox lucius*) through the diet or the medium, followed similar pathways: entry via the gills or gastrointestinal system, metabolism in the liver, and excretion in the urine and bile (Balk et al. 1984). Benthic marine fishes exposed to naphthalene or benzo[a]pyrene, either in diet or through contaminated sediments, accumulated substantial concentrations in tissues and body fluids (Varanasi and Gmur 1981). The tendency of fish to metabolize PAHs extensively and rapidly may explain why benzo[a]pyrene, for example, is frequently undetected, or only detected in low concentrations in livers of fish from environments heavily contaminated with PAHs (Varanasi and Gmur 1980, 1981). Extensive metabolism of benzo[a]pyrene plus the presence of large

proportions of polyhydroxy metabolites in liver of English sole indicates the formation of reactive intermediates such as diol epoxides and phenol epoxides of benzo[*a*]pyrene, both of which are implicated in mammalian mutagenesis and carcinogenesis (Varanasi and Gmür 1981).

Cytotoxic, mutagenic, and carcinogenic effects of many PAHs are generally believed to be mediated through active epoxides formed by interaction with microsomal monooxygenases. These highly active arene oxides can interact with macromolecular tissue components and can be further metabolized or rearranged to phenols or various conjugates. They can also be affected by epoxide hydrolase to form dihydrodiols, which are precursors of biologically active diol epoxides — a group that has been implicated as ultimate carcinogens. Investigators generally agree that marine and freshwater fishes:

- Are as well equipped as mammals with liver PAH-metabolizing enzymes
- Rapidly metabolize PAHs by liver mixed-function oxidases, with little evidence of accumulation
- Translocate conjugated PAH metabolites to the gall bladder prior to excretion in feces and urine
- Have mixed-function oxidase degradation rates that are significantly modified by sex, age, diet, water temperature, dose-time relationships, and other variables.

In addition, many species of fishes can convert PAHs, benzo[*a*]pyrene for example, to potent mutagenic metabolites, but because detection of the 7,8-dihydrodiol-9,10-epoxide by analytical methods is difficult, most investigators must use biological assays, such as the Ames test, to detect mutagenic agents. The interaction effects of PAHs with inorganic and other organic compounds are poorly understood. Specific examples of the above-listed phenomena for PAH compounds and teleosts are documented for benzo[*a*]pyrene (Ahokas et al. 1975; Lu et al. 1977; Gerhart and Carlson 1978; Melius et al. 1980; Varanasi et al. 1980, 1984; Stegeman et al. 1982; Couch et al. 1983; Hendricks 1984; Melius 1984; Schoor 1984; Schoor and Srivastava 1984; Hendricks et al. 1985; Neff 1985; Fair 1986; von Hofe and Puffer 1986; Baumann and Whittle 1988; Ueng et al. 1994), 3-methylcholanthrene (Gerhart and Carlson 1978; Melius et al. 1980; Melius and Elam 1983; Schoor and Srivastava 1984; Neff 1985; Ueng et al. 1994), benz[*a*]anthracene, chrysene and pyrene (Gerhart and Carlson 1978; Gagne et al. 1995), fluoranthene (Baumann and Whittle 1988; Gagne et al. 1995), and 7,12-dimethylbenz[*a*]anthracene (Stegeman et al. 1982).

Baumann et al. (1982) summarized reports on increasing frequencies of liver tumors in wild populations of fish during the past decade, especially in brown bullhead (*Ictalurus nebulosus*) from the Fox River, Illinois (12% tumor frequency), in Atlantic hagfish (*Myxine glutinosa*) from Swedish estuaries (6%), in English sole from the Duwamish estuary, Washington (32%), and in tomcod (*Microgadus tomcod*) from the Hudson River, New York (25%). In all of these instances, significant levels of contaminants were present in the sediments, including PAHs. PAHs have been identified as genotoxic pollutants in sediments from the Black River, Ohio, where a high incidence of hepatoma and other tumors has been observed in ictalurid fishes (West et al. 1984, 1986). Reports of tumors in Great Lakes fish populations have been increasing. Tumors of thyroid, gonad, skin, and liver are reported, with tumor frequency greatest near areas contaminated by industrial effluents such as PAHs; liver tumors were common among brown bullhead populations at sites with large amounts of PAHs in sediments (Baumann 1984; Baumann and Whittle 1988). A positive relationship was finally established between sediment PAH levels and prevalence of liver lesions in English sole in Puget Sound, Washington (Malins et al. 1984; Varanasi et al. 1984), and sediment levels and liver tumor frequency in brown bullheads from the Black River, Ohio (Baumann and Harshbarger 1985; Black et al. 1985). Sediment PAH levels in the Black River, Ohio, from the vicinity of a coke plant outfall, were up to 10,000 times greater than those from a control location: concentrations were greater than 100 mg/kg for pyrene, fluoranthene, and phenanthrene; between 50 and 100 mg/kg for benz[*a*]anthracene, chrysene, and benzofluoranthenes; and between 10 and 50 mg/kg for individual naphthalenes, benzo[*e*]pyrene, benzo[*a*]pyrene, perylene, indeno[*1,2,3-cd*]pyrene, benzo[*g,h,i*]perylene, and anthanthrene (Baumann et al. 1982). Brown bullheads from this

location contained >1.0 mg/kg of acenaphthalene (2.4), phenanthrene (5.7), fluoranthene (1.9), and pyrene (1.1), and lower concentrations of heavier molecular weight PAHs. Bullheads also exhibited a high (33%) liver tumor frequency, which seemed to correspond to their PAH body burdens. Investigators concluded that the elevated frequency of liver neoplasia in Black River bullheads was chemically induced and was the result of exposure to PAHs (Baumann et al. 1982; Baumann and Harshbarger 1985).

Neoplasms in several species of fishes have been produced experimentally with 3-methylcholanthrene, acetylaminofluorene, benzo[a]pyrene, and 7,12-dimethylbenz[a]anthracene, with tumors evident 3 to 12 months postexposure (Couch and Harshbarger 1985; Hendricks et al. 1985; Hawkins et al. 1989). Under laboratory conditions, liver neoplasms were induced in two species of minnows (*Poeciliopsis* spp.) by repeated short-term exposures (6 h once a week, for 5 weeks) to an aqueous suspension of 5 mg/L of 7,12-dimethylbenz[a]anthracene. About 44% of the fish surviving this treatment developed hepatocellular neoplasms 6 to 9 months postexposure (Schultz and Schultz 1982). Guppies developed hepatic and extrahepatic neoplasms within 6 months following brief (6-h exposure, once weekly for 4 weeks) waterborne exposures to very low (20 to 35 µg/L) concentrations of 7,12-dimethylbenz[a]anthracene (Hawkins et al. 1989). Eastern mudminnows (*Umbra pygmaea*) kept in water containing up to 700 µg PAHs/L for 11 days showed increased frequencies of chromosomal aberrations in gills: 30% vs. 8% in controls (Prein et al. 1978). High dietary benzo[a]pyrene levels of 500 mg/kg produced significant elevations in hepatic mixed-function oxidase levels in rainbow trout after 9 weeks (Hendricks et al. 1985). Rainbow trout fed diets containing 1006 mg benzo[a]pyrene/kg for 12 months developed liver tumors (Couch et al. 1983). About 25% of rainbow trout kept on diets containing 1000 mg benzo[a]pyrene/kg for 18 months had histologically confirmed liver neoplasms as compared to 15% after 12 months, with no evidence of neoplasia in controls (Hendricks et al. 1985). Young English sole may activate and degrade carcinogenic PAHs, such as benzo[a]pyrene, to a greater extent than adults, but additional research is needed to determine if younger fish are at greater risk than older sole to PAH-induced toxicity (Varanasi et al. 1984). In English sole, a high significant positive correlation between PAH metabolites (1- and 3-hydroxy benzo[a]pyrene, hydroxy and dehydrodiol metabolites of pyrene and fluoranthene) in bile, and idiopathic liver lesions, prevalence of neoplasms, megalocytic hepatosis, and total number of hepatic lesions (Krahn et al. 1986) suggests that selected PAH metabolites and key organs or tissues may be the most effective monitors of PAH contamination in aquatic organisms.

In addition to those effects of PAHs emphasizing survival, uptake, depuration, and carcinogenesis previously listed, a wide variety of additional effects have been documented for aquatic organisms. These include:

- Inhibited reproduction of daphnids and delayed emergence of larval midges by fluorene (Finger et al. 1985)
- Reproductive impairment in fish by anthracene (Hall and Oris 1991) and elevated concentrations of total PAHs in sediments (Johnson et al. 1998)
- Generalized disruption of cell membrane function in fishes by anthracene (McCloskey and Oris 1993)
- Decreased respiration and heart rate in mussels (*Mytilus californianus*) by benzo[a]pyrene (Sabourin and Tullis 1981)
- Increased weight of liver, kidney, gall bladder, and spleen of sea catfish (*Arius felis*) by 3-methylcholanthrene, which was dose-related (Melius and Elam 1983)
- Photosynthetic inhibition of algae and macrophytes by anthracene, naphthalene, phenanthrene, pyrene (Neff 1985), and fluorene (Finger et al. 1985)
- Immobilization of the protozoan *Paramecium caudatum* by anthracene, with an EC50 (60 min) of 0.1 µg/L (USEPA 1980)
- Perylene accumulation by algae (Stegeman 1981)

- Accumulation without activation of benzo[a]pyrene and benzo[a]anthracene by a marine protozoan (*Parauronema acutum*), and biotransformation of various fluorenes by *P. acutum* to mutagenic metabolites (Lindmark 1981)
- Interference by toluene and anthracene with benzo[a]pyrene uptake by freshwater amphipods (Landrum 1983)
- Abnormal blood chemistry in oysters (*Crassostrea virginica*) exposed for 1 year to 5 µg 3-methylcholanthrene/L (Couch et al. 1983)
- Enlarged livers in brown bullheads from a PAH-contaminated river (Fabacher and Baumann 1985).

25.4.5 Amphibians and Reptiles

In vitro studies with abdominal skin of *Rana pipiens* demonstrated that naphthalene inhibited sodium transport after exposure to 4.4 mg/L for 30 min (Blankemeyer and Hefler 1990). Some data were available on biological effects of benzo[a]pyrene, 3-methylcholanthrene, and perylene to reptiles and amphibians (Balls 1964; Stegeman 1981; Anderson et al. 1982; Schwen and Mannering 1982a, 1982b; Couch et al. 1983). Implantation of 1.5 mg benzo[a]pyrene crystals into the abdominal cavity of adult South African clawed frogs (*Xenopus laevis*) produced lymphosarcomas in 11 of the 13 frogs (85%) after 86 to 288 days (Balls 1964). Immature frogs were more resistant, with only 45% bearing lymphoid tumors of liver, kidney, spleen, or abdominal muscle 272 to 310 days after implantation of 1.5 mg of benzo[a]pyrene crystals in the dorsal lymph sac or abdominal cavity. Implantation of 3-methylcholanthrene crystals into *X. laevis* provokes development of lymphoid tumors similar to those occurring naturally in this species. Moreover, these tumors are readily transplantable into other *Xenopus* or into the urodele species *Triturus cristatus* (Balls 1964). Intraperitoneal injection of perylene into tiger salamanders can result in hepatic tumors (Couch et al. 1983).

A critical point of interaction between PAHs and reptiles or amphibians involves the transformation of these compounds by cytochrome P-450-dependent monooxygenase systems (Stegeman 1981); in general, reaction rates in this group are considerably slower than those observed in hepatic microsomes from mammals (Schwen and Mannering 1982a). Mixed-function oxidation systems can be induced in liver and skin of tiger salamanders by perylene (Couch et al. 1983) and 3-methylcholanthrene (Anderson et al. 1982), and in liver of the leopard frog (*Rana pipiens*) and garter snake (*Thamnophis* sp.) by benzo[a]pyrene and 3-methylcholanthrene (Stegeman 1981; Schwen and Mannering 1982a, 1982b). A single dose of 40 mg/kg body weight of 3-methylcholanthrene was sufficient to induce mixed-function oxidase activity for several weeks in the leopard frog (Schwen and Mannering 1982b). Amphibians, including tiger salamanders, are quite resistant to PAH carcinogenesis when compared to mammals, according to Anderson et al. (1982). This conclusion was based on studies with *Ambystoma* hepatic microsomes and their inability to produce mutagenic metabolites of benzo[a]pyrene and perylene (as measured by bacterial *Salmonella typhimurium* strains used in the Ames test). However, rat liver preparations did produce mutagenic metabolites under these procedures (Anderson et al. 1982).

25.4.6 Birds

In birds, PAHs were associated with impaired reproduction, growth retardation, morphological abnormalities, behavioral changes, and alterations in Vitamin A and thyroid hormone metabolism (Murk et al. 1996). In one study, fertilized eggs of the chicken (*Gallus domesticus*) and the common eider duck (*Somateria mollissima*) were injected with a mixture of 16 PAHs at 0.2 mg PAH/kg egg FW on day 4 of incubation (Naf et al. 1992). In chicken eggs, 94% of the administered dose was metabolized within the egg by day 18. In embryos of both chickens and eiders, PAH concentrations were highest in gallbladder, followed by liver, kidney, and adipose tissues. Eiders had 40% of the total PAH content in these organs vs. 16% for chickens. Chick embryos, eider embryos, and

juvenile eiders had similar PAH concentrations and PAH profiles. The largest PAH molecule studied, coronene, was not taken up from the yolk by the embryo as efficiently as other PAHs, but once taken up it was metabolized as readily as the other PAHs. AHH activities of chick and eider embryos were of similar magnitude (Naf et al. 1992). Studies with European starlings (*Sturnus vulgaris*) and 7,12-dimethylbenz[*a*]anthracene show that effects on the immune function and hepatic mixed-function oxygenase activity were more pronounced when administered by subcutaneous injection when compared to an oral route of exposure, and more pronounced in nestlings than in adults. Serious adverse effects were noted in adults at total administered doses of 125 mg/kg BW via injection or orally, and 100 mg/kg BW in nestlings (Trust et al. 1994).

Mallards (*Anas platyrhynchos*) fed diets that contained 4000 mg PAHs/kg (mostly as naphthalenes, naphthenes, and phenanthrene) for a period of 7 months had normal survival and no visible signs of toxicity during exposure. However, liver weight increased 25% and blood flow to liver increased 30%, when compared to controls (Patton and Dieter 1980). In another study with mallards, Hoffman and Gay (1981) measured embryotoxicity of various PAHs applied externally, in a comparatively innocuous synthetic petroleum mixture, to the surface of mallard eggs. The most embryotoxic PAH tested was 7,12-dimethylbenz[*a*]anthracene: approximately 0.002 µg/egg (equivalent to about 0.036 µg/kg fresh weight, based on an average weight of 55 g per egg) caused 26% mortality in 18 days, and, among survivors, produced significant reduction in embryonic growth and a significant increase in the percent of anomalies (e.g., incomplete skeletal ossification, defects in eye, brain, liver, feathers, and bill). At 0.01 µg 7,12-dimethylbenz[*a*]anthracene/egg, only 10% survived to day 18. Similar results were obtained with 0.015 µg (and higher) chrysene/egg. For benzo[*a*]pyrene, 0.002 µg/egg did not affect mallard survival, but did cause embryonic growth reduction and an increased incidence of abnormal survivors. At 0.01 µg benzo[*a*]pyrene/egg, 60% died in 18 days; at 0.05 µg/egg, 75% were dead within 3 days of treatment (Hoffman and Gay 1981). Embryos may contain microsomal enzymes that can metabolize PAHs to more highly toxic intermediates than can adults, and avian embryos may have a greater capacity to metabolize PAHs in this manner than do mammalian embryos and fetuses (as quoted in Hoffman and Gay 1981); this observation warrants additional research. Several investigators have suggested that the presence of PAHs in petroleum, including benzo[*a*]pyrene, chrysene, and 7,12-dimethylbenz[*a*]anthracene, significantly enhances the overall embryotoxicity in avian species, and that the relatively small percent of aromatic hydrocarbons contributed by PAHs in petroleum may confer much of the adverse biological effects reported after eggs have been exposed to microliter quantities of polluting oils (Hoffman and Gay 1981; Albers 1983).

25.4.7 Mammals

Numerous PAH compounds are distinct in their ability to produce tumors in skin and in most epithelial tissues of practically all animal species tested. Malignancies were often induced by acute exposures to microgram quantities. In some cases, the latency period can be as short as 4 to 8 weeks, with the tumors resembling human carcinomas (USEPA 1980). Carcinogenic potential values of individual PAHs via dermal exposure, when compared to benzo[*a*]pyrene with an assigned value of 1.0, were 5.0 for dibenz[*a,h*]anthracene; 0.1 for benzo[*a*]anthracene, benzo[*b,k*]fluoranthene, and indeno[1,2,3-*cd*]perylene; 0.01 for benzo[*g,h,i*]perylene and chrysene; and 0.001 for fluoranthene, fluorene, phenanthrene, and pyrene (Hussain et al. 1998). Certain carcinogenic PAHs are capable of passage across skin, lungs, and intestine, and can enter the rat fetus, for example, following intragastric or intravenous administration to pregnant dams (USEPA 1980). In most cases, the process of carcinogenesis occurs over a period of many months in experimental animals, and many years in humans. The tissue affected is determined by the route of administration and species under investigation. Thus, 7,12-dimethylbenz[*a*]anthracene is a potent carcinogen for the mammary gland of young female rats after oral or intravenous administration; dietary benzo[*a*]pyrene leads

to leukemia, lung adenoma, and stomach tumors in mice, and both PAH compounds can induce hepatomas in skin of male mice when injected shortly after birth (Dipple 1985). Mammary tumors were observed in female rats 6 weeks after they were given the first of 4 weekly intragastric doses of 5 mg 7,12-dimethylbenz[a]anthracene/rat; exposure to magnetic fields of low flux density may promote the growth and development of mammary tumors (Mevissen et al. 1998). Acute and chronic exposure to various carcinogenic PAHs have resulted in destruction of hematopoietic and lymphoid tissues, ovotoxicity, antispermatozoic effects, adrenal necrosis, changes in the intestinal and respiratory epithelia, and other effects (Table 25.8) (USEPA 1980; Lee and Grant 1981). For the most part, however, tissue damage occurs at dose levels that would also be expected to induce carcinomas, and thus the threat of malignancy predominates in evaluating PAH toxicity. There is a scarcity of data available on the toxicological properties of PAHs that are not demonstrably carcinogenic to mammals (USEPA 1980; Lee and Grant 1981).

Table 25.8 Some Effects of PAHs on Selected Laboratory Mammals

Effect (units), Organism, PAH Compound	Concentration	Reference ^a
LD50, ACUTE ORAL (mg/kg body weight)		
Rodents (<i>Rattus</i> spp., <i>Mus</i> spp.)		
Benzo[a]pyrene	50	1
Phenanthrene	700	1
Naphthalene	1780	1
Fluoranthene	2000	1
CARCINOGENICITY, CHRONIC ORAL (mg/kg body weight)		
Rodents		
7,12-Dimethylbenz[a]anthracene	0.00004–0.00025	2
Benzo[a]pyrene	0.002	1
Dibenz[a,h]anthracene	0.006	1
Benz[a]anthracene	2.0	1
Benzo[b]fluoranthene	40.0	1
Benzo[k]fluoranthene	72.0	1
Indeno[1,2,3-cd]pyrene	72.0	1
Chrysene	99.0	1
Anthracene	3300.0	1
CARCINOGENICITY, APPLIED EXTERNALLY AS TOPICAL (mg)		
Mice, <i>Mus</i> spp.		
Benzo[a]pyrene	0.001	2
Dibenz[a,c]anthracene	0.001	2
7,12-Dimethylbenz[a]anthracene	0.02	2
Dibenz[a,j]anthracene	0.039	2
Anthracene	0.08	2
Benzo[g,h,i]perylene	0.8	2
Benzo[a]anthracene	1.0	2
CARCINOGENICITY, SUBCUTANEOUS (mg)		
Mice		
Dibenz[a,h]anthracene		
Adults	>0.0002	2
Newborn	>0.00008	2
Dibenzo[a,j]pyrene		
In sesame oil	0.05	2
In peanut oil	0.6	2
Benzo[a]pyrene	0.06	2
Dibenzo[a,e]pyrene	>0.6	2

Table 25.8 (continued) Some Effects of PAHs on Selected Laboratory Mammals

Effect (units), Organism, PAH Compound	Concentration	Reference^a
Benzo[<i>b</i>]fluoranthene	1.8	2
Benz[<i>a</i>]anthracene	5.0	2
Dibenz[<i>a,h</i>]pyrene	6.0	2
TESTICULAR DAMAGE (mg)		
Rat, <i>Rattus</i> spp.		
Benzo[<i>a</i>]pyrene, oral	100.0 (no effect)	4
7,12-Dimethylbenz[<i>a</i>]anthracene		
Intravenous		
Young rats	0.5–2.0	4
Older rats	5.0	4
Oral	20.0	4
OOCYTE AND FOLLICLE DESTRUCTION, SINGLE INTRAPERITONEAL INJECTION (mg/kg body weight)		
Mice		
Benzo[<i>a</i>]pyrene	80.0	5
3-Methylcholanthrene	80.0	5
7,12-Dimethylbenz[<i>a</i>]anthracene	80.0	5
ALTERED BLOOD SERUM CHEMISTRY AND NEPHROTOXICITY, SINGLE INTRAPERITONEAL INJECTION (mg/kg body weight)		
Rat		
Phenanthrene	150.0	6
Pyrene	150.0	6
FOOD CONSUMPTION, DAILY FOR 5 DAYS (mg/kg body weight)		
Deer mice, <i>Peromyscus maniculatus</i>		
2-Methoxynaphthalene		
30% reduction	825	3
2-Ethoxynaphthalene		
3% reduction	1213	3
House mice, <i>Mus musculus</i>		
2-Methoxynaphthalene		
50% reduction	825	3
2-Ethyoxynaphthalene		
50% reduction	1213	3

^a 1, Sims and Overcash 1983; 2, Lo and Sandi 1978; 3, Schafer and Bowles 1985; 4, USEPA 1980; 5, Mattison 1980; 6, Yoshikawa et al. 1985.

Target organs for PAH toxic action are diverse, due partly to extensive distribution in the body and also to selective attack by these chemicals on proliferating cells (USEPA 1980). Damage to the hematopoietic and lymphoid system in experimental animals is a particularly common observation (USEPA 1980). In rats, the target organs for 7,12-dimethylbenz[*a*]anthracene are skin, small intestine, kidney, and mammary gland, whereas in fish the primary target organ is liver (Schultz and Schultz 1982). Application of carcinogenic PAHs to mouse skin leads to destruction of sebaceous glands and to hyperplasia, hyperkeratosis, and ulceration (USEPA 1980). Tumors are induced in mouse skin by the repeated application of small doses of PAHs, by a single application of a large dose, or by the single application of a subcarcinogenic dose (initiation) followed by repeated application of certain noncarcinogenic agents (promotion) (Dipple 1985). Newborn mice were highly susceptible to 3-methylcholanthrene, with many mice dying from acute or chronic wasting disease following treatment; some strains of mice eventually developed thymomas, but other strains showed no evidence despite serious damage to the thymus (USEPA 1980). In general, PAH

carcinogens transform cells through genetic injury involving metabolism of the parent compound to a reactive diol epoxide. This, in turn, can then form adducts with cellular molecules, such as DNA, RNA, and proteins, resulting in cell transformation (Dipple 1985; Ward et al. 1985). In the case of benzo[*a*]pyrene, one isomer of the 7,8-diol,9,10-epoxide is an exceptionally potent carcinogen to newborn mice and is believed to be the ultimate carcinogenic metabolite of this PAH (Slaga et al. 1978). One of the most toxicologically significant processes involved in the response to PAH absorption is the interaction with drug-metabolizing enzyme systems (Lee and Grant 1981). Increased production of mixed-function oxidase enzymes in various small mammals has been induced by halogenated naphthalenes (Campbell et al. 1983), 3-methylcholanthrene (Miranda and Chhabra 1980), and numerous other PAHs (USEPA 1980). PAH metabolites produced by microsomal enzymes in mammals can be arbitrarily divided into water-soluble groups, and organosoluble groups such as phenols, dihydrodiols, hydroxymethyl derivatives, quinones, and epoxides (USEPA 1980). In the case of benzo[*a*]pyrene, the diol epoxides are usually considered as the ultimate carcinogens. Other microsomal enzymes convert epoxide metabolites to easily excreted water soluble compounds, with excretion primarily through feces and the hepatobiliary system (USEPA 1980). Interspecies differences in sensitivity to PAH-induced carcinogenesis are due largely to differences in levels of fixed function oxidase activities, and these will directly affect rates at which active metabolites are converted to less-active products (Neff 1979).

Investigators (Neff 1979; USEPA 1980; Dipple 1985) agree that:

- Unsubstituted aromatic PAHs with fewer than 4 condensed rings have not shown tumorigenic activity
- That many, but not all, four-, five-, and six-ring PAH compounds are carcinogenic
- That only a few unsubstituted hydrocarbons with seven rings or more are tumorigenic or carcinogenic

Many PAH compounds containing four and five rings, and some containing six or more rings, provoke local tumors after repeated application to the dorsal skin of mice; the tumor incidence exhibited a significant dose-response relationship (Grimmer et al. 1985). Among unsubstituted PAHs containing a nonaromatic ring (e.g., cholanthrene and acenaphthanthracene), all active carcinogens retained an intact phenanthrene segment (USEPA 1980). The addition of alkyl substituents in certain positions in the ring system of a fully aromatic PAH will often confer carcinogenic activity or dramatically enhance existing carcinogenic potency. For example, monomethyl substitution of benz[*a*]anthracene can lead to strong carcinogenicity in mice, with potency depending on the position of substitution in the order $7 > 6 > 8 = 12 > 9$; a further enhancement of carcinogenic activity is produced by appropriate dimethyl substitution, with 7,12-dimethylbenz[*a*]anthracene among the most potent PAH carcinogens known. Alkyl substitution of partially aromatic condensed ring systems may also add considerable carcinogenic activity as is the case with 3-methylcholanthrene. With alkyl substitutes longer than methyl, carcinogenicity levels decrease, possibly due to a decrease in transport through cell membranes (USEPA 1980).

A good correlation exists between skin tumor-initiating activities of various benzo[*a*]pyrene metabolites and their mutagenic activity in mammalian cell mutagenesis systems (Slaga et al. 1978), although variations in chromosome number and structure may accompany tumors induced by various carcinogenic PAHs in rats, mice, and hamsters (Bayer 1978; USEPA 1980). Active PAH metabolites (e.g., dihydrodiols or diol epoxides) can produce sister chromatid exchanges in Chinese hamster ovary cells (Bayer 1978; USEPA 1980; Pal 1984). When exchanges were induced by the diol epoxide, a close relationship exists between the frequency of sister chromatid exchanges and the levels of deoxyribonucleoside-diol-epoxide adduct formation (Pal 1984). In general, noncarcinogenic PAHs were not mutagenic (USEPA 1980). Laboratory studies with mice have shown that many carcinogenic PAHs adversely affect the immune system, thus directly impacting an organism's general health, although noncarcinogenic analogs had no immunosuppressive effect. Further, the more carcinogenic the PAH, the greater the immunosuppression (Ward et al. 1985). Destruction of

oocytes and follicles in mouse ovary is documented following intraperitoneal injection of benzo[*a*]pyrene, 3-methylcholanthrene, and 7,12-dimethylbenz[*a*]anthracene; the rate of destruction was proportional to the activity of the ovarian cytochrome P-450-dependent monooxygenase, as well as the carcinogenicity of the PAH (Mattison 1980). However, no information is presently available to indicate whether PAHs present a hazard to reproductive success. In those cases where teratogenic effects are clearly evident (e.g., 7,12-dimethylbenz[*a*]anthracene), the required doses were far in excess of realistic environmental exposures (Lee and Grant 1981). Numerous studies show that unsubstituted PAHs do not accumulate in mammalian adipose tissues despite their high lipid solubility, probably because they tend to be rapidly and extensively metabolized (USEPA 1980; Lee and Grant 1981).

The biological half-life (T_b 1/2) of PAHs is limited, as judged by rodent studies. In the case of oral doses of benzo[*a*]pyrene and rat blood and liver, T_b 1/2 values of 5 to 10 min were recorded; the initial rapid elimination phase was followed by a slower disappearance phase lasting 6 h or more (USEPA 1980). The T_b 1/2 value of benzo[*a*]pyrene from blood of rats given 15 mg/kg BW by intravenous injection was 400 min (Moir et al. 1998). In that study, adipose and lung tissues had comparatively high concentrations of benzo[*a*]pyrene 32 h after dosing, and fecal excretion was the dominant route of BaP loss, being 4 to 10 times higher than urinary excretion (Moir et al. 1998). T_b 1/2 values from the site of subcutaneous injection in mice were 1.75 weeks for benzo[*a*]pyrene, 3.5 weeks for 3-methylcholanthrene, and 12 weeks for dibenz[*a,h*]anthracene; the relative carcinogenicity of each compound was directly proportional to the time of retention at the injection site (Pucknat 1981).

Many chemicals are known to modify the action of carcinogenic PAHs in experimental animals, including other PAHs that are weakly carcinogenic or noncarcinogenic. The effects of these modifiers on PAH metabolism appear to fall into three major categories (DiGiovanni and Slaga 1981b):

- Those that alter the metabolism of the carcinogen, causing decreased activation or increased detoxification
- Those that scavenge active molecular species of carcinogens to prevent their reaching critical target sites in the cell
- Those that exhibit competitive antagonism

For example, pyrene given to rats by intravenous injection or orally at 20 mg/kg BW alone or in combination with other PAHs produce the following observations: bioavailability of pyrene is increased in combination with fluoranthene or benz[*a*]anthracene; pyrene enhances the carcinogenic effect of benzo[*a*]pyrene, and carcinogenicity of benzo[*a*]pyrene can be inhibited by pyrene, phenanthrene, or anthracene; and some PAHs present in the environment accelerate the clearance of pyrene but reduce the level of 1-hydroxypyrene in urine (Lipniak-Gawlik 1998). Benz[*a*]anthracene, a weak carcinogen when applied simultaneously with dibenz[*a,h*]anthracene, inhibits the carcinogenic action of the latter in mouse skin; a similar case is made for benzo[*e*]pyrene or dibenz[*a,c*]anthracene applied to mouse skin shortly prior to initiation with 7,12-dimethylbenz[*a*]anthracene, or 3-methylcholanthrene (DiGiovanni and Slaga 1981a). Benzo[*a*]pyrene, a known carcinogen, interacts synergistically with cyclopenta[*cd*]pyrene, a moderately strong carcinogen found in automobile exhausts, according to results of mouse skin carcinogenicity studies (Rogan et al. 1983). Other PAH combinations were cocarcinogenic, such as benzo[*e*]pyrene, pyrene, and fluoranthene applied repeatedly with benzo[*a*]pyrene to the skins of mice (DiGiovanni and Slaga 1981a). Effective inhibitors of PAH-induced tumor development include selenium, Vitamin E, ascorbic acid, butylated hydroxytoluene, and hydroxyanisole (USEPA 1980). In addition, protective effects against PAH-induced tumor formation have been reported for various naturally occurring compounds such as flavones, retinoids, and Vitamin A (USEPA 1980). Until these interaction effects are clarified, the results of single-substance laboratory studies may be extremely difficult to apply to field situations of suspected PAH contamination. Additional work is also needed on PAH dose-

response relationships, testing relevant environmental PAHs for carcinogenicity, and elucidating effects of PAH mixtures on tumor formation (Grimmer 1983).

25.5 RECOMMENDATIONS

No standards have been promulgated for PAHs by any regulatory agency for the protection of sensitive species of aquatic organisms or wildlife, although some criteria have been proposed for aquatic life protection ([Table 25.9](#)). This observation is not unexpected in view of several factors:

1. The paucity of data on PAH background concentrations in wildlife and other natural resources
2. The absence of information on results of chronic oral feeding studies of PAH mixtures and the lack of a representative PAH mixture for test purposes
3. The demonstrable — and as yet poorly understood — effects of biological modifiers, such as sex, age, and diet, and interaction effects of PAHs with inorganic and other organic compounds, including other PAHs.

Nevertheless, the growing database for aquatic life indicates a number of generalizations: (1) many PAHs are acutely toxic at concentrations between 50 and 1000 µg/L; (2) deleterious sublethal responses are sometimes observed at concentrations in the range of 0.1 to 5.0 µg/L; (3) uptake can be substantial, but depuration is usually rapid except in some species of invertebrates; and (4) whole-body burdens in excess of 300 µg benzo[*a*]pyrene/kg (and presumably other PAHs) in certain teleosts would be accompanied by a rise in the activity of detoxifying enzymes.

Aquatic research has focused on PAHs because of their known relationship with carcinogenesis and mutagenesis (Black et al. 1988; Hawkins et al. 1990; Steard et al. 1990, 1991; Collier and Varanasi 1991; Smolowitz et al. 1992; Fernandez and L'Haridon 1994). Many reports exist of high incidences of cancer-like growths and developmental anomalies in natural populations of aquatic animals and plants, but none conclusively demonstrate the induction of cancer by exposure of aquatic animals to environmentally realistic levels of carcinogenic PAHs in the water column, diet, or sediments (Neff 1982b, 1985). However, studies by Baumann, Malins, Black, Varanasi, and their co-workers, among others, have now established that sediments heavily contaminated with PAHs from industrial sources were the direct cause of elevated PAH body burdens and elevated frequencies of liver neoplasia in fishes from these locales. Only a few sites containing high PAH concentrations in sediments have been identified (Couch and Harshbarger 1985), suggesting a need to identify and to evaluate other PAH-contaminated aquatic sites. Most fishery products consumed by upper trophic levels, including humans, contain PAH concentrations similar to those in green vegetables and smoked and charcoal-broiled meats, and would probably represent a minor source of PAH toxicity; however, consumption of aquatic organisms, especially filter-feeding bivalve molluscs, from regions severely contaminated with petroleum or PAH-containing industrial wastes, should be avoided (Jackim and Lake 1978; Neff 1982b). Neff (1982b) has suggested that repeated consumption of PAH-contaminated shellfish may pose a cancer risk to humans, and Al-Yakoob et al. (1994) aver that consumption of PAH-contaminated fish from the Arabian Gulf poses a risk to human health. If true, this needs to be evaluated using seabirds, pinnipeds, and other wildlife groups which feed extensively on molluscs and teleosts that are capable of accumulating high burdens of carcinogenic PAHs, in order to determine if similar risks exist.

For avian wildlife, data are incomplete on PAH background concentrations and on acute and chronic toxicity. Studies with mallard embryos and PAHs applied to the egg surface showed toxic and adverse sublethal effects at concentrations between 0.036 and 0.18 µg PAH/kg whole egg (Hoffman and Gay 1981). Additional research is needed on petroleum-derived PAHs and their effects on developing embryos of seabirds and other waterfowl. There is an urgent need for specific avian biomarkers of PAH exposure (Murk et al. 1996).

PAH criteria for human health protection ([Table 25.9](#)) were derived from tests with small laboratory mammals, primarily rodents. Accordingly, these proposed criteria should become interim guidelines for protection of nonhuman mammalian resources pending acquisition of more definitive data. The proposed PAH criteria are controversial. Pucknat (1981) states that there was no way to quantify the potential human health risks incurred by the interaction of any PAH with other PAHs or with other agents in the environment, including tumor initiators, promoters, and inhibitors. The problem arises primarily from the diversity of test systems and bioassay conditions used for determining carcinogenic potential of individual PAHs in experimental animals, and is confounded by the lack of a representative PAH mixture for test purposes, the absence of data for animal and human chronic oral exposures to PAH mixtures, and the reliance on data derived from studies with benzo[*a*]pyrene to produce generalizations concerning environmental effects of PAHs — generalizations which may not be scientifically sound — according to Pucknat (1981). The USEPA (1980) emphasizes that only a small percentage of PAH compounds are known to be carcinogenic, and that measurements of total PAHs (i.e., the sum of all multiple fused-ring hydrocarbons having no heteroatoms) cannot be equated with carcinogenic potential. Furthermore, when the term “total PAHs” is used, the compounds being considered should be specified for each case. Lee and Grant (1981) state that an analysis of dose-response relationships for PAH-induced tumors in animals shows, in some cases, deviation from linearity in dose-response curves, especially at low doses, suggesting a two-stage model consistent with a linear nonthreshold pattern. Because overt tumor induction follows a dose-response relationship consistent with a multihit promotion process, the multihit component of carcinogenesis may be supplied by environmental stimuli not necessarily linked or related to PAH exposure.

The well-documented existence of carcinogenic and anticarcinogenic agents strongly suggests that a time assessment of carcinogenic risk for a particular PAH can be evaluated only through a multifactorial analysis (Lee and Grant 1981). One of the most toxicologically significant processes involved in the response to PAH absorption is the interaction with drug metabolizing enzyme systems. The induction of this enzyme activity in various body tissues by PAHs and other xenobiotics is probably critical to the generation of reactive PAH metabolites at the target site for tumor induction. At present, wide variations occur in human and animal carcinogen-metabolizing capacity. Moreover, it has not yet been possible to definitely correlate enzyme activity with susceptibility to carcinogenesis. The obligatory coupling of metabolic activation with PAH-induced neoplasia in animals indicates that the modulation of drug-metabolizing enzymes is central to carcinogenesis (Lee and Grant 1981).

PAHs from drinking water contribute only a small proportion of the average total human intake (Harrison et al. 1975). The drinking water quality criterion for carcinogenic PAH compounds is based on the assumption that each compound is as potent as benzo[*a*]pyrene and that the carcinogenic effect of the compounds is proportional to the sum of their concentrations (USEPA 1980). Based on an oral feeding study of benzo[*a*]pyrene in mice, the concentration of this compound estimated to result in additional risk of one additional case for every 100,000 individuals exposed (i.e., 10^{-5}) is 0.028 µg/L. Therefore, with this assumption, the sum of the concentrations of all carcinogenic PAH compounds should be less than 0.028 µg/L in order to keep the lifetime cancer risk below 10^{-4} (USEPA 1980). The corresponding recommended criteria which may result in an incremental cancer risk of 10^{-6} and 10^{-7} over the lifetime are 0.0028 and 0.00028 µg/L, respectively ([Table 25.9](#)). If the above estimates are made for consumption of aquatic organisms only, the levels are 0.311 (10^{-5}), 0.031(10^{-6}), and 0.003(10^{-7}) µg/kg, respectively (USEPA 1980). The use of contaminated water for irrigation can also spread PAHs into other vegetable foodstuffs (USEPA 1980). When vegetables grown in a PAH-polluted area are thoroughly washed and peeled, their contribution to total PAH intake in humans is not significant (Wang and Meresz 1982). Herbivorous wildlife, however, may ingest significant quantities of various PAHs from contaminated vegetables — but no data were available on this subject.

Table 25.9 Proposed PAH Criteria for Protection of Human Health and Aquatic Life

Criterion, PAH Group, and Units	Concentration	Reference ⁱ
HUMAN HEALTH		
Air		
Total PAHs, µg/m ³	0.0109	1
Total PAHs, daily intake, µg ^f	0.164–0.251	1
Cyclohexane extractable fractions; coke oven emissions, coal tar products, µg/m ³ , 8–10 h-weighted average	100.0–150.0	1
Benzene-soluble fractions; coal tar pitch volatiles, µg/m ³ , 8-h average	200.0	1
Benzo[a]pyrene		
µg/m ³	0.0005	1
Daily intake, µg ^f	0.005–0.0115	1
Acceptable, µg/m ³		
AZ	0.79 for 1-h; 0.21 for 24 h; 0.00057 for 1 year	5
CT, IN	0.1 for 8-h	5
FL, KS, MI	0.0003 for 1 year	5
ME	0.0006 for 1 year	5
NC	0.03 for 1 year	5
PA	0.0007 for 1 year	5
TX	0.03 for 30 min; 0.003 for 1 year	5
Carcinogenic PAHs		
µg/m ³	0.002	1
Daily intake, µg ^f	0.03–0.046	1
Drinking water		
Total PAHs		
µg/L ^a	0.0135–0.2	1
Daily intake, µg ^a	0.027–0.4	1
Yearly intake, µg	4.0	1
Europe, µg/L ^h	<0.2	5
Benz[a]anthracene, µg/L	<0.1	5
Benzo[a]pyrene		
µg/L, U.S.	<0.2	5
µg/L, most states	0.03–0.003	5
Daily intake, µg	0.0011	1
Dibenzanthracene, µg/L	<0.3	5
Carcinogenic PAHs		
µg/L ^b	0.0021	1
Daily intake, µg ^b	0.0042	1
µg/L ^c		
Cancer risk 10 ⁻⁵	0.028	1
Cancer risk 10 ⁻⁶	0.0028	1
Cancer risk 10 ⁻⁷	0.00028	1
Daily intake, µg ^c		
Cancer risk 10 ⁻⁵	0.056	1
Cancer risk 10 ⁻⁶	0.0056	1
Cancer risk 10 ⁻⁷	0.00056	1
Food		
Total PAHs		
Daily intake, µg ^d	1.6–16.0	1
Yearly intake, µg	4150.0	1
Benzo[a]pyrene		
Daily intake, µg ^e	0.16–1.6	1

Table 25.9 (continued) Proposed PAH Criteria for Protection of Human Health and Aquatic Life

Criterion, PAH Group, and Units	Concentration	Referenceⁱ
Low-risk range; oral intake; mg/kg BW daily for up to 364 days		
Acenaphthene	0.06	5
Anthracene	0.03	5
Fluoranthene	0.04	5
Fluorene	0.04	5
Pyrene	0.03	5
All sources		
Total PAHs		
Daily, µg	1.79–16.6	1
Benzo[a]pyrene		
Daily intake, µg	0.166–1.61	1
Daily allowable limit, µg	0.048	2
Carcinogenic PAHs (except diet)		
Daily intake, µg ^b	0.086–0.102	1
Land disposal restrictions (proposed)		
Maximum allowed; nonwastewaters; mg/kg FW		
Benz[a]anthracene, benzo[a]pyrene, chrysene, or I(1,2,3-cd)P	3.4	5
B(b)F, B(k)F	6.8	5
Dibenz[a,h]anthracene	8.2	5
Maximum allowed; wastewaters, mg/L		
B(a)A, chrysene	0.059	5
BaP	0.061	5
BbF, BkF	0.11	5
I(1,2,3-cd)P	0.0055	5
Dibenz[a,h]anthracene	0.055	5
AQUATIC LIFE		
Sediment criteria to protect freshwater organisms, in mg/kg DW^g		
Naphthalene	<0.01	3
Phenanthrene	<0.04	3
Benzo[a]pyrene	<0.06	3
Acenaphthene	<0.15	3
Fluorene	<0.2	3
Benz[a]anthracene	<0.2	3
Anthracene	<0.6	3
Acridine	<1.0	3
Fluoranthene	<2.0	3
Sediment criteria to protect marine life, in mg/kg DW^g		
Naphthalene	<0.01	3
Benzo[a]pyrene	<0.06	3
Acenaphthene	<0.15	3
Fluorene	<0.2	3
Chrysene	<0.2	3
Water criteria, in g/L, to protect freshwater biota under conditions of chronic exposure		
Benzo[a]pyrene	<0.01	3

Table 25.9 (continued) Proposed PAH Criteria for Protection of Human Health and Aquatic Life

Criterion, PAH Group, and Units	Concentration	Reference ⁱ
Acridine	<0.05 (phototoxic effects); <3.0 (no phototoxicity)	3
Benz[a]anthracene	<0.1	3
Anthracene	<0.1 (phototoxic effects); <4.0 (no phototoxicity)	3
Fluoranthene	<0.2 (phototoxic effects); <4.0 (no phototoxicity)	3
Naphthalene	<1.0	3
Acenaphthene	<6.0	3
Fluorene	<12.0	3
Total PAHs (n = 13); Ohio	<310.0	5
Marine water criteria, in g/L, to protect biota under conditions of chronic exposure		
Benzo[a]pyrene	<0.01	3
Chrysene	<0.1	3
Naphthalene and methylated naphthalenes	<1.0	3
Acenaphthene	<6.0	3
Fluorene	<12.0	3
Anthracene		
Fathead minnow, <i>Pimephales promelas</i>		
Reproduction impaired	>15 mg/kg body weight	4
Reproduction normal	<15 mg/kg BW; <6 µg/L medium	4
Bluegill, <i>Lepomis macrochirus</i>		
No adverse effect	<13.5 mg/kg BW	4

^a Total of 6 PAHs: fluoranthene, benzo[a]pyrene, benzo[g,h,i]perylene, benzo[b]fluoranthene, benzo[k]fluoranthene, and indeno[1,2,3-cd]pyrene.

^b Total of 3 PAHs: benzo[a]pyrene, benzo[j]fluoranthene, and indeno[1,2,3-cd]pyrene.

^c Based on all carcinogenic PAHs.

^d Assuming 1600 g food daily, 70-kg adult, 1–10 mg total PAHs/diet.

^e As above, except 0.1–1.0 mg benzo[a]pyrene/diet.

^f Assuming average of 15–23 m³ of air inhaled daily.

^g To derive PAH criteria, a safety factor of 0.1 was used with most chronic data, but ranged between 0.1 and 0.01 of the lowest observed effective concentration in freshwater and 0.1 and 0.5 in marine waters.

^h Total of 6 PAHs: benzo[a]pyrene, benzo[b]fluoranthene, benzo[a]fluoranthene, benzo[k]fluoranthene, fluoranthene, and indeno[1,2,3-cd]pyrene

ⁱ 1, As quoted in Eisler 1987; 2, Wang and Meresz 1982; 3, Nagpal 1994; 4, Hall 1993; 5, USPHS 1995.

PAHs are widely distributed in the environment as evidenced by their detection in sediments, soils, air, surface waters, and plant and animal tissues. However, the ecological impact of PAHs is uncertain. PAHs show little tendency for bioconcentration despite their high lipid solubility (Pucknat 1981), probably because most PAHs are rapidly metabolized. Sims and Overcash (1983) list a variety of research needs regarding PAHs in soil-plant systems. Specifically, research is needed to establish: the rates of PAH decomposition in soils; the soil PAH levels above which PAH constituents adversely affect the food chain; and enhancement factors that increase degradation rates of PAHs, especially PAHs with more than three rings. Once these factors have been determined, PAH disposal into soils may become feasible at environmentally nonhazardous levels.

Diet is the major source of PAHs to humans. Authorities agree that most foods contain 1 to 10 µg total PAHs/kg fresh weight, that smoking or barbecuing fish and meats increases total PAH content up to 100-fold, that contaminated molluscs and crustaceans may contribute significantly to PAH intake, and that PAH carcinogenic risk to humans has existed at least since man began to

cook his food (Barnett 1976; USEPA 1980; Lee and Grant 1981; Lawrence and Weber 1984a). A total of 22 PAHs has been identified in foods, of which 11 have been found to be carcinogenic in experimental animals. Of these, only 5 (benzo[*a*]pyrene, benz[*a*]anthracene, 3-methylcholanthrene, dibenz[*a,h*]anthracene, and 7,12-dimethylbenz[*a*]anthracene) have been demonstrated to induce tumors following oral administration to rats and mice, and only 3 of the 11 exhibited positive dose-response relationships in chronic studies with mice (Lo and Sandi 1978). There is no credible evidence that any of the 11 known carcinogenic PAHs or their combinations can cause cancer in human beings via the oral route, especially in quantities likely to be present in foods (Lo and Sandi 1978). There is, however, a need for a complete risk assessment to human health from consumption of PAH-contaminated foods, especially in areas of the Middle East where PAH concentrations for anthracene and pyrene in food items greatly exceed the carcinogenic and mutagenic risk based on benzo[*a*]pyrene equivalents (Al-Yakoob et al. 1994).

In view of the carcinogenic characteristics of many PAH compounds, their increasing concentrations in the environment should be considered alarming, and efforts should be made to reduce or eliminate them wherever possible (Suess 1976). Current research, not unexpectedly, has focused on PAH removal from contaminated environments and on bioindicators of PAH exposure. Fernandez and L'Haridon (1994) recommend irradiation (with UV light or daylight) of certain PAHs or hydrocarbon-rich mixtures prior to disposal into the environment to help reduce their harmful effects. Roy and Liu (1997) have successfully used flushing with anionic surfactants to remove anthracene from contaminated soils, and recommend surfactant soil flushing to remove PAHs as an alternative new technology to groundwater flushing with water. Biomarkers proposed as indicators of PAH exposure include elevated excretion rate of 1-OH pyrene in bile of eels from contaminated sites (van der Oost et al. 1994), intestinal P-450 activity as an indicator of dietary PAH exposure and liver P-450 activity as an indicator of sediment PAH concentrations in marine teleosts (Van Veld et al. 1990), loss rate of 5-methyl deoxycytidine from DNA (Shugart 1990), and elevated hepatic EROD activity and concentrations of biliary PAH metabolites (McDonald et al. 1995; Yu et al. 1995). However, levels of bile conjugates as a biomarker of PAH exposure should be interpreted with caution, particularly if some fish are known to have chronic liver disease (Smith et al. 1993). Synchronous fluorescent spectroscopy (SFS) has been used successfully to identify pyrene- and benzo[*a*]pyrene-type metabolites in bile of brown bullheads from Lake Erie tributaries in 1990/91 (Lin et al. 1994). SFS is recommended for screening large numbers of fish samples for evidence of PAH exposure. Increased benzo[*a*]pyrene monooxygenase activity was evident in several species of freshwater fishes exposed to benzo[*a*]pyrene, as reflected by measurement of bile fluorescence (Britvic et al. 1993). Finally, there is a need for additional PAH toxicokinetic models that emphasize uptake, retention, translocation, and biotransformation rates (Law et al. 1991).

25.6 SUMMARY

Polycyclic aromatic hydrocarbons (PAHs) consist of hydrogen and carbon arranged in the form of two or more fused benzene rings. There are thousands of PAH compounds, each differing in the number and position of aromatic rings, and in the position of substituents on the basic ring system. Environmental concern has focused on PAHs that range in molecular weight from 128.16 (naphthalene, 2-ring structure) to 300.36 (coronene, 7-ring structure). Unsubstituted lower-molecular-weight PAH compounds, containing two or three rings, exhibit significant acute toxicity and other adverse effects to some organisms, but are noncarcinogenic. The higher-molecular-weight PAHs, containing four to seven rings, are significantly less toxic, but many of these compounds are demonstrably carcinogenic, mutagenic, or teratogenic to a wide variety of organisms, including fish and other aquatic life, amphibians, birds, and mammals. In general, PAHs show little tendency to biomagnify in food chains, despite their high lipid solubility, probably because most PAHs are

rapidly metabolized. Inter- and intraspecies responses to individual PAHs are quite variable, and are significantly modified by many inorganic and organic compounds, including other PAHs. Until these interaction effects are clarified, the results of single-substance laboratory tests may be extremely difficult to apply to field situations of suspected PAH contamination.

PAHs are ubiquitous in nature — as evidenced by their detection in sediments, soils, air, surface waters, and plant and animal tissues — primarily as a result of natural processes such as forest fires, microbial synthesis, and volcanic activities. Anthropogenic activities associated with significant production of PAHs — leading, in some cases, to localized areas of high contamination — include high-temperature ($>700^{\circ}\text{C}$) pyrolysis of organic materials typical of some processes used in the iron and steel industry, heating and power generation, and petroleum refining. Aquatic environments may receive PAHs from accidental releases of petroleum and its products, from sewage effluents, and from other sources. Sediments heavily contaminated with industrial PAH wastes have directly caused elevated PAH body burdens and increased frequency of liver neoplasia in fishes. At present, no criteria or standards have been promulgated for PAHs by any regulatory agency for the protection of sensitive species of aquatic organisms or wildlife. This observation was not unexpected in view of the paucity of data on PAH background concentrations in wildlife and other natural resources, the absence of information on results of chronic oral feeding studies of PAH mixtures, the lack of a representative PAH mixture for test purposes, and the demonstrable — and, as yet, poorly understood — effects of biological and nonbiological modifiers on PAH toxicity and metabolism. By contrast, criteria for human health protection and total PAHs, carcinogenic PAHs, and benzo[a]pyrene have been proposed for drinking water and air, and for total PAHs and benzo[a]pyrene in food: drinking water, 0.01 to $<0.2\text{ }\mu\text{g}$ total PAHs/L, $<0.002\text{ }\mu\text{g}$ carcinogenic PAHs/L, and $<0.0006\text{ }\mu\text{g}$ benzo[a]pyrene/L; air, $<0.01\text{ }\mu\text{g}$ total PAHs/m³, $<0.002\text{ }\mu\text{g}$ carcinogenic PAHs/m³, and $<0.0005\text{ }\mu\text{g}$ benzo[a]pyrene/m³; food, 1.6 to $<16.0\text{ }\mu\text{g}$ total PAHs daily, and 0.16 to $<1.6\text{ }\mu\text{g}$ benzo[a]pyrene daily. In view of the carcinogenic characteristics of many PAH compounds and their increasing concentrations in the environment, it now seems prudent to reduce or eliminate them wherever possible, pending acquisition of more definitive ecotoxicological data.

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CHAPTER 26

Sodium Monofluoroacetate (Compound 1080)

26.1 INTRODUCTION

Sodium monofluoroacetate (CH_2FCOONa), also known as 1080 or Compound 1080, belongs to a class of chemicals known as the fluoroacetates (Pattison 1959). It is a tasteless and odorless water-soluble poison of extraordinary potency that has been used widely against rodents and other mammalian pests (Anonymous 1946; Negherbon 1959; Rammell and Fleming 1978; McIlroy 1981a; Hornshaw et al. 1986; Aulerich et al. 1987; Connolly and Burns 1990; Eisler 1995). The widespread use of 1080 in pest control has resulted in accidental deaths of livestock, wildlife, pets (cats and dogs), and humans (Anonymous 1946; Chenoweth 1949; Sayama and Brunetti 1952; Negherbon 1959; U.S. Environmental Protection Agency [USEPA] 1976; McIlroy 1982a), and several suicides in Asia from drinking 1080 rat poison solutions (Howard 1983). There is no effective antidote to 1080 (Mead et al. 1991). When consumed, fluoroacetate is converted to fluorocitrate, inhibiting the enzymes aconitase and succinate dehydrogenase. The accumulated citrate interferes with energy production and cellular function (Aulerich et al. 1987).

Monofluoroacetic acid (CH_2FCOOH) was first synthesized in Belgium in 1896 but attracted little attention from chemists and pharmacologists at that time (Chenoweth 1949; Atzert 1971). In 1927, sodium monofluoroacetate was patented as a preservative against moths (Sayama and Brunetti 1952). The toxic nature of monofluoroacetate compounds was first noted in Germany in 1934 (Atzert 1971). In the late 1930s and early 1940s Polish scientists conducted additional research on the toxic properties of fluoroacetate compounds, especially on the methyl ester of fluoroacetic acid that they had synthesized (Anonymous 1946; Chenoweth 1949). In 1942, British scientists further refined this compound to the sodium salt, which became known as 1080 (Anonymous 1946). In 1944, potassium monofluoroacetate (CH_2FCOOK) was isolated from *Dichapetalum cymosum*, a South African plant, and was the first known example of a naturally occurring organic fluoride; the plant, known locally as Gifblaar, caused many livestock deaths (Chenoweth 1949) and was recognized by Europeans as poisonous as early as 1890 (Peacock 1964). Fluoroacetate compounds have since been isolated from poisonous plants in Australia (*Acacia georginae*, *Gastrolobium* spp.), Brazil (rat weed, *Palicourea marginata*), and Africa (*Dichapetalum* spp.) (Atzert 1971). Ratsbane (*Dichapetalum toxicarium*), a west African plant, was known to contain a poison — subsequently identified as a fluoroacetate — that was lethal to rats, livestock, and humans and reportedly used by African natives during the 1800s to poison the wells and water supplies of hostile tribes (Anonymous 1946).

During World War II (1939 to 1945), as a result of acute domestic shortages of common rodenticides, such as thallium, strichnine, and red squill, a testing program was initiated for

alternative chemicals (Anonymous 1946). In June 1944, the U.S. Office of Scientific Research and Development supplied the Patuxent Wildlife Research Center (PWRC) — then a U.S. Fish and Wildlife Service laboratory — with sodium monofluoroacetate and other chemicals for testing as rodenticides (Atzert 1971). Sodium monofluoroacetate received the PWRC acquisition number 1080, which subsequently was adopted as its name by the chemical's manufacturer. Samples of 1080 were also shipped to the Denver Wildlife Research Center, another former U.S. Fish and Wildlife Service laboratory, for testing on additional species. Results of these tests gave evidence of the value of 1080 as an effective method of controlling animal predators of livestock and other animal pests (Atzert 1971). During World War II, 1080 protected Allied troops in the Pacific theater against scrub typhus, also known as "tsut sugamushi," a louse-borne rickettsial disease with rodents as vectors (Peacock 1964). In the United States, 1080 was first used in 1945 to control rodents, and later coyotes (*Canis latrans*), rabbits, prairie dogs, and gophers (Hornshaw et al. 1986; Aulerich et al. 1987). Between 1946 and 1949, at least 12 humans died accidentally in the United States from 1080 poisoning when it was used as a rodenticide; a child became ill but recovered after eating the cooked flesh of a 1080-poisoned squirrel (USEPA 1976). Since 1955, 1080 has been used extensively in a variety of baits — especially in Australia and New Zealand — to control European rabbits (*Oryctolagus cuniculus*), dingoes (*Canis familiaris dingo*), feral pigs (*Sus scrofa*), brush-tailed possums (*Trichosurus vulpecula*), and various species of wallabies (McIlroy 1981a, 1981b, 1982a, 1984; Twigg and King 1991). In Australia, vegetable baits are sometimes eaten by nontarget herbivores, such as sheep (*Ovis aries*), cattle (*Bos taurus*), and various species of wildlife, causing both primary and secondary poisoning of nontarget animals (McIlroy 1982a). In the United States, most uses of 1080 were canceled in 1972 due, in part, to deaths of nontarget animals (Balcomb et al. 1983). At present, the use of 1080 in the United States is restricted to livestock protection collars on sheep and goats (*Capra hircus*) against predation by coyotes (Palmateer 1989, 1990). Useful reviews on ecotoxicological aspects of 1080 include those by Chenoweth (1949), Peacock (1964), Atzert (1971), Kun (1982), Twigg and King (1991), Seawright and Eason (1994), and Eisler (1995).

26.2 USES

The use of 1080 in the United States is now restricted to livestock collars on sheep and goats for protection against predation by coyotes. Other countries, most notably Australia and New Zealand, use 1080 extensively in a variety of baits to control many species of vertebrate pests.

26.2.1 Domestic Use

Compound 1080 is highly poisonous to all tested mammals as well as humans (Green 1946). There is no known antidote to 1080, and it has been impossible to resuscitate any animal or human poisoned with 1080 once final stages of poisoning have appeared (Kalbach 1945; Green 1946; Connolly 1989, 1993a). In 25 years of use in the United States, there have been four suicides and at least 12 accidental human deaths; between 1959 and 1969, 37 known incidents of domestic animal poisoning have resulted from federal use of 1080 (Atzert 1971). Compound 1080 is not recommended for use in residential areas or for distribution in places where the public might be exposed (Green 1946); only licensed pest control operators can use 1080 (Green 1946; Peacock 1964; USEPA 1985; Murphy 1986). Tull Chemical in Oxford, Alabama, is the sole domestic producer of 1080; none is imported (USEPA 1985). When handling 1080, human operators should wear protective clothing, including gloves and a respirator; extreme caution is recommended at all times (Green 1946). Each applicator must carry syrup of ipecac to induce vomiting in case of accidental 1080 poisoning when attaching, removing, or disposing of livestock protection collars (Connolly 1989, 1993a).

Compound 1080 was first used in the United States in the late 1940s to control gophers, ground squirrels, prairie dogs, field mice, commensal rodents, and coyotes (Chenoweth 1949; Fry et al. 1986). Coyote damage to livestock in California alone is estimated at \$75 million annually (Howard 1983). Yearly amounts of 1080 used in the United States for predator control were 23 kg in the early 1960s, 7727 kg in the late 1960s, and only 8 kg in 1971 (Connolly 1982). Total production of 1080 in the United States between 1968 and 1970 averaged about 1182 kg annually (Atzert 1971). In 1977, 277,545 kg of 1080-containing baits (272 kg of 1080) were used to control ground squirrels (76%), prairie dogs (7%), and mice, rats, chipmunks, and other rodents (17%); California used 83% of all 1080 baits, Colorado 12%, and Nevada and Oregon 5% (USEPA 1985). About 0.3 kg 1080 per year are used in the livestock protection collar, but only about 35 g per year is released into the environment (Connolly 1993b). In March 1972, the use of 1080 for predator control was prohibited on federal lands. Later that year, all uses of 1080 for predator control were banned in the United States because of adverse effects on nontarget organisms, including endangered species (Palmateer 1989, 1990). In the period since 1080 was banned, the number of grazing livestock reported lost to predation on western national forests has increased. Between 1960 and 1971, 1.42% (range 1.0 to 1.9%) of all sheep and goats grazed were lost to predators vs. 2.17% (1.7 to 2.5%) in 1970 to 1978 (Lynch and Nass 1981). Until it was banned in 1972, the use of 1080 as a predator control agent in the United States was strictly controlled. The chemical was registered under the Federal Insecticide, Fungicide and Rodenticide Act (61 Stat 163; 7 U.S.C. 135-135K) for use only by governmental agencies and experienced pest control operators (Atzert 1971). The use of 1080 as a rodenticide was disallowed in 1985 for three reasons:

1. Lack of emergency treatment, namely a viable medical antidote
2. High acute toxicity to nontarget mammals and birds
3. A significant reduction in populations of nontarget organisms and fatalities to endangered species (USEPA 1985)

In 1985, 1080 use was conditionally permitted in livestock protection collars and in single lethal dose baits; a registration for the livestock protection collar was issued to the U.S. Department of the Interior on July 18, 1985 (USEPA 1985). On February 21, 1989, the registration for 1080 was canceled, effectively prohibiting all uses. In June 1989, however, technical 1080 was conditionally approved for use only in the 1080 livestock protection collar. The 30-mL collar is registered for use by the U.S. Department of Agriculture; by the states of Montana, Wyoming, South Dakota, and New Mexico; and by Rancher's Supply, Alpine, Texas (Palmateer 1989, 1990).

Compound 1080 was highly effective against all species of rats, prairie dogs, and ground squirrels, and satisfactory for the control of mice (Peacock 1964). The chemical was formulated in grain baits or chopped greens for crop and range rodents, and in water bait stations to control rats (USEPA 1985). The concentration of 1080 in baits was lowered to 0.02% both in the range of the California condor (*Gymnogyps californianus*) and for prairie dog control because of possible impacts on the endangered black-footed ferret (*Mustela nigripes*) (USEPA 1985). Commercial 1080 was commonly colored with 0.5% nigrosine and sold as a compound containing >90% sodium monofluoroacetate, to be mixed with foods at 2226 mg/kg in preparing baits, or dissolved in water at 3756 mg/L for poisoning drinking water in indoor control of rodents (Anonymous 1946; Green 1946; Negherbon 1959). Bait acceptance by rats was not significantly reduced by the dye (Peacock 1964). Compound 1080 was adequately accepted by rats and mice when present in water; solid food baits poisoned with 1080 were not always accepted as readily and sometimes required special preparation to insure the ingestion of lethal amounts (Green 1946). A water solution of 1080 was the most effective rodenticide tested for rat control in southern states, and 1080-grain baits were the most effective field rodenticides against ground squirrels, prairie dogs, and mice in California, South Dakota, and Colorado (Kalmach 1945). Seeds and cereal grains were the most effective baits

for small rodents: 1 kg 1080 was sufficient to kill 3.96 million squirrels (Peacock 1964). Grain baits were colored brilliant yellow or green to heighten repellency to birds; coloring baits did not affect their acceptance by rodents (Peacock 1964; Atzert 1971). Rats did not develop any significant tolerance to 1080 from ingestion of sublethal doses, although rats that survived a poisoning incident may develop an aversion to 1080 (Green 1946; Peacock 1964).

To kill coyotes and wolves (*Canis lupus*) in the United States and Canada, meat baits containing 35 mg 1080/kg were recommended, usually by injecting a water solution of 1080 into horse meat baits; only 28 to 56 g of a poisoned bait was sufficient to kill (Peacock 1964). Meat baits were usually placed during the autumn in areas with maximum coyote use and minimum use by most nontarget carnivores (Atzert 1971). The most widely publicized technique for poisoning predators was the 1080 large bait station: a 22- to 45-kg livestock meat bait injected with 35 mg 1080/kg bait (Connolly 1982). The use of 1080 stations peaked in the early 1960s, at which time 15 to 16 thousand stations were placed each winter in the western United States. After 1964, the number of stations declined annually, to 7289 stations in 1971 (Connolly 1982). Against canine predators of livestock, 1080 was more selective and less hazardous to nontarget species than strichnine or traps (Peacock 1964). Meat baits used to control coyotes were seldom fatal to hawks, owls, and eagles, even when these raptors gorged themselves on the 1080-poisoned baits (Peacock 1964). In addition to the large bait stations, an unknown number of U.S. government hunters used 1080 in smaller baits at various stations (Connolly 1982).

The introduction of 1080-livestock protection collars to protect goats and sheep against coyote depredation was initiated in 1985. Its use was limited to certified applicators (Burns et al. 1991). The 1080-filled rubber collars are attached to the throats of sheep and goats; 1080 is released when coyotes attack collared livestock with characteristic bites to the throat (Walton 1990; Burns et al. 1991). The livestock protection collars contain 30 mL of a 1% 1080 solution (Walton 1990) and tartrazine (Burns and Savarie 1989; Connolly 1993a) as a marker. The livestock protection collar may not be used in areas known to be frequented by endangered species of wildlife, and this includes various geographic areas in California, Michigan, Minnesota, Montana, Washington, Wisconsin, and Wyoming (Connolly 1989, 1993a). Compound 1080 is reportedly more effective and safer in livestock protection collars than sodium cyanide, diphacinone, or methomyl (Connolly 1982). Pen tests with compound 1080 in livestock protection collars began in late 1976, and field tests in 1978 (Connolly and Burns 1990). Under field conditions, 1080 livestock protection collars on sheep seem to protect selectively against predation by coyotes; no adverse effects on humans, domestic animals, and nontarget wildlife were recorded (Connolly and Burns 1990). The decision to permit limited use of 1080 in livestock protection collars is now being contested by at least 14 conservation groups because of its alleged hazard to nontarget organisms (bears, badgers, dogs, eagles) and to human health, and to the availability of alternate and more successful methods of coyote control (Sibbison 1984). In Texas, for example, annual predation losses of sheep and goats to coyotes are estimated at \$5 million. But very few Texas ranchers have taken advantage of the opportunity to use livestock protection collars, and only 23 coyotes were killed in 1989 by the collars vs. 473 by cyanide, snares, aerial gunning, and other control measures (Walton 1990). Toxic livestock protection collars in full operation would probably kill <1000 coyotes annually vs. 1 million coyotes killed annually in sport hunting and other control measures (Sibbison 1984).

Compound 1080 was also effective against jackrabbits, foxes, and moles. Baits containing 0.05 to 0.1% 1080 on vegetables were used in California to kill jackrabbits (*Lepus* spp.) and various rodents (Schitoskey 1975). The Arctic fox (*Alopex lagopus*), intentionally introduced onto the Aleutian Islands in 1835 (Bailey 1993), almost eliminated the Aleutian Canada goose (*Branta canadensis leucoparlia*) by 1967. 1080-tallow baits were successfully used to control fox populations (Byrd et al. 1988; Tietjen et al. 1988; Bailey 1993). Earthworm baits are used to kill moles. The earthworms are soaked for 45 min in a 2.5% solution of 1080 and placed in mole burrows. The solution can be used several times for additional lots of worms; however, the use of the manure worm (*Eisenia foetida*) should be avoided because it is seldom eaten by moles (Peacock 1964).

Secondary poisoning of domestic cats and dogs from consumption of 1080-poisoned rodents was frequently noted (Anonymous 1946). Cats and dogs are highly susceptible to 1080 and may die after eating freshly poisoned rodents, dried carcasses, or 1080 baits, or after drinking 1080-poisoned water (Green 1946). All pets should be confined or removed from the area to be poisoned and released after the entire program has been completed. Pigs and carnivorous wildlife are also at risk from consumption of 1080-poisoned rodents (Peacock 1964). Secondary poisoning of kit foxes (*Vulpes* spp.) is theoretically possible after eating a single kangaroo rat (*Dipodomys* spp.) that had swallowed or stuffed its cheeks with 1 g of a 0.1% vegetable/cereal bait and contained a total whole-body burden of about 1 mg 1080 per rat (Schitoskey 1975). To prevent secondary poisoning, all uneaten baits and carcasses of poisoned rodents should be recovered and incinerated (Green 1946), and no 1080-contaminated animal should be eaten by humans or fed to animals (Connolly 1989, 1993a).

26.2.2 Nondomestic Use

Compound 1080 has had limited use as a vertebrate pesticide in Canada, India, Mexico, and South Africa, and extensive use in Australia (Calver et al. 1989b) and New Zealand (Rammell and Fleming 1978). In Canada, 1080 was first used in 1950 in British Columbia to control wolves and coyotes preying on livestock (Peacock 1964). Poisoned 1080 baits were used in India to control (67 to 100% effective) populations of the Indian crested porcupine (*Hystrix indica*) throughout its range because of porcupine-caused damage and losses to agriculture crops; however, 1080 baits were not as effective as fumigants in controlling this species (Khan et al. 1992). In Mexico, 1080 was used against rabid coyotes, although many domestic dogs were also killed (Peacock 1964). In South Africa, beginning in 1961, 1080 was used to control the black-backed jackal (*Canis mesomelas*) preying on livestock, and baboons (*Papio anubis*) and moles that consumed agricultural crops (Peacock 1964). Livestock protection collars containing 30 mL of a 1% 1080 solution are now used in South Africa to combat predation by the Asiatic jackal (*Canis aureus*) (Walton 1990).

Compound 1080 was first used in Australia in the 1950s to kill the introduced European rabbit (*Oryctolagus cuniculus*). Principal target species in Australia now include other introductions such as dingoes, foxes (*Vulpes vulpes*), feral pigs (*Sus scrofa*), feral cats (*Felis cattus*), as well as native brush-tailed possums (*Trichosurus vulpecula*), red-necked wallabies (*Macropus rufogriseus*), and pademelons (*Thylogale billardierii*) (McIlroy 1981a, 1981b, 1982, 1984; Calver et al. 1989a, 1989b; Wong et al. 1991). In Australia, different baits contained different concentrations of 1080; meat baits contained 144 mg/kg, grain baits 288 to 300 mg/kg, fruits and vegetables 330 mg/kg, and pellets 500 mg/kg (McIlroy 1983a).

One method of killing rabbits in many areas of Australia is to apply 1080-poisoned bait (carrots, oat grains, pellets of bran or pollard) to furrows made in the earth or broadcast across the area from the air or ground (McIlroy 1984; McIlroy and Gifford 1991). Aerial dropping of diced carrots treated with 1080 was found to be almost 100% effective for rabbits (Anonymous 1964). In Victoria, more than 6.5 million ha were treated with 1080-poisoned carrots. To attract rabbits to the kill area, nonpoisoned carrots were applied to rabbit trails at more than 8.3 kg/km; nonpoisoned baits were offered twice, 3 days apart, followed by 1080-poisoned carrots 1 week later (Woodfield et al. 1964). Bait avoidance is reported in some populations of European rabbits exposed repeatedly to 1080 baits through sustained control programs. Behavioral resistance may reduce the effectiveness of sustained control and should be considered in pest management plans (Hickling 1994). Individuals — but not populations — of some native species of Australian animals and birds face a greater risk of being poisoned by 1080 during rabbit-poisoning campaigns than rabbits, particularly herbivorous macropodids, rodents, and birds with no prior exposure history to naturally occurring fluoroacetates (McIlroy 1992). Foxes, dingoes, dogs, and cats seem to be at greater risk of secondary poisoning than native birds and mammals, particularly from eating muscle from poisoned rabbits that contained as much as 5 mg 1080 per rabbit (McIlroy 1992).

The injection method of fresh meat baits for use in control of dingoes produced baits more uniform with respect to the amount of 1080 in the bait when compared with mixed baits prepared by tumbling in 1080 solutions. Both techniques, however, produced baits containing variable quantities of 1080 (Kramer et al. 1987). Use of 1080-poisoned baits to control wild dogs (*Canis familiaris familiaris*) and dingoes was not as successful as traps: 22% control for 1080 vs. 56% control for traps. Factors that reduced the success of poisoned baits included rapid loss in toxicity of the baits after their distribution; the rapid rate at which they were removed by other animals, particularly foxes and birds; and the dogs' apparent preference for natural prey (McIlroy et al. 1986a).

Feral pigs in Australia damage crops, degrade pasture, kill and eat lambs, and are potential vectors and reservoirs of exotic pathogens (O'Brien et al. 1986; O'Brien 1988). Control of feral pigs with poisoned baits, including 1080 bait, is difficult because most pigs regurgitate these baits shortly after ingestion (O'Brien et al. 1986). The vomitus may cause secondary poisoning of nontarget species, and pigs surviving sublethal exposure to 1080 as a result of vomiting may develop an aversion to 1080, thus decreasing their susceptibility to subsequent poisoning programs. The incorporation of antiemetics into 1080 baits should reduce or prevent vomiting, but those tested were not completely successful (O'Brien et al. 1986). Feral cats have altered ecosystems and depleted populations of indigenous lizards and birds on Australia, New Zealand, and numerous island habitats throughout the world. Fresh fish baits injected with 2 mg 1080 per bait are used as a humane and lethal poison for feral cats (Eason and Frampton 1991).

The use of 1080 in New Zealand is restricted to licensed operators employed by pest destruction boards and government departments (Temple and Edwards 1985). In Australia, and other locations, the addition of dye to identify toxic baits is standard practice (Temple and Edwards 1985; Statham 1989). The main purpose of such addition is to reduce the unintentional poisoning of birds; birds eat significantly less blue- or green-dyed feed than undyed feed (Statham 1989). Although birds prefer undyed baits to those dyed green, Canada geese (*Branta canadensis*) when feeding at night are unable to distinguish between dyed and undyed baits and consume both with equal frequency (Temple and Edwards 1985). Carrots used as wallaby baits in New Zealand are dyed with special green or blue pigments; however, the red-necked wallaby (*Macropus rufogriseus*) accepted both dyed and undyed carrots equally (Statham 1989). Mice (*Mus* spp.) readily consumed dyed wheat (Twigg and Kay 1992). Compound 1080 is used in jam-type baits to control brush-tailed possums. These baits contained 1080 at concentrations as high as 1500 mg 1080/kg FW bait and were dyed green to protect birds. Cinnamon was added to mask the flavor of the 1080 poison, and 800 mg potassium sorbate/kg was added as an antifungal bait preservative (Goodwin and Ten Houten 1991).

The Norway rat (*Rattus norvegicus*) had a severe effect on island populations of New Zealand birds, reptiles, and invertebrates (Moors 1985). In one case, rats on Big South Island exterminated five species of native forest birds within 3 years, including the last known population of the bush wren (*Xenicus longipes*). A paste containing petroleum jelly, soya oil, sugar, green dye, and 800 mg 1080/kg remained toxic for 6 to 9 months to rats preying on grey-faced petrels (*Pterodroma macroura*) and other birds. Because 1080 produces a poison-shyness in any Norway rat that eats a sublethal dose, complete eradication of this species by 1080 is improbable (Moors 1985). The use of anticoagulants — such as warfarin (multiple doses needed), brodifacoum (single dose) or coumatetralyl — seems more promising than 1080 in rat control programs (Moors 1985), although secondary poisoning of owls and hawks may occur (Hegdal and Colvin 1988).

In New Zealand, compound 1080 in a gel carrier is sometimes applied to the leaves of broadleaf (*Griselinia littoralis*) to poison red deer (*Cervus elephas*), feral goats, white-tailed deer (*Odocoileus virginianus*), and red-necked wallabies (Batcheler and Challies 1988). Use of 1080 gel baits reduced feral goat populations by 90% (Parkes 1983). Wallaby populations were reduced 87 to 91% using a 1080 gel applied to the foliage of palatable plants, and this compares favorably to reductions achieved using aerially sown baits (Warburton 1990). The gel carrier was an effective phytotoxin,

causing withering, death, or loss of chlorophyll from leaves within 10 days, and sometimes within 24 h (Parkes 1983).

Feral pigs are sometimes poisoned by inserting as many as 10 gelatin capsules (each containing 100 mg 1080) into carcass or offal baits. Poisoned carcasses may remain edible for more than 2 months during autumn and winter when poisoning campaigns are conducted. The 1080 is leached out when the carcass has disintegrated (McIlroy 1983a). Other techniques to control feral pigs include injection of 1080 gel into beef lung baits or insertion of capsules containing 1080 into apple, potato, or other fruit and vegetable baits. However, these techniques are potentially the most dangerous to applicators because 1080 powder, rather than a diluted solution, is used. Also, the baits are lethal to nontarget scavengers (McIlroy 1983a).

26.3 ENVIRONMENTAL CHEMISTRY

26.3.1 General

Sodium monofluoroacetate is a whitish powder, soluble in water to at least 263 mg/L but relatively insoluble in organic solvents. Some aqueous solutions of 1080 retain their rodenticidal properties for at least 12 months, but others lose as much as 54% of their toxicity after 24 days. Compound 1080 is unstable at $>110^{\circ}\text{C}$ and decomposes at $>200^{\circ}\text{C}$, although 1080 in baits or poisoned carcasses is comparatively stable. Losses of 1080 from meat baits are due primarily to microbial defluorination, and also to leaching from rainfall and consumption by maggots. Leachates from 1080 baits are not likely to be transported long distances by groundwater because they tend to be held in the upper soil layers. Compound 1080 can be measured in water at concentrations as low as 0.6 $\mu\text{g}/\text{L}$ and in biological samples at 10 to 15 $\mu\text{g}/\text{kg}$. As discussed later, 1080 is readily absorbed through the gastrointestinal tract, mucous membranes, and pulmonary epithelia. Once absorbed, it is uniformly distributed in the tissues. Metabolic conversion of high concentrations of fluoroacetate to fluorocitrate results in large accumulations of citrate in the tissues and eventual death from ventricular fibrillation or respiratory failure. Regardless of dose and in all tested species, no signs or symptoms of 1080 poisoning were evident during a latent period of 30 min to 2 h; however, death usually occurred within 24 h of exposure. Repeated sublethal doses of 1080 have increased the tolerance of some species of tested birds and mammals to lethal 1080 doses. Reptiles are more resistant to 1080 than mammals because of their low facility to convert fluoroacetate to fluorocitrate and their high defluorination capability. No effective antidote is now available to treat advanced cases of fluoroacetate poisoning; accidental poisoning of livestock and dogs by 1080 is likely to be fatal. Partial protection against 1080 poisoning in mammals has been demonstrated with glycerol monoacetate, a sodium acetate/ethanol mixture, and a calcium glutonate/sodium succinate mixture.

26.3.2 Chemical Properties

Some chemical and other properties of 1080 are summarized in [Table 26.1](#). In water, trace amounts (0.6 $\mu\text{g}/\text{L}$) of 1080 were detected using gas chromatography (GC) with electron capture detection; recoveries from environmental water spiked at 5 to 10 $\mu\text{g}/\text{L}$ ranged from 93 to 97% (Ozawa and Tsukioka 1987). Recent advances make it possible to measure 1080 in solutions at concentrations as low as 0.2 $\mu\text{g}/\text{L}$ (Kimball and Mishalanie 1993). In biological tissues, various methods have been used to determine fluoroacetic acid, including colorimetry, fluoride-ion electrodes, gas-liquid chromatography, and high-pressure chromatography. However, these methods involve lengthy extraction procedures, have low recoveries, or show lack of selectivity (Allender 1990). A sensitive gas chromatographic technique was developed and used successfully to determine

Table 26.1 Some Properties of Sodium Monofluoroacetate

Variable	Data
Alternate names	1080; Compound 1080; fratol; monosodium fluoroacetate; sodium fluoacetate; sodium fluoroacetate; ten-eighty
Chemical formula	CH_2FCOONa
Molecular weight	100.03
Physical state	White, odorless, almost tasteless, hygroscopic powdery salt, resembling powdered sugar or baking powder
Primary use	Rodenticide; mammal control agent
Purity	96.0–98.6%
Solubility	
Water	263 mg/L
Acetone, alcohol, animal and vegetable fats, kerosene, oils	Relatively insoluble
Stability	Unstable at >110°C and decomposes at >200°C. Hydrogen fluoride (20% by weight) is a decomposition product which readily reacts with metals or metal compounds to form stable inorganic fluoride compounds

^a Data from Chenoweth 1949; Negherbon 1959; Peacock 1964; Tucker and Crabtree 1970; Atzert 1971; Hudson et al. 1984.

fluoroacetate levels in organs from a magpie (*Gymnorhina tibicen*) that had ingested a bait containing 1080 poison. The procedure involved extraction of 1080 with acetone:water (8:1), followed by derivatization with pentafluorobenzyl bromide. Bait samples were initially screened by thin-layer chromatography, and identification of derivatized extracts was confirmed by gas chromatography–mass spectrometry GC–MS (Allender 1990). A new method for fluoroacetate determination in biological samples involves isolation of fluoroacetate as its potassium salt by ion-exchange chromatography and conversion to its dodecyl ester. The ester is quantified by capillary GC with a flame ionization detector for the range 1 to 10 mg/kg and by selected ion monitoring using GC–MS for the range 0.01 to 1.00 mg/kg (Burke et al. 1989). The detection limit for 1080 in tissues and baits is 15 µg/kg using a reaction-capillary GC procedure with photoionization detection; the detection limit is 100 µg/kg using flame ionization procedures. The detection limit using these procedures is less sensitive than GC–MS; however, GC–MS is not normally available in veterinary diagnostic laboratories (Hoogenboom and Rammell 1987).

26.3.3 Persistence

Significant water contamination is unlikely after aerial distribution of 1080 baits (Eason et al. 1993a). In one New Zealand field trial in which >20 metric tons of 1080 baits were aerially sown over a 2300-ha island to control brushtail possums (*Trichosurus vulpecula*) and rock wallabies (*Petrogale penicillata*), no 1080 was detected in surface or groundwater of the island for at least 6 months after baits were dropped. A similar case was made for streams and rivers after 100 metric tons of 1080 baits were sown by airplane over 17,000 ha of forest (Eason et al. 1992, 1993b). Laboratory studies on 1080 persistence in solutions suggest that degradation to nontoxic metabolites is most rapid at elevated temperatures and in biologically conditioned media, but is highly variable. In general, aqueous solutions of the salt or esters decrease in toxicity over time through spontaneous decarboxylation to sodium bicarbonate and to the highly volatile, relatively nontoxic, methyl fluoride. Solutions refrigerated at 5°C lost about 54% of their initial toxicity to laboratory rats after 24 days and about 40% after 7 days at room temperature, but 1080 solutions remained toxic to yeast for at least 1 month after storage at 3 to 5°C (Chenoweth 1949). In an aquarium containing plants and invertebrates and 0.1 mg 1080/L, water concentration of 1080 declined 70% in 24 h and was not detectable after 100 h; residues in plants were not detectable after 330 h (Eason et al.

1993b). In a distilled water aquarium without biota, 1080 residues declined only 16% in 170 h (Eason et al. 1993b). In another study, 1080 solutions prepared in distilled water and stored at room temperature for 10 years showed no significant breakdown; moreover, solutions of 1080 prepared in stagnant algal-laden water did not lose biocidal properties over a 12-month period (McIlroy 1981a). More research seems needed on 1080 persistence in aquatic environments.

In soils, 1080 is degraded to nontoxic metabolites by soil bacteria and fungi, usually through cleavage of the carbon–fluoride bond (Eason et al. 1991, 1993a). Soil microorganisms capable of defluorinating 1080 include *Aspergillus fumigatus*, *Fusarium oxysporum*, at least three species of *Pseudomonas*, *Nocardia* spp., and two species of *Penicillium* (Wong et al. 1992a). These microorganisms can defluorinate 1080 when grown in solution with 1080 as the sole carbon source, and also in autoclaved soil; the amount of defluorination ranged from 2 to 89% in soils and 2 to 85% in 1080 solutions. Some indigenous soil microflora were able to defluorinate 50 to 87% of the 1080 within 5 to 9 days in soil at 10% moisture at 15 to 28°C. The most effective defluorinators in solution and in soils were certain strains of *Pseudomonas*, *Fusarium*, and *Penicillium* (Wong et al. 1991, 1992a; Walker 1994). *Pseudomonas cepacia*, for example, isolated from the seeds of various fluoroacetate-accumulating plants can grow and degrade fluoroacetate in fluoroacetate concentrations as high as 10,000 mg/kg (Meyer 1994). Biodeflourination of 1080 by soil bacteria was maximal under conditions of neutral to alkaline pH, fluctuating temperatures between 11 and 24°C, and at soil moisture contents of 8 to 15%; biodeflourination of 1080 by soil fungi was maximal at pH 5 (Wong et al. 1992b).

Losses of 1080 from meat baits were most likely due to consumption of the bait by blowfly maggots, leaching by rainfall, defluorination by microorganisms, and leakage from baits during their decomposition (McIlroy et al. 1988). The 1080 in baits will persist under hot and dry conditions where leaching from rain is unlikely (Wong et al. 1992a). Baits remained toxic to dogs for over 32 days during winter when maggots were absent and 6 to 31 days during summer when maggots were present. Baits contained an average LD₅₀ dose to tiger quolls (*Dasyurus maculatus*) — a raccoon-like marsupial — for 4 to 15 days in winter and 2 to 4 days in summer (McIlroy et al. 1988). Meat baits that initially contained 4.6 mg 1080 retained 62% after 3 days, 29% after 6 days, and 28% after 8 days (McIlroy et al. 1986a). The persistence of 1080 in fatty meat baits for control of wild dogs in Australia was measured over a period of 226 days (Fleming and Parker 1991). Baits that initially contained 5.4 mg 1080 retained 73% at day 7, 64% at day 20, 25% at day 48, and 15% at day 226. These baits retained LD₅₀ kill values after 52 days to wild dogs, 93 days to cattle dogs, and 171 days to sheep dogs. In that study, loss of 1080 from the baits was not correlated with rainfall, temperature, or humidity. Losses were attributed to metabolism of 1080 bound to the fatty meat bait, leaching, consumption by maggots, and bacterial defluorination (Fleming and Parker 1991). When it is desirable for baits to remain toxic for long periods, the defluorination activity and microbial growth can be reduced significantly by incorporating bacteriostats and fungistats. Conversely, baits may be inoculated with suitable defluorinating microbes that rapidly detoxify 1080-poisoned baits (Wong et al. 1991).

Compound 1080 was found to be highly persistent in diets formulated for mink (*Mustela vison*). Mink diets analyzed 30 months after formulation lost 19 to 29% of the 1080 when the initial concentration ranged between 0.9 and 5.25 mg 1080/kg; loss was negligible at 0.5 mg 1080/kg ration (Hornshaw et al. 1986). A paste containing 0.08% 1080 plus petroleum jelly, soya oil, sugar, and green dye retained its rodenticidal properties for 6 to 9 months. But a rolled oats/cat food 1080 bait, because of its moistness, became fly-infested in warm weather, tended to rot, and lost its rodenticidal properties in a few days (Moors 1985). Gel baits set to kill deer were sampled after 45 days of weathering; only 10% of the 1080-treated leaves retained toxic gel after 45 days (Batcheler and Challies 1988). About 1.4% of 1080 was lost from the leaves per millimeter of rainfall; about 90% was lost in two trials in which 81 and 207 mm of rainfall were recorded. Compound 1080 decreased from 604 mg/bait at the start, to 76 mg/bait after 30 days, and to 5 mg/bait after 45 days. Significant losses of compound 1080 also resulted from biodegradation in

storage. *Penicillium* spp. from broadleaf samples degraded 1080 at pH 5.4 and 23°C and grew vigorously on 1080-poisoned gels; other species of microorganisms can also degrade 1080 (Batcheler and Challies 1988).

Leachates from 1080-poisoned baits are not likely to be transported long distances by the leaching water because they are held in the upper soil layers (Atzert 1971). This statement is predicated on the facts that: (1) salts of monofluoroacetic acid rapidly adsorb to plant tissues and other cellulosic materials; (2) some plants can decompose 29% of the adsorbed 1080 in 48 h; and (3) 1080 in soils is decomposed by soil microorganisms (Atzert 1971). The percent of 1080 defluorinated from various bait materials after 30 days as a result of microbial action ranged between 0.0 and 7.2% for cereals, eggs, horse meat, and beef; 14% for kangaroo meat; and 71% for oats (Wong et al. 1991). The defluorinating ability of fungi and bacteria was low when 1080 was the sole carbon source and high when alternative carbon sources such as peptone-meat extracts were present. The extent of defluorination varied among the different types of organisms associated with the baits. Microorganisms isolated from oats and kangaroo meat had the highest defluorinating activity, and those from cereals and eggs the lowest (Wong et al. 1991).

26.3.4 Metabolism

Sodium monofluoroacetate is absorbed through the gastrointestinal tract, open wounds, mucous membranes, and the pulmonary epithelium. It is not readily absorbed through intact skin (Negherbon 1959; Atzert 1971). Once absorbed, it seems to be uniformly distributed in the tissues, including the brain, heart, liver, and kidney (Peacock 1964). All tested routes of 1080 administration are equally toxic: there is no noteworthy difference in the acute toxicity of 1080 when administered orally, subcutaneously, intramuscularly, intraperitoneally, or intravenously (Chenoweth 1949; Peacock 1964; Atzert 1971). Moreover, the oral toxicity of 1080 is independent of the carrier, including water, meat, grain, oil, gum acacia suspension, or gelatin capsule carriers (Atzert 1971).

All students of the action of fluoroacetate have been impressed with the unusually long and variable latent period between administration and response. This latent period occurred in all species studied, regardless of route of administration (Chenoweth 1949; Negherbon 1959; Peacock 1964; Tucker and Crabtree 1970; Atzert 1971; Hudson et al. 1984). With few exceptions, the latent period ranges between 30 min and 2 h and massive doses — such as 50 times an LD₉₅ dose — do not elicit immediate responses. The time between 1080 treatment and death was relatively constant in all tested species, and usually ranged between 1 h and 1 day. The latent period associated with 1080 may result from three major factors: (1) the time required for hydrolysis of monofluoroacetate to monofluoroacetic acid, and its subsequent translocation and cell penetration; (2) the time required for biochemical synthesis of a lethal quantity of fluorocitrate; and (3) the time required for the fluorocitrate to disrupt intracellular functions on a large enough scale to induce gross signs of poisoning (Chenoweth 1949; Atzert 1971).

Many authorities agree that the toxicity of 1080 to mammals is due to its conversion to fluorocitrate, a fluorotricarboxylic acid (Gal et al. 1961; Atzert 1971; Roy et al. 1980; McIlroy 1981b; Kun 1982; Mead et al. 1985a, 1985b; Hornshaw et al. 1986; Twigg et al. 1986, 1988a, 1988b; Murphy 1986). These authorities concur that enzymatic conversion of fluoroacetate via fluoroacetyl coenzyme A plus oxalacetate in mitochondria is the metabolic pathway that converts the nontoxic fluoroacetate to fluorocitrate. Fluorocitrate blocks the Krebs cycle, also known as the tricarboxylic acid cycle, which is the major mechanism for realizing energy from food. Fluorocitrate inhibits the enzyme aconitase and thereby inhibits the conversion of citrate to isocitrate. Fluorocitrate also inhibits succinate dehydrogenase, which plays a key role in succinate metabolism. The inhibition of these two enzymes results in large accumulations of citrate in the tissues, blocking glucose metabolism through phosphofructokinase inhibition, and eventually destroying cellular permeability, cell function, and finally the cell itself. The classical explanation of fluorocitrate toxicity through aconitase inhibition has been questioned (Kun 1982; Savarie 1984). A more recent

explanation is that fluorocitrate binds with mitochondrial protein, thereby preventing citrate transport and its utilization by cells for energy production, although the underlying biochemical mechanisms are not completely understood (Kun 1982). Based on calculated metabolic rates of fluorocarboxylic acids, secondary poisoning of animals that have consumed 1080-poisoned prey is probably due to unmetabolized fluoroacetate rather than to fluorocitric acid (Kun 1982).

Dogs, rats, and rabbits metabolize fluoroacetate compounds to nontoxic metabolites and excrete fluoroacetate and fluorocitrate compounds; peak rate of excretion occurs during the first day after dosing and drops shortly thereafter. Rats dosed with radiolabeled 1080 at 5 mg/kg BW had seven different radioactive compounds in their urine. Monofluoroacetate comprised only 13% of the urinary radioactive material, fluorocitrate only 11%, and an unidentified toxic metabolite 3%; two nontoxic metabolites accounted for almost 73% of the urinary radioactivity (Atzert 1971). Animal muscle usually contained nondetectable residues of any 1080 component within 1 to 5 days of treatment (Marsh et al. 1987; Eason et al. 1993c). Defluorination occurred in the liver by way of an enzymic glutathione-dependent mechanism, which in the brush-tailed opossum resulted in the formation of S-carboxymethylcysteine and free fluoride ion (Twigg et al. 1986). A rapid rate of defluorination together with a low reliance on aerobic respiration favored detoxification of fluoroacetate rather than its conversion into fluorocitrate, and may account for the resistance of reptiles to 1080 when compared to mammals (Twigg et al. 1986).

Sublethal doses of 1080 have led to a tolerance to subsequent challenging doses in certain animals. In other species, however, repeated sublethal doses have resulted in accumulation of a lethal concentration (Atzert 1971). Repeated sublethal doses of 1080 have increased the tolerance of some eagles, rats, mice, and monkeys, but not dogs. Conversely, repeated sublethal doses of 1080 have accumulated to lethal levels in dogs, guinea pigs, rabbits, and mallards. Continued sublethal doses of 1080 to rats caused regressive changes in the germinal epithelium of the seminiferous tubules (Atzert 1971). Altered behavior in mice following high sublethal doses of 1080 probably resulted from neuronal damage caused by concurrent energy deficiency, further accentuated by the CNS stimulant action of fluoroacetate/fluorocitrate and the brain anoxia that occurred during 1080-induced intermittent convulsions. A similar pattern has been reported in two human patients (Omara and Sisodia 1990). Anuria in some 1080-dosed mice probably resulted from renal shutdown caused by hypocalcemic tension (Omara and Sisodia 1990). Tolerance to 1080 is a time-related phenomenon (Atzert 1971). Laboratory rats given 0.5 mg 1080/kg BW were more resistant to 5.0 mg/kg BW given >4 and <24 h later than nontested rats (Atzert 1971). Accumulation of 1080 is also a time-related phenomenon (Chenoweth 1949; Atzert 1971). Domestic dogs given 25 µg 1080/kg BW daily were unaffected until the fifth dose, when convulsions and death occurred. Also, larger sublethal doses could be administered to dogs on alternate days without adverse effects (Atzert 1971).

Fish, amphibians, and reptiles are usually less sensitive to 1080 than warm-blooded animals (Atzert 1971). Reptiles, for example, are more resistant to 1080 than mammals (Twigg et al. 1986). The relatively small elevation of plasma citrate levels in skinks (*Tiliqua rugosa*) given 100 mg 1080/kg BW reflects the exceptional tolerance of this lizard species. The minimal effect of fluoroacetate on aerobic respiration in *T. rugosa* could be explained by a low conversion of fluoroacetate into fluorocitrate or by a low susceptibility of aconitase to the fluorocitrate formed. Although defluorination in skinks helped to minimize the immediate effects of fluoroacetate in aerobic respiration, it resulted in rapid depletion of liver glutathione levels (Twigg et al. 1986).

The breakdown in intracellular processes caused by fluorocitrate or decreased energy production may result in death from gradual cardiac failure or ventricular fibrillation, death from progressive depression of the CNS with either cardiac or respiratory failure, or death from respiratory arrest following severe convulsions. Signs of 1080 intoxication included labored breathing, vomiting, lethargy, muscular incoordination, weakness, and tremors (Chenoweth 1949; Negherbon 1959; Tucker and Crabtree 1970; Atzert 1971; Hudson et al. 1984; Murphy 1986; Eason and Frampton 1991). Among herbivores, 1080-induced deaths were due primarily to cardiac disorders; among

carnivores, deaths were from CNS disorders; and among omnivores, deaths were from both cardiac and CNS disorders (Atzert 1971). Other signs of 1080 intoxication included kidney and testicular damage (Savarie 1984) and altered blood chemistry — specifically, elevated concentrations of citrate (Twigg et al. 1986), glucose, lactic acid, pyruvic acid, acetate, inorganic phosphate, potassium, and fluorine (Negherbon 1959). Some mammals additionally displayed parasympathetic nervous system effects, including increased salivation, urination, and defecation, with eventual cardiac failure (Hudson et al. 1984).

Vomiting probably evolved among carrion eaters as a natural protective mechanism, but it does not necessarily ensure survival from 1080 poisoning (McIlroy 1981b). For example, although 90% of eastern native quolls (*Dasyurus viverrinus*) and 95% of tasmanian devils (*Sarcophilus harrisii*) vomited within 26 to 55 min after ingesting 1080, this was still sufficient time for many to absorb a lethal dose. Loud sounds, sudden movements of an observer, or convulsions by another animal nearby sometimes stimulated convulsions. However, variability was great between species and among conspecifics. Signs preceding convulsions usually included restlessness; hyperexcitability or increased response to stimuli; trembling; rapid, shallow breathing; incontinence or diarrhea; excessive salivation; twitching of facial muscles; abnormal eye movements; incoordination; vocalization; and sudden bursts of violent activity. All affected animals subsequently fall to the ground in a tetanic seizure, with hind limbs or all four limbs and sometimes the tail extended rigidly from their arched bodies. This tonic phase is followed by a clonic phase in which the animals kick with the front legs, and eventually begin to relax. After this phase, animals either recover gradually, die shortly afterwards, experience additional seizures and then die or recover, or remain comatose until death up to 6 days later (McIlroy 1981b).

26.3.5 Antidotes

No highly effective treatment of well-established fluoroacetate poisoning is available (Chenoweth 1949; Peacock 1964; Atzert 1971), and accidental poisoning of livestock and domestic dogs is likely to be fatal (Mead et al. 1991). The following compounds were tested and had no effect on ameliorating 1080 intoxication: salts of fatty acids, anticonvulsants, vitamins, and metabolic intermediates (Chenoweth 1949); and nonphysiological sulfhydryl compounds, such as *N*-acetyl-cysteine and cysteamine (Mead et al. 1985a). As discussed later, sodium acetate/ethanol mixtures, barbiturates, glycerol monoacetate, calcium glutonate/sodium succinate mixtures, and 4-methyl-pyrazole offer partial protection to 1080-poisoned mammals, possibly because they compete with fluoroacetate in the Krebs cycle.

Sodium acetate partially protects mice against 1080, as does ethanol. Ethanol and sodium acetate administered together are twice as effective as either alone, suggesting a synergistic effect (Chenoweth 1949). Mixtures of acetate and ethanol reduced mortality of 1080-poisoned mice (given 2 times an LD₅₀ dose) from 80 to 30% (Tourtellotte and Coon 1950). Mice given 170 mg 1080/kg BW (about 10 times an LD₅₀ dose) plus an intraperitoneal injection of sodium acetate (2 to 3 g/kg BW) dissolved in ethanol (1.6 g/kg BW) reduced mortality by 90%. But the beneficial effect of the acetate/ethanol treatment to mice decreased rapidly with increasing time after the administration of 1080. Ethanol/acetate mixtures had some antidotal effect on 1080-poisoned dogs provided that treatment was administered within 30 min of poisoning (Tourtellotte and Coon 1950). A mixture of 2 g sodium acetate/kg BW plus 2 g ethanol/kg BW is recommended for treatment of 1080-poisoned monkeys (Peacock 1964).

Barbiturates were marginally effective in protecting domestic dogs against fluoroacetate poisoning, but not laboratory mice (Chenoweth 1949; Peacock 1964). Barbiturates administered to dogs within 30 min of 1080 poisoning (4 times an LD₅₀ dose) resulted in 80% survival; when therapy was given 3 h after poisoning, survival was 17% (Tourtellotte and Coon 1950). At higher

1080 doses (i.e., 6 times the LD₅₀ value), barbiturates were ineffective. Repeated intravenous injections of 20 mg pentobarbital/kg BW to a 1080-poisoned dog (0.3 mg 1080/kg BW) prevented death when administered within 8.5 h of poisoning (Tourtellotte and Coon 1950).

Glycerol monoacetate at 2 to 4 g/kg BW partially protects 1080-poisoned rats, rabbits, dogs, and rhesus monkeys (Chenoweth 1949; Peacock 1964; Murphy 1986). But its effectiveness is apparent only when administered intramuscularly in large amounts immediately after 1080 ingestion (Mead et al. 1991). A single dose of magnesium sulfate at 800 mg/kg BW given intramuscularly as a 50% solution shortly after 1080 exposure prevented death of rats dosed with marginally lethal amounts of 1080 (Peacock 1964).

A reduced level of blood calcium is one explanation for the toxic effects of fluoroacetate, and may account for the gap between chemical manifestations and the biochemistry of 1080 poisoning (Roy et al. 1980). Cats poisoned with 1080 showed a 27% drop in blood calcium levels within 40 min; intravenous administration of calcium chloride prolonged the life of treated cats from 94 min to 167 min (Roy et al. 1980). In a search for effective antidotes to fluoroacetate poisoning, calcium gluconate was chosen to antagonize hypocalcemia, and sodium alpha-ketoglutarate, and sodium succinate were selected to revive the TCA cycle (Omara and Sisodia 1990). Effectiveness of each of these antidotes individually and in certain combinations was tested in laboratory mice exposed to lethal doses (15 mg/kg BW, intraperitoneal injection) of 1080. Antidotal treatments were administered from 15 min to 36 h after dosing. All three antidotes alone, and a combination of calcium glutonate with sodium alpha-ketoglutarate, were ineffective in reducing mortality in treated mice. However, a combination of calcium glutonate (130 mg/kg BW) and sodium succinate (240 mg/kg BW) was effective if the two solutions were either injected at separate sites or mixed in the same syringe just prior to injection. Increasing the dose of sodium succinate to 360 or 480 mg/kg BW with calcium glutonate (130 mg/kg BW) was unrewarding. Additional studies are needed to confirm the efficacy and mechanisms of action of this combination (Omara and Sisodia 1990).

Intraperitoneal injection of 4-methylpyrazole to rats at 90 mg/kg BW, given 2 h prior to 1080 administration, offered partial protection against accumulations of citrate or fluorocitrate in the kidney (Feldwick et al. 1994). The antidotal effects of 4-methylpyrazole are attributed to its inhibition of NAD⁺-dependent alcohol dehydrogenase that converts 1,3-difluoro-2-propanol to difluoroacetone, an intermediate in the pathway of erythrofluorocitrate metabolism (Feldwick et al. 1994). A disadvantage of 4-methylpyrazole is that it needs to be administered before significant exposure to fluoroacetate.

First aid treatment for humans accidentally poisoned with 1080 includes immediate emesis and gastric lavage, followed by an oral dose of magnesium sulfate or sodium sulfate to remove the poison from the alimentary tract before absorption of lethal quantities can occur (Peacock 1964; Atzert 1971). When the stomach is emptied, oral administration of ethanol may be beneficial (Temple and Edwards 1985). The patient should be put at complete rest and given barbiturates having moderate duration of action, such as sodium amytole, to control convulsions (Anonymous 1964; Atzert 1971). Intramuscular injections of undiluted glycerol monoacetate at 0.5 mg/kg BW are recommended every 30 min for several hours and then at a reduced level for at least 12 h (Atzert 1971; Temple and Edwards 1985). If intramuscular administration is not feasible, a mixture of 100 mL undiluted glycerol monoacetate in 500 mL water can be given orally and repeated in an hour (Atzert 1971). If glycerol monoacetate is not available, acetamide or a combination of sodium acetate and ethanol may be given in the same dose (Atzert 1971). If ventricular fibrillation occurs, the heroic treatment of 5 mL 1% procaine hydrochloride via intracardiac puncture is justified (Anonymous 1964). Intravenous administration of procainamide is also effective in restoring normal rhythm in ventricular fibrillations (Atzert 1971). Symptoms of 1080 poisoning usually subside in 12 to 24 h, but the patient should be kept in bed for at least 3 days (Anonymous 1946).

26.4 LETHAL AND SUBLETHAL EFFECTS

26.4.1 General

Mammals were the least-resistant group tested against 1080. Individuals of sensitive species died after receiving a single dose of 0.05 to 0.2 mg/kg BW. As discussed later, adverse sublethal effects included testicular damage in rats (*Rattus* sp.) after drinking water containing 2.2 to 20.0 mg 1080/L for 7 days (0.07 to 0.71 mg/kg BW daily), impaired reproduction in mink fed diets containing 0.8 mg 1080/kg ration for 60 days, and altered blood chemistry in European ferrets given diets containing 1.1 mg 1080/kg feed for 28 days. Elevated fluoroacetate residues were measured in some 1080-poisoned mammals, notably European rabbits, of 34 mg/kg DW muscle and 423 mg/kg DW liver. Birds belonging to sensitive species died after a single 1080 dose of 0.6 to 2.5 mg/kg BW, daily doses of 0.5 mg/kg BW for 30 days, 47 mg/kg diet for 5 days, or 18 mg/L drinking water for 5 days. Accumulation and adverse sublethal effects in birds occurred at dietary loadings of 10 to 13 mg 1080/kg ration. The risk to human consumers of cooked meat from 1080-poisoned waterfowl seems negligible. Amphibians and reptiles were more resistant to 1080 than mammals and birds because of their greater ability to detoxify fluoroacetate by defluorination, a reduced ability to convert fluoroacetate to fluorocitrate, and an aconitase hydratase enzyme that is comparatively insensitive to fluorocitrate inhibition. LD₅₀ values for amphibians were >44 mg 1080/kg BW; for reptiles, this value was >54 mg 1080/kg BW. Other studies with 1080 and sensitive species showed death of mosquito larvae at water concentrations of 0.025 to 0.05 mg/L, death of terrestrial beetle and lepidopteran larvae at 1.1 to 3.9 mg/kg BW, no phytotoxicity to terrestrial flora at water concentrations of 10 mg/L, and — based on limited data — no adverse effects on freshwater fish at 370 mg/L.

26.4.2 Terrestrial Plants and Invertebrates

Fluoroacetate was first isolated in South Africa in 1944 from the gifblaar plant (*Dichapetalum cymosum*) (Negherbon 1959). Seeds of the South African *Dichapetalum braunii* may contain as much as 8000 mg fluoroacetate/kg DW (Meyer 1994). Several other species of *Dichapetalum* produce fluoroacetate, as well as *Palicourea marcgravii*, a South American species known to be poisonous (Twigg et al. 1986; Twigg and King 1991). In Australia, fluoroacetate occurs naturally in the leaves, flowers, and seeds of more than 35 species of leguminous plants of the genera *Gastrolobium* and *Acacia* (Mead et al. 1985; Twigg et al. 1986, 1988, 1990; Twigg and King 1991; McIlroy 1992). All but two of these species are confined to the southwest corner of western Australia; the other two species are found in northern and central Australia. Fluoroacetate concentrations varied regionally, seasonally, among species, and among parts of the plants. Fluoroacetate content of these plants is usually greatest in flowers, seeds, and young leaves, and this is consistent with chemically mediated defense strategies in which plants use poisonous compounds to protect those parts most essential to them (Twigg and King 1991). In Australia, the highest fluoroacetate concentrations measured were in air-dried leaves and seeds of two species from western Australia: concentrations reached 2650 mg/kg in leaves and 6500 mg/kg in seeds of *Gastrolobium* spp. Air-dried samples of the two species from northern and central Australia, *Acacia georginae* and *Gastrolobium grandiflorum*, contained as much as 25 mg fluoroacetate/kg leaf and 185 mg/kg seed (Twigg and King 1991).

Significant economic losses of domestic livestock have occurred in Africa and Australia after ingestion of fluoroacetate-bearing vegetation (Twigg and King 1991). Herbivores that have had evolutionary exposure to this vegetation are much less susceptible to fluoroacetate intoxication than geographically separate, unchallenged species (Mead et al. 1985; Twigg et al. 1986). The development of tolerance to fluoroacetate by insects, reptiles, birds, and mammals has evolved on at least three continents where indigenous plants produce fluoroacetate which protects them against herbivores

(Twigg and King 1991). In Australia, for example, animal populations that have coexisted with fluoroacetate-bearing vegetation for at least several thousands of years have developed varying degrees of tolerance to this potent toxin. Tolerance depends on their diet and habitat, size of their home range, mobility, and length of evolutionary exposure to fluoroacetate-bearing vegetation. Once developed, this tolerance is retained by animal populations even after isolation from the toxic vegetation for 70 to 100 centuries. Biochemical mechanisms responsible for the large toxicity differential between conspecifics with and without exposure to fluoroacetate-bearing vegetation are poorly understood (Twigg and King 1991).

Fluoroacetate and fluorocitrate have also been isolated from forage crops grown in an environment rich in atmospheric or inorganic fluoride (Lovelace et al. 1968; Ward and Huskisson 1969; Atzert 1971; Savarie 1984; Twigg and King 1991). For example, soybeans (*Glycine max*) can synthesize fluoroacetic acid when grown in an atmosphere containing elevated levels of hydrogen fluoride or in media containing high levels of sodium fluoride. Forage crops, including alfalfa (*Medicago sativa*) and crested wheat grass (*Agropyron cristatum*), found growing near a phosphate plant that discharged inorganic fluoride contained as much as 179 mg fluoroacetate/kg DW, 896 mg fluorocitrate/kg DW, and 1000 mg total fluoride/kg. The plants were not adversely affected, but horses (*Equus caballus*) grazing these crops showed signs of fluoride poisoning, suggesting that the toxic effect of inorganic fluoride adsorbed or absorbed by plants and not incorporated into monofluoroacetic acid was greater than the toxic effect of monofluoroacetic acid synthesized by the plants (Lovelace et al. 1968; Atzert 1971). Lettuce (*Lactuca sativa*) can absorb radiolabeled 1080 through its roots or leaves, resulting in elevated citrate concentrations and active retention of radioactivity when compared to controls (Ward and Huskisson 1969). Plants can degrade 1080 by cleaving the carbon–fluorine bond, as judged by studies with germinating seeds of the peanut, *Arachis hypogaea* (Atzert 1971).

Compound 1080 mixed with gel, paste, or grease carriers smeared on leaves of palatable plants has been used to control ungulate and marsupial pests in New Zealand, including feral goats (*Capra* sp.), red deer (*Cervus elephas*), and white-tailed deer (*Odocoileus virginianus*) (Parkes 1991). The effectiveness of 1080 in carbopol gel or petrolatum grease on leaves of the mahoe (*Melicytus ramiflorus*) was significantly modified by the phytotoxicity of these carriers. Both carriers caused baited leaves to abscise, and the rate of abscission increased when 1080 was included. Petrolatum was one third as phytotoxic as carbopol and retained 1080 for longer periods — at least 1 year. Carbopol lost about 95% of its 1080 after 64 days of exposure and 100 mm of rain vs. 22% loss in petrolatum under similar conditions. Carbopol with 1080 is recommended for use where its distribution is sufficient to place goats and other target species at immediate risk; petrolatum can be used in areas where a long-lasting bait is needed (Parkes 1991).

Compound 1080 has systemic insecticidal properties against insects feeding on treated plants. Cabbage (*Brassica oleracea capitata*) that had accumulated 1080 through its roots from solution or soil cultures, or following leaf application, was toxic by contact to eggs and larvae of the large white butterfly (*Pieris brassicae*), and various species of aphids (Negherbon 1959). Compound 1080 was not phytotoxic at 10 mg/L or several times the concentration necessary for insecticidal action, but its use as an insecticide is not recommended because of its high mammalian toxicity (Negherbon 1959; Spurr 1991).

At least nine groups of terrestrial invertebrates are adversely affected by eating 1080-poisoned baits, living in habitats contaminated by residues leaching from 1080 baits, or consuming animal by-products and carcasses contaminated with 1080 (Chenoweth 1949; Notman 1989). Lethal effects are reported in houseflies, moths, aphids, ants, bees, and mites that ate 1080-poisoned baits and in fleas that ate 1080-poisoned rats (Notman 1989). Cockroaches, collembolids, and slugs that ate poisoned baits experienced adverse effects. Egg production in wasps was disrupted after a single sublethal dose of 1080, and butterfly eggs treated with 1080 had 98% mortality of resultant larvae (Notman 1989). Harvester ants (*Pogono myrmex*) and darkling ground beetles (Tentyridae) removed and consumed 1080 bait, leaving bait and dead ants concentrated on the ground near the nest

(Hegdal et al. 1986). In a wasp control program, German wasps (*Vespula germanica*) and common wasps (*Vespula vulgaris*) fed 1080-poisoned canned sardines in aspic jelly were not affected at concentrations <100 mg 1080/kg bait (Spurr 1991). At 1000 mg/kg, however, wasp traffic at nest entrances was reduced 17%; at 5000 to 10,000 mg/kg, traffic was reduced 78 to 89%, and almost all wasps died within 100 m of bait stations after 6 h (Spurr 1991). Honeybees (*Apis mellifera*) feed readily on 1080 jam baits used to control opossums (*Trichosurus vulpecula*) in New Zealand (Goodwin and Ten Houten 1991). Bee kills have been documented in the vicinity of jam baits and dead bees contained 3.1 to 10.0 mg 1080/kg whole bee. The oral LD₅₀ for the honey bee is 0.8 µg/bee. Because no deaths occur within 2 h after feeding, poisoned bees may make several foraging trips before dying. Molasses or oxalic acid is now added to 1080 jam baits to repel bees (Goodwin and Ten Houten 1991). Poisoned insects may cause secondary poisoning of insectivores. Accordingly, 1080 should not be used in the vicinity of susceptible nontarget species of invertebrates or endangered insectivores (Notman 1989).

Tested insect larvae showed great variability in sensitivity to 1080 after abdominal injection (Twigg 1990). The LD₅₀ value, in mg 1080/kg BW — administered by way of fluoroacetate-bearing vegetation — was 1.05 for *Perga dorsalis* (Hymenoptera); for Lepidoptera, these values were 3.9 for *Mnesampla privata*, 42.7 for *Spilosoma* sp., and about 130.0 for *Ochrogaster lunifer*. For all species tested, death occurred within 2 to 48 h after injection, and total body citrate concentrations were significantly higher than that of unpoisoned conspecifics. Enhanced tolerance to 1080 was shown in larvae of Western Australian insects feeding on fluoroacetate-bearing vegetation (Twigg 1990).

Populations of terrestrial invertebrates were not adversely affected by 1080 poisoning operations to control brushtail possums in New Zealand, including populations of amphipods, ants, beetles, collembolids, millipedes, mites, weevils, slugs, spiders, and snails (Spurr 1994). Residues of 1080 in nontarget terrestrial invertebrates were low or negligible after an aerial poisoning campaign (Eason et al. 1993b). Residues of 1080 were measured in various species of terrestrial invertebrates in New Zealand before and after aerial application of possum baits containing 800 mg 1080/kg and sown at 5 kg/ha. No residues of 1080 were found in spiders, beetles, millipedes, centipedes, or earthworms at any stage. Residues of 1080 were detectable in some orthopteran insects (2 mg/kg FW) and cockroaches (4 mg/kg FW). Laboratory studies indicated that 90% of all 1080 was eliminated from insects within 4 to 6 days after dosing, suggesting low risk to insectivorous birds (Eason et al. 1993b).

26.4.3 Aquatic Organisms

Despite an intensive literature search, very little data were found on the toxicity of 1080 to aquatic life. King and Penfound (1946) report that fingerling bream and bass (species unidentified) tolerated 370 mg 1080/L for an indefinite period with no apparent discomfort. Deonier et al. (1946) aver that fourth instar larvae of the mosquito *Anopheles quadrimaculatus* were comparatively sensitive to 1080, and that 1080 was among the most toxic 3% of 6000 organic compounds screened against this life stage. In 48 h, concentrations of 0.025, 0.05, and 0.1 mg 1080/L were fatal to 15%, 40%, and 65% of these larvae, respectively. The common duckweed (*Spirodela oligorrhiza*) seems to be unusually sensitive to 1080. Growth inhibition of duckweed was recorded at 0.5 mg/L (Walker 1994), but this needs verification.

Recent unpublished data (as quoted in Fagerstone et al. 1994) on the acute toxicity of 1080 to rainbow trout (*Oncorhynchus mykiss*), bluegill (*Lepomis macrochirus*), and daphnid (*Daphnia magna*) suggest that these organisms are comparatively tolerant to 1080. For example, bluegills exposed to 970 mg 1080/L for 96 h showed no observable adverse effects. For rainbow trout, the no-observable-effect concentration during 96-h exposure was 13 mg 1080/L and the LC₅₀ (96 h) value was 54 mg/L with a 95% confidence interval of 39 to 74 mg/L. For *Daphnia*, no adverse

effects were noted at 130 mg 1080/L during exposure for 48 h, although 50% were immobilized at 350 mg/L in 48 h (Fagerstone et al. 1994). No data were available on effects of 1080 to aquatic biota during life-cycle or long-term exposures. Studies need to be initiated on effects of chronic exposure of 1080 to nontarget species of aquatic arthropods and macrophytes.

26.4.4 Amphibians and Reptiles

In general, the onset of action and time to death or recovery was slowest in amphibians and reptiles and they were among the most resistant to 1080 of all vertebrate animals tested (McIlroy et al. 1985; McIlroy 1986). LD₅₀ values for representative species of amphibians ranged from 54 to 2000 mg 1080/kg BW and for reptiles 44 to 800 mg/kg BW (Table 26.2). Frogs and lizards given a lethal oral dose of 1080 did not show signs of poisoning for 22 to 56 h and survived for 78 to 131 h (McIlroy et al. 1985). Frogs seem to be more sensitive to 1080 in summer than in winter (Chenowith 1949). Amphibians and reptiles possess an innate tolerance to 1080 when compared to mammals because of their greater ability to detoxify fluoroacetate by defluorination, a reduced ability to convert fluoroacetate to fluorocitrate, and an aconitase hydratase enzyme system that is less sensitive to inhibition by fluorocitrate (Twigg and Mead 1990).

One of the most tolerant reptiles tested against 1080 was the shingle-back lizard (*Tiliqua rugosa*) (McIlroy 1986), but populations of *T. rugosa* from western Australia that coexist with fluoroacetate-bearing vegetation were much less sensitive to 1080 intoxication than conspecifics from South Australia not exposed to the toxic plants (Table 26.2; McIlroy et al. 1985; Twigg et al. 1988a; Twigg and Mead 1990). The shingle-back lizard is an omnivore that feeds on flowers, leaves, and seeds, and probably evolved an increased tolerance to fluoroacetate through feeding on toxic plants such as *Gastrolobium* and *Oxylobium*, which are abundant in southwestern Australia (McIlroy et al. 1985).

Reptiles are unlikely to be affected by either primary or secondary poisoning during 1080-poisoning campaigns (McIlroy 1992). In Australia, 1080-poisoned baits contained 330 mg 1080/kg in carrot baits for rabbits and oat baits for pigs, 400 mg 1080/kg in oat baits for rabbits, 500 mg 1080/kg in pellet baits for rabbits and pigs, 14 mg 1080/kg in meat baits for dingos, and 144 mg/kg in meat baits for pigs (McIlroy et al. 1985). These data indicate that most species of reptiles tested would need to ingest unrealistic quantities of bait to be adversely affected by 1080. Most lizards, for example, would need to eat 43 to 172% of their body weight of poisoned rabbit baits, and 143 to 393% of their body weight of meat baits intended for pigs. However, Gould's monitor (*Varanus gouldi*) may ingest lethal amounts of meat baits intended for pigs after eating 31% of its body weight of poisoned baits. By comparison, a large pig (130 kg) needs to eat about 2 kg of meat bait (1.6% of its body weight) for an LD₉₉ dose (McIlroy et al. 1985).

Table 26.2 Effects of 1080 on Representative Amphibians and Reptiles

Group, Species, Dose, and Other Variables	Effect	Reference ^a
AMPHIBIANS		
Spotted grass frog, <i>Limnodynastes tasmaniensis</i> ; 60 mg/kg body weight (BW); single dose	LD ₅₀ , adults	1
Bullfrog, <i>Rana catesbeiana</i> ; 54.4 (95% confidence interval [=CI] of 25.6–115.0) mg/kg BW; single dose	LD ₅₀	2, 6
Frogs, various; 1000–2000 mg/kg BW; single dose	LD ₅₀	7, 8
Leopard frog, <i>Rana pipiens</i> ; 150 mg/kg BW; single dose	LD ₅₀	2, 9
South African clawed frog, <i>Xenopus laevis</i> ; >500 mg/kg BW; single dose	LD ₅₀	2, 9

Table 26.2 (continued) Effects of 1080 on Representative Amphibians and Reptiles

Group, Species, Dose, and Other Variables	Effect	Reference ^a
REPTILES		
Australian reptiles		
163 (44–336) mg/kg BW	LD50 mean and range for 5 species with no previous exposure to naturally occurring fluoroacetates	10
250 and 800 mg/kg BW	LD50 for 2 species with prior or continuing exposure to naturally occurring fluoroacetates	10
Gopher snake, <i>Pituophis catenifer</i> ; fed dead or moribund rodents poisoned with high concentrations of 1080	In 21 separate trials, 14 snakes regurgitated rodents and 7 had no significant effects within 5 days of ingestion	11
Bearded dragon, <i>Pogona barbatus</i> ; <110 mg/kg BW; single dose	LD50	1
Blotched blue-tongued lizard, <i>Tiliqua nigrolutea</i> ; 336 (95% CI of 232–487) mg/kg BW; single dose	LD50	1, 5
Shingle-back lizard, <i>Tiliqua rugosa</i> ; single dose 25 mg/kg BW	No effect on plasma testosterone concentration	3
100 mg/kg BW	Plasma testosterone concentration decreased 52%	3
100 mg/kg BW	Plasma citrate levels increased 3.4 times after 48 h	4
206 (95% CI of 147–289) mg/kg BW	LD50; nontolerant populations from South Australia	1, 5
300 mg/kg BW	Oxygen consumption reduced 2.5–11.0% over a 22-h postdosing observation period	4
525 (95% CI of 487–589 mg/kg BW)	LD50; tolerant populations from West Australia	1
Gould's monitor, <i>Varanus gouldi</i> ; 43.6 (95% CI of 27.5–69.2) mg/kg BW; single dose	LD50	1, 5
Lace monitor, <i>Varanus varius</i> ; <119 mg/kg BW; single dose	LD50	1

^a **1**, McIlroy et al. 1985; **2**, Atzert 1971; **3**, Twigg et al. 1988a; **4**, Twigg et al. 1986; **5**, McIlroy and Gifford 1992; **6**, Tucker and Crabtree 1970; **7**, Negherbon 1959; **8**, Anonymous 1946; **9**, Chenoweth 1949; **10**, McIlroy 1992; **11**, Brock 1965.

26.4.5 Birds

Laboratory studies with birds (Table 26.3) indicated several trends:

1. Death occurred in orally-dosed sensitive species after a single dose of 0.6 to 2.5 mg 1080/kg BW, daily doses of 0.5 mg 1080/kg BW for 30 days, 47 mg/kg diet for 5 days, or 18 mg/L drinking water for 5 days.
2. Single doses >10 mg/kg BW were usually fatal.
3. 1080 toxicity was enhanced at lower temperatures.
4. Younger birds were more sensitive than older birds.
5. Birds tended to avoid diets and drinking water containing high sublethal concentrations of 1080.
6. Accumulations and adverse effects were noted at dietary concentrations of 10 to 13 mg 1080/kg feed.
7. Birds with prior or continuing exposure to naturally occurring fluoroacetates were more resistant to 1080 than conspecifics lacking such exposure

Drinking water LC50 values were about 10 times higher (i.e., 10 times less toxic) than dietary LC50s for mallards (*Anas platyrhynchos*) and common bobwhites (*Colinus virginianus*). However, both species of birds consumed 5 to 10 times more water than food on a daily mg/kg BW basis

(Kononen et al. 1991). The minimum repeated daily oral dosage that was lethal to mallards in 30-day tests was 0.5 mg/kg BW, suggesting a high degree of cumulative action for this species (Tucker and Crabtree 1970). But European starlings (*Sturnus vulgaris*) tolerated 13.5 mg 1080/kg diet for extended periods without significant adverse effects (Balcomb et al. 1983). Studies with the galah (*Cacatua roseicapilla*) showed that 1080 lethality was not affected by the age or sex of the bird or the route of administration (McIlroy 1981a). But breeding adult female Pacific black ducks were more sensitive to 1080 than either males or nonbreeding females (McIlroy 1984).

The most common external signs of avian 1080 poisoning included depression, fluffed feathers, a reluctance to move, and convulsions (McIlroy 1984). Signs of 1080 poisoning first appeared 1 to 60 h after dosing, and deaths occurred 1 h to almost 11 days after dosing (McIlroy 1984). Death of 1080-poisoned California quail (*Callipepla californica*) usually occurred within 3 h, although birds were inactive within 2 h of dosing and comatose until death (Sayama and Brunetti 1952). The most common internal sign of 1080 poisoning was a dose-related increase in plasma citrate concentration, and this was a useful indicator of fluoroacetate sensitivity among birds of similar metabolic rates and phylogenetic affinities (Twigg and King 1989). Some birds poisoned with 1080 either vomited (little crow, *Corvus bennetti*; emu, *Dromaius novaehollandiae*; wedge-tailed eagle, *Aquila audax*; sulphur-crested cockatoo, *Cacatua galerita*) or had saliva or fluid dripping from their beaks (Pacific black duck, *Anas superciliosa*) (McIlroy 1984). Early signs of poisoning, such as vomiting, were seen at oral doses of 10 mg/kg BW in various raptors, including the rough-legged hawk (*Buteo lagopus*), the ferruginous rough-legged hawk (*Buteo regalis*), the northern harrier (*Circus cyaneus*), and the great horned owl (*Bubo virginianus*) (Atzert 1971). The onset of convulsions was preceded by rapid panting, squawking, shrieking or other vocalizations and then a brief period (5 to 120 s) of violent wing flapping, loss of balance, or paddling or running motions with the feet. Birds then fell to the ground while undergoing tetanic seizures, breathing slowly and laboriously, with wings and tail outstretched (McIlroy 1984). Turkey vultures (*Cathartes aura*) fatally poisoned by 1080 died 4 to 32 h after dosing; prior to death, birds displayed tremors, ataxia, lethargy, wing drooping, and emesis. Turkey vultures were more sensitive to 1080 at colder temperatures of 8 to 9°C than at 23 to 28°C; this may be due to inhibition by 1080 of mitochondrial oxidative phosphorylation at colder temperatures, making animals more sensitive at times of increased metabolic demand (Fry et al. 1986).

Some bird species probably developed a tolerance to 1080 from eating plants that contain fluoroacetate, or insects and other organisms that have fed on such plants (McIlroy 1984). Birds indigenous to geographic areas of Australia where fluoroacetate-bearing vegetation is abundant were more tolerant to 1080 than birds distributed outside the range of the toxic plants. Fluoroacetate tolerance in birds is postulated to increase with increasing evolutionary exposure to the toxic plants and decreasing mobility (Twigg and King 1989). In the low-nutrient environment of western Australia, fluoroacetate-tolerant herbivores clearly have a potential advantage over nontolerant herbivores in their broadened choice of fluoroacetate-bearing vegetation in the diet (Twigg et al. 1988b). The most sensitive Australian bird tested was the red-browed firetail (*Emblema temporalis*), with an LD₅₀ of 0.63 mg 1080/kg BW (0.007 mg/whole bird). The most resistant bird tested was the emu with an LD₅₀ of about 250 mg 1080/kg BW or about 8000 mg/whole bird (McIlroy 1983a, 1984, 1986). Emus in the southwest portion of Western Australia with evolutionary exposure to fluoroacetate-bearing vegetation have unusually high tolerance to 1080. Emu tolerance was attributed to: (1) their ability to detoxify fluoroacetate by defluorination; (2) a limited ability to convert fluoroacetate into fluorocitrate; and (3) possession of an aconitase hydratase enzyme that is relatively insensitive to fluorocitrate (Twigg et al. 1988b).

Deaths of nontarget species of birds after eating 1080-poisoned baits have been reported (Spurr 1979; McIlroy 1984; Fry et al. 1986; Hegdal et al. 1986; McIlroy et al. 1986a), although population effects have not yet been demonstrated. Birds of several species were found dead after 1080 baits were applied to kill California ground squirrels (*Spermophilus beecheyi*), but only Brewer's blackbird

(*Euphagus cyanocephalus*) contained measurable 1080 residues. Nontarget seed-eating birds that died after eating 1080-poisoned baits included sparrows, blackbirds, towhees (*Pipilo* spp.), horned larks (*Eremophila lepestris*), McCown's longspurs (*Calcarius mccownii*), chestnut-collared longspurs (*Calcarius ornatus*), and western meadowlarks (*Sturnella neglecta*) (Hegdal et al. 1986). Individuals of at least 20 species of Australian birds are at risk from dingo and pig poisoning campaigns that use meat baits containing 14 to 140 mg 1080/kg bait, and 39 species are at risk from rabbit and pig poisoning campaigns using vegetable baits that contain 330 to 500 mg 1080/kg bait. The extent of bird mortality and possible population effects depend on several factors (McIlroy 1984):

- Bait palatability to each species
- Availability of other foods
- Amount of 1080 ingested
- Number of birds in each population that consume baits before the target species or other nontarget groups
- Rate of 1080 leaching from baits by dew or rainfall

Birds seen feeding on 1080-poisoned baits for control of wild dogs included the pied currawong (*Strepera graculina*), the Australian raven (*Corvus coronoides*), the Australian magpie (*Gymnorhina tibicen*), and the wedge-tailed eagle (*Aquila audax*) (McIlroy 1981b; McIlroy et al. 1986a). Avian scavengers such as vultures, condors, hawks, and ravens are likely to find poisoned food items as they search for carcasses (Fry et al. 1986).

Secondary 1080 poisoning of birds is documented. Australian birds found dead after eating 1080-poisoned carcasses of pigs (*Sus* sp.) included kites (whistling kite, *Haliastur sphenurus*; black kite, *Milvus migrans*), eagles (Australian little eagle, *Hieraetus morphnoides*; wedge-tailed eagle), brown falcon (*Falco berigora*), Australian kestrel (*Falco cenchroides*), brown goshawk (*Accipiter fasciatus*), Australian magpie-lark (*Grallina cyanoleuca*), Australian raven, and crows (Australian crow, *Corvus orru*; little crow, *Corvus bennetti*) (McIlroy 1983a). Insectivorous birds that may have died after eating 1080-poisoned ants (*Veromessor andrei*, *Liometopum occidentale*) in the United States include acorn woodpeckers (*Melanerpes formicivorus*), the white-breasted nuthatch (*Sitta carolinensis*), and the ash-throated flycatcher (*Myiarchus cinerascens*) (Hegdal et al. 1986).

Little or no secondary hazards to raptors were evident — as judged by the absence of carcasses — from 1080 ground squirrel baiting operations among hawks, harriers, eagles, ravens, vultures, and condors. However, some species of owls were comparatively susceptible to 1080, including burrowing owls (*Athene cunicularia*) and barn owls (*Tyto alba*) (Hegdal et al. 1986). Raptors are less susceptible to secondary poisoning from 1080 than mammalian predators because birds have higher LD50 values, refuse to eat large amounts of 1080-poisoned meats, and sometimes regurgitate poisoned baits (Hegdal et al. 1986). The reduced hazard of acute 1080 poisoning via secondary sources for raptors is illustrated for the golden eagle (*Aquila chrysaetos*), a bird that normally consumes the internal organs of its prey before consuming other portions of the carcass (Atzert 1971). Golden eagles fed diets containing 7.7 mg 1080/kg diet — about 3 times the highest concentration of 1080 detected in carcasses of coyotes killed by 1080 livestock protection collars — all survived, although some eagles showed signs of 1080 intoxication, including loss of strength and coordination, lethargy, and tremors (Burns et al. 1991). For a 3.2-kg golden eagle to obtain an LD50 dose (1.25 to 5.00 mg 1080/kg BW), it would have to consume the internal organs of 7 to 30 coyotes killed by 1080, assuming that each coyote ingested 0.1 mg 1080/kg BW and did not excrete, detoxify, or regurgitate any of the toxicant and that, as in rats, about 40% of the dose is present in the internal organs at death (Atzert 1971). Since the internal organs of a coyote account for 20 to 25% of its live weight or 2.7 to 3.2 kg/coyote, and a golden eagle's daily consumption

of food is about 30% of its live weight or 0.9 kg (Atzert 1971), it seems unlikely for raptors to be at great risk from consuming coyotes killed by 1080 livestock protection collars (Burns et al. 1991).

Human consumers of meat from 1080-killed ducks would probably not be adversely affected after eating an average cooked portion (Temple and Edwards 1985). Moreover, oven-baking or grilling at temperatures >200°C will cause breakdown of 1080. For example, if a mallard received a triple lethal dose of 1080, then a 1-kg mallard would contain an estimated 14.4 mg of 1080. A 70-kg human would have to consume 25.4 kg of poisoned duck flesh to receive a lethal dose, as judged by LD₅₀ values of 4.8 mg/kg BW for mallards and 5 mg/kg BW for humans. Theoretically, consumption of only two whole ducks poisoned by 1080 may cause transient toxicity (Temple and Edwards 1985).

Avian populations that were reduced in numbers during 1080 poisoning for possum control usually recovered quickly if they had high potential for reproduction and dispersal (Spurr 1979). Birds from Australia or New Zealand with poor reproductive potential and poor dispersal had a high risk of nonrecovery; this group includes the three species of kiwi (*Apteryx* spp.), takake (*Notornis mantelli*), kakapo (*Strigops habroptilus*), laughing owl (*Sceloglaux albifacies*), bush wren (*Xenicus longipes*), rock wren (*Xenicus gilviventris*), fernbird (*Bowdleria punctata*), yellowhead (*Mohoua ochrocephala*), stitchbird (*Notiomystis cincta*), saddleback (*Philesturnus carunculatus*), kokako (*Callaeas cinerea*), and New Zealand thrush (*Turnagra capensis*) (Spurr 1979, 1993). Poison control programs against wild dogs, dingoes, and their hybrids using 1080 meat baits did not significantly affect nontarget populations of birds in the treated areas (McIlroy et al. 1986b). Baiting with 1080 to control rabbits and foxes in Australia usually had no significant permanent adverse effects on nontarget birds, although 15 of the 30 bird species in the treated areas during the poisoning campaign showed a temporary negative trend in abundance, especially welcome swallows (*Hirundo neoxena*), tree martins (*Hirundo nigricans*), and crimson rosellas (*Platycercus elegans*) (McIlroy and Gifford 1991). Aerial drops of 1080-laced pellets (11.8 kg/ha) to control brushtail possums and rock wallabies (*Petrogale penicillata*) on Rangitoto Island, New Zealand, had no observed effect on island bird populations over the next 12 months (Miller and Anderson 1992). No species of bird showed a population decline and several showed significant increases in numbers, including greenfinch (*Carduelis chloris*), Australian harrier hawk (*Circus approximans*), and tui (*Prosthemadera novae-seelandiae*). Increases were attributed to the reduction in numbers of mammalian browsers, which led to increased vegetation and improved habitat for nontarget bird species (Miller and Anderson 1992).

Mortality of nontarget birds in 1080 poisonings may be underreported because many die in their nests or roosts and are never found (Koenig and Reynolds 1987). Raptors of several species were found dead shortly after application of 1080 baits. However, no 1080 residues were detected in any of these birds and the cause of death was not established (Hegdal et al. 1986). Application of 1080 baits to control California ground squirrels was associated with deaths of yellow-billed magpies (*Pica nuttalli*) which contained about 1.02 mg 1080/kg FW of internal organs (Koenig and Reynolds 1987) vs. 0.6 to 0.7 mg 1080/kg FW in stomachs of black-billed magpies (*Pica*) treated with lethal doses of 1.6 to 3.2 mg 1080/kg BW (Okuno et al. 1984). It is not known if *P. nuttalli* ingested the 1080 bait directly, ate other poisoned animals, or both (Koenig and Reynolds 1987). Risks of 1080 poisoning to birds can be reduced by (McIlroy 1984; McIlroy et al. 1986a):

1. Setting meat baits out just before sunset and removing them early next morning
2. Burying baits for pigs below ground
3. Using baits that only the target animals prefer
4. Reducing the number of available small bait fragments
5. Masking the appearance of baits and enhancing their specificity by the use of dyes — although some birds in Australia seem to prefer green-dyed meat baits

Table 26.3 Effects of 1080 on Representative Birds

Species, Dose, and Other Variables	Effect	Reference^a
Chukar, <i>Alectoris graeca</i> ; 3.5 (95% confidence interval [=CI] of 2.6–4.8) mg/kg body weight (BW); single dose	LD50	1–4
Northern pintail, <i>Anas acuta</i> ; 8–10 mg/kg BW; single dose	50–100% dead	2, 5
American wigeon, <i>Anas americana</i> ; single dose 4.0 mg/kg BW; males 11.0 mg/kg BW; females	LD100 LD100	5 5
Mallard, <i>Anas platyrhynchos</i> 0.5 mg/kg BW; daily oral dose for 30 days 3.7 (95% CI of 21.5–5.5) mg/kg BW; single dose; age 7 days 4.8 (95% CI of 2.6–9.0) mg/kg BW; single dose; age 6 months 6.0 (95% CI of 4.2–8.4) mg/kg BW; single dose; ducklings 7.0–7.5 mg/kg BW; single dose 8.0 mg/kg BW; adult females; single dose 9.1 (95% CI of 5.6–14.6) mg/kg BW; single dose; adults 10.0 mg/kg BW; adult males; single dose 13–24 mg/L drinking water for 5 days plus 3-day observation period; age 10 days 18–24 mg/L drinking water for 5 days plus 3-day observation period; age 10 days >236 mg/kg diet fresh weight (FW) for 5 days plus 3-day observation period; age 10 days 527 mg/kg diet FW for 5 days plus 3-day observation period; age 10 days	Some deaths in 30 days, but less than 50% LD50 LD50 LD50 LD75-LD100 LD50 LD50 LD50 Avoidance of water containing 1080 when given choice 50–90% dead Avoidance of diets containing 1080 when given choice 50% dead	3, 4 6 6 3, 4 5 2 1, 3, 4 2 7 7 7 7 7
Pacific black duck, <i>Anas superciliosa</i> ; single dose 10.0 (95% CI of 7.4–13.5) mg/kg BW; adult breeding females 18.9 (95% CI of 16.3–219) mg/kg BW; adult males 23.8 (95% CI of 15.3–37.0) mg/kg BW; adult nonbreeding females	LD50 LD50 LD50	8 8, 9 8
Wedge-tailed eagle, <i>Aquila audax</i> ; 9.5 (95% CI of 7.2–12.5) mg/kg BW; single dose	LD50	8, 10
Golden eagle, <i>Aquila chrysaetos</i> ; single dose 1.25–5.00 mg/kg BW 3.5 (95% CI of 0.5–25.1) mg/kg BW	LD50 LD50	2, 3, 5, 26 4, 11
Australian birds; various species; single dose 7.8 (0.6–25.0) mg/kg BW 28.4 (1.8–102.0) mg/kg BW	LD50 mean and range for 45 species with no known past exposure to naturally occurring fluoroacetates LD50 mean and range for 14 species with prior or continuing exposure to naturally occurring fluoroacetates	27 27
Australian birds, 41 species; single dose 0.6–0.99 mg/kg BW 1.0–9.9 mg/kg BW 20.0–49.9 mg/kg BW >200 mg/kg BW	LD50, 2 species LD50, 27 species LD50, 11 species LD50, 1 species	8 8 8 8
Port Lincoln parrot, <i>Barnardius zonarius</i> ; 11.5 (95% CI of 9.6–13.7) mg/kg BW; single dose	LD50	9, 12
Great horned owl, <i>Bubo virginianus</i> ; 20 mg/kg BW; single dose	LD50	5
Rough-legged hawk, <i>Buteo lagopus</i> ; 10 mg/kg BW; single dose	LD50	5

Table 26.3 (continued) Effects of 1080 on Representative Birds

Species, Dose, and Other Variables	Effect	Reference^a
Ferruginous rough-legged hawk, <i>Buteo regalis</i> ; 10 mg/kg BW; single dose	LD50	5
Sulphur-crested cockatoo, <i>Cacatua galerita</i> ; 3.5 (95% CI of 2.9–4.1) mg/kg BW; single dose	LD50	8, 13
Galah, <i>Cacatua roseicapilla</i> ; ~5.6 (95% CI of 3.1–10.5) mg/kg BW; single dose	LD50	8, 14
California quail, <i>Callipepla californica</i>		
0.5 or 1.0 mg/kg BW; single dose	No deaths	15
0.5 or 1.0 mg/kg BW on day 1; 2.5 mg/kg BW on days 2, 3, and 4	All dead	15
4.6 (95% CI of 2.7–8.1) mg/kg BW; single dose	LD50	4
>5.0 mg/kg BW; single dose	All dead	15
Turkey vulture, <i>Cathartes aura</i> ; single dose		
20 mg/kg BW	Lethargy and wing-drooping at 13°C	24
30 mg/kg BW	Tremors, lethargy, ataxia, incoordination at 11–17°C	24
40 mg/kg BW	Lethal at 7–9°C; lethargy, ataxia, and incoordination at 15°C	24
60 mg/kg BW	Tremors, lethargy, and wing-droop at 15–20°C	24
80 mg/kg BW	All dead within 4 h at 20°C; no regurgitation	24
100 mg/kg BW	75% dead at 23–28°C	24
Maned duck, <i>Chenonetta jubata</i> ; 12.6 (95% CI of 10.1–15.7 mg 1080/kg BW); single dose	LD50	8, 9
Northern harrier, <i>Circus cyaneus</i> ; 10 mg/kg BW; single dose	LD50	5
Common bobwhite, <i>Colinus virginianus</i>		
>9 mg/L drinking water daily for 5 days plus 3-day observation period	Avoidance of water containing 1080 when given choice	7
31 mg/L drinking water daily for 5 days plus 3-day observation period	50% dead	7
93 mg/L drinking water daily for 5 days plus 3-day observation period	All dead	7
>95 mg/kg diet daily for 5 days plus 3-day observation period	Avoidance of 1080 diets when given choice	7
385 mg/kg diet daily for 5 days plus 3-day observation period	50% dead	7
Grey shrike thrush, <i>Colluricincla harmonica</i> ; ~12.0 mg/kg BW; single dose	LD50	13
Rock dove, <i>Columba livia</i> ; 4.2 (95% CI of 3.4–5.3) mg/kg BW; single dose	LD50	1–3
Black vulture, <i>Coragyps atratus</i> ; 15 mg/kg BW; single dose	LD50	2, 5
Little crow, <i>Corvus bennetti</i> ; 13.4 (95% CI of 11.7–15.2) mg/kg BW; single dose	LD50	8, 10, 13
Australian raven, <i>Corvus coronoides</i> ; 5.1 mg/kg BW; single dose	LD50	10, 13
Little raven, <i>Corvus mellori</i> ; 3.1 (95% CI of 2.7–3.6) mg/kg BW; single dose	LD50	8
Japanese quail, <i>Coturnix japonica</i> ; 16.2 (95% CI of 7.2–28.7) mg/kg BW; single dose	LD50	2, 4
Laughing kookaburra, <i>Dacelo novaeguineae</i> ; ~6.0 mg/kg BW; single dose	LD50	10, 13
Emu, <i>Dromaius novaehollandiae</i> ; 102–278 mg/kg BW; single dose	LD50	8, 12, 13
Red-browed firetail, <i>Emblema temporalis</i> ; 0.6 (95% CI of 0.4–1.0) mg/kg BW; single dose	LD50	8
Brewer's blackbird, <i>Euphagus cyanocephalus</i> ; 2.5–3.0 mg/kg BW; single dose	LD33–LD50	2, 5

Table 26.3 (continued) Effects of 1080 on Representative Birds

Species, Dose, and Other Variables	Effect	Reference^a
Finches, 7 species; 2.7 (95% CI of 0.8–4.6) mg/kg BW; single dose	LD50	16
Flycatchers, 4 species; 13.2 (95% CI of 8.7–20.0) mg/kg BW; single dose	LD50	16
Domestic chicken, <i>Gallus</i> spp.; 5.0–18.0 mg/kg BW; single dose	LD50–LD100	2, 5, 15, 17–19, 25, 26
Gamebirds, 8 species; 7.3 (95% CI of 0.0–16.4) mg/kg BW; single dose	LD50	16
Australian magpie-lark, <i>Grallina cyanoleuca</i> ; 8.8 (95% CI of 4.0–13.5) mg/kg BW; single dose	LD50	8, 13
Australian magpie, <i>Gymnorhina tibicen</i> ; 9.9 (95% CI of 7.6–12.9) mg/kg BW; single dose	LD50	8, 10, 13
Honeyeaters, 5 species; 8.1 (95% CI of 6.9–9.5) mg/kg BW; single dose	LD50	16
Gambel's quail, <i>Lophortyx gambeli</i> ; 20 mg/kg BW; single dose	LD50–LD57	2, 5, 26
Turkey, <i>Meleagris gallopavo</i> ; 4.8 (95% CI of 1.2–19.0) mg/kg BW; single dose	LD50	4
Black kite, <i>Milvus migrans</i> ; 18.5 (95% CI of 15.0–23.2) mg/kg BW; single dose	LD50	8, 10, 13
Parrots, single dose		
8 species; 4.0 (95% CI of 0.0–9.3) mg/kg BW	LD50	16
5 species, 5–75 mg/kg BW	LD50	9
House sparrow, <i>Passer domesticus</i> ; single dose		
2.5 mg/kg BW	LD43	5
3.0 (95% CI of 2.4–3.8) mg/kg BW	LD50–LD100	1–4, 20, 26
Zebra finch, <i>Peophila guttata</i> ; fed diet containing 10 mg 1080/kg; equivalent to 11–15 mg/kg BW daily	Maximum fluoroacetate concentrations, in mg/kg FW, were 12.6 in crop, 2.0 in stomach, 2 in liver, 6.0 in heart, 3.9 in intestine, and 1.2 in muscle; mean concentrations were about 1 mg/kg FW for all tissues except heart (2.0 mg/kg FW)	21
Ring-necked pheasant, <i>Phasianus colchicus</i> ; 6.5 (95% CI of 3.9–10.8) mg/kg BW; single dose	LD50	1–4
Black-billed magpie, <i>Pica pica</i> ; single dose		
0.67 mg/kg BW	No deaths	5
1.3 mg/kg BW	LD100	5
1.6 mg/kg BW; survivors sacrificed at 24 h	Residues of 1080, in mg/kg FW, in survivors were 0.05–0.34 in muscle and 0.07–0.49 in stomach. Dead birds contained 0.2 mg/kg FW in muscle and 0.25 in stomach	22
2.0, 2.5, or 3.2 mg/kg BW	All dead within 24 h. Mean (max.) 1080 residue concentrations, in mg/kg FW, were 0.4 (0.6), 0.7 (1.0) and 0.9 (1.4) in muscle, respectively; for stomach, these values were 0.4 (0.9), 0.7 (1.1), and 1.0 (1.5), respectively	22
Pigeons and doves, single dose		
3 species, 10.6 (6–40) mg/kg BW	LD50	9
5 species; 10.6 (95% CI of 1.9–60.9) mg/kg BW	LD50	8, 16, 26
Red-rumped parrot, <i>Psephotus haematonotus</i> ; ~5.3 mg/kg BW; single dose	LD50	13
Raptors, 5 species; 9.1 (95% CI of 5.1–13.1) mg/kg BW; single dose	LD50	16
Seed-eating birds; 4 species; single dose; from Western Australia, exposed to fluoroacetate-bearing vegetation; 25–75 mg/kg BW	LD50	12
Pied currawong, <i>Strepera graculina</i> ; 13.1 (95% CI of 10.9–15.7) mg/kg BW; single dose	LD50	8

Table 26.3 (continued) Effects of 1080 on Representative Birds

Species, Dose, and Other Variables	Effect	Reference^a
Laughing dove, <i>Streptopelea senegalensis</i> ; 5.9 (95% CI of 4.2–8.2) mg/kg BW; single dose	LD50	9
European starling, <i>Sturnus vulgaris</i>		
13.5 mg 1080/kg diet for 4 weeks	Treated birds had slightly lower body weight and testes weight than controls, but differences were not statistically significant	23
27 mg 1080/kg diet	No deaths in 5 days	23
47 (95% CI of 27–108) mg 1080/kg diet for 5 days	50% dead	23
54 mg 1080/kg diet for 5 days	67% dead	23
108 mg 1080/kg diet for 3 days	50% dead	23
198 (95% CI of 119–400) mg 1080/kg diet for 24 h	50% dead	23
432 mg 1080/kg diet for 48 h	All dead	23
Waterfowl, 7 species; 7.1 (95% CI of 1.9–25.6) mg/kg BW; single dose	LD50	16
Mourning dove, <i>Zenaida macroura</i> ; 8.6–14.6 mg/kg BW; single dose	LD25–LD50	1, 2, 4, 5, 20

^a 1, Tucker and Haeghele 1971; 2, Atzert 1971; 3, Tucker and Crabtree 1970; 4, Hudson et al. 1984; 5, Peacock 1964; 6, Hudson et al. 1972; 7, Kononen et al. 1991; 8, McIlroy 1984; 9, Twigg and King 1989; 10, McIlroy and Gifford 1992; 11, Burns et al. 1991; 12, Twigg et al. 1988b; 13, McIlroy 1983a; 14, McIlroy 1981a; 15, Sayama and Brunetti 1952; 16, McIlroy 1986; 17, Anonymous 1946; 18, Kalmbach 1945; 19, Negherbon 1959; 20, Green 1946; 21, Burke et al. 1989; 22, Okuno et al. 1984; 23, Balcomb et al. 1983; 24, Fry et al. 1986; 25, Robison 1970; 26, Chenoweth 1949; 27, McIlroy 1992.

26.4.6 Mammals

Studies with mammals (Table 26.4) showed several trends:

1. Individuals of sensitive species died after receiving a single dose between 0.05 and 0.2 mg/kg BW, including species of livestock, marsupials, canids, felids, rodents, and foxes.
2. Most individuals of tested species died after a single dose between 1 and 3 mg/kg BW.
3. A latent period was evident between exposure and signs of intoxication.
4. Mortality patterns usually stabilized within 24 h after exposure.
5. Species from fluoroacetate-bearing vegetation areas were more resistant than conspecifics from nonfluoroacetate vegetation areas.
6. Route of administration had little effect on survival patterns.
7. Younger animals were more sensitive than adults.
8. High residues were detected in some 1080-poisoned animals, notably rabbits with 34 mg/kg DW muscle and 423 mg/kg DW liver.
9. Secondary poisoning was evident among carnivores after eating 1080-poisoned mammals.
10. Sublethal effects included testicular damage in rats after drinking water containing 2.2 to 20.0 mg 1080/L for 7 days (0.07 to 0.71 mg/kg BW daily), impaired reproduction in mink fed diets containing 0.8 mg 1080/kg ration for 60 days, and altered blood chemistry in ferrets given diets containing 1.1 mg 1080/kg ration for 28 days.

The most sensitive mammal tested was the Texas pocket gopher (*Geomys personatus*), with an LD50 of <0.05 mg 1080/kg BW (McIlroy 1986). In general, carnivorous eutherian mammals were most sensitive to 1080 and amphibians most resistant; intermediate in sensitivity were herbivorous eutherian mammals and marsupials, carnivorous marsupials, herbivorous-granivorous rodents, omnivorous mammals, and birds — in that order (McIlroy 1992). Very young mammals seemed more sensitive to 1080 than other members of their populations (McIlroy 1981a); no other differences in sensitivity to 1080 were found that could be related to sex, age, or nutritional status

(McIlroy 1981a, 1981b; O'Brien 1988; O'Brien and Lukins 1988). Route of administration had little effect on 1080 toxicity. Oral dosages were as toxic as subcutaneous, intramuscular, intravenous, and intraperitoneal dosages (Negherbon 1959; McIlroy 1981a, 1983a). There are species differences, as yet unexplained, in fatal 1080 poisonings: dogs died of convulsions or respiratory paralysis, but monkeys, horses, rabbits, and humans died of ventricular fibrillations (Murphy 1986). Individuals of most species dosed with 1080 died within 7 days, but feral pigs and wedge-tailed eagles took longer (McIlroy 1981a). Ambient air temperatures in the range 4 to 33°C modified the sensitivity of small mammals to 1080. In mice (*Mus* spp.) and guinea pigs (*Cavia* spp.), sensitivity was greater at the extremes of the thermal regimes than at intermediate temperatures (McIlroy 1981b; Oliver and King 1983). Raccoons (*Procyon lotor*) and feral pigs were more sensitive at elevated ambient temperatures (Eastland and Beasom 1986b; O'Brien 1988), but opossums and domestic sheep were more sensitive at low temperatures (McIlroy 1982a; Eastland and Beasom 1986b). At elevated temperatures, 1080 was more toxic to feral pigs when administered via drinking water vs. oat baits, and in wheat baits vs. pellet baits (O'Brien 1988).

Warm-blooded species varied considerably in response to sodium fluoroacetate, with primates more resistant and rodents and carnivores more susceptible. Based on fatal or near-fatal cases of human poisonings, the dangerous dose for humans is 0.5 to 2.0 mg/kg BW (Negherbon 1959). Among the 171 species of mammals tested, for which there are data, there was considerable variability in the time until signs of poisoning became apparent (0.1 h to >7 days), the time to death (0.1 h to >21 days), and the time until animals began to show signs of recovery (2 h to 18 days) (McIlroy 1986). Signs of poisoning among herbivorous species of marsupials first appeared 1 to 39 h after dosing; death, followed 3 to 156 h after dosing (McIlroy 1982a). Australian carnivores did not show signs of 1080 poisoning for 0.6 to 4.8 h; first deaths occurred between 1.6 and 21 h and recovery in 0.4 to >26 h (McIlroy 1981b). Marsupial carnivores generally showed signs of 1080 poisoning earlier and died or recovered more quickly than did marsupial herbivores and placental mammals (McIlroy 1986). After the latent period, common signs of 1080 poisoning in caged mammals included hyperexcitation, rapid breathing, and trembling. Some animals then recovered, while others began to vomit, convulse, or both (McIlroy 1981b). The most common signs of 1080 poisoning in 14 species of Australian rodents were depression, hypersensitivity to stimuli, respiratory distress, and convulsions; signs usually appeared 0.4 to 38.1 h after dosing; deaths occurred 0.7 to 206 h after dosing. A few species were more tolerant, perhaps because of exposure to indigenous plants that contained fluoroacetate (McIlroy 1982b). Rabbits (*Oryctolagus* sp.) poisoned by 1080 showed increased sensitivity to noise or disturbance; those surviving high sublethal doses began recovering 5 to 23 h after dosing (McIlroy 1982a). Cows (*Bos* spp.) showed no signs of fatal 1080 poisoning until shortly before death; signs appeared in the following sequence: urination, staggering, falling down, slight spasms, and death 1.5 to 29 h after treatment (Robison 1970). Prairie dogs showed no signs of 1080 poisoning for several hours after consuming a fatal dose; death occurred 8 to 13 h after dosing and was preceded by a rapid respiratory rate, hyperactivity, and convulsions (Huggins et al. 1988). In feral pigs, signs of poisoning such as vomiting, increasing lethargy, and labored breathing appeared about 6.2 h after dosing (range 1.9 to 47.3 h), and death after 16.1 h (range 2.8 to 80 h) after dosing (McIlroy 1983a). Vomiting occurred in 98% of poisoned pigs, but was unrelated to dose (O'Brien 1988) or bait type (O'Brien et al. 1988). With some animals, particularly the eastern native cat (*Dasyurus viverrinus*), the tiger cat (*Dasyurus maculatus*), and the tasmanian devil, the first sign of 1080 poisoning is the sudden onset of vomiting. Vomiting was independent of dose ingested or mode of administration. Thereafter, animals may either recover or experience hyperexcitation, convulsions, and death (McIlroy 1981b).

Many 1080 control programs report high effectiveness without significant effect on nontarget species. Australian baits used to control various mammal pests usually contain 15 to 110 mg 1080/kg bait, although concentrations as high as 1200 mg/kg bait are documented (McIlroy 1981b). Baiting with 1080 to control European rabbits and red foxes (*Vulpes vulpes*) in New South Wales, Australia, caused a 90% reduction in numbers of rabbits and 75% of foxes; populations of both species began

to recover soon after the campaign ended, indicating the need for continued control measures. Populations of nontarget birds and mammals did not appear to be affected, and no dead birds or nontarget mammals were found (McIlroy and Gifford 1991). A similar case is reported for 1080 control programs in Australia against wild dogs, dingoes, and their hybrids (McIlroy et al. 1986b). In Tasmania, deliberate poisoning of forest-browsing pests with carrot baits containing 0.014% 1080 — the same concentration used elsewhere in Tasmania for rabbit control — resulted in 94% mortality of brushtail possum populations, 96% mortality of red-bellied pademelons, and 86% mortality of Bennett's wallabies (McIlroy 1982a). The use of 1080 to protect island-dwelling rare or endangered species of herbivorous marsupials — a comparatively tolerant group — to kill more sensitive introduced competitors or predators such as rabbits, foxes, and feral cats was suggested by McIlroy (1982a) as an interesting possibility.

Compound 1080 is highly toxic to some species of nontarget mammals, including domestic cats and dogs (Kalmbach 1945). Hazards to wildlife associated with 1080 baiting for California ground squirrels that reduced squirrel populations by 85% included some deaths of Heermann's kangaroo rats (*Dipodomys heermanni*), the little pocket mouse (*Perognathus longimembris*), the desert woodrat (*Neotoma lepida*), deer mice (*Peromyscus* spp.), and the western harvest mouse (*Reithrodontomys megalotis*). Poisoned rodents contained between 5.2 and 23.1 mg 1080/kg BW and 1080-poisoned desert cottontails (*Sylvilagus audubonii*) contained 8.2 mg 1080/kg stomach contents (Hegdal et al. 1986). Nontarget animals found dead in New South Wales state forest areas after 22 rabbit poisoning operations between 1971 and 1975 included, in decreasing order of frequency, foxes, wallabies, possums, gray kangaroos, wombats, rats, hares, birds, cats, sheep, and dogs. This pattern may reflect the relative abundance of each species in the areas involved, their access to and acceptance of baits, and their ease of detection after death by forestry personnel (McIlroy 1982a). In Australia, the animals alleged to be most at risk during rabbit- or pig-poisoning campaigns using pellet, grain, or carrot baits are the kangaroos, wallabies, and wombats. For example, common wombats (*Vombatus ursinus*) and hairy-nosed wombats (*Lasiorhinus latifrons*) need to consume only 10 to 16 g of pellet, grain, or carrot baits containing 0.33 to 0.5 mg of 1080 to receive an LD₅₀. Hairy-nosed wombats eat 120 to 570 g of food daily, and common wombats can eat over 500 g of unpoisoned carrots daily, indicating that both species could easily consume lethal quantities of bait. Livestock were next at theoretical risk, followed by brushtail possums, pigs, and various rodents and birds (McIlroy 1986). More data are needed on bait consumption rates of nontarget mammals if risk from 1080-poisoning campaigns is to be satisfactorily assessed.

Laboratory studies may overestimate the risk to nontarget species from 1080 baiting. The northern quoll (*Dasyurus hallucatus*), for example, was found to be at highest theoretical risk from aerial baiting programs, as judged by LD₅₀ laboratory studies with 15 species of rodents and dasyurids. But no quolls were found dead during aerial baiting to control dingoes, and all seemed to have normal movements as judged by radiotelemetry (King 1989). Alternatives to LD₅₀ testing now include tissue culture techniques, monitoring of metabolite levels in blood or tissues, and estimating the lowest dose likely to cause death (Calver et al. 1989a). Monitoring the level of citrate in blood plasma of animals that received a sublethal dose of 1080 has been used successfully with species large enough to provide adequate samples of blood plasma in several bleeds over a 24-h period, but these other alternatives have not been attempted on Australian fauna (Calver et al. 1989a).

Because 1080 acts as an emetic, especially on coyotes and feral pigs, there is a risk of primary poisoning to nontarget animals from eating the vomitus (Atzert 1971; McIlroy 1983a; Rathore 1985; O'Brien et al. 1986, 1988). Wild pigs poisoned by carrot baits placed for European rabbits were observed to leave trails of vomitus containing carrot and other ingested foods (Rathore 1985). The antiemetic compound metoclopramide (Maxolon®) prevents vomiting in pigs by blocking dopamine receptors in the chemoreceptor trigger zones. The addition of metoclopramide to 1080 poison baits for wild pigs reduces vomiting and thereby reduces the poisoning risk to nontarget species. The addition of metoclopramide improves the efficiency and percentage of the kill of wild pigs because they will not develop taste aversion to the baits. A similar case is made for dogs.

Baits containing this antiemetic at an effective concentration of 1 mg/kg BW shortened the median time for death for dogs from 151 min postdose for 1080 baits without metoclopramide to 132 min (Rathore 1985). At tested doses (1 to 16 mg/kg BW), metoclopramide did not decrease the frequency of vomiting by dogs, but did decrease the amount of vomitus (O'Brien et al. 1986).

Secondary poisoning is likely among carrion eaters feeding on rabbits and other herbivores poisoned with 1080-treated carrots, especially foxes and dingoes (secondary target species), and dogs and cats (McIlroy 1981b; McIlroy and Gifford 1992). Secondary poisoning was reported for dogs feeding on 1080-treated rodents and prairie dogs, and for cats feeding on treated rats and mice (Anonymous 1946). Some domestic dogs and cats were found dead within 450 m of a 1080-treatment area; signs of 1080 poisoning were evident but no 1080 residues were detected by chemical analyses (Hegdal et al. 1986). Ground squirrel control with 1080 baits caused secondary poisoning of dogs, cats, coyotes, bobcats (*Lynx rufus*), skunks, and kit foxes (Hegdal et al. 1986). The high susceptibility of threatened and endangered species of kit foxes to 1080 rodenticides, as judged by studies with nonthreatened species of kit foxes, suggests that 1080 could be a factor in their population decline (Schitoskey 1975). Sodium monofluoroacetate has a high degree of secondary toxicity in mammals, as evidenced by deaths of domestic ferrets that ate 1080-poisoned white-footed mice (*Peromyscus leucopus*) (Hudson et al. 1984). Similarly, coyotes died after ingestion of 1080-poisoned ground squirrels that contained 3 to 6 mg of 1080 equivalent to 0.24 to 0.63 mg/kg BW coyote (Casper et al. 1986; Marsh et al. 1987). Coyotes that ate a single 1080-poisoned squirrel daily for 5 days, for an estimated total dose of 0.12 to 0.27 mg/kg BW, usually survived, suggesting that there is little secondary hazard from multiple doses when they are small (Marsh et al. 1987). Carcasses and viscera from coyotes that died after ingesting 5 to 15 mg 1080 were fed for 14 to 35 days to other coyotes, domestic dogs, striped skunks (*Mephitis mephitis*), and black-billed magpies; no evidence of secondary poisoning was seen in any species tested. Maximum residues of 1080 in dead coyote tissues, in mg/kg FW, were 0.66 in muscle, 0.79 in small intestine, and 0.76 in stomach tissue (Burns et al. 1986). Tissues of 1080-poisoned coyotes did not produce secondary poisoning in opossums (*Didelphis virginiana*) (Eastland and Beason 1986a), striped skunks (Eastland and Beason 1986a; Burns et al. 1991), raccoons (Eastland and Beason 1986a; Hegdal et al. 1986), or badgers (*Taxidea taxus*) (Hegdal et al. 1986). The hazard of secondary poisoning to predators is minimal after consuming tissues of 1080-killed black-tailed prairie dogs (*Cynomys ludovicianus*), as their tissues contained <0.1 mg fluoroacetate/kg FW (Huggins et al. 1988). No mink died when fed 1080-poisoned rabbits at 40% of the total diet, provided that the rabbit gastrointestinal tract had been removed from the carcass. This suggests that secondary toxicity from 1080 is due primarily to consumption of the unmetabolized compound from the gut of prey species (Aulerich et al. 1987). The risk to different individuals or populations depends on the species' sensitivity to 1080, the number of poisoned animals consumed, and the amounts of different tissues or organs consumed (McIlroy and Gifford 1992).

Animals in Australia vary greatly in their sensitivity to 1080 poison, with known LD₅₀ values ranging from 0.11 to >800 mg/kg BW. Many native species, particularly in Western Australia have evolved tolerances to 1080 through ingestion of native plants that contain fluoroacetate or prey that consume these plants (McIlroy 1982a; McIlroy 1992). The degree to which this tolerance is developed depends on the extent of the toxic plants in the microhabitat, the need of each species to include those food species that contain fluoroacetate in its diet, and the length of evolutionary exposure to the toxic plants (Twigg et al. 1988b; King et al. 1989; Twigg and Mead 1990). This naturally occurring resistance to the toxins allows control programs that use 1080 to be more specific for introduced test species (Mead et al. 1985). Tolerance to fluoroacetate is present in insects, reptiles, mammals, and birds and is in the order of herbivores > omnivores > carnivores (Twigg and King 1991). Mammals with lower metabolic rates — such as marsupial carnivores — seem to be more tolerant to a metabolically interfering poison such as 1080 than mammals with a higher metabolism such as eutherian carnivores (McIlroy 1981a; 1981b). Tolerance to gradually increasing doses of fluoroacetate can be induced in the mouse, rat, and rhesus monkey, but not in

dog or rabbit; however, the protective effect of prior exposure to 1080 seldom persisted for more than 48 h (Chenoweth 1949). Laboratory white rats may acquire tolerance to 1080 by the ingestion of sublethal doses over a period of 5 to 14 days; cessation of dosing for 7 days caused a loss of tolerance (Kalmbach 1945). Some species acquired tolerance to 1080 after repeated sublethal doses and others accumulated the chemical until a lethal threshold was reached (McIlroy 1981a). Both phenomena were unpredictable if 1080 residues in the tissues remained between doses. Time required for complete elimination of 1080 from tissues varied among species: dogs required 2 to 3 days, rats 36 h, and sheep as long as 1 month (McIlroy 1981a).

Sublethal concentrations of 1080 may adversely affect reproduction, growth, and behavior. In rats (*Rattus* sp.), the organ most vulnerable to 1080 poisoning is the testes, and this is consistent with 1080-impaired energy production via blockage of the Krebs cycle and subsequent impairment of carbohydrate metabolism (Sullivan et al. 1979). Subacute dietary exposure to 1080 caused dose-dependent decreases in body weights and feed consumption in mink and European ferrets (Hornshaw et al. 1986). Toxic 1080 meat baits were usually avoided by the majority of tested nontarget dasyurids and rodents when alternative foods were available. Twelve of the 24 groups tested did not sample meat baits under these conditions (Calver et al. 1989a). Adult wild pigs given a sublethal dose of 1080 (0.5 mg/kg BW) in apple baits vomited within 30 min after eating the treated bait and avoided apple baits in future tests (Rathore 1985). Caged wild Norway rats (*Rattus norvegicus*) and black rats (*Rattus rattus*) developed a gradually increasing aversion to drinking water solutions of 1080, although this aversion was not sufficient to disrupt growth and reproduction (Kalmbach 1945).

Table 26.4 Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference ^a
Arctic fox, <i>Alopex lagopus</i>		
Fed a single bait containing 4 mg 1080	Muscle contained 0.39 (0.24–0.65) mg 1080/kg fresh weight (FW)	1
Muscle from 66 foxes found dead on Kiska Island, Alaska, after 1080 poisoning; analysis 60 days after collection	Muscle from males contained 0.7 (0.12–2.2) mg 1080/kg FW; for females, it was 0.81 (0.09–2.8) mg/kg FW	1
Brown antechinus, <i>Antechinus stuartii</i>		
1.1–3.5 mg/kg body weight (BW)	LD50, from non-fluoroacetate-bearing vegetation area	2–4
11.0 mg/kg BW	LD50, from fluoroacetate vegetation area	4
Dusky antechinus, <i>Antechinus swainsonii</i> ; 3.2 (95% confidence interval [=CI] of 2.4–4.2) mg/kg BW	LD50	3
Black-handed spider monkey, <i>Ateles geoffroyi</i> ; 10.0–15.0 mg/kg BW	LD50	5–8
Australian mammals, various; 1.6–20.0 mg/kg BW	Lethal to 8 species of marsupials and 5 species of rodents	9
Australian rodents		
3.1 (0.7–9.0) mg/kg BW	LD50 mean (range) for 10 species with no known exposure to naturally occurring fluoroacetates	10
21.6 (3.5–80.0) mg/kg BW	LD50 mean (range) for 10 species with known past or continuing exposure to naturally occurring fluoroacetates	10
Burrowing bettong, <i>Bettongia lesueuer</i> ; 10–20 mg/kg BW	LD50	11
Cow, <i>Bos</i> spp.; single dose		
0.078 mg/kg BW	Not fatal to calves and adults	12
0.156 mg/kg BW	Not fatal to cows; LD20 for calves	12
0.22 (95% CI of 0.15–0.33) mg/kg BW	LD50 for steers and calves	5, 11, 12
0.312 mg/kg BW	LD67 for cows; LD80 for calves	12
0.39 (95% CI of 0.25–0.63) mg/kg BW	LD50 for Hereford cows	5, 11
0.624 mg/kg BW	LD100 for cows and calves	12

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Canids, 6 species; 0.15 (95% CI of <0.1–0.3) mg/kg BW	LD50	13
Dog, <i>Canis familiaris</i>		
0.06 mg/kg BW, single oral dose	LD50; death in 5–9 h	6, 14
0.1–0.35 mg/kg BW, single oral dose	LD100; death in 4–6 h	6, 7, 14–16
Ingested about 1.96 mg of 1080 (56 g of a 1080-poisoned bait containing 35 mg 1080/kg horse meat)	Vomiting at 1.75 h post ingestion; seizure and a short yip 20 min later; seizures and exhaustion for the next 50 min; death at about 3 h after ingestion	16
Dingo, <i>Canis familiaris dingo</i>		
0.11 (95% CI of 0.09–0.15) mg/kg BW	LD50	3
0.123 (95% CI of 0.110–0.137) mg/kg BW	LD99	13
Coyote, <i>Canis latrans</i>		
Fed 1080-poisoned ground squirrels (<i>Spermophilus</i> sp.) that contained 0.01–0.09 mg fluoroacetate/kg FW	Maximum residues in dead coyotes, in mg 1080/kg FW, were 0.14 in large intestine, 0.09 in kidney, 0.07 in brain, 0.05 in stomach, and 0.03 in liver	17
0.1–0.2 mg/kg BW	LD50	5–8, 16
0.13–0.16 mg/kg BW by gavage	Muscle residues were 0.10–0.11 mg/kg FW	18
0.23–0.5 mg/kg BW; poisoned bait	Muscle residues of 0.08–0.15 mg/kg FW	18
0.5–1.0 mg/kg BW by gavage	Muscle residue of 0.08–0.15 mg/kg FW	18
1 mg/kg BW; poisoned bait	Muscle residue of 0.21 mg/kg FW	18
Ingestion of bait containing 5 mg 1080 (about 2.28 mg 1080/kg BW)	Signs of poisoning noted in 17–18 min after bait ingestion; death in 243–313 min after ingestion	19
Single lethal oral dose of 5 mg/kg BW		
Nonrefrigerated muscle tissue	Muscle contained 2.3 mg/kg FW <3 h after death; 1.5 mg/kg FW at 7 days	18
Frozen muscle tissue	Residue of 2.3 mg/kg FW after 30 days, 2.1 mg/kg FW after 60 days	18
Room temperature, muscle tissue	Residues ranged from 1.8–2.0 mg/kg FW between <3 h and 28 days	18
<3 h after death	Residues, in mg/kg FW, were 11.0 in stomach; 2.1–2.4 in heart, muscle, kidney and intestine; and 1.2 in liver	18
30.0 mg/kg BW by gavage	19.5 mg/kg FW in muscle	18
In pen tests, 25 coyotes were offered lambs with collars containing 5 or 10 mg 1080/mL	A total of 23 coyotes attacked and 21 died after collars were punctured in their first (n = 17), second (n = 3), or fifth (n = 1) tests. The average time to death was 217 min (range 115–436 min)	20
Goat, <i>Capra</i> sp.		
0.1 mg/kg BW; single oral dose	Half-time persistence of 5.4 h in plasma	21
0.3–0.7 mg/kg BW	LD50	5–8, 11, 16
Guinea pig, <i>Cavia</i> spp.		
0.18 mg/kg BW	LD50 at 4°C	22
0.23 mg/kg BW	LD50 at 32°C	22
0.38 mg/kg BW	LD50 at 17°C	22
0.39 mg/kg BW	LD50 at 24°C	22
Ground squirrels, <i>Citellus</i> spp.; 0.3–0.9 mg/kg BW	LD50	5–7, 15, 16
Hamsters, <i>Cricetus</i> spp.; 3.0 mg/kg BW	LD50	6
Black-tailed prairie dog, <i>Cynomys ludovicianus</i>		
0.125 mg/kg BW	No deaths	7, 23
0.17–0.3 mg/kg BW	LD50	5, 8, 23, 50
0.4–2.5 mg/kg BW	LD50–LD100	15, 16, 50
Dasyurids, 11 species; 3–12 mg/kg BW	LD50	24
Kowari, <i>Dasyuroides byrnei</i> ; ~2.8 mg/kg BW	LD50	3

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Northern native cat, <i>Dasyurus hallucatus</i> ; 5.7 (95% CI of 3.9–8.2) mg/kg BW	LD50	3
Tiger cat, <i>Dasyurus maculatus</i> ; 1.8 (95% CI of 1.3–2.7) mg/kg BW	LD50	3
Quolls, <i>Dasyurus</i> spp.		
1.5 mg/kg BW	LD50, nontolerant population from southeastern Australia	4
7.5 mg/kg BW	LD50, tolerant populations from Western Australia	4
Eastern native cat, <i>Dasyurus viverrinus</i> ; 3.7 (95% CI of 3.2–4.4) mg/kg BW	LD50	3
Opossum, <i>Didelphis marsupialis</i> ; 60.0 mg/kg BW	LD50	5
Kangaroo rats, <i>Dipodomys</i> spp.		
0.1–0.2 mg/kg BW	LD47–LD85	5, 6, 16
0.2–1.0 mg/kg BW	LD100	16
Mule, <i>Equus asinus</i> X <i>E. caballus</i> ; 0.22–0.44 mg/kg BW	LD50	5, 11, 25
Horse, <i>Equus caballus</i> ; 0.32–1.00 mg/kg BW	LD50	5–8, 11, 12, 16, 25
North American porcupine, <i>Erethizon dorsatum</i> ; ~1.0 mg/kg BW	LD50	5
Eutherian mammals, Australia		
0.36 (95% CI of 0.04–3.5) mg/kg BW	LD50, 13 species of carnivores	13
0.44 (95% CI of 0.21–0.60) mg/kg BW	LD50, 7 species of herbivores	13
Feral cat, <i>Felis cattus</i>		
0.1–0.19 mg/kg BW	No deaths using poisoned fish baits	26
0.2–0.3 mg/kg BW	LD50, intravenous injection	26
0.28 (95% CI of 0.07–0.49) mg/kg BW	LD50, poisoned fish baits	26
0.35 mg/kg BW	LD50, acute oral route	26
0.35 mg/kg BW	LD90, poisoned fish baits	26
0.4 (95% CI of 0.31–0.52) mg/kg BW	LD50, oral intubation	3
1.3 mg/kg BW	All dead within 24 h when ingested as a fish bait	26
Domestic cat, <i>Felis domesticus</i>		
0.2–0.3 mg/kg BW	LD50	5–8, 16
0.5 mg/kg BW	LD100	16
Breviceps pocket gopher, <i>Geomys breviceps</i>		
<0.05 mg/kg BW	LD50	5, 6
0.05 mg/kg BW	LD100	16
Tuza pocket gopher, <i>Geomys floridanus</i>		
0.2 mg/kg BW	LD50	5, 6
0.25–0.5 mg/kg BW	LD60–LD100	16
Human, <i>Homo sapiens</i>		
0.7–2.1 mg/kg BW	LD50 (estimated)	5
2.0 mg/kg BW	LD100 (estimated) for children	16
2.0–10.0 mg/kg BW	LD50 (estimated) for adults	6, 27
Water-rat, <i>Hydromys chrysogaster</i> ; 2.9 mg/kg BW	LD50	28, 29
Golden bandicoot, <i>Isoodon auratus barrowensis</i> ; 8.9 (95% CI of 7.2–11.0) mg/kg BW	LD50	30
Northern brown bandicoot, <i>Isoodon macrourus</i> ; 3.5 mg/kg BW	LD50	30, 31
Southern brown bandicoot, <i>Isoodon obesulus</i>		
7.0–8.0 mg/kg BW	LD50; maximum latent period, 183 h; time until death, 7–206 h; time for survivors to recover, 27 h	30, 31

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference^a
20.0 mg/kg BW; from area of fluoroacetate-bearing vegetation	Tolerated	30
Southern hairy-nosed wombat, <i>Lasiorhinus latifrons</i> ; 0.21 (95% CI of 0.15–0.29) mg/kg BW	LD50	11
Black-tailed jack rabbit, <i>Lepus californicus</i> ; 5.6 mg/kg BW	LD50	5, 11
Bobcat, <i>Lynx rufus</i> ; 0.67 mg/kg BW	LD50–LD100	7, 8, 16
Rhesus monkey, <i>Macaca mulatta</i> ; 4–12 mg/kg BW	LD50	5–7, 16
Macropodids, 7 species; 0.23 (95% CI of 0.1–0.6) mg/kg BW	LD50	13
Agile wallaby, <i>Macropus agilis</i> ; 0.22 mg/kg BW	LD50	11
Tammar wallaby, <i>Macropus eugenii</i>		
0.15 mg/kg BW	LD50, pouch young	11
0.27 mg/kg BW vs. 2.0–10.0 mg/kg BW	LD50, adults from nonfluoroacetate- vs. fluoroacetate-vegetation areas	11
Gel containing 12.5 mg 1080 applied to a single leaf of edible foliage	Population reduced 91% in North Island, New Zealand field trial	32
Marsupials		
Various species; fatally poisoned with 1080 under laboratory conditions	Mean residue concentrations, in mg 1080/kg FW, were 0.2 in muscle, 6.1 in viscera, and 29.7 in stomach and contents	33
0.25 (95% CI of 0.1–0.7) mg/kg BW; 10 species of herbivores	LD50, eastern Australia (nonfluoroacetate-vegetation area)	10, 13
2.6 (95% CI of 0.9–7.6) mg/kg BW; 9 species of carnivores	LD50	13
24.2–42.0 (95% CI of 1.5–389.4) mg/kg BW; 10 species of herbivores	LD50, Western Australia (fluoroacetate-vegetation area)	10, 13
From area of fluoroacetate-bearing vegetation		
Red kangaroo, <i>Macropus rufus</i> ; 2.0–4.4 mg/kg BW	LD50	11
Western brush wallaby, <i>Macropus irma</i> ; 5–10 mg/kg BW	LD50	11
Western gray kangaroo, <i>Macropus fuliginosus</i> ; 40–60 mg/kg BW	LD50	11
Brush-tailed bettong, <i>Bettongia penicillata</i> and banded hare-wallaby, <i>Lagostrophus fasciatus</i> ; 100–200 mg/kg BW	LD50	11
Eastern gray kangaroo, <i>Macropus giganteus</i> ; 0.1–0.4 mg/kg BW	LD50	11
Bennett's wallaby, <i>Macropus rufogriseus</i>		
0.2 mg/kg BW	LD50	11
Gel containing about 25 mg 1080 applied to single leaf of edible foliage	Population reduced 87% in South Island, New Zealand, field trial	32
Greater bilby (bandicoot), <i>Macrotis lagotis</i> ; 15 mg/kg BW; from area of fluoroacetate-bearing vegetation	Tolerated	30
Marten, <i>Martes marten</i> ; ~1.0 mg/kg BW	LD50	5
Grassland melomys rat, <i>Melomys burtoni</i> ; 2.6 (95% CI of 2.2–3.1) mg/kg BW	LD50	28
Striped skunk, <i>Mephitis mephitis</i>		
Diet		
Fed diet containing 4.1 mg 1080/kg ration for 5 days (about 2 times level found in 1080-poisoned coyotes)	No deaths or signs of poisoning other than reduced feeding and loss in body weight	35

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference ^a
Fed coyote muscle for 14–35 days; coyote had been poisoned with massive (400 mg) dose of 1080	Fatal to all 3 skunks tested	19
Single dose		
0.125 mg/kg BW	No deaths in 7 days	34
0.25 mg/kg BW	LD40	34
0.35 (95% CI of 0.21–0.54) mg/kg BW	LD50	34
0.75 mg/kg BW	LD100	34
Tristram jird, <i>Meriones tristrami</i> ; fed wheat grain baits		
0.38–0.47 mg/kg BW	50% dead in 3 days	36
1.7–2.5 mg/kg BW	All dead within 24 h	36
Levant vole, <i>Microtus guentheri</i> ; fed wheat grain baits		
0.24–0.43 mg/kg BW	LD50	36
0.44 mg/kg BW	LD73	36
0.2–2.5 mg/kg BW	All dead within 24 h	36
Meadow mouse, <i>Microtus haydeni</i> ; 0.3–0.5 mg/kg BW	LD33–LD100	16
Meadow vole, <i>Microtus pennsylvanicus</i> ; 0.92 mg/kg BW	LD50	5
House mouse, <i>Mus musculus</i>		
2.6 mg/kg BW	LD50 at 12.2°C	22
4.5 mg/kg BW	LD50 at 33°C	22
5.8 mg/kg BW	LD50 at 17.9°C	22
7.4 mg/kg BW	LD50 at 30°C	22
8.3 (95% CI of 6.3–11.0) mg/kg BW	LD50	28
10.0 mg/kg BW	LD66	16
12.8 mg/kg BW	LD50 at 24°C	22
Mice, <i>Mus</i> spp.		
5.0–19.3 mg/kg BW	LD50	6, 14
13.5 (95% CI of 11.0–16.6) mg/kg BW	LD50; survivors exhibited persistent abnormal behavior, ranging from circling to resting with their heads tucked under the abdomen or brisket	37
15 mg 1080/kg BW alone, or followed by intraperitoneal injection of mixture of 130 mg calcium glutonate/kg BW plus 240 mg sodium succinate/kg BW	Alone, 1080 resulted in 80% dead in 48 h and 100% in 120 h. If antidote is administered within 15 min of 1080 exposure, survival increased to 70% at 48 h and 50% at 120 h after 1080 treatment; antidote survivors recovered much earlier and resumed feeding within 3 days of 1080 injection	37
150 mg 1080/kg bait	In pen tests, population numbers were reduced 88% in 20 days	38
Domestic ferret, <i>Mustela putorius</i>		
1.41 (95% CI of 1.00–2.00) mg/kg BW	LD50	39
Fed one 1080-poisoned white-footed mouse (<i>Peromyscus leucopus</i>) equivalent to 1, 2, 4, or 8 mg/kg BW ferret	All died at all doses except 1 ferret at 2 mg/kg BW	39
European ferret, <i>Mustela putorius furo</i>		
Fed internal organs for 3 days of 1080-killed black-tailed prairie dogs	1 of 10 ferrets died and 5 others showed signs of 1080 poisoning; all affected ferrets recovered 24–48 h after exposure	50
Fed ground whole carcasses (less skin, skull, and feet) of black-tailed prairie dogs that died of 1080 poisoning. Carcasses contained 0.05–0.1 mg fluoracetate/kg FW and composed 90% of diet	No adverse effects after 28 days	23

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference^a
1.1 mg/kg diet for 28 days	Reduction in red and white blood cell numbers	40
1.2–1.4 mg/kg BW, single dose	LD50	5, 25, 40, 50
9.4 mg/kg diet for 28 days	LD50	40
Mink, <i>Mustela vison</i>		
0.1 mg/kg BW	No deaths in 3 days	40
0.25 mg/kg BW	50% dead in 3 days	40
0.5 mg/kg BW	2.5–2.8 h to death	40
0.8 mg/kg diet for 2 months prior to breeding	Impaired reproduction	40
1.0 mg/kg BW	1.5 h to death	40
2.9 mg/kg diet for 28 days	40% dead	40
3.2 (95% CI of 2.4–4.5) mg/kg diet for 28 days	50% dead	40
5.25 mg/kg diet for 28 days	Partial paralysis of hind limbs and reduced feed intake by day 5; 90% dead at 28 days	40
Nutria, <i>Myocaster coypus</i> ; 0.6 mg/kg BW	LD50	5
White-throated wood rat, <i>Neotoma albigula</i>		
<0.8 mg/kg BW	LD50	5
0.8 mg/kg BW	LD100	16
Wood rat, <i>Neotoma intermedia</i>		
1.0 mg/kg BW	LD20	16
1.5 mg/kg BW	LD50	5
2.0 mg/kg BW	LD100	16
Spinifex hopping-mouse, <i>Notomys alexis</i> ; 32.7 (95% CI of 27.4–39.3) mg/kg BW	LD50	28
Mitchell's hopping mouse, <i>Notomys mitchelli</i> ; 19.4 (95% CI of 15.8–23.9) mg/kg BW	LD50	28
Mule deer, <i>Odocoileus hemionus hemionus</i> ; 0.3–1.0 mg/kg BW	LD50, 8–11 months of age	5, 11, 25, 39
European rabbit, <i>Oryctolagus cuniculus</i>		
Found dead after consuming 1080-treated carrots; New South Wales, Australia; February 1986	Maximum concentrations of 1080, in mg/kg DW, were 263 in kidney, 423 in liver, 151 in heart, 34 in muscle, 136 in stomach, and 243 in stomach contents. Total 1080 content was 7.04 mg whole body and 4.87 mg in whole body less stomach and contents	33
0.36 (95% CI of 0.30–0.42) mg/kg BW	LD50, immatures	11
0.42 (95% CI of 0.26–0.58) mg/kg BW	LD50, adults	11
0.51 (95% CI of 0.44–0.58) mg/kg BW	LD90	11
Fed pellets containing 10 mg 1080/kg pellet	All dead within 6 h	41
Sheep, <i>Ovis aries</i>		
0.1 mg/kg BW; single oral dose	Residues after 2.5 h, in mg/kg, were 0.1 in plasma and 0.02–0.06 in other tissues; after 96 h, the maximum value in any tissue was 0.003 mg/kg. Half-time persistence of 1080 in plasma was 10.8 h	21
0.25–0.64 mg/kg BW	LD50	5, 11
2.0 mg/kg BW	LD50	6, 12
Gunn's bandicoot, <i>Perameles gunni</i> ; 5.4 mg/kg BW	LD50; latent period, 2–6 h; time until death, 4–86 h	31
Long-nosed bandicoot, <i>Perameles nasuta</i> ; 7.7 (95% CI of 5.3–11.2) mg/kg BW	LD50; maximum latent period, 6.4 h; time until death 4–56 h; time for survivors to recover, 26–42 h	3, 31
Pocket mouse, <i>Perognathus inornatus</i> ; 1.0 mg/kg BW	LD100	16
Deer mouse, <i>Peromyscus</i> sp.		
2.0–4.0 mg/kg BW	LD39–LD50	16
4.0–5.0 mg/kg BW	LD50	5, 6, 15

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Raccoon, <i>Procyon lotor</i> ; single oral dose Ambient air temperature of 23–27°C vs. 13–23°C		
0.5 mg/kg BW	LD40 vs. none dead	42
1.0–1.85 mg/kg BW	LD60 vs. LD20	42
2.45 mg/kg BW	LD80 vs. LD60	42
2.82 mg/kg BW	LD100 vs. LD75	42
3.24 mg/kg BW	All dead	42
Plains mouse, <i>Pseudomys australis</i> ; 1.2 (95% CI of 1.1–1.4) mg/kg BW	LD50	28
Sandy inland mouse, <i>Pseudomys hermannsburgensis</i>		
1.6 (95% CI of 1.3–2.0) mg/kg BW	LD50, New Zealand	9
39.3 (95% CI of 23.6–65.4) mg/kg BW	LD50, Australia	28
Long-tailed mouse, <i>Pseudomys higginsi</i> ; 9.0 (95% CI of 6.2–13.1) mg/kg BW	LD50	28
Western chestnut mouse, <i>Pseudomys nanus</i> ; 14.7 (95% CI of 13.7–15.9) mg/kg BW	LD50	28
Alexandrine rat, <i>Rattus alexandricus</i>		
0.5 mg/kg BW	LD50	5, 6
1.0–2.0 mg/kg BW	LD92–LD100	16
Bush rat, <i>Rattus fuscipes</i> ; 1.1 (95% CI of 0.9–1.5) mg/kg BW	LD50	28, 29
Swamp rat, <i>Rattus lutreolus</i> ; 1.7 (95% CI of 1.4–2.1) mg/kg BW	LD50	28
Norway rat, <i>Rattus norvegicus</i>		
0.22–3.0 mg/kg BW	LD50, wild strains	6, 43
2.0 mg/kg BW	Oxygen consumption reduced 28–57% in 24 h	43
2.1–2.2 mg/kg BW	LD50, laboratory strains	5
3.0 mg/kg BW	5-fold increase in plasma citrate levels in 4 h	43
4.0–8.0 mg/kg BW	LD72–LD100	16
Black rat, <i>Rattus rattus</i> ; 1.7 (95% CI of 1.2–2.4) mg/kg BW	LD50	28
Canefield rat, <i>Rattus sordidus</i> ; 1.3 (95% CI of 1.0–1.6) mg/kg BW	LD50	28, 29
Laboratory white rat, <i>Rattus</i> sp.		
Single dose		
0.2 mg/kg BW	LD50	27
4.0 mg/kg BW	LD60	16
7.5 mg/kg BW	LD100	16
10.53 mg radiolabeled 1080/kg BW	After 4 h, radioactivity was highest in carcass (60%), liver (12%), intestine and stomach (10%) and brain, kidney, testes, and spleen (2–3% each)	5
Multiple doses		
Males given drinking water containing 2.2, 6.6, or 20 mg 1080/L for 7 days then observed for 21 days. Daily dose rates, in mg/kg BW, were 0.07 (2.2 mg/L), 0.18, and 0.71 (20 mg/L), respectively	No overt signs of acute toxicity in any group. However, all groups had testes damage (altered appearance, decreased number of spermatids, formation of spermatid and spermatocyte giant cells). The two high-dose groups had reduction in testicular weight and seminiferous tubule atrophy; regeneration of tubules was incomplete at day 21 postexposure	44
Tunney's rat, <i>Rattus tunneyi</i> ; 2.6 (95% CI of 2.2–2.9) mg/kg BW	LD50	9
Rodents, 32 species		
<0.1 mg/kg BW	LD50, 4 species	28
0.1–0.25 mg/kg BW	LD50, 6 species	28
0.26–1.0 mg/kg BW	LD50, 15 species	28
>1.0 mg/kg BW	LD50, 7 species	28

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Rodents, various, single dose 0.83 (95% CI of 0.1–6.3) mg/kg BW 1.05 (95% CI 0.02–2.1) mg/kg BW 2.0–20.0 mg/kg BW 19.4 (95% CI <0.05–48.1) mg/kg BW	LD50, 11 species of cricetids LD50, 5 species of <i>Rattus</i> Lethal, 8 species LD50, 6 species of pseudo-mice	13 13 24 13
Tasmanian devil, <i>Sarcophilus harrisii</i> ; 4.2 (95% CI of 2.8–6.6) mg/kg BW	LD50	3
Quokka (kangaroo), <i>Setonix brachyurus</i> 3.5 mg/kg BW	Nontolerant populations had significantly increased plasma citrate levels in 12 h, but none died	45
10–40 mg/kg BW	10 mg/kg BW killed 50% of a nontolerant population; tolerant populations survived	45
60 mg/kg BW	All populations dead within 12 h; plasma citrate levels elevated	45
Cotton rat, <i>Sigmodon hispidus</i> 0.1 mg/kg BW 5.0 mg/kg BW	LD50 LD100	5, 6, 16 16
Fat-tailed dunnart, <i>Sminthopsis crassicaudata</i> ; 2.1 (95% CI of 1.6–2.7) mg/kg BW	LD50	3
Stripe-faced dunnart, <i>Sminthopsis macroura</i> ; 0.9 (95% CI of 0.6–1.6) mg/kg BW	LD50	3
Ground squirrel, <i>Spermophilus beecheyi</i> ; fatally poisoned with 1080 0.8 mg/kg BW	Tissue residues, in mg fluoroacetate/kg FW, were 0.2–0.7 in brain, kidney, liver, muscle, and lung; 1.0 in caecum; 1.3 in spleen; and 11.8 in stomach	17
4.8 mg/kg BW	Tissue residues, in mg fluoroacetate/kg FW, were 0.5–0.7 in brain and muscle; 1.1–1.8 in caecum, kidney, liver, and lung; 9.7 in spleen; and 55.9 in stomach	17
Feral pig, <i>Sus scrofa</i> 0.4 mg/kg BW <1.0 mg/kg BW 1.0 (95% CI of 0.8–1.3) mg/kg BW 1.8 (95% CI of 1.3–185.9) mg/kg BW 2.3 (95% CI of 1.6–3381) mg/kg BW 4.3 mg/kg BW 21.3 mg/kg BW	LD50, juveniles LD50, adults LD50 LD95 LD99 LD28 with pellet baits; LD60 with wheat baits LD100; median time to death of 244 min (range 131–7200 min)	46 46 29 29 29 47 47
Domestic pig, <i>Sus</i> sp. 0.3–0.4 mg/kg BW <1.0 mg/kg BW	LD50, juveniles LD50, adults	5, 7, 8, 16 5
Badger, <i>Taxidea taxus</i> ; 1.0–1.5 mg/kg BW	LD50–LD100	5, 16
Red-bellied pademelon, <i>Thylogale billardierii</i> ; 0.13 (95% CI of 0.09–0.19) mg/kg BW	LD50	11, 31
Brush-tailed possum, <i>Trichosurus vulpecula</i> 0.3–1.0 mg/kg BW 16.9 (95% CI of 11.6–24.7) mg/kg BW 41.2 (95% CI of 30.2–56.1) mg/kg BW >100–>125 mg/kg BW	LD50, from nonfluoroacetate vegetation area LD50 at 10.5°C LD50 at 23.5°C LD50, from fluoroacetate-bearing vegetation area	2, 11 22 22 11, 45
Grey fox, <i>Urocyon cinereoargenteus</i> ; 0.3 mg/kg BW	Lethal	5, 16
Bears, <i>Ursus</i> spp.; 0.5–1.0 mg/kg BW	LD50	5

Table 26.4 (continued) Effects of 1080 on Representative Mammals

Species, Dose, and Other Variables	Effect	Reference ^a
Common wombat, <i>Vombatus ursinus</i>		
0.15 (95% CI of 0.12–0.19) mg/kg BW	LD50, free-ranging	11
0.22 (95% CI of 0.18–0.27) mg/kg BW	LD50, captive wombats	11
Desert kit fox, <i>Vulpes macrotis arsipus</i>		
0.22 (95% CI of 0.15–0.34) mg/kg BW; single dose	LD50	48
Fed a 1080-poisoned kangaroo rat (<i>Dipodomys</i> sp.). Approximate dose to fox of 0.434 mg/kg BW	Death within 12 h	48
Red fox, <i>Vulpes vulpes</i>		
0.08–0.10 mg/kg BW	No deaths	49
0.125–0.15 mg/kg BW	All dead	49
Thick-tailed rat, <i>Zyzomys argurus</i> ; 3.2–5.8 mg/kg BW	LD50	9

^a 1, Tietjen et al. 1988; 2, McIlroy 1981a; 3, McIlroy 1981b; 4, King et al. 1989; 5, Atzert 1971; 6, Chenoweth 1949; 7, Anonymous 1946; 8, Negherbon 1959; 9, Calver et al. 1989b; 10, McIlroy 1992; 11, McIlroy 1982a; 12, Robison 1970; 13, McIlroy 1986; 14, Tourtellotte and Coon 1950; 15, Kalmbach 1945; 16, Peacock 1964; 17, Casper et al. 1986; 18, Okuno et al. 1984; 19, Burns et al. 1986; 20, Connolly and Burns 1990; 21, Eason et al. 1994; 22, Oliver and King 1983; 23, Huggins et al. 1988; 24, Calver et al. 1989a; 25, Tucker and Crabtree 1970; 26, Eason and Frampton 1991; 27, Murphy 1986; 28, McIlroy 1982b; 29, McIlroy 1983a; 30, Twigg et al. 1990; 31, McIlroy 1983b; 32, Warburton 1990; 33, McIlroy and Gifford 1992; 34, Eastland and Beasom 1987; 35, Burns et al. 1991; 36, Moran 1991; 37, Omara and Sisodia 1990; 38, Twigg and Kay 1992; 39, Hudson et al. 1984; 40, Hornshaw et al. 1986; 41, Aulerich et al. 1987; 42, Eastland and Beasom 1986b; 43, Twigg et al. 1986; 44, Sullivan et al. 1979; 45, Mead et al. 1985b; 46, Rathore 1985; 47, O'Brien et al. 1988; 48, Schitoskey 1975; 49, McIlroy and King 1990; 50, Savarie et al. 1994.

26.5 RECOMMENDATIONS

It is emphasized that 1080 is a restricted pesticide that can only be used by certified applicators who have received special training (Green 1946; Negherbon 1959; USEPA 1985; Connolly 1993a), and that carcasses of all organisms found dead from 1080 poisoning must be buried or incinerated (USEPA 1985). Some authorities aver that continued use of 1080 is justified and desirable, and that risk is minimal to nontarget organisms. As discussed earlier, 1080 is a natural plant product, is generally highly toxic to most pests at low concentrations, is readily lost from baits following heavy dews or rainfall, is biodegraded by fungi and bacteria, and does not persist in soil or water. In New Zealand, 1080 has been used since 1954 and is still considered an essential pesticide for limiting forest and crop damage and for containing the spread of tuberculosis to livestock by brush-tailed possums (Eason et al. 1993b). It has been used to control isolated island populations of mammals that prey on endangered or threatened species of birds, as was the case for Arctic foxes preying on Aleutian Canada geese in the Aleutian Islands (Tietjen et al. 1988; Bailey 1993). In Australia and New Zealand, results of field studies suggest that 1080-poisoning campaigns had no significant effect on almost all populations of common nontarget species (McIlroy 1982a, 1992; McIlroy et al. 1986b; McIlroy and Gifford 1991; Spurr 1994), although more studies are recommended on vulnerable, rare, endangered, or uncommon species (McIlroy 1992).

There is, however, a growing body of information on 1080 that questions its usefulness in the United States. This database includes adverse effects on some nontarget organisms and endangered species; the confounding effects of the latent period, behavioral alterations, and application routes; and the development of suitable alternative chemicals. On the basis of acute oral toxicity tests, it is likely that sensitive nontarget mammals and birds will consume lethal quantities of 1080 from poisoned baits or from consumption of organisms fatally poisoned with 1080 (USEPA 1985). Field studies record deaths among sensitive nontarget species that ate 1080 baits, including bees (Goodwin

and Ten Houten 1991), insectivorous birds, (McIlroy 1982a; Hegdal et al. 1986), rabbits, rodents (Hegdal et al. 1986), cats, dogs (Kalmbach 1945; Green 1946; Hegdal et al. 1986), and livestock (McIlroy 1982a, 1986). Secondary poisoning is reported for carrion eaters and mammalian predators — especially canids and felines — after feeding on 1080-poisoned prey (Hegdal et al. 1986; McIlroy and Gifford 1992). Sublethal effects of 1080 on growth of ferrets and reproduction of mink are reported (Hudson et al. 1984; Hornshaw et al. 1986). Some endangered species are at risk from direct consumption of the 1080 baits or from secondary poisoning (USEPA 1985). In general, the use of 1080 within the geographic range of any endangered species is discouraged, or disallowed outright in the case of the California condor, the San Joaquin kit fox (*Vulpes macrotis mutica*), the Aleutian Canada goose, the Morrow Bay kangaroo rat (*Dipodomys heermanni morroensis*), and the salt marsh harvest mouse (*Reithrodontomys raviventris*). When exceptions are made, or when 1080 use is permitted in an area known to be frequented by an endangered species, restrictions are placed on the maximum concentration of 1080 in the baits (USEPA 1985).

It is unlikely that human consumers of meat from 1080-killed ducks would be adversely affected after eating an average cooked portion (Temple and Edwards 1985). The risk to humans is minimal to low from eating meat of domestic animals accidentally poisoned with high sublethal concentrations of 1080 because it is cleared rapidly from domestic animals, usually within a few days (Eason et al. 1994). In the absence of additional data, it seems prudent to postpone for at least 3 weeks the slaughter or marketing of livestock that survived 1080 exposure. No livestock in the United States contaminated with 1080 are marketed (Connolly 1993a).

No effective antidote to 1080 is currently available, and accidental poisoning of livestock and dogs is likely to be fatal (Green 1946; Chenoweth 1949; Peacock 1964; Atzert 1971; Mead et al. 1991). The lack of emergency human treatment in cases of 1080 poisoning, coupled with the observation that monoacetin — potentially the most effective medication for compound 1080 poisoning — is not available in a pharmaceutical grade (USEPA 1985), strongly indicates the need for a viable 1080 antidote. The search for an effective 1080 antidote is ongoing, and some candidate compounds offer partial protection, including mixtures of sodium acetate and ethanol, barbiturates (Tourtellotte and Coon 1950; Peacock 1964), glycerol monoacetate (Peacock 1964; Murphy 1986), a mixture of calcium glutonate and sodium succinate (Roy et al. 1980; Omara and Sisodia 1990), and 4-methylpyrazole (Feldwick et al. 1994). The development and availability of an effective 1080 antidote should constitute a high research priority. Until such time when this antidote is distributed, it seems reasonable to use 1080 in the United States only after other alternatives have been considered.

The interval between 1080 dosage and signs of intoxication is at least 30 min, regardless of dose or species tested, and needs to be considered when evaluating the efficacy of 1080. Coyotes, for example, may continue to kill livestock after receiving a lethal dose (Connolly and Burns 1990). And coyotes may travel some distance from their prey prior to incapacitation, making carcass recovery and program evaluation difficult, as was the case for 1080-poisoned quolls in Australia (King 1989). Similarly, many 1080-poisoned nontarget animals may have left the treated area before succumbing, thus leading to underestimation of mortality among this group (Collins 1965). Tolerance to fluoroacetates and avoidance of 1080 baits should also be considered in future 1080 poisoning campaigns by wildlife managers and animal damage control operators. Avoidance of 1080 toxic baits by target mammals is documented when alternative foods are available (Calver et al. 1989a), and among pigs and rats surviving sublethal exposures (Kalmbach 1945; Rathore 1985). Indigenous populations of mammals, birds, and reptiles that coexist with fluoroacetate-bearing vegetation are much less sensitive to 1080 poisoning, perhaps by as much as 2 orders of magnitude, than conspecifics lacking such exposure (Twigg et al. 1988; King et al. 1989; Twigg and Mean 1990).

The timing of application of 1080 baits is critical. In one mishap, baits were dropped aerially while many ground squirrels — the targeted species — were still in hibernation underground for the winter and had not emerged (Collins 1965). Aerial application of 1080 baits in a ground squirrel

control program in California, although effective in controlling the squirrels, resulted in great overuse of the baits. As many as 70 to 77% of the poisoned baits were not eaten by the squirrels and were not recovered. Also, the yellow dye used to color the baits — as a deterrent to birds — faded rapidly (Collins 1964, 1965). To protect migratory waterfowl, 1080 baits should not be applied immediately preceding or during the main waterfowl hunting season or whenever birds are abundant (Temple and Edwards 1985). To protect honeybees, 1080-poisoned jam baits should be deposited >400 m from apiary sites. If 1080 baits are dispersed <400 m from apiary sites, then beekeepers should remove their hives to a more distant site (Goodwin and Ten Houten 1991). The 1080 toxicity database for aquatic organisms is insufficient for practicable formulation of criteria to protect this ecosystem. This seems to be a high priority research need in geographic areas of intensive 1080 application.

Potential replacement chemicals for 1080 include PAPP (*para*-aminopropiophenone), DFP (1,3-difluoro-2-propanol), and various anticoagulant and nonanticoagulant toxins. PAPP is highly toxic to coyotes and domestic cats (each with LD50s of 5.6 mg/kg BW) and lethal to rats and mice (LD50s of 177 and 233 mg/kg BW, respectively); intermediate in sensitivity were bobcats (10.0), and kit foxes (14.1 mg/kg BW) (Savarie et al. 1983). DFP is under investigation in Australia as an alternative to 1080 in faunal management programs because it has a mode of action similar to that of 1080 and has an antidote in pyrazole (Mead et al. 1991). DFP is the major ingredient of the pesticide glifor used in Russia to control rodents, particularly voles of the genus *Microtus*. Also deserving of evaluation are 4-methylpyrazole and related compounds to function as antidotes to DFP intoxication (Mead et al. 1991). In New Zealand, alternatives to 1080 under evaluation include several nonanticoagulant toxins (glifor, cholecalciferol, calciferol, alpha-chloralase, nicotine, malathion) and anticoagulants, including brodifacoum and pindone (Eason et al. 1993a).

26.6 SUMMARY

Sodium monofluoroacetate (CH_2FCOONa), also known as 1080, was first used in the United States to control gophers, squirrels, prairie dogs, rodents, and coyotes (*Canis latrans*); 1080 domestic use is currently restricted to livestock protection collars on sheep and goats to selectively kill depredating coyotes. However, Australia, New Zealand, and some other nations continue to use 1080 to control rabbits, possums, deer, foxes, feral pigs and cats, wild dogs, wallabies, rodents, and other mammals. The chemical is readily absorbed by ingestion or inhalation. At lethal doses, metabolic conversion of fluoroacetate to fluorocitrate results in the accumulation of citrate in the tissues and death within 24 h from ventricular fibrillation or respiratory failure; no antidote is available. At sublethal doses, the toxic effects of 1080 are reversible. Primary and secondary poisoning of nontarget vertebrates may accompany use of 1080. Sensitive mammals died after receiving a single dose of 0.05 to 0.2 mg 1080/kg body weight (BW), including representative species of livestock, marsupials, canids, felids, rodents, and foxes. Most tested species died after a single dose of 1 to 3 mg/kg BW. High residues were measured in some 1080-poisoned target mammals and this contributed to secondary poisoning of carnivores ingesting 1080-poisoned prey organisms. Sublethal effects occurred in sensitive mammals at >2.2 mg 1080/L drinking water or 0.8 to 1.1 mg 1080/kg diet. Sensitive species of birds died after a single 1080 dose of 0.6 to 2.5 mg/kg BW, daily doses of 0.5 mg/kg BW for 30 days, 47 mg/kg in diets for 5 days, or 18 mg/L in drinking water for 5 days. Adverse effects occurred in birds at dietary loadings as low as 10 to 13 mg 1080/kg ration. Amphibians and reptiles were more resistant to 1080 than birds and mammals. LD50 values were >44 mg/kg BW for tested amphibians and >54 mg/kg BW for tested reptiles; resistance to 1080 was attributed to their reduced ability to convert fluoroacetate to fluorocitrate and their increased ability to detoxify fluoroacetate by defluorination. Mosquito larvae reportedly died at 0.025 to 0.05 mg 1080/L but fish seemed unaffected at 13 mg/L. However, data on 1080 in aquatic ecosystems are incomplete. Acute LD50 values for terrestrial insects ranged from 1.1 to

3.9 mg/kg BW to 130.0 mg/kg BW for larvae feeding on fluoroacetate-bearing vegetation. Residues of 1080 in exposed insects were usually low (<4 mg 1080/kg fresh weight) or negligible, and were usually eliminated completely within 6 days, suggesting low risk to insectivorous birds. Loss of 1080 from baits occurs primarily due to microbial defluorination and secondarily to leaching by rainfall and consumption by insect larvae; leachates from 1080 baits are likely to be held in the upper soil layers. The use of 1080 seems warranted in the absence of suitable alternative control methods.

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CHAPTER 27

Toxaphene

27.1 INTRODUCTION

Toxaphene is a complex mixture of chlorinated bornanes and bornenes containing as many as 670 individual compounds. Heavy past usage, environmental persistence, and long-range atmospheric transport caused ecosystem-wide toxaphene contamination of biota from regions with little or no historical toxaphene application — including Arctic invertebrates, fishes, and mammals, Baltic seals and whales, and the atmosphere of the Great Lakes (Kucklick et al. 1993; Vetter et al. 1996). Environmental hazards and increasing public concerns associated with toxaphene (chlorinated camphene, 67 to 69% chlorine) are documented in a series of useful review articles (Pollock and Kilgore 1978; U.S. Environmental Protection Agency [USEPA] 1979, 1980a; Cohen et al. 1982; Rice and Evans 1984; Eisler and Jacknow 1985; Sullivan and Armstrong 1985; Saleh 1991; Bidleman and Muir 1993; U.S. Public Health Service [USPHS] 1994).

Toxaphene was introduced in the mid-1940s as a new insecticide, but only a few years elapsed before it was being used commercially on a large scale to effectively control a variety of pests — especially pests of cotton, corn, fruits, vegetables, grains, soybeans, and ectoparasites of livestock (USPHS 1994). Toxaphene solutions were often mixed with other pesticides, including methyl and ethyl parathion, DDT, and lindane (USPHS 1994). In the mid-1950s, toxaphene was first used in ponds, lakes, and streams as a piscicide. By 1966, toxaphene was the chemical of choice in fish eradication programs in Canada and second in the United States after rotenone (Lennon et al. 1970). Its use for this purpose was discontinued in the 1960s due to its lengthy persistence in water, high acute toxicity to aquatic biota, and significant bioaccumulation and biomagnification in various environmental compartments. By 1974, cumulative world use of toxaphene, mainly against insect pests of cotton, was estimated at 450,000 metric tons. Production of toxaphene declined from 1973 to 1980; however, annual consumption in 1980 was estimated at 105,000 tons, thus qualifying toxaphene as one of the most heavily utilized agricultural chemicals worldwide. In the early 1980s, toxaphene was extensively applied in California to control fruitworms on tomatoes, bollworm on cotton, and a wide range of pestiferous insects that infested alfalfa, broccoli, celery, beans, clover, lettuce, cauliflower, and pears. In time, toxaphene-resistant strains of cotton pests, including bollworm and lygus bug, appeared in California, Texas, Egypt, and India (USEPA 1979; USPHS 1994).

In November 1982, most registered uses of toxaphene were canceled by the U.S. Environmental Protection Agency, although existing available stocks could be used through 1986 (USEPA 1982). Prior to the USEPA action, similar actions that banned or restricted toxaphene use had been implemented in a number of countries, including Canada, England, Sweden, Finland, Denmark, France, Switzerland, Hungary, Italy, Egypt, and Algeria (Cohen et al. 1982; Swackhamer et al. 1993; Wideqvist et al. 1993). In 1990, the USEPA banned all uses of toxaphene in the United States or any of its territories because of adverse effects on human and animal health (USPHS 1994). In

1993, the USEPA banned the importation of food containing toxaphene residues in the United States or any of its territories. And on September 1, 1993, all tolerances, interim tolerances, and food additive regulations for toxaphene on all agricultural commodities were revoked (USPHS 1994). However, toxaphene-like pesticides are currently produced and used in many countries, including India, many South and Central American countries, Eastern bloc countries in the former Soviet Union, and many African countries (Kucklick et al. 1993; Voldner and Li 1993; USPHS 1994).

27.2 ENVIRONMENTAL CHEMISTRY

The commercial production of toxaphene involves the reaction of camphene, chlorine activated by ultraviolet radiation, and certain catalysts to yield chlorinated camphene with a chlorine content of 67 to 69% by weight. This product is a relatively stable material composed of at least 177 — as many as 670 are predicted — chlorinated bornanes and bornenes (Saleh 1991; McConnell et al. 1993). Of these components, 26 have been isolated and 10 identified; these 26 components comprise 40% of the toxaphene. Information on chemical properties and the fate and effects of the remaining components is missing or incomplete (Cohen et al. 1982). Several components that have been tested are more toxic to houseflies than the technical mixture, especially di-, tri-, and tetrachlorobornane compounds (Pollock and Kilgore 1978). Technical toxaphene is a yellow, waxy solid of empirical formula $C_{10}H_{10}Cl_8$ and an average molecular weight of 414. It melts at 65 to 99°C. Toxaphene is soluble in water to 3 mg/L and is readily soluble in fats and organic solvents, based on its high partition coefficient of 10 to the power 3.3 to 6.4. Toxaphene has a tendency to adsorb on sediments and to bioaccumulate in aquatic organisms (USEPA 1979; USPHS 1994).

Because toxaphene consists of numerous compounds, it seems inappropriate and misleading to continue using the name toxaphene to describe this insecticide. It is known that chemical properties, such as solubility, toxicity, volatility, and other properties, are the sum of the individual contribution of many different compounds in differing relative amounts. A 50-fold difference between toxicities of toxaphene components can occur, and, with a wide range in the polarity of different fractions, there probably are also significant solubility differences. In addition, the composition of toxaphene changes with time, and residues in fat are not of the same composition as parent toxaphene (Pollock and Kilgore 1978). The metabolism of toxaphene has been an area of limited research activity, owing to the analytical difficulties involved in detecting a multicomponent substance (Pollock and Kilgore 1978). However, toxaphene has been reported more often in biological samples in recent years. This increased recognition is probably due to better analytical methods for toxaphene analysis (Ribick et al. 1982), especially electron capture negative ion mass spectrometry (Muir and de Boer 1993), greater awareness by analysts, and the continuing use of toxaphene, while use of potentially interfering organochlorine insecticides has slowly decreased. Toxaphene was available as an emulsifiable concentrate, wettable powder, or dust. The commercial product is relatively stable but may decay upon prolonged exposure to sunlight, alkalis, or temperatures above 120°C. Toxaphene is also known as Agracide Maggot Killer, CAS 8001-35-2, Camphofene Huilex, Motox, Toxafeed, (USPHS 1994), chlorinated camphene, Synthetic 3956, Octachlorocamphene, Alltox, Geniphene, Toxakil (Negherbon 1959), polychlorocamphene, camphechlor, Clor Chem T-590, Cristoxo, Moto, Phenacide, Phenatox, Strobane-T, Toxon 63, and Vapotone (Johnson and Finley 1980). Chemically, it is known as a mixture of various chlorinated camphenes (Tucker and Crabtree 1970). The actual global production of toxaphene between 1950 and 1993 is unknown, but estimates range as high as 1.3 million metric tons (McConnell et al. 1993; Voldner and Li 1993).

Toxaphene partitions to the atmosphere, surface and groundwaters, soil and sediment particulates, and adipose tissue. As a result of its volatility and resistance to photolytic transformation, toxaphene has been transported over long distances in the atmosphere (USPHS 1994). Toxaphene residues have been detected in various environmental compartments hundreds of kilometers distant

from known applications of this insecticide. Prevailing winds, rainfall, and sediment runoff probably account for substantial portions of this transport (Kucklick et al. 1993; USPHS 1994). Rainfall, for example, has been implicated as a significant toxaphene vector in South Carolina estuaries (Harder et al. 1980). During and immediately after the summer use season, toxaphene levels in rain exceeded, by several times, the concentrations reported to produce bone damage in fish under controlled laboratory conditions. Toxaphene becomes sorbed to soils when it is used in agriculture. Therefore, a major mode of toxaphene transport in areas planted continuously in cotton is through sediment loss in runoff (McDowell et al. 1981). In soils, toxaphene is relatively immobile. Under anaerobic conditions, toxaphene is rapidly biotransformed in soils and sediments with a half-time persistence of 2 to 4 months. However, under aerobic conditions, toxaphene may persist for years — Tb 1/2 of 11 years — in aerated surface soils and sediments (USPHS 1994). Measurements indicated a linear relation between toxaphene yield and sediment yield in runoff water. Atmospheric transport of toxaphene is well documented. Air samples from the western North Atlantic contained measurable levels of toxaphene at distances up to 1200 km from the nearest point source of application on land (Bidleman and Olney 1975). Similarly, nationwide monitoring of toxaphene in fish showed increases during 1970 to 1974 (Schmitt et al. 1981), especially in areas where the insecticide was not used, suggesting that atmospheric transport is essential to widespread distribution. Airborne toxaphene is resistant to photodecomposition; however, selective volatilization of toxaphene components is a major cause of degradation, resulting in an estimated half-time of 15 days while in the atmosphere (Cohen et al. 1982).

Toxaphene degrades more rapidly in most environmental compartments than other chlorinated pesticides, such as DDT and dieldrin (Matsumura 1978). The major metabolic degradation mechanisms for toxaphene in all organisms from bacteria to primates are now believed to be the reductive dechlorination, reductive dehydrochlorination, and in some cases oxidative dechlorination to produce hydroxyl derivatives, acids, or ketones (Saleh 1991). Toxaphene persistence and degradation in soil, water, and biota are modified by numerous and disparate biological and abiotic factors. Under laboratory conditions, toxaphene in water has a half-time persistence of more than 10 years under conditions of high oxygen content, 25°C, and pH 5 to 8 (USPHS 1994). In lakes, toxaphene persistence was significantly related to lake depth, stratification, and turnover, but not related to surface area, pH, temperature, sunlight, and oxygen (Cohen et al. 1982). Data from studies where toxaphene was used to control nongame fish in lakes suggest that it may persist in water from several months to more than 9 years. For example, two mountain lakes in Oregon that were treated with toxaphene in fish eradication programs remained toxic for 1 to 6 years (Terrierre et al. 1966). Davis Lake, a shallow lake rich in aquatic life, which was treated with 88 µg toxaphene/L, could be restocked with rainbow trout (*Oncorhynchus mykiss*) within 1 year when water toxaphene levels were 0.63 µg/L. Trout grew rapidly, although whole-body burdens up to 24 mg/kg were recorded. Miller Lake, a deep, biologically sparse lake, was treated with 40 µg/L toxaphene; trout could not be restocked for 6 years until water levels had dropped to 0.8 µg toxaphene/L. Toxaphene at 50 µg/L was used to eradicate fish from Clayton Lake, New Mexico (Kallman et al. 1962). Water concentrations of 1.0 µg/L were measured 250 days posttreatment, but the lake remained toxic for 9 months, with restocking possible only after 12 months. Residues in fish surviving treatment were 3.5 mg/kg whole-body wet weight shortly after exposure, and 0.3 mg/kg about 5 months postapplication. Some lakes treated with toxaphene to kill fish have remained toxic for 3 to 4 years (Webb 1980). In another study (Johnson et al. 1966), lake water that contained 1.0 µg toxaphene/L (9 years after toxaphene treatment) supported healthy fish populations. In this lake, particulate matter contained 70 µg toxaphene/kg, and plankton contained 15,000 µg/kg. However, there were changes in gas chromatographic profiles of toxaphene residues taken from the lakes, suggesting that the parent toxaphene had been altered or degraded into compounds with lower environmental hazards to biota. Clearly, this subject area merits additional research effort.

In soils, toxaphene can persist for lengthy periods, with microbial degradation occurring under aerobic and anaerobic conditions (Cohen et al. 1982). Pimentel (1971) reported that toxaphene,

applied at 140 mg/kg soil, persisted for more than 6 years; when applied at 50 mg/kg, half the toxaphene was measurable after 11 years. Further, in sandy loam soils, 45% of the toxaphene remained 14 years after initial application of 100 mg/kg. Some investigators suggest that toxaphene degradation is more rapid under anaerobic conditions (Pollock and Kilgore 1978). Thus, toxaphene in anaerobic salt marsh sediments generally degraded within a few days to shorter-lived components (Williams and Bidleman 1978). Toxaphene accumulated only slightly in anaerobic marsh soils not flooded daily by tides (Gallagher et al. 1979), and the highest pesticide concentrations were associated with roots of dead plants.

Degradation of toxaphene in plant, air, and soil samples was evident following toxaphene application of 9 kg/ha to a San Joaquin Valley, California, cotton field (Seiber et al. 1979). Cotton leaves contained 661 mg toxaphene/kg immediately after application and 135 mg toxaphene/kg after 58 days, with the greatest loss attributed to components of highest volatility. Air samples were essentially the same at 2 and 14 days postapplication (1.8 to 1.9 $\mu\text{g}/\text{m}^3$). This was attributed to a corresponding enrichment of volatile components. Topsoil samples immediately after application and 58 days later contained 13.1 and 6.4 mg/kg, respectively; loss was primarily via vaporization, but at least one component was significantly degraded. One year later, soil cores and irrigation ditch samples showed extensive toxaphene degradation resulting in a selective decline of some components; anaerobic reduction occurred in these environmental compartments.

Toxaphene elimination rates vary between species. In rats, the half-time persistence of toxaphene (time to 50% excretion = $T_{1/2}$) was 1 to 3 days (USEPA 1980a). If the trend persisted, virtually all toxaphene would be eliminated in five half-lives. Elevated blood toxaphene levels in a human subject who had eaten catfish fillets containing 52 mg of toxaphene/kg dropped 67% in 11 days. By 14 days after the initial measurement, toxaphene blood levels were below analytical detection limits (USEPA 1980a). Persistence seems to be longer in some fishes. Lake trout (*Salvelinus namaycush*) given a single intraperitoneal injection of 7 mg toxaphene/kg BW had a $T_{1/2}$ of 322 days; for white suckers (*Catostomus commersoni*), this value was 524 days (Delorme et al. 1993).

27.3 CONCENTRATIONS IN FIELD POPULATIONS

Long-range atmospheric transport of toxaphene has resulted in measurable toxaphene residues in tissues of fishes from remote lakes in northern Canada; fishes from pristine areas of the North Atlantic, North Pacific, and Antarctic Oceans; and fishes, birds, and seals from the western North Atlantic Ocean, Arctic Ocean, Greenland, Sweden, Canada, and the drainage basin of Chesapeake Bay (Table 27.1) (Saleh 1991; USPHS 1994). In Lake Baikal, Russia, the toxaphene congener pattern in water was similar to that in the air, indicating the importance of atmospheric deposition processes to this water body (McConnell et al. 1993). Atmospheric toxaphene concentrations vary markedly with season, being lower in winter and higher in summer (Barrie et al. 1993).

National contaminant monitoring surveys, conducted in the period 1974 to 1976, show that toxaphene was detected in about 6% of all fish sampled. This is a higher percentage than recorded in fruits, vegetables, poultry, and meat (Ludke and Schmitt 1980). Fish collected nationwide at 109 stations between 1976 and 1979 had measurable toxaphene residues at about 60% of all stations sampled; concentrations in fish from the Great Lakes stations exceeded those in fish from most of the rest of the United States, including locations within the cotton-growing areas (Schmitt et al. 1983). Lake trout (*Salvelinus namaycush*) from Lake Michigan typically contained 5 to 10 mg of toxaphene/kg whole body on a wet weight basis; lake trout from Lake Huron contained 9 mg/kg. These residues are considered harmful to various sensitive species of freshwater teleosts (Schmitt et al. 1983). Since relatively little toxaphene has been used in the Great Lakes region when compared to cotton-growing areas in the mid-South, Northeast, and Southeast, it is postulated that atmospheric transport from areas to the south and southwest are the sources of toxaphene contamination in the

Great Lakes (Schmitt et al. 1983). Between 1976 and 1984, mean toxaphene concentrations in whole fish collected nationwide declined significantly from 0.34 mg/kg FW, maximum 12.7 mg/kg FW in 1976/77 to 0.14 mg/kg FW, maximum 8.2 mg/kg FW, in 1984 (Schmitt et al. 1990). Declines in toxaphene concentrations were also recorded in eggs of the guillemot (*Cephus* sp.) population from the Baltic Sea between 1974 and 1989 (Wideqvist et al. 1993) (Table 27.1).

Freshwater fishes of the Arroyo Colorado, a major waterway traversing the lower Rio Grande Valley in southern Texas, were highly contaminated with toxaphene and DDE residues when compared to fish collected elsewhere in the Valley; toxaphene concentrations ranged up to 31.5 mg/kg wet weight in whole-fish composite samples (Table 27.1). These values were within or above the range producing adverse effects in sensitive species of fish. In addition, toxaphene residues in carcasses of fish-eating birds contained up to 3 mg toxaphene/kg (Table 27.1). Unlike fishes, avian species readily metabolize and excrete toxaphene, so that little accumulation occurs in tissues. In any event, these levels of toxaphene in carcasses of piscivorous birds are probably biologically insignificant (White et al. 1983). In the Arroyo Colorado area, toxaphene was being used, to some extent, on crops such as cotton, not only as an insecticide, but as a carrier for more effective chemicals. Another possible source of contamination is a former pesticide plant at Mission, Texas, near the headwaters of the Arroyo Colorado. Soil at this site contained high concentrations of various pesticides, including toxaphene. Contaminant-laden runoff from this site could eventually reach the Arroyo from storm sewers and other water diversion facilities. The contaminated Arroyo Colorado, in turn, empties into the Laguna Madre, one of the more important breeding and nursery grounds for fish and wildlife in the United States. The Texas Department of Health, in an advisory to consumers, has stated that consumption of fishes from the Arroyo Colorado, especially blue catfish (*Ictalurus furcatus*) and gizzard shad (*Dorosoma cepedianum*), is not advised (White et al. 1983).

Birds, unlike fish, generally contained low or nondetectable levels of toxaphene, and the frequency of occurrence was relatively low when compared with that of other organochlorine pesticides (Table 27.1). This generalization held for eggs of the osprey (*Pandion haliaetus*) collected in southern New Jersey in 1974 (Wiemeyer et al. 1978); carcasses of 103 skinned shorebirds from Corpus Christi, Texas, during winter 1976/77 (White et al. 1980); eggs of the brown pelican (*Pelecanus occidentalis*) from 1971 to 1976 in Louisiana (Blus (et al. 1979); eggs of clapper rails (*Rallus longirostris*), purple gallinules (*Porphyrrula martinica*), and limpkins (*Aramus guarauna*) from the Southeast in 1972 to 1974 (Klass et al. 1980); and all avian tissues in Texas between 1965 and 1988 (Mora 1995). Among 105 herons found dead nationwide since 1976, only nine contained measurable quantities of toxaphene; for DDE, PCBs, dieldrin, and DDD, these frequencies were 96, 90, 37 and 35, respectively (Ohlendorf et al. 1981). Levels of toxaphene and other organochlorines in canvasbacks (*Aythya valisineria*) from Chesapeake Bay, Maryland, during 1973 to 1976 were below the levels known to cause problems in other species (White et al. 1979). However, adipose tissues from 55 male wild turkeys (*Meleagris gallopavo*) killed during the 1974 hunting season in southern Illinois contained 0.2 to 0.9 mg/kg of toxaphene (Bridges and Andrews 1977), suggesting that certain species of birds may selectively accumulate low concentrations of toxaphene.

Two bird kills reported in California have been attributed to toxaphene poisoning (Pollock and Kilgore 1978). In one case, the apparent route of exposure was from contaminated fish, with bird poisoning the result of toxaphene biomagnification in the food chain. In that case, algae contained 0.1 to 0.3 mg toxaphene/kg wet weight, snails and daphnids 0.2, fish 3 to 8, and fish-eating birds 39 mg/kg. The last value is substantially in excess of 3 mg/kg, a concentration considered biologically insignificant to fish-eating birds (White et al. 1983). The second incident involved some birds that were apparently killed by toxaphene when it was used to control grasshoppers on a shortgrass range. At 2 to 3 weeks postspray, bird carcasses contained 0.1 to 9.6 mg toxaphene/kg.

Toxaphene accumulates in tissues of many aquatic species, especially in lipid-rich tissues of polar fish and marine mammals (Swackhamer and McConnell 1993). Toxaphene concentrations in livers of Arctic fishes of 2.9 mg/kg FW and in Canadian cod liver oil of 28 mg/kg FW are recorded

(de Boer and Wester 1993). Toxaphene concentrations — up to 39.7 mg/kg FW blubber — in marine mammals from Newfoundland were higher than other groups of organochlorines measured and were probably due to elevated toxaphene concentrations in their diet of Atlantic cod (*Gadus morhua*) and herring (*Clupea harengus harengus*) (Muir et al. 1988). Only a few of the many polychlorobornane congeners accumulate in liver and blubber of marine mammals, perhaps because some of the higher chlorinated compounds with more than six chlorine atoms remain unmetabolized or are highly accumulated (Vetter et al. 1992). The two main toxaphene congeners identified in fish liver, dolphin blubber, and human milk were 2-exo, 3-endo, 5-exo, 6-endo, 8,8,9,10,10-nonachlorobornane, and 2-exo, 3-endo, 5-exo, 6-endo, 8,8,10,10-octachlorobornane (de Boer and Wester 1993). The three main congeners found in blubber (two octa- and one nonachloro compound) accounted for about 30 to 40% of the total toxaphene burden (Oehme et al. 1996). The major peak in the Baikal seal chromatogram was an 8-chlorinated bornane similar to that of ringed seals from the Canadian Arctic (Kucklick et al. 1993). But cod liver oils contained up to 10 major congeners and exceeded the maximum acceptable concentration for food in Germany of 0.1 to 0.4 mg total toxaphenes/kg lipid weight (de Boer and Wester 1993; Oehme et al. 1996). The octachlorobornane and nonachlorobornane congeners that dominated in Arctic amphipods, fishes, and marine mammals (narwhals and belugas) comprised only 8 to 11% in the ringed seal (*Phoca hispida*)–polar bear (*Ursus maritimus*) food chain (Zhu and Norstrom 1993).

Toxaphene is biomagnified through the food web by marine mammals, with factors ranging from about 40 to 100 for dolphins and porpoises (de Boer and Wester 1993). In Lake Michigan, toxaphene was biomagnified in aquatic food webs by about 5 from plankton to fish (sculpin, *Myoxocephalus* sp.) and 14 from mysids to fish (Evans et al. 1991). Biomagnification of toxaphene through food webs was clearly demonstrated in 16 species of organisms collected from oxbow lakes in northeastern Louisiana during 1980 (Neithammer et al. 1984). Without exception, residues were highest (3.6 mg/kg whole-body wet weight, range 1.7 to 5.5) in tertiary consumers, such as green-backed heron (*Butorides striatus*), various species of snakes, spotted gar (*Lepisosteus osseus*), and largemouth bass (*Micropterus salmoides*). Secondary consumers, such as bluegill (*Lepomis macrochirus*), blacktail shiner (*Notropis venustus*), and yellow-crowned night-heron (*Nycticorax violaceus*), contained lower residues (0.9 mg/kg wet weight, range 0.1 to 1.2). Primary consumers, including crayfish (*Procambarus* spp.) and threadfin shad (*Dorosoma petenense*), contained the lowest levels (0.8 mg/kg wet weight, range 0.6 to 1.0) of all consumer groups. Toxaphene levels were not detectable in water and sediments from these oxbow lakes (Neithammer et al. 1984). Variability in tissue toxaphene concentrations of fishes from Canadian Yukon lakes are related, in part, to differences in the food chains of the lakes (Kidd et al. 1993), with emphasis on prey lipid content (Hargrove et al. 1993).

Table 27.1 Toxaphene Concentrations in Field Collections of Selected Living Organisms and Abiotic Materials (Concentrations are in mg toxaphene per kg fresh weight [FW], dry weight [DW], or lipid weight [LW], except where noted.)

Material, Organism, and Other Variables	Concentration (mg/kg)	Reference ^b
AIR		
Arctic, 1992		
January–February	<0.002 µg/m ³	8
June	0.027 µg/m ³	8
Lake Baikal, Russia, June 1991	0.016 µg/m ³	6
United States		
1972, 16 states	Max. 8700 ng/m ³	4
1981		
Greenville, Mississippi	Max. 9.1 ng/m ³	4
St. Louis, Missouri	Max. 1.7 ng/m ³	4

Table 27.1 (continued) Toxaphene Concentrations in Field Collections of Selected Living Organisms and Abiotic Materials (Concentrations are in mg toxaphene per kg fresh weight [FW], dry weight [DW], or lipid weight [LW], except where noted.)

Material, Organism, and Other Variables	Concentration (mg/kg)	Reference ^b
Bridgeman, Michigan	Max. 0.44 ng/m ³	4
Beaver Island, Michigan	Max. 0.14 ng/m ³	4
Western North Atlantic Ocean, 1973–74	Max. 1.6 ng/m ³	4
RAIN		
Southern France	Max. 53 ng/L	4
SEDIMENTS		
Bering Sea, August 1988	0.0003 FW	7
Mississippi, Yazoo National Wildlife Refuge (NWR), 1987–88	0.07–0.12 FW; Max. 4.6 FW	2
SURFACE WATERS		
United States, 1980–82		
Ambient surface waters	0.05 µg/L	4
Municipal runoff	ND	4
Lake Baikal, Russia, June 1991	0.064 (0.034–0.143) µg/L	5
ALGAE AND MACROPHYTES		
Phytoplankton, Bering Sea, August 1988	0.001–0.002 FW	7
INVERTEBRATES		
Crustaceans, Bering Sea, August 1988	0.001–0.002 FW	7
Amphipods, Arctic Ocean, whole, 1986–89	Max. 2.3 FW, Max. 16.5 LW	16
FISH		
Arctic Ocean, 1986–89 Arctic cod, <i>Boreogadus saida</i> , muscle	Max. 0.05 FW	16
Glacial eelpout, <i>Lycodes frigidus</i> , liver	Max. 0.05 FW	16
Arctic char, <i>Salvelinus alpinus</i> , whole	Max. 0.15 FW	16
Arroyo Colorado, Texas		
1978, whole		
Blue catfish, <i>Ictalurus furcatus</i>	9.7–31.5 FW	1
Gizzard shad, <i>Dorosoma cepedianum</i>	11.2–29.6 FW	1
Sea catfish, <i>Arius felis</i>	ND ^a –0.4 FW	1
Spotted seatrout, <i>Cynoscion nebulosus</i>	ND	1
1979, whole		
Blue catfish	19.5–24.8 FW	1
Gizzard shad	5.4 FW	1
Channel catfish, <i>Ictalurus punctatus</i>	0.8–19.5 FW	1
Striped mullet, <i>Mugil cephalus</i>	4.4 FW	1
Bering Sea, August 1988		
Walleye pollock, <i>Theragra chalcogrammus</i> , whole	0.013 FW	7
Lake Baikal, Russia, June 1991		
Omul, <i>Coregonus autumnalis migratorius</i> , whole	1.1 (0.9–1.3) LW	5
Sculpin, <i>Comephorus dybowskii</i> , whole	1.9 (1.6–2.1) LW	5
Mississippi, Yazoo NWR, 1987–88, whole		
Bowfin, <i>Amia calva</i>	2.7 (0.3–8.6) FW	2
Common carp, <i>Cyprinus carpio</i>	3.1 (0.5–6.2 FW)	2
Mosquitofish, <i>Gambusia affinis</i>	0.25 FW	2

Table 27.1 (continued) Toxaphene Concentrations in Field Collections of Selected Living Organisms and Abiotic Materials (Concentrations are in mg toxaphene per kg fresh weight [FW], dry weight [DW], or lipid weight [LW], except where noted.)

Material, Organism, and Other Variables	Concentration (mg/kg)	Reference ^b
Smallmouth buffalo, <i>Ictiobus bubalus</i>	5.8 (0.8–15) FW	2
Spotted gar, <i>Lepisosteus oculatus</i>	2.7, Max. 16 FW	2
North Atlantic Ocean		
Atlantic cod, <i>Gadus morhua</i> , liver	0.3–0.8 LW	10
Raw fish oils	0.37–0.56 LW	10
Refined fish oils	Max. 0.097 LW	10
North Sea and northeast Atlantic Ocean, liver, 1990–92		
Twaite shad, <i>Alosa fallax</i>	0.02 FW	11
Atlantic cod, <i>Gadus morhua</i>	Max. 0.6 FW	11
Dab, <i>Limanda limanda</i>	Max. 0.01 FW	11
Haddock, <i>Melanogrammus aeglefinus</i>	Max. 0.43 FW	11
Hake, <i>Merluccius</i> sp.	Max. 1.3 FW	11
Spiny dogfish, <i>Squalus acanthias</i>	0.2 FW	11
United States, freshwater, nationwide, whole, 1976–84		
1976–77	0.34 FW; Max. 12.7 FW; detectable in 59% of all samples	9
1978–79	0.28 FW; Max. 18.7 FW; found in 61% of all samples	9
1980–81	0.28 FW; Max. 21.0 FW; found in 88% of all samples	9
1984	0.14 FW; Max. 8.2 FW; found in 69% of samples	9
REPTILES		
Mississippi, Yazoo NWR, 1987–88, whole		
Cottonmouth, <i>Agkistrodon piscivorus</i>	0.03, Max. 1.3 FW	2
Water snakes, <i>Nerodia</i> spp.	0.3, Max. 27 FW	2
BIRDS		
Arizona, 1977–85, eggs		
Bald eagle, <i>Haliaeetus leucocephalus</i>	0.04 FW	17
Arroyo Colorado, Texas		
1978, whole		
Laughing gull, <i>Larus atricilla</i>	ND–3.0 FW	1
Ringed-billed gull, <i>Larus delawarensis</i>	ND–3.0 FW	1
Franklin's gull, <i>Larus pipixcan</i>	ND–2.0 FW	1
Herring gull, <i>Larus argentatus</i>	ND	1
Pied-billed grebe, <i>Podilymbus podiceps</i>	ND	1
Forster's tern, <i>Sterna forsteri</i>	1.7 FW	1
Great-tailed grackle, <i>Quiscalus mexicanus</i>	ND	1
Red-winged blackbird, <i>Agelaius phoeniceus</i>	ND	1
1979, whole		
Laughing gull	ND–0.4 FW	1
Baltic Sea, 1974–89, Guillemot, <i>Cephus</i> sp., eggs		
1974	13 LW	13
1976	14–23 LW	13
1978	9.5 LW	13
1982	8.0 LW	13
1987	5.2 LW	13
1989	6.1–15.0 LW	13
Texas, 1965–88		
All avian tissues	Usually <1.0 FW; geometric mean 0.32 FW, range 0.06–1.7 FW	15
Forster's tern, <i>Sterna forsteri</i> , carcass, 1978	1.7 FW	15

Table 27.1 (continued) Toxaphene Concentrations in Field Collections of Selected Living Organisms and Abiotic Materials (Concentrations are in mg toxaphene per kg fresh weight [FW], dry weight [DW], or lipid weight [LW], except where noted.)

Material, Organism, and Other Variables	Concentration (mg/kg)	Reference ^b
MAMMALS		
Arctic Ocean 1986–89, blubber		
Beluga, <i>Delphinopterus leucas</i>	1.4–8.1 FW	16
Narwhal, <i>Monodon monoceros</i>	2.4–9.2 FW	16
Ringed seal, <i>Phoca hispida</i>	Max. 0.48 FW	16
Lake Baikal, Russia, June 1991		
Baikal seal, <i>Phoca sibirica</i> , blubber	2.3 (2.2–2.3) LW	5
Mississippi, Yazoo NWR, 1988		
Raccoon, <i>Procyon lotor</i> , adipose tissue	0.02 FW, Max. 31.0 FW	3
Newfoundland, 1980–82, blubber		
Long-finned pilot whale, <i>Globicephala melaena</i>		
Females	3.5 (0.5–11.8) FW	14
Males	9.0 (4.3–14.7) FW	14
White-beaked dolphin, <i>Lagenorhynchus albirostris</i>		
Females	22 (9.6–39.7) FW	14
Males	34 (13–87) FW	14
North Sea, 1990		
Harbor porpoise, <i>Phoceania phocoena</i> , blubber	6.8 FW	11
Sweden, various locations, blubber		
Harbor seal, <i>Phoca vitulina</i>		
Adult males	0.4 FW	12
Juveniles, 1988	0.3–1.5 FW	12
Gray seal, <i>Halichoerus grypus</i>		
Adult males	1.9 FW	12
Adult females	3.1–10.0 FW	12
Ringed seal, <i>Phoca hispida</i>	3.1 FW, Max. 14.0 FW	12
Sweden, human milk fat	0.1 FW	18

^a ND = not detectable.

^b 1, White et al. 1983; 2, Ford and Hill 1991; 3, Ford and Hill 1990; 4, USPHS 1994; 5, Kucklick et al. 1993; 6, McConnell et al. 1993; 7, Rice 1993; 8, Barrie et al. 1993; 9, Schmitt et al. 1990; 10, Oehme et al. 1996; 11, de Boer and Wester 1993; 12, Andersson and Wartanian 1992; 13, Wideqvist et al. 1993; 14, Muir et al. 1988; 15, Mora 1995; 16, Hargrove et al. 1993; 17, Grubb et al. 1990; 18, Saleh 1991.

27.4 LETHAL EFFECTS

Toxaphene is extremely toxic to freshwater and marine biota. In laboratory tests of 96-h duration, 50% mortality was recorded for the most sensitive species of freshwater and marine teleosts, marine crustaceans, and freshwater insects at nominal water concentrations of less than 10 µg/L of toxaphene, and, in several cases, less than 1 µg/L (Table 27.2). Bioassays of longer duration, based on exposure of aquatic organisms for the entire or most of the life cycle, produced significant adverse effects on growth, survival, and reproduction at toxaphene concentrations between 0.025 and 1.0 µg/L (Table 27.3). Toxaphene was most toxic to freshwater fishes in soft water at elevated temperatures (Saleh 1991). Based on its high toxicity and extensive use, it is not surprising that toxaphene was considered a major cause of nationwide fish kills in 1977 (USEPA 1980b).

Warm-blooded organisms are relatively resistant to toxaphene, as determined from results of short-term tests involving oral, dermal, and dietary routes of administration. In acute oral toxicity tests with birds and mammals, LD50 values ranged between 10 and 160 mg/kg body weight (Table 27.4). The dietary LC50 values for four species of birds ranged between 538 and 828 mg toxaphene/kg ration (Saleh 1991). The acute oral toxicities of toxaphene to rats, mice, dogs, guinea

Table 27.2 Acute Toxicity of Toxaphene to Aquatic Organisms
 (Concentrations shown are in micrograms of toxaphene per liter
 [g/L] of medium fatal to 50% of the test organisms in 96 h.)

Type of Water, Taxonomic Group, Species	LC50 (96 h)	Reference ^a
FRESHWATER		
Insects		
Stonefly, <i>Claassenia</i> sp.	1.3	1
Stonefly, <i>Pteronarcys</i> sp.	2.3	1
Crane fly, <i>Tipula</i> sp.	18.0	1
Midge, <i>Chironomus</i> sp.	30.0 ^b	1
Snipe fly, <i>Atherix</i> sp.	40.0	1
Crustaceans		
Daphnid, <i>Daphnia magna</i>	10.0 ^b	1
Daphnid, <i>Daphnia pulex</i>	14.2 ^b	1
Daphnid, <i>Simocephalus</i> sp.	19.0 ^b	1
Amphipod, <i>Gammarus fasciatus</i>	26.0	1
Glass shrimp, <i>Palaemonetes kadlakensis</i>	28.0	3
Fish		
Largemouth bass, <i>Micropterus salmoides</i>	2.0	1
Bluegill, <i>Lepomis macrochirus</i>	2.4–29.0	1, 3, 4
Brown trout, <i>Salmo trutta</i>	3.1	1
Common carp, <i>Cyprinus carpio</i>	3.7	1
Channel catfish, <i>Ictalurus punctatus</i>	4.2–13.1	1, 3
Black bullhead, <i>Ictalurus melas</i>	5.8	1
Coho salmon, <i>Oncorhynchus kisutch</i>	8.0	1
Rainbow trout, <i>Oncorhynchus mykiss</i>	10.6	1
Yellow perch, <i>Perca flavescens</i>	12.0	1
Green sunfish, <i>Lepomis cyanellus</i>	13.0	1
Redear sunfish, <i>Lepomis microlophus</i>	13.0	3
Goldfish, <i>Carassius auratus</i>	14.0	1
Fathead minnow, <i>Pimephales promelas</i>	18.0	1
Guppy, <i>Poecilia reticulata</i>	20.0	3
Amphibians		
Leopard Frog, <i>Rana sphenocephala</i>	32.0–54.0	2
SALTWATER		
Molluscs		
American oyster, <i>Crassostrea virginica</i>	16.0 ^c	3, 5
Quahog clam, embryo, <i>Mercenaria mercenaria</i>	1120.0	3
Crustaceans		
Drift-line crab, <i>Sesarma cinereum</i>	0.05–8.8	3
Copepod, <i>Acartia tonsa</i>	0.11	3
Pink shrimp, <i>Penaeus duorarum</i>	1.4–2.2	3, 5
Grass shrimp, <i>Palaemonetes pugio</i>	4.4	3, 5
Mysid shrimp, <i>Mysidopsis bahia</i>	4.5	3
Korean shrimp, <i>Palaemon macrodactylus</i>	21.0	3
Mud crab, larva, <i>Rithropanopeus harrisi</i>	43.8	3
Blue crab, <i>Callinectes sapidus</i>	824.0	3
Fish		
Pinfish, <i>Lagodon rhomboides</i>	0.5	3, 5
Sheepshead minnow, <i>Cyprinodon variegatus</i>	1.1	3, 5
Striped bass, <i>Morone saxatilis</i>	4.4	3
Threespine stickleback, <i>Gasterosteus aculeatus</i>	8.2	3

^a 1, Johnson and Finley 1980; 2, Hall and Swineford 1980; 3, USEPA 1980a; 4, Isensee et al. 1979; 5, Schimmel et al. 1977.

^b 48-hour value.

^c New shell growth reduced 50% in 96 h.

Table 27.3 Maximum Acceptable Toxicant Concentration Values (MATC) for Toxaphene and Aquatic Organisms, Based on Exposure for the Entire or Most of the Life Cycle (Concentrations are in micrograms of toxaphene per liter [ppb].)

Type of Water, Organism	MATC (g/L)	Reference ^a
FRESHWATER		
Arthropods		
Daphnid, <i>Daphnia magna</i>	0.07–0.12	1
Amphipod, <i>Gammarus pseudolimnaeus</i>	0.13–0.25	1
Midge, larva, <i>Chironomus plumosus</i>	1.0–3.2	1
Fish		
Fathead minnow, <i>Pimephales promelas</i>	0.025–0.054	2
Channel catfish, <i>Ictalurus punctatus</i>	0.049–0.072	2
SALTWATER		
Fish		
Sheepshead minnow, <i>Cyprinodon variegatus</i>		
Early life stage	1.1–2.5	3

^a 1, Sanders 1980; 2, Mayer et al. 1977; 3, USEPA 1980a.

Table 27.4 Acute Oral Toxicity of Toxaphene to Birds and Mammals

Organism	LD50 (mg/kg BW)
BIRDS	
California quail, <i>Callipepla californica</i>	
Sharp-tailed grouse, <i>Tympanuchus phasianellus</i>	12–47
Gray partridge, <i>Perdix perdix</i>	14–28
Ring-necked pheasant, <i>Phasianus colchicus</i>	20–28
Mallard, <i>Anas platyrhynchos</i>	20–80
Duckling	23–40
Adult	37–133
Fulvous whistling-duck, <i>Dendrocygna bicolor</i>	37–264
Northern bobwhite, <i>Colinus virginianus</i>	59–123
Lesser sandhill crane, <i>Grus canadensis canadensis</i>	100–316
Horned lark, <i>Eremophila alpestris</i>	425–794
MAMMALS	
Domestic cat, <i>Felis domesticus</i>	25–40
Dog, <i>Canis familiaris</i>	49
Human, <i>Homo sapiens</i>	60 (estimated)
Laboratory white rat, <i>Rattus</i> sp.	80–90
Mouse, <i>Mus</i> sp.	120
Mule deer, <i>Odocoileus hemionus hemionus</i>	139–240
Domestic goat, <i>Capra hircus</i>	>160
Cattle, <i>Bos</i> sp.	144
Sheep, <i>Ovis aries</i>	200
Goat, <i>Capra hircus</i>	200
Guinea pig, <i>Cavia</i> sp.	270

Note: Concentrations shown are in milligrams of toxaphene ingested per kilogram body weight (BW) fatal to 50% of test animals. A single dose was administered orally and survival data gathered over a 14-day posttreatment observation period.

Data from Tucker and Crabtree 1970; Hudson et al. 1984; Saleh 1991.

pigs, cats, rabbits, cattle, goats, and sheep extended from 25 to 270 mg/kg body weight (Pollock and Kilgore 1978; USEPA 1980a). These values are in good agreement with those shown in [Table 27.4](#). For reasons unknown, pregnant rodents were 5 to 10 times more resistant to oral toxaphene than were nonpregnant rodents (USPHS 1994). Dermal toxicities of toxaphene ranged from 250 mg/kg body weight for rabbits and 930 mg/kg for rats, to 25,000 mg/kg for cattle (Pollock and Kilgore 1978). As was true for acute oral and dermal toxicity data, comparatively high levels of dietary toxaphene were required (i.e., 538 to 828 mg/kg diet) to produce significant death rates in various species of birds (Heath et al. 1972). In their study on four species of gamebirds, each aged 2 weeks, Heath et al. (1972) fed them diets containing graded concentrations of toxaphene for 5 days, followed by 3 days of untreated food. LD₅₀ values at the end of day 8 were 828 mg toxaphene/kg diet for northern bobwhite, 686 for Japanese quail (*Coturnix coturnix japonica*), 542 for ring-necked pheasant (*Phasianus colchicus*), and 538 for mallard (*Anas platyrhynchos*). It appears that toxaphene is not a major hazard to bird survival at previously recommended field application rates (Hoffman and Albers 1984). However, at toxaphene levels not considered life-threatening to birds and mammals, fetotoxic effects have been recorded. For example, ring-necked pheasants fed 100 mg/kg dietary toxaphene produced eggs with significantly reduced hatch over controls. Similarly, toxaphene administered orally to pregnant rats and mice during organogenesis caused fetal toxicity at 15 mg/kg body weight (Pollock and Kilgore 1978).

Some human deaths, especially those of children, have been reported following the ingestion of toxaphene-contaminated foods (USEPA 1980a). Known toxaphene residues in food items of victims ranged from 9.7 to 47 mg/kg; a total dose of 2 to 7 g of toxaphene is considered acutely toxic to a 70-kg adult. For comparison purposes, a 4.5-kg bird would probably die after consumption of 45 to 450 mg toxaphene (USEPA 1980a).

27.5 SUBLETHAL EFFECTS

Among sensitive species of marine and freshwater fish and invertebrates, water concentrations of 0.054 to 0.299 µg/L of toxaphene were associated with growth inhibition, reduced reproduction, backbone abnormalities, or histopathology ([Table 27.5](#)). Aquatic biota are capable of spectacular accumulations of toxaphene from the medium; bioconcentration factors ranged between 1270 and 52,000 those of water under laboratory conditions ([Table 27.6](#)). A similar pattern was observed in Big Bear Lake, California, where toxaphene was applied at 200 µg/L to eradicate goldfish (Pimentel 1971). Biomagnification factors of 365 were calculated for plankton, 1000 for goldfish, and 8500 in pelican fat, representing residues of 73 mg toxaphene/kg in phytoplankton, 200 in goldfish, and 1700 in pelican fat. Accumulation of toxaphene by various species of fish food organisms is dependent on exposure time and concentration. For example, insect nymphs subjected to 20 µg/L of toxaphene for less than 24 h did not accumulate doses lethal to fish. However, algae, diatoms, and protozoan ciliates held for 24 h in 20 µg toxaphene/L solutions, and *Daphnia magna* held 120 h in 10 µg/L, were lethal when fed to fish (Schoettger and Olive 1961).

Fish accumulated part-per-million (mg/kg) toxaphene concentrations in various tissues within a few days when placed in toxaphene-treated lakes that contained less than 1.0 µg/L (Cohen et al. 1982). Freshwater teleosts experienced acute and chronic effects when whole-body levels were in excess of 0.4 mg/kg but less than 5 mg/kg (this latter value being the Food and Drug Administration “action level” for human consumption) (Cohen et al. 1982). Thus, groups of brook trout eggs containing 900 µg toxaphene/kg had drastically reduced survival when compared to controls (Cohen et al. 1982), and brook trout tissue residues exceeding 400 µg toxaphene/kg were associated with reductions in growth, abnormal bone development, and reduced fecundity (Mayer and Mehrle 1977). Fathead minnows containing more than 400 µg toxaphene/kg grew more slowly than controls (Mayer and Mehrle 1977); similar results were reported in channel catfish fry containing 600 to 3400 µg toxaphene/kg (Mayer and Mehrle 1977). Toxaphene retention by aquatic organisms is

Table 27.5 Sublethal Effects of Toxaphene to Aquatic Biota

Type of Medium, Organism	Toxaphene Concentration in Medium (g/L [ppb])	Exposure Duration (days)	Effect	Reference ^a
FRESHWATER				
Daphnid, <i>Daphnia magna</i>	0.12	14	Reduced reproduction	1
Midge, <i>Chironomus plumosus</i>	3.2	20	Delayed emergence	1
Goldfish, <i>Carassius auratus</i>	0.44–1.8	4	Behavioral disruption	2
Brook trout, <i>Salvelinus fontinalis</i>	0.068	161	Reduced reproduction	3
Brook trout	0.288	161	Growth inhibition	4
Fathead minnow, <i>Pimephales promelas</i>				
Adult	0.097	30	Growth inhibition	4
Fry	0.054	30	Growth inhibition	4
Channel catfish, <i>Ictalurus punctatus</i>				
Adult	0.299	30	Growth inhibition	4
Fry	0.072	15	Backbone abnormalities	4
Largemouth bass, <i>Micropterus salmoides</i>				
Larvae	0.2	14	Histopathology of kidney and GI tract	2
SALTWATER				
American oyster, <i>Crassostrea virginica</i>	100.0	1	Growth inhibition	5
Mysid shrimp, <i>Mysidopsis bahia</i>	0.14	28	Reduced reproduction	5
Spot, (teleost) <i>Leiostomus xanthurus</i>	0.1	Long-term	Histopathology	2

^a 1, Sanders 1980; 2, Pollock and Kilgore 1978; 3, Mayer et al. 1975; 4, Mayer et al. 1977; 5, USEPA 1980a.

relatively lengthy when compared to mammals. In one case, American oysters (*Crassostrea virginica*) held for 24 weeks in 10 µg/L toxaphene solutions contained 32.4 mg/kg in soft tissues; after 16 weeks in noncontaminated seawater, oysters still contained 3.0 mg/kg (Pollock and Kilgore 1978).

Sublethal effects of toxaphene observed in mammals (Table 27.7), small laboratory animals, and birds were similar to those recorded for aquatic organisms. However, there was general agreement that effects were induced at much higher concentrations. In domestic white leghorn chickens, for example, toxaphene at 100 mg/kg in the diet for 30 weeks did not significantly alter egg production, hatchability, or fertility, although some bone deformation and kidney lesions were recorded (Bush et al. 1977). The highest dietary dose of toxaphene fed to chickens in lifetime exposure studies, which produced no effect on any parameter measured, ranged between 3.8 and 5 mg/kg (Bush et al. 1977). Several studies with the American black duck (*Anas rubripes*) produced effects similar to those recorded in chickens. In one study, ducklings fed diets containing 10 or 50 mg toxaphene/kg for 90 days had reduced growth and impaired backbone development (Mehrle et al. 1979). Collagen, the organic matrix of bone, was significantly decreased in cervical vertebrae of ducklings fed the diet containing 50 mg toxaphene/kg ration. Calcium concentrations increased in vertebrae of ducklings fed either 10 or 50 mg/kg dietary toxaphene; effects were observed only in female ducklings. In a long-term feeding study lasting 19 months, which included two breeding seasons, American black ducks, fed 10 or 50 mg toxaphene/kg in a dry mash diet, showed no significant differences when compared to control birds in survival, egg production, fertility, hatchability, eggshell thickness, or growth and survival of young (Haseltine et al. 1980). The only negative effects recorded included weight loss among treated males during summer and a slight delay in the number of days required to complete a clutch. Carcass toxaphene residues, which seldom exceeded 0.5 mg/kg, were found in only one duck fed the 50 mg/kg diet (Haseltine et al. 1980),

Table 27.6 Bioconcentration Factors (BCF) for Toxaphene and Selected Species of Aquatic Biota

Medium, Tissue, Species, Developmental Stage	BCF	Exposure Duration (days)
FRESHWATER		
Whole body		
Brook trout, <i>Salvelinus fontinalis</i>	10,000	140
Fathead minnow, <i>Pimephales promelas</i>	52,000	98
Channel catfish, <i>Ictalurus punctatus</i>		
Adults	22,000	100
Fry	40,000	90
Muscle		
Brook trout	3400	161
Channel catfish	7800	137
SALTWATER		
Whole body		
American oyster,		
<i>Crassostrea virginica</i>	32,800	168
<i>C. virginica</i>	9000	4
Sheepshead minnow,		
<i>Cyprinodon variegatus</i>	9800	28
<i>C. variegatus</i>	5000	4
Longnose killifish, <i>Fundulus similis</i>		
Fry	27,900	28
Juvenile	29,400	28
Adult	5400	32
Egg	1270	14
Egg	3700	52
Pinfish, <i>Lagodon rhomboides</i>	5300	4

Modified from Schimmel et al. 1977; and USEPA 1980a.

suggesting low body accumulations in American black duck. However, toxaphene residues were present in the liver of all birds fed toxaphene. At dietary concentrations of 10 or 50 mg/kg, there was no change in avoidance behavior of young American black ducks (Heinz and Finley 1978), which, if interrupted, is considered life-threatening.

Ring-necked pheasants (*Phasianus colchicus*) fed diets containing 300 mg toxaphene/kg showed decreases in egg deposition, egg hatch, food intake, and weight gain. At 100 mg/kg, all of these parameters, except reduced hatch, were the same as controls (Pollock and Kilgore 1978). In a field study, aerial applications of a DDT/toxaphene mixture in southwestern Idaho during 1970, at recommended concentrations to control pests, had no major impact on penned or feral ring-necked pheasants (Messick et al. 1974), suggesting that conformance with recommended application rates should be endorsed whenever possible. However, it is emphasized that recommended toxaphene application rates varied widely and depended, in part, on the pest species to be controlled, the number and type of other pesticides applied jointly, and climatic conditions. Laboratory studies with mallard eggs suggest that recommended toxaphene application rates in excess of 1.12 kg/ha, which is generally exceeded in most cases, may produce severe embryotoxic effects, including dislocated joints and poor growth (Hoffman and Eastin 1982).

Northern bobwhite fed 5 mg/kg dietary toxaphene for 4 months showed thyroid hypertrophy (Pollock and Kilgore 1978) and interference with the ability of bobwhites to discriminate patterns (Kreitzer 1980). In the latter investigation, Kreitzer fed 10 or 50 mg/kg dietary toxaphene to 3-day-old bobwhites for 20 weeks and found that toxaphene-treated birds made 50% more errors than

controls on initial testing. These effects appeared as early as 30 days after toxaphene exposure. In a second test, there was no difference between experimentals and controls, indicating that the ability to learn these tasks was not permanently impaired.

Rats, mice, dogs, deer, sheep, and cattle are all relatively resistant to toxaphene. No-effect levels of 20 to 25 mg/kg dietary toxaphene were documented during multigeneration exposure of rats and during 2-year feeding studies with mice and dogs (USEPA 1980a). No effects were observed in monkeys over a 2-year period during which they were fed diets containing 0.7 ppm toxaphene (Pollock and Kilgore 1978). Toxaphene is carcinogenic in rodents, inducing malignant neoplasms of the liver and other sites (Saleh 1991). Cancers were induced in mice and rats by toxaphene when residues in the diet exceeded 50 mg/kg during lifetime exposure (USEPA 1980a). Toxaphene increases the frequency of sister chromatid exchanges of chromosomes in a human lymphoid cell culture line (USPHS 1994). These results, together with the positive mutagenic response (to *Salmonella* bacteria), constitute substantial evidence that toxaphene is likely to be a human carcinogen (USEPA 1979, 1980a). Penned and wild deer fed toxaphene at 1000 mg/kg appeared normal but showed a decreased digestion rate, which was attributed to a decrease in rumen bacteria (Schwartz and Nagy 1974). Steers fed alfalfa hay containing 306 mg toxaphene/kg for 19 weeks stored 772 mg/kg in abdominal fat and 27 mg/kg in lean meat without apparent ill effects, demonstrating the lipophilicity of toxaphene and the relatively low accumulation rates. For sheep under an identical regimen, these values were 317 mg/kg in fat and 36 mg/kg in meat (Pollock and Kilgore 1978). Milk from dairy cows had measurable concentrations of toxaphene after the cows had been sprayed with emulsions, suspensions, or oil solutions of toxaphene at entomologically effective doses; toxaphene residues in milk were highest on days 1 and 2 postexposure (0.7 to 0.8 mg/L) and declined to control values of 0.06 to 0.08 mg/L by days 14 to 21 (Claborn et al. 1963).

Table 27.7 Sublethal Effects of Toxaphene on Selected Mammals

Organism	Effect	Reference ^a
COW, <i>Bos</i> sp.		
Fed diets containing 20, 60, 100, or 140 mg toxaphene/kg ration for 8 weeks followed by 21-day postexposure observation period. Milk analyzed periodically	Toxaphene concentrations in milk, in mg/L, after 8 weeks of exposure (21 days postexposure) were 0.23 (0.02) in the 20 mg/kg group, 0.48 (0.07) in the 60 mg/kg group, 0.91 (0.12) in the 100 mg/kg group, and 1.82 (0.20) in the 140 mg/kg group	1
Oral exposure to single dose of 50, 100, or 150 mg/kg of ¹⁴ C-labeled toxaphene	Toxaphene residues in tissues 7 days later were dose dependent and ranged, in mg/kg fresh weight (FW), from 2.9–22.3 in liver, 3.5–5.5 in kidney, and 2.7–3.9 in brain	2
GUINEA PIG, <i>Cavia</i> sp.		
2 or 5 mg/kg BW daily via oral route for 60 days	Histopathology of brain, liver, and kidney	3
DOG, <i>Canis familiaris</i>		
Given oral doses of 0.0, 0.2, 2, or 5 mg toxaphene/kg body weight (BW) daily for 13 weeks	Food consumption, growth, and survival normal in all groups. No adverse effects in 0.2 mg/kg group. Mild to moderate dose-dependent histological changes in liver and thyroid in high-dose groups. After 13 weeks, toxaphene residues, in mg/kg FW, increased in a dose-dependent manner in liver from 0.8 (0.2 mg/kg group) to 8.5 (5 mg/kg group), and in fat from 4 (0.2 mg/kg) to 92–105 (5 mg/kg BW daily)	4
HUMAN, <i>Homo sapiens</i>		
Inhalation, 500 mg/m ³ , 30 min daily for 10 days	No toxic effects	2

Table 27.7 (continued) Sublethal Effects of Toxaphene on Selected Mammals

Organism	Effect	Reference ^a
LABORATORY WHITE RAT, <i>Rattus</i> sp.		
Fed diets containing 0, 4, 20, 100, or 500 mg toxaphene/kg ration for 13 weeks	Growth, food consumption, and survival normal in all groups. No adverse effects at 4 mg/kg ration, equivalent to 0.35 mg/kg BW daily. Adverse effects in the high-dose group (500 mg toxaphene/kg ration) included enlarged liver, increased hepatic microsomal enzyme activities, and kidney damage; toxaphene residues in this group after 13 weeks, in mg/kg FW, were 7–10 in liver and 57–103 in fat	4
Weanlings were fed diets containing 0, 4, 20, 100, or 500 mg toxaphene/kg ration for 1 generation and 2 litters	No adverse effects on litter size, pup weight, fertility, gestation, or survival. Toxic effects — mostly associated only with the 500-mg/kg group — included depressed weight gain, elevated serum cholesterol, increased liver and kidney weight, and increased hepatic microsomal enzyme activities. Treatment-related changes in liver, kidney, and thyroid of adult rats were observed at diets as low as 20 mg/kg ration	6
Fed diets of >100 or >1000 mg toxaphene/kg ration for 12 weeks Given 0.05–15 mg/kg BW daily, chronic exposure	Liver pathology at >100 mg/kg ration and central nervous system effects at >1000 mg/kg diet Offspring showed behavioral effects at all doses; at 15 mg/kg BW daily, reproduction was inhibited and offspring showed immunosuppression	7 2
Pregnant females given toxaphene on days 6–15 of gestation at 32 mg/kg BW daily	Maternal survival was 87% on day 8 and 50% on day 16. Survivors had weight loss in whole body, thymus, and spleen. Adverse developmental effect (supernumerary ribs) in litters	5
Inhalation of 40 mg toxaphene dust/m ³ for 3 months	Slight hepatocellular necrosis	2

^a 1, Claborn et al. 1963; 2, USPHS 1994; 3; Chandra and Durairaj 1992; 4, Chu et al. 1986; 5, Chernoff et al. 1990; 6, Chu et al. 1988; 7, Saleh 1991.

27.6 RECOMMENDATIONS

In November 1982, the U.S. Environmental Protection Agency canceled the registration of toxaphene for most uses and, thus, joined a growing number of nations in Western Europe, Scandinavia, North America, and North Africa that had previously initiated similar actions. With some restrictions, toxaphene was used domestically through the mid-1980s for treatment of scabies in cattle and sheep; controlling sporadic infestations of armyworms, cutworms, and grasshoppers on cotton, corn, and small grains; and, in Puerto Rico and the Virgin Islands, to control mealy bugs, pineapple gummosis moths, and banana weevils. Existing stocks of toxaphene were used through 1986 for control of sicklepod in soybeans and peanuts, for insects in corn cultivated without tillage, and for pests of dry and southern peas (USEPA 1982). In 1993, all uses and manufacture of toxaphene were banned in the United States (USPHS 1994). To understand the potential global budget of toxaphene, it is now necessary to obtain information on the present and historical uses in third world and former Eastern bloc countries (Swackhamer and McConnell 1993).

Although toxaphene is not markedly hazardous to most wildlife species for which data were available, the decision to withdraw or curtail agricultural uses of toxaphene was popular with most natural resource managers. Their concerns, apparently shared by others, were based, in part, on the following observations:

- Toxaphene causes death and deleterious effects to nontarget aquatic biota at extremely low concentrations (i.e., <1.0 µg/L).
- Toxaphene is persistent in soils, water, and other environmental compartments, with residence times measured in years.
- Toxaphene accumulates in aquatic organisms and biomagnifies through food chains.
- Toxaphene is widely distributed, even when the initial application point is hundreds of kilometers distant; transport is presumably by atmospheric and other vectors.
- Technical difficulties continue to exist in the chemical analysis of toxaphene, a compound with at least 177 isomers.
- There is an imperfect understanding of the fate and effects of individual toxaphene components.
- There is inadequate knowledge of interaction effects of toxaphene with other agricultural chemicals (especially when mixtures are applied simultaneously) and with other persistent compounds in aquatic ecosystems, such as PCBs, DDT and its isomers, and petroleum.
- There is the perception that suitable alternative pesticidal chemicals are available, including some carbamates, organophosphorus compounds, and synthetic pyrethroids.

At present, large but unknown quantities of toxaphene that were discharged into the environment over the past several decades remain undegraded and potentially bioavailable. Also, knowledge of toxaphene ecotoxicology is incomplete or inadequate. Limits for toxaphene residues in air, water, biota, and other environmental compartments for the protection of fish, livestock, and human health vary considerably ([Table 27.8](#)). The concentration of toxaphene in seawater considered safe for marine life protection is 0.07 µg/L; for sensitive freshwater species, this lies between 0.008 and 0.013 µg/L. This contrasts sharply with some recommended drinking water criteria for human health protection of 5.0 to 8.8 µg/L. Other existing criteria for human health protection, which range in various foods from 0.1 to 7.0 mg/kg, appear adequate at this time to protect sensitive wildlife species. It is emphasized that these values, and others shown in [Table 27.8](#), are considered criteria and not administratively legislated standards.

No standard reference materials have been certified for analysis of chlorobornanes, although several may be suitable — including fish oils and whale blubber. Analytical standards for several chlorobornanes are now available, but there is a need to identify other remaining environmentally significant congeners (Muir and de Boer 1993). More research is now recommended in the following areas:

- Partitioning between air/water (including snow), air/plant, and air/soil interfaces (Swackhamer and McConnell 1993)
- Processes that control degradation in soils and sediments and transformations during atmospheric transport (Swackhamer and McConnell 1993)
- Effects of inhalation and dermal exposure to toxaphene, especially studies of an intermediate or chronic exposure (USPHS 1994)
- Toxicities of specific toxaphene congeners and their chemical analysis (USPHS 1994)
- Bioconcentration and biomagnification of individual congeners in terrestrial food chains (Swackhamer and McConnell 1993)
- Acute management of toxaphene-induced seizures in humans with anticonvulsants, especially diazepam, phenobarbital, and phenytoin (USPHS 1994).

27.7 SUMMARY

Toxaphene (chlorinated camphene, 67 to 69% chlorine) is a broad-spectrum insecticide, which was formerly one of the most heavily used agricultural chemicals on a global scale, especially

Table 27.8 Proposed Toxaphene Criteria for Protection of Natural Resources and Human Health

Compartment	Allowable Concentration
AQUATIC LIFE PROTECTION	
Freshwater ^a	0.013 µg/L (24-h average); 1.6 µg/L maximum at any time (USEPA 1980a)
Freshwater Most states Acute Chronic	0.073 µg/L (USPHS 1994) 0.0002 µg/L (USPHS 1994)
Wisconsin Acute, Great Lakes Acute, cold water Acute, warm water Chronic; Great Lakes, cold water, warm water	0.61 µg/L (USPHS 1994) 0.81 µg/L (USPHS 1994) 0.61 µg/L (USPHS 1994) 0.01 µg/L (USPHS 1994)
Marine	0.07 µg/L maximum at any time (USEPA 1980a)
Marine Most states Acute Chronic	0.21 µg/L (USPHS 1994) 0.0002 µg/L (USPHS 1994)
Residues in fish tissues	5.0 mg/kg maximum, wet weight basis USEPA 1980a); 0.4–0.6 µg/kg maximum, wet weight basis (Mayer and Mehrle 1977)
LABORATORY WHITE RAT	
Diet No adverse effect level	4.0 mg/kg ration, equivalent to 0.29–0.38 mg toxaphene/kg body weight daily (Chu et al. 1988)
Lowest adverse effect level (histological damage)	20.0 mg/kg ration (Chu et al. 1988)
HUMAN HEALTH	
Minimum risk level, oral	5 µg/kg body weight daily for acute duration oral exposure of 14 days or less ^b ; 1 µg/kg BW daily for intermediate duration exposure of 15–364 days (USPHS 1994)
Safe daily dose	3.4 µg/kg body weight (USEPA 1980a)
Acceptable daily intake	1.25 µg/kg body weight (USEPA 1980a)
Air Arizona 1-h average 24-h average	3.7 µg/m ³ (USPHS 1994) 1.5 µg/m ³ (USPHS 1994)
New York, 1-year average	1.67 µg/m ³ (USPHS 1994)
Oklahoma, 24-h average	5.0 µg/m ³ (USPHS 1994)
Texas, 30-min average	0.5 µg/m ³ (USPHS 1994)
Daily intake	0.00018 µg/kg body weight (USEPA 1980a)
Immediately hazardous	200 mg/m ³ (USPHS 1994)
Drinking water California Maryland Missouri	5 µg/L; maximum of 500 µg/L for 1 day or 40 µg/L for 10 days (USPHS 1994) 0.21 µg/L (USPHS 1994) 5 µg/L (USPHS 1994) 0.000071 µg/L (USPHS 1994)
Diet Fish consumption Germany U.S.	0.4 mg/kg lipid weight (de Boer and Wester 1993) 5.0 mg/kg fresh weight (de Boer and Wester 1993)
Fat of meat from livestock	7.0 mg/kg (USEPA 1980a)
Milk and milk products, fat weight basis	0.5 mg/kg (USEPA 1980a)
Soybean oil	6 mg/L (USPHS 1994)
Sunflower seeds	0.1 mg/kg wet weight basis (USEPA 1980a)

Table 27.8 (continued) Proposed Toxaphene Criteria for Protection of Natural Resources and Human**Compartment****Allowable Concentration**

Citrus fruits	5.0–7.0 mg/kg wet weight basis (Canada); 0.4 mg/kg wet weight (W. Germany, Netherlands) (USEPA 1980a)
Groundwater	5 µg/L (USPHS 1994)
WILDLIFE PROPAGATION	
Nevada	
Irrigation	5 µg/L (USPHS 1994)
Watering of livestock	0.01 µg/L (USPHS 1994)

^a The International Joint Commission of the United States and Canada recommend a water quality standard of 0.008 µg/L for the protection of freshwater aquatic life. This standard is based on the study by Mayer et al. (1975), who found that toxaphene at 0.039 µg/L in water caused a significant increase in mortality and a significant decrease in growth of surviving brook trout fry over a 90-day period. The standard of 0.008 µg/L is obtained by applying an uncertainty value of 5.

^b Based on a LOAEL of 5.0 mg/kg BW daily for decreased hepatic biliary function in rats treated with toxaphene in the diet for 8 days and an uncertainty factor of 1000.

against pests of cotton. In 1982, the U.S. Environmental Protection Agency canceled the registrations of toxaphene for most uses; stocks of toxaphene could be used, with some restrictions, through 1986. Considerable, but unknown, quantities of toxaphene previously discharged into the environment over the past several decades may remain undegraded and potentially available to living resources. Since 1993, all domestic uses and manufacture of toxaphene were prohibited; however, toxaphene use in other countries is continuing.

Toxaphene is extremely persistent in soil and water, with documented half-times of 9 to 11 years. However, in air and in warm-blooded organisms, toxaphene degradation is rapid with half-times of 15 and 3 days, respectively. Toxaphene is especially hazardous to nontarget marine and freshwater organisms, with death recorded at ambient water concentrations substantially below 10 µg/L, and adverse effects observed on growth, reproduction, and metabolism at water concentrations between 0.05 and 0.3 µg/L. Aquatic organisms readily accumulate toxaphene from the ambient medium and diet, sometimes spectacularly, retain it for lengthy periods, and biomagnify the chemical through food chains. These phenomena could account for the numerous fish kills recorded after toxaphene application, as well as the high residues measured in fish from the Rio Grande Valley in southern Texas and other locations of former high agricultural use of toxaphene. Atmospheric vectors, including prevailing winds and rainfall, may transport toxaphene hundreds of kilometers from known point sources of application. This, in part, would explain the levels of 5 to 10 mg/kg whole-body wet weight recorded in various species of fish from the Great Lakes.

Based on estimated environmental exposure levels, toxaphene does not appear to constitute a major threat to warm-blooded animals, including migratory birds and other wildlife, domestic poultry and livestock, small laboratory mammals, and humans. Wildlife typically contain low or nondetectable levels of toxaphene, except for some species of fish-eating raptors, and the frequency of occurrence is low when compared with that of other organochlorine agricultural compounds. However, toxaphene has been implicated as a human carcinogen and mutagen at relatively high test dosages and was associated with some bird kills following aerial applications.

In water, the concentration of toxaphene considered safe for protection of freshwater life is conservatively estimated to lie between 0.008 and 0.013 µg/L; for marine life, it is 0.07 µg/L. This is in sharp contrast to the current recommended drinking water criterion for human health protection of 5.0 to 8.8 µg/L. Similarly, residues in fish tissue in excess of 0.4 to 0.6 mg/kg wet weight may be hazardous to fish health and should be considered as presumptive evidence of significant environmental contamination, although fish may contain up to 5.0 mg/kg before they are considered hazardous to human consumers. Toxaphene criteria for human health protection — which range in various foods from 0.1 mg/kg for sunflower seeds to 7.0 mg/kg in meat, fats, and citrus fruits — also appear adequate to safeguard sensitive species of wildlife.

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CHAPTER 28

Arsenic

28.1 INTRODUCTION

Anxiety over arsenic (As) is understandable and frequently justifiable. Arsenic compounds were the preferred homicidal and suicidal agents during the Middle Ages, and arsenicals have been regarded largely in terms of their poisonous characteristics in the nonscientific literature (National Academy of Sciences [NAS] 1977). Acute arsenic poisoning was reported in the 1800s in horses, cows, deer, and foxes as a result of emissions from metal smelters (Ismail and Roberts 1992). In 1885, arsenic accounted for nearly one third of the homicide poisonings in France (North et al. 1997). Data collected on animals, including humans, indicated that inorganic arsenic can cross the placenta and produce mutagenic, teratogenic, and carcinogenic effects in offspring (Nagymajtenyi et al. 1985; Agency for Toxic Substances and Disease Registry [ATSDR] 1992). Correlations between elevated atmospheric arsenic levels and mortalities from cancer, bronchitis, and pneumonia were established in an epidemiological study in England and Wales, where deaths from respiratory cancer were increased at air concentrations $>3 \mu\text{g As/m}^3$ (National Research Council of Canada [NRCC] 1978). Chronic arsenical poisoning, including skin cancer and a gangrenous condition of the hands and feet called Blackfoot's disease, has occurred in people from several communities in Europe, South America, and Taiwan who were exposed to elevated concentrations of arsenic in drinking water (U.S. Environmental Protection Agency [USEPA] 1980; Lin et al. 1998). Inorganic arsenic in dietary staples such as yams and rice may have contributed substantially to exposure and adverse health effects observed in an endemic Taiwanese population historically exposed to arsenic in drinking water (Schoof et al. 1998). Severe health effects, including cancer and death, have recently been documented in Mongolia (Luo et al. 1997; Ma et al. 1998), Bangladesh (Biswas et al. 1998), Chile (Smith et al. 1998), and India (Chowdhury et al. 1997) from ingestion of naturally elevated levels of arsenic in the drinking water, and in Thailand from the use of traditional arsenic-containing medicines and arsenical wastes from mining activities (Choprapawon and Rodcline 1997). In Japan, about 12,000 infants were poisoned (128 deaths) after consuming dry milk containing 15 to 24 mg inorganic As/kg, which originated from contaminated sodium phosphate used as a milk stabilizer. Fifteen years after exposure, the survivors sustained an elevated frequency of severe hearing loss and brain-wave abnormalities (Pershagen and Vahter 1979).

Many reviews on ecotoxicological aspects of arsenic in the environment are available, including those by Woolson (1975), NAS (1977), NRCC (1978), Pershagen and Vahter (1979), USEPA (1980, 1985), Hood (1985), Andreae (1986), Sorensen (1987), Eisler (1988, 1994), Phillips (1990), ATSDR (1992), Abernathy et al. (1997), Society for Environmental Geochemistry and Health [SEGH] (1998) and the U.S. Public Health Service [USPHS] (1998). These authorities agree on six points:

1. Arsenic is a relatively common element and is present in air, water, soil, plants, and in all living tissues.
2. Arsenicals have been used in medicine as chemotherapeutics since 400 BCE, and organoarsenicals were used extensively for this purpose until about 1945, with no serious effects when judiciously administered.
3. Large quantities of arsenicals are released into the environment as a result of industrial and especially agricultural activities, and these may pose potent ecological dangers.
4. Exposure of humans and wildlife to arsenic may occur through air (emissions from smelters, coal-fired power plants, herbicide sprays), water (mine tailings runoff, smelter wastes, natural mineralization), and food (especially seafoods).
5. Chronic exposure to arsenicals by way of the air, diet, and other routes has been associated with liver, kidney, and heart damage, hearing loss, brain-wave abnormalities, and impaired resistance to viral infections.
6. Exposure to arsenic has been associated with different types of human cancers such as respiratory cancers and epidermoid carcinomas of the skin, as well as precancerous dermal keratosis. The epidemiological evidence of human carcinogenicity is supported by carcinogenesis in experimental animals (Deknudt et al. 1986).

28.2 SOURCES, FATE, AND USES

Global production of arsenic is estimated to be 75,000 to 100,000 tons annually, of which the United States produces about 21,000 tons and uses about 44,000 tons. Major quantities are imported from Sweden, the world's leading producer (NAS 1977; USEPA 1980). Imports of arsenic trioxide (As_2O_3) to the United States have increased from about 16 million kg in 1985 to about 30 million kg in 1989; imports of elemental arsenic have increased from about 0.45 million kg in 1985/88 to 1.2 million kg in 1989 (ATSDR 1992). The United States exports about 0.3 million kg arsenic compounds annually, mainly as arsenic acid, sodium arsenate, and lead arsenate (ATSDR 1992). Almost all (97%) of the arsenic made worldwide enters end-product manufacture in the form of arsenic trioxide, and the rest is used as additives in producing special lead and copper alloys (NAS 1977). About 74% of the total arsenic trioxide is in products used for wood preservation (ATSDR 1992). Most of the rest (about 19%) is used in production of agricultural chemicals, such as insecticides, herbicides, fungicides, algicides, and growth stimulants for plants and animals (ATSDR 1992). Smaller amounts are used in the production of glass, in the electronic industry, dyestuffs, and in veterinary and human medicines, including medicines for the eradication of tapeworm in sheep and cattle (NAS 1977; ATSDR 1992; Eisler 1994). The sole producer and refiner of As_2O_3 in the United States is a copper smelter in Tacoma, Washington (NAS 1977).

Arsenic naturally occurs as sulfides and as complex sulfides of iron, nickel, and cobalt (Woolson 1975). In one form or another, arsenic is present in rocks, soils, water, and living organisms at concentrations of parts per billion to parts per million (NAS 1977). Soil arsenic levels are normally elevated near arseniferous deposits and in mineralized zones containing gold, silver, and sulfides of lead and zinc (Dudas 1984; Thornton and Farago 1997). Secondary iron oxides formed from the weathering of pyrite act as scavengers of arsenic (Dudas 1984). Pyrite is a known carrier of arsenic and may contain up to 5600 mg/kg. For example, total arsenic is 10 times above normal background levels in soils derived from pyritic shale (Dudas 1984). Natural weathering of rocks and soils adds about 40,000 tons of arsenic to the oceans yearly, accounting for <0.01 mg/L input to water on a global basis (NRCC 1978). Many species of marine plants and animals often contain naturally high concentrations of arsenic (NAS 1977), but it is usually present in a harmless organic form (Woolson 1975). Anthropogenic input of arsenic to the environment is substantial and exceeds that contributed by natural weathering processes by a factor of about 3 (NRCC 1978).

The most important concept with respect to arsenic cycling in the environment is constant change. Arsenic is ubiquitous in living tissue and is constantly being oxidized, reduced, or otherwise

metabolized. In soils, insoluble or slightly soluble arsenic compounds are constantly being resolubilized, and the arsenic is being presented for plant uptake or reduction by organisms and chemical processes. Humans reportedly modify the arsenic cycle only by causing localized high concentrations (NAS 1977). The speciation of arsenic in the environment is affected partly by indiscriminate biological uptake, which consumes about 20% of the dissolved arsenate pool and results in measurable concentrations of reduced and methylated arsenic species. The overall arsenic cycle is similar to the phosphate cycle; however, regeneration time for arsenic is much slower — on the order of several months (Sanders 1980). The ubiquity of arsenic in the environment is evidence of the redistribution processes that have been operating since early geologic time (Woolson 1975). A prehuman steady-state solution to the global arsenic cycle (Austin and Millward 1984) indicates that major reservoirs of arsenic (in kilotons) are magma (50 billion), sediments (25 billion), oceanic deep waters (1.56 million), land (1.4 million), and ocean mixed layers (270,000); minor amounts occur in ocean particulates (100), and in continental (2.5) and marine tropospheres (0.069). Arsenic is significantly mobilized from the land to the troposphere by both natural and anthropogenic processes. Industrial emissions account for about 30% of the present-day burden of arsenic in the troposphere (Austin and Millward 1984). Agronomic ecosystems, for example, may receive arsenic from agricultural sources such as organic herbicides, irrigation waters, and fertilizers, and from such nonagricultural sources as fossil fuels and industrial and municipal wastes (Woolson 1975). Arsenic is mobile and nonaccumulative in air, plant, and water phases of agronomic ecosystems; arsenicals sometimes accumulate in soils, but redistribution mechanisms usually preclude hazardous accumulations (Woolson 1975).

Arsenic compounds have been used in medicine since the time of Hippocrates, ca. 400 BCE (Woolson 1975). Inorganic arsenicals have been used for centuries, and organoarsenicals for at least a century in the treatment of syphilis, yaws, amoebic dysentery, and trypanosomiasis (NAS 1977). During the period 1200 to 1650, however, arsenic was used extensively in homicides (NRCC 1978). In 1815, the first accidental death was reported from arsine (AsH_3) poisoning; and between 1900 and 1903, accidental poisonings from consumption of arsenic-contaminated beer were widely reported (NRCC 1978). In 1938, it was established that arsenic can counteract selenium toxicity (NRCC 1978; ATSDR 1992). The introduction of arsphenamine, an organoarsenical, to control venereal disease earlier this century gave rise to intensive research by organic chemists, which resulted in the synthesis of at least 32,000 arsenic compounds. But the advent of penicillin and other newer drugs nearly eliminated the use of organic arsenicals as human therapeutic agents (USEPA 1980). Arsenical drugs are still used in treating certain tropical diseases, such as African sleeping sickness and amoebic dysentery, and are used in veterinary medicine to treat parasitic diseases, including filariasis in dogs (*Canis familiaris*) and blackhead in turkeys (*Meleagris gallopavo*) and chickens, *Gallus* spp. (NAS 1977). Today, abnormal sources of arsenic that can enter the food chain from plants or animals include arsenical pesticides such as lead arsenate; arsenic acid, HAsO_3 ; sodium arsenite, NaAsO_2 ; sodium arsenate, Na_2AsO_4 ; and cacodylic acid, $(\text{CH}_3)_2\text{As}(\text{OH})$ (NAS 1977).

The major uses of arsenic are in the production of herbicides, insecticides, desiccants, growth stimulants for plants and animals, and especially wood preservatives. Much smaller amounts are used in the manufacture of glass (nearly all of which contains 0.2% to 1.0% arsenic as an additive — primarily as a decolorizing agent) and textiles, and in medical and veterinary applications (NAS 1977; USEPA 1980; Hamasaki et al. 1995). Arsenic is also an ingredient in lewisite, a blistering poison gas developed (but not used) during World War I, and in various police riot-control agents (NAS 1977). The availability of arsenic in certain local areas has been increased by various human activities:

- Smelting and refining of gold, silver, copper, zinc, uranium, and lead ores
- Combustion of fossil fuels, such as coal and gasoline
- Burning of vegetation from cotton gins treated with arsenical pesticides
- Careless or extensive use of arsenical herbicides, pesticides, and defoliants

- Dumping of land wastes and sewage sludge (1.1 mg/L) in areas that allow leaching into groundwater
- Use of domestic detergents in wash water (2.5 to 1000 mg As/L)
- Manufacture of glass
- Sinking of drinking water wells into naturally arseniferous rock (NRCC 1978; USEPA 1980).

There are several major anthropogenic sources of environmental arsenic contamination: industrial smelters — the effluent from a copper smelter in Tacoma, Washington, contained up to 70 tons arsenic discharged yearly into nearby Puget Sound (NRCC 1978); coal-fired power plants, which collectively emit about 3000 tons arsenic annually in the United States (USEPA 1980); and production and use of arsenical pesticides, coupled with careless disposal of used pesticide containers (NAS 1977). Elevated levels of arsenic have been reported in soils near smelters, in acid mine spoils, and in orchards receiving heavy applications of lead arsenate (NAS 1977; Dudas 1984). Air concentrations of arsenic are elevated near metal smelters, near sources of coal burning, and wherever arsenical pesticides are applied (NAS 1977). Atmospheric deposition of arsenic has steadily increased for at least 30 years, as judged by sedimentary evidence from lakes in upstate New York (Smith et al. 1987). Arsenic is introduced into the aquatic environment through atmospheric deposition of combustion products and through runoff from flyash storage areas near power plants and nonferrous smelters (Smith et al. 1987). Elevated arsenic concentrations in water were recorded near mining operations and from mineral springs and other natural waters — usually alkaline and with high sodium and bicarbonate contents (NAS 1977). In the United States, the most widespread and frequent increases in dissolved arsenic concentrations in river waters were in the northern Midwest. All evidence suggests that increased atmospheric deposition of fossil fuel combustion products was the predominant cause of the trend (Smith et al. 1987).

Agricultural applications provide the largest anthropogenic source of arsenic in the environment (Woolson 1975). Inorganic arsenicals (arsenic trioxide; arsenic acid; arsenates of calcium, copper, lead, and sodium; and arsenites of sodium and potassium) have been used widely for centuries as insecticides, herbicides, algicides, and desiccants. Paris green (cuprous arsenite) was successfully used in 1867 to control the Colorado potato beetle (*Leptinotarsa decemlineata*) in the eastern United States. Arsenic trioxide has been applied widely as a soil sterilant. Sodium arsenite has been used for aquatic weed control, as a defoliant to kill potato vines before tuber harvest, as a weed killer along roadsides and railroad rights-of-way, and for control of crabgrass (*Digitaria sanguinalis*). Calcium arsenates have been applied to cotton and tobacco fields to protect against the boll weevil (*Anthonomus grandis*) and other insects. Lead arsenate has been used to control insect pests of fruit trees, and for many years was the only insecticide that controlled the codling moth (*Carpocapsa pomonella*) in apple orchards and the horn worm larva (Sphingidae) on tobacco. Much smaller quantities of lead arsenate are now used in orchards because fruit growers rely primarily on carbamate and organophosphorus compounds to control insect pests; however, lead arsenate is still being used by some growers to protect orchards from certain chewing insects. The use of inorganic arsenicals has decreased due to the banning of sodium arsenite and some other arsenicals for most purposes, although they continue to be used on golf greens and fairways in certain areas to control annual bluegrass (*Poa annua*). In recent decades, inorganic arsenicals have been replaced by organoarsenicals for herbicidal application, and by carbamate and organophosphorus compounds for insect control (Woolson 1975). By the mid-1950s, organoarsenicals were used extensively as desiccants, defoliants, and herbicides (NRCC 1978). Organoarsenicals marketed in agriculture today, which are used primarily for herbicidal application, include cacodylic acid (also known as dimethylarsinic acid) and its salts — monosodium and disodium methanearsonate (Woolson 1975; NAS 1977). Organoarsenicals are used as selective herbicides for weedy grasses in turf, and around cotton and noncrop areas for weed control. At least 1.8 million ha (4.4 million acres) have been treated with more than 8000 tons of organoarsenicals (NAS 1977). In 1945, it was discovered that one organoarsenical (3-nitro-4-hydroxyphenyl arsonic acid) controlled coccidiosis and promoted growth in domestic chicken (Woolson 1975). Since that time, other substituted phenylarsonic acids

have been shown to have both therapeutic and growth-promoting properties as feed additives for poultry and swine (*Sus* spp.), and are used for this purpose today under existing regulations (Woolson 1975; NAS 1977) — although the use of arsenicals in poultry food was banned in France in 1959 (NRCC 1978).

28.3 CHEMICAL AND BIOCHEMICAL PROPERTIES

Elemental arsenic is a gray, crystalline material characterized by atomic number 33, atomic weight of 74.92, density of 5.727, melting point of 817°C, sublimation at 613°C, and chemical properties similar to those of phosphorus (Woolson 1975; NAS 1977; NRCC 1978; USEPA 1980, 1985; ATSDR 1992). Arsenic has four valence states: -3, 0, +3, and +5. Arsines and methylarsines, which are characteristic of arsenic in the -3 oxidation state, are generally unstable in air. Elemental arsenic, As⁰ is formed by the reduction of arsenic oxides. Arsenic trioxide (As⁺³) is a product of smelting operations and is the material used in synthesizing most arsenicals. It is oxidized catalytically or by bacteria to arsenic pentoxide (As⁺⁵) or orthoarsenic acid (H₃AsO₄). Arsenic in nature is rarely in its free state. Usually, it is a component of sulfidic ores, occurring as arsenides and arsenates, along with arsenic trioxide, which is a weathering product of arsenides. Most arsenicals degrade or weather to form arsenate, although arsenite may form under anaerobic conditions. Biotransformations may occur, resulting in volatile arsenicals that normally are returned to the land where soil adsorption, plant uptake, erosion, leaching, reduction to arsines, and other processes occur. This natural arsenic cycle reflects a constant shifting of arsenic between environmental compartments. Atomic absorption spectrometry is the most common procedure for measuring arsenic in biological materials, although other methods are used, including neutron activation (ATSDR 1992). A variety of sensitive techniques have been used to obtain speciation data for the forms of arsenic at trace levels (Hamasaki et al. 1995; Crecelius et al. 1998).

Arsenic species in flooded soils and water are subject to chemically and microbiologically mediated oxidation or reduction and methylation reactions (Tamaki and Frankenberger 1992; Hamasaki et al. 1995). At high Eh values (i.e., high oxidation-reduction potential) typical of those encountered in oxygenated waters, pentavalent As⁺⁵ tends to exist as H₃AsO₄, H₂AsO₄, HAsO₂, and AsO₄⁻³. At lower Eh, the corresponding trivalent arsenic species can be present, as well as AsS₂ (Thanabalasingam and Pickering 1986). In aerobic soils, the dominant arsenic species is As⁺⁵, and small quantities of arsenite and monomethylarsonic acid are present in mineralized areas. In anaerobic soils, As⁺³ is the major soluble species (Haswell et al. 1985). Inorganic arsenic is more mobile than organic arsenic, and thus poses greater problems by leaching into surface waters and groundwater (NRCC 1978). The trivalent arsenic species are generally considered to be more toxic, more soluble, and more mobile than As⁺⁵ species (Thanabalasingam and Pickering 1986). Soil microorganisms metabolize arsenic into volatile arsine derivatives. Depending on conditions, 17% to 60% of the total arsenic present in soil may be volatilized (NRCC 1978). Estimates of the half-life of arsenic in soil vary from 6.5 years for arsenic trioxide to 16 years for lead arsenate (NRCC 1978).

In water, arsenic occurs in both inorganic and organic forms, and in dissolved and gaseous states (USEPA 1980). The form of arsenic in water depends on Eh, pH, organic content, suspended solids, dissolved oxygen, and other variables (USEPA 1985). Arsenic in water exists primarily as a dissolved ionic species; particulates account for less than 1% of the total measurable arsenic (Maher 1985a). Arsenic is rarely found in water in the elemental state (0) and is found in the -3 state only at extremely low Eh values (Lima et al. 1984). Common forms of arsenic encountered in water are arsenate, arsenite, methanearsonic acid, and dimethylarsinic acid (USEPA 1985). The formation of inorganic pentavalent arsenic, the most common species in water, is favored under conditions of high dissolved oxygen, basic pH, high Eh, and reduced content of organic material; reverse conditions usually favor the formation of arsenites and arsenic sulfides (NRCC 1978;

Pershagen and Vahter 1979; USEPA 1980), although some arsenite is attributed to biological activity (Maher 1985a). Water temperature seems to affect arsenic species composition in the estuary of the River Beaulieu in the United Kingdom, where reduced and methylated species predominate during warmer months and inorganic As⁺⁵ predominates during the colder months. The appearance of methylated arsenicals during the warmer months is attributed both to bacterial and abiotic release from decaying plankton and to grazing by zooplankton (Howard et al. 1984). Also contributing to higher water or mobile levels are the natural levels of polyvalent anions, especially phosphate species. Phosphate, for example, displaces arsenic held by humic acids, and it sorbs strongly to the hydrous oxides of arsenates (Thanabalingam and Pickering 1986).

Marine algae transform arsenate into nonvolatile methylated arsenic compounds such as methanearsonic and dimethylarsinic acids (Tamaki and Frankenberger 1992). Freshwater algae and macrophytes, like marine algae, synthesize lipid-soluble arsenic compounds and do not produce volatile methylarsines. Terrestrial plants preferentially accumulate arsenate over arsenite by a factor of about 4. Phosphate inhibits arsenate uptake by plants, but not the reverse. The mode of toxicity of arsenate in plants is to partially block protein synthesis and interfere with protein phosphorylation — a process that is prevented by phosphate (Tamaki and Frankenberger 1992).

Physical processes play a key role in governing arsenic bioavailability in aquatic environments. For example, arsenates are readily sorbed by colloidal humic material under conditions of high organic content, low pH, low phosphate, and low mineral content (USEPA 1980; Thanabalingam and Pickering 1986). Arsenates also coprecipitate with, or adsorb on, hydrous iron oxides and form insoluble precipitates with calcium, sulfur, aluminum, and barium compounds (USEPA 1980). Removal of arsenic from seawater by iron hydroxide scavenging seems to be a predominant factor in certain estuaries. The process involves both As⁺³ and As⁺⁵ and results in a measurable increase in arsenic levels in particulate matter, especially at low salinities (Sloot et al. 1985; Tremblay and Gobeil 1990). Arsenic sulfides are comparatively insoluble under conditions prevalent in anaerobic aqueous and sedimentary media containing hydrogen sulfide. Accordingly, these compounds may accumulate as precipitates and thus remove arsenic from the aqueous environment. In the absence of hydrogen sulfide, these sulfides decompose within several days to form arsenic oxides, sulfur, and hydrogen sulfide (NAS 1977).

In reduced environments, such as sediments, arsenate is reduced to arsenite and methylated to methylarsinic acid or dimethylarsenic acids: these compounds may be further methylated to trimethylarsine or reduced to dimethylarsine, and may volatilize to the atmosphere where oxidation reactions result in the formation of dimethylarsinic acid (Woolson 1975). Arsenates are more strongly adsorbed to sediments than are other arsenic forms, the adsorption processes depending strongly on arsenic concentration, sediment characteristics, pH, and ionic concentration of other compounds (USEPA 1980). An important mechanism of arsenic adsorption onto lake sediments involves the interaction of anionic arsenates and hydrous iron oxides. Evidence suggests that arsenic is incorporated into sediments at the time of hydrous oxide formation, rather than by adsorption onto existing surfaces (Aggett and Roberts 1986). Arsenic concentrations in lake sediments are also correlated with manganese; hydrous manganese oxides — positively charged for the adsorption of Mn⁺² ions — play a significant role in arsenic adsorption onto the surface of lake sediments (Takamatsu et al. 1985). The mobility of arsenic in lake sediments and its release to the overlying water is related partly to seasonal changes. In areas that become stratified in summer, arsenic released from sediments accumulates in the hypolimnion until turnover, when it is mixed with epilimnetic waters. This mixing may result in a 10 to 20% increase in arsenic concentration (Aggett and O'Brien 1985). Microorganisms (including four species of fungi) in lake sediments oxidized inorganic As⁺³ to As⁺⁵ and reduced inorganic As⁺⁵ to As⁺³ under aerobic conditions; under anaerobic conditions, only reduction was observed (Freeman et al. 1986). Inorganic arsenic can be converted to organic alkyl arsenic acids and methylated arsines under anaerobic conditions by fungi, yeasts, and bacteria — although biomethylation may also occur under aerobic conditions (USEPA 1980).

Most arsenic investigators now agree on the following points:

1. Arsenic may be absorbed by ingestion, inhalation, or through permeation of the skin or mucous membranes.
2. Cells accumulate arsenic using an active transport system normally used in phosphate transport.
3. Arsenicals are readily absorbed after ingestion, most being rapidly excreted in the urine during the first few days, or at most a week (the effects seen after long-term exposure are probably a result of continuous daily exposure, rather than of accumulation).
4. The toxicity of arsenicals conforms to the following order, from greatest to least toxicity: arsines > inorganic arsenites > organic trivalent compounds (arsenoxides) > inorganic arsenates > organic pentavalent compounds > arsonium compounds > elemental arsenic.
5. Solubility in water and body fluids appears to be directly related to toxicity (the low toxicity of elemental arsenic is attributed to its virtual insolubility in water and body fluids, whereas the highly toxic arsenic trioxide, for example, is soluble in water to 12.0 g/L at 0°C, 21.0 g/L at 25°C, and 56.0 g/L at 75°C).
6. The mechanisms of arsenical toxicity differ considerably among arsenic species, although signs of poisoning appear similar for all arsenicals (Woolson 1975; NRCC 1978; Pershagen and Vahter 1979; Eisler 1988, 1994; ATSDR 1992; Abernathy et al. 1997; SEGH 1998).

The primary toxicity mode of inorganic As⁺³ is through reaction with sulfhydryl groups of proteins and subsequent enzyme inhibition; inorganic pentavalent arsenate does not react as readily as As⁺³ with sulfhydryl groups, but may uncouple oxidative phosphorylation (Howard et al. 1984; USEPA 1985). Inorganic As⁺³ interrupts oxidative metabolic pathways and sometimes causes morphological changes in liver mitochondria. Arsenite *in vitro* reacts with protein-SH groups to inactivate enzymes such as dihydrolipoyle dehydrogenase and thiolase, producing inhibited oxidation of pyruvate and beta-oxidation of fatty acids (Belton et al. 1985). Inorganic As⁺³ may also exert toxic effects by the reaction of arsenous acid (HAsO) with the sulfhydryl (SH) groups of enzymes. In the first reaction, arsenous acid is reduced to arsionous acid (AsOH₂), which then condenses to either monothiols or dithiols to yield dithioesters of arsionous acid. Arsionous acid may then condense with enzyme SH groups to form a binary complex (Knowles and Benson 1984a, 1984b).

Methylation to methylarsonic acid [(CH₃)₂AsO₃H₂] and dimethylarsinic acid [(CH₃)₂AsO₂H] is usually the major detoxification mechanism for inorganic pentavalent arsenates and trivalent arsenites in mammals. Methylated arsenicals rapidly clear from all tissues, except perhaps the thyroid (Marafante et al. 1985; Vahter and Marafante 1985; Yamauchi et al. 1986). Methylated arsenicals are probably common in nature. Methylation of arsenic (unlike methylation of mercury) greatly reduces toxicity and is a true detoxification process (Woolson 1975; Hamasaki et al. 1995; Aposhian et al. 1997). Before methylation (which occurs largely in the liver), As⁺⁵ is reduced to As⁺³ — the kidney being an important site for this transformation (Belton et al. 1985). Arsenate reduction and subsequent methylation are rapid: both arsenite and dimethylarsinate were present in hamster (*Cricetus* sp.) plasma only 12 min postinjection of inorganic As⁺⁵ (Hanlon and Ferm 1986c). Demethylation of methylated arsenicals formed *in vivo* has not yet been reported (USEPA 1980). Although terrestrial biota usually contain much lower total concentrations of arsenic than marine biota, metabolism of arsenic is similar in marine and terrestrial systems (Irgolic et al. 1998).

Toxic effects of organoarsenicals are exerted by initial metabolism to the trivalent arsenoxide form, and then by reaction with sulfhydryl groups of tissue proteins and enzymes to form an arylbis (organylthio) arsine (NAS 1977). This form, in turn, inhibits oxidative degradation of carbohydrates and decreases cellular ATP, the energy-storage molecule of the cell (NRCC 1978). Among the organoarsenicals, those physiologically most injurious are methylarsonous acid [CH₃As(OH)₂] and dimethylarsinous acid [(CH₃)₂AsOH] (Knowles and Benson 1984b). The enzyme inhibitory forms of organoarsenicals (arsionous acid) are formed from arsenous acid and the corresponding arsonic acids by a wide variety of enzymes and subcellular particles (Knowles and Benson 1984a). Organoarsenicals used as growth promoters and drugs are converted to more easily excreted (and sometimes more toxic) substances, although most organoarsenicals are eliminated without being

converted to inorganic arsenic or to demethylarsinic acids (Pershagen and Vahter 1979; Edmonds et al. 1993).

28.4 ESSENTIALITY, SYNERGISM, AND ANTAGONISM

Limited data are available on the beneficial, protective, and essential properties of arsenic and on its interactions with other chemicals. Arsenic apparently behaves more like an environmental contaminant than as a nutritionally essential mineral (NAS 1977). Nevertheless, low doses (<2 µg/day) of arsenic stimulated growth and metamorphosis in tadpoles and increased viability and cocoon yield in silkworm caterpillars (NAS 1977). Arsenic deficiency has been observed in rats: signs include rough haircoat, low growth rate, decreased hematocrit, increased fragility of red cells, and enlarged spleen (NAS 1977). Similar results have been documented in goats and pigs fed diets containing less than 0.05 mg As/kg (NAS 1977). In these animals, reproductive performance was impaired, neonatal mortality was increased, birth weight was lower, and weight gains in second-generation animals were decreased. These effects were not evident in animals fed diets containing 0.35 mg As/kg (NAS 1977; ATSDR 1992).

The use of phenylarsonic feed additives to promote growth in poultry and swine and to treat specific diseases does not seem to constitute a hazard to the animal or to its consumers. Animal deaths and elevated tissue arsenic residues occur only when the arsenicals are fed at excessive dosages for long periods (NAS 1977). Arsenic can be detected at low levels in tissues of animals fed organoarsenicals, but it is rapidly eliminated when the arsenicals are removed from the feed for the required 5-day period before marketing (Woolson 1975).

Selenium and arsenic are antagonists in several animal species. Dietary arsenic, as arsenate, alleviates the toxic effects of selenium, as seleno-DL-methionine, on mallard (*Anas platyrhynchos*) reproduction and duckling growth and survival (Stanley et al. 1994). Mallard ducklings fed arsenate in the diet at 200 mg As/kg ration were protected against the toxic effects of 60 mg Se/kg ration as selenomethionine, including selenium-induced mortality, impaired growth, hepatic lesions, and enzyme disruptions (Hoffman et al. 1992). In rats, dogs, swine, cattle, and poultry, the arsenic protects against selenium poisoning if arsenic is administered in the drinking water and selenium through the diet (NAS 1977; NRCC 1978; Pershagen and Vahter 1979). Inorganic arsenic compounds decrease the toxicity of inorganic selenium compounds by increasing biliary excretion (NRCC 1978). However, in contrast to antagonism shown by inorganic arsenic/inorganic selenium mixtures, the toxic effects of naturally methylated selenium compounds (trimethylselenonium chloride and dimethyl selenide) are markedly enhanced by inorganic arsenicals (NRCC 1978).

The toxic effects of arsenic can be counteracted with:

1. Saline purgatives
2. Various demulcents that coat irritated gastrointestinal mucous membranes
3. Sodium thiosulfate (NAS 1977)
4. Mono- and dithiol-containing compounds and 2,3-dimercaptopropanol (Pershagen and Vahter 1979)

Arsenic uptake in rabbit intestine is inhibited by phosphate, casein, and various metal-chelating agents (USEPA 1980). Mice and rabbits are significantly protected against sodium arsenite intoxication by *N*-(2,3-dimercaptopropyl)phthalimidic acid (Stine et al. 1984). Conversely, the toxic effects of arsenite are potentiated by excess dithiols, cadmium, and lead, as evidenced by reduced food efficiency and disrupted blood chemistry in rodents (Pershagen and Vahter 1979).

Arsenic effectively controls filariasis in cattle; new protective uses are under investigation. The control of parasitic nematodes (*Parafilaria bovicola*) in cattle was successful after 30 weekly treatments in plunge dips containing 1600 mg As₂O₃/L. However, the muscle of treated cattle

contained up to 1.3 mg As/kg, or 12 times the amount in controls (Nevill 1985). Existing anionic organic arsenicals used to control tropical nematode infections in humans have sporadic and unacceptable lethal side effects. Cationic derivatives have been synthesized in an attempt to avoid the side effects and have been examined for effects on adult nematodes (*Brugia pahangi*) in gerbils (*Meriones unguiculatus*). All arsenicals were potent filaricides; the most effective compounds tested killed 95% of adult *B. pahangi* after five daily subcutaneous injections of 3.1 mg As/kg body weight (Denham et al. 1986).

Animals previously exposed to sublethal levels of arsenic may develop tolerance to arsenic on reexposure. Although the mechanism of this process is not fully understood, it probably includes the efficiency of *in vivo* methylation processes (USEPA 1980). For example, resistance to toxic doses of As⁺³ or As⁺⁵ increases in mouse fibroblast cells pretreated with a low As⁺³ concentration (Fischer et al. 1985). Also, growth is better in arsenic-conditioned mouse cells in the presence of arsenic than in previously unexposed cells, and inorganic arsenic is more efficiently methylated. *In vivo* biotransformation and excretion of inorganic arsenic as monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) have been demonstrated in a number of mammalian species, including humans. It seems that cells may adapt to arsenic by increasing the biotransformation rate of the element to methylated forms, such as MMA and DMA (Fischer et al. 1985). Pretreatment of Chinese hamster (*Cricetus* spp.) ovary cells with sodium arsenite provided partial protection against adverse effects of methyl methanesulfonate (MMS) and may even benefit the MMS-treated cells. However, posttreatment dramatically increases the cytotoxic, clastogenic, and mitotic effects induced by MMS (Lee et al. 1986b).

Although arsenic is not an essential plant nutrient, small yield increases have sometimes been observed at low soil arsenic levels, especially for tolerant crops such as potatoes, corn, rye, and wheat (Woolson 1975). Arsenic phytotoxicity of soils is reduced with increasing lime, organic matter, iron, zinc, and phosphates (NRCC 1978). In most soil systems, the chemistry of As becomes the chemistry of arsenate; the estimated half-time of arsenic in soils is about 6.5 years, although losses of 60% in 3 years and 67% in 7 years have been reported (Woolson 1975). Additional research is warranted on the role of arsenic in crop production, and in nutrition, with special reference to essentiality for aquatic and terrestrial wildlife.

28.5 CONCENTRATIONS IN FIELD COLLECTIONS

28.5.1 General

In abundance, arsenic ranks 20th among the elements in the earth's crust (1.5 to 2 mg/kg), 14th in seawater, and 12th in the human body (Woolson 1975). It occurs in various forms, including inorganic and organic compounds and trivalent and pentavalent states (Pershagen and Vahter 1979). In aquatic environments, higher arsenic concentrations are reported in hot springs, in groundwaters from areas of thermal activity or in areas containing rocks with high arsenic content, and in some waters with high dissolved salt content (NAS 1977). Most of the other elevated values reported in lakes, rivers, and sediments are probably due to anthropogenic sources, which include smelting and mining operations; combustion of fossil fuel; arsenical grasshopper baits; synthetic detergent and sewage sludge wastes; and arsenical defoliants, herbicides, and pesticides (NAS 1977). Most living organisms normally contain measurable concentrations of arsenic, but except for marine biota, these are usually less than 1 mg/kg fresh weight. Marine organisms, especially crustaceans, may contain more than 100 mg As/kg dry weight, usually as arsenobetaine, a water-soluble organoarsenical that poses little risk to the organism or its consumer. Plants and animals collected from naturally arseniferous areas or near anthropogenic sources may contain significantly elevated tissue residues of arsenic. Additional and more detailed information on background concentrations

of arsenic in abiotic and living resources has been given by NAS (1977), Hall et al. (1978), NRCC (1978), USEPA (1980), Jenkins (1980), Eisler (1981, 1994), and Phillips (1990).

28.5.2 Nonbiological Samples

Arsenic is a major constituent of at least 245 mineral species, of which arsenopyrite is the most common (NAS 1977). In general, background concentrations of arsenic are 0.2 to 15 mg/kg in the lithosphere, 0.005 to 0.1 µg/m³ in air, <10 µg/L in water, and <15 mg/kg in soil (NRCC 1978; ATSDR 1992). The commercial use and production of arsenic compounds have raised local concentrations in the environment far above the natural background concentrations ([Table 28.1](#)).

Weathering of rocks and soils adds about 45,000 tons of arsenic to the oceans annually, accounting for less than 0.01 mg/L on a global basis (NRCC 1978). However, arsenic inputs to oceans have increased during the past century, both from natural sources and as a result of industrial use, agricultural and deforestation activities, emissions from coal and oil combustion, and loss during mining of metal ores. If present activities continue, arsenic concentrations in oceanic surface waters will have increased overall by about 2% by the year 2000, with most of the increased burden in estuaries and coastal oceans (e.g., Puget Sound, Washington; the Tamar, England; and the Tejo, Portugal) (Sanders 1985). Estimates of the residence times of arsenic are 60,000 years in the ocean and 45 years in a freshwater lake (NRCC 1978). In the hydrosphere, inorganic arsenic occurs predominantly as As⁺⁵ in surface water, and significantly as As⁺³ in groundwater containing high levels of total arsenic. The main organic species in freshwater are methylarsonic acid and dimethylarsinic acid, and these are usually present in lower concentrations than inorganic arsenites and arsenates (Pershagen and Vahter 1979). Total arsenic concentrations in surface water and groundwater are usually <10 µg/L. In certain areas, however, levels above 1 mg/L have been recorded (Pershagen and Vahter 1979).

In air, most arsenic particulates consist of inorganic arsenic compounds, often as As⁺³. Burning of coal and arsenic-treated wood, and smelting of metals are major sources of atmospheric arsenic contamination (i.e., >1 µg/m³). In general, atmospheric arsenic levels are higher in winter, due to increased use of coal for heating (Pershagen and Vahter 1979).

The main carrier of arsenic in rocks and in most types of mineral deposits is iron pyrite (FeS₂), which may contain >2000 mg As/kg (NRCC 1978). In localized areas, soils are contaminated by arsenic oxide fallout from smelting ores (especially sulfide ores) and combustion of arsenic-rich coal (Woolson 1975).

Arsenic in lacustrine sediment columns is subject to control by diagenetic processes and adsorption mechanisms, as well as anthropogenic influences (Farmer and Lovell 1986; Farag et al. 1995). For example, elevated levels of arsenic in surface or near-surface sediments may have several causes (Farmer and Lovell 1986), including natural processes (Loch Lomond, Scotland) and human activities such as smelting (Lake Washington, Washington; Kelly Lake, Ontario, Canada), manufacture of arsenical herbicides (Brown's Lake, Wisconsin), and mining operations (Northwest Territories, Canada; Clark Fork River, Montana). Elevated levels of arsenic in sediments of the Wailoa River, Hawaii, are the result of As₂O₃ applied as an anti-termite agent between 1932 and 1963. These elevated levels are found mainly in anaerobic sediment regions where the chemical has been relatively undisturbed by activity. Low levels of arsenic in the biota of the Wailoa River estuary suggest that arsenic is trapped in the anaerobic sediment layers (Hallacher et al. 1985).

Arsenic geochemistry in Chesapeake Bay, Maryland, depends on anthropogenic inputs and phytoplankton species composition (Sanders 1985). Inputs of anthropogenic arsenic into Chesapeake Bay are estimated at 100 kg daily, or 39 tons/year — probably from sources such as unreported industrial discharges, use of arsenical herbicides, and from wood preservatives (Sanders 1985). The chemical form of the arsenic in solution varies seasonally and along the axis of the bay. Arsenic is present only as arsenate in winter, but substantial quantities of reduced and methylated forms are present in summer in different areas. The forms and distribution patterns of arsenic

during the summer suggest that separate formation processes exist. Arsenite, present in low salinity regions, may have been formed by chemical reduction in anoxic, subsurface waters and then mixed into the surface layer. Methylated arsenicals are highly correlated with standing crops of algae. One particular form, methylarsonate, is significantly correlated with the dominant alga, *Chroomonas*. Since both arsenic reactivity and toxicity are altered by transformation of chemical form, the observed variations in arsenic speciation have considerable geochemical and ecological significance (Sanders 1985).

Table 28.1 Total Arsenic Concentrations in Selected Nonbiological Materials

Material and Units (in parentheses)	Concentration ^a	Reference ^b
AIR (µg/m³)		
Remote areas	<0.02	1
Urban areas	(0.0–0.16)	1
Near smelters		
U.S.S.R.	(0.5–1.9)	2
Texas	Max. 1.4	2
Tacoma, Washington	Max. 1.5	2
Romania	Max. 1.6	2
Germany	(0.9–1.5)	2
Coal-fired power plant, Czechoslovakia	(19–69)	3
Orchard spraying of Pb arsenate	Max. 260,000	3
Near U.S. cotton gin burning vegetation treated with arsenic	Max. 400	3
DRINKING WATER (mg/L)		
Nationwide, U.S.	2.4 (0.5–214)	4
Fairbanks, Alaska	224 (1–2450)	4
Bakersfield, California	(6–393)	4
Nevada, 3 communities	(51–123)	4
Mexico, from plant producing As ₂ O ₃	(4000–6000)	2
Japan, near factory producing arsenic sulfide	3000	2
Ghana, near gold mine	1400	2
Minnesota, contaminated by residual arsenical grasshopper bait	(11,800–21,000)	1
Methylated arsenicals use areas, U.S.	Usually <0.3 (0.01–1.0)	5
DUST (mg/kg)		
Tacoma, Washington		
Near smelter	1300	1
Remote from smelter	70	1
FOSSIL FUELS (mg/kg)		
Coal		
Canada	4 (0.3–100)	3
United States	5	2
Czechoslovakia	Max. 1500	2
Worldwide	13 (0.0–2000)	1
Coal ash	(<20–8000)	3
Flyash	(2.8–200)	3
Petroleum	0.2	3
Petroleum ash	Max. 100,000	3
Automobile particulates	298	3

Table 28.1 (continued) Total Arsenic Concentrations in Selected Nonbiological Materials

Material and Units (in parentheses)	Concentration ^a	Reference ^b
GROUNDWATER (μg/L)		
Near polymetallic sulfide deposits	Max. 400,000	3
Near gold mining activities	>50	2
U.S., Atlantic coastal plain	Usually <10	2, 20
U.S., Southwest and New England	17.9 (0.01–800)	3, 20
LAKE WATER (μg/L)		
Dissolved solids		
<2000 mg/L	(0.0–100)	6
>2000 mg/L	(0.1–2000)	6
Lake Superior	(0.1–1.6)	6
Japan, various	(0.2–1.9)	6
Germany, Elbe River	(20–25)	6
Searles Lake, California	(198,000–243,000)	1, 4
California, other lakes	(0.0–100)	1, 4
Michigan	Max. 2.4	1, 4
Wisconsin	(4–117)	1, 4
Florida	Max. 3.6	1, 4
Lake Chataqua, New York	(3.5–35.6)	1, 4
Lake Ohakuri, New Zealand	(30–60)	7
Finfeather Lake, Texas	Max. 240,000	8
Thermal waters, worldwide	Usually 20–3800; Max. 276,000	1, 2, 3, 9
RAIN (μg/L)		
Canada	(0.01–5)	3
Rhode Island	0.8	1
Seattle, Washington	17	1
RIVER WATER (μg/L)		
Polluted, U.S.	Max. 6000	4
Nonpolluted, U.S.	Usually <5	4
Nationwide, U.S., 1974–1981		
25th percentile	<1	10
50th percentile	1	10
75th percentile	3	10
ROCK (mg/kg)		
Limestones	1.7 (0.1–20)	1
Sandstones	2 (0.6–120)	1
Shales and clays	14.5 (0.3–490)	1
Phosphates	22.6 (0.4–188)	1
Igneous, various	1.5–3 (0.06–113)	1
SEAWATER (μg/L)		
Worldwide	2 (0.15–6)	6
Pacific Ocean	(1.4–1.8)	11
Atlantic Ocean	(1.0–1.5)	11
South Australia		
Total dissolved As	1.3 (1.1–1.6)	12
As ⁺⁵	1.29	12
As ⁺³	0.03	12
Particulate As	<0.0006	12

Table 28.1 (continued) Total Arsenic Concentrations in Selected Nonbiological Materials

Material and Units (in parentheses)	Concentration^a	Reference^b
U.K., Beaulieu estuary		
Water temperature <12°C		
Inorganic arsenic	(0.4–0.9)	13
Suspended arsenic	(0.02–0.24)	13
Organoarsenicals	(0.19–0.75)	13
Water temperature >12°C		
Inorganic arsenic	(0.6–1.1)	13
Suspended arsenic	(0.2–0.6)	13
Organoarsenicals	ND	13
SEDIMENTS (mg/kg dry weight)		
Near sewer outfall	35	3
From areas contaminated by smelters, arsenical herbicides, or mine tailings		
Surface	(198–3500)	1, 7, 9, 14, 15
Subsurface	(12–25)	1, 7, 9, 14, 15
Upper Mississippi River	2.6 (0.6–6.2)	16
Lake Michigan	(5–30)	1
Naturally elevated	>500	1, 9
Oceanic	33.7 (<0.4–455)	3
Lacustrine	Usually 5–26.9; Max. 13,000	3
SNOW (mg/kg)		
Near smelter	>1000	3
SOIL PORE WATERS (µg/L)		
Mineralized areas		
Arsenate	(79–210)	17
Arsenite	(2–11)	17
Monomethyl arsonic acid (MMAA)	(4–22)	17
Total arsenic	(93–240)	17
Unmineralized areas		
Arsenate	(18–49)	17
Arsenite	(1–7)	17
MMAA	<1	17
Total arsenic	(13–59)	17
SOILS (mg/kg dry weight)		
U.S., uncontaminated	7.4	18
Worldwide, uncontaminated	7.2	18
Canada		
Near gold mine		
Air levels 3.9 mg As/m ³	21,213	3
80 km distant	(10–25)	3
England		
Near arsenic refinery	156	19
Reference site	5	19
Near smelter		
Japan	Max. 2470	2
Tacoma, Washington	Max. 380	2
Treated with arsenical pesticides		
U.S.	165 (1–2554)	6
Canada	121	6

Table 28.1 (continued) Total Arsenic Concentrations in Selected Nonbiological Materials

Material and Units (in parentheses)	Concentration ^a	Reference ^b
SYNTHETIC DETERGENTS (mg/kg)		
Household, heavy duty	(1–73)	1, 2
^a Concentrations are listed as mean, minimum–maximum (in parentheses), and maximum (Max.).		
^b 1, NAS 1977; 2, Pershagen and Vahter 1979; 3, NRCC 1978; 4, USEPA 1989; 5, Hood 1985; 6, Woolson 1975; 7, Freeman et al. 1986; 8, Sorensen et al. 1985; 9, Farmer and Lovell 1986; 10, Smith et al. 1987; 11, Sanders 1980; 12, Maher 1985a; 13, Howard et al. 1984; 14, Hallacher et al. 1985; 15, Takamatsu 1985; 16, Wiener et al. 1984; 17, Haswell et al. 1985; 18, Dudas 1984; 19, Ismail and Roberts 1992; 20, Welch et al. 1998.		

28.5.3 Biological Samples

Background arsenic concentrations in living organisms are usually <1 mg/kg fresh weight in terrestrial flora and fauna, birds, and freshwater biota. These levels are higher, sometimes markedly so, in biota collected from mine waste sites, arsenic-treated areas, near smelters and mining areas, near areas with high geothermal activity, and near manufacturers of arsenical defoliants and pesticides (Table 28.2). For example, bloater (*Coregonus hoyi*) collected in Lake Michigan near a facility that produced arsenical herbicides consistently had the highest (1.5 to 2.9 mg As/kg fresh weight whole body) arsenic concentrations measured in freshwater fishes in the United States between 1976 and 1984 (Schmitt and Brumbaugh 1990). Marine organisms normally contain arsenic residues of several to more than 100 mg/kg dry weight (Lunde 1977). However, as will be discussed later, these concentrations present little hazard to the organism or its consumers.

Arsenic concentrations in tissues of marine biota show a wide range of values, being highest in lipids, liver, and muscle tissues, and varying with the age of the organism, geographic locale, and proximity to anthropogenic activities (Table 28.2). In general, tissues with high lipid content contained high levels of arsenic. Crustacean tissues sold for human consumption and collected in U.S. coastal waters usually contained 3 to 10 mg As/kg fresh weight (Hall et al. 1978), or 1 to 100 mg/kg dry weight (Fowler and Unlu 1978), and were somewhat higher than those reported for finfish and molluscan tissues. Marine finfish tissues usually contained 2 to 5 mg As/kg fresh weight (Table 28.2). However, postmortem reduction of As⁺⁵ to As⁺³ occurs rapidly in fish tissues (Reinke et al. 1975), suggesting a need for additional research in this area. Maximum arsenic values recorded in elasmobranchs (mg/kg fresh weight) were 30 in the muscle of a shark (*Mustelus antarcticus*) and 16.2 in the muscle of a ray (*Raja* sp.) (Eisler 1981). The highest arsenic concentration recorded in a marine mammal, 2.8 mg As/kg fresh weight lipid, was from a whale (Eisler 1981).

Arsenic appears to be elevated in marine biota because of their ability to accumulate arsenic from seawater or food sources — and not because of localized pollution (Maher 1985b). The great majority of arsenic in marine organisms exists as water-soluble and lipid-soluble organoarsenicals that include arsenolipids, arenosugars, arsenocholine, arsenobetaine [(CH₃)₃AsCH₂COOH], monomethylarsonate [CH₃AsO(OH)₂], and demethylarsinate [(CH₃)₂AsO(OH)], as well as other forms (Edmonds et al. 1993). There is no convincing hypothesis to account for the existence of all the various forms of organoarsenicals found in marine organisms. One suggested hypothesis is that each form involves a single anabolic/catabolic pathway concerned with the synthesis and turnover of phosphatidylcholine (Phillips and Depledge 1986). Arenosugars (arsenobetaine precursors) are the dominant arsenic species in brown kelp (*Ecklonia radiata*), giant clam (*Tridacna maxima*), shrimp (*Pandalus borealis*), and ivory shell (*Buccinum striatum*) (Shiomii et al. 1984a, 1984b; Francesconi et al. 1985; Matsuto et al. 1986; Phillips and Depledge 1986). For most marine species, however, there is general agreement that arsenic exists primarily as arsenobetaine, a water-soluble organoarsenical that has been identified in tissues of western rock lobster (*Panulirus cygnus*),

American lobster (*Homarus americanus*), octopus (*Paroctopus* sp.), sea cucumber (*Stichopus japonicus*), blue shark (*Prionace glauca*), sole (*Limanda* sp.), squid (*Sepioteuthis australis*), prawn (*Penaeus latisulcatus*), scallop (*Pecten alba*), and many other species (including teleosts, molluscs, tunicates, and crustaceans) (Shiomii et al. 1984b; Francesconi et al. 1985; Hanaoka and Tagawa 1985a, 1985b; Maher 1985b; Norin et al. 1985; Matsuto et al. 1986; Ozretic et al. 1990; Phillips 1990; Kaise and Fukui 1992; Edmonds et al. 1993). Degradation of arsenobetaine in muscle and liver of the star spotted shark (*Mustelus manazo*) to inorganic arsenic occurs in a natural environment and suggests that arsenobetaine bioconverted from inorganic arsenic in seawater is degraded to original inorganic arsenic. About 13% of the arsenobetaine in shark muscle and 4% in liver was degraded to inorganic arsenic within 40 days (Hanaoka et al. 1993). The potential risks associated with consumption of seafoods containing arsenobetaine seem to be minor. The chemical was not mutagenic in the bacterial *Salmonella typhimurium* assay (Ames test), had no effect on metabolic inhibition of Chinese hamster ovary cells at 10,000 mg/L, and showed no synergism or antagonism on the action of other contaminants (Jongen et al. 1985). Arsenobetaine was not toxic to mice at oral doses of 10,000 mg/kg body weight during a 7-day observation period and was rapidly absorbed from the gastrointestinal tract and rapidly excreted in urine without metabolism, owing to its high polar and hydrophilic characteristics (Kaise et al. 1985; Kaise and Fukui 1992).

Shorebirds (seven species) wintering in the Corpus Christi, Texas, area contained an average of 0.3 mg As/kg fresh weight in livers (maximum of 1.5 mg/kg), despite the presence of smelters and the heavy use of arsenical herbicides and defoliants. These values probably reflect normal background concentrations (White et al. 1980). Similar arsenic levels were reported in livers of brown pelicans (*Pelecanus occidentalis*) collected from South Carolina (Blus et al. 1977). Bone arsenic concentrations in 23 species of birds collected in southwestern Russia during 1993 to 1995 ranged from 0.1 to 1.7 mg As/kg DW; arsenic concentrations were similar for terrestrial and aquatic birds, and for urban and rural environments (Lebedeva 1997). The highest arsenic concentration recorded in seemingly unstressed coastal birds was 13.2 mg/kg fresh weight lipids (Table 28.2). This tends to corroborate the findings of others that arsenic concentrates in lipid fractions of marine plants, invertebrates, and higher organisms. An abnormal concentration of 16.7 mg As/kg fresh weight was recorded in the liver of an osprey (*Pandion haliaetus*) from the Chesapeake Bay region (Wiemeyer et al. 1980). This bird was alive but weak, with serious histopathology including the absence of subcutaneous fat, presence of serous fluid in the pericardial sac, and disorders of the lung and kidney. The bird died shortly after collection. Arsenic concentrations in the livers of other ospreys collected in the same area were usually <1.5 mg As/kg fresh weight. Chicks of the avocet (*Recurvirostra americana*) reared from eggs taken near arsenic-contaminated ponds in California (127 to 1100 µg As/L) had reduced hatch, as well as impaired growth and immune function, when compared to chicks from a reference site (29 µg As/L). Other contaminants present included boron and selenium, although the authors concluded that arsenic played a significant role in observed effects (Fairbrother et al. 1994).

Arsenic concentrations in tissues of small mammals (field mouse, *Apodemus sylvaticus*; bank vole, *Clethrionomys glareolus*; field vole, *Microtus agrestis*; common shrew, *Sorex araneus*) from the vicinity of an English arsenic refinery were usually less than 1 mg/kg FW and did not reflect arsenic levels of the surrounding soil or vegetation (Ismail and Roberts 1992). In general, mean arsenic concentrations were highest in spleen, followed — in descending order — by bone, heart, kidney, brain, muscle, and liver (Ismail and Roberts 1992). For human adults, seafood contributes 74% to 96% of the total daily arsenic intake, and rice and rice cereals most of the remainder. For infants, 41% of the estimated total arsenic intakes arise from seafood and 34% from rice and rice cereals (Tao and Bolger 1998). Effective biomarkers of arsenic exposure in humans include elevated arsenic concentrations in hair, fingernails, and especially urine (Lin et al. 1998). In Taiwan, urinary levels of inorganic and organic arsenic metabolites are associated with previous exposure to high-arsenic artesian well water (Hsueh et al. 1998). Humans who had previously been exposed to high-arsenic drinking water and had switched to tap water containing <50 µg total As/L had — after 30 years — elevated levels of arsenic in urine, especially MMA and DMA (Hsueh et al. 1998).

Table 28.2 Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals
 (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
TERRESTRIAL PLANTS		
Colonial bentgrass, <i>Agrostis tenuis</i>		
On mine waste site	1480 DW; Max. 3470 DW	1
On low arsenic soil	(0.3–3) DW	1
Scotch heather, <i>Calluna vulgaris</i>		
On mine waste site	1260 DW	1
On low arsenic soil	0.3 DW	1
Coontail, <i>Ceratophyllum demersum</i>		
From geothermal area, New Zealand	(20–1060) DW	1
Cereal grains		
From arsenic treated areas	Usually <3 DW; Max. 252 DW	2
Nontreated areas	Usually <0.5 DW; Max. 5 DW	2
Grasses		
From arsenic treated areas	(0.5–60,000) DW	2
Nontreated areas	(0.1–0.9) DW	2
Apple, <i>Malus sylvestris</i>		
Fruit	<0.1 FW; <1.8 DW	1
Alfalfa, <i>Medicago sativa</i>		
U.S.	1.6 FW	1
Montana, smelter area	(0.4–5.7) FW	1
Mushrooms; Austria; 1995; near arsenic roasting facility in operation for about 500 years and closed for about 100 years; soil had 730 mg total As/kg DW		
<i>Collybia maculata</i>		
Total	30.0 DW	60
Arsenobetaine	>27.0 DW	60
<i>Collybia butyracea</i>		
Total	10.9 DW	60
Arsenobetaine	8.8 DW	60
Dimethylarsinic acid	1.9 DW	60
<i>Amantia muscaria</i>		
Total	21.9–22.0 DW	60, 61
Arsenate	Trace–0.3 DW	60, 61
Arsenite	Trace–0.4 DW	60, 61
Arsenobetaine	Max. 15.1 DW	60
Arsenocholine	2.5–2.7 DW	60, 61
Dimethylarsinic acid	Trace–0.7 DW	60, 61
Tetramethylarsonium salt	0.5–0.8 DW	60, 61
White spruce, <i>Picea alba</i>		
Arsenic-contaminated soil		
Branch	(2.8–14.3) DW	1
Leaf	(2.1–9.5)	1
Trunk	(0.3–55) DW	1
Root	(45–130) DW	1
Control site		
All samples	<2.4 DW	1
Pine, <i>Pinus silvestris</i> , needles		
Near U.S.S.R. metals smelter; soil levels 120.0 mg As/kg	22 FW	3
Peppers, <i>Piper spp.</i> ; China		
Fresh	<1 FW	56
Dried over arsenic-rich (35 g As/kg) coal fires	500 DW	56
Trees, nontreated areas	Usually <1 DW	2
Lowbush blueberry, <i>Vaccinium angustifolium</i>		
Maine, leaf		
Arsenic-treated soil	(6.8–15) DW	1

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Control	0.8 DW	1
Various species		
From uncontaminated soils	(<0.01–5) DW	2
From arsenic-impacted (80 mg/kg) soils	1.2 (<0.2–5.8) DW	4
Vegetables		
From arsenic-treated areas	Usually <3 DW; Max. 145 DW	2
Nontreated areas	Usually <1 DW; Max. 8 DW	2
Vegetation		
Near gold mine, Canada		
Air levels up to 3.9 mg As/m ³	Max. 11,438 DW	5
80 km distant	(12–20) DW	5
Near arsenic refinery (vs. control site), England	37 DW vs. 0.2 DW	54

FRESHWATER PLANTS

Aquatic Plants		
Arsenic-treated areas	(20–1450) DW	2
Untreated areas	(1.4–13) DW	2
Irish moss, <i>Chondrus crispus</i>		
Whole	(5–12) DW	1
Pondweeds, <i>Potamogeton</i> spp.		
Whole		
Near geothermal area	(11–436) DW	1
Control site	<6 DW	1
Widgeongrass, <i>Ruppia maritima</i>		
From Kern National Wildlife Refuge, California, contaminated by agricultural drainwater of 12–190 µg As/L	Max. 430 DW	32

FRESHWATER FISHES

Alewife, <i>Alosa pseudoharengus</i>		
Whole, Michigan	0.02 FW	1
Muscle, Wisconsin	0 FW	1
California; San Joaquin River; September–November 1986; whole fish		
Common carp, <i>Cyprinus carpio</i>	0.2–0.5 (0.1–0.6) DW	50
Mosquitofish, <i>Gambusia affinis</i>	0.5–1.1 (0.4–1.6) DW	50
Bluegill, <i>Lepomis macrochirus</i>	0.3–1.0 (0.2–1.3) DW	50
Largemouth bass, <i>Micropterus salmoides</i>	0.2–0.3 DW	50
Sacramento blackfish, <i>Orthodon microlepidotus</i>	0.7 DW	50
White sucker, <i>Catostomus commersoni</i>		
Muscle	(0.03–0.13) FW	1
Whole	(0.05–0.16) FW	1
Common carp, <i>Cyprinus carpio</i>		
Upper Mississippi River, 1979		
Whole	0.4 (0.2–0.6) DW	6
Liver	0.4 (0.3–1) DW	6
Nationwide		
Whole	0.05 FW	1
Muscle	(0.0–0.2) FW	1
Northern pike, <i>Esox lucius</i>		
Muscle		
Canada	(0.05–0.09) FW	1
Great Lakes	<0.05 FW	1
Sweden	0.03 FW	1
New York	<0.1 FW	1
Wisconsin	<0.01 FW	1

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Fish, various species		
Whole	Max. 1.9 FW	2
Whole	(0.04–0.2) FW	7
Netherlands, 1977–1984		
Muscle	(0.04–0.15) FW	8
Nationwide, U.S., whole fish		
1976–1977	0.27 FW; Max. 2.9 FW	9, 33
1978–1979	0.16 FW; Max. 2.1 FW	33
1980–81	0.15 FW; Max. 1.7 FW	33
1984	0.14 FW; Max. 1.5 FW	33
Near smelter (water arsenic 2.3–2.9 mg/L)		
Muscle, 3 species		
Total arsenic	0.05–0.24) FW	10
Inorganic arsenic	(0.01–0.02) FW	10
Liver, 2 species		
Total arsenic	0.15 FW	10
Inorganic arsenic	0.01 FW	10
Control location (water arsenic <0.5 mg/L)		
Muscle		
Total arsenic	(0.06–0.09) FW	10
Inorganic arsenic	<0.03 FW	10
Liver		
Total arsenic	0.09 FW	10
Inorganic arsenic	<0.01 FW	10
Channel catfish, <i>Ictalurus punctatus</i>		
Muscle		
Native	(0.0–0.3) FW	1
Cultured	(0.2–3.1) FW	1
Whole, nationwide	(<0.05–0.3) FW	1
Green sunfish, <i>Lepomis cyanellus</i> ; liver		
Polluted waters (from manufacturer of arsenical defoliants and pesticides), Texas. Mean water concentration 13.5 mg As/L; sediment content of 4700 mg/kg		
Age 1–2 years	(19.7–64.2) DW	11
Age 3	15 DW	11
Age 4	(6.1–11.5) DW	11
Bluegill, <i>Lepomis macrochirus</i>		
From pools treated with arsenic		
Muscle	1.3 FW	1
Skin and scales	2.4 FW	1
Gills and GI tract	17.6 FW	1
Liver	11.6 FW	1
Kidney	5.9 FW	1
Ovary	8.4 FW	1
Control locations		
All tissues	<0.2 FW	1
Whole		
Nationwide	(<0.05–0.15) FW	1
Upper Mississippi River, 1979	0.3 (0.2–0.4) DW	6
Smallmouth bass, <i>Micropterus dolomieu</i>		
Muscle		
Wisconsin	<0.13 FW	1
Lake Erie	0.22 FW	1
New York	(0.03–0.51) FW	1
Whole, nationwide	(<0.05–0.28) FW	1

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Largemouth bass, <i>Micropterus salmoides</i>		
Whole, nationwide	(<0.05–0.22) FW	1
Muscle		
Wisconsin	(0.0–0.12) FW	1
New York	(0.03–0.16) FW	1
Striped bass, <i>Morone saxatilis</i>		
Muscle	(0.2–0.7) FW	1
Coho salmon, <i>Oncorhynchus kisutch</i>		
Muscle		
Wisconsin	<0.15 FW	1
Lake Erie	(0.07–0.17) FW	1
New York	<0.5 FW	1
U.S.	0.09 FW	1
Yellow perch, <i>Perca flavescens</i>		
All tissues	<0.16 FW	1
Rainbow trout, <i>Oncorhynchus mykiss</i>		
All tissues	<0.4 FW	1
Atlantic salmon, <i>Salmo salar</i>		
Oil		
Liver	6.7 FW	1
Muscle	(0.8–3.1) FW	1
Brown trout, <i>Salmo trutta</i>		
Kidney; Clark Fork River, Montana vs. reference site	11.3 DW vs. 1.8 DW	37
Lake trout, <i>Salvelinus namaycush</i>		
Whole, nationwide	(0.06–0.68) FW	1
MARINE PLANTS		
Algae		
Green	(0.5–5) DW	2
Brown	Max. 30 DW	2
11 species	(2–58) DW	12
Various species	(10–100) DW	13
Seaweed, <i>Chondrus crispus</i>	5.2 DW	2
Alga, <i>Fucus</i> spp.		
Oil	(6–27) FW	2
Fatty acid	(5–6) FW	2
Brown alga, <i>Fucus vesiculosus</i>		
Whole	(35.2–80) DW	1
Brown alga, <i>Laminaria digitata</i>		
Whole	94 DW	2
Whole	(42–50) DW	1
Oil	(155–221) DW	2
Fatty acid	(8–36) DW	2
Alga, <i>Laminaria hyperborea</i>		
Total arsenic	142 DW	12
Organic arsenic	139 DW	12
Sargassum weed, <i>Sargassum fluitans</i>		
Total arsenic	19.5 FW	7
As ⁺³	1.8 FW	7
As ⁺⁵	17.7 FW	7
Organoarsenicals	0.2 FW	7
Seaweed, <i>Sargassum</i> sp.		
Total arsenic	(4.1–8.7) FW	5
As ⁺³	(0.14–0.35) FW	5

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
As ⁺⁵	(1.9–7.3) FW	5
Organoarsenicals	Max. 0.1 FW	5
Seaweeds		
Whole	(3.8–93.8) DW	2
Whole	(10–109) DW	12
Oil fraction	(5.7–221) FW	12
MARINE MOLLUSCS		
Bivalves, California, 1984–1986, soft parts		
Clam, <i>Corbicula</i> sp.	5.4–11.5 DW	34
Clam, <i>Macoma balthica</i>	7.6–12.1	34
Ivory shell, <i>Buccinum striatissimum</i>		
Muscle		
Total arsenic	38 FW	14
Arsenobetaine	24.2 FW	14
Midgut gland		
Total arsenic	18 FW	14
Arsenobetaine	10.8 FW	14
Oysters, <i>Crassostrea</i> spp.		
Soft parts	(1.3–10) DW; (0.3–3.4) FW	12
American oyster, <i>Crassostrea virginica</i>		
Soft parts	2.9 FW	1
Soft parts	10.3 DW	15
Spindle shells, <i>Hemifusus</i> spp.		
Hong Kong, 1984, Muscle		
Total arsenic	Max. 500 FW	16
Inorganic arsenic	<0.5 FW	16
Limpet, <i>Littorina littorea</i>		
Soft parts		
Near arsenic source	11.5 DW	12
Offshore	4 DW	12
Squid, <i>Loligo vulgaris</i>		
Soft parts	(0.8–7.5) FW	1
Hardshell clam, <i>Mercenaria mercenaria</i>		
Soft parts		
Age 3 years	3.8 DW	12
Age 4 years	4.7 DW	12
Age 10 years	9.3 DW	12
Age 15 years	8.4 DW	12
Molluscs, edible tissues		
Hong Kong, 1976–1978		
Bivalves	(3.2–39.6) FW	17
Gastropods	(19–176) FW	17
Cephalopods	(0.7–5.5)	17
United States.		
6 species	(2–3) FW	18
8 species	(3–4) FW	18
3 species	(4–5) FW	18
4 species	(7–20) FW	18
Yugoslavia, northern Adriatic Sea, summer 1986, 6 species	21–31 FW	35
Mussel, <i>Mytilus edulis</i>		
Soft parts	2.5 (1.4–4.6) FW	8
Soft parts	(1.6–16) DW	12
Scallop, <i>Placopecten magellanicus</i>		
Soft parts	1.6 (1.3–2.4) FW	1

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
MARINE CRUSTACEANS		
Blue crab, <i>Callinectes sapidus</i>		
Florida, whole	7.7 FW	1
Maryland, soft parts	(0.5–1.8) FW	1
Dungeness crab, <i>Cancer magister</i>		
Muscle	6.5 (2.2–37.8) FW	1
Muscle	4 FW	19
Alaskan snow crab, <i>Chinocetes bairdii</i>		
Muscle	7.4 FW	19
Copepods		
Whole	(2–8.2) DW; (0.4–1.3) FW	12
Shrimp, <i>Crangon crangon</i>		
Netherlands, 1977–1984		
Muscle	3 (2–6.8) FW	8
Crustaceans, edible tissues		
Hong Kong, 1976–1978		
Crabs	(5.4–19.1) FW	17
Lobsters	(26.7–52.8) FW	17
Prawns and shrimps	(1.2–44) FW	17
United States		
6 species	(3–5) FW	18
3 species	(5–10) FW	18
4 species	(10–20) FW	18
2 species	(20–30) FW	18
1 species	(40–50) FW	18
American lobster, <i>Homarus americanus</i>		
Muscle	(3.8–7.6) DW; Max. 40.5 FW	1
Hepatopancreas	22.5 FW	1
Whole	(3.8–16) DW; (1–3) FW	12
Stone crab, <i>Menippe mercenaria</i>		
Whole	(9–11.8) FW	1
Deep sea prawn, <i>Pandalus borealis</i>		
Head and shell	68.3 DW	1
Muscle	61.6 DW	1
Oil	42 DW; 10.1 FW	1
Egg	3.7–14 FW	1
Prawns, <i>Pandalus</i> spp.		
Whole	(7.3–11.5) FW	12
Alaskan king crab, <i>Paralithodes camtschatica</i>		
Muscle	8.6 FW	19
Brown shrimp, <i>Penaeus aztecus</i>		
Muscle	(3.1–5.2) FW	1
Whole	0.6 DW	1
White shrimp, <i>Penaeus setiferus</i>		
Muscle		
Mississippi	(1.7–4.4) FW	1
Florida	(2.8–7.7) FW	1
Shrimp, <i>Sergestes lucens</i>		
Muscle		
Total arsenic	5.5 FW	20
Arsenobetaine	4.5 FW	20
Shrimps		
Exoskeleton	15.3 FW	7
Muscle, 2 species	(18.8–41.6) FW; (3.8–128) DW	2

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
MARINE FISHES AND ELASMOBRANCHS		
Whitetip shark, <i>Carcharhinus longimanus</i>		
Muscle	3.1 FW	21
Black sea bass, <i>Centropristes striata</i>		
Muscle	6.4 DW	1
Elasmobranchs		
Muscle		
Sharks	Max. 30 FW	12
Rays	Max. 16.2 FW	12
Roundnose flounder, <i>Eopsetta grigorjewi</i>		
Muscle	20.1 FW	22
Finfishes		
Near metal smelter, water concentration 2.3–2.9 mg As/L		
Muscle, 6 species		
Total arsenic	(0.2–2.6) FW	10
Inorganic arsenic	(0.02–0.1) FW	10
Liver, 4 species		
Total arsenic	(0.4–1.8) FW	10
Inorganic arsenic	(0.02–0.07) FW	10
Control location, water concentration <2.0 mg As/L		
Muscle, 5 species		
Total arsenic	(0.1–1.2) FW	10
Inorganic arsenic	(0.02–0.15) FW	10
Liver, 4 species		
Total arsenic	(0.2–1.5) FW	10
Inorganic arsenic	(0.02–0.05) FW	10
Finfish, Hong Kong, 1976–1978		
Edible tissues	Max. 21.1 FW	17
Finfish, Netherlands, 1977–1984		
Muscle, 4 species	(2.8–10.9) FW	8
Finfish, North America		
Liver		
49 species	(0.7–5) FW	18
26 species	(5–20) FW	18
6 species	(20–50) FW	18
Muscle		
91 species	(0.6–4) FW	18
41 species	(4–8) FW	18
27 species	(8–30) FW	18
6 species	(0.18–0.30) DW	36
4 species		
Total arsenic	(1.4–10) FW	23
Inorganic arsenic	<0.5 FW	23
Whole		
16 species	(1–8) FW	18
Finfish, worldwide		
Various tissues		
Total arsenic	(ND–142) FW	2
Inorganic arsenic	(0.7–3.2) FW	2
Organic arsenic	(3.4–139) FW	2
Atlantic cod, <i>Gadus morhua</i>		
Muscle	2.2 FW	2
Liver	9.8 FW	2

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
North East Irish Sea; total As (<1% inorganic); muscle; sludge disposal site vs. reference site		
Plaice, <i>Pleuronectes platessa</i>	20.5 FW vs. <7.5 FW	39
Whiting, <i>Merlangius merlangus</i>	6.2 FW vs. <4.0 FW	39
Blue pointer, <i>Isurus oxyrinchus</i>		
Muscle	9.5 FW	21
Striped bass, <i>Morone saxatilis</i>		
Muscle	(0.3–0.5) FW; 1.8 DW	12
Liver	0.7 FW	12
Striped mullet, <i>Mugil cephalus</i>		
Viscera	Max. 1.3 FW	24
Norway; Glomma estuary; March–December 1988; muscle		
Atlantic cod	4.1 FW	38
Flounder, <i>Platichthys flesus</i>	5.2 FW	38
English sole, <i>Pleuronectes vetulus</i>		
Muscle	1.1 (0.6–11.5) FW	1
Skate, <i>Raja</i> sp.		
Muscle	16.2 FW	1
Windowpane flounder, <i>Scophthalmus aquosus</i>		
Muscle	(1.4–2.8) FW	1
Spiny dogfish, <i>Squalus acanthias</i>		
Muscle	10 DW	25
Liver	5.7 DW	25
Spleen	9.8 DW	25
Yolk sac	9.1 DW	25
Embryo	2.6 DW	25
Muscle		
Arsenate	<0.03 DW	58
Arsenite	<0.03 DW	58
Arsenobetaine	15.6–16.0 DW	58
Arsenocholine	0.02–0.04 DW	58
Dimethylarsinic acid	0.28–0.49 DW	58
Methylarsonic acid	<0.03 DW	58
Tetramethylarsonium	0.23–0.38 DW	58
Trimethylarsine oxide	<0.03 DW	58
Unknown	0.16–0.32 DW	58

AMPHIBIANS AND REPTILES

Alligator, <i>Alligator mississippiensis</i>		
Egg	(0.05–0.2) FW	1
Southern toad, <i>Bufo terrestris</i> ; adults; whole body		
From coal ash settling basins (sediments with 39.6 mg As/kg DW) vs. reference site (0.3 mg As/kg DW sediment)	1.6 DW vs. 0.2 DW	63
From reference site to settling basin for 7–12 weeks	0.2 DW vs. 0.8–1.2 DW	63
Crocodile, <i>Crocodylus acutus</i>		
Egg	0.2 FW	26
Bullfrog, <i>Rana catesbeiana</i> ; tadpoles; South Carolina; 1997		
With digestive tract		
Body	0.8 FW; 3.9 DW	65
Tail	0.3 FW; 1.8 DW	65
Whole	0.6 FW; 3.1 DW	65
Without digestive tract		
Body without gut	3.3 DW	65
Tail	1.9 DW	65

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Digestive tract	17.3 DW	65
Whole	3.1 DW	65
Frogs, <i>Rana</i> spp.		
All tissues	<0.4 FW	1
Toads, 2 species		
All tissues	<0.05 FW	1
BIRDS		
American black duck, <i>Anas rubripes</i>		
Egg	0.2 FW	12
Ducks, <i>Anas</i> spp.		
All tissues	<0.4 FW	1
Scaup, <i>Aythya</i> spp.		
All tissues	<0.4 FW	1
California; 1986–87; eggs; Merced County vs. Fresno County; mallard, <i>Anas platyrhynchos</i> and gadwall, <i>Anas strepera</i>		
1986	<0.3 FW in 97% of eggs; Max. 0.84 FW	40
1987	All <0.3 FW	40
Canada; Vancouver Island, British Columbia; near copper mine; 1976 vs. 1981–82		
Western grebe, <i>Aechmophorus occidentalis</i> ; liver	1.1 FW vs. 0.08 FW	43
Glaucous-winged gull, <i>Larus glaucescens</i> ; liver	1.6 FW vs. 0.1 FW	43
Marbled murrelet, <i>Synthliboramphus antiquus</i>		
Liver	3.2 FW vs. 0.8 FW	43
Diet, all locations	0.03–0.15 FW	43
Willet, <i>Catoptrophorus semipalmatus</i>		
Southwest Texas; summer 1986; 4 locations; sediments had 2.1–11.0 mg As/kg DW		
Liver	1.3–7.5 (ND–15.0) DW	41
Stomach contents	1.2–2.3 (ND–4.7) DW	41
Gulls, 3 species		
Oil	(0.6–13.2) FW	12
Kenya, Lake Nakuru; 1990 vs. 1970		
White pelican, <i>Pelecanus onocrotalus</i>		
Kidney	0.05 (0.03–0.8) FW vs. 0.009 FW	53
Liver	0.04 FW vs. 0.01 FW	53
White-necked cormorant, <i>Phalacrocorax carbo</i>		
Kidney	0.05 (0.04–0.11) FW vs. no data	53
Liver	0.04 (0.03–0.06) FW vs. no data	53
Lesser flamingo, <i>Phoeniconaias minor</i>		
Kidney	0.06 FW vs. 0.10 FW	53
Liver	0.04 FW vs. 0.07 FW	53
Osprey, <i>Pandion haliaetus</i>		
Liver	Max. 16.7 FW	27
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg		
South Carolina, 1971–72	0.3 (0.08–0.8) FW	28
Florida, 1969–70	0.1 (0.07–0.2) FW	28
Liver, 1971–72, GA, FL, SC		
Found dead	(0.2–1) FW	28
Shot	(0.3–0.9) FW	28
Russia, southwestern region, 1993–95, bone		
Heros, <i>Ardea</i> spp.	0.12 DW	52
21 species	0.15–1.6 DW	52
Hawks, <i>Buteo</i> spp.	1.7 DW	52

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Shorebirds		
Corpus Cristi, Texas; 1976–1977		
Liver, 7 species	(0.05–1.5) FW	29
New Zealand, 5 species		
Feather	<1 FW	12
Liver	Max. 2.6 FW	12
Spain; Ebro Delta bird sanctuary; livers; January–April 1989; found dead		
7 species	ND	42
5 species	0.2–0.5 FW	42
2 species	1.0–1.2 FW	42
Starling, <i>Sturnus vulgaris</i>		
Whole, nationwide, U.S., 1971	(<0.01–0.21) FW	2
Icelandic redshank, <i>Tringa totanus robusta</i>		
Netherlands, 1979–1982		
Feather		
Juveniles	Max. 0.8 FW	30
Adults	(0.5–3.2) FW	30
MAMMALS		
Fin whale, <i>Balaenoptera physalis</i>		
Blubber oil	1.8 FW	1
Cow, <i>Bos bovis</i>		
Downwind from copper smelter		
16–21 km		
Hair	8.9 FW	1
Milk	0.013 FW	1
Blood	0.026 FW	1
60 km		
Hair	0.46 FW	1
Milk	0.002 FW	1
Blood	0.009 FW	1
Controls		
Milk	<0.001 FW	31
Muscle	0.005 FW	31
Liver	(0.008–0.012) FW	31
Kidney	(0.017–0.053) FW	31
Red deer, <i>Cervus elaphus</i> vs. roe deer, <i>Capreolus capreolus</i> ; Slovakia, Europe		
Hair	0.1–0.3 (Max. 1.0) DW vs. 0.1 (Max. 25.2) DW	51
Internal tissues	<0.1 DW vs.<0.1 DW	51
Domestic animals		
All tissues	<0.3 FW	2
Humans, <i>Homo sapiens</i>		
U.S.; 1991–96; total daily intake, in µg		
Age 6–11 months	2	57
Age 2 years	22	57
Age 6 years	19	57
Age 10 years	13	57
14–16-year-old males	15	57
14–16-year-old females	21	57
25–30-year-old males	54	57
25–30-year-old females	26	57
40–45-year-old males	44	57
40–45-year-old females	35	57

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
60–65-year-old males	87	57
60–65-year-old females	68	57
70-year-old male	66	57
70-year-old female	43	57
Finland; urine; drinking water contains 17–980 µg As/L		
Current users	0.058 FW	66
Ex-users (ceased drinking from As-contaminated source 2–4 months previously)	0.017 FW	66
Controls (<1 µg As/L)	0.005 FW	66
Taiwan; urine; more than 20 years after consumption of high As-contaminated well water		
Total	0.267 FW	67
Inorganic	0.086 FW	67
Livestock		
All tissues	<0.6 FW	2
Marine mammals		
Four species; liver		
Total	0.17–2.40 FW	59
Arsenobetaine	0.05–1.7 FW	59
Arsenocholine	0.005–0.044 FW	59
Arsenic acid	<0.001 FW	59
Arsenos acid	<0.001 FW	59
Dimethylarsinic acid	<0.001–0.11 FW	59
Methylarsonic acid	<0.001–0.025 FW	59
Tetramethylarsonium cation		
Pinnipeds	<0.009–0.043 FW	59
Cetaceans	ND	59
Unidentified compound	0.002–0.027 FW	59
Pinnipeds		
All tissues	Max. 1.7 FW	12
Cetaceans		
Muscle	0.4 DW	12
Oil	(0.6–2.8) FW	12
White-tailed deer, <i>Odocoileus virginianus</i>		
New York; found dead		
Kidney	56.0 FW	44
Liver	102.0 FW	44
Tennessee, killed from arsenic herbicide		
Liver	19 FW	1
Kidney	17.8 FW	1
Rumen contents	22.5 FW	1
Harbor seal, <i>Phoca vitulina</i>		
UK, all tissues	<0.3 FW	1
Mammals, (mice, voles, shrews); England; near arsenic refinery		
Spleen	Max. 33.9 FW	54
Brain	Max. 9.7 FW	54
Bone	Max. 9.5 FW	54
Heart	Max. 7.0 FW	54
Kidney	Max. 6.2 FW	54
Liver	Max. 5.2 FW	54
Muscle	Max. 4.4 FW	54
Whole body	Max. 3.2 FW	54
Mexican free-tailed bat, <i>Tadarida brasiliensis</i> ; New Mexico and Oklahoma; May–August 1991; livers	Usually ND; Max. 0.35 FW	45

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Fox, <i>Vulpes</i> sp.		
All tissues	<0.7 FW	1
Wildlife		
All tissues	<1 FW	2
INTEGRATED STUDIES		
Alaska; Cook Inlet; summer 1997; edible portions of seafood products		
Total arsenic	0.6 FW (salmon)–5.0 FW (clams, cod, flounder)	55
Dimethylarsinic acid	0.02–0.6 FW	55
As ⁺³ plus As ⁺⁵	0.001–0.01 FW	55
Monomethylarsinic acid	Trace	55
Germany; near former arsenic roasting facility; total As		
Ants, <i>Formica</i> sp.; whole	12.6 DW	62
Ant-hill material	5420.0 DW	62
Spruce, <i>Picea</i> sp.; needles	1.2 DW	62
Larch, <i>Larix</i> sp.; needles	3.7 DW	62
Korea; near silver and gold mine closed in 1970; surveyed October/November 1997		
Tailings	5000 DW	68
Downstream		
Sediments	Max. 4400 DW	68
Irrigation water	Max. 1.89 FW	68
Rice; mine area vs. reference site		
Grain	Max. 0.6 DW vs. Max. 0.3 DW	68
Stalks and leaves	Max. 9.1 DW vs. Max. 3.6 DW	68
South Texas; Lower Laguna Madre; 1986–87		
Sediments	1.9 (0.4–8.2) DW	46
Shoalgrass, <i>Halodule wrightii</i> ; rhizomes	12.2 (2–25) DW	46
Grass shrimp, <i>Palaemonetes</i> sp.; whole	26.9 (9.7–55.0) DW	46
Brown shrimp, <i>Penaeus aztecus</i> ; whole	17.9 (8.1–50.0) DW	46
Blue crab, <i>Callinectes sapidus</i> ; whole minus legs, carapace and abdomen	18.4 (2.7–50.0) DW	46
Pinfish, <i>Lagodon rhomboides</i> ; whole	9.4 (1.7–20.0) DW	46
Montana; mining waste-contaminated wetland vs. reference site; 1990–92		
Sediments	45.3 DW vs. 5.8 DW	47, 48
Soil	52.5–67.1 DW vs. 7.7 DW	47, 48
Surface water	0.014 FW vs. no data	47, 48
Vegetation		
Above ground		
Forbs	1.1–1.9 DW vs. 0.4–0.5 DW	47, 48
Grasses	6.7 DW vs. 2.1 DW	47, 48
Floating macrophytes	18.9–35.2 DW vs. <0.02 DW	47
Below ground		
Forbs	9.3 DW vs. 2.1 DW	47, 48
Grasses	100.1 DW vs. 6.4 DW	47, 48
Macrophytes	52.0 DW vs. <0.2 DW	47
Invertebrates		
Aquatic		
Arthropods	7.7 DW vs. <0.02 DW	47
Snails	<0.02 DW vs. <0.02 DW	47
Terrestrial		
Grasshoppers	3.9 DW vs. <0.02 DW	47
Earthworms	10.9 DW vs. 1.7 DW	47

Table 28.2 (continued) Arsenic Concentrations in Field Collections of Selected Species of Plants and Animals (Values listed are in mg As/kg fresh weight [FW] or dry weight [DW].)

Ecosystem, Species, and Other Variables	Concentration (mg/kg ^a)	Reference ^b
Fishes, whole	0.15 FW vs. 0.05–0.12 FW	47
Bird eggs	<0.1 DW vs. no data	47
Deer mice, <i>Peromyscus maniculatus</i>		
Carcass	<0.02 FW vs. no data	48
Liver, kidney, gonads	ND vs. no data	48
Meadow vole, <i>Microtus pennsylvanicus</i>		
Carcass	0.25 FW vs. no data	48
Liver, kidney, gonads	ND vs. no data	48
Ontario, Canada; Moira Lake (recipient of mining wastes — including arsenic — since the 1830s); June 1991		
Water	Max. 0.106 FW	49
Sediments	Max. 1000 DW	49
Fishes; 13 species; whole	0.03–0.34 FW	49
Creek chub, <i>Semotilus atromaculatus</i> ; whole	2.4 FW	49
Rock bass, <i>Ambloplites rupestris</i>		
Bone	0.5 FW	49
Intestine	0.6 FW	49
Liver	0.04 FW	49
Muscle	0.08 FW	49
Whole	0.13 (0.07–1.9) FW	49
Taiwan, 1995–96		
Fish; 8 species; muscle	Max. 5.3 DW	64
Shrimp; 2 species; muscle	Max. 5.1 DW	64
Clam, <i>Meretrix lusoria</i> ; soft parts	13.7 (9.5–20.1) DW	64
Pacific oyster, <i>Crassostrea gigas</i> ; soft parts	11.8 (7.2–16.3) DW	64

^a Concentrations are listed as mean, minimum-maximum (in parentheses), nondetectable (ND), and maximum (Max.).

^b 1, Jenkins 1980; 2, NAS 1977; 3, Mankovska 1986; 4, Merry et al. 1986; 5, NRCC 1978; 6, Wiener et al. 1984; 7, Woolson 1975; 8, Vos and Hovens 1986; 9, Lima et al. 1984; 10, Norin et al. 1985; 11, Sorensen et al. 1985; 12, Eisler 1981; 13, Pershagen and Vahter 1979; 14, Shiomi et al. 1984a; 15, Zaroogian and Hoffman 1982; 16, Phillips and Depledge 1986; 17, Phillips et al. 1982; 18, Hall et al. 1978; 19, Francesconi et al. 1985; 20, Shiomi et al. 1984b; 21, Hanaoka and Tagawa 1985a; 22, Hanaoka and Tagawa 1985b; 23, Reinke et al. 1975; 24, Hallacher et al. 1985; 25, Windom et al. 1973; 26, Hall 1980; 27, Wiemeyer et al. 1980; 28, Blus et al. 1977; 29, White et al. 1980; 30, Goede 1985; 31, Vreman et al. 1986; 32, Camardese et al. 1990; 33, Schmitt and Brumbaugh 1990; 34, Johns and Luoma 1990; 35, Ozretic et al. 1990; 36, Ramelow et al. 1989; 37, Farag et al. 1995; 38, Stavelind et al. 1993; 39, Leah et al. 1992; 40, Hothem and Welsh 1994; 41, Custer and Mitchell 1991; 42, Guitart et al. 1994; 43, Vermeer and Thompson 1992; 44, Mathews and Porter 1989; 45, Thies and Gregory 1994; 46, Custer and Mitchell 1993; 47, Pascoe et al. 1996; 48, Pascoe et al. 1994; 49, Azcue and Dixon 1994; 50, Saiki et al. 1992; 51, Findo et al. 1993; 52, Lebedeva 1997; 53, Kairu 1996; 54, Ismail and Roberts 1992; 55, Bigler and Crecelius 1998; 56, Finkelman et al. 1998; 57, Tao and Bolger 1998; 58, Goessler et al. 1998a; 59, Goessler et al. 1998b; 60, Kuehnelt et al. 1997a; 61, Kuehnelt et al. 1997b; 62, Kuehnelt et al. 1997c; 63, Hopkins et al. 1998; 64, Han et al. 1998; 65, Burger and Snodgrass 1998; 66, Kurttio et al. 1998; 67, Hsueh et al. 1998; 68, Ahn et al. 1999.

28.6 LETHAL AND SUBLETHAL EFFECTS

28.6.1 General

As will be discussed later, most authorities agree on ten points:

1. Inorganic arsenicals are more toxic than organic arsenicals, and trivalent forms are more toxic than pentavalent forms.
2. Episodes of arsenic poisoning are either acute or subacute; cases of chronic arsenosis are rarely encountered, except in humans.

3. Sensitivity to arsenic is greatest during the early developmental stages.
4. Arsenic can traverse placental barriers: as little as 1.7 mg As⁺⁵/kg body weight at critical stages of hamster embryogenesis, for example, can produce fetal death and malformation.
5. Biomethylation is the preferred detoxification mechanism for inorganic arsenicals.
6. Arsenic is bioconcentrated by organisms, but not biomagnified in the food chain.
7. In soils, depressed crop yields were recorded at 3 to 28 mg of water-soluble As/L, or about 25 to 85 mg total As/kg soil; adverse effects on vegetation were recorded at concentrations in air of >3.9 µg As/m³.
8. Some aquatic species were adversely affected at water concentrations of 19 to 48 µg As/L, or 120 mg As/kg in the diet, or tissue residue of 1.3 to 5 mg As/kg fresh weight.
9. Sensitive species of birds died following single oral doses of 17.4 to 47.6 mg As/kg body weight.
10. Adverse effects were noted in mammals at single oral doses of 2.5 to 33 mg As/kg body weight, at chronic oral doses of 1 to 10 mg As/kg body weight, and at feeding levels of 50 mg — and sometimes only 5 mg — As/kg in the diet.

The literature emphasizes that arsenic metabolism and toxicity vary greatly between species and that its effects are significantly altered by numerous physical, chemical, and biological modifiers. Adverse health effects, for example, may involve respiratory, gastrointestinal, cardiovascular, and hematopoietic systems, and may range from reversible effects to cancer and death, depending partly on the physical and chemical forms of arsenic tested, the route of administration, and the dose.

28.6.2 Carcinogenesis, Mutagenesis, and Teratogenesis

Inorganic arsenic is a known human carcinogen and has been assigned Group A classification by the U.S. Environmental Protection Agency, Group 1 classification by the International Agency for Research on Cancer, and been designated Category A1 by the American Conference of Governmental Industrial Hygienists (ATSDR 1992; USPHS 1998). Epidemiological studies show that an increased risk of cancers in the skin, lung, liver, and lymph and hematopoietic systems of humans is associated with exposure to inorganic arsenicals. These increased cancer risks are especially prevalent among smelter workers and in those engaged in the production and use of arsenical pesticides where atmospheric levels exceed 54.6 µg As/m³ (NRCC 1978; Belton et al. 1985; Pershagen and Bjorklund 1985). Skin tumors, mainly of low malignancy, have been reported after consumption of arsenic-rich drinking waters; a total dose of several grams, probably as As⁺³, is usually required for the development of skin tumors (Pershagen and Vahter 1979). High incidences of skin cancer and hyperpigmentation were noted among several population groups, especially Taiwanese and Chileans, consuming water containing more than 0.6 mg As/L. The frequency of cancer was highest among people over age 60 who demonstrated symptoms of chronic arsenic poisoning (NRCC 1978). In some areas of India, however, as many as 60% of the children between age 4 and 10 years had arsenical melanosis because of the exceptionally high levels of arsenic in the drinking water (Chowdhury et al. 1997). Elimination of arsenic in drinking water decreased the mortality incidence of arsenic-related cancers of the liver, lung, kidney, and skin in communities where blackfoot disease is endemic (Tsai et al. 1998).

Arsenic reportedly inhibits cancer formation in species having a high incidence of spontaneous cancers (NRCC 1978). In fact, arsenic may be the only chemical for which there is sufficient evidence for carcinogenicity in humans but not in other animals (Woolson 1975; Belton et al. 1985; Lee et al. 1985). In general, animal carcinogenicity tests with inorganic and organic arsenicals have been negative (Hood 1985), even when the chemicals were administered at or near the highest tolerated dosages for long periods (NAS 1977). Most studies of arsenic carcinogenesis in animals were presumably of insufficient duration to simulate conditions in long-lived species such as humans (NRCC 1978). However, mice developed leukemia and lymphoma after 20 subcutaneous injections of 0.5 mg As⁺⁵/kg body weight: 46% of the experimental group developed these signs vs. none of the controls (NRCC 1978). And mice given 500 µg As/L (as sodium arsenite) in the drinking water for lifetime exposures developed tumors in the lung, liver, and GI tract (Ng et al. 1998). Pulmonary

tumorigenicity has been demonstrated in hamsters administered calcium arsenate intratracheally (Pershagen and Bjorklund 1985). Inorganic arsenic interacts with benzo[a]pyrene in the induction of lung adenocarcinomas in hamsters (ATSDR 1992). Cacodylic acid and other organoarsenicals are not carcinogenic, but may be mutagenic at very high doses (Hood 1985). Monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) are primary metabolites of inorganic arsenic, a known human carcinogen. However, the rapid elimination ($T_{1/2} = 2$ h) and low retention (<2%) of MMA and DMA explain, in part, their low acute toxicity and cancer risk (Hughes and Kenyon 1998).

Several inorganic arsenic compounds are weak inducers of chromosomal aberrations, sister chromatid exchange, and *in vitro* transformation of mammalian and piscine cells. However, there is no conclusive evidence that arsenic causes point mutations in any cellular system (Pershagen and Vahter 1979; Belton et al. 1985; Lee et al. 1985; Deknudt et al. 1986; Manna and Mukherjee 1989). Studies with bacteria suggest that arsenite is a comutagen, or may inhibit DNA repair (Belton et al. 1985).

Arsenic is a known teratogen in several classes of vertebrates and has been implicated as a cause of birth defects in humans (Domingo 1994). Specific developmental malformations have been produced experimentally in mammals using inorganic As^{+3} or As^{+5} , either through a single dose or a continuous dose during embryogenesis (Hanlon and Ferm 1986b). Teratogenic effects are initiated no later than 4 h after administration of arsenic; fetal abnormalities are primarily neural tube defects (Hanlon and Ferm 1985c) but might also include protruding eyes, incomplete development of the skull, abnormally small jaws, and other skeletal anomalies (NRCC 1978). Inorganic As^{+3} and As^{+5} , but not organoarsenicals, cross placental barriers in many species of mammals and result in fetal deaths and malformations (NRCC 1978; USEPA 1980; Domingo 1994). Studies with hamsters, for example, showed that sodium arsenite can induce chromatid breaks and chromatid exchanges in Chinese hamster ovary cells in a dose-dependent manner (Lee et al. 1986b). In an earlier study (Lee et al. 1985), As^{+3} was about 10 times more potent than As^{+5} in causing transformations. The birth defects were most pronounced in golden hamsters exposed to As^{+5} during the 24-hr period of critical embryogenesis — day 8 of gestation (Ferm and Hanlon 1985) — when 1.7 mg As^{+5}/kg body weight induced neural tube defects in about 90% of the fetuses. Hanlon and Ferm (1986a) showed that hamsters exposed to As^{+5} and heat stress (39°C for 50 min) on day 8 of gestation produced a greater percentage of malformed offspring (18% to 39%) than did hamsters exposed to As^{+5} alone (4% to 8%).

28.6.3 Terrestrial Plants and Invertebrates

In general, arsenic availability to plants is highest in coarse-textured soils having little colloidal material and little ion exchange capacity, and lowest in fine-textured soils high in clay, organic material, iron, calcium, and phosphate (NRCC 1978). To be absorbed by plants, arsenic compounds must be in a mobile form in the soil solution. Except for locations where arsenic content is high (e.g., around smelters), the accumulated arsenic is distributed throughout the plant body in nontoxic amounts (NAS 1977). For most plants, a significant depression in crop yields was evident at soil arsenic concentrations of 3 to 28 mg/L of water-soluble arsenic and 25 to 85 mg/kg of total arsenic (NRCC 1978). Yields of peas (*Pisum sativum*), a sensitive species, were decreased at 1 mg/L of water-soluble arsenic or 25 mg/kg of total soil arsenic. Rice (*Oryza sativum*) yields were decreased 75% at 50 mg/L of disodium methylarsonate in silty loam, and soybeans (*Glycine max*) grew poorly when residues exceeded 1 mg As/kg (Table 28.3) (NRCC 1978). Forage plants grown in soils contaminated with up to 80 mg total As/kg from arsenical orchard sprays contained up to 5.8 mg As/kg dry weight; however, these plants were considered nonhazardous to grazing ruminants (Merry et al. 1986).

Attention focused on inorganic arsenical pesticides after accumulations of arsenic in soils eventually became toxic to several agricultural crops, especially in former orchards and cotton fields. Once toxicity is observed, it persists for several years even if no additional arsenic treatment is made (Woolson 1975). Poor crop growth was associated with bioavailability of arsenic in soils. For example, alfalfa (*Medicago sativa*) and barley (*Hordeum vulgare*) grew poorly in soils con-

taining only 3.4 to 9.5 mg As/kg, provided the soils were acidic, lightly textured, low in phosphorus and aluminum, high in iron and calcium, and contained excess moisture (Woolson 1975). Use of inorganic arsenical herbicides, such as calcium arsenate, to golf course turfs for control of fungal blight sometimes exacerbates the disease. The use of arsenicals on Kentucky bluegrass (*Poa pratensis*) is discouraged under conditions of high moisture and root stress induced by previous arsenical applications (Smiley et al. 1985).

Methylated arsenicals, whether herbicides or defoliants, are sprayed on plant surfaces. They can reach the soil during application or can be washed from the plants. Additional arsenic enters soils by exchange from the roots or when dead plant materials decay (Hood 1985). Cacodylic acid and sodium cacodylate are nonselective herbicides used in at least 82 products to eliminate weeds and grasses around trees and shrubs, and to eradicate vegetation from rights-of-way and other noncrop areas (Hood 1985). Normal application rates of various organoarsenicals for crop and noncrop purposes rarely exceed 5 kg/ha (Woolson 1975). At recommended treatment levels, organoarsenical soil residues are not toxic to crops, and those tested (soybean, beet, wheat) were more resistant to organoarsenicals than to comparable levels of inorganic arsenicals (Woolson 1975).

Air concentrations up to 3.9 µg As/m³ near gold mining operations were associated with adverse effects on vegetation. Higher concentrations of 19 to 69 µg As/m³, near a coal-fired power plant in Czechoslovakia, produced measurable contamination in soils and vegetation in a 6-km radius (NRCC 1978).

The phytotoxic actions of inorganic and organic arsenicals are different, and each is significantly modified by physical processes. The primary mode of action of arsenite in plants is inhibition of light activation, probably through interference with the pentose phosphate pathway (Marques and Anderson 1986). Arsenites penetrate the plant cuticle to a greater degree than arsenates (NAS 1977). One of the first indications of plant injury by sodium arsenite is wilting caused by loss of turgor, whereas stress due to sodium arsenate does not involve rapid loss of turgor (NAS 1977). Organoarsenicals, such as cacodylic acid, enter plants mostly by absorption of sprays; uptake from the soil contributes only a minor fraction (Hood 1985). The phytotoxicity of organoarsenical herbicides is characterized by chlorosis, cessation of growth, gradual browning, dehydration, and death (NAS 1977). In general, plants cease to grow and develop after the roots have absorbed much arsenic (NRCC 1978). Plants can absorb arsenic through the roots and foliage, although translocation is species dependent. Concentrations of arsenic in plants correlate highly and consistently with water-extractable soil arsenic, and usually poorly with total soil arsenic (NRCC 1978). For example, concentrations of arsenic in corn (*Zea mays*) grown in calcareous soils for 25 days were significantly correlated with the soil water-extractable arsenic fraction, but not other fractions. Extractable phosphorus was correlated positively to both arsenic in corn and to the water-soluble arsenic fraction (Sadiq 1986). In the moss *Hylocomium splendens*, arsenate accumulation from solution was through living shoots, optimum uptake being between pH 3 and 5 (Wells and Richardson 1985). Some plants, such as beets (*Beta vulgaris*), accumulated arsenic more readily at elevated temperatures, but the addition of phosphate fertilizers markedly depressed uptake (Merry et al. 1986).

Soils amended with arsenic-contaminated plant tissues were not measurably affected in CO₂ evolution and nitrification, suggesting that the effects of adding arsenic to soils does not influence the decomposition rate of plant tissues by soil microorganisms (Wang et al. 1984). The half-life of cacodylic acid is about 20 days in untreated soils and 31 days in arsenic-amended soils (Hood 1985). Estimates of the half-time of inorganic arsenicals in soils are much longer, ranging from 6.5 years for arsenic trioxide to 16 years for lead arsenate (NRCC 1978).

Data on arsenic effects to soil biota and insects are limited. In general, soil microorganisms are capable of tolerating and metabolizing relatively high concentrations of arsenic (Wang et al. 1984). This adaptation seems usually to be due to decreased permeability of the microorganism to arsenic (NAS 1977). Tolerant soil microbiota can withstand concentrations up to 1600 mg/kg; however, growth and metabolism were reduced in sensitive species at 375 mg As/kg and, at 150 to 165 mg As/kg, soils were devoid of earthworms and showed diminished quantities of bacteria and proto-

zoans (NRCC 1978). Earthworms (*Lumbricus terrestris*) held in soils containing 40 to 100 mg As⁺⁵/kg DW soil for 8 to 23 days had significantly reduced survival, especially among worms held in soils less than 70 mm in depth when compared to worms held at 500 to 700 mm. Survivors had negligible arsenic residues. Dead worms had higher concentrations, suggesting that arsenic homeostasis breaks down after death (Meharg et al. 1998). Honeybees (*Apis mellifera*) killed accidentally by sprayed As⁺³ contained 4 to 5 µg As per bee (NAS 1977), equivalent to 21 to 31 mg/kg body weight (Table 28.3). Larvae of the western spruce budworm (*Choristoneura occidentalis*) continued to feed on As⁺³-contaminated vegetation until a threshold level of about 2300 to 3300 mg As/kg dry weight whole larvae was reached; death then sometimes occurred (Table 28.3) (Robertson and McLean 1985). Larvae that had accumulated sufficient energy reserves completed the first stage of metamorphosis but developed into pupae of subnormal weight. Larvae containing <2600 mg As⁺³/kg ultimately developed into adults of less than normal weight, and some containing >2600 mg/kg dry weight died as pupae (Robertson and McLean 1985).

Table 28.3 Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Terrestrial Plants and Invertebrates

Ecosystem, Organism, and Other Variables	Arsenic Concentration and Effects	Reference ^a
TERRESTRIAL PLANTS		
Crops		
Total water soluble As in soils	Depressed crop yields at 3–28 mg/L	1
Total soil As concentrations	Depressed crop yields at 25–85 mg/kg	1
Common bermudagrass, <i>Cynodon dactylon</i>		
Arsenite	Plants grown on As-amended soils (up to 90 mg As ⁺³ /kg) contained up to 17 mg As/kg dry weight in stems, 20 in leaves, and 304 in roots	2
Fruit orchards		
Inorganic arsenites and arsenates	Soils contain 31–94 mg/kg dry weight (vs. 2.4 in untreated orchards); whole rodents contain <0.002 mg As/kg fresh weight (vs. ND in untreated orchards)	3
Soybean, <i>Glycine max</i>		
Total As	Toxic signs at plant residues >1 mg total As/kg	1
Grasslands		
Cacodylic acid	Kill of 75 to 90% of all species at 17 kg/ha; recovery modest	3
Rice, <i>Oryza sativum</i>		
Disodium methylarsonate	75% decrease in yield at soil (silty loam) concentrations of 50 mg/kg	1
Scots pine, <i>Pinus sylvestris</i>		
Inorganic As ⁺⁵	Seedlings die when soil (sandy) concentrations exceed 250 mg/kg DW. Maximum BCF factors low: 0.6 for roots; 0.1 for shoots. Residues >62 mg As/kg DW in shoots are toxic, and 3300 mg/kg DW is usually fatal	4
Pea, <i>Pisum sativum</i>		
Sodium arsenite	15 mg/L inhibits light activation and photosynthetic CO ₂ fixation in chloroplasts	5
Sandhill plant communities		
Cacodylic acid	No lasting effect at 2.25 kg/ha. Some species defoliated at 6.8 kg/ha. Significant effect, including 75% defoliation of oaks and death of all pine trees, at 34 kg/ha	3
Cowpea, <i>Vigna</i> sp.		
Total water soluble As in soils	Decreased yields at 1 mg/L	1
Total soil As concentrations (loamy sand)	Toxic at 25 mg/kg	1
Yeast		
Arsenate	At 75 mg/L, 60% reduction in phosphate transport and glucose metabolism in 30 min; at 375 mg/L, 100% reduction	1

Table 28.3 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Terrestrial Plants and Invertebrates

Ecosystem, Organism, and Other Variables	Arsenic Concentration and Effects	Reference ^a
TERRESTRIAL INVERTEBRATES		
Honeybee, <i>Apis mellifera</i>		
Inorganic arsenite	Following arsenic spray dusting, dead bees contained 20.8–31.2 mg/kg FW (adults) or 5–13 mg/kg FW (larvae)	6
Beetles		
Cacodylic acid	Dietary levels of 100–1000 mg/kg fatal to certain pestiferous species	3
Western spruce budworm, <i>Christoneura occidentalis</i> , sixth instar stage		
Arsenic trioxide	Dietary levels of 99.5 mg/kg FW killed 10%, 2250 mg/kg killed 50%, and 65,300 mg/kg was fatal to 90%. Newly molted pupae and adults of As-exposed larvae had reduced weight. Regardless of dietary levels, concentrations of As ranged up to 2640 mg/kg DW in dead pupae, and 1708 mg/kg DW in adults	7
Earthworm, <i>Lumbricus terrestris</i>		
As ⁺⁵	Earthworms held in soils containing 40 mg As/kg DW for 23 days had no accumulations in first 12 days, with BCF of 3 by day 23	8
As ⁺⁵	100 mg As/kg DW soil was fatal to 50% in 8 days	8
As ⁺⁵	400 mg As/kg DW soil was fatal to 50% in 2 days	8

^a 1, NRCC 1978; 2, Wang et al. 1984; 3, Hood 1985 4, Sheppard et al. 1985; 5, Marques and Anderson 1986; 6, Jenkins 1980; 7, Robertson and McLean 1985; 8, Meharg et al. 1998.

28.6.4 Aquatic Biota

Adverse effects of arsenicals on aquatic organisms have been reported at concentrations of 19 to 48 µg/L in water, 33 mg/kg in diets, and 1.3 to 5 mg/kg fresh weight in tissues (Table 28.4). The most sensitive of the aquatic species tested that showed adverse effects were three species of marine algae, which showed reduced growth in the range of 19 to 22 µg As⁺³/L; developing embryos of the narrow-mouthed toad (*Gastrophryne carolinensis*), of which 50% were dead or malformed in 7 days at 40 µg As⁺³/L; and a freshwater alga (*Scenedesmus obliquus*), in which growth was inhibited 50% in 14 days at 48 µg As⁺⁵/L (Table 28.4). Chronic studies with mass cultures of natural phytoplankton communities exposed to low levels of arsenate (1.0 to 15.2 µg/L) showed that As⁺⁵ differentially inhibits certain plants, causing a marked change in species composition, succession, and predator-prey relations. The significance of these changes on carbon transfer between trophic levels is unknown (Sanders and Cibik 1985; Sanders 1986). Adverse biological effects have also been documented at water concentrations of 75 to 100 µg As/L:

- At 75 µg As⁺⁵/L, growth and biomass in freshwater and marine algae was reduced.
- At 85 to 88 µg/L of As⁺⁵ or various methylated arsenicals, mortality was 10% to 32% in amphipods (*Gammarus pseudolimnaeus*) in 28 days.
- At 95 µg As⁺³/L, marine red alga failed to reproduce sexually.
- At 100 µg As⁺⁵/L, marine copepods died and goldfish behavior was impaired (Table 28.4).

Rainbow trout (*Oncorhynchus mykiss*) fed diets containing up to 90 mg As⁺⁵/kg were slightly affected, but those given diets containing >120 mg As/kg (as As⁺³ or As⁺⁵) grew poorly, avoided food, and failed to metabolize food efficiently. No toxic effects were reported over 8 weeks of exposure to diets containing 1600 mg/kg, as methylated arsenicals (Table 28.4). Dietary disodium

heptahydrate (DSA) is more toxic to juvenile rainbow trout than dietary arsenic trioxide, dimethylarsinic acid, or arsanilic acid (Cockell et al. 1991; Cockell and Bettger 1993). Diets containing 55 to 60 mg As⁺⁵/kg ration as DSA were associated with changes in the hepatobiliary system of juvenile rainbow trout after 12 weeks of feeding (Cockell et al. 1992). The most sensitive indicator of DSA insult in juvenile rainbow trout was chronic inflammation of the gallbladder wall, as found in 71% of trout exposed to 33 mg As/kg ration for 24 weeks and 100% of those exposed to 65 mg As/kg ration for 24 weeks. There was no damage at 13 mg/kg ration and lower in the 24-week study (Cockell et al. 1991). The whole-body arsenic concentrations in moribund rainbow trout poisoned by arsenate compounds in 11-week exposures ranged between 4 and 6 mg As/kg fresh weight (vs. 2.0 mg/kg fresh weight in controls) — and dead whole trout had 8 to 12 mg As/kg fresh weight — suggesting that a critical arsenic body concentration is reached before death or toxicant insult occurs (McGeachy and Dixon 1990). In bluegills (*Lepomis macrochirus*), tissue residues of 1.35 mg As/kg fresh weight in juveniles and 5 mg/kg in adults are considered elevated and potentially hazardous (NRCC 1978).

Toxic and other effects of arsenicals to aquatic life are significantly modified by numerous biological and abiotic factors (Woolson 1975; NAS 1977; NRCC 1978; USEPA 1980, 1985; Howard et al. 1984; Michnowicz and Weakley 1984; Bryant et al. 1985; Sanders 1986; Hamilton and Buhl 1990; McGeachy and Dixon 1990). The LC50 values, for example, are markedly affected by water temperature, pH, Eh, organic content, phosphate concentration, suspended solids, and presence of other substances and toxicants, as well as arsenic speciation, and duration of exposure. In general, inorganic arsenicals are more toxic than organoarsenicals to aquatic biota, and trivalent species are more toxic than pentavalent species. Early life stages are most sensitive, and large interspecies differences are recorded, even among species closely related taxonomically.

Arsenic is accumulated from the water by a variety of organisms. However, there is no evidence of magnification along the aquatic food chain (Woolson 1975; NAS 1977; NRCC 1978; Hallacher et al. 1985; Hood 1985; Lindsay and Sanders 1990; Woodward et al. 1995). In a marine ecosystem based on the alga *Fucus vesiculosus*, arsenate (7.5 µg As⁺⁵/L) was accumulated by all biota. After 3 months, arsenic was concentrated most efficiently by *Fucus* (120 mg/kg dry weight in apical fronds) and filamentous algal species (30 mg/kg dry weight); little or no bioaccumulation occurred in invertebrates, although arsenic seemed to be retained by gastropods and mussels (Rosemarin et al. 1985). In a simplified estuarine food chain, there was no significant increase in arsenic content of grass shrimp (*Palaemonetes pugio*) exposed to arsenate-contaminated food or to elevated water concentrations (Lindsay and Sanders 1990). In a freshwater food chain composed of algae, daphnids, and fish, water concentrations of 0.1 mg cacodylic acid/L produced residues (mg As/kg dry weight), after 48 h, of 4.5 in algae and 3.9 in daphnids, but only 0.09 in fish (NAS 1977). Microcosms of a Delaware cordgrass (*Spartina alterniflora*) salt marsh exposed to elevated levels of As⁺⁵ showed that virtually all arsenic was incorporated into plant tissue or strongly sorbed to cell surfaces (Sanders and Osman 1985). Studies with radioarsenic and mussels (*Mytilus galloprovincialis*) showed that accumulation varied with nominal arsenic concentrations, tissue, age of the mussel, and temperature and salinity of the medium (Unlu and Fowler 1979). Arsenate uptake increased with increasing arsenic concentration in the medium, but the response was not linear, accumulation being suppressed at higher external arsenic concentrations. Smaller mussels took up more arsenic than larger ones. In both size groups, arsenic was concentrated in the byssus and digestive gland. In general, arsenic uptake and loss increased at increasing temperatures. Uptake was significantly higher at 1.9% salinity than at 3.8%, but loss rate was about the same at both salinities. Radioarsenic loss followed a biphasic pattern; the biological half-life was 3 and 32 days for the fast and slow compartments, respectively; secretion of the byssal thread played a key role in elimination (Unlu and Fowler 1979). Factors known to modify rates of arsenic accumulation and retention in a marine shrimp (*Lysmata seticaudata*) include water temperature and salinity, arsenic concentration, age, and especially frequency of molting (Fowler and Unlu 1978).

Bioconcentration factors (BCF) experimentally determined for arsenic in aquatic organisms are, except for algae, relatively low. The BCF values for inorganic As⁺³ in most aquatic invertebrates and fish exposed for 21 to 30 days did not exceed 17 times; the maxima were 6 times for As⁺⁵, and 9 times for organoarsenicals (USEPA 1980, 1985). Significantly higher BCF values were recorded in other aquatic organisms (NRCC 1978), but they were based on mean arsenic concentrations in natural waters that seemed artificially high. A BCF of 350 times was reported for the American oyster (*Crassostrea virginica*) held in 5 µg As⁺⁵/L for 112 days (Zaroogian and Hoffman 1982). There was no relation between oyster body burdens of arsenic and exposure concentrations. However, diet seemed to contribute more to arsenic uptake than did seawater concentrations (Zaroogian and Hoffman 1982). An arsenic-tolerant strain of freshwater alga (*Chlorella vulgaris*) from an arsenic-polluted environment showed increasing growth up to 2000 mg As⁺⁵/L, and it could survive at 10,000 mg As⁺⁵/L (Maeda et al. 1985). Accumulations up to 50,000 mg As/kg dry weight were recorded (Maeda et al. 1985), suggesting a need for additional research on the extent of this phenomenon and its implications on food-web dynamics.

Some investigators have suggested that arsenic in the form of arsenite is preferentially utilized by marine algae and bacteria (Johnson 1972; Bottino et al. 1978; Johnson and Burke 1978). Arsenate reduction to arsenite in seawater depends on phosphorus in solution and available algal biomass (Johnson and Burke 1978). During algal growth, as phosphate is depleted and the P⁺⁵:As⁺⁵ ratio drops, the rate of As⁺⁵ reduction increases. The resultant As⁺³, after an initial peak, is rapidly oxidized to As⁺⁵, indicating the possibility of biological catalysis of oxidation as well as mediation of As⁺⁵ reduction. Researchers generally agree that As⁺³ is more toxic than arsenates to higher organisms; however, As⁺⁵ had a more profound effect on growth and morphology of marine algae than As⁺³. It is possible that marine algae erect a barrier against the absorption of As⁺³, but not against As⁺⁵. Within the cell, As⁺⁵ can then be reduced to the possibly more toxic As⁺³. For example, the culture of two species of marine algae (*Tetraselmis chui* and *Hymenomonas carterae*) in media containing various concentrations of As⁺⁵ or As⁺³ showed that arsenic effects varied with oxidation state, concentration, and light intensity. Arsenate was incorporated and later partly released by both species. Differences between rates of uptake and release suggest that arsenic undergoes chemical changes after incorporation into algal cells (Bottino et al. 1978). When bacterial cultures from the Sargasso Sea and from marine waters of Rhode Island were grown in As⁺³-enriched media, the bacteria reduced all available As⁺⁵ and utilized As⁺³ during the exponential growth phase, presumably as an essential trace nutrient. The arsenate reduction rate per cell was estimated to be 75×10^{-11} mg As/minute (Johnson 1972).

The ability of marine phytoplankton to accumulate high concentrations of inorganic arsenicals and transform them to methylated arsenicals that are later efficiently transferred in the food chain is well documented (Irgolic et al. 1977; Benson 1984; Matsuto et al. 1984; Freeman 1985; Froelich et al. 1985; Maeda et al. 1985; Norin et al. 1985; Sanders 1985; Yamaoka and Takimura 1986). Algae constitute an important source of organoarsenic compounds in marine food webs. In the food chain composed of the alga *Dunaliella marina*, the grazing shrimp *Artemia salina*, and the carnivorous shrimp *Lysmata seticaudata*, organic forms of arsenic were derived from *in vivo* synthesis by *Dunaliella* and efficiently transferred, without magnification, along the food chain (Wrench et al. 1979). Laboratory studies with five species of euryhaline algae grown in freshwater or seawater showed that all species synthesized fat-soluble and water-soluble arsено-organic compounds from inorganic As⁺³ and As⁺⁵. The BCF values in the five species examined ranged from 200 times to about 3000 times — accumulations being highest in lipid phases (Lunde 1973). In Charlotte Harbor, Florida, a region that has become phosphate enriched due to agricultural activity, virtually all of the arsenic taken up by phytoplankton was biomethylated and returned to the estuary, usually as monomethylarsonic and dimethylarsenic acids (Froelich et al. 1985). The ability of marine phytoplankton to methylate arsenic and release the products to a surrounding environment varies between species and even within a particular species in relation to their possession of necessary

methylating enzymes (Sanders 1985). The processes involved in detoxifying arsenate after its absorption by phytoplankton are not firmly established, but seem to be nearly identical in all plants, suggesting a similar evolutionary development. Like phosphates and sulfates, arsenate may be fixed with ADP, reduced to the arsonous level, and successfully methylated and adenosylated, ultimately producing the 5-dimethylarsenosoribosyl derivatives accumulating in algae (Benson 1984).

Sodium arsenite has been used extensively as an herbicide for control of mixed submerged aquatic vegetation in freshwater ponds and lakes. Concentrations of 1.5 to 3.8 mg As⁺³/L have usually been effective and are considered safe for fish (NAS 1977). However, As⁺³ concentrations considered effective for aquatic weed control may be harmful to several species of freshwater teleosts, including bluegills, flagfish (*Jordenella floridae*), fathead minnows (*Pimephales promelas*), and rainbow trout (*Oncorhynchus mykiss*) (Table 28.4). Fish exposed to 1 to 2 mg total As/L for 2 to 3 days may show one or more of several signs: hemorrhagic spheres on gills; fatty infiltration of liver; and necrosis of heart, liver, and ovarian tissues (NRCC 1978). In green sunfish (*Lepomis cyanellus*), hepatocyte changes parallel arsenic accumulations in the liver (Sorensen et al. 1985). Organoarsenicals are usually eliminated rapidly by fish and other aquatic fauna. Rainbow trout, for example, fed a marine diet containing 15 mg organic arsenic/kg had only negligible tissue residues 6 to 10 days later, although some enrichment was noted in the eyes, throat, gills, and pyloric caeca (Pershagen and Vahter 1979). Oral administration of sodium arsenate to estuary catfish (*Cnidoglanis macrocephalus*) and school whiting (*Sillago bassensis*) resulted in tissue accumulations of trimethylarsine oxide. Arsenobetaine levels, which occur naturally in these teleosts, were not affected by As⁺⁵ dosing. The toxicity of trimethylarsine oxide is unknown, but the ease with which it can be reduced to the highly toxic trimethylarsine is cause for concern (Edmonds and Francesconi 1987). Recent studies, however, suggest that humans are capable of metabolizing trimethylarsine to the comparatively innocuous arsenobetaine (Goessler et al. 1997).

Table 28.4 Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Ecosystem, Species, Arsenic Compound ^a , and Other Variables	Arsenic Concentration (mg/L)	Effect	Reference ^b
FRESHWATER PLANTS			
Algae, various species			
As ⁺³	1.7	Toxic	1
As ⁺³	4	Decomposition	1
As ⁺³	2.3	95%–100% kill in 2–4 weeks of 4 species	2, 3
As ⁺⁵	0.075	Decreased growth	3
Alga, <i>Ankistrodesmus falcatus</i>			
As ⁺⁵	0.26	EC50 (14 days)	3
Alga, <i>Scenedesmus obliquus</i>			
As ⁺⁵	0.048	EC50 (14 days)	3
Alga, <i>Selenastrum capricornutum</i>			
As ⁺⁵	0.69	EC50 (4 days)	3
FRESHWATER INVERTEBRATES			
Cladoceran, <i>Bosmina longirostris</i>			
As ⁺⁵	0.85	50% immobilization in 96 h	4
Cladoceran, <i>Daphnia magna</i>			
As ⁺³	0.63–1.32	MATC ^c	3

Table 28.4 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Ecosystem, Species, Arsenic Compound ^a , and Other Variables	Arsenic Concentration (mg/L)	Effect	Reference ^b
As ⁺³	0.96	LC5 (28 days)	5
As ⁺³			
Starved	1.5	50% immobilization (96 h)	6
Fed	4.3	50% immobilization (96 h)	6
As ⁺⁵	0.52	Reproductive impairment of 16% in 3 weeks	3
As ⁺⁵	0.93	LC5 (28 days); maximum bioconcentration factor (BCF) of 219	5
As ⁺⁵	7.4	LC50 (96 h)	2
DSMA	0.83	LC0 (28 days)	5
SDMA	1.1	LC0 (28 days)	5
Total As	1	18% decrease in body weight in 3 weeks	1
Total As	1.4	50% reproductive impairment in 3 weeks	1
Total As	2.8	LC50 (21 days)	1
Total As	4.3–7.5	Immobilization (21 days)	1
Cladoceran, <i>Daphnia pulex</i>			
As ⁺⁵	49.6	50% immobilization (48 h)	4
As ⁺³	1.3	LC50 (96 h)	2, 3
As ⁺³	3	EC50 (48 h)	7
Amphipod, <i>Gammarus pseudolimnaeus</i>			
As ⁺³	0.87	50% immobilization (96 h)	6
As ⁺³	0.088	LC20 (28 days)	5
As ⁺³	0.96	LC100 (28 days)	5
As ⁺⁵	0.97	LC20 (28 days); no accumulations	5
DSMA	0.086	LC10 (28 days)	5
DSMA	0.97	LC40 (28 days)	5
SDMA	0.85	LC0 (28 days)	5
Snail, <i>Helisoma campanulata</i>			
As ⁺³	0.96	LC10 (28 days)	5
As ⁺⁵	0.97	LC0 (28 days); maximum BCF of 99	5
DSMA	0.97	LC0 (28 days)	5
SDMA	0.085	LC0 (28 days)	5
SDMA	0.085	LC32 (28 days)	5
Red crayfish, <i>Procambarus clarkii</i>			
MSMA	Nominal concentration of 0.5 mg/L, equivalent to 0.23 mg As/L	Whole-body As concentration after 8-week exposure plus 8-week depuration was 0.3 mg/kg DW whole body vs. 0.4 for controls	15
MSMA	Nominal exposure of 5 mg/L, equivalent to 2.3 mg As/L	Exposure and depuration as above; maximum As concentration was 4.3 mg/kg DW whole body during exposure, 0.6 at end of depuration	15
MSMA	Nominal concentration of 50 mg/L, equivalent to 23.1 mg As/L	Exposure and depuration as above; maximum As concentration during exposure was 9 mg/kg DW whole animal and 2.1 at end of depuration	15
MSMA	Nominal exposure of 100 mg/L, equivalent to 46.3 mg As/L	No effect on growth or survival during 24-week exposure, but hatching success reduced to 17% vs. 78% for controls	16
MSMA	1019	LC50 (96 h)	16
Stonefly, <i>Pteronarcys californica</i>			
As ⁺³	38	LC50 (96 h)	7

Table 28.4 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Ecosystem, Species, Arsenic Compound ^a , and Other Variables	Arsenic Concentration (mg/L)	Effect	Reference ^b
Stonefly, <i>Pteronarcys dorsata</i>			
As ⁺³	0.96	LC0 (28 days)	5
As ⁺⁵	0.97	LC20 (28 days); maximum BCF of 131	5
DSMA	0.97	LC0 (28 days)	5
SDMA	0.85	LC0 (28 days)	5
Cladoceran, <i>Simocephalus serrulatus</i>			
As ⁺³	0.81	LC50 (96 h)	3
Zooplankton			
As ⁺³	0.4	No effect	1
As ⁺³	1.2	Population reduction	1
FRESHWATER VERTEBRATES			
Marbled salamander, <i>Ambystoma opacum</i>			
As ⁺³	4.5	EC50 (8 days) concentration producing death and malformations in developing embryos	3
Goldfish, <i>Carassius auratus</i>			
As ⁺⁵	0.1	15% behavioral impairment in 24 h; 30% impairment in 48 h	1
As ⁺⁵	24.6–41.6	LC50 (7 days)	1
As ⁺³	0.49	EC50 (7 days)	3
MSMA	5	LC50 (96 h)	3
Narrow-mouthed toad, <i>Gastrophryne carolinensis</i>			
As ⁺³	0.04	50% death or malformations in developing embryos in 7 days	3
Channel catfish, <i>Ictalurus punctatus</i>			
As ⁺³	25.9	LC50 (96 h)	8
Flagfish, <i>Jordanella floridae</i>			
As ⁺³	14.4	LC50 (96 h)	6
As ⁺³	2.1–4.1	MATC ^c	3
Bluegill, <i>Lepomis macrochirus</i>			
As ⁺³			
Juveniles	0.69	Reduced survival 16 weeks after a single treatment	2, 3
Adults	0.69	Histopathology after 16 weekly treatments	2
As ⁺³	4	Population reduction of 42% after several monthly applications	8
As ⁺³	30–35	LC50 (96 h)	7, 8
MSMA	1.9	LC50 (96 h)	3
Total As	Tissue levels of 1.35 mg/kg fresh weight (juveniles) and 5 mg/kg (adults)	Threshold acute toxic value	1
Spottail shiner, <i>Notropis hudsonius</i>			
As ⁺³	45	LC50 (25 h)	8
As ⁺³	29	LC50 (48 h); survivors with fin and scale damage	8

Table 28.4 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Ecosystem, Species, Arsenic Compound ^a , and Other Variables	Arsenic Concentration (mg/L)	Effect	Reference ^b
Chum salmon, <i>Oncorhynchus keta</i>			
As ⁺³	11	LC50 (48 h)	8
Chinook salmon, <i>Oncorhynchus tshawytscha</i>			
Mean weight 0.5 g; fresh water			
As ⁺³	25.1	LC50 (96 h)	21
As ⁺⁵	90.0	LC50 (96 h)	21
Mean weight 2.0 g; brackish water			
As ⁺³	21.4	LC50 (96 h)	21
As ⁺⁵	66.5	LC50 (96 h)	21
Minnow, <i>Phoxinus phoxinus</i>			
As ⁺³	20	Equilibrium loss in 36 h	8
As ⁺⁵	234–250	Lethal	8
Fathead minnow, <i>Pimephales promelas</i>			
As ⁺⁵	0.53–1.50	MATC ^c	3
As ⁺³	2.1–4.8	MATC ^c	6
As ⁺³	6.0	LC30 (96 h)	17
As ⁺³	14.1	LC50 (96 h)	6
As ⁺³	17.7	LC76 (96 h)	17
As ⁺⁵	25.6	LC50 (96 h)	3
Rainbow trout, <i>Oncorhynchus mykiss</i>			
As ⁺³	0.13	EC10 (28 days)	3
As ⁺³			
Embryos	0.54	LC50 (28 days)	2
Adults	23–26.6	LC50 (96 h)	5
As ⁺³	0.96	LC50 (28 days)	7, 8
As ⁺⁵	60 at 15°C	50% loss of equilibrium (LOE) in 210 h; whole-body arsenic concentration (WBC) of 8.1 mg/kg FW	18
As ⁺⁵	120 at 5°C	50% LOE in 57 h; WBC of 8.6 FW	18
As ⁺⁵	120 at 15°C	50% LOE in 35 h; WBC of 8.6 FW	18
As ⁺⁵	240 at 5°C	50% LOE in 32 h; WBC of 13.5 FW	18
As ⁺³ or As ⁺⁵	Fed diets of 120–1600 mg As/kg for 8 weeks	Growth depression, food avoidance, and impaired feed efficiency at all levels	9
As ⁺⁵	Fed diets of 10–90 mg As/kg for 16 weeks	No effect level at about 10 mg/kg diet. Some adaptation to dietary As observed in trout fed 90 mg/kg diet, as initial negative growth gave way to slow positive growth over time	9
As ⁺⁵	0.97	LC0 (28 days); no accumulations	5
DSA	13–33 mg As/kg ration for 12–24 weeks or 0.281–0.525 mg As/kg BW daily	MATC ^c	19
DSA	55–60 mg As ⁺⁵ per kg ration for 8–12 weeks	Elevated accumulations in tissues; adverse effects on hepatobiliary system	20

Table 28.4 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Ecosystem, Species, Arsenic Compound ^a , and Other Variables	Arsenic Concentration (mg/L)	Effect	Reference ^b
DSA	58 mg As ⁺⁵ /kg ration for 12 weeks	Diet avoidance and reduced growth. Gallbladder lesions within 24 h of exposure developing to chronic inflammation with fibrosis of the gallbladder wall. Tissue arsenic concentrations at day 84, in mg As/kg DW, were 21 in liver, 39 in gallbladder, and 60 (as As ⁺³) in bile vs. <0.5 for all control tissues	22
DSMA	0.97	LC0 (28 days)	5
SDMA	0.85	LC0 (28 days)	5
SC	1000	LC0 (28 days)	14
DMA or ABA	Fed diet containing 120–1600 mg/kg for 8 weeks	No toxic response at any level tested	9
Brook trout, <i>Salvelinus fontinalis</i>			
As ⁺³	15	LC50 (96 h)	3
MARINE PLANTS			
Algae, 2 species			
As ⁺³ or As ⁺⁵	1	No effect	10
As ⁺⁵	1000	No deaths	10
Algae, 3 species			
As ⁺³	0.019–0.022	Reduced growth	3
Red alga, <i>Champia parvula</i>			
As ⁺³	0.065	Normal sexual reproduction	10
As ⁺³	0.095	No sexual reproduction	10
As ⁺³	0.30	Death	10
As ⁺⁵	10	Normal growth, but no sexual reproduction	10
Phytoplankton			
As ⁺⁵	0.075	Reduced biomass of populations in 4 days	3
Red alga, <i>Plumaria elegans</i>			
As ⁺³	0.58	Arrested sporeling development 7 days posttreatment after exposure for 18 h	12
Alga, <i>Skeletonema costatum</i>			
As ⁺⁵	0.13	Growth inhibition	3
Alga, <i>Thalassiosira aestivalis</i>			
As ⁺⁵	0.075	Reduced chlorophyll a	3
MARINE INVERTEBRATES			
Copepod, <i>Acartia clausi</i>			
As ⁺³	0.51	LC50 (96 h)	3
Dungeness crab, <i>Cancer magister</i>			
As ⁺³	0.23	LC50 (96 h), zoea	3
Amphipod, <i>Corophium volutator</i>			
As ⁺⁵			
Water temperature, °C			
5	8	LC50 (230 h)	11
10	8	LC50 (150 h)	11

Table 28.4 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

Ecosystem, Species, Arsenic Compound ^a , and Other Variables	Arsenic Concentration (mg/L)	Effect	Reference ^b
15	8	LC50 (74 h)	11
15	4	LC50 (140 h)	11
15	2	LC50 (192 h)	11
Pacific oyster, <i>Crassostrea gigas</i>			
As ⁺³	0.33	LC50 (96 h) for embryos	3
American oyster, <i>Crassostrea virginica</i>			
As ⁺³ (eggs)	7.5	LC50 (48 h)	8
Copepod, <i>Eurytemora affinis</i>			
As ⁺⁵	0.025	No effect	12
As ⁺⁵	0.1	Reduced juvenile survival	12
As ⁺⁵	1	Reduced adult survival	12
Clam, <i>Macoma balthica</i>			
As ⁺⁵			
Water temperature, °C			
5	220	LC50 (192 h)	11
10	60	LC50 (192 h)	11
15	15	LC50 (192 h)	11
Mysid, <i>Mysidopsis bahia</i>			
As ⁺³	0.63–1.27	MATC ^c	3
As ⁺⁵	2.3	LC50 (96 h)	3
Blue mussel, <i>Mytilus edulis</i>			
As ⁺³	16	Lethal in 3–16 days	8
Mud snail, <i>Nassarius obsoletus</i>			
As ⁺³	2	Depressed oxygen consumption in 72 h	8
Oligochaete annelid, <i>Tubifex costatus</i>			
As ⁺⁵			
Water temperature, °C			
5	500	LC50 (130 h)	11
10	500	LC50 (115 h)	11
15	500	LC50 (85 h)	11

MARINE VERTEBRATES

Grey mullet, <i>Chelon labrosus</i>			
As ⁺³	27.3	LC50 (96 h); some skin discoloration	13
Dab, <i>Limanda limanda</i>			
As ⁺³	28.5	LC50 (96 h); respiratory problems	13
Pink salmon, <i>Oncorhynchus gorbuscha</i>			
As ⁺³	2.5	LC0 (10 days)	8
As ⁺³	3.8	LC54 (10 days)	3
As ⁺³	7.2	LC100 (7 days)	3
Winter flounder, <i>Pleuronectes americanus</i>			
As ⁺³	28, 56, or 112 mg As/kg BW by sc injection	All doses induced liver metallothionein protein within 24 h	23
Teleosts, 3 species			
As ⁺³	12.7–16	LC50 (96 h)	3

Table 28.4 (continued) Lethal and Sublethal Effects of Various Arsenic Compounds on Selected Species of Aquatic Biota

- ^a As⁺³, inorganic trivalent arsenite; As⁺⁵, inorganic pentavalent arsenate; DMA, dimethylarsinic acid; ABA, *p*-amino-benzeneearsonic acid; DSA, disodium arsenate heptahydrate; DMSA, disodium methylarsenate [CH₃AsO(ONa)₂]; SDMA, sodium dimethylarsenate [(CH₃)₂AsO(ONa)]; MSMA, monosodium methaneearsonate; SC, sodium cacodylate.
- ^b 1, NRCC 1978; 2, USEPA 1980; 3, USEPA 1985; 4, Passino and Novak 1984; 5, Spehar et al. 1980; 6, Lima et al. 1984; 7, Johnson and Finley 1980; 8, NAS 1977; 9, Cockell and Hilton 1985; 10, Thursby and Steele 1984; 11, Bryant et al. 1985; 12, Sanders 1986; 13, Taylor et al. 1985; 14, Hood 1985; 15, Naqvi et al. 1990; 16, Naqvi and Flagge 1990; 17, Dyer et al. 1993; 18, McGeachy and Dixon 1992; 19, Cockell et al. 1991; 20, Cockell et al. 1992; 21, Hamilton and Buhl 1990; 22, Cockell and Bettger 1992; 23, Jensen-Eller and Crivello 1998.
- ^c Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

28.6.5 Birds

Signs of inorganic trivalent arsenite poisoning in birds (muscular incoordination, debility, slowness, jerkiness, falling, hyperactivity, fluffed feathers, drooped eyelid, huddled position, unkempt appearance, loss of righting reflex, immobility, seizures) were similar to those induced by many other toxicants and did not seem to be specific for arsenosis. Signs occurred within 1 h and deaths within 1 to 6 days postadministration; remission took up to 1 month (Hudson et al. 1984). Internal examination suggested that lethal effects of acute inorganic arsenic poisoning were due to the destruction of blood vessels lining the gut, which resulted in decreased blood pressure and subsequent shock (Nystrom 1984). *Coturnix* (*Coturnix coturnix*), for example, exposed to acute oral doses of As⁺³ showed hepatocyte damage (i.e., swelling of granular endoplasmic reticulum); these effects were attributed to osmotic imbalance, possibly induced by direct inhibition of the sodium pump by arsenic (Nystrom 1984).

Arsenic, as arsenate, in aquatic plants (up to 430 mg As/kg plant dry weight) from agricultural drainwater areas can impair normal development of mallard ducklings that consume these plants (Camardese et al. 1990) (Table 28.5). Pen studies with ducklings showed that a diet of 30 mg As/kg ration adversely affects growth and physiology, and a 300 mg As/kg diet alters brain biochemistry and nesting behavior. Decreased energy levels and altered behavior can further decrease duckling survival in a natural environment (Camardese et al. 1990).

Western grasshoppers (*Melanophis* spp.) poisoned by arsenic trioxide were fed, with essentially no deleterious effects, to nestling northern bobwhites (*Colinus virginianus*), mockingbirds (*Mimus polyglottos*), American robins (*Turdus migratorius*), and other songbirds (NAS 1977). Up to 134 poisoned grasshoppers, containing a total of about 40 mg As, were fed to individual nestlings with no apparent toxic effect. Species tested that were most sensitive to various arsenicals were the brown-headed cowbird (*Molothrus ater*) with an LD₅₀ (11-day) value of 99.8 mg copper acetoarsenite/kg diet; California quail (*Callipepla californica*) with an LD₅₀ single oral dose value of 47.6 mg sodium arsenite/kg body weight; and chicken with 33 and turkey with 17.4 mg/kg body weight of 3-nitro-4-hydroxy phenylarsonic acid as a single oral dose (Table 28.5).

Chickens rapidly excrete arsenicals; only 2% of dietary sodium arsenite remained after 60 h (NAS 1977), and arsanilic acid was excreted largely unchanged (Woolson 1975). Excretion of arsanilic acid by chickens was affected by uptake route: excretion was more rapid if administration was by intramuscular injection than if it was oral (NRCC 1978). Studies with inorganic As⁺⁵ and chickens indicated that (Fullmer and Wasserman 1986):

1. Arsenates rapidly penetrated mucosal and serosal surfaces of epithelial membranes.
2. As⁺⁵ intestinal absorption was essentially complete within 1 h at 370 mg As⁺⁵/kg BW, but only 50% complete at 3700 mg/kg BW.
3. Vitamin D₃ was effective in enhancing duodenal As⁺⁵ absorption in rachitic chicks.
4. As⁺⁵ and phosphate did not appear to share a common transport pathway in the avian duodenum.

Table 28.5 Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Birds

Species and Arsenic Compound	Effect	Reference ^a
CHUKAR, <i>Alectoris chukar</i> Silvisar-510 (mixture of cacodylic acid and triethanolamine cacodylate)	Single oral LD50 dose of 2000 mg/kg body weight (BW); signs of poisoning evident within 10 min and mortalities within 1–2 days postadministration. Remission took up to 1 month	1
MALLARD, <i>Anas platyrhynchos</i> Sodium arsenate	Adult breeding pairs fed diets with 0, 25, 100, or 400 mg As/kg ration for up to 173 days. Ducklings produced were fed the same diet as their parents for 14 days. Dose-dependent increase in liver arsenic from 0.23 mg As/kg DW in controls to 6.6 in the 400-mg/kg group and in eggs from 0.23 in controls to 3.6 mg/kg DW in the 400-mg/kg group. Dose-dependent adverse effects on growth, onset of egg laying, and eggshell thinning. In ducklings, arsenic accumulated in the liver from 0.2 mg As/kg DW in controls to 33.0 in the 400-mg/kg group and caused dose-dependent decrease in whole-body and liver growth rate	9
Sodium arsenate	Ducklings were fed 30, 100, or 300 mg As/kg diet for 10 weeks. All treatment levels produced elevated hepatic glutathione and ATP concentrations and decreased overall weight gain and rate of growth in females. Arsenic concentrations were elevated in brain and liver of ducklings fed 100 or 300 mg/kg diets; at 300 mg/kg, all ducklings had altered behavior, i.e., increased resting time; males had reduced growth	6
Sodium arsenate	Day-old ducklings fed diets containing 200 mg As/kg ration for 4 weeks. When protein was adequate (22%), some growth reduction resulted. With only 7% protein in diet, growth and survival was reduced and frequency of liver histopathology increased	7
Sodium arsenate	Adult males fed diets containing 300 mg As/kg ration. Equilibrium reached in 10–30 days; 50% loss from liver in 1–3 days on transfer to uncontaminated diet	8
Sodium arsenite	323 mg/kg BW is LD50 acute oral value	1–3
Sodium arsenite	500 mg/kg diet is fatal to 50% in 32 days; 1000 mg/kg diet fatal to 50% in 6 days	2
Sodium cacodylate	1740–5000 mg/kg diet fatal to 50% in 5 days	4
Silvisar 510	Single oral LD50 >2400 mg/kg BW; regurgitation and excessive drinking noted	1
Lead arsenate	5000 mg/kg diet not fatal in 11 days	2
Copper acetoarsenite	5000 mg/kg diet fatal to 20% in 11 days	2
CALIFORNIA QUAIL, <i>Callipepla californica</i>	LD50 single oral dose of 47.6 mg/kg BW	1
COMMON BOBWHITE, <i>Colinus virginianus</i>	480 mg/kg in diet fatal to 50% in 11 days	2
Copper acetoarsenite	1740 mg/kg in diet for 5 days produced no effect on behavior, no signs of intoxication, and negative necropsy	4
Sodium cacodylate	Single oral LD50 dose of 3300 mg/kg BW	4
Monosodium methane-arsonate, $\text{CH}_4\text{AsNaO}_3$		
CHICKEN, <i>Gallus gallus</i>	Up to 34% dead embryos at dose range of 0.01–1 mg $\text{As}^{+3}/\text{embryo}$; threshold for malformations at dose range 0.03–0.3 mg/embryo	3
Inorganic trivalent arsenite	Up to 8% dead at dose range 0.01–1 mg $\text{As}^{+5}/\text{embryo}$; threshold for malformations at dose range 0.3–3 mg/embryo	3
Inorganic pentavalent arsenate	Teratogenic to embryos when injected at 1–2 mg/egg	3, 4
Disodium methyl arsenate	Developmental abnormalities at embryonic injected doses of 1–2 mg/egg	4
Sodium cacodylate	At dietary levels of 23.3 mg/kg, liver residues were 2.9 mg/kg FW at 9 weeks. No ill effects noted	5

Table 28.5 (continued) Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Birds

Species and Arsenic Compound	Effect	Reference^a
3-Nitro-4-hydroxyphenyl-arsonic acid	At 18.7 mg/kg diet for 9 weeks, liver residues of 2.4 mg/kg FW. Those fed diets containing 187 mg/kg for 9 weeks had no ill effects; liver content of 7.5 mg/kg FW	5
3-Nitro-4-hydroxyphenyl-arsonic acid	LC50 dose of 33 mg/kg BW (single oral) or 9.7 mg/kg BW (intraperitoneal injection)	2
Arsanilic acid	Fed diets containing 45 mg/kg for 9 weeks; no effect except slightly elevated liver content of 1.2 mg/kg fresh weight. At dietary levels of 455 mg/kg, liver residues were 6.4 mg/kg FW after 9 weeks; no other effects evident	5
Cacodylic acid	Dosed orally without effect at 100 mg/kg BW daily for 10 days	4
CHICKENS, <i>Gallus</i> spp.		
Arsanilic acid	50% excreted in 36–38 h	3
Arsenate	50% excreted in 60–63 h	3
TURKEY, <i>Meleagris gallopavo</i>		
3-Nitro-4-hydroxyphenyl-arsonic acid	Single oral LD50 dose of 17.4 mg/kg BW	2
BROWN-HEADED COWBIRD, <i>Molothrus ater</i>		
Copper acetoarsenite	All survived 11 mg/kg diet for 6 months; maximum whole-body residue of 1.7 mg As/kg dry weight	2
Copper acetoarsenite	All survived 33 mg/kg diet for 6 months (whole-body content of 6.6 mg As/kg dry weight) or 7 months (8.6 DW)	2
Copper acetoarsenite	99.8 mg/kg in diet fatal to 50% in 11 days	2
Copper acetoarsenite	100 mg/kg in diet for 3 months fatal to 100%; tissue residues of 6.1 dry weight in brain, 40.6 in liver	2
GRAY PARTRIDGE, <i>Perdix perdix</i>		
Lead arsenate	300 mg/kg BW fatal in 52 h	2
RING-NECKED PHEASANT, <i>Phasianus colchicus</i>		
Sodium arsenite	Single oral dose of 386 mg/kg BW is LD50 value	1
Copper acetoarsenite	Single oral dose of 1403 mg/kg BW is LD50 value	3
Lead arsenate	4989 mg/kg in diet fatal	2

^a 1, Hudson et al. 1984; 2, NAS 1977; 3, NRCC 1978; 4, Hood 1985; 5, Woolson 1975; 6, Camardese et al. 1990; 7, Hoffman et al. 1992; 8, Pendleton et al. 1995; 9, Stanley et al. 1994.

28.6.6 Mammals

Mammals are exposed to arsenic primarily through the ingestion of naturally contaminated vegetation and water, or through human activity. In addition, feed additives containing arsanilic acid derivatives are often fed to domestic livestock to promote growth and retard disease. Some commercial pet foods contain up to 2.3 mg As/kg dry weight (NRCC 1978). Uptake may occur by ingestion (the most likely route), inhalation, and absorption through skin and mucous membranes. Soluble arsenicals are absorbed more rapidly and completely than are the sparingly soluble arsenicals, regardless of the route of administration (NRCC 1978). In humans, inorganic arsenic at high concentrations is associated with adverse reproductive outcomes, including increased rates of spontaneous abortion, low birth weight, congenital malformations, and death (Hopenhayn-Rich et al. 1998). However, at environmentally relevant levels and routes of exposure, humans are not at risk for birth defects due to arsenic (Holton et al. 1998). *In vitro* tests with human erythrocytes demonstrate that inorganic As⁺⁵ as sodium arsenite was up to 1000 times more effective than inorganic As⁺³ as sodium arsenite after exposure for 5 h to 750 mg As/L in causing death, morphologic changes, and ATP depletion (Winski and Carter 1998).

Acute episodes of poisoning in warm-blooded organisms by inorganic and organic arsenicals are usually characterized by high mortality and morbidity over a period of 2 to 3 days (NAS 1977;

Selby et al. 1977). General signs of arsenic toxicosis include intense abdominal pain, staggering gait, extreme weakness, trembling, salivation, vomiting, diarrhea, fast and feeble pulse, prostration, collapse, and death. Gross necropsy shows a reddening of gastric mucosa and intestinal mucosa, a soft yellow liver, and red edematous lungs. Histopathological findings show edema of gastrointestinal mucosa and submucosa, necrosis and sloughing of mucosal epithelium, renal tubular degeneration, hepatic fatty changes and necrosis, and capillary degeneration in the gastrointestinal tract, vascular beds, skin, and other organs. In subacute episodes, where animals live for several days, signs of arsenosis include depression, anorexia, increased urination, dehydration, thirst, partial paralysis of rear limbs, trembling, stupor, coldness of extremities, and subnormal body temperatures (NAS 1977; Selby et al. 1977; ATSDR 1992). In cases involving cutaneous exposure to arsenicals, a dry, cracked, leathery, and peeling skin may be a prominent feature (Selby et al. 1977). Nasal discharges and eye irritation were documented in rodents exposed to organoarsenicals in inhalation toxicity tests (Hood 1985). Subacute effects in humans and laboratory animals include peripheral nervous disturbances, melanosis, anemia, leukopenia, cardiac abnormalities, and liver changes. Most adverse signs rapidly disappear after exposure ceases (Pershagen and Vahter 1979).

Arsenic poisoning in most animals is usually manifested by acute or subacute signs; chronic poisoning is infrequently seen (NAS 1977). The probability of chronic arsenic poisoning from continuous ingestion of small doses is rare because detoxification and excretion are rapid (Woolson 1975). Chronic toxicity of inorganic arsenicals is associated with weakness, paralysis, conjunctivitis, dermatitis, decreased growth, and liver damage (NRCC 1978). Arsenosis, produced as a result of chronic exposure to organic arsenicals, was associated with demyelination of the optic and sciatic nerves, depressed growth, and decreased resistance to infection (NRCC 1978).

Research results on arsenic poisoning in mammals ([Table 28.6](#)) show general agreement on eight points:

1. Arsenic metabolism and effects are significantly influenced by the organism tested, the route of administration, the physical and chemical form of the arsenical, and the dose.
2. Inorganic arsenic compounds are more toxic than organic arsenic compounds, and trivalent species are more toxic than pentavalent species.
3. Inorganic arsenicals can cross the placenta in most species of mammals.
4. Early developmental stages are the most sensitive, and humans appear to be one of the more susceptible species.
5. Animal tissues usually contain low levels (<0.3 mg As/kg fresh weight) of arsenic. After the administration of arsenicals, these levels are elevated, especially in liver, kidney, spleen, and lung; and several weeks later, arsenic is translocated to ectodermal tissues (hair, nails) because of the high concentration of sulfur-containing proteins in these tissues.
6. Inorganic arsenicals are oxidized *in vivo*, biomethylated, and usually excreted rapidly in the urine, but organoarsenicals are usually not subject to similar transformations.
7. Acute or subacute arsenic exposure can lead to elevated tissue residues, appetite loss, reduced growth, loss of hearing, dermatitis, blindness, degenerative changes in liver and kidney, cancer, chromosomal damage, birth defects, and death.
8. Death or malformations have been documented at single oral doses of 2.5 to 33 mg As/kg body weight, at chronic doses of 1 to 10 mg As/kg body weight, and at dietary levels >5 and <50 mg As/kg diet.

Episodes of wildlife poisoning by arsenic are infrequent. White-tailed deer (*Odocoileus virginianus*) consumed, by licking, fatal amounts of sodium arsenite used to debark trees. The practice of debarking trees with arsenicals for commercial use has been almost completely replaced by mechanical debarking equipment (NAS 1977). In another incident, white-tailed deer were found dead of arsenic poisoning in a northern New York forest and had 102 mg As/kg fresh weight in liver and 56 mg As/kg FW in kidney. These tissue concentrations are 2 to 3 times higher than those in cattle that died of arsenic poisoning — estimated at 241 to 337 mg As/kg BW (Mathews and

Porter 1989). It is speculated that these deer licked trees injected with Silvisar 550, which contains monosodium methanearsonate, probably because of its salty taste (Mathews and Porter 1989). Snowshoe hares (*Lepus* sp.) appear to be especially sensitive to methylated arsenicals; hares died after consuming plants heavily contaminated with monosodium methanearsonate as a result of careless silviculture practices (Hood 1985).

Unlike wildlife, reports of arsenosis in domestic animals are common in bovines and felines, less common in ovines and equines, and rare in porcines and poultry (NAS 1977). In practice, the most dangerous arsenic preparations are dips, herbicides, and defoliants in which the arsenical is in a highly soluble trivalent form, usually as trioxide or arsenite (Selby et al. 1977). Accidental poisoning of cattle with arsenicals, for example, is well documented. In one instance, more than 100 cattle died after accidental overdosing with arsenic trioxide applied topically to control lice. On necropsy, there were subcutaneous edematous swellings and petechial hemorrhages in the area of application, and histopathology of the intestine, mucosa, kidney, and epidermis (Robertson et al. 1984). In Bangladesh, poisoned cattle showed depression, trembling, bloody diarrhea, restlessness, unsteady gait, stumbling, convulsions, groaning, shallow labored breathing, teeth grinding, and salivation (Samad and Chowdhury 1984). Cattle usually died 12 to 36 h after the onset of signs; necropsy showed extensive submucosal hemorrhages of the gastrointestinal tract (Samad and Chowdhury 1984) and tissue residues >10 mg/kg fresh weight in liver and kidney (Thatcher et al. 1985). It sometimes appears that animals, especially cattle, develop an increased preference for weeds sprayed with an arsenic weed killer, not because of a change in the palatability of the plant, but probably because arsenic compounds are salty and thus attractive to animals (Selby et al. 1977).

When extrapolating animal data from one species to another, the species tested must be considered. For example, the metabolism of arsenic in the rat (*Rattus* sp.) is unique and very different from that in man and other animals. Rats store arsenic in blood hemoglobin, excreting it very slowly — unlike most mammals which rapidly excrete ingested inorganic arsenic in the urine as methylated derivatives (NAS 1977). Blood arsenic, whether given as As^{+3} or As^{+5} , rapidly clears from humans, mice, rabbits, dogs, and primates; the half-life is 6 h for the fast phase and about 60 h for the slow phase (USEPA 1980). In the rat, however, blood arsenic is mostly retained in erythrocytes and clears slowly; the half-life is 60 to 90 days (USEPA 1980). In rats, the excretion of arsenic into bile is 40 times faster than in rabbits and up to 800 times faster than in dogs (Pershagen and Vähter 1979). Most researchers now agree that the rat is unsatisfactory for use in arsenic research (NAS 1977; NRCC 1978; Pershagen and Vähter 1979; USEPA 1980; Webb et al. 1986).

Dimethylarsinic acid is the major metabolite of orally administered arsenic trioxide, and is excreted rapidly in the urine (Yamauchi and Yamamura 1985). The methylation process is true detoxification, since methanearsonates and cacodylates are about 200 times less toxic than sodium arsenite (NAS 1977). The marmoset monkey (*Callithrix jacchus*), unlike all other animal species studied to date, was not able (for unknown reasons) to metabolize administered As^{+5} to dimethylarsinic acid; most was reduced to As^{+3} . Only 20% of the total dose was excreted in urine as unchanged As^{+5} , and another 20% as As^{+3} . The rest was bound to tissues, giving distribution patterns similar to arsenite (Vähter and Marafante 1985). Accordingly, the marmoset, like the rat, may be unsuitable for research with arsenicals.

Arsenicals were ineffective in controlling certain bacterial and viral infections. Mice experimentally infected with bacteria (*Klebsiella pneumoniae*) or viruses (pseudorabies, encephalitis, encephalomyocarditis) showed a significant increase in mortality when treated with large doses of arsenicals compared to nonarsenic-treated groups (NAS 1977; Aranyi et al. 1985).

It has been suggested, but not yet verified, that many small mammals avoid arsenic-supplemented feeds and consume other foods if given the choice (NAS 1977), and that cacodylic acid, which has negligible effects on wildlife, reduces species diversity due to selective destruction of vegetation (Hood 1985). Both topics merit more research.

Table 28.6 Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Mammals

Organism and Arsenical	Effect	Reference ^a
COW, <i>Bos bovis</i>		
Arsenate	Cows fed 33 mg As ⁺⁵ daily per animal for 3 months had slightly elevated levels in muscle (0.02 mg/kg fresh weight vs. 0.005 in controls) and liver (0.03 vs. 0.012), but normal levels in milk and kidney	1
Arsenite	Cows fed 33 mg As ⁺³ daily per animal for 15–28 months had tissue levels, in mg/kg fresh weight, of 0.002 for milk (vs. <0.001 for controls), 0.03 for muscle (vs. 0.005), 0.1 for liver (vs. 0.012), and 0.16 for kidney (vs. 0.053)	1
CATTLE, <i>Bos</i> spp.		
Arsenic pentoxide (wood ashes treated with arsenic preservative)	Several deaths after eating ashes (780 mg/kg dry weight); tissue residues, in mg As/kg fresh weight, of 13.9 in liver, 23.7 in kidney, and 25.8 in rumen contents (vs. normal values of <0.5)	2
Arsenic trioxide	Single oral dose of 15–45 grams per animal is fatal	3
Arsenic trioxide	Toxic dose is 33–55 mg/kg body weight (BW), or 13.2–22 g for a 400-kg animal. Animals accidentally poisoned topically contained up to 15 mg As/kg fresh weight liver, 23 in kidney, and 45 in urine (vs. <1 for all normal tissues)	4
Cacodylic acid, (CH ₃) ₂ AsO(OH)	Calves were anorexic in 3–6 days when fed diets containing 4700 mg/kg. Adult oral dose of 10 mg/kg BW daily for 3 weeks, followed by 20 mg/kg BW daily for 5–6 weeks was lethal. Adverse effects at 25 mg/kg BW daily for 10 days	5
Methanearsonic acid	Calves were anorexic in 3–6 days when fed diets containing 4000 mg/kg	5
Monosodium methanearsonate	10 mg/kg BW daily for 10 days was fatal	3
Sodium arsenite	Single oral dose of 1–4 g fatal	3
DOG, <i>Canis familiaris</i>		
Cacodylic acid	Single oral LD ₅₀ value of 1000 mg/kg BW; diets containing 30 mg/kg for 90 days had no ill effects	5
Methanearsonic acid	Fed diets containing 30 mg/kg for 90 days with no ill effects	5
Sodium arsenite	50–150 mg fatal	3
DOMESTIC GOAT, <i>Capra</i> sp.		
Arsenic acid	Single oral dose of 2.5–7.5 mg/kg BW (50–150 mg) was acutely toxic	3
GUINEA PIG, <i>Cavia</i> sp.		
Arsenic acid	Dietary levels of 350 mg/kg resulted in blindness and optic disc atrophy in 25–30 days	6
Arsenic trioxide	Fed diets containing 50 mg/kg for 21 days; elevated As residues, in mg/kg fresh weight, of 4 in blood, 15 in heart (vs. <1 for all control tissues)	7
Sodium arsanilate	Subcutaneous injection of 70 mg/kg BW caused degeneration of sensory walls of inner ear; elevated As residues in cochlea	6
Sodium arsenate	Intraperitoneal injection of 0.2 mg/kg BW at age 2 months causes deafness	6
HAMSTER, <i>Cricetus</i> sp.		
Arsenate	Maternal dose of 5 mg As ⁺⁵ /kg BW caused some fetal mortality, but no malformations; higher dose of 20 mg/kg BW caused 54% fetal deaths and malformations	3
Calcium arsenate	Pulmonary tumorigenicity demonstrated 70 weeks after 15 intratracheal weekly injections of 3 mg/kg BW	8

Table 28.6 (continued) Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Mammals

Organism and Arsenical	Effect	Reference^a
Dimethylarsinate	50% growth reduction in Chinese hamster ovary cells (CHOC) at 90–112 mg/L	9
Gallium arsenide	Single oral dose of 100 mg/kg BW mostly (85%) eliminated in 5 days, usually in form of organoarsenicals; all tissue levels <0.25 mg/kg	10
Sodium arsenate	Dosed intravenously on day 8 of gestation: 2 mg/kg BW had no measurable effect; 8 mg/kg produced increased incidence of malformation and resorption; 16 mg/kg BW killed all embryos	6
Sodium arsenate	50% growth reduction in CHOC at 2.25 mg/L	9
Sodium arsenite	Chinese hamster ovary cells (CHOC) show 50% growth reduction at 0.3 mg/L	9
Sodium cacodylate	Single intraperitoneal injection of 900–1000 mg/kg during midgestation results in some maternal deaths and increased incidences of fetal malformations	5
HORSE, <i>Equus caballus</i>		
Sodium arsenite	Daily doses of 2–6 mg/kg BW (1–3 grams) for 14 weeks is fatal	3
CAT, <i>Felis domesticus</i>		
Inorganic arsenate or arsenite	Chronic oral toxicity at 1.5 mg/kg BW	6
HUMAN, <i>Homo sapiens</i>		
Arsenic trioxide	Fatal at 70–189 mg, equivalent to about 1–2.6 mg As/kg BW	6
Arsenic trioxide	LD50 dose of 7 mg/kg BW	3
Cacodylic acid	LD50 of 1350 mg/kg BW	3
Lead arsenate	Some deaths at 7 mg/kg BW	3
Total arsenic	Accumulations of 1 mg/kg BW daily for 3 months in children, or 80 mg/kg BW daily for 3 years in adults produced symptoms of chronic arsenic poisoning	3
Total arsenic, daily oral dose	Prolonged dosages of 3–4 mg daily produced clinical symptoms of chronic arsenic intoxication	3
Total arsenic in drinking and cooking water	Prolonged use produced symptoms of chronic arsenic intoxication (0.6 mg/L) or skin cancer (0.29 mg/L)	3
Total arsenic, probably arsenate	12,000 Japanese infants poisoned (128 deaths) from consumption of dry milk contaminated with arsenic; average exposure of 3.5 mg As daily for 1 month. Severe hearing loss, brain wave abnormalities, and other CNS disturbances noted 15 years after exposure	6
Total inorganic arsenic	Daily dose of 3 mg for 2 weeks may cause severe poisoning in infants, and symptoms of toxicity in adults	6
CYNOMOLGUS MONKEY, <i>Macaca</i> sp.		
Fish-arsenic meal (witch flounder, <i>Glyptocephalus cynoglossus</i>) containing 77 mg total As/kg	Given a single meal at 1 mg/kg BW; tissue residues normal after 14 days	11
As above, except arsenic trioxide substituted for total As	As above	11
MAMMALS, many species		
Calcium arsenate	Single oral LD50 range of 35–100 mg/kg BW	3
Lead arsenate	Single oral LD50 range of 10–50 mg/kg BW	3
MAMMALS, most species		
Arsenic trioxide	3–250 mg/kg BW lethal	12
Sodium arsenite	1–25 mg/kg BW lethal	12

Table 28.6 (continued) Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Mammals

Organism and Arsenical	Effect	Reference ^a
MOUSE, <i>Mus</i> spp.		
Arsenate	Maternal dose of 10 mg As ⁺⁵ /kg BW results in some fetal deaths and malformations	3
Arsenic trioxide	Single oral LD50 (96 h) value of 39.4 mg/kg BW; LD0 (96 h) of 10.4 mg/kg BW	12
Arsenic trioxide	"Adapted" group (50 mg As/L in drinking water for 3 months) had subcutaneous LD50 value of 14 mg/kg BW vs. 11 for nonadapted group	12
Arsenic trioxide	Air concentrations of 28.5 mg/m ³ for 4 h daily on days 9–12 of gestation caused fetotoxic effects and chromosomal damage to liver cells by day 18; effects included reduced survival, impaired growth, retarded limb ossification, and bone abnormalities. At 2.9 mg/m ³ , a 9.9% decrease in fetal weight was recorded; at 0.26 mg/m ³ , a 3.1% decrease was measured	13
Cacodylic acid	Oral dosages of 400–600 mg/kg BW on days 7–16 of gestation produces fetal malformations (cleft palate), delayed skeletal ossification, and fetal weight reduction	5
Dimethylarsinic acid	200–600 mg/kg BW daily for 10 days (DMA) produced fetal and maternal toxicity	25
Single oral dose		
Arsenous oxide	34 mg As/kg BW fatal to 50%	21
Tetramethylarsonium iodide	890 mg As/kg BW fatal to 50%	21
Dimethylarsinic acid	1200 mg As/kg BW fatal to 50%	21
Dimethylarsonic acid	1800 mg As/kg BW fatal to 50%	21
Arsenocholine	6500 mg As/kg BW fatal to 50%	21
Trimethylarsinoxide	10,600 mg As/kg BW fatal to 50%	21
Arsenobetaine	>100,000 mg As/kg BW fatal to 50%	21
Sodium arsenate	Maximum tolerated doses in terms of abortion or maternal death over 24 h in 18-day pregnant mice were 20 mg As ⁺⁵ /kg BW, intraperitoneal route, and 50 mg/kg BW when administered orally. Residue half-life was about 10 h, regardless of route of administration	14
Sodium arsenate	Given 500 µg As/L in drinking water for as long as 26 months, equivalent to 0.07–0.08 mg As/kg BW daily. No tumors in controls vs. 41.1% of mice in treated groups with 1 or more tumors — mostly of the lung, liver, and GI tract	22
Sodium arsenite	Fed 5 mg/kg diet for 3 generations: reduced litter size, but outwardly normal	6
Sodium arsenite	LD50 of 9.6 mg/kg BW, sc route; LD90 (7 days postadministration) of 11.3 mg/kg BW, sc route	15
Sodium arsenite	LD50 of 12 mg/kg BW intraperitoneal route. At 10 mg/kg BW, damage to bone marrow and sperm	16
Sodium cacodylate	Single intraperitoneal injection of 1200 mg/kg BW during midgestation results in increased rates of fetal skeletal malformations	5
MULE DEER, <i>Odocoileus hemionus hemionus</i>		
Silvisar-510 (mixture of cacodylic acid and triethanolamine cacodylate)	Single oral LD50 dose >320 mg/kg BW; appetite loss	17
WHITE-TAILED DEER, <i>Odocoileus virginianus</i>		
Sodium arsenite (used to debark trees)	Lethal dose of 923–2770 mg equivalent to about 34 mg/kg BW; liver residues of 40 mg/kg fresh weight	12
Arsenic acid (to control Johnson grass)	23 deer killed from apparent misuse. Arsenic levels, in mg/kg fresh weight, in deer found dead were 19 in liver, 18 in kidney, and 22.5 in rumen. Soils from area contained ~2.4 mg As/kg, and water 0.42 mg As/L	12

Table 28.6 (continued) Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Mammals

Organism and Arsenical	Effect	Reference^a
RABBIT, <i>Oryctolagus</i> sp.		
Monomethylarsonic acid (MMA)	50 mg/kg ration for 7–12 weeks produces hepatotoxicity	25
DOMESTIC SHEEP, <i>Ovis aries</i>		
Arsanilic acid	One-year-old castrates fed diets with 273 mg As/kg for 28 days had 0.54 mg As/L in blood, 29 mg/kg dry weight in liver, 24 in kidney, and 1.2 in muscle (vs. <0.01 in all control tissues). After 6 days on an As-free diet, liver residues were <5 mg/kg DW. Maximum tissue levels in sheep fed diets containing 27 mg As/kg for 28 days were 3.2 mg/kg DW kidney; for a 144 mg/kg DW diet, the maximum tissue level was 27 mg/kg DW liver	7
Sodium arsenite	Single oral dose of 5–12 mg/kg BW (0.2–0.5 g) was acutely toxic	3
Soluble arsenic	Lambs fed supplemental arsenic for 3 months at 2 mg As/kg DW diet contained maximum concentrations of 2 mg/kg FW brain (vs. 1 in controls), 14 in muscle (2), 24 in liver (4), and 57 in kidney (10)	18
Total arsenic	Sheep fed diets containing lakeweed (<i>Lagarosiphon major</i>) (288 mg As/kg DW) at 58 mg total As/kg diet for 3 weeks without ill effect. Tissue residues increased during feeding, but rapidly declined when lakeweed was removed from diet	7
RAT, <i>Rattus</i> spp.		
Arsanilic acid	No teratogenesis observed in 7 generations at dietary level of 17.5 mg/kg; positive effect on litter size and survival	6
Arsenate	Fed diets containing 50 mg/kg for 10 weeks with no effect on serum uric acid levels	19
Arsenic trioxide	Single oral LD50 (96 h) value of 15.1 mg/kg BW	12
Arsenic trioxide	Single dose of 17 mg/kg BW administered intratracheally is maximally tolerated nonlethal dose; 2 weeks later, blood As elevated (36 mg/L) and lung histopathology evident	20
Arsenic trioxide	After 21 days on diet containing 50 mg/kg, tissue arsenic levels were elevated in blood (125 mg/L vs. 15 in controls), heart (43 mg/kg FW vs. 3.3), spleen (60 vs. <0.7), and kidney (25 vs. 1.5)	7
Arsenite	Oral administration of 1.2 mg/kg BW daily for 6 weeks reduced uric acid levels in plasma by 67%	19
Arsenite	10 mg As/L in drinking water for 7 months; urinary metabolites were mainly methylated arsenic metabolites with about 6% in inorganic form	24
Arsenobetaine	100 mg As/L in drinking water for 7 months; eliminated in urine unchanged without transformation	24
Cacodylic acid	Fetal and maternal deaths noted when pregnant rats dosed by gavage at 50–60 mg/kg BW daily during gestation days 6–13. Fetal abnormalities observed when dams given oral dosages of 40–60 mg/kg BW on days 7–16 of gestation	5
Dimethylarsinic acid (DMA)	Main metabolites in urine after 7 months of exposure to 100 mg As/L drinking water were DMA and trimethylarsin oxide (TMAO) with minute amounts of tetramethylarsonium (TMA)	24
Dimethylarsinic acid	40–60 mg/kg BW daily for 10 days associated with fetal and maternal toxicity	25
Monomethylarsonic acid (MMA)	100 mg As/L in drinking water for 7 months produced main products in urine of unchanged MMA and DMA, plus small amounts of TMA and TMAO	24
3-Nitro-4-hydroxyphenylarsonic acid	Single oral LD50 value of 44 mg/kg BW	12
Sodium arsenate	LD75 (48 h) value of 14–18 mg/kg BW (intraperitoneal route)	12

Table 28.6 (continued) Lethal and Sublethal Effects of Various Arsenicals on Selected Species of Mammals

Organism and Arsenical	Effect	Reference ^a
Sodium arsenite	Single intraperitoneal injection of 5–12 mg/kg on days 7–12 of gestation produced eye defects, exencephaly, and faulty development of kidney and gonads	6
Sodium arsenite	LD75 (48 h) value of 4.5 mg/kg BW (intraperitoneal injection)	12
Trimethylarsin oxide (TMAO)	100 mg As/L in drinking water for 7 months was excreted in urine mostly unchanged with some TMA	24
RODENTS, various species		
Cacodylic acid	LD50 (various routes) values range from 470–830 mg/kg BW	5
Sodium cacodylate	LD50 (various routes) values range from 600–2600 mg/kg BW	5
COTTON RAT, <i>Sigmodon hispidus</i>		
Sodium arsenite	Adult males given 0, 5, or 10 mg As ⁺³ /L drinking water for 6 weeks had dose-dependent decrease in daily food intake. Minimal effects on immune function, tissue weights, and blood chemistry	23
PIG, <i>Sus</i> sp.		
Sodium arsenite	Drinking water containing 500 mg/L lethal at 100–200 mg/kg BW	12
3-Nitro-4-hydroxyphenylarsonic acid	Arsenosis documented after 2 months on diets containing 100 mg/kg, or after 3–10 days on diets containing 250 mg/kg	12
RABBIT, <i>Sylvilagus</i> sp.		
Cacodylic acid	Adverse effects at dermal dosages equivalent to 4–6 g/kg BW	5
Calcium arsenate	Single oral dose of 23 mg/kg BW fatal in 3 days	12
Copper acetoarsenite	Single oral dose of 10.5 mg/kg BW fatal in 50 h	12
Inorganic arsenate	Single oral LD50 value of 8 mg/kg BW	3
Lead arsenate	Single oral dose of 40.4 mg/kg BW fatal in 52 h	12

^a 1, Vreman et al. 1986; 2, Thatcher et al. 1985; 3, NRCC 1978; 4, Robertson et al. 1884; 5, Hood 1985; 6, Pershagen and Vahter 1979; 7, Woolson 1975; 8, Pershagen and Bjorklund 1985; 9, Belton et al. 1985; 10, Yamauchi et al. 1986; 11, Charbonneau et al. 1978; 12, NAS 1977; 13, Nagymajtenyi et al. 1985; 14, Hood et al. 1987; 15, Stine et al. 1984; 16, Deknudt et al. 1986; 17, Hudson et al. 1984; 18, Veen and Vreman 1986; 19, Jauge and Del-Razo 1985; 20, Webb et al. 1986; 21, Hamasaki et al. 1995; 22, Ng et al. 1998; 23, Savabieasfahani et al. 1998; 24, Yoshida et al. 1998; 25, Hughes and Kenyon 1998.

28.7 RECOMMENDATIONS

Numerous criteria for arsenic have been proposed to protect natural resources and human health (Table 28.7). But many authorities recognize that these criteria are not sufficient for adequate or (in some cases) reasonable protection, and that many additional data are required if meaningful standards are to be promulgated (NAS 1977; NRCC 1978; Pershagen and Vahter 1979; USEPA 1980, 1985; Eisler 1994; Abernathy et al. 1997; SEGH 1998). Specifically, data are needed on the following subjects:

1. Cancer incidence and other abnormalities in natural resources from areas with elevated arsenic levels, and the relation to potential carcinogenicity of arsenic compounds
2. Interaction effects of arsenic with other carcinogens, cocarcinogens, promoting agents, inhibitors, and common environmental contaminants
3. Controlled studies with aquatic and terrestrial indicator organisms on physiological and biochemical effects of long-term, low-dose exposures to inorganic and organic arsenicals, including effects on reproduction and genetic makeup

4. Methodologies for establishing maximum permissible tissue concentrations for arsenic
5. Effects of arsenic in combination with infectious agents
6. Mechanisms of arsenical growth-promoting agents
7. Role of arsenic in nutrition
8. Extent of animal adaptation to arsenicals and the mechanisms of action
9. Identification and quantification of mineral and chemical forms of arsenic in rocks, soils, and sediments that constitute the natural forms of arsenic entering water and the food chain
10. Physicochemical processes influencing arsenic cycling.

In addition, the following techniques should be developed and implemented: (1) more sophisticated measurements of the chemical forms of arsenic in plant and animal tissues; (2) correlation of biologically observable effects with particular chemical forms of arsenic; and (3) management of arsenical wastes that accommodates recycling, reuse, and long-term storage.

Some proposed arsenic criteria merit additional comment, such as those on aquatic life protection, levels in seafoods and drinking water, and use in food-producing animals as growth stimulants or for disease prevention and treatment.

For saltwater life protection, the current water quality criterion of 36 µg As⁺³/L (USEPA 1985; [Table 28.7](#)) seems to offer a reasonable degree of safety. Only a few species of algae show adverse effects at <36 µg/L (e.g., reduced growth at 19 to 22 µg/L). In 1980, this criterion was 508 µg/L (USEPA 1980), about 14 times higher than the current criterion. The downward modification seems to be indicative of the increasingly stringent arsenic criteria formulated by regulatory agencies. The current criterion for freshwater-life protection of 190 µg As⁺³/L (USEPA 1985; [Table 28.7](#)), however, which is down from 440 µg As⁺³/L in 1980 (USEPA 1980), is unsatisfactory. Many species of freshwater biota are adversely affected at <190 µg/L of As⁺³, As⁺⁵, or various organoarsenicals ([Table 28.4](#)). These adverse effects include death and malformations of toad embryos at 40 µg/L, growth inhibition of algae at 48 to 75 µg/L, mortality of amphipods and gastropods at 85 to 88 µg/L, and behavioral impairment of goldfish (*Carassius auratus*) at 100 µg/L. A downward adjustment in the current freshwater aquatic-life protection criterion seems warranted.

In Hong Kong, permissible concentrations of arsenic in seafood destined for human consumption range from 6 to 10 mg/kg fresh weight ([Table 28.7](#)). However, these values are routinely exceeded in 22% of finfish, 20% of bivalve molluscs, 67% of gastropods, 29% of crabs, 21% of shrimp and prawns, and 100% of lobsters (Phillips et al. 1982). The highest arsenic concentrations recorded in Hong Kong seafood products were in gastropods (*Hemifusus* spp.), in which the concentrations of 152 to 176 mg/kg FW were among the highest recorded in any species to date (Phillips et al. 1982). A similar situation exists in Yugoslavia, where almost all seafoods exceed the upper limit prescribed by food quality regulations (Ozretic et al. 1990). Most of the arsenic in seafood products is usually arsenobetaine or some other comparatively harmless form. In effect, arsenic criteria for seafoods are neither enforced nor enforceable. Some toxicologists from the U.S. Food and Drug Administration believe that the average daily intake of arsenic in the different food commodities does not pose a hazard to the consumer (Jelinek and Corneliusen 1977). It is now clear that formulation of maximum permissible concentrations of arsenic in seafoods for health regulation purposes should recognize the chemical nature of arsenic (McGeachy and Dixon 1990; [Table 28.7](#)).

For maximum protection of human health from the potential carcinogenic effects of exposure to arsenic through drinking water or contaminated aquatic organisms, the ambient water concentration should be zero, based on the nonthreshold assumption for arsenic. But a zero level may not be attainable. Accordingly, the levels established are those that are estimated to increase cancer risk over a lifetime to only one additional case per 100,000 population. These values are estimated at 0.022 µg As/L for drinking water and 0.175 µg As/L for water containing edible aquatic resources (USEPA 1980; [Table 28.7](#)).

Various phenylarsonic acids — especially arsanilic acid, sodium arsanilate, and 3-nitro-4-hydroxyphenylarsonic acid — have been used as feed additives for disease control and for improvement of weight gain in swine and poultry for almost 40 years (NAS 1977). The arsenic is present as As⁺⁵

and is rapidly excreted; present regulations require withdrawal of arsenical feed additives 5 days before slaughter for satisfactory depuration (NAS 1977). Under these conditions, total arsenic residues in edible tissues do not exceed the maximum permissible limit of 2 mg/kg fresh weight (Jelinek and Corneliusen 1977). Organoarsenicals probably will continue to be used as feed additives unless new evidence indicates they should not be.

Table 28.7 Proposed Arsenic Criteria for the Protection of Selected Natural Resources and Human Health

Resource and Other Variables	Criterion or Effective Arsenic Concentration (Reference)
AQUATIC LIFE	
Freshwater biota: medium concentrations	4-day mean water concentration not to exceed 190 µg total recoverable inorganic As ⁺³ /L more than once every 3 years; 1-h mean not to exceed 360 µg inorganic As ⁺³ /L more than once every 3 years. Insufficient data for criteria formulation for inorganic As ⁺⁵ , or for any organoarsenical (USEPA 1985)
Freshwater biota: tissue residues	Diminished growth and survival reported in immature bluegills (<i>Lepomis macrochirus</i>) when total arsenic residues in muscle are >1.3 mg/kg fresh weight (FW) or >5 mg/kg in adults (NRCC 1978)
Saltwater biota: medium concentration	4-day average water concentration not to exceed 36 µg As ⁺³ /L more than once every 3 years; 1-h mean not to exceed 69 µg As ⁺³ /L more than once every 3 years. Insufficient data for criteria formulation for inorganic As ⁺⁵ , or for any organoarsenical (USEPA 1985)
Saltwater biota: tissue residues	Depending on chemical form of arsenic, certain marine teleosts may be unaffected at muscle total arsenic residues of 40 mg/kg FW (NRCC 1978)
BIRDS	
Tissue residues	Residues, in mg total As/kg FW, liver or kidney in 2–10 range are considered elevated; residues >10 mg/kg are indicative of arsenic poisoning (Goede 1985)
Mallard, <i>Anas platyrhynchos</i> Sodium arsenite in diet	Reduced growth in ducklings fed more than 30 mg As/kg diet (Camardese et al. 1990)
Turkey, <i>Meleagris gallopavo</i> Arsanilic acid in diet	Maximum dietary concentration for turkeys less than 28 days old is 300–400 mg/kg feed (NAS 1977) Maximum levels in diets, in mg/kg feed, are 50–100 for arsanilic acid, 25–188 for 3-nitro-4-hydroxy-phenylarsonic acid (for chickens and turkeys, not recommended for ducks and geese), and 180–370 for others (NAS 1977)
Phenylarsonic feed additives for disease control and improvement of weight gain in domestic poultry; safe dietary levels	
DOMESTIC LIVESTOCK	
Prescribed limits for arsenic in feedstuffs	
Straight feedstuffs, except those listed below	<2 mg total As/kg FW (Vreman et al. 1986)
Meals from grass, dried lucerne, or dried clover	<4 mg total As/kg FW (Vreman et al. 1986)
Phosphate mealstuffs	<10 mg total As/kg FW (Vreman et al. 1986)
Fish meals	<10 mg total As/kg FW (Vreman et al. 1986)
Tissue residues	
Poisoned	
Liver, kidney	5–>10 total As/kg FW (Thatcher et al. 1985; Vreman et al. 1986)
Normal, muscle	<0.3 mg total As/kg FW (Veen and Vreman 1986)
VEGETATION	
No observable effects	<1 mg total water-soluble soil As/L; <25 mg total As/kg soil; <3.9 µg As/m ³ air (NRCC 1978)

Table 28.7 (continued) Proposed Arsenic Criteria for the Protection of Selected Natural Resources and Human Health

Resource and Other Variables	Criterion or Effective Arsenic Concentration (Reference)
HUMAN HEALTH	
Diet	
Permissible levels	
Total diet	<0.5 mg As/kg dry weight diet (Sorensen et al. 1985); 0.0003–0.0008 mg/kg body weight (BW) daily (ATSDR 1992)
Fruits, vegetables	The tolerance for arsenic residues as As_2O_3 , resulting from pesticidal use of copper, magnesium, and sodium arsenates is 3.5 mg/kg (Jelinek and Corneliusen 1977)
Muscle of poultry and swine, eggs, swine edible by-products	<2 mg total As/kg FW (Jelinek and Corneliusen 1977)
Edible by-products of chickens and turkey, liver and kidney of swine	<2 mg total As/kg FW (Jelinek and Corneliusen 1977)
Seafood products	In Hong Kong, limited to <6 mg As^{+3}/kg FW for edible tissues of finfish and <10 mg As^{+3}/kg for molluscs and crustaceans (Phillips et al. 1982; Edmonds and Francesconi 1993); in Yugoslavia, these values are 2 for fish and 4 for molluscs and crustaceans (Ozretic et al. 1990); in Australia, <1 mg inorganic As/kg FW and in New Zealand <2 mg inorganic As/kg FW — there is no limit on organoarsenicals (Edmonds and Francesconi 1993). In the UK, seafood products should contain <1 mg As/kg FW contributed as a result of contamination (Edmonds and Francesconi 1993)
Adverse effects	
Consumption of aquatic organisms living in As-contaminated waters	
Cancer risk of	
10^{-5}	0.175 µg As/L (USEPA 1980)
10^{-6}	0.0175 µg As/L (USEPA 1980) ^a
10^{-7}	0.00175 µg As/L (USEPA 1980)
Drinking water	
Allowable concentrations	
Total arsenic	<10 µg/L (NAS 1977; Hering et al. 1997; Kurttio et al. 1998)
Total arsenic	<50 µg/L (Pershagen and Vahter 1979; USEPA 1980; Norin et al. 1985; ATSDR 1992; USPHS 1998)
Total arsenic, Maine	<30 µg/L (ATSDR 1992)
Adverse effects	
Cancer risk of	
10^{-5}	0.022 µg As/L (USEPA 1980)
10^{-6}	0.0022 µg As/L (USEPA 1980) ^a
10^{-7}	0.00022 µg As/L (USEPA 1980)
Symptoms of arsenic toxicity observed	9% incidence at 50 µg As/L, 16% at 50–100 µg/L, and 44% at >100 µg As/L (NRCC 1978)
Harmful after prolonged consumption “Cancer”	>50–960 µg As/L (NRCC 1978)
Skin cancer	In Chile, cancer rate estimated at 0.01% at 82 µg As/L, 0.17% at 600 µg As/L (NRCC 1978)
Total intake	0.26% frequency at 290 µg/L and 2.14% at 600 µg/L (USEPA 1980)
No observable effect	
North America	0.007–0.06 mg As daily (Pershagen and Vahter 1979); 2 µg/kg BW daily (ATSDR 1992)
Japan	0.07–0.17 mg As daily (Pershagen and Vahter 1979)
United States	
1960s	0.05–0.1 mg As daily (Pershagen and Vahter 1979)
1974	0.015 mg As daily (Pershagen and Vahter 1979)
1998	<0.021 mg As daily, based on <0.0003 mg/kg BW daily for 70-kg adult (USPHS 1998)
Canada	0.03 mg As daily (NRCC 1978)

Table 28.7 (continued) Proposed Arsenic Criteria for the Protection of Selected Natural Resources and Human Health

Resource and Other Variables	Criterion or Effective Arsenic Concentration (Reference)
Netherlands	
Acceptable	2 µg total inorganic As/kg body weight (BW) (about 0.14 mg daily for 70 kg adult); 0.094 mg daily through fishery products (Vos and Hovens 1986)
Adverse effects (prolonged exposure)	
Subclinical symptoms	0.15–0.6 mg As daily (NRCC 1978)
Intoxication	3–4 mg As daily (NRCC 1978)
Blackfoot disease	Total dose of 20 g over several years increases prevalence of disease by 3% Pershagen and Vahter 1979)
Mild chronic poisoning	0.15 mg As daily or about 2 µg/kg BW daily (NRCC 1978)
Chronic arsenic poisoning	Lifetime cumulative absorption of 1 g As, or intake of 0.7–2.6 g/year for several years (in medications) can produce symptoms after latent period of 4–24 years (NRCC 1978)
Tissue residues	
No observed effect levels	
Urine	<0.05 mg As/L (NRCC 1978)
Liver, kidney	<0.5 mg As/L (NRCC 1978)
Blood	<0.7 As/kg (NRCC 1978)
Hair ^b	<2 mg As/kg (NRCC 1978)
Fingernail	<5 mg As/kg (NRCC 1978)
Arsenic-poisoned	
Liver, kidney	2–100 mg As/kg FW; confirmatory tests >10 mg As/kg FW; residues in survivors several days later were 2–4 mg/kg FW (NAS 1977)
Whole body	In children, symptoms of chronic arsenicism evident at 1 mg As/kg BW, equivalent to intake of about 10 mg/month for 3 months; for adults, these values were 80 mg/kg BW, equivalent to about 2 g/year for 3 years (NRCC 1978)
Air	
Allowable concentrations	
Arsine	<200 µg/m ³ for U.S. industrial workers; proposed mean arsine limit of <4 µg/m ³ in 8-h period and <10 µg/m ³ maximum in 15 min (NAS 1977) <4 µg/m ³ (NRCC 1978)
Arsine	<2 µg/m ³ (ATSDR 1992)
Inorganic arsenic	<10 µg/m ³ (ATSDR 1992; USPHS 1998)
Occupational	<500 µg/m ³ (ATSDR 1992)
Residential	<3 µg/m ³ in U.S.S.R. and Czechoslovakia, <500 µg/m ³ for U.S. industrial workers (NAS 1977)
Organic arsenic	Proposed limit of <50 µg/m ³ , maximum of 2 µg/m ³ in 15 min, <10 µg airborne inorganic As/m ³ (USEPA 1980)
Total As	<0.3 µg/m ³ in U.S.S.R., <0.1 µg/m ³ in U.S. (Nagymajtenyi et al. 1985)
Total As (threshold limit value-time weighted mean:8 h/day, 40-h work week)	
Arsenic trioxide	
Adverse effects	
Increased mortality	Associated with daily time-weighted average arsenic exposure of >3 µg/m ³ for 1 year (NRCC 1978)
Respiratory cancer (increased risk)	Associated with chronic exposure >3 µg/m ³ , or occupational exposure (lifetime) of >54.6 µg As/m ³ (NRCC 1978)
Respiratory cancer (increased risk)	Exposure to 50 µg As/m ³ for more than 25 years associated with 3-fold increase (Pershagen and Vahter 1979)
Skin diseases	Associated with ambient air concentrations of 60–13,000 µg As/m ³ (NRCC 1978)
Dermatitis	Associated with ambient air concentrations of 300–81,500 µg As/m ³ (NRCC 1978)

^a One excess cancer per million population (10^{-6}) is estimated during lifetime exposure to 0.00022 µg arsenic per liter of drinking water, or to lifetime consumption of aquatic organisms residing in waters containing 0.0175 µg As/L (USEPA 1980).

^b Thai children, age 6–9 years from the Ronpiboon district with >5 mg As/kg DW hair had abnormally low IQs compared to those with 2.01–5 mg As/kg DW. Both groups had significantly lower IQs than controls (<1 mg As/kg DW hair), as measured by the Wechsler Intelligence Scale Test for Children (Unchalee et al. 1999). This study needs verification.

28.8 SUMMARY

Arsenic (As) is a relatively common element that occurs in air, water, soil, and all living tissues. It ranks 20th in abundance in Earth's crust, 14th in seawater, and 12th in the human body. Arsenic is a teratogen and carcinogen that can traverse placental barriers and produce fetal death and malformations in many species of mammals. Although it is carcinogenic in humans, evidence for arsenic-induced carcinogenicity in other mammals is scarce. Paradoxically, evidence is accumulating that arsenic is nutritionally essential or beneficial. Arsenic deficiency effects, such as poor growth, reduced survival, and inhibited reproduction, have been recorded in mammals fed diets containing <0.05 mg As/kg, but not in those fed diets with 0.35 mg As/kg. At comparatively low doses, arsenic stimulates growth and development in various species of plants and animals.

Most arsenic produced domestically is used in the manufacture of agricultural products such as insecticides, herbicides, fungicides, algicides, wood preservatives, and growth stimulants for plants and animals. Living resources are exposed to arsenic by way of atmospheric emissions from smelters, coal-fired power plants, and arsenical herbicide sprays; from water contaminated by mine tailings, smelter wastes, and natural mineralization; and from diet, especially from consumption of marine biota. Arsenic concentrations are usually low (<1.0 mg/kg fresh weight) in most living organisms, but they are elevated in marine biota (in which arsenic occurs as arsenobetaine and poses little risk to organisms or their consumers) and in plants and animals from areas that are naturally arseniferous or are near industrial manufacturers and agricultural users of arsenicals. Arsenic is bioconcentrated by organisms but is not biomagnified in the food chain.

Arsenic exists in four oxidation states, as inorganic or organic forms. Its bioavailability and toxic properties are significantly modified by numerous biological and abiotic factors, including the physical and chemical forms of arsenic tested, the route of administration, the dose, and the species of animal. In general, inorganic arsenic compounds are more toxic than organic compounds, and trivalent species are more toxic than pentavalent species. Arsenic may be absorbed by ingestion, inhalation, or through permeation of the skin or mucous membranes; cells take up arsenic through an active transport system normally used in phosphate transport. The mechanisms of arsenic toxicity differ greatly among chemical species, although all appear to cause similar signs of poisoning. Biomethylation is the preferred detoxification mechanism for absorbed inorganic arsenicals; methylated arsenicals usually clear from tissues within a few days.

Episodes of arsenic poisoning are either acute or subacute. Chronic cases of arsenosis are seldom encountered in any species except human beings. Single oral doses of arsenicals fatal to 50% of sensitive species tested ranged from 17 to 48 mg/kg body weight (BW) in birds and from 2.5 to 33 mg/kg BW in mammals. Susceptible species of mammals were adversely affected at chronic doses of 1 to 10 mg As/kg BW, or 50 mg As/kg diet. Sensitive aquatic species were damaged at water concentrations of 19 to 48 µg As/L (the U.S. Environmental Protection Agency drinking water criterion for human health protection is 50 µg/L), 120 mg As/kg diet, or (in the case of freshwater fish) tissue residues >1.3 mg/kg fresh weight. Adverse effects to crops and vegetation were recorded at 3 to 28 mg of water-soluble As/L (equivalent to about 25 to 85 mg total As/kg soil) and at atmospheric concentrations >3.9 µg As/m³.

Numerous and disparate arsenic criteria have been proposed for the protection of sensitive natural resources. However, the consensus is that many of these criteria are inadequate and that additional information is needed in at least five categories:

1. Developing standardized procedures to permit correlation of biologically observable effects with suitable chemical forms of arsenic
2. Conducting studies under controlled conditions with appropriate aquatic and terrestrial indicator organisms to determine the effects of chronic exposure to low doses of inorganic and organic arsenicals on reproduction, genetic makeup, adaptation, disease resistance, growth, and other variables

3. Measuring interaction effects of arsenic with other common environmental contaminants, including carcinogens, cocarcinogens, and promoting agents
4. Monitoring the incidence of cancer and other abnormalities in the natural resources of areas with relatively high arsenic levels, and correlating these with the possible carcinogenicity of arsenic compounds
5. Developing appropriate models of arsenic cycling and budgets in natural ecosystems.

28.9 LITERATURE CITED

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CHAPTER 29

Boron

29.1 INTRODUCTION

Borax ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$) was the first of the boron (B) minerals to be traded by the Babylonians more than 4000 years ago for use in the working and welding of gold (Greenwood and Thomas 1973). Borax has been known as a cleaning agent since the days of the ancient Greek and Roman empires and was used as a food preservative in Europe and America, although its use for the latter purpose has been discontinued (Weir and Fisher 1972). Boron and its compounds were used in the Egyptian and Roman eras to prepare borosilicate glass. Borax glazes were known from about the year 200; by 1556, borax was widely used throughout Europe as a flux (Greenwood and Thomas 1973). Boric acid (H_3BO_3) was first synthesized in 1707 (Greenwood and Thomas 1973). Boric acid and borates are the main boron compounds of ecological significance; other boron compounds usually degrade or are transformed to borates or boric acid (Sprague 1972).

Boron is an essential trace element for the growth and development of higher plants, although the range between insufficiency and excess is generally narrow, varying with the plant; boron is not required in fungi and animals (Sprague 1972; Weir and Fisher 1972; Birge and Black 1977; Goldbach and Amberger 1986; Stone 1990). In the southwestern United States, naturally elevated boron concentrations in surface waters used for irrigation may be sufficiently high to cause toxicity to plants of commercial importance (Benson et al. 1984). Another major source of boron entering ground and surface waters results from the use of borax-containing laundry products, coupled with ineffective removal of boron by conventional sewage processes (Benson et al. 1984). Agricultural drainwaters contaminated with boron are considered potentially hazardous to waterfowl and other wildlife populations throughout areas of the western United States (Smith and Anders 1989).

Medical and household uses of boric acid solutions as antiseptics have led to numerous accidental poisonings by ingestion or absorption through abraded skin, particularly in infants (U.S. Environmental Protection Agency [USEPA] 1975; Dixon et al. 1976; Landolph 1985; Siegel and Wason 1986). Poisonings have been reported in English children consuming milk containing 0.7 g boric acid/L, and in burn patients treated topically with saturated boric acid solutions (NAS 1980). In the 1940s, topical preparations of boric acid became a popular remedy for diaper rash in England. By 1953, at least 60 fatal cases of boric acid poisoning had been reported in English infants (O'Sullivan and Taylor 1983). Inhalation of boranes, especially diborane (B_2H_6), pentaborane (B_5H_9), and decaborane ($\text{B}_{10}\text{H}_{14}$) — which is used as a rocket propellant — is toxic to exposed workers (Dixon et al. 1976; NAS 1980). Boron compounds, especially boric acid, can also accumulate in animal tissues and produce a reduction in fertility, an increase in developmental abnormalities — especially those involving the skeletal system — stillbirth, and death (Weir and Fisher 1972; Lee et al. 1978; Landolph 1985). There seems to be a reasonable margin between a toxic dose in man and other vertebrates and in boron levels that may occur as incidental residues from

the use of borax and boric acid in agriculture and industry (Weir and Fisher 1972). Additional, and more extensive, information on ecological and toxicological aspects of boron in the environment is presented in reviews by Sprague (1972), USEPA (1975), NAS (1980), Anonymous (1983), Klasing and Pilch (1988), Butterwick et al. (1989), Eisler (1990), Stone (1990), U.S. Public Health Service [USPHS] (1991), and Culver et al. (1998).

29.2 ENVIRONMENTAL CHEMISTRY

29.2.1 General

The United States supplies about 70% of the global boron demand, and Turkey supplies 18%. Of the total annual U.S. production of about 500,000 tons, 45% is used in the manufacture of glass and glassware, 15% in laundry products, 10% in enamels and glazes, and 8% in agricultural chemicals. It is estimated that boron compounds enter the North American environment at a rate of 32,000 tons annually as a result of human activities, primarily from laundry products, irrigation drainwater, agricultural chemicals, coal combustion, and mining and processing. Boron compounds tend to accumulate in aquatic ecosystems because of the relatively high water solubility of these compounds.

The chemistry of boron is exceedingly complex and rivals that of carbon in its diversity. Most boron compounds, however, enter or degrade in the environment to borates (B-O compounds), such as borax and boric acid, and these are considered to be the most significant ecologically.

Toxicosis in animals has resulted from ingestion of boric acid or borax solutions, from topical applications of boric acid solutions to damaged skin, and from inhalation of boranes; the exact mechanisms of action are not understood. Boron and its compounds are potent teratogens when applied directly to the embryo, but there is no evidence of mutagenicity or carcinogenicity. Boron's unique affinity for cancerous tissues has been exploited in neutron capture radiation therapy of malignant human brain tumors.

29.2.2 Sources and Uses

Boron is a dark brown element that is widespread in the environment but occurs naturally only in combined form, usually as borax, colemanite ($\text{Ca}_2\text{B}_6\text{O}_{11} \cdot 5\text{H}_2\text{O}$), boronatrocacite ($\text{CaB}_4\text{O}_7\text{NaBO}_2 \cdot 8\text{H}_2\text{O}$), and boracite ($\text{Mg}_7\text{Cl}_2\text{B}_{16}\text{O}_{30}$) (USEPA 1975; NAS 1980). In the United States, boron deposits in the form of borax are concentrated in the desert areas of southern California, especially near Boron, California (USEPA 1975; USPHS 1991). Proven deposits of sodium tetraborates — from which borax is prepared and from which boron can be isolated — also exist in Nevada, Oregon, Turkey, Russia, and China (Sprague 1972; NAS 1980). About 300,000 metric tons of boron are removed from mined ore each year (Argust 1998). The United States supplies about 70% of the world boron demand, and Turkey supplies 18%; the most common commercial compounds are boric acid and borax (Sprague 1972; Butterwick et al. 1989; USPHS 1991).

In 1988, the United States produced 566,093 metric tons of boric oxide, imported an additional 60,000 metric tons of boron-containing minerals, and exported 589,680 metric tons of boric acid and borates (USPHS 1991). The majority of the boron produced annually at facilities in Oklahoma, New Jersey, Nevada, and Pennsylvania is in the form of sodium tetraborate compounds (USPHS 1991). Of the total production, about 42% occurs as anhydrous borax ($\text{Na}_2\text{B}_4\text{O}_7$), 29% as borax pentahydrate ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 5\text{H}_2\text{O}$), 10% as borax decahydrate or borax, and 16% as boric acid or boric oxide (B_2O_3) (Sprague 1972; USEPA 1975). Boron and its compounds are used in the manufacture of glassware (40% to 45%); soaps and cleansers (15%); enamels, frits, and glazes (10%); fertilizers

(5%); and herbicides (2% to 3%); 22% to 28% goes for other uses including cosmetics, insecticides, antifreeze, as neutron absorbers in atomic reactors, and leather tanning (Sprague 1972; USEPA 1975; NAS 1980; USPHS 1991; Woods 1994; Argust 1998). Borates have some toxicity to insects and, in relatively high concentrations, can control cockroaches, woodboring insects, gypsy moths, and larvae of flies in manure piles and in dog runs (Sprague 1972; USEPA 1975). Some organoboron compounds are used to sterilize fuel distribution and storage systems against fungi and bacteria (Sprague 1972). Radioboron-10 is widely used in radiation therapy against brain tumors, especially in Japan (Hatanaka 1986). In medicine, certain amine-carboxyborane derivatives show promise in reducing serum cholesterol and triglyceride concentrations, in alleviating some forms of chronic arthritis, and as antineoplastic agents (Hall et al. 1994; Newnham 1994). Other boron compounds are used widely as thermal protection materials in space probes, in fireproofing of fabrics and wood, in leather manufacture, in numerous pharmaceuticals and hygiene products, in steel hardening, in deoxidation of bronze, as a high-energy fuel, as neutron-absorbing shielding near atomic reactors, and as water softeners, pH adjusters, emulsifiers, neutralizers, stabilizers, buffers, and viscosifiers (NAS 1980; Parry and Kodama 1980; Schillinger et al. 1982; Siegel and Wason 1986; USPHS 1991).

The major global environmental reservoirs of boron (metric tons) include continental and oceanic crusts (10^{15}), oceans (10^{12}), groundwater (10^8), ice (10^8), coal deposits (10^7), commercial borate deposits (10^7), biomass (10^7), and surface waters (10^5) (Argust 1998). The largest flows of boron in the environment arise from the movement of boron into the atmosphere from the oceans at 1.3 to 4.5×10^6 tons annually. Drainage from soil systems into groundwaters and surface waters accounts for 1.3×10^5 to 1.3×10^6 tons yearly. And boron mining and volcanic eruptions account for 4×10^5 and 2×10^5 tons of boron per annum, respectively (Argust 1998).

Boron enters the environment at about 32,000 metric tons annually in the United States (Table 29.1). Most ends up in the aquatic environment because of the relatively high water solubility of all boron compounds, especially boron-containing laundry products and sewage (USEPA 1975). Conventional sewage treatment removes little or no boron (USEPA 1975; Vengosh 1998). Studies of domestic wastewaters in California and Israel, using boron isotopic composition techniques, show that boron in sewage is derived from sodium borate components used in household detergents (Vengosh 1998). Of the total boron in coal, as much as 71% may be lost to the atmosphere upon combustion. More than 50% of the boron found in coal ash is readily water soluble (Pagenkopf and Connolly 1982). The release of boron from coal flyash to leachate water is dependent on the ash to water ratio: at 1 g ash/L, up to 90% of the boron is soluble; at 50 g/L, only 40% is released; at 100 g/L, less than 30% is released. Coating of coal ash with aluminum solution reduces boron solubility by about 90% due to the formation of an insoluble aluminum–borate complex (Pagenkopf and Connolly 1982).

Table 29.1 Environmental Sources of Domestic Boron

Source	Metric Tons, Annually
Laundry products	14,000
Agricultural chemicals and fertilizers	7000
Coal combustion	4000
Mining and processing	3000
Glass and ceramics	1500
Miscellaneous	2500
Total	32,000

Data from U.S. Environmental Protection Agency (USEPA). 1975. Preliminary Investigation of Effects on the Environment of Boron, Indium, Nickel, Selenium, Tin, Vanadium and Their Compounds. Vol. 1. Boron. U.S. Environ. Protection Agen. Rep. 56/2-75-005A. 111 pp.

Boron compounds listed in the “Commodity List of Explosives and Other Dangerous Articles” are boron trichloride (BCl_3), boron trifluoride (BF_3), decaborane ($\text{B}_{10}\text{H}_{14}$), and pentaborane (B_5H_9) (USEPA 1975). Boron trichloride is a corrosive liquid; the maximum quantity allowed in containers by rail is 1 L, and by air only one container is permitted per aircraft. Boron trifluoride is a nonflammable gas restricted to 140 kg in one outside container by rail, and to 140 kg in cargo planes only. Decaborane is a flammable solid, and transport by rail or air is limited to 12 kg. Pentaborane is a flammable liquid and is prohibited for transport by air or rail. Diborane (B_2H_6) and higher boranes are unstable and are classified as dangerous articles in transport; no more than 0.1 kg can be shipped in a cylinder (USEPA 1975). Organic boron–oxygen compounds readily hydrolyze and should be stored and transferred in an inert atmosphere; usually, glass containers are used for shipping small quantities, and steel containers or tank cars are used for bulk items. Hazardous atmospheric conditions resulting from high concentrations of boron compounds are localized and are not considered a serious environmental problem (USEPA 1975).

29.2.3 Chemical Properties

The element boron has an atomic number of 5, a molecular weight of 10.811, an oxidation state of 3 for simple compounds (but other oxidation states for carboranes and other polyhedral cage boron compounds), a specific gravity of 2.34, a melting point of 2300°C, sublimation at 2550°C, and is almost insoluble in water. Boron exists as B-10 (19.78%) and B-11 (80.22%) isotopes, and it contributes about 0.001% to Earth’s crust, although it does not occur free in nature (USEPA 1975; Smith 1985). The chemistry of boron is exceedingly complex and rivals that of carbon in diversity. Reviews on boron’s chemistry are especially abundant and include those by Steinberg and McCloskey (1964), Brotherton and Steinberg (1970a, 1970b), Greenwood and Thomas (1973), Grimes (1982), Evans and Sparks (1983), Smith (1985), Emin et al. (1986), Heller (1986), Niedenzu and Trofimenko (1986), Hermanek (1987), and USPHS (1991).

Most boron compounds degrade in the environment to B–O (borate) compounds, and these are the boron compounds of ecological significance — especially borax and boric acid (Sprague 1972; Antia and Cheng 1975; Thompson et al. 1976). Sodium tetraborate decahydrate (borax) has a melting point of 75°C, a boiling point of 320°C, and is soluble in water to 20 g/L at 0°C and to 1700 g/L at 100°C (USEPA 1975). Boric acid has a melting point of 169°C, a boiling point of 300°C and, like borax, is exceedingly soluble in water: 63.5 g/L at 30°C and 276 g/L at 100°C (USEPA 1975; USPHS 1991).

Boron exists in several forms in the soil (USEPA 1975); in soil solution, it exists largely as the undissociated weak monobasic acid that accepts hydroxyl groups (Gupta and Macleod 1982). Most plant-available boron in soils is associated with soil organic matter (Gupta and Macleod 1982), with the hot-water soluble boron fraction (Hingston 1986), and with soil solution pH ranges of 5.5 to 8.5 and 10 to 11.5 (Goldberg and Glaubig 1986). It is assumed that boron adsorbs to soil particles and aluminum and iron oxide minerals (Goldberg and Glaubig 1986). Boron mobility in soils is reduced under conditions of pH 7.5 to 9.0, and with high abundance of amorphous aluminum oxide, iron oxide, and organic content (USPHS 1991).

In water, boron readily hydrolyzes to form the electrically neutral, weak monobasic acid H_3BO_3 and the monovalent ion $\text{B}(\text{OH})_4^-$. Waterborne boron may be adsorbed by soils and sediments (USPHS 1991). The predominant boron species in seawater is boric acid (Thompson et al. 1976); concentrations are higher at higher salinities and in proximity to industrial waste discharges (Liddicoat et al. 1983; Narvekar et al. 1983). In seawater, borate or boric acid occurs naturally at 4.5 to 5.5 mg/L. About 76% of the total inorganic boron in seawater occurs as undissociated boric acid [$\text{B}(\text{OH})_3$], and the remainder is identified as the borate ion [$\text{B}(\text{OH})_4^-$]. Of the total borate ion, 44% appears to be complexed with sodium, magnesium, and calcium (Antia and Cheng 1975).

Other evidence suggests additional complexation of borate with ferric ions and polyhydroxylated organic compounds (Antia and Cheng 1975).

Atmospheric boron is in the form of particulates or aerosols of borides, boron oxide, borates, boranes, organoboron compounds, trihalide boron compounds, or borazines. The half-time persistence of airborne boron particles is short, usually on the order of days (USPHS 1991).

Despite the development of sophisticated instrumentation and techniques, the accurate determination of boron in biological materials is difficult at concentrations less than 1 mg B/kg (Downing et al. 1998). Problems associated with analysis of boron from biological sources include contamination from Teflon® vessels during microwave digestion; losses due to freeze drying; variations in boron isotope ratios, standards preparation, and reagent backgrounds; and instrumental interference (Downing et al. 1998). Inductively coupled plasma-mass spectrometry now allows quantitation of percutaneous absorption of ^{10}B in ^{10}B -enriched boric acid, borax, and disodium octaborate tetrahydrate in biological materials (Wester et al. 1998a), although absorption through intact human skin is significantly less than the mean daily dietary intake (Wester et al. 1998b).

29.2.4 Mode of Action

A proposed essential role for boron is as a regulator of enzymatic pathways closely involved with energy substrate metabolism, insulin release, and the immune system. Boron influences the activities of at least 26 enzymes — including reductases, transferases, hydrolases, and isomerases — examined in various biological systems by acting on the enzyme directly and binding to cofactors or substrates (Hunt 1998). The complexing ability of the boron atom is considered to be the key explanation of why it is essential to higher plants (USEPA 1975), although the exact mechanism of action is still unknown. In biological systems, boron probably is complexed with hydroxylated species, and inhibition or stimulation of enzymes and coenzymes is pivotal in its mode of action (Woods 1994). Boron interacts with substances of biological interest, including polysaccharides, pyridoxine, riboflavin, dehydroascorbic acid, and pyridine nucleotides (Sammam et al. 1998). Boron's complexing ability is thought to beneficially influence transport of sugars and other organic compounds, production of plant growth regulators, biosynthesis of nucleic acids and phenolic acid, carbohydrate metabolism, respiration, and pollen germination (USEPA 1975; Nielsen 1986).

Boron poisoning in animals is primarily an experimental phenomenon, although livestock in certain regions may be exposed to high concentrations in drinking water — up to 80 mg B/L — that have not been shown to be toxic (NAS 1980). Toxicosis in humans has resulted from ingestion of boric acid or borax solutions, topical applications of boric acid solutions to burn-damaged skin, and inhalation of boranes (NAS 1980). In mammals, boron is thought to regulate parathyroid function through metabolism of phosphorus, magnesium, and especially calcium. Boron has a close relationship with calcium metabolism, most likely at the cell membrane level (Nielsen 1986). The toxicological effects of boric acid and borax are similar for different species. Other inorganic borates that dissociate to boric acid display similar toxicity, whereas those that do not dissociate to boric acid may display a different toxicological profile (Hubbard 1998).

Dietary boron at nontoxic concentrations, as sodium borate or boric acid, is rapidly and almost completely absorbed from the gastrointestinal tract, does not seem to accumulate in healthy tissues, and is excreted largely in urine, usually within hours, but sometimes as long as 23 days. Similar patterns are evident for humans, dogs, cows, rabbits, rodents, and guinea pigs (NAS 1980; Benson et al. 1984; Nielsen 1986; Siegel and Wason 1986; USPHS 1991; Murray 1998). Urinary boron excretion changes rapidly with changes in boron intake, suggesting that the kidney is the site of homeostatic regulation (Sutherland et al. 1998). Boron does not seem to accumulate in soft tissues of animals, but does accumulate in bone; cessation of exposure to dietary boron resulted in a rapid drop in bone boron, usually within 24 h (Moseman 1994). Boric acid poisoning in animals,

regardless of route of administration, is characterized by the following signs: generalized erythema (boiled lobster appearance) starting in the axillary, inguinal, and face regions, eventually covering the entire body with conjunctival redness, followed by massive desquamation 2 to 3 days later; acute gastroenteritis, including nausea and vomiting; diarrhea; anorexia; cardiac weakness; excessive urinary excretion of riboflavin; decreased oxygen uptake by the brain; hypoacidity; altered enzyme activity levels; impaired growth and reproduction; and death from circulatory collapse and shock, usually within 5 days (Dani et al. 1971; Sprague 1972; USEPA 1975; NAS 1980; Schillinger et al. 1982; Settimi et al. 1982; Siegel and Wason 1986; USPHS 1991).

Boron hydrides or boranes, such as B_2H_6 , B_4H_{10} , and B_5H_9 , from chemical processes produce acute central nervous system (CNS) pulmonary damage and lung disease through inhalation (NAS 1980; Klaassen et al. 1986). Boranes produce toxic effects by creating embolisms of hydrogen gas as they react with tissue, and by depleting biogenic amines of the CNS and inhibiting aminotransferases and other pyridoxol-dependent enzymes (Korty and Scott 1970; USEPA 1975). Boranes produce similar effects in humans and animals, and these are generally ascribable to CNS depression and excitation (Naeger and Leibman 1972; Smith 1985). Symptoms of borane intoxication include pulmonary irritation, headache, chills, fatigue, muscular weakness and pain, cramps, dizziness, chest tightness, and pneumonia (NAS 1980). Boranes may adversely affect male reproductive capacity (Klaassen et al. 1986), but this requires verification. Decaborane ($B_{10}H_{14}$), as one example, is a highly lipid-soluble compound that can enter the body through inhalation, ingestion, or the skin. In water, decaborane is rapidly transformed into intermediate products that are eventually degraded to boric acid. The intermediate products, but not decaborane or boric acid, reduce phosphomolybdic acid and inhibit glutamic-oxaloacetic transaminase; treatment of intermediates with pyridoxol phosphate tends to reverse the inhibitory activity (Naeger and Leibman 1972). Low decaborane doses cause behavioral effects such as depression, catatonia, and convulsions (USEPA 1975).

Inorganic borates are comparatively toxic, apparently complexing hydroxy compounds and interfering with protein synthesis (USEPA 1975). Organoborate compounds exert physiological effects on the CNS and peripheral nervous system, acting as spasmolytics, sedatives, and convulsants, depending on their structure (USEPA 1975). Boron trihalides such as BBr_3 , BCl_3 , and BF_3 are corrosive to the eyes, skin, and mucous membranes, and will cause burns on the skin — apparently due to the hydrolysis of the trihalides to their halogen acids, and not to boron (USEPA 1975; Smith 1985).

Boron is a potent teratogen when applied directly to the embryo. Boric acid injected into chicken and amphibian embryos produced abnormal development of the neural tube, notochord, tail, and limbs, perhaps through complexing polyhydroxy compounds and interfering with riboflavin metabolism (Landauer 1952, 1953a, 1953b, 1953c; Landauer and Clark 1964; USEPA 1975; Settimi et al. 1982). Boron and its compounds, however, are neither mutagenic nor carcinogenic (Landolph 1985; Dieter 1994). Nonmutagenicity is based on results of the *Salmonella typhimurium*-mammalian microsome mutagenicity assay; boron neither enhances nor inhibits the activity of benzo[*a*]pyrene, a known mutagen (Anonymous 1983; Benson et al. 1984). There is no evidence that boron is a possible carcinogen, although long-term, selective uptake of boron by tumors has been reported (USEPA 1975).

Boron seems to have an affinity for cancerous tumors, and this property has been exploited in radiation therapy (Hamada et al. 1983; Hatanaka 1986). Boron-10 has been used in neutron capture therapy to cure malignant sarcomas implanted in the hind legs of mice, as well as spontaneous malignant melanomas in pigs (Slatkin et al. 1986). The sulfhydral borane monomer ($B_{12}H_{11}SH$)²⁻ is used as a B-10 carrier in neutron therapy of malignant human brain tumors and seems to be most effective at 30 µg B-10/kg tissue (Hatanaka 1986). Polyhedral boranes attached to monoclonal antibodies that are tumor specific may become useful in tumor therapy by neutron irradiation (Parry

and Kodama 1980). It is possible, however, that uptake of boron may be a nonspecific attribute of tumors and of a variety of normal tissues that lack a blood-brain barrier. Thus, the potential usefulness of selected B-10 carriers for treating extracranial neoplasms seems questionable at this time (Slatkin et al. 1986).

29.3 CONCENTRATIONS IN FIELD COLLECTIONS

29.3.1 General

Terrestrial plants are normally rich sources of boron. Levels in meat and fish are usually low. But these generalizations are based on limited data. Boron is ubiquitous in the environment as a result of natural weathering processes (Woods 1994). However, human activities such as mining, coal burning, and use of borax laundry detergents have resulted in elevated boron loadings in air, water, and soils (USPHS 1991). Comparatively high levels of boron occur in fish, aquatic plants, and insects at Kesterson National Wildlife Refuge that was contaminated by agricultural drainwater (Hothem and Ohlendorf 1989; Eisler 1990). The availability of inductively coupled plasma-mass spectrometry (ICP-MS) technology enables measurement of boron concentrations and isotope ratios in a large number of biological samples with minimal sample preparation at detection limits of 0.11 µg/L (Vanderpool et al. 1994).

29.3.2 Nonbiological Materials

Boron is distributed widely in the environment (Ahl and Jonsson 1972; USEPA 1975). Naturally elevated boron levels are usually associated with marine sediments, thermal springs, large deposits of boron minerals, seawater, and certain groundwaters ([Table 29.2](#)). Human activities, however, have resulted in elevated boron concentrations near coal-fired plants, in mine drainage waters, in municipal wastes, and in agricultural drainage waters. In one case, agricultural drainwater practices in western California produced boron concentrations in local rivers, groundwaters, and surface waters that exceeded the established limits for the protection of crops and aquatic life (Schuler 1987; Klasing and Pilch 1988; [Table 29.2](#)). Contamination of pristine groundwaters (<0.05 mg B/L) by domestic wastewater and agriculture-return flows (0.5 to 1.0 mg B/L) is documented by the isotopically distinguished signature of borate compounds. For example, in areas where calcium borates are applied as fertilizers, the B¹¹/B¹⁰ ratios of the soil water and leachates are expected to be low and can be used as diagnostic tools for tracing agriculture-return flows (Vengosh 1998).

Coal-fired power plants are major sources of atmospheric boron contamination. At least 30% of boron in coal is lost in this manner (Cox et al. 1978; Gladney et al. 1978). The apparently large amounts of boron lost to the environment through stack emissions may be directly related to the organic content of coal ([Table 29.2](#)) (Gladney et al. 1978). Also, disposal of B-laden drainage waters from boron mines is a major problem in certain geographic areas. In Turkey, for example, which possesses about 60% of the world's boron reserves — localized in a rectangular area about 100 × 200 km near the Simav River — drainage waters discharged from the mines as a result of borate production have elevated boron concentrations in the Simav River to levels unsuitable for crop irrigation purposes. About 68,000 ha of agricultural land irrigated by the Simav River is now threatened by boron pollution (Okay et al. 1985). In the United States, laundry detergents originating from household use may contribute as much as 50% of the boron loadings in effluents discharged into aquatic environments; lesser amounts are contributed by soil minerals, rainfall, and industry and sewage effluents (USEPA 1975).

Table 29.2 Boron Concentrations in Selected Nonbiological Materials (Concentrations are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW], except where noted.)

Material	Concentration, (mg/kg or mg/L)	Reference ^a
AIR		
Workplace (borax mining and refining plants, sites where boric acid is manufactured)	1–14 mg/m ³	18
Non-workplace locations	0.02 (<0.0005–0.08) µg/m ³	19
AFFECTED BY AGRICULTURAL DRAINAGE WATERS		
Western San Joaquin Valley, California		
River waters	Median 1.1 FW	16
Surface waters	Median 3.1 (Max. 83.0) FW	16
Groundwaters	Median 7.4 (Max. 120.0) FW; frequently >100 FW	16, 18
Kesterson National Wildlife Refuge, 1984		
Subsurface waters	20 (12–41) FW	17
Sediments	20 (10–71) DW	17
COAL-FIRED POWER PLANTS		
Chalk Point Power Plant, Maryland		
Coal	13 AW	1
Bottom slag	19 AW	1
Flyash	33 AW	1
Four Corners Power Plant, New Mexico		
Coal	92 AW	1
Bottom slag	120 AW	1
Flyash	240 AW	1
Coal ash		
Anthracite	90 AW	1
Volatile bituminous		
Low	123 AW	1
Medium	218 AW	1
High	770 AW	1
Lignite	1020 AW	1
Coal ash	5–200 DW	2, 15
DRINKING WATER		
Worldwide	Usually <0.4 FW, range 0.0005–>2.0 FW	18
California		
50th percentile	0.1 FW	20
90th percentile	0.4 FW	20
Northern Chile	0.31–15.2 FW	20
Bottled water; U.S. and Europe	0.75 (<0.005–4.35) FW	20
GROUNDWATERS		
Pristine	Usually <0.05 FW	21
Worldwide	Usually <0.5 FW	9
Greece	2.3–5.4 FW	4
United States	Max. 5.0 FW	12
MINE DRAINAGE WATERS		
Turkish boron mines		
Avsar mine	16 FW	4
Simav mine	260 FW	4
Yenikoy mine	390 FW	4

Table 29.2 (continued) Boron Concentrations in Selected Nonbiological Materials (Concentrations are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW], except where noted.)

Material	Concentration, (mg/kg or mg/L)	Reference ^a
RAIN		
Sweden	0.002 FW	7
France	0.002–0.004 FW	7
U.S.		
Mississippi	Usually <0.01 FW	11
Florida	~0.01 FW	7, 8
India	0.03 (0.002–0.007) FW	11
England	0.08 FW	7
Japan	0.1 FW	7
RIVER WATER		
Germany	0.02 FW; Max. 0.18 FW	20
U.K., northern Italy	0.002–0.87 FW	20
SEAWATER		
British Columbia		
Surface	3.5 (0.2–4.7) FW	13
Depth 5 m	3.9 FW	13
Open ocean	4.5 FW	8
Coastal	4.6 FW	8, 18, 20
Total inorganic	4.5–5.5 FW	14
As undissociated boric acid	3.4–4.2 FW	14
As borate ion, $B(OH)_4^-$	1.1–1.3 FW	14
As complex with sodium, magnesium, and calcium	0.5–0.6 FW	14
SEDIMENTS		
Nonmarine clays	<10 DW	3
Postglacial marine	Max. 500 DW	3
SOILS		
Worldwide	Usually 45–124 DW, range 4–200, mostly as biologically unavailable tourmaline	5, 6
United States	30 (10–300) DW	7, 18, 19
SEWAGE WATERS		
Scandinavia	0.4 (Max. 0.7) FW	3
SURFACE FRESHWATERS		
Canada, 1988	0.16 FW	20
Worldwide	0.0001–<0.5 FW	8–10, 16
Norway, 1970	Usually <0.004 FW, median 0.013, range 0.001–1.05 FW	3
Sweden, 1970	0.12 (0.001–1.0) FW	3, 7
Southeastern U.S., 1969–1970		
Streams, swamps, ponds	Usually <0.1 FW	11
Reservoirs	0.007 (<0.001–0.09) FW	11
In regions where marine deposits are common	>0.06 FW	3
United States	Generally <0.1 FW; frequently 0.1–0.3 FW; rarely 360 FW in areas of boron-rich deposits	8, 12, 18, 19

Table 29.2 (continued) Boron Concentrations in Selected Nonbiological Materials (Concentrations are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW], except where noted.)

Material	Concentration, (mg/kg or mg/L)	Reference ^a
United States		
10th percentile	0.01 FW	20
50th percentile	0.076 FW	20
90th percentile	0.387 FW	20
Nevada		
Humboldt River	0.2 FW	6
Borax Flat	Up to 80 FW	6
Turkey		
Uncontaminated	<0.5 FW	4
Contaminated with boron mine wastes	4 (Max. 7) FW	4
Western U.S.	Sometimes 5–15 FW	10, 12
Japan	1–15 FW	7
THERMAL SPRINGS		
Greece	43 FW	4
WELL WATER		
India	0.08–0.5 FW	7

^a 1, Gladney et al. 1978; 2, Pagenkopf and Connolly 1982; 3, Ahl and Jonsson 1972; 4, Okay et al. 1985; 5, Gupta and Macleod 1982; 6, NAS 1980; 7, Sprague 1972; 8, USEPA 1975; 9, Benson et al. 1984; 10, Lewis and Valentine 1981; 11, Boyd and Walley 1972; 12, Birge and Black 1977; 13, Thompson et al. 1976; 14, Antia and Cheng 1975; 15, Cox et al. 1978; 16, Klasing and Pilch 1988; 17, Schuler 1987; 18, USPHS 1991; 19, Howe 1998; 20, Coughlin 1998; 21, Vengosh 1998.

29.3.3 Plants and Animals

Boron accumulates in both aquatic and terrestrial plants but it does not seem to biomagnify in the food chain (Howe 1998). Boron does not biomagnify in aquatic food chains and has low potential to accumulate in aquatic organisms, as judged by studies in the San Joaquin River, California, and its tributaries (Saiki et al. 1993). Marine and freshwater plants, fishes, and invertebrates concentrated boron from the medium by factors of less than 100, suggesting that biota is not a significant removal mechanism of boron from water (USPHS 1991). Boron concentrations in livers of birds collected from Baja California, Mexico, in 1986 were highest in the seed-eating mourning dove *Zenaida macroura* (maximum 28.5 mg B/kg FW) and lowest (maximum 8.7 mg B/kg FW) in fish-eating and omnivorous species (Mora and Anderson 1995).

Boron occurred at high concentrations in plants, insects, and fish at Kesterson National Wildlife Refuge in California — the recipient of contaminated agricultural drainwater — when compared to a nearby control area (Table 29.3) (Ohlendorf et al. 1986; Schuler 1987). The authors indicated that little is known about the effect of boron ingestion on bird reproduction, although both boric acid and borax produced mortality and teratogenic development when injected into eggs. Studies on the effects of boron on waterfowl growth, physiology (Hoffman et al. 1990), and reproduction (Smith and Anders 1989) are discussed later.

Terrestrial plants, especially nuts and some fruits and vegetables, are rich sources of boron (Table 29.3). Honey is another good source of boron, and concentrations up to 7.2 mg/kg dry weight have been reported (Nielsen 1986). Boron concentrations are also elevated in marine plants, zooplankton, and corals, but are low in fish and certain marine invertebrates (Table 29.3). No data were found on boron levels in terrestrial mammalian wildlife. The average daily intake of boron in humans ranges between 1 and 25 mg; however, populations residing in areas of the western

United States with natural boron-rich deposits may be exposed to higher-than-average levels of boron (USPHS 1991). Boron intake from drinking water is highly variable and dependent on the geographic source, the quantity of water consumed, and the water sources used to bottle other beverages (Coughlin 1998). Current estimates of boron in domestic diets for normal human adults is about 1 mg daily; however, toddlers age 2 years consumed 3.7 times more boron than mature males when adjusted for body weight (Meacham and Hunt 1998). There is great variability in the human diet, and people from different countries have different sources of dietary boron. In the United States, for example, major sources of dietary boron include coffee, milk, orange juice, peanut butter, wine, pinto beans, and other juices and fruits. By contrast, in Mexico and Kenya, major sources of dietary boron include corn, kidney beans, maguey (an alcoholic drink from fermented bananas), cactus, and mangoes (Rainey and Nyquist 1998). In rats, increasing concentrations of boron in drinking water were associated with increasing tissue boron concentrations, plasma testosterone, and Vitamin D, and a decrease in HDL cholesterol (Samman et al. 1998). Data for humans and domestic animals indicate that boron levels are elevated in bony tissues, but are always less than 0.6 mg B/kg fresh weight or 1.5 mg/kg dry weight in other tissues examined (Table 29.3).

**Table 29.3 Boron Concentrations in Field Collections of Selected Species of Plants and Animals
(Values shown are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)**

Ecosystem, Organism, and Other Variables	Concentration (mg/kg)	Reference ^a
TERRESTRIAL PLANTS		
Cereal grains	1–5 DW	1, 2, 19
Box thorn, <i>Lycium andersonii</i>		
Stem	7–26 DW	8
Leaf	26–163 DW	8
Root	25–74 DW	8
Prunes, raisins, dates	9–27 DW	2
Tropical fruits	Usually <10 FW	1
Nuts	16–23 DW	2
Vegetables	Usually >13 DW	2
Angiosperms	50 DW	8
Gymnosperms	63 DW	8
Pteridophytes	77 DW	8
Beet, <i>Beta vulgaris</i>	76 DW	19
Dandelion, <i>Taraxacum</i> sp.	80 DW	19
Sagebrush, <i>Artemisia tridentata</i>		
On high B soil		
Whole	Max. 250 DW	8
Leaf	Max. 156 DW	8
Stem	Max. 54 DW	8
Quince, <i>Cydonia</i> sp.	160 FW	19
Apple, pear, tomato, red pepper	440–1250 DW	2
FRESHWATER ORGANISMS		
Lake trout, <i>Salvelinus namaycush</i> , muscle	0.2–0.6 FW	8
Cattail, <i>Typha latifolia</i> , whole	15–30 DW	8
Aquatic macrophytes		
22 species	Usually <20 DW; mean 11.3 (1.2–100) DW	4
Various	2–19 DW	5
Waterweed, <i>Elodea</i> spp., whole	18–44 DW	8
Pondweed, <i>Potamogeton</i> spp., whole	18–170 DW	8
Yellow pond lily, <i>Nuphar</i> spp., whole	23–31 DW	8
Watermilfoil, <i>Myriophyllum</i> spp., whole	25–54 DW	8

Table 29.3 (continued) Boron Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, and Other Variables	Concentration, (mg/kg)	Reference ^a
Kesterson National Wildlife Refuge, California, contaminated with irrigation drainwater		
1983		
Aquatic plants	382 (270–510) DW	3
Aquatic insects	45 (36–54) DW	3
Mosquitofish, <i>Gambusia affinis</i> , whole	11 (8–20) DW	3
1984		
Widgeongrass, <i>Ruppia maritima</i>		
Whole	371 (120–780) DW	9, 13
Seeds	1860 (450–3500) DW	9, 13
Filamentous algae	501 (390–787) DW	9, 13
Aquatic insects	43–186 (22–340) DW	9
1985		
Water	20.0 FW	16
Aquatic plants, whole	340–1800 DW	16
Aquatic insects, whole	Max. 280 DW	16
Mosquitofish, whole	20.6 DW; Max. 32.0 DW	16
Volta Wildlife area, California (control area)		
1983		
Aquatic plants	34 DW	3
Aquatic insects	13 (6–35) DW	3
Mosquitofish, whole	2.8 (Max. 3.6) DW	3
1984		
Widgeongrass		
Whole	100 (37–540) DW	9
Seeds	36 (32–43) DW	9
Filamentous algae	85 (64–140) DW	9
Aquatic insects	12–32 (7–47) DW	9
1985		
Water	1.8 FW	16
Aquatic plants, whole	220–520 DW	16
Aquatic insects, whole	Max. 60 DW	16
Mosquitofish, whole	4.9 DW; Max. 7.4 DW	16
Western San Joaquin Valley, California, contaminated with irrigation drainwater		
Vegetation and seeds	Max. 3390 DW	10
Clams, 2 species, muscle	Max. 9.3 FW	10
Bluegill, <i>Lepomis macrochirus</i> , whole	<0.8–1.9 FW; Max. 3.9 FW	10
Common carp, <i>Cyprinus carpio</i> , whole	0.5–5.7 FW; Max. 6.2 FW	10
San Joaquin River, California; 1987; maximum concentrations		
Water	2.9 FW	17
Sediments	6.9 DW	17
Detritus	190.0 DW	17
Filamentous algae, whole	280.0 DW	17
Plankton	47.0 DW	17
Chironomid larvae, whole	27.0 DW	17
Amphipods, whole	22.0 DW	17
Crayfish, whole	23.0 DW	17
Mosquitofish, whole	8.4 DW	17
Bluegill, whole	7.9 DW	17
Largemouth bass, whole	2.0 DW	17
MARINE ORGANISMS		
Seaweeds, whole, Japan, 41 species	106 (16–319) DW; 762 (231–3038) AW	6
Marine algae	4–120 DW	8

Table 29.3 (continued) Boron Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, and Other Variables	Concentration, (mg/kg)	Reference ^a
Zooplankton	18–216 DW	7
Ctenophore, <i>Beroe cucumis</i>	115 AW	6
Corals, 34 species		
Deep open ocean	50–85 DW	6
Shallow open ocean	65–100 DW	6
Shallow coastal zone	40–110 DW	6
Tunicate, <i>Salpa fusiformis</i> , whole	50 AW	6
Chaetognath, <i>Sagitta elega</i>	130 AW	6
Dungeness crab, <i>Cancer magister</i> , whole	1.8 (0.9–3.3) FW	6, 7
Molluscs, bivalves		
Soft parts, 11 species	1.6–4.5 FW	6
Soft parts, British Columbia		
Clams, 8 species	0.9–5.3 FW	7
Oysters, 2 species	3.1–4.0 FW	7
Mussels, 2 species	2.0–5.5 FW	7
Octopus, <i>Polypus bimaculatus</i> , whole	1.3 FW	7
Sockeye salmon, <i>Oncorhynchus nerka</i>		
Soft tissues	0.5–0.7 FW	6, 7
Bone	1.5 (1.1–4.4) FW	6, 7
Anchovetta, <i>Cetengraulis mysticetus</i> , whole	3.3–3.8 AW	8
Yellowfin tuna, <i>Thunnus albacares</i>		
Muscle	39.0 AW	8
Whole	9.0 AW	8
Eyeball	5.6 AW	8
Spleen	3.3 AW	8
Gill	1.8 AW	8
Heart	1.5 AW	8
Harbor seal, <i>Phoca vitulina</i>		
Blood	2.0 FW	8
Spleen	0.5 FW	8
Muscle	0.3 FW	8
Liver	0.2 FW	8
Heart	0.1 FW	8
Kidney	0.01 FW	8

BIRDS

Aquatic birds; central California, 1985–88; livers; South Grasslands (contaminated) vs. North Grasslands; freshwater substituted for irrigation drainwater in fall 1985

Cinnamon teal, <i>Anas cyanoptera</i>		
1987	4.1 DW vs. not detected (ND)	11
1988	3.0 DW vs. ND	11
Mallard, <i>Anas platyrhynchos</i>		
1985	7.4 DW vs. 6.6 DW	11
1988	29.0 DW vs. 1.8 DW	11
Gadwall, <i>Anas strepera</i>		
1987	6.9 DW vs. ND	11
1988	4.3 DW vs. 2.5 DW	11
American coot, <i>Fulica americana</i>		
1985	27.0 DW vs. 11.0 DW	11
1987	9.1 DW vs. 5.3 DW	11
1988	8.5 DW vs. 3.8 DW	11
Mexicali Valley, Baja California; 1986; livers; 5 species	1.2–28.5 FW	12
Willet, <i>Catoptrophorus semipalmatus</i> ; 1994; San Diego Bay; sediments vs. stomach contents		
Naval Air Station	<10 DW vs. 3.9 DW	20
Tijuana Slough National Wildlife Refuge	21 DW vs. 6.5 DW	20

Table 29.3 (continued) Boron Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, and Other Variables	Concentration, (mg/kg)	Reference ^a
Sandhill crane, <i>Grus canadensis</i> ; Nebraska; 1989–90; liver; found dead after collision with powerline	1.2 (1.0–2.4) DW	13
Whooping crane, <i>Grus americana</i>		
Male; 4-months old; Colorado; 1985		
Muscle	4.9 FW	14
Liver	10.0 FW	14
Egg; NWT, Canada		
1986	4.7–5.0 FW	14
1987	1.0 FW	14
1989	1.0 FW	14
Aransas/Wood Buffalo National Park, Canada; 1989		
Male; 1.5 years old		
Muscle	<0.05 FW	14
Liver	<1.0 FW	14
Female; 4-years old		
Muscle, liver	Not detected	14
Avocet, <i>Recurvirostra americana</i> ; south Central Valley of California; 1991		
Contaminated ponds (29–109 mg B/L)		
Egg	8.3–10.5 DW	15
Kidney	1.9 DW	15
Liver	4.5–10.3 DW	15
Reference ponds (<1.0 mg B/L)		
Egg	8.5 DW	15
Kidney	Not detected	15
Liver	9.6 DW	15
MAMMALS, TERRESTRIAL		
Animal tissues, blood, urine		
Normal	Usually <10 FW	19
Poisoned	Max. 2000 FW	19
Human, <i>Homo sapiens</i>		
Teeth	18.2 (0.5–69) DW	1
Nails	16 (7.5–83) FW	19
Rib	6.2–10.2 AW	1
Hair	4.3 (0.8–10.2) FW	19
Kidney, lung, lymph nodes	0.6 FW	1, 2
Urine	0.75 (0.2–2.9) FW	19
Blood	0.06–0.4 FW	1, 2, 19
Serum	0.02–0.2 FW	2, 19
Muscle	0.1 FW	1, 2
Testes	0.09 FW	2
Milk	0.06–0.08 FW	2
Brain	0.06 FW	1, 2
Diet (foods with the highest boron concentrations)		
Avocado	11.1–14.3 FW	21
Peanut butter	5.9–14.5 FW	21
Prune juice	5.2–5.6 FW	21
Chocolate powder	4.3 FW	21
Wine	3.6 FW	21
Grape juice	3.4–3.7 FW	21
Pecans	2.6–6.6 FW	21
Animal meat for human consumption	0.2 DW	2
Animal muscle and organs	0.5–1.5 DW	1
Milk, cow	0.2–1.0 FW	1, 19
Dairy products	1.1 DW	2

Table 29.3 (continued) Boron Concentrations in Field Collections of Selected Species of Plants and Animals (Values shown are in mg B/kg fresh weight [FW], dry weight [DW], or ash weight [AW].)

^a 1, NAS 1980; 2, Nielsen 1986; 3, Ohlendorf et al. 1986; 4, Boyd and Walley 1972; 5, Ahl and Jonsson 1972; 6, Eisler 1981; 7, Thompson et al. 1976; 8, Jenkins 1980; 9, Schuler 1987; 10, Klasing and Pilch 1988; 11, Pavaglio et al. 1992; 12, Mora and Anderson 1995; 13, Fannin 1991; 14, Lewis et al. 1991; 15, Fairbrother et al. 1994; 16, Hothem and Ohlendorf 1989; 17, Saiki et al. 1993; 18, Whitworth et al. 1991; 19, Moseman 1994; 20, Hui and Beyer 1998; 21, Meacham and Hunt 1998.

29.4 EFFECTS

29.4.1 General

Boron is essential for the growth of higher plants and has been applied to boron-deficient soils for at least 50 years to improve yields of many crops. Phytotoxic levels of boron usually occur as a result of human activities, such as boron-contaminated irrigation waters and excess applications of boron-rich fertilizers, sewage sludges, and flyashes. Boron compounds at comparatively high concentrations are used to control pestiferous insects through direct biocidal action, enhancement of disease sensitivity, or use as a chemosterilant.

Representative species of aquatic plants, invertebrates, fishes, and amphibians can usually tolerate up to 10 mg B/L medium for extended periods without adverse effects, although it has been suggested that concentrations greater than 0.1 mg B/L may ultimately affect reproduction in rainbow trout (*Oncorhynchus mykiss*), and greater than 0.2 mg/L may impair survival of other fish species. In waterfowl, diets that contain 30 or 100 mg B/kg fresh weight adversely affect growth rate. Elevated tissue residues were recorded in ducks fed diets containing between 100 and 300 mg B/kg, and reduced survival occurred at dietary levels of 1000 mg B/kg. Boron is a potent avian teratogen when injected directly into embryos during the first 96 h of development. In mammals, the lethal dose of boron, as boric acid, varies according to species, and usually ranges between 210 and 603 mg B/kg body weight (BW); early development stages are especially sensitive. Excessive boron consumption adversely affects growth and reproduction in sensitive species of mammals (i.e., >1000 mg B/kg diet, >15 mg B/kg BW daily, >1.0 mg B/L drinking water, or >3 g B/kg BW single dose on the first day of pregnancy). Boron is not considered essential for mammalian growth but does protect against fluorosis and bone demineralization.

29.4.2 Terrestrial Plants

Boron was accepted as being an essential micronutrient for higher plants in 1923, with toxicity owing to excess boron much less common in the environment than boron deficiency (Howe 1998; Samman et al. 1998). The role of boron in nutrition and toxicity of terrestrial crops and forest trees has been reviewed extensively by Eaton (1944), USEPA (1975), Gupta (1979, 1983), Gupta and Macleod (1982), Pilbeam and Kirkby (1983), Gupta et al. (1985), Eisler (1990), and Stone (1990). It is generally agreed that boron is essential for the growth of higher plants and some species of fungi, bacteria, and algae, and that excess boron is phytotoxic. It is also agreed that plants vary greatly in their sensitivity to B toxicity (Boyd and Walley 1972; USEPA 1975; Birge and Black 1977; Goldberg and Glaubig 1986; Dear and Lipsett 1987; USPHS 1991). The exact mode of action of boron is unknown; however, its complexing ability facilitates the movement of sugars and other materials, and it is involved in cell wall bonding, conversion of glucose-1-phosphate to starch, and metabolism of nucleic acids (Sprague 1972; Gupta et al. 1985; Goldbach and Amberger 1986). Blevins and Lukaszewski (1994) suggest that boron toxicity to plants is attributed, in part, to interactions between borates and divalent cations like manganese, resulting in altered metabolic pathways of allantoate aminohydrolase in the case of manganese. The boron level in plants depends on the content and availability of soil boron, season, disease state, inherent species or variety

differences, and interactions with other substances (USEPA 1975; Gestring and Soltanpour 1987). Most of the plant-available boron comes from the decomposition of soil organic matter and from boron adsorbed and precipitated onto soil surface particles. However, soil solution boron is the most important form, and plants take it up directly from this source (Gupta et al. 1985). Boron availability to plants is strongly associated with the hot-water-soluble fraction. This usually ranges from 0.4 to 4.7% of the total boron. The highest percentage occurs in fine-textured soils, and the lowest occurs in coarse-textured soils (Gupta and Macleod 1982). Uptake of boron by plants is about 4 times higher at pH 4 than at pH 9, highest in the temperature range 10 to 30°C, and higher with increased light intensity (Sprague 1972).

For the past 60 years, boron has been applied to B-deficient soils to improve crop yields of grains, fruits, vegetables, legumes, pine trees, tobacco, cotton, sunflowers, and peanuts (USEPA 1975; Gupta 1979; Lipsett et al. 1979; Shorrocks and Nicholson 1980; Hopmans and Flinn 1984; Gupta and Cutcliffe 1985; Willett et al. 1985; Combrink and Davies 1987; Dear and Lipsett 1987; Mozafer 1987; Nuttall et al. 1987; Rerkasem et al. 1988; Stone 1990). Boron is unique among the essential micronutrients because it is the only element normally present in soil solution as a non-ionized molecule over the pH range suitable for plant growth (Gupta 1979). Boron deficiency in plants is widespread and has been reported in one or more crops in at least 43 states, almost all Canadian provinces, and many other countries (Gupta 1979). Boron deficiency in crops is more widespread than that of any other micronutrient (Gupta et al. 1985). It is more likely to occur in light-textured acid soils in humid regions because of boron's tendency to leach. However, deficiency may also occur in heavy-textured soils with high pH because boron is readily adsorbed under these conditions (Gupta et al. 1985). Deficiency signs include browning and spotting of leaves, chlorosis, abnormal thickening of cell walls, increased production of indoleacetic acid, accumulation of polyphenolic compounds, changes in membrane permeability, necrosis, and finally death (USEPA 1975; Gupta 1979). Visible signs of deficiency in corn are accentuated by calcium deficiency, and are least evident when calcium is added to excess. Under conditions of boron and calcium deficiency combined, yields are low, and starch phosphorylase activity in corn leaves increases markedly, as does that of ribonuclease and polyphenol oxidase (Chatterjee et al. 1987). Interaction effects were also measured between boron and potassium in alfalfa (Walker et al. 1987). Boron deficiency is usually corrected by application of 0.5 to 3 kg B/ha, depending on crop and formulation (Gupta 1979). Adding boron promotes translocation rate of photosynthetic products and increases CO₂ incorporation into free amino acids (Gupta 1979).

Boron toxicity has been reported in many species of grasses, fruits, vegetables, grains, trees, and other terrestrial plants (Gupta and Macleod 1982; Dye et al. 1983; Glaubig and Bingham 1985; Francois 1986; Nicholaichuk et al. 1988; Stone 1990) ([Table 29.4](#)). Toxic levels generally do not occur on agricultural lands unless boron compounds have been added in excessive quantities, such as with fertilizer materials, irrigation water, sewage sludge, or coal ash (Gupta and Macleod 1982; Gestring and Soltanpour 1987). Boron-contaminated irrigation water is one of the main causes of boron toxicity to plants. The continued use and concentration of boron in the soil due to evapotranspiration is the reason for eventual toxicity problems (Gupta et al. 1985). Borates have also been used as herbicides for complete kill of vegetation at application rates of 2244 kg/ha (equivalent to 2000 pounds/acre) (Sprague 1972). Borates are frequently applied at elevated concentrations (i.e., >2 g/kg soil) in combination with organic pesticides in order to produce bacteriostatic effects. The resultant B-produced reduction in microbial degradation of the pesticide effectively extends the pesticide's biocidal properties (Sprague 1972). In some cases, cooling tower drift from geothermal steam containing boron may cause foliar boron toxicity in the vicinity of generating units (Glaubig and Bingham 1985; Sage et al. 1989).

Boron poisoning in plants is characterized by stunted growth, leaf malformation, browning and yellowing, chlorosis, necrosis, increased sensitivity to mildew, wilting, and inhibition of pollen germination and pollen tube growth (USEPA 1975; Glaubig and Bingham 1985; Mitchell et al. 1987).

In barley (*Hordeum vulgare*), for example, excess boron caused decreased growth and grain yield, elevated residues in leaves, and increased rate of leaf senescence (Riley 1987; [Table 29.4](#)). Barley grown on zinc-deficient soils tended to accumulate boron up to 2.5 times within 7 days; a similar pattern was evident for excess phosphorus (Graham et al. 1987). Thus, under conditions of marginally high boron in the rooting zone, low zinc, and high phosphorus, boron may accumulate to toxic levels in plants (Graham et al. 1987). Toxic effects in plants — including leaf injury — were observed in 26% of plants at or below substrate concentrations that resulted in greatest growth, indicating considerable overlap between injurious and beneficial effects of boron in plants (Eaton 1944). In general, deficiency effects in plants were evident when boron concentrations in soil solution were <2 mg/L; optimal growth occurred at 2 to 5 mg/L; and toxic effects were evident at 5 to 12 mg B/L (Gupta et al. 1985). However, there is considerable variation in resistance to boron between species ([Table 29.5](#)). Sensitive species are known to include citrus, stone fruits, and nut trees; semitolerant species include cotton, tubers, cereals, grains, and olives; tolerant species usually include most vegetables (Gupta et al. 1985).

Table 29.4 Boron Toxicity to Some Terrestrial Plants

Species, Dose, and Other Variables	Effect (Reference ^a)
BIGLEAF MAPLE, <i>Acer macrophyllum</i> 0.9–5.4 mg B/L, in saturated soil extracts	Reduced growth; >25% foliar damage; leaf residues of 76–324 mg B/kg ash weight (1)
MADRONE, <i>Arbutus menziesii</i> 2.2–5.4 mg B/L, in saturated soil extracts	Growth inhibition; >25% foliar damage; leaf residues of 216–540 mg B/kg ash weight (1)
BEET, <i>Beta vulgaris</i> Soil B solutions 5 mg/L 15 mg/L	Optimal growth (2) Injury evident (2)
BROCCOLI, <i>Brassica oleracea italica</i> Grown in nutrient solutions containing 0.08 mg B/L 4.1 and 8.1 mg B/L	Chlorophyll levels and net photosynthetic rates were significantly lower than those grown in 0.41–0.81 mg B/L solutions (3) Leaf damage evident; lower chlorophyll levels and lower net photosynthetic rate than 0.4 and 0.8 mg B/L groups (3)
RHODES GRASS, <i>Chloris gayana</i> Grown in flyash containing 3 mg hot-water-soluble B/L	Toxic. Residues >149 mg/kg DW (4)
LEMON, <i>Citrus limonia osbeck</i> Soil B concentrations 0.03–0.04 mg/L 1 mg/L	Optimal growth (2) Injury evident (2)
SOYBEAN, <i>Glycine max</i> Grown in soils amended with scrubber sludge residues (4.1 g B/kg) from coal-fired power plant for 2–3 years	Higher sludge B levels of 2 mg B/kg soil surface at year 1, and 1.2 mg B/kg at year 2 produced signs of B toxicity, including decreased growth and elevated residues (>83 mg/kg DW) in leaf and (>47 mg/kg DW) in seeds (5)
SUNFLOWER, <i>Helianthus annuus</i> 50 mg B/L growth medium 10 mg B/L growth medium	Adversely affects phospholipid composition and synthesis in roots and microsomes from seedlings by inhibition of choline phosphotransferase (6) Tolerated level (6)
BARLEY, <i>Hordeum vulgare</i> Residues, in mg B/kg DW 0.5–1.0 in soil 30 in shoots 50–70 in shoots 60–80 in leaf 80–120 in shoots 120–130 in shoots	Residues of 46–100 mg/kg DW in leaves (7) Damage to older leaves (8) Reduction of 10% in dry weight of shoots (7) Toxicity evident (8) Toxic signs, but no yield reductions (8) Grain yield reduced 10% (8)

Table 29.4 (continued) Boron Toxicity to Some Terrestrial Plants

Species, Dose, and Other Variables	Effect (Reference^a)
ALFALFA, <i>Medicago sativa</i> 850–975 mg B/kg dry weight plant	Reduced yield (9)
RICE, <i>Oryza sativa</i> Whole plant B residues 38 mg/kg DW 43–55 mg/kg DW	No signs of toxicity (10) Signs of toxicity evident (10)
Soil waters 2.5–5 mg B/L	Toxic (10)
FRENCH BEAN, <i>Phaseolus vulgaris</i> Grown in flyash containing 3 mg hot-water-soluble B/L	Toxic. Residues >209 mg/kg DW (4)
Residues in whole plant, in mg B/kg dry weight 9–12 >125	Slow flowering and pod formation; general yellowing of tips (11) Reduced growth; burned older leaves dark brown (11)
DIGGER PINE, <i>Pinus sabiniana</i>, seedlings 13–17 mg B/L in saturated soil extracts	Growth reduction; foliar damage >25%; needle residues 1242–1512 mg B/kg ash weight (1)
PEAR, <i>Pyrus communis</i> 82–164 kg B/ha applied to soil around pear trees in a nonirrigated orchard over a 6-year period	Toxicity observed during application and during 4 years postapplication. Toxicity was associated with residues, in mg B/kg DW, of 90–115 in blossom clusters and 45–55 in fruit. Within 5 years postapplication, soil B levels were <2 mg/kg, and all visible signs of toxicity had disappeared (12)
VEGETATION, various species 2244 kg borates/ha (2000 lbs/acre)	Total kill of most species (2)
CORN, <i>Zea mays</i> Soil B concentrations 1 mg/L 5 mg/L	Optimal growth (2) Injury evident (2)
Plant residues >98 mg B/kg DW	Marginal burning and dark brown tips of older leaves (11)

^a 1, Glaubig and Bingham 1985; 2, Sprague 1972; 3, Petracek and Sams 1987; 4, Aitken and Bell 1985; 5, Ransome and Dowdy 1987; 6, Belver and Donaire 1987; 7, Riley 1987; 8, Kluge and Podlesak 1985; 9, Gestring and Soltanpour 1987; 10, Cayton 1985; 11, Gupta 1983; 12, Crandall et al. 1981.

Table 29.5 Boron Concentrations in Soil Water Associated with Optimal Growth and Plant Injury

Plant Category	Boron Concentration in Soil Water (mg/L)	
	Optimal Growth	Plant Injury
Sensitive species	Trace–1	Usually 1–5
Semitoriental species	Usually 1–5	Usually 5–15
Tolerant species	Usually 5–10	Usually 5–25

Data from Sprague, R.W. 1972. The ecological significance of boron. United States Borax and Chemical Corp., Los Angeles, 58 pp.

29.4.3 Terrestrial Invertebrates

Relatively high concentrations of boron compounds are used to control fruitflies, cockroaches, gypsy moth larvae, houseflies, and woodboring insects (Sprague 1972; USEPA 1975; Table 29.6). Boric acid is an effective stomach poison for several insect species, including German cockroaches (*Blattella germanica*), that are unable to detect the presence of boric acid (USEPA 1975). Insect infestation of wood and other substrates can be prevented by pretreatment with boric acid or borax at

Table 29.6 Lethal and Sublethal Effects of Boron on Terrestrial Invertebrates

Organism, Dose, and Other Variables	Effect (Reference ^a)
FRUITFLY, <i>Anastrepha ludens</i> Baits containing cottonseed hydrolysate and borax	Reduced infestation in oranges by 68%, and in mangoes by 98% (1)
HONEY BEE, <i>Apis mellifera</i> 8.7 mg B/L syrup (50 mg boric acid/L) 17.5 mg B/L syrup (100 mg boric acid/L)	No effect on survival (2) Fatal to about 50% (2)
GERMAN COCKROACH, <i>Blattella germanica</i> Baits containing 25% boric acid plus honey	Population reduction of 50% in about 5 days, 80% in 4 weeks, and 98% in 6–9 months (3)
Sugar diet containing 11% boric acid 25% boric acid 50% boric acid 100% boric acid	44% dead in 72 hours (1) 79% dead in 72 hours (1) 80% dead in 72 hours (1) 91% dead in 72 hours (1)
Baits containing 20% boric acid	88% population reduction in 2 weeks; 92 to 95% reduction in 4–12 weeks (4)
GYPSY MOTH, <i>Lymantria dispar</i>, larvae 0.25% boric acid solution (436 mg B/L) 0.5% boric acid 1% boric acid	No effect on gypsy moth nucleopolyhedrosis virus (NPV) (5) Enhanced NPV activity by 2-fold (5) Enhanced NPV activity by 11-fold (5)
HOUSEFLIES, <i>Musca domestica</i> 250–5000 mg B/kg diet, as boric acid Isobornyl thiocyanoacetate 27.3 µg/fly Aerosols, >2%	Inhibits reproduction (2) LD50 (1) 50% knockdown in 6 minutes (1)
AMERICAN COCKROACH, <i>Periplaneta americana</i> Baits containing 1.5% boric acid	All dead in 6 days (6)
WOODBORING INSECTS Common houseborer 430 mg boric acid/m ³ wood	Adequate wood protection (2)
Termites, 3 species >10,000 mg boric acid/m ³ wood	Required for wood protection (2)

^a 1, USEPA 1975; 2, Sprague 1972; 3, Gupta and Parrish 1984; 4, Wright and Dupree 1982; 5, Shapiro and Bell 1982; 6, Lizzio 1986.

doses of 0.25 to 0.55 kg/m³ of wood (USEPA 1975). Boric acid and other boron compounds are effective chemosterilants of the cotton boll weevil (*Anthonomus grandis*) and houseflies (USEPA 1975).

29.4.4 Aquatic Organisms

Boron effects on aquatic plants are highly species specific (Glandon and McNabb 1978; Rao 1981) (Table 29.7). Borate, like silicate, is an essential micronutrient for the growth of aquatic plants, such as diatoms, and it seems that a chemical combination of both nutrients in the form of silicoborate may be required by certain diatoms (Antia and Cheng 1975). In aquatic plants, boron affects nucleic acid metabolism, carbohydrate biosynthesis and transport, and membrane integrity, and it interacts with growth substances (Frick 1985). Diatoms (*Cylindrotheca fusiformis*) cultured under B-deficient conditions stop dividing and swell in size despite increased photosynthetic rates. Boron-deficient diatoms accumulate rubidium, phenolic compounds, nitrates, and phosphates, and they show increased activity of various enzymes, especially glucose-6-phosphate dehydrogenase. However, respiratory adjustment is negligible until nutrient stress becomes irreversible in about 48 h (Smyth and Dugger 1980, 1981). Boron, under conditions of excess, alleviates nutrient deficiency in some phytoplanktoners and can cause temporal variations of phytoplankton composition

in coastal waters (Rao 1981). Phytoplankton can tolerate up to 10 mg inorganic B/L in the absence of stress from pH adversity and nutrient deficiency, although higher borate concentrations up to 100 mg/L are expected to cause species redistribution by favoring the growth of some species and suppressing that of others (Antia and Cheng 1975; Table 29.7).

Available data for aquatic invertebrates and boron suggest that the no-observable-effect levels were 13.6 mg B/L for freshwater organisms and 37 mg B/L for marine biota (Table 29.7). Juvenile Pacific oysters (*Crassostrea gigas*) accumulated boron in relation to availability, but showed no prolonged retention following cessation of exposure (Thompson et al. 1976). At industrial discharge levels of about 1.0 mg B/L, no hazard is apparent to oysters and aquatic vertebrates (Thompson et al. 1976).

Boron may be an essential nutrient in several species of aquatic vertebrates. Insufficient boron (<3 µg B/L; 62 µg B/kg ration) interfered with the normal development of the South African clawed frog (*Xenopus laevis*) during organogenesis, and substantially impaired normal reproductive function in adult frogs (Fort et al. 1998). Impaired growth of rainbow trout (*Oncorhynchus mykiss*) embryos was documented at <90 µg B/L, and death of zebrafish (*Brachydanio rerio*) embryos at <2 µg B/L (Rowe et al. 1998).

The most sensitive aquatic vertebrates tested for which data are available were coho salmon (*Oncorhynchus kisutch*), with an LC50 (16-day) value of 12 mg B/L in seawater, and sockeye salmon (*O. nerka*), showing elevated tissue residues after exposure for 3 weeks in seawater containing 10 mg B/L (Table 29.7). Boron concentrations between 0.001 and 0.1 mg/L had little effect on survival of rainbow trout embryos after exposure for 28 days (Table 29.7). These low levels may represent a reduction in reproductive potential of rainbow trout, and concentrations more than 0.2 mg B/L may impair survival of other fish species, according to Birge and Black (1977). However, additional data are needed to verify these speculations. Birge and Black (1977) reported that concentrations of 100 to 300 mg B/L killed all species of aquatic vertebrates tested, that embryonic mortality and teratogenesis were greater in hard water than in soft water, but that larval mortality of fish and amphibians was higher in soft water than in hard water, and that boron compounds were more toxic to embryos and larvae than to adults. Moreover, they found no measurable effect on boron toxicity to aquatic vertebrates in water temperature in the range of 13 to 29°C, dissolved oxygen between 6.4 and 10.3 mg/L, and pH between 7.5 and 8.5. Elevated boron concentrations of 50 to 100 mg B/L adversely affects the development of amphibian embryos (Laposata and Dunson 1998). In central Pennsylvania ponds, embryos from two species of salamanders (spotted salamander, *Ambystoma maculatum*; Jefferson salamander, *Ambystoma jeffersonianum*), the wood frog (*Rana sylvatica*), and the American toad (*Bufo americanus*) were exposed to wastewater effluents of 0, 50, or 100 mg B/L. At 50 and 100 mg B/L, there were significant increases in the frequency of deformed larvae and reduced hatching success (Laposata and Dunson 1998).

Table 29.7 Lethal and Sublethal Effects of Boron on Aquatic Organisms

Taxonomic Group, Organism, Compound, Dose, and Other Variables	Effect	Reference ^a
AQUATIC PLANTS		
Blue-green alga, <i>Anacystis nidulans</i> , boric acid, H_3BO_3 0.01–4.0 mg B/L	Grows well in B-deficient media; growth neither stimulated nor inhibited at higher levels	1, 15
50 mg B/L	No effect on growth or organic constituents	2
75–100 mg B/L	Growth and chlorophyll content reduced; at 72 hours, photosynthetic pigments depleted	2
100 mg B/L	Decrease in protein content causing inhibition in nitrate uptake and nitrate reductase activity. Decreased chlorophyll content and photosynthesis inhibition within 72 h	2, 15

Table 29.7 (continued) Lethal and Sublethal Effects of Boron on Aquatic Organisms

Taxonomic Group, Organism, Compound, Dose, and Other Variables	Effect	Reference ^a
Green alga, <i>Chlorella pyrenoidosa</i> , boric acid 10 mg B/L	No effect on growth or cell composition. Bioconcentration factor (BCF) of 4 after 7 days	3
50 mg B/L	BCF of 5 after 7 days	3
50–100 mg B/L	Altered cell division and amino acid activity after 72 h; reversible photosynthesis inhibition. Giant cells formed with increased nitrate and protein	4
100 mg B/L	BCF of 4.8 after 7 days	3
>100 mg B/L	100% inhibitory for cell division and biomass synthesis in 72 h	4
Duckweed, <i>Lemna minor</i> , boric acid Control media, 10–20 mg B/L, pH 5.0	Normal growth	5
100 mg B/L, pH 5.0	Growth inhibited; recovery on transfer to control media	5
20 mg B/L, pH 4.0	Residues of 93 mg B/kg FW vs. 63 in controls	5
20 mg B/L, pH 7.0	Growth inhibited. Residues of 257 mg/kg FW vs. 49 in controls	5
Marine algae, 19 species, boric acid 5–10 mg B/L	No inhibitory effect on growth rate in 60 days; stimulatory to some species	6
10–50 mg B/L	Prolonged survival of peak populations of certain diatoms after growth cessation: <i>Bellerochea polymorpha</i> at 10 mg B/L, <i>Skeletonema costatum</i> at 50 mg B/L	6
50 mg B/L	Growth inhibition in 26% of species tested; adaptation and recovery by most species	6
100 mg B/L	Growth inhibition in 12 of 19 species tested; 8 species did not recover and died	6
Marine phytoplankton 30 mg B/L, high nitrates, phosphates, silicates, and low temperatures	Increased primary production and carbon assimilation	7
30 mg B/L, low nutrients, high temperatures	Photosynthesis inhibited up to 62%	7
30 mg B/L, unicellular cultures, 5-days-old	Photosynthesis inhibition	7
As above, 14-days-old	Enhanced photosynthesis in certain species	7
INVERTEBRATES		
Sea urchin, <i>Anthocidaris crassispina</i> , embryos, boric acid 37 mg B/L	Normal development	8
75 mg B/L	Fatal	8
Chironomid, <i>Chironomus decorus</i> , fourth instar 20 mg/L	Growth rate reduced in 96 h	21
1376 mg/L	LC50 (48 h)	21
Cladoceran, <i>Daphnia magna</i> 6.4 mg B/L	Highest concentration tested in 21-day exposure producing no measurable effect	9, 10
13.6 mg B/L	Lowest concentration tested in 21-day exposure causing reduction in number of broods, total young produced, mean brood size, and mean size	9, 10
27 mg B/L	LC14 (21 days)	10
53 mg B/L	LC50 (21 days)	10
54–200 mg B/L	No deaths in 48 h	9, 10
106 mg B/L	LC100 (21 days)	10

Table 29.7 (continued) Lethal and Sublethal Effects of Boron on Aquatic Organisms

Taxonomic Group, Organism, Compound, Dose, and Other Variables	Effect	Reference ^a
115–246 mg B/L	LC50 (48 h)	9, 10, 21
420 mg B/L	LC100 (48 h)	9
Mosquito larvae, 3 species, boric acid, mg/L		
250 (43.7 mg B/L)	LC97–LC99 through hatching	11
4000 (700 mg B/L)	LC100 (48 h), freshly-hatched	11
3000 (524 mg B/L)	LC100 (48 h), second instar	11
10,000 (1748 mg B/L)	LC100 (48 h), third instar	11
16,000 (2797 mg B/L)	LC100 (48 h), pupae	11
VERTEBRATES		
Amphibians; 3 species; eggs; exposed to 0, 50 or 100 mg B/L		
Jefferson salamander, <i>Ambystoma jeffersonianum</i> ; spotted salamander, <i>Ambystoma maculatum</i> ; wood frog, <i>Rana sylvatica</i>	At 50 and 100 mg B/L, there was a significant increase in frequency of deformed larvae	23
American toad, <i>Bufo americanus</i>	Reduced hatching success at 100 mg B/L	23
Zebrafish, <i>Brachydanio rerio</i> ; exposed for 6 months from embryos to adults		
0.002 mg/L	Embryonic death	25
>9.2 mg/L	Adult death	25
Fowler's toad, <i>Bufo fowleri</i> , embryos, through day 4 posthatch		
Boric acid		
Soft water, 50 mg CaCO ₃ /L		
25 mg B/L	LC1 (7.5 days)	12
145 mg B/L	LC50 (7.5 days)	12
Hard water, 200 mg CaCO ₃ /L		
5 mg B/L	LC1 (7.5 days)	12
123 mg B/L	LC50 (7.5 days)	12
Toad, <i>Bufo vulgaris</i> , embryos		
874 mg B/L, as boric acid. Exposure for 24 h from 2-cell stage to tailbud stage	Malformations included edema, microcephalia, short tail, and suppressed forebrain development	11
Goldfish, <i>Carassius auratus</i> , embryos, through day 4 posthatch		
Boric acid		
Soft water		
0.6 mg B/L	LC1 (7 days)	12
46 mg B/L	LC50 (7 days)	12
Hard water		
0.2 mg B/L	LC1 (7 days)	12
75 mg B/L	LC50 (7 days)	12
Borax, Na ₂ B ₄ O ₇ ·10H ₂ O		
Soft water		
1.4 mg B/L	LC1 (7 days)	12
65 mg B/L	LC50 (7 days)	12
Hard water		
0.9 mg B/L	LC1 (7 days)	12
59 mg B/L	LC50 (7 days)	12
Endangered fishes, three species, Green River, Utah; boron tested as boric acid		
Bonytail, <i>Gila elegans</i>		
280 (226–347) mg B/L	LC50 (96 h), fry	17
552 (452–707) mg B/L	LC50 (96 h), juveniles	17
Colorado squawfish, <i>Ptychocheilus lucius</i>		
279 (216–360) mg B/L	LC50 (96h), fry	17
527 (430–667) mg B/L	LC50 (96 h), juveniles	17

Table 29.7 (continued) Lethal and Sublethal Effects of Boron on Aquatic Organisms

Taxonomic Group, Organism, Compound, Dose, and Other Variables	Effect	Reference ^a
Razorback sucker, <i>Xyrauchen texanus</i>		
233 (172–293) mg B/L	LC50 (96 h), fry	17
279 (216–360) mg B/L	LC50 (96 h), juveniles	17
Mosquitofish, <i>Gambusia affinis</i> , adults		
Boric acid		
5600 mg/L (979 mg B/L)	LC50 (96 h)	12
Sodium borate		
3600 mg/L	LC50 (96 h)	12
Channel catfish, <i>Ictalurus punctatus</i> , embryos, through day 4 posthatch		
Boric acid		
Soft water		
0.5 mg B/L	LC1 (9 days)	12
155 mg B/L	LC50 (9 days)	12
Hard water		
0.2 mg B/L	LC1 (9 days)	12
22 mg B/L	LC50 (9 days)	12
Borax		
Soft water		
5.5 mg B/L	LC1 (9 days)	12
155 mg B/L	LC50 (9 days)	12
Hard water		
1.7 mg B/L	LC1 (9 days)	12
71 mg B/L	LC50 (9 days)	12
Bluegill, <i>Lepomis macrochirus</i>		
Boron trifluoride, BF ₃		
15,000 mg B/L	LC50 (24 h)	12
Dab, <i>Limanda limanda</i>		
74.0 mg B/L	LC50 (96 h)	13
88.3 mg B/L	LC50 (24 h)	13
Largemouth bass, <i>Micropterus salmoides</i> ; embryos exposed 2–4 h after fertilization through 8 days posthatch (about 11 days after fertilization)		
1.39 mg B/L	No observable effect	20
12.2 mg B/L	Lowest observable effect concentration (reduced survival, increased developmental abnormalities)	20
92 (84–100) mg B/L	LC50	20
Striped bass, <i>Morone saxatilis</i>		
Juveniles exposed continuously to full strength agricultural drainwater containing 48.8 mg B/L	All dead in 23 days	22
Coho salmon, <i>Oncorhynchus kisutch</i>		
Fry		
447 (356–561) mg B/L	LC50 (96 h), freshwater	18
600 (511–705) mg B/L	LC50 (96 h), brackish water	18
Underyearlings		
12 mg B/L	LC50 (283–384 h), seawater	14
113 mg B/L	LC50 (283–552 h), freshwater	14
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Embryos exposed until hatch to various concentrations of borates		
<0.09 mg B/L	Impaired growth	25
>0.09–5.0 mg B/L	Dose-dependent increase in embryonic growth	25
>100 mg B/L	Lethal	25

Table 29.7 (continued) Lethal and Sublethal Effects of Boron on Aquatic Organisms

Taxonomic Group, Organism, Compound, Dose, and Other Variables	Effect	Reference ^a
Embryos, through day 4 posthatch		
Boric acid		
Soft water		
0.1 mg B/L	LC1 (28 days)	12
100 mg B/L	LC50 (28 days)	12
Hard water		
0.001 mg B/L	LC1 (28 days)	12
79 mg B/L	LC50 (28 days)	12
Borax		
Soft water		
0.07 mg B/L	LC1 (28 days)	12
27 mg B/L	LC50 (28 days)	12
Hard water		
0.07 mg B/L	LC1 (28 days)	12
54 mg B/L	LC50 (28 days)	12
Adults		
339 mg B/L	LC50 (48 h)	10,12, 16
350 mg B/L	No effect in 30 min	16
3500 mg B/L	All alive after 30 min, but in obvious distress	16
14,000 mg B/L	After exposure for 30 min, all recovered if placed in flowing boron-free water	16
Sockeye salmon, <i>Oncorhynchus nerka</i>		
10 mg B/L, exposure in seawater for 3 weeks	Maximum residues, in mg/kg FW, were 17 in bone, 12 in kidney, 10 in gill, 9 in liver, and 8 in muscle. Max. control values were always <1.0, except bone, which was 4.4 mg/kg FW	14
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
Fry		
600 mg B/L	LC50 (96 h), brackish water	18
725 mg B/L	LC50 (96 h), freshwater	18
Juveniles exposed to boron concentrations as high as 6.05 mg/L as boric acid for 90 days in freshwater	No increase in whole-body B concentrations	19
Juveniles exposed to full-strength agricultural drainwater from San Joaquin Valley, California, for 28 days. Drainwater had 48.8 (44–53) mg B/L	77% dead; survivors had reduced growth and 192 (190–200) mg B/kg DW whole body vs. 3.1 mg B/kg DW in controls	22
Leopard frog, <i>Rana pipiens</i> , embryos, through day 4 posthatch		
Boric acid		
Soft water		
13 mg B/L	LC1 (7.5 days)	12
130 mg B/L	LC50 (7.5 days)	12
Hard water		
22 mg B/L	LC1 (7.5 days)	12
135 mg B/L	LC50 (7.5 days)	12
Borax		
Soft water		
5 mg B/L	LC1 (7.5 days)	12
47 mg B/L	LC50 (7.5 days)	12
Hard water		
3 mg B/L	LC1 (7.5 days)	12
54 mg B/L	LC50 (7.5 days)	12
South African clawed frog, <i>Xenopus laevis</i>		
Embryos allowed to develop in media containing from <1 to 5000 µg/L	Developmental malformations at <3 µg B/L, but not at higher concentrations. Malformations included abnormal	24

Table 29.7 (continued) Lethal and Sublethal Effects of Boron on Aquatic Organisms

Taxonomic Group, Organism, Compound, Dose, and Other Variables	Effect	Reference ^a
Adults fed diets containing 62 or 1851 µg B/kg ration for 28 days, then mated and offspring cultured in media with various levels of B	development of the gut, craniofacial region and eye, visceral edema, myotomes, and notochord Frogs fed diets containing 62 µg B/kg produced a greater number of necrotic eggs and abnormal embryos than those given 1851 µg B/kg ration. Embryos cultured in media with less than 4 µg B/L had a high incidence of malformations when compared to those raised in media of 4 µg B/L and higher	24

^a 1, Martinez et al. 1986b; 2, Martinez et al. 1986a; 3, Fernandez et al. 1984; 4, Maeso et al. 1985; 5, Frick 1985; 6, Antia and Cheng 1975; 7, Rao 1981; 8, Kobayashi 1971; 9, Gersich 1984; 10, Lewis and Valentine 1981; 11, USEPA 1975; 12, Birge and Black 1977; 13, Taylor et al. 1985; 14, Thompson et al. 1976; 15, Mateo et al. 1987; 16, Sprague 1972; 17, Hamilton 1995; 18, Hamilton and Buhl 1990; 19, Hamilton and Wiedmeyer 1990; 20, Black et al. 1993; 21, Maier and Knight 1991; 22, Saiki et al. 1992; 23, Laposata and Dunson 1998; 24, Fort et al. 1998; 25, Rowe et al. 1998.

29.4.5 Birds

Boron stimulated growth in Vitamin D₃-deficient chicks. Supplemental dietary boron alleviated or corrected cholecalciferol deficiency-induced elevations in plasma glucose concentrations in chicks (Hunt 1994). There is no need to supplement the diets of laying hens with boron, provided that basal diets contained about 11 mg B/kg ration (Qin and Klandorf 1991).

Boron is a potent teratogen to domestic chicken embryos when injected into eggs. Injection of boron into the yolk sac of chicken embryos during the first 96 h of development with 1.0 to 2.5 mg of boric acid — equivalent to 3.2 to 8.0 mg B/kg fresh weight egg (55 g egg) — produced a wide range of developmental abnormalities (Table 29.8). Several compounds are known to counteract B-induced avian developmental abnormalities, or to reduce the frequency of malformations, although the mode of action is unclear. These compounds include sodium pyruvate, to counteract rumplessness (Landauer 1952); nicotinamide, to decrease frequency of facial defects (Landauer 1952) and melanin formation (Landauer 1953c); and riboflavin, which greatly reduced the teratogenic effects of boric acid (Landauer 1952, 1953a, 1953b; Landauer and Clark 1964). Other polyhydroxy compounds, such as D-ribose, pyridoxine hydrochloride, and D-sorbitol hydrate, also reduced or abolished boric acid-induced teratogenicity in chick embryos (Landauer 1953b).

High concentrations of boron have been found in the San Joaquin Valley of California in irrigation drainwater and in aquatic plants consumed by waterfowl. Measured boron concentrations in that locale exceeded 20 mg/L in subsurface agricultural drainage waters, 400 mg/kg dry weight in widgeongrass (*Ruppia maritima*) and algae, 150 mg/kg dry weight in aquatic insects, 1860 mg/kg dry weight in some aquatic plants, and up to 3390 mg/kg dry weight in seeds consumed by waterfowl (Schuler 1987; Klasing and Pilch 1988; Smith and Anders 1989; Hoffman et al. 1990). At present, only selenium has been implicated as the cause of abnormal development among waterfowl in western areas impacted by irrigation drainwaters (Ohlendorf et al. 1986; Hoffman et al. 1988, 1990). However, studies by Smith and Anders (1989) and Hoffman et al. (1990) with mallards demonstrate that dietary boron concentrations well below levels that can occur in the environment represent a toxicological hazard that has not been considered in the management of agricultural drainwater. For example, dietary concentrations of 300 to 400 mg B/kg of feed on a fresh weight basis — substantially lower than boron levels reported in the vicinity of some western wildlife refuges contaminated by agricultural drainwater — adversely affect mallard growth, behavior, and brain biochemistry and are often associated with elevated tissue boron levels (Table 29.8). Dietary levels

of 100 mg B/kg fresh weight result in reduced growth of female mallard ducklings (Hoffman et al. 1990), and diets containing as little as 30 mg B/kg fresh weight fed to mallard adults adversely affected the growth rate of their ducklings (Smith and Anders 1989). Resource managers must now consider boron, as well as selenium, and their possible interactions, as a toxic hazard to wildlife populations throughout areas of the western United States (Smith and Anders 1989).

Table 29.8 Lethal and Sublethal Effects of Boron on Birds

Species, Dose, and Other Variables	Effect (Reference ^a)
MALLARD, <i>Anas platyrhynchos</i>	
Adults fed diets containing various concentrations of B, as boric acid, for 3 weeks, then mated. Resultant ducklings continued on same diets for 21 days. Data collected on reproduction, survival, residues, and histopathology when ducklings were age 21 days.	
8 mg B/kg diet fresh weight (controls). Diets contained about 10% moisture	Boron residues in egg, liver, and brain of adults and ducklings were always <3 mg B/kg dry weight (8)
30 mg B/kg diet FW	Duckling weight gain reduced compared to controls. Residues in egg and duckling liver and brain about 3–4 mg B/kg DW; residues <3 in adult liver and brain (8)
300 mg B/kg diet FW	Duckling body weights at hatch significantly lower than controls; duckling weight gain reduced. Mean residues, in mg B/kg dry weight, were 13 in egg, 15 in adult liver (Max. 24), 17 in duckling liver (Max. 36), 14 in adult brain (Max. 24), and 19 in duckling brain (Max. 44) (8)
1000 mg B/kg diet FW	No observable effect on adults. No effect on egg fertility or shell thickness. Significantly reduced hatching success; duckling mortality through age 7 days significantly greater than controls, and body weight lower. Total number of 21-day-old ducklings produced per female and brain:body weight ratios were significantly higher than controls. Mean B residues, in mg/kg DW, were 49 in egg, 33 in adult liver (Max. 74), 51 in duckling liver (Max. 89), 41 in adult brain (Max. 89), and 66 in duckling brain (Max. 110). No histopathology evident in liver, brain, kidney, or heart (8)
Breeding adults fed diets containing 0, 450, or 900 mg B/kg ration as boric acid for as long as 24 weeks. Ducklings produced received the same treatment as their parents for 14 days, then killed	No histopathology and no adverse effects on survival. B residues in the 900 mg B/kg group, in mg/kg B/kg FW, were 11 in egg vs. 2 in controls, 8.5 in adult liver vs. 0.6 in controls, and 13 in duckling liver vs. 0.3 in controls; values for the 450 mg/kg group were intermediate. Adults in the high-dose group had weight loss and decreased hemoglobin; eggs produced were lower in weight and fertility than controls. Hatching success and duckling weight in the high-dose group were reduced; duckling growth was reduced; altered duckling liver biochemistry (14)
Adult males fed diet containing 1600 mg B/kg ration as boric acid for 32 days	Boron accumulated in blood, brain, and liver, reaching 30–67 mg B/kg DW in 2–15 days. Boron was eliminated rapidly, with few detectable residues after 1 day on a boron-free diet (12)
Ducklings, age 1 day, fed diets containing 0, 100, 400, or 1600 mg B/kg ration as boric acid for 9 weeks	Only the high-dose group had consistently altered activity schedules, including decreases in amount of time spent in alert behaviors and in the water. Overall feeding time was increased, but did not result in an increase in the amount of food consumed (13)
Ducklings, age 1 day, 2-week dietary exposure 1000 mg B/kg FW diet, as boric acid 5000 mg B/kg diet, as boric acid	Adverse effects on growth (9) Some deaths (9)
Ducklings, age 1 day, 4-week dietary exposure. Diets contained as much as 1000 mg B/kg ration as boric acid alone or in combination with 15 or 60 mg Se/kg ration as selenomethionine. Diets contained either 22% or 7% protein	Boron alone caused growth reduction, with effect exacerbated by selenium and low protein (11)

Table 29.8 (continued) Lethal and Sublethal Effects of Boron on Birds

Species, Dose, and Other Variables	Effect (Reference^a)
Ducklings age 1 day, 10-week dietary exposure to boric acid	
Controls, 13 mg B/kg FW diet. Diets contained 12% to 14% moisture	Brain B concentration of 2 mg/kg DW (9)
100 mg B/kg FW diet	Delayed growth of females, plasma triglyceride levels elevated, abnormal liver metabolism, brain residue of 4 mg/kg DW (9)
400 mg B/kg FW diet	Delayed growth of females, plasma triglyceride elevated, brain B residue of 5 mg/kg DW, decrease in brain ATP, altered duckling behavior in bathing and resting (9)
1600 mg B/kg FW diet	Some deaths (10%), delayed growth, decreased food consumption, plasma triglyceride elevated, brain B residue of 51 mg/kg DW (Max. 99), decrease in brain calcium and ATP, reduction in time spent bathing and standing, increase in time spent resting, increased serum calcium, lower hematocrit and hemoglobin; no histopathology of brain, liver, or kidney (9)
DOMESTIC CHICKEN, <i>Gallus domesticus</i>	
Embryo, yolk injection	
Boric acid	
0.01 mg B/kg body weight (BW)	LD1 (1)
1.0 mg B/kg BW	LD50 (1)
1.0 mg at age 28 h	Developmental abnormalities (2)
2.0 mg at 28 h of development	Malformations of nervous system, eyes, and spinal cord (3)
2.5 mg at 24 h of development	Rumplessness (7)
2.5 mg at 84 h of development	Foot defects (7)
2.5 mg at 96 h of development	Skeletal deformities, cleft palate, missing toes, eye deformities (4–6)
15.8 mg B/kg egg at 96 h of development	LD50 (96 h). Most (70 to 85%) of the survivors at age 18 days had edema, inhibited feather growth, pale body coloration, and reduced body weight (10)
Borax	
0.01 mg B/kg BW	LD1 (1)
0.5 mg B/kg BW	LD50 (1)
Embryo, chorioallantoic membrane injection on day 8 of incubation with 0.1, 0.5, or 1.0 mg B/egg as sodium tetraborate	Chicks had a dose-dependent decrease in bone organic matrix, hatchability, and bone growth (16)
Adult	
Basal diets (11 mg B/kg ration) supplemented with 100 mg B/kg ration for 2 weeks, then reduced to 60 mg B/kg ration for 3 additional weeks	Egg production reduced (15)
875 mg B/kg diet, as boric acid, for 6 days	Egg production ceased; production normal 14 days after B withdrawn (1)

^a 1, Birge and Black 1977; 2, Schowling and Cuevas 1975; 3, Schowling et al. 1976; 4, Landauer 1953a; 5, Landauer 1953b; 6, Landauer 1953c; 7, Landauer 1952; 8, Smith and Anders 1989; 9, Hoffman et al. 1990; 10, Ridgway and Karnofsky 1952; 11, Hoffman et al. 1991; 12, Pendleton et al. 1995; 13, Whitworth et al. 1991; 14, Stanley et al. 1996; 15, Qin and Klandorf 1991; 16, King et al. 1991.

29.4.6 Mammals

No requirement for boron in mammals is proven, although evidence is accumulating suggesting that boron may be an essential nutrient. Boron is related to normal energy utilization, immune function, and metabolism of bone, minerals, and lipids (Penland 1998). Boron deficiency (<0.04

mg B/kg ration of dams) impairs early embryonic development in rodents. These effects were not observed at 2 mg B/kg ration (Lanoue et al. 1998). Boron deprivation in animals and humans results in decreased brain electrical activity similar to that observed in nonspecific malnutrition, and reduced cognitive and psychomotor function (Penland 1998). Learning performance (manual dexterity, eye-hand coordination, memory, attention, perception) in humans was significantly higher when the daily boron ingestion rate was 3 mg vs. 0.23 mg (Penland 1994). Boron dietary supplements to postmenopausal women age 48 to 82 years induced changes consistent with the prevention of calcium loss and bone demineralization (Nielson et al. 1987; Nielsen 1994). In rats, adequate dietary boron protected against premature senescence (Massie 1994) and alleviated the signs of Vitamin D₃ deficiency through improved absorption and retention of calcium and phosphorus, and retention of femur magnesium (Hunt 1994). In cattle, increases in boron ingestion were associated with elevated boron levels in plasma and urine, increased boron excretion, decreased plasma phosphate concentrations, and increased renal and urinary clearance of phosphates (Weeth et al. 1981). Boron accumulations in rat testes were associated with progressive germ cell depletion that persisted long after toxic exposure to boron had occurred (Lee et al. 1978).

Boron effectively counteracts symptoms of fluoride intoxication in humans (Zhou et al. 1987) and in rabbits poisoned experimentally (Elsair et al. 1980a, 1980b, 1981). Humans suffering from skeletal fluorosis experienced 50 to 80% improvement after drinking solutions containing 300 to 1100 mg of borax per liter daily, 3 weeks a month for 3 months (Zhou et al. 1987). Boron enhances sequestration of fluoride from bone and excretion through kidneys and possibly the intestinal tract (Elsair et al. 1980a, 1981).

Inorganic borates, including boric acid, and sodium, ammonium, potassium, and zinc borates display low acute toxicity to mammals via oral, dermal, and inhalation routes of exposure. The critical effects in several species of mammals during chronic exposure to boron compounds are male reproductive toxicity and developmental abnormalities (Hubbard 1998). For example, prenatal exposure to elevated levels of boric acid causes reduced incidences of supernumerary ribs and a shortening or absence of the 13th rib in several species of laboratory animals (Narotsky et al. 1998). The doses that cause these effects are far higher than any levels to which human populations could be exposed. Humans would need to consume 3.3 g of boric acid or 5.0 g of borax to ingest the same dose level at the lowest animal NOAEL (Hubbard 1998). Boron has no measurable effect on human fertility or reproduction among workers exposed to borates or to populations exposed to high environmental borate levels (Hubbard 1998; Sayli 1998; Tuccar et al. 1998). Adult Turkish females, for example, residing in boron-rich areas (29 mg B/L drinking water) or boron-poor areas (0.3 to 0.5 mg B/L drinking water) did not differ in rate of spontaneous abortions, stillbirths, or congenital malformations (Tuccar et al. 1998).

Long-term exposure of humans to airborne boron dust may cause irritation of the nose, throat, and eyes, and large amounts of boron ingested over short periods of time can adversely affect the gastrointestinal tract, liver, kidney, and brain, and may lead to death (USPHS 1991). However, borax mean air exposures of 18 mg/m³ measured for high-exposure workers together with dietary boron, resulted in an estimated absorption of only 0.38 mg B/kg BW daily. At this level, there was no progressive accumulation across the work week (Culver et al. 1994). Epidemics and sporadic cases of oral intoxication in people are often due to inadvertent addition of boric acid to infant formulas (Siegel and Wason 1986). Five of 11 human infants died within 3 days of exposure after ingesting formula prepared with a 2.5% aqueous solution of boric acid, equivalent to 4.5 to 14.0 g of boron ingested. Prior to death, these infants were lethargic and vomiting; postmortem degenerative changes were observed in liver, kidney, and brain (USPHS 1991). Some products containing boron compounds, such as pacifiers, have been sold in Ireland despite a recommendation from the Pharmaceutical Society of Great Britain that they should not be sold because of hazards to infants (O'Sullivan and Taylor 1983). Fatal cases of boron poisoning have involved misuse of boron compounds in hospitals, either from accidental substitution of boric acid solution for water in infant formula or from accidental use of boric acid as a diapering powder (USEPA 1975). In an adult fatality, the victim died after inundation by borax solution (USEPA 1975). In one case, a 12-month-old girl developed violent vomiting, coughing, irritability, tremors, seizures, and a delirious reaction

after accidentally swallowing a mixture containing 3 g boric acid and 300 mg cinchocaine chloride prescribed due to a painful dental protrusion (Egfjord et al. 1988). Her plasma boric acid level 6 h later was 26 mg/L; the half-time persistence ($T_{1/2}$) for boric acid in plasma is about 7 h (Egfjord et al. 1988). The lethal dose of boric acid varies according to the species. In mammals, it ranges from 210 to 603 mg B/kg BW, and death is due to CNS paralysis and gastrointestinal irritation (Table 29.9; NAS 1980; USPHS 1991). Human newborns are especially sensitive, and accidental deaths have been recorded at doses between 50 and 140 mg B/kg BW (Table 29.9).

In mammals, excessive boron consumption results in a reduced growth rate and sometimes loss in body weight. These may not be due entirely to reduced feed and water consumption (Table 29.9; Seal and Weeth 1980). Growth retardation has been reported in cattle given 150 mg B/L drinking water (about 15 mg B/kg BW daily), in dogs consuming diets containing 1750 mg B/kg, in rabbits eating rations equivalent to >140 mg B/kg BW daily, and in rats given 150 mg B/L drinking water or 1060 mg B/kg diet (Table 29.9). In some cases, animals will avoid B-contaminated drinking water if given a choice. Rats, for example, will reject drinking water containing as little as 1.0 mg B/L (Dixon et al. 1976), and cattle will avoid water containing >29 mg B/L (Green and Weeth 1977).

Male workers engaged in boric acid production showed weakened sexual activity, decreased seminal volume, low sperm count and motility, and increased seminal fructose (USEPA 1975). Animal studies demonstrated that the testes atrophy or degenerate if large amounts of boron are eaten or drunk; these effects have not been reported in humans (USPHS 1991). Adverse effects on reproduction of laboratory animals have been reported in sensitive species fed diets containing more than 1000 mg B/kg, or given drinking water containing 1.0 mg B/L (equivalent to about 0.3 mg B/kg BW daily), or given a single oral dose of 3000 mg B/kg BW on the first day of pregnancy (Table 29.9). Boric acid caused developmental toxicity — including fetal weight reduction, prenatal mortality and malformations, decreased survival — in rats, mice, and rabbits in the range of 16 to 80 mg B/kg BW daily given either throughout gestation or only during major organogenesis (Heindel et al. 1994).

Volatile boron compounds, especially boranes, are usually more toxic than boric acid or soluble borates (Table 29.9) (NAS 1980). However, there is little commercial production of synthetic boranes, except for sodium borohydride — one of the least toxic boranes (Sprague 1972). Boron trifluoride is a gas used as a catalyst in several industrial systems, but on exposure to moisture in air, it reacts to form a stable dihydride (Rusch et al. 1986). For boric oxide dusts, occupational exposures to 4.1 mg/m³ (range 1.2 to 8.5) are associated with eye irritation; dryness of mouth, nose and throat; sore throat; and cough (Garabrant et al. 1984).

Table 29.9 Lethal and Sublethal Effects of Boron on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect (Reference ^a)
CATTLE, <i>Bos</i> spp.	
Drinking water	
Supplemented with 15, 30, 60, or 120 mg B/L for 10 days	Boron levels in plasma rose from 2.7 mg/L in controls to 4.4 (15 mg/L group) to 5.3 (30 mg/L group) to 8.3 (60 mg/L group) to 13.4 mg/L in the 120 mg B/L drinking water supplement (5)
29 mg B/L, and higher	When given choice, cattle preferred tap water to drinking water supplemented with B compounds (1)
120 mg B/L, as borax, for 10 days	No effect on feed or water consumption; no overt signs of toxicosis (2)
150 mg B/L, as borax, for 30 days, equivalent to 15.3 mg B/kg BW daily	Decreased feed consumption, weight loss, edema, inflammation of legs, daily elevated plasma B levels of 1.2 mg/L vs. 0.5 in controls, abnormal blood chemistry (1–5)
Diet	
Consumed feed containing 157 mg B/kg, as borax, for 42 days	No adverse effects (3)

Table 29.9 (continued) Lethal and Sublethal Effects of Boron on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect (Reference^a)
Fed 2–2.5 g boron daily as borax, for 40 days	No observable adverse effects; all B excreted, mostly in urine (6)
Fed 20 g borax daily	Milk B residues increased from <1.0 mg/L to >3 mg/L (5)
Ingested total dose of 100–300 g boron, equivalent to 200–600 mg B/kg BW	Toxic dose (7)
Found dead after consuming 1 kg borax, or about 250 g B	Residues, in mg B/kg FW, were 1300 in ruminal fluids, 1900 in abomasal fluids, 24 in liver, 19 in rumen, and 21 in abomasum (7)
DOG, <i>Canis familiaris</i>	
Diet	
350 mg B/kg feed, 2 years	Tolerated (8)
1540 mg borax/kg or 3000 mg boric acid/kg, chronic study (174–524 mg B/kg diet)	No adverse effects (6, 9)
1170 mg B/kg, 38 weeks	Testicular degeneration, spermatogenesis cessation (5, 8)
Inhalation	
92 mg pentaborane/m ³ for 15 min	LC50 (9)
GUINEA PIG, <i>Cavia</i> spp.	
Inhalation	
0.018 mg decaborane/m ³ , 6 h daily, 5–6 exposures	Eye inflammation, listlessness, emaciation, convulsions (3)
HUMAN, <i>Homo sapiens</i>	
Dermal	
7-month-old infant treated for dermatitis with 3% boric acid powder	Fatal. Boron concentrations elevated in bile, intestinal contents, and spleen (9)
Adult administered about 645 g of boric acid dermally	Toxicosis observed (10)
Inhalation	
Borax dust, 1.1–14.4 mg/m ³ , occupational exposure for at least 5 years	At 14.4 mg/m ³ , 33% of workers noted dryness of mouth, nose, or throat; 28% had eye irritation problems; 15% had nosebleeds and cough; 13% had sore throat or shortness of breath and chest tightness. At 4.0 and 1.1 mg/m ³ , no symptoms except eye irritation were noted by more than 5% and 3% of exposed participants (11) Irritation of nose, throat, and eyes (27) Pulmonary irritation, headache, nausea, fatigue, muscular weakness, liver and kidney pathology (3)
Boron dust, >4.1 mg/m ³ for 11 years	
Boranes, various	
Oral	
3 mg B daily for 119 days to diet containing 0.25 mg B	Reduction in urinary excretion of calcium and magnesium by postmenopausal women (12)
20 mg B daily	Normal adult intake (6)
Solutions >88 mg B/L or >500 mg boric acid/L	Fatal to infants (13)
895 mg B/kg BW; single attempted suicidal dose of a boric-acid-containing insecticide by adult female	Vomiting; hospitalized for 96h; asymptomatic after release (27)
1–3 g boric acid, or 0.3–0.8 g/kg BW	Lethal to newborns. (14, 27)
2–4.5 g boric acid or 0.5–1.2 g/kg BW	Nonfatal to infants, but serum levels elevated from 20–150 mg borate/L (14)
>3.5 g boric acid daily	Probably harmful or lethal to infants and newborns (10)
4 g boric acid or borates daily	No toxicosis in adults (6, 9)
4.5–15 g boric acid, equivalent to 1.25–4.2 g/kg BW, in accidentally contaminated formula in newborn nursery	Death preceded by severe symptomology; serum levels of 400–1000 mg borate/L (13, 14)
5–6 g of borates, or 0.7 g/kg BW	Fatal to infants (14, 15)
15–20 g of boric acid, equivalent to 0.25–0.3 g/kg BW	Fatal to adults (9, 14, 15, 27)

Table 29.9 (continued) Lethal and Sublethal Effects of Boron on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect (Reference^a)
Infants, age 6–16 weeks, given pacifiers dipped in a proprietary borax (107 g/L) and honey compound. Dose during 1-month-exposure period estimated at 3–9 g borax	Some developed seizure disorders characterized by vomiting, loose stools, irritability, diarrhea; elevated blood B values of 2.6–8.5 mg B/L vs. <0.6 in controls. When preparation withheld, seizures stopped and children remained well for at least 5 years (13)
Injection, intravenous	
Adult males, age 22–28 years, given single infusion of 562–611 mg boric acid, equivalent to 8.0–8.7 mg B/kg BW	Tb 1/2 persistence of boric acid was 21 h. Most excreted in urine in 24 h, 94% in 96 h, and ~99% in 120 h; plasma boric acid concentrations after infusion was about 16 mg/L vs. 0.5 at start; no discomfort during or after infusion (16)
Adults given total dose of 20 g boric acid	No permanent adverse effects (9)
MONKEY, <i>Macaca</i> spp.	
Inhalation	
Pentaborane, 640 mg/m ³ , 2 min	LC50 (9)
Intraperitoneal injection	
Decaborane, 1 mg/kg BW daily, multiple injections	Altered brain wave activity (9)
Decaborane, 6 mg/kg BW, single injection	LC50 (9)
MICE, <i>Mus</i> sp.	
Drinking water	
5 mg B/L, lifetime exposure	No effect on growth, longevity, or tumor incidence (2, 5)
Ingestion	
3 g B/kg BW, first day of pregnancy	94% of embryos did not develop past blastocyst stage vs. 9% in controls (9)
Diet	
Equivalent to 27 mg B/kg BW daily	No adverse reproductive effects (33)
48 mg B/kg BW daily for 103 weeks	40% dead (27)
96 mg/kg BW daily for 103 weeks	Testicular atrophy (27)
Equivalent to 111 mg B/kg BW daily	Reduced fertility (33)
144 mg/kg BW daily for 13 weeks	Decreased survival (27)
288 mg/kg BW daily for 13 weeks	Testicular degeneration (27)
1500 mg boric acid/kg (262 mg B/kg) daily	All dead within 10 days (17)
Injection, intravenous	
1.32 g sodium borate per kg BW, single dose	LD50 (18)
Injection, intraperitoneal	
25.2 mg decaborane/kg BW, single dose	LD50 (9)
44.7 mg decaborane/kg BW, single dose, prior treatment for 8 days at 250 mg/kg BW with pyridoxine hydrochloride	LD50 (9)
2817 mg sodium borate/kg BW, single dose	LD50 (18)
Inhalation	
Pentaborane	
0.011 mg/m ³ for 4 h	LC50 (3)
50 mg/m ³ , 15 min	LC50 (9)
342 mg/m ³ , 2 min	LC50 (9)
1034 mg/m ³ , 30 seconds	LC50 (9)
RABBIT, <i>Oryctolagus</i> sp.	
Diet	
Equivalent to 800–1000 mg borates/kg BW daily for 4 days	Growth retardation (18)
Intragastric route	
Daily dose of 100 mg calcium borate for 4 months	Altered serum chemistry (9)
Intravenous injection	
Single dose of 800–900 mg boric acid/kg BW	LD50 (18)

Table 29.9 (continued) Lethal and Sublethal Effects of Boron on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect (Reference ^a)
Intraperitoneal injection	
30 mg decaborane/kg BW	Death within 24 h (3)
Dermal	
25–200 mg boric acid/kg BW daily	Not irritating or toxic when applied to intact skin (18)
Sodium borate solutions of 50,000 or 100,000 mg borates/L applied to skin	Mildly or moderately irritating (18)
Boron oxide dust	Application to skin produced erythema that lasted 2–3 days; instillation in eyes produced immediate conjunctivitis as a result of exothermic hydration of boron oxide to boric acid (19)
Inhalation	
120–150 mg calcium borate/m ³ , 2 h daily, 10 weeks exposure	Respiratory tract pathology, growth inhibition, enlarged liver (9)
RAT, <i>Rattus</i> sp.	
Drinking water	
Free access for 90 days to drinking water containing 0.3, 1.0, or 6.0 mg B/L	Rats refused to drink water at 1.0 or 6.0 mg/L (15)
0.3 mg boric acid/L for 6 months	No effect on gonadotoxicity (20)
1.0 mg boric acid/L for 6 months, equivalent to 0.05 mg B/kg BW daily	Decreased spermatozoid count, reduction in spermatozoid activity (20)
6 mg B/L, 90 days	No toxic effect on male reproductive system, blood chemistry, or growth (5, 15)
6 mg B/L for 6 months, equivalent to 0.3 mg B/kg BW daily	Gonadotoxicity in male rats; altered enzyme activity levels in blood and liver (20, 21)
75 mg B/L, as borax, for 45 days	No effect on growth or reproduction (3)
100 mg B/L for 21 days	Tissue B levels in kidney, liver, brain, and blood increased for first 9 days but returned to normal by day 21 except for blood, which continued to rise (21)
150 mg B/L for 70 days, or 170 mg B/L for 25 days	Slight reduction in growth rate (5)
>150 mg B/L for extended periods	Adverse effects probable (5)
300 mg B/L for 49–70 days	Growth rate reduced 21%, but no change in food consumption; coarse coat; atrophied scrotal sacs (4)
440 mg B/L for 25 days	Growth inhibition (4)
880 mg B/L for 70 days	Inhibited sperm production (27)
3 g sodium tetraborate/L for 10–14 weeks	Increase in activity of cerebral succinic dehydrogenase and brain acid proteinase, and in brain RNA concentration; decrease in liver cytochrome P-450 activity (22)
Diet	
Females fed diets with 0.04 (low) or 2 (adequate) mg B/kg ration for 6 weeks before breeding and through pregnancy; reproductive outcome monitored on gestation day 20	Low dietary B significantly lowered maternal blood, liver, and bone B concentrations; however, it had no clear effects on fetal growth or development (35)
Day 10 embryos from dams fed either the low (0.04 mg/kg ration) or adequate (2 mg/kg ration) boron diets for at least 12 weeks were cultured in serum collected from male rats exposed to the low or adequate dietary B treatments	Dams fed the low B diet had a significant reduction in number of implantation sites when compared to dams fed the B-adequate diet; however, embryonic growth <i>in vitro</i> was not affected by B treatment (35)
Pregnant rats fed diets with boric acid equivalent to <0.35 (controls), 3, 6, 10, 13, or 25 mg B/kg BW daily from gestational days 0–20. About half the dams in each group were killed on gestational day 20 and blood and prenatal outcome evaluated. Remaining dams received a control diet beginning on gestational day 20 and their litters monitored throughout lactation	Maternal blood boron concentrations were elevated in all boron groups in a dose-dependent manner. On gestational day 20, blood B concentrations of 1.3 mg/kg FW were associated with the no-observed-adverse-effect level (NOAEL) and 1.53 mg/kg FW with the lowest-observed-adverse effect level (LOAEL), equivalent to dietary intakes of 10 and 13 mg B/kg BW daily, respectively, for developmental toxicity. Developmental toxicity persisted postnatally only at 25 mg B/kg BW daily, a dose associated with more than a 10-fold increase in maternal blood B (2.8 mg B/kg FW) vs. 0.23 mg/kg FW in controls (34)

Table 29.9 (continued) Lethal and Sublethal Effects of Boron on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect (Reference^a)
Equivalent to 17.5 mg B/kg BW daily	No adverse reproductive effects (33)
Equivalent to 26 mg B/kg BW daily	Mild reversible inhibition of spermatiation (33)
Equivalent to 58.5 mg B/kg BW daily	Testicular atrophy; reduced fertility (33)
Fed diets containing 0, 200, 1000, 3000, or 9000 mg B/kg ration as boric acid for up to 12 weeks, equivalent to <0.2 (control), 1.7, 8.5, 26, or 68 mg B/kg BW daily; resistance to destructive testing was measured on femurs, tibias, and lumbar vertebrae	Vertebral resistance to a crushing force was increased by about 10% at all boron dose levels (200–9000 mg B/kg ration); no effect on femurs and tibias. Dietary loadings of 3000 and 9000 mg/kg were reproductively toxic to males and the developing fetus (31)
0.09–1.71 mg boric acid/kg BW daily for 6 months (0.015–0.3 mg B/kg BW daily)	Adverse changes in testes (18)
0.16 or 2.7 mg B/kg ration for 12 weeks to Vitamin D-deprived rats	Abnormal mineral balance in low-dose diet; normal calcium, magnesium, and phosphorus balance in 2.7 mg/kg supplement (28)
350 or 525 mg B/kg diet, as borax or boric acid, for 2 years	No observable adverse effects on fertility, lactation, litter size, weight, or appearance (6)
500, 1000, or 2000 mg B/kg diet, as borax, for 30–60 days, equivalent to 12, 25, or 50 mg B ingested daily	No adverse effects at 500 mg B/kg diet for 60 days. At 1000 and 2000 mg B/kg, adverse effects measured on male reproductive capacity, including germinal aplasia and infertility; effects persisted for at least 8 months following B exposure at highest dose (23)
525 mg B/kg diet for 90 days	Tolerated (8); testes damage (27)
1000 mg boric acid or borax/kg BW daily	Weight loss after 1 week on borax diet, or 2 weeks on boric acid diet; toxic signs after 3 weeks on both diets (24)
1050 mg B/kg diet, as borax or boric acid, for 2 years	Testicular degeneration (6)
1060 mg B/kg diet, as sodium borate, chronic exposure	Growth retardation and testicular atrophy (18)
1170 mg B/kg diet for 2 months	Coarse coat, scaly tails, hunched position, bloody discharge from eyes, depressed hemoglobin and hematocrit (5)
1170 mg B/kg diet, as borax or boric acid, 2 years	Sterility in males and females (6, 8)
1575 mg B/kg ration for 28 days as boric acid, adult males	Testicular lesions after 7 days, atrophy after 28 days (29); no return of spermatogenesis after resumption of normal diet for as long as 32 weeks (30)
1750 mg B/kg diet, 25 days	Reduction of 50% in growth rate (4)
1750 mg B/kg diet, as sodium borate, chronic	Severe testicular atrophy (18)
10,250 mg B/kg ration	Dead after 1 day (27)
Oral, single dose, except where noted	
450 mg B/kg BW	No effect on male fertility (15)
500 mg B/kg BW by gavage on gestation days 5–9, 6–9, 6–10, or on single days between gestation days 6 and 11	After multiday exposures, there was an increased frequency of malformations of the axial skeleton involving the head, sternum, ribs, and vertebrae. About 90% of the fetuses exposed on gestation day 9 had only 6 cervical vertebrae; 60% of the fetuses exposed on gestation day 10 had reduced survival and a reduction in the number of thoracic and lumbar vertebrae (32)
510–690 mg B/kg BW, as borax	LD50 (8, 9, 24)
550–710 mg B/kg BW, as boric acid	LD50 (8, 9, 24)
600 mg B/kg BW	LD50 (2)
3.45–5.14 g sodium borate/kg BW	LD50 (18)
5.1 g boric acid/kg BW	LD50 (6)
6.1 g borax/kg BW	LD50 (6)
Injection, subcutaneous	
1.4 g boric acid/kg BW	LD50 (18)
Injection, intravenous	
5–75 mg boric acid/kg BW	Slight reduction in arterial blood pressure (21)

Table 29.9 (continued) Lethal and Sublethal Effects of Boron on Mammals

Organism, Route of Administration, Dose, and Other Variables	Effect (Reference ^a)
Injection, intraperitoneal	
42 mg sodium borate/kg BW, single injection	Tissue residues after 30 min, in mg B/kg FW, were 25 in blood, 30 in liver, and 50 in kidney vs. <5 in all control tissues. After 3 months, residues were 20 mg B/kg FW in brain, 45 in heart, 60 in liver, and 75 in kidney (21)
Inhalation, boron trifluoride	
2, 6, or 17 mg BF ₃ /m ³ , 6 h daily, 5 days weekly, 13 weeks	At 17 mg/m ³ , altered proximal tubular epithelium of kidney and abnormal serum chemistry. At 6 mg/m ³ , elevated fluoride levels in urine, serum, and bone, but no toxic response. No difference from controls at 2 mg/m ³ (26)
24 or 66 mg/m ³ , 6 h daily, 9 days	Clinical signs of respiratory irritation, nasal discharge, weight loss, increased lung weight, depressed liver weight, kidney pathology at 66 but not 24 mg/m ³ (26)
55 mg/m ³ , 4–7 h daily, 5 days weekly, 6 weeks	Some deaths in rats and other rodent species tested, but no deaths in nonrodent species (26)
180 mg/m ³ , 6 hours daily, consecutive days	All dead prior to sixth exposure (26)
259 mg/m ³ , 4–7 h daily, 2 days	All dead. Mortality was lower for guinea pigs, dogs, rabbits, mice, and cats. Lung and kidney damage in all species (26)
1210 mg/m ³ , 4 h	50% dead (26)
Inhalation, boron oxide	
470 mg/m ³ , 10 weeks	Reddish exudates from nose, but no deaths or signs of lung damage (19)
470 mg/m ³ , 24 weeks	No signs of toxicosis (9)
Inhalation, decaborane	
20 mg/m ³ , 6 h daily, 5 days weekly	Tremors, convulsions, nervousness, restlessness, weight loss, belligerence (3)
36 mg/m ³ , 4 h	LC50 (3)
Inhalation, pentaborane	
3 mg/m ³ , 6 h daily, 5 days weekly	Extreme belligerence, tremors, weight loss (3)
18 mg/m ³ , 4 h	LC50 (3)

^a 1, Green and Weeth 1977; 2, Weeth et al. 1981; 3, NAS 1980; 4, Seal and Weeth 1980; 5, Nielsen 1986; 6, Sprague 1972; 7, Brockman et al. 1985; 8, Weir and Fisher 1972; 9, USEPA 1975; 10, Gupta and Parrish 1984; 11, Garabrant et al. 1985; 12, Nielsen et al. 1987; 13, O'Sullivan and Taylor 1983; 14, Siegel and Wason 1986; 15, Dixon et al. 1976; 16, Jansen et al. 1984; 17, Lizzio 1986; 18, Anonymous 1983; 19, Garabrant et al. 1984; 20, Krasovskii et al. 1976; 21, Magour et al. 1982; 22, Settimi et al. 1982; 23, Lee et al. 1978; 24, Dani et al. 1971; 25, Benson et al. 1984; 26, Rusch et al. 1986; 27, USPHS 1991; 28, Dupre et al. 1994; 29, Ku and Chapin 1994; 30, Chapin and Ku 1994; 31, Chapin et al. 1998; 32, Narotsky et al. 1998; 33, Hubbard 1998; 34, Price et al. 1998; 35, Lenoue et al. 1998.

29.5 RECOMMENDATIONS

Many boron criteria have been proposed for the protection of crops, aquatic life, waterfowl, livestock, and human health (Table 29.10). The risk to aquatic ecosystems from boron is low (Howe 1998). Boron concentrations in contaminated industrial effluents seldom exceed 1.0 mg B/L, a level considered nonhazardous to aquatic life (Table 29.10) (Thompson et al. 1976). In a few boron-rich areas, natural levels will be higher, although organisms may adapt to local conditions (Howe 1998). However, future accumulations of boron in groundwater through wider uses of boron-containing cleansing agents may adversely affect aquatic organisms and other species of plants and animals, as now occurs in areas where natural boron deposits exist (USEPA 1975). Long-term monitoring of groundwaters and surface waters for boron levels seems warranted.

Results of chronic feeding studies using mallards demonstrate that diets containing 13 mg B/kg FW produce no adverse effects, but those containing 30 or 100 mg B/kg FW are associated with elevated tissue boron residues and growth reduction, and diets containing 1000 mg B/kg are fatal

(Table 29.10). More research is needed on the fate and effects of boron on waterfowl and raptors, especially in those areas where high dietary boron loadings are encountered as a result of agricultural drainwater disposal practices.

Minimum concentrations of dietary boron needed to maintain animal health are not known with certainty. However, diets containing <0.4 mg B/kg fresh weight may adversely affect metabolism of rats and chicks. Accordingly, animal diets should contain >0.3 mg B/kg fresh weight until necessary feeding data become available (Nielsen 1986). Also, the defensible boron maximum for livestock drinking water may be considerably higher than 5 mg/L (Table 29.10) because several “safe” water sources in Nevada exceeded this upper maximum and approached 80 mg B/L (Green and Weeth 1977). Data are unavailable on boron effects on terrestrial wildlife. Until these data become available, it seems reasonable to apply the same criteria proposed for livestock protection (Table 29.10) to mammalian wildlife, that is, diets should contain more than 0.4 mg B/kg DW but less than 100 mg/kg, and drinking water <5 mg/L.

Medicinal use of boric acid and borax for babies has resulted in anorexia, nausea, vomiting, diarrhea, marked cardiac weakness, a red eruption over the entire body, and (rarely) death (NAS 1980). The medical community has since abandoned the use of boric acid solutions as irrigants and antiseptics (Siegel and Wason 1986), abandoned all medical uses in Denmark (Egfjord et al. 1988), and severely limited availability (prescription only) in Ireland (O’Sullivan and Taylor 1983). Increased use of boric acid as a household pesticide should be viewed with concern, especially in households where children have access to non-safety-capped boric acid containers (Siegel and Wason 1986). However, the amine-carboxyborane derivatives show promise as therapeutic agents for a number of disease states. More research is needed on medical aspects of amine-carboxyborane compounds and their ability to reduce serum cholesterol and to relieve, through their anti-inflammatory properties, the effects of chronic arthritis (Hall et al. 1994; Newnham 1994). This group of compounds were effective antineoplastic agents with selective activity against single cell and solid tumors derived from human and rodent leukemias, lymphomas, sarcomas, and carcinomas (Hall et al. 1994). Health benefits of borates and boron compounds and their role in fertility and pregnancy merit additional investigation (Mastromatteo and Sullivan 1994). Boron, for example, may be essential to normal bone growth and composition and protect against bone loss associated with aging (McCoy et al. 1994).

The fact that boron is essential to plants is firmly established (NAS 1980; USPHS 1991). However, when boron concentrations in irrigation waters exceed 2 mg/L, extensive plant toxicity should be expected (Pagenkopf and Connolly 1982). High concentrations of boron in some potential irrigation waters in parts of the western United States at levels capable of causing crop damage have prompted implementation of boron criteria for irrigation waters (Table 29.10), although no legally enforceable boron standards have been promulgated (USEPA 1975). More information is needed on crop plants in the following subjects: interaction of boron with other elements in the soil and its effects on boron availability to plants, the role of boron on pollination as it affects seed yield and sugar content of crops, and distinguishing signs of boron deficiency in plants from similar signs of molybdenum deficiency (Gupta and Macleod 1982; Mastromatteo and Sullivan 1994).

More research is needed on the accurate measurement of boron in biological materials when the concentrations are <1.0 mg B/kg (Sullivan and Culver 1998). Standard biological reference materials with low boron levels need to be produced for use in interlaboratory comparisons. This becomes especially important in studies on boron-deficiency states and the ability of the organism to conserve boron at very low intakes (Sullivan and Culver 1998). More research is needed on homeostatic regulation of boron and functional markers of boron metabolism (Sutherland et al. 1998). Sullivan and Culver (1998) recommend additional studies to establish:

- The availability of boron from the diet and its distribution to the tissues
- Boron essentiality in higher organisms
- The beneficial effects of boron on health
- The role of borates in behavioral disorders and cognitive performance

New advances in boron nutrition research should include better characterization of the mechanisms through which boron modulates immune function and insulin release (Hunt 1998). Epidemiological studies should be initiated to identify health conditions associated with inadequate dietary boron (Sutherland et al. 1998). Finally, Dourson et al. (1998) recommend more research on uncertainty factors used in establishing tolerable daily intake values for the protection of human health, with emphasis on variations in interspecies and intraspecies differences in resistance to boron.

Table 29.10 Proposed Boron Criteria for the Protection of Natural Resources and Human Health

Resource and Other Variables	Criterion	Reference ^a
CROPS		
Irrigation waters		
Sensitive crops	0.3–<0.75 mg B/L	1–3, 19
Semitorient crops	0.67–2.5 mg B/L	1–3
Tolerant crops	1–4 mg B/L	1–3
Maximum safe concentration	4 mg B/L	2
Residues in crops		
Boron deficiency	<15 mg B/kg dry weight (DW) plant	4, 5
Toxicosis	>200 mg B/kg DW plant	4, 5
Soil concentrations		
Optimal growth of several species	>0.1–<0.5 mg B/kg DW soil	19
Deficiency, Bangladesh	<0.2 mg B/kg DW surface layer	26
FOREST TREES		
Conifers, sensitive species		
Deficient	<4 mg B/kg DW foliage	23
Low	>4–<8 mg B/kg DW foliage	23
Intermediate	13–20 mg B/kg DW foliage	23
Toxic	>75 mg B/kg DW foliage	23
Angiosperms, sensitive species		
Deficient	8–16 mg B/kg DW foliage	23
Toxic	>180 mg B/kg DW foliage	23
AQUATIC ORGANISMS		
Nonhazardous levels in water		
Fish, oysters	<1–5 mg B/L	2, 6, 25
Aquatic communities	1–2 mg/L	25
Aquatic plants	4 mg B/L	2
Aquatic invertebrates	6–10 mg B/L	25
“Safe” levels in water		
Largemouth bass, <i>Micropterus salmoides</i>	<30 mg B/L	1, 7
Bluegill, <i>Lepomis macrochirus</i>	<33 mg B/L	1, 7
Rainbow trout, <i>Oncorhynchus mykiss</i> , embryos and larvae	0.75–1.0 mg B/L	20
Adverse effects, sensitive species		
	10–12 mg B/L	6, 20
WATERFOWL		
Diet		
No observed adverse effect	<13 mg B/kg fresh weight (FW)	17
Adverse effects	30–100 mg B/kg FW	17, 18
Fatal	1000 mg B/kg FW	18
LABORATORY ANIMALS		
No observed adverse effect		
Rat	<15.6 mg/kg body weight (BW) daily during gestation	22
Rabbit	<25 mg B/kg BW daily	22

Table 29.10 (continued) Proposed Boron Criteria for the Protection of Natural Resources and Human Health

Resource and Other Variables	Criterion	Reference^a
Mouse	<50 mg B/kg BW daily	22
Adverse effect level		
Rat	>15.6 mg B/kg BW daily during gestation	22
Rabbit	>50 mg B/kg BW daily	22
Mouse	90 mg B/kg BW daily during gestation	22
LIVESTOCK		
Diet		
Boron deficiency	<0.4 mg B/kg DW	5
Toxic signs probable	>100 mg B/kg DW	5
Maximum tolerable level, as borax	150 mg B/kg DW	4, 5
Total dose, toxic	100–300 g of B (equivalent to 200–600 mg B/kg BW)	9
Drinking water		
Maximum allowable	5 mg B/L	4, 8, 10, 11
Maximum tolerated	40 mg B/L	10
“Safe”	40–150 mg B/L	11
Adverse effects	>150 mg B/L	5
PESTICIDE APPLICATIONS		
Boric acid, 99% powder	Effective for control of household cockroaches, ants, and fleas	2
Boric acid, 8% solution	Fungicide for vegetables, fruits, and trees	12
HUMAN HEALTH		
Air		
Threshold Limit Value (8 h daily, 5 days weekly)		
Pentaborane	0.01 mg/L	4
Diborane	0.1 mg/L	4
Decaborane	0.5 mg/L	4
Sodium borate	1–5 mg/m ³	16, 17
Boron trifluoride	<3 mg/m ³	19
Calcium borate	4–6 mg/m ³	3
Boron tribromide	10 mg/m ³	19
Boron oxide		
Total dust	10 mg/m ³	19
Respirable fraction	<5 mg/m ³	19
Sodium tetraborate	10 mg/m ³	19
Decahydrate	<5 mg/m ³	19
Anhydrous and pentahydrate	<1 mg/m ³	19
Borate dusts		
Safe	<1 mg B/m ³ daily	21
Infrequent effects	1.1 mg B/m ³ daily	21
Adverse effects	4–14.6 mg B/m ³ daily	21
Daily intake		
Total tolerable	0.4 mg/kg BW ^b	24
Worldwide	Range 0.3–41 mg B, means usually 10–20 mg B ^c	4, 5, 13
Finland	1.7 mg B	5
England	2.8 mg B	5
U.S.	3 mg B	4
No effect level	4 g boric acid	14
Adverse effect level		
Chronic intoxication	4–5 g boric acid	14
Lethal to infants and small children	5–6 g boric acid	14

Table 29.10 (continued) Proposed Boron Criteria for the Protection of Natural Resources and Human Health

Resource and Other Variables	Criterion	Reference ^a
Lethal to adults	18–20 g boric acid, single dose	14
Dermal, ocular		
Sodium borate and boric acid	Safe as cosmetic ingredients at <5% concentrations; not recommended on infant skin or injured skin	12, 16
Diet		
Citrus fruits	<8 mg B/kg FW	19
Cottonseed	<30 mg B/kg FW	19
Hop extracts	<310 mg B/kg FW	19
Minimal risk level	<3.2 mg B/kg ration FW	19
Adverse effects, including death	>4161 mg B/kg ration FW	19
Drinking water		
Recommended	<0.3 mg B/L	15
Former Soviet Union	<0.5 mg B/L	10
U.S.	<1.0 mg B/L	4, 11
"Safe"	<20 mg B/L	2, 10
No toxic effects	20–30 mg B/L	2
Tissue residues		
Blood, children and infants		
Normal	<1.25 mg B/L FW	19
Adverse systemic effects	20–150 mg B/L FW	19
Fatal	200–1600 mg B/L FW	19
Serum, adults		
No significant toxicity	<2320 mg B/L FW	19
Urine, adults		
Normal	0.7–1.5 mg B/L FW	19

^a 1, Sprague 1972; 2, Papachristou et al. 1987; 3, USEPA 1975; 4, NAS 1980; 5, Nielsen 1986; 6, Thompson et al. 1976; 7, Birge and Black 1977; 8, Weeth et al. 1981; 9, Brockman et al. 1985; 10, Seal and Weeth 1980; 11, Green and Weeth 1977; 12, Siegel and Wason 1986; 13, Benson et al. 1984; 14, Schillinger et al. 1982; 15, Krasovskii et al. 1976; 16, Anonymous 1983; 17, Hoffman et al. 1989; 18, Smith and Anders 1989; 19, USPHS 1991; 20, Black et al. 1993; 21, Wegman et al. 1994; 22, Heindel et al. 1994; 23, Stone 1990; 24, Becking and Chen 1998; 25, Howe 1998; 26, Miah 1999.

^b Based on NOAEL of 9.6 mg B/kg BW daily for reproductive effects in rats and an uncertainty factor of 25.

^c Becking and Chen (1998) estimate global mean daily intake of B by humans as 1.9 mg, mostly from food (65%) and drinking water (30%). For a 70-kg adult, this is equivalent to 0.027 mg B/kg BW daily.

29.6 SUMMARY

The United States is the major global producer of boron compounds and supplies about 70% of the annual demand. Although boron is ubiquitous in the environment, human activities such as mining, coal burning, drainwater disposal, and use of borax laundry detergents have resulted in elevated boron loadings in the atmosphere and in irrigation waters. The chemistry of boron is complex and rivals that of carbon in its diversity. However, most boron compounds enter or degrade in the environment to B–O compounds (borates) — such as borax and boric acid — and these are considered to be the most significant ecologically.

Boron is an essential trace element for the growth of terrestrial crop plants and for some species of fungi, bacteria, and algae, but excess boron is phytotoxic. Representative species of aquatic organisms, including plants, invertebrates, fishes, and amphibians, usually tolerated up to 10 mg B/L medium for extended periods without harm. In waterfowl, growth was adversely affected at dietary levels of 30 to 100 mg B/kg fresh weight, tissue boron concentrations were elevated at 100 to 300 mg B/kg diet, and survival was reduced at dietary levels of 1000 mg B/kg. All of these dietary levels currently exist near agricultural drainwater disposal sites in the western United States. Boron is not now considered essential in mammalian nutrition, although low dietary levels protect

against fluorosis and bone demineralization. Excessive consumption (i.e., >1000 mg B/kg diet, >15 mg B/kg body weight daily, >1.0 mg B/L drinking water, or >210 mg B/kg body weight in a single dose) adversely affects growth, survival, or reproduction in sensitive mammals. Boron and its compounds are potent teratogens when applied directly to the mammalian embryo, but there is no evidence of mutagenicity or carcinogenicity. Boron's unique affinity for cancerous tissues has been exploited in neutron capture radiation therapy of malignant human brain tumors.

Boron criteria recommended for the protection of sensitive species include:

- <0.3 mg B/L in water for irrigation of crops
- <1.0 mg B/L for aquatic life
- <5.0 mg B/L in livestock drinking waters
- <30 mg B/kg in diets of waterfowl
- <100 mg B/kg in diets of livestock.

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CHAPTER 30

Molybdenum

30.1 INTRODUCTION

Molybdenum (Mo) is present in all plant, human, and animal tissues, and is considered an essential micronutrient for most life forms (Schroeder et al. 1970; Underwood 1971; Chappell and Peterson 1976; Chappell et al. 1979; Goyer 1986). The first indication of an essential role for molybdenum in animal nutrition came in 1953 when it was discovered that a flavoprotein enzyme, xanthine oxidase, was dependent on molybdenum for its activity (Underwood 1971). It was later determined that molybdenum is essential in the diet of lambs, chicks, and turkey poult (Underwood 1971). Molybdenum compounds are now routinely added to soils, plants, and waters to achieve various enrichment or balance effects (Friberg et al. 1975; Friberg and Lener 1986).

There are certain locations where plants will not grow optimally because of a deficiency in molybdenum, and other places where the levels of molybdenum in plants are toxic to livestock grazing on the plants (Chappell and Peterson 1976). Molybdenum poisoning in cattle was first diagnosed in England in 1938; molybdenosis was shown to be associated with consumption of herbage containing large amounts of this element, and to be controllable by treatment with copper sulfate (Underwood 1971). Molybdenum poisoning of ruminants, especially cattle, has been reported in at least 15 states, and in Canada, England, Australia, New Zealand, Ireland, the Netherlands, Japan, and Hungary. Molybdenosis was most pronounced in areas where soils were alkaline, high in molybdenum and low in copper, or near industrial point sources such as coal, aluminum, uranium, or molybdenum mines; steel alloy mills; or oil refineries (Dollahite et al. 1972; Alloway 1973; Kubota 1975; Buck 1978; Ward 1978; Chappell et al. 1979; Kincaid 1980; King et al. 1984; Kume et al. 1984; Sas 1987). All cattle are susceptible to molybdenosis, milking cows and young stock being the most sensitive (Underwood 1971). Industrial molybdenosis in domestic cattle and sheep, which usually involved a single farm or pasture, has been widely documented (Ward 1978):

- In Colorado in 1958 from contaminated river waters used in irrigation
- In Alabama in 1960 from mine spoil erosion
- In North Dakota in 1968 from flyash from a lignite burning plant
- In Missouri in 1970-1972 from clay pit erosion
- In Pennsylvania in 1971 from aerial contamination by a molybdenum smelter
- In South Dakota in 1975 from molybdenum-contaminated magnesium oxide
- In Texas in 1965-1972 from uranium mine waste leachate

In humans, a gout-like disease in two villages in Armenia was attributed to the ingestion of local foods high in molybdenum and grown in soils high in molybdenum (Friberg and Lener 1986).

Esophageal cancer was prevalent in various parts of southern Africa where food was grown in low molybdenum soils; it was reported in China in a low frequency rate that was significantly correlated with increasing molybdenum concentrations in cereals and drinking water (Luo et al. 1983). Additional and more extensive data on ecological and toxicological aspects of molybdenum in the environment were reviewed by Schroeder et al. (1970), Underwood (1971), Friberg et al. (1975), Chappell and Peterson (1976, 1977), Ward (1978), Chappell et al. (1979), Gupta and Lipsett (1981), Friberg and Lener (1986), and Eisler (1989).

30.2 ENVIRONMENTAL CHEMISTRY

30.2.1 General

Molybdenum is a comparatively rare element that is used primarily in the manufacture of steel alloys for the aircraft and weapons industries. Most of the global production of about 100,000 tons annually comes from the United States — primarily Colorado. Anthropogenic activities that have contributed to environmental molybdenum contamination include combustion of fossil fuels, and smelting, mining, and milling operations for steel, copper, and uranium, as well as for molybdenum. In general, the chemistry of molybdenum is complex and inadequately known. Its toxicological properties are governed to a remarkable extent by interactions with copper and sulfur, although other metals and compounds may confound this interrelation.

30.2.2 Sources and Uses

Molybdenum is used in the manufacture of high-strength, low-alloy steels and other steel alloys in the aircraft and weapons industries, and in the production of spark plugs, X-ray tubes and electrodes, catalysts, pigments, and chemical reagents (Friberg et al. 1975; Kummer 1980; Goyer 1986). The most important industrial compound is the trioxide, Mo_3O_8 , which is resistant to most acids and is oxidized in air at $>500^\circ\text{C}$ (Shamberger 1979).

Molybdenum, discovered about 200 years ago, entered the commercial market in the 1920s as a result of extensive metallurgical research into its alloying properties and to the finding at Climax, Colorado, of the largest proven reserves of molybdenum worldwide (King et al. 1973). Molybdenum does not occur free in nature and is found only in combination with sulfur, oxygen, tungsten, lead, uranium, iron, magnesium, cobalt, vanadium, bismuth, or calcium. The most economically important ores are molybdenite (MoS_2), jordisite (amorphous MoS_2), and ferrimolybdate ($\text{FeMoO}_3 \cdot \text{H}_2\text{O}$); less important are wulfenite (PbMoO_4), powellite (CaMoO_4), and ilsemannite (Mo_3O_8) (Friberg et al. 1975; Chappell et al. 1979; Friberg and Lener 1986; Goyer 1986).

World molybdenum production has increased from about 90 metric tons in 1900 — half from Australia and Norway, half from the United States — to 136 tons in 1906, 1364 in 1932 (an order of magnitude increase in 26 years), 10,909 in 1946, and 91,000 tons in 1973. Through the years, molybdenum has been produced in about 30 countries. In 1973, about 60% of the worldwide production was from the United States, 15% from Canada, 15% from the U.S.S.R. and China combined, and 10% from other nations — Chile, Japan, Korea, Norway, and Mexico (King et al. 1973). By 1979, the United States produced about 62% of the world production of 103,000 metric tons, and exported about half, chiefly to western Europe and Japan; other major producers in 1979 were Canada, Chile, and the U.S.S.R. (Kummer 1980). In the United States, only three mines in Colorado account for almost 70% of domestic production. Other active molybdenum mining sites in North America are in Arizona, Nevada, New Mexico, Utah, and California; molybdenum reserves have also been proven in Idaho, Alaska, Pennsylvania, and British Columbia (Kummer 1980). About 65% of domestic molybdenum is recovered from ores rich in molybdenum; the rest is a by-product from ores of copper, tungsten, and uranium (Chappell et al. 1979).

As a result of various human activities, molybdenum enters the environment from many sources (King et al. 1973; Friberg et al. 1975; Chappell et al. 1979). Coal combustion is the largest atmospheric source of molybdenum, contributing about 550 metric tons annually, or 61% of all atmospheric molybdenum worldwide that comes from anthropogenic sources. In Sweden alone, about 2.5 tons molybdenum are emitted into the atmosphere yearly from oil combustion (Friberg et al. 1975). Molybdenum mining and milling are the source of about 100 metric tons annually to aquatic systems. At the world's largest molybdenum mine in Climax, Colorado, where about 36,000 tons of tailings are generated daily, the operation releases up to 100 tons of molybdenum annually as aqueous effluent. Other sources are molybdenum smelting, uranium mining and milling, steel and copper milling, oil refining, shale oil production, and claypit mining.

30.2.3 Chemical Properties

Molybdenum, which can function both as a metal and metalloid, is an essential component in a large number of biochemical systems — including xanthine oxidase. At least four metalloenzymes are known to be molybdenum dependent, and all are molybdoflavoproteins (Schroeder et al. 1970). Molybdenum is characterized by the following physical and chemical properties: atomic number 42; atomic weight 95.94; density 10.2; melting point 2617°C; boiling point 4612°C; oxidation states 0, +2, +3, +4, +5, and +6; crystalline forms as gray-black powder, or silver-white metal; mass numbers (percent contribution of naturally occurring molybdenum) of 92 (15.86%), 94 (9.12%), 95 (15.7%), 96 (16.5%), 97 (9.45%), 98 (23.75%), and 100 (9.62.%); and radioactive isotopes of mass number 90, 91, 93, 99 (Tb 1/2 of 67 h, frequently used as a tracer), 101, 102, and 105 (Busev 1969; Schroeder et al. 1970; Shamberger 1979; Friberg and Lener 1986). In water at pH >7, molybdenum exists primarily as the molybdate ion, MoO_4^{2-} ; at pH <7, various polymeric compounds are formed, including the paramolybdate ion, $\text{Mo}_7\text{O}_{24}^{6-}$ (Busev 1969). In soils, molybdate was sorbed most readily to alkaline, high calcium, high chloride soils; retention was least in low pH, low sulfate soils (Smith et al. 1987). There is general agreement that molybdenum chemistry is complex and inadequately known. Additional and more extensive information on its properties was summarized in major reviews by Busev (1969), Boschke (1978), Brewer (1980), Coughlan (1980), Newton and Otsuka (1980), Parker (1983), and Mitchell and Sykes (1986).

30.2.4 Mode of Action

Interactions among some trace metals are so pervading and so biologically influential that the results of nutritional and toxicological studies conducted with a single element can be misleading unless the dietary and body tissue levels of interacting elements are clearly defined (Underwood 1979). For molybdenum, interactions are so dominant — especially in ruminant species — that a particular level of intake in the diet can lead to molybdenum deficiency or to molybdenum toxicity in the animal, depending on the relative intakes of copper and inorganic sulfate (Schroeder et al. 1970; Underwood 1971, 1979; Clawson et al. 1972; Suttle 1973, 1983a; Friberg et al. 1975; Buck 1978; Ward 1978; Chappell et al. 1979; Shamberger 1979; Van Ryssen and Stielau 1980; Gupta and Lipsett 1981; Ivan and Veira 1985; Friberg and Lener 1986; Goyer 1986; Kincaid et al. 1986; Osman and Sykes 1989).

The first indications of interaction between copper and molybdenum came more than 40 years ago from studies of grazing cattle in certain areas of England. Afflicted animals lost weight, developed severe diarrhea, and (in extreme cases) died. The disease is sometimes called teart (rhymes with heart) or molybdenosis, and is caused by eating herbage rich in molybdenum (i.e., 20 to 100 mg/kg dry weight diet compared to <5 mg/kg in nearby healthy pastures) and low or deficient in copper and inorganic sulfate (Underwood 1979). Molybdenosis is a copper deficiency

disease that occurs particularly in cattle and sheep and is usually caused by the depressing effect of molybdenum on the physiological availability of copper (Clawson et al. 1972; Dollahite et al. 1972; Alloway 1973; Erdman et al. 1978; Mills and Breamer 1980; Van Ryssen and Stielau 1980; Nederbragt 1982; Suttle 1983a; Goyer 1986; Osman and Sykes 1989). The disease was treated successfully with copper sulfate at 1 to 2 g daily in the diet, or 200 to 300 mg daily by intravenous injection (Buck 1978; Underwood 1979; Ivan and Veira 1985). When ruminant diets contained copper at 8 to 11 mg/kg weight — a normal range — cattle were poisoned at molybdenum levels of 5 to 6 mg/kg and sheep at 10 to 12 mg/kg. When dietary copper was low (i.e., <8 mg/kg) or sulfate ion level was high, molybdenum at 1 to 2 mg/kg ration was sometimes toxic to cattle. Increasing the copper in diets to 13 to 16 mg/kg protected cattle against concentrations up to 150 mg/kg of dietary molybdenum (Buck 1978). Studies of molybdenum metabolism are of limited value unless one knows the status in the diet of inorganic sulfate, which alleviates molybdenum toxicity in all known species by increasing urinary molybdenum excretion (Underwood 1971, 1979).

Copper prevents the accumulation of molybdenum in the liver and may antagonize the absorption of molybdenum from food. The antagonism of copper to molybdenum depends on sulfate, which may displace molybdate (Goyer 1986). In certain sheep pastures, for example, the herbage may contain up to 15 mg copper/kg dry weight and <0.2 mg Mo/kg dry weight — conditions favoring the development of a high copper status that may lead to copper poisoning. Treatment consists of providing molybdate salt licks, which are highly effective in reducing copper levels in grazing sheep (Buck 1978; Underwood 1979). A low copper:molybdenum ratio (i.e., <2), rather than the absolute dietary concentration of molybdenum, is the primary determinant of susceptibility to molybdenum poisoning; molybdenosis is not expected when this ratio is near 5 (Buck 1978; Ward 1978; Mills and Breamer 1980). Ratios of copper to molybdenum in sweet clover (*Melilotus* spp., a known molybdenum accumulator plant) growing in coal mine spoils in the Dakotas, Montana, and Wyoming ranged from 0.4 to 5, suggesting that molybdenosis can be expected to occur in cattle and sheep grazing in low Cu:Mo areas (Erdman et al. 1978). A similar situation existed in British Columbia, where 19% of all fodders and grains had a Cu:Mo ratio <2 (Underwood 1979).

There are several explanations for the high sensitivity of ruminants to increased dietary molybdenum and sulfur, the most plausible being the role of thiomolybdates (Penumarthy and Oehme 1978; Lamand et al. 1980; Nederbragt 1980, 1982; Suttle 1980, 1983b; Mills et al. 1981; Suttle and Field 1983; Weber et al. 1983; Hynes et al. 1985; Friberg and Lener 1986; Allen and Gawthorne 1987; Sas 1987; Strickland et al. 1987). Thiomolybdates are compounds formed by the progressive substitution for sulfur and oxygen in the molybdate (MoO_4^{2-}) anion when hydrogen sulfide and MoO_4^{2-} interact *in vitro* at neutral pH. Di-, tri-, and tetrathiomolybdates are formed, but only the last of these effectively impairs copper absorption. When sufficient tetrathiomolybdate (MoS_4) is formed in the rumen, it and copper in the gut combine and the resultant complex is bound strongly to proteins of high molecular weight. The molybdoproteins so formed are strong chelators of copper, and may be the agents responsible for copper deficiency through formation of biologically unavailable copper complexes in gut, blood, and tissues of animals that consume diets containing high concentrations of molybdenum. To confound matters, the complex molybdenum–copper–sulfur interrelationship can be modified, or disrupted entirely, by many compounds or mixtures. These include the salts of tungsten (Schroeder et al. 1970; Underwood 1971; Mills and Breamer 1980; Luo et al. 1983; Goyer 1986), zinc (Penumarthy and Oehme 1978; Parada 1981; Alary et al. 1983), lead and manganese (Underwood 1971), iron (Phillippo et al. 1987b), vanadium (Vaishampayan 1983), chromium (Vaishampayan 1983; Chung et al. 1985), phosphorus (Underwood 1971; Baldwin et al. 1981), cystine and methionine (Underwood 1971, 1979), fluoride (Goyer 1986), and proteins (Underwood 1971, 1979; Friberg and Lener 1986; Kincaid et al. 1986).

30.3 CONCENTRATIONS IN FIELD COLLECTIONS

30.3.1 General

Molybdenum levels tend to be elevated in nonbiological materials and in terrestrial flora in the vicinity of molybdenum mining and reclamation activities, fossil-fuel power plants, and disposal areas for molybdenum-contaminated sewage sludge, flyash, and irrigation waters. Concentrations of molybdenum in fish, wildlife, and invertebrates were low when compared to those in terrestrial plants, although certain aquatic invertebrates were capable of high bioconcentration. Concentrations of molybdenum alone, however, were not sufficient to diagnose molybdenum deficiency or toxicosis.

30.3.2 Nonbiological Samples

Elevated levels of molybdenum in nonbiological materials have been reported near certain mines, power plants, and oil shale deposits, as well as in various sewage sludges, fertilizers, and agricultural drainwaters ([Table 30.1](#)). Molybdenum is concentrated in coal and petroleum, and the burning of these fuels contributes heavily to atmospheric molybdenum (King et al. 1973). Combustion of fossil fuels contributes about 5000 metric tons of molybdenum annually to the atmosphere; atmospheric particulates contain about 0.001 µg Mo/m³ air (Goyer 1986).

Natural molybdenum concentrations in ground and surface waters rarely exceed 20 µg/L; significantly higher concentrations are probably due to industrial contamination. Existing wastewater and water treatment facilities remove less than 20% of the molybdenum; accordingly, drinking water concentrations are near those of the untreated source (Chappell et al. 1979). Molybdenum concentrations in saline waters appear to be directly related to salinity (Prange and Kremling 1985; Sloot et al. 1985). In the Wadden Sea, for example, molybdenum concentrations were 0.08, 0.4, and 1.0 µg/L at salinities of 0.07, 1.2, and 3.3%, respectively (Sloot et al. 1985).

The molybdenum content of soil may vary by more than an order of magnitude, causing both deficient and excessive concentrations for plants and ruminants in some parts of the world (Friberg et al. 1975). Native soils may contain enough molybdenum to cause molybdenosis in range livestock in some areas of the United States, particularly in Oregon, Nevada, and California (Kubota et al. 1967; Erdman et al. 1978). Elevated soil molybdenum levels can result from both natural and industrial sources. Usually when soil molybdenum levels exceed 5 mg/kg dry weight, a geological anomaly or industrial contamination is the likely explanation (Chappell et al. 1979). Molybdenum is more available biologically to herbage plants in alkaline soils than in neutral or acidic soils (Underwood 1971; Friberg et al. 1975; Shacklette et al. 1978; Wright and Hossner 1984). Liming of acidic soils or treatment with molybdenum-containing fertilizers can effectively raise the molybdenum content of herbage (Underwood 1971; Pierzynski and Jacobs 1986).

The disposal of sewage sludge, flyash from coal combustion, and molybdenum-contaminated irrigation waters to agricultural fields may result in the production of molybdenum-rich herbage. Sewage sludges rich in molybdenum and applied to agricultural soils resulted in elevated molybdenum content in corn and soybeans in a dose-dependent pattern (Pierzynski and Jacobs 1986). Similarly, flyash from coal combustion applied to pasture and croplands at rates sufficient to provide molybdenum at concentrations of 40 g/kg and higher resulted in potentially hazardous levels in vegetation to ruminant grazers. Molybdenum in flyash applied to soils remained biologically available for extended periods, especially in calcareous soils (Elseewi and Page 1984). Irrigation has also been proposed as a possible disposal method for large quantities of water having molybdenum concentrations of 5 to 100 mg/L that result from mining and reclamation activities. This method of disposal is not recommended unless all animals are kept off irrigated sites and the vegetation can be harvested and destroyed until molybdenum levels in the plants remain below 10 mg/kg dry weight (Smith et al. 1987).

Table 30.1 Molybdenum Concentrations in Selected Nonbiological Materials

Material, Unit, and Location	Concentration^a	Reference^b
SEAWATER (µg/L)		
Worldwide	<1–10	1–3
Worldwide	4–12	4
Pacific Ocean, all depths	10.3	5
DRINKING WATER (µg/L)		
U.S.S.R.		
Winter	0.03–0.06	1
Summer	0.11–0.15	1
U.S.	0.1–6.2	2
U.S.	Usually <5, Max. 500	1, 4
Switzerland	Usually <1, Max. 29	1
SURFACE WATER (µg/L)		
North American rivers	0.4	4
California lakes	0.4 (<3–100)	1
U.S. rivers	1.2–4.1	1
Mineral waters	2–3	2
Near Mo mine and mill, Colorado	(100–10,000)	4
Ash pond effluent from coal-fired power plant, New Mexico	170	4
Power station effluent, Victoria, Australia	330	6
Near Mo tailings pile, New Mexico	600	4
Evaporation ponds, California, 1985–86	1100 (630–2600)	7
Leachate from oil shale retort, Colorado	4100 (2500–8300)	4
Irrigation water from Mo mining and reclamation	5000–100,000	8
GROUNDWATER (µg/L)		
U.S.	Usually <1	4
U.S.S.R.	3	4
California, agricultural drainwater, 1985–86	1200–5500	7
Colorado		
Mining areas	Max. 25,000	1
Near uranium mill	50,000	4
SEDIMENTS (mg/kg, dry weight)		
U.S. rivers	5–57	1
Evaporation ponds, California	18 (<2–22)	7
Near Mo tailings pile, Colorado	21	4
Baltic Sea	80	3
Near Mo mine and mill, Colorado	530, Max. 1800	1, 4
SOILS (mg/kg, dry weight)		
Natural soils		
Worldwide	0.1–10, usually 0.2–0.7	1, 2
Worldwide	1–2 (0.6–3.5)	4
U.S.	1.2 (0.1–40)	4
Molybdenosis areas	2–>6	9
Elevated Mo	12–76 (2–190)	4
Economic Mo deposits	>200	4
Impacted soils		
In upper 5 cm at 0.3 or 3 km from Mo ore processing plant in 1982 and 1983		
0.3 km		
1982, Total	28	10
1982, Extractable	5	10
1983, Total	73	10

Table 30.1 (continued) Molybdenum Concentrations in Selected Nonbiological Materials

Material, Unit, and Location	Concentration ^a	Reference ^b
1983, Extractable 3 km	3	10
1982, Total	3	10
1982, Extractable	0.4	10
1983, Total	8	10
1983, Extractable	0.8	10
Near Mo mine and mill, Colorado, irrigated with Mo-contaminated effluent from uranium mill	61 (49–72)	4
Ireland, highly mineralized	170 (11–4000)	17
SEWAGE SLUDGE (mg/kg, dry weight)		
Iowa	<1–75	11
U.S.	2–30	2
Most states, U.S.	5–39	11
North America	<10 (2–100)	1, 12
Michigan	32 (6–3700)	11
AIR (mg/m³)		
Rural, U.S.	0.0001–0.003	1, 2
Urban, U.S.	0.01–0.03	1, 2
Worldwide	<0.0005	13
FERTILIZERS (mg/kg, dry weight)		
Domestic	3–6	1, 14
OIL, OIL SHALE, COAL, AND WASTE PRODUCTS (liquids, mg/L; solids, mg/kg dry weight)		
Coal conversion process waters	0.001–0.5	15
Oil shale retort water	0.06–0.3	15
Light oil	<0.1	1
Heavy oil	Max. 0.5	1
Spent oil shale	0.6	15
Coal	1–73	15
Coal	3 (0.3–15)	1, 16
Oil shale	5–87	15
Coal ash	7–160	16
Flyash from power stations	Usually 10–40, Max. 180	1

^a Concentrations are shown as means, range (in parentheses), and maximum (Max.).

^b 1, Friberg et al. 1975; 2, Friberg and Lener 1986; 3, Prange and Kremling 1985; 4, Chappell et al. 1979; 5, Collier 1985; 6, Ahsanullah 1982; 7, Fujii 1988; 8, Smith et al. 1987; 9, Kubota et al. 1967; 10, Schalscha et al. 1987; 11, Pierzynski and Jacobs 1986; 12, Lahann 1976; 13, Schroeder et al. 1970; 14, Goyer 1986; 15, Birge et al. 1980; 16, Elseewi and Page 1984; 17, Talbot and Ryan 1988.

30.3.3 Biological Samples

All plants contain molybdenum, and it is essential for the growth of all terrestrial flora (Schroeder et al. 1970). Molybdenum concentrations were elevated in terrestrial plants, especially in those collected from soils amended with flyash, liquid sludge, or molybdenum-contaminated irrigation waters, in naturally occurring teat pastures, and in the vicinity of molybdenum mining and ore processing activities, steelworks, and other metal processors. Molybdenum concentrations greater than 20 mg/kg dry weight were frequently documented in plants from contaminated areas (Table 30.2). Legumes, especially trefoil clovers (*Lotus* sp.) selectively accumulated molybdenum; concentrations of 5 to 30 mg/kg dry weight were common in molybdenum-contaminated areas (Friberg et al. 1975; Shacklette et al. 1978). The molybdenum levels were sometimes high and potentially toxic in legumes from

poorly drained acidic soils (Kubota et al. 1967; Underwood 1971). Some terrestrial grasses displayed copper:molybdenum ratios between 0.5 and 3.7. Since ratios greater than 2 were within the range where molybdenosis is likely, and since most of the molybdenum concentrations were greater than the maximum tolerable level of 6 mg/kg dry weight, hypocuprosis (molybdenosis) in cattle was expected (Schalscha et al. 1987). Major sources of molybdenum overload in fodder were in plants grown on high-molybdenum alkaline soils and from industrial contamination by coal and uranium mines and alloy mills (Sas 1987). Variations in molybdenum content of pasture species ranged from 0.1 to 200 mg/kg dry weight, and most variations were due to soil and species differences (Underwood 1971). Pasture plants collected from mountainous areas of southern Norway were usually deficient in copper, and low to partly deficient in molybdenum. As a result, the copper:molybdenum ratios were generally high and may explain the occurrence of chronic copper poisoning in grazing sheep in that region (Garmo et al. 1986).

Except in terrestrial plants, molybdenum concentrations were low in all groups examined; maximum concentrations reported from all sampling locales were about 6 mg/kg dry weight in aquatic plants, about 4 mg/kg fresh weight in aquatic invertebrates, 2 mg/kg fresh weight in fishes (except for rainbow trout liver and kidney — 26 to 43 mg/kg fresh weight — from fish collected near a molybdenum tailings outfall), 4 mg/kg dry weight in birds, 30 mg/kg dry weight in domestic ruminant liver, 85 mg/kg dry weight in the horse, and <4 mg/kg dry weight in mammalian wildlife and humans (Table 30.2).

No food chain biomagnification of molybdenum was found in 1987 in aquatic organisms from the San Joaquin River, California (Saiki et al. 1993). Maximum concentrations of molybdenum recorded in the San Joaquin River in 1987 were 10 µg/L in water, and — in mg/kg DW — 3.1 in detritus, 1.4 in algae, 0.54 in chironomid larvae, 0.64 in whole crustaceans, and 0.51 in bluegills (Saiki et al. 1993). Molybdenum did not biomagnify in the fish/crustacean/hump-backed dolphin (*Sousa chinensis*) food chain (Parsons 1998). Molybdenum concentrations from cetacean liver tissues were 4.1 times lower than those of whole prey organisms, i.e., 0.8 vs. 3.3 mg Mo/kg DW. Hump-backed dolphins from Hong Kong consume about 4.3 mg of molybdenum daily, equivalent to about 0.02 mg Mo/kg BW (Parsons 1998). Large interspecies differences were evident among aquatic organisms in their ability to accumulate molybdenum from the medium. Marine bivalve molluscs usually contained 30 to 90 times more molybdenum than the ambient seawater; however, some species from Greek waters had bioconcentration factors up to 1300 (Eisler 1981). Marine plankton accumulated molybdenum from seawater by factors up to 25 (Goyer 1986). But growth in aquatic phytoplankton populations was inhibited under conditions of low or missing molybdenum, nitrogen, and organic matter concentrations. The role of molybdenum in this process requires clarification (Paerl et al. 1987). In rainbow trout (*Oncorhynchus mykiss*), residues of molybdenum in tissues were affected only slightly by the concentrations in water; tissue residues ranged from 5 to 118 µg/kg fresh weight in water containing trace (<6 µg/L) concentrations; 10 to 146 µg/kg in water containing low (6 µg/L) concentrations; and from 13 to 322 µg/kg in water containing high (300 µg/L) concentrations (Ward 1973). A similar pattern was reported for kokanee salmon, *Oncorhynchus nerka* (Ward 1973). Rainbow trout held for 2 weeks in live traps 1.6 km downstream from a molybdenum mine tailings outfall survived, but liver and kidney had significantly elevated levels of molybdenum, calcium, manganese, iron, zinc, strontium, and zirconium, and 10% less potassium. The observed mineral changes may have been due to outfalls from nonmolybdenum mines discharged into the river system (Kienholz 1977).

In moles (*Talpa europaea*), adults had significantly higher concentrations of molybdenum in liver than did juveniles (Pankakoski et al. 1993). The significance of this observation is imperfectly understood. Molybdenum mining operations are not detrimental to mammalian wildlife, as judged by normal appearance and low molybdenum levels in liver and kidney of nine species — including deer, squirrel, chipmunk, badger, beaver, marmot, and pika — collected from areas with high environmental molybdenum levels (Kienholz 1977). It is emphasized that molybdenum concentrations in animal tissues give little indication of the dietary molybdenum status, and are of little diagnostic value for this purpose unless the sulfate, protein, and copper status of the diet are also known. This point is discussed in greater detail later.

Table 30.2 Molybdenum Concentrations in Field Collections of Selected Species of Animals and Plants (Values shown are in mg Mo/kg [ppm Mo] fresh weight [FW], dry weight [DW], or ash weight [AW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
TERRESTRIAL PLANTS		
Bermuda grass, <i>Cynodon dactylon</i>		
Soil amended with molybdenum-contaminated irrigation water		
Control	5 DW	1
6 mg Mo/kg soil	225 DW	1
13 mg Mo/kg soil	309 DW	1
26 mg Mo/kg soil	447 DW	1
Herbage (forage)		
Normal	1–3 DW	2
Teart pastures	20–100 DW	2
Barley, <i>Hordeum vulgare</i>		
Soil amended with flyash		
40 g/kg soil	6 DW	3
80 g/kg soil	11 DW	3
Moss, <i>Hypnum cupressiforme</i> , Sweden		
Normal	1 DW	4
Near waste disposal plant	8 DW	4
Near metal processor	400 DW	4
Near steelworks	560 DW	4
Legumes		
From molybdenosis areas	17–125 DW	5
From nonmolybdenosis areas	6–28 DW	5
Black medic, <i>Medicago lupulina</i> , Carson Valley, Nevada	Max. 372 DW	6
Alfalfa, <i>Medicago sativa</i>		
Soil amended with flyash		
40 g/kg soil	10 DW	3
80 g/kg soil	12 DW	3
Pasture plants, southern Norway	0.3 (0.01–4) DW	7
Peas, <i>Pisum sativum</i>		
Canada	0.2 FW	4
U.S.	0.3–5 FW	4
India	0.7–2 FW	4
Romania, Germany	1 FW	4
Russia	6 FW	4
Ballica grass, <i>Lolium perenne</i>		
Distance from Mo ore processing plant		
1982		
0.3 km	29–40 DW	8
1.0 km	8–10 DW	8
1983		
0.3 km	6–10 DW	8
1.0 km	7–10 DW	8
9.0 km	4–5 DW	8
In soil amended with liquid sludge to contain 410 mg Mo/ha	20 DW	9
White clover, <i>Trifolium repens</i>		
Soil amended with flyash		
40 g/kg soil	27 DW	3
80 g/kg soil	36 DW	3
Soil amended with liquid sludge		
17 mg Mo/ha	31 DW	9
410 mg Mo/ha	90 DW	9
Wheat, <i>Triticum aestivum</i>		
Germany, Romania, Russia	0.2–0.8 FW	4

Table 30.2 (continued) Molybdenum Concentrations in Field Collections of Selected Species of Animals and Plants (Values shown are in mg Mo/kg [ppm Mo] fresh weight [FW], dry weight [DW], or ash weight [AW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
India	0.5 FW	4
U.S.	0.6–6 FW	4
Vegetables		
Mo symptoms in humans	11–82 DW	4
Control site	3–5 DW	4
Vegetation		
Near Mo mine	Max. 5400 AW	6
Normal	<2–500 AW	6
AQUATIC PLANTS		
Algae, whole		
Marine	0.03–0.2 FW; 0.1–1.3 DW	4
Canada, 11 species	0.2–1.4 DW	10
Marine plants	0.5 FW	11
Marsh plants, whole		
Texas, 14 species	0.4–2.5 DW	10
Seaweeds, whole		
U.K., 5 species	0.2–1.3 DW; 0.04–0.2 FW	10
Norway, 11 species	0.3–6 DW	4
AQUATIC INVERTEBRATES		
Aquatic insects, 4 species		
Near low Mo waters (<1.0 µg Mo/L)	0.3–1.4 DW	12
Upstream	Max. 0.2 DW	12
Downstream	Max. 0.3 DW	12
Corals, marine, 34 species	<2 DW	13
Crustaceans, marine		
Tissues sold for human consumption, 16 species	0.1–0.4 FW	14
Molluscs, marine		
Soft parts		
15 species	<0.1–0.6 FW	14
3 species	0.7–4 FW	14
Common mussel, <i>Mytilus edulis</i> ; southeast Alaska; 1980–82; soft parts	<1.9 DW	27
Mussel, <i>Mytilus edulis aoteanus</i>		
Soft parts	0.6 DW	15
Gill	0.6 DW	15
Visceral mass	2 DW	15
Shell	11 DW	15
Other tissues	<0.1 DW	15
Scallop, <i>Pecten novae-zelandiae</i>		
Soft parts	0.9 DW	15
Mantle	2 DW	15
Gill	3 DW	15
Intestine	4 DW	15
Kidney	3 DW	15
Foot	0.4 DW	15
Plankton, Baltic Sea	2 DW	16
FISH		
Fishes, marine		
Liver		
43 species	0.1–0.3 FW	14
29 species	0.4–2.0 FW	14
2 species	0.4–1.0 DW	17

Table 30.2 (continued) Molybdenum Concentrations in Field Collections of Selected Species of Animals and Plants (Values shown are in mg Mo/kg [ppm Mo] fresh weight [FW], dry weight [DW], or ash weight [AW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Muscle		
130 species	0.1–0.3 FW	14
29 species	0.4–0.6 FW	14
Various	Max. 0.04 FW	11
Whole		
17 species	0.1–0.6 FW	14
8 species	0.012–0.15 FW	18
Rainbow trout, <i>Oncorhynchus mykiss</i>		
From waters with <6 µg Mo/L		
Liver	0.04–0.1 FW	19
Spleen	0.05–0.9 FW	19
Kidney	0.1 FW	19
Skin	0.07 FW	19
Bone	0.1–0.15 FW	19
Muscle	0.01 FW	19
Intestine	0.01–0.07 FW	19
Stomach	0.04 FW	19
Brain	0.02 FW	19
From waters with 300 µg Mo/L		
Liver	0.2 FW	19
Spleen	0.2 FW	19
Kidney	0.15 FW	19
Skin	0.1 FW	19
Bone	0.2 FW	19
Muscle	0.01 FW	19
Intestine	0.1 FW	19
Stomach	0.3 FW	19
Brain	0.09 FW	19
Held 2 weeks in live traps 1.6 km downstream from molybdenum tailings outfall		
Liver	43 DW	20
Kidney	26 DW	20
Control location		
Liver	1 DW	20
Kidney	<2 DW	20

BIRDS

Alaska, near Ketchikan; 1980–82

Barrows goldeneye, <i>Bucephala islandica</i>		
Kidney	5.2–7.8 DW	27
Liver	4.8–6.2 DW	27
Common merganser, <i>Mergus merganser</i>		
Kidney	2.4–8.0 DW	27
Liver	<1.9–5.7 DW	27
Chicken, <i>Gallus</i> sp.		
Liver	3.6 DW	21
Kidney	4.4 DW	21
Muscle	0.1 DW	21
Robin, <i>Turdus migratorius</i> , from molybdenum mine site		
Liver	1.6 DW	20
Kidney	1.9 DW	20

MAMMALS

Alaskan moose, *Alces alces gigas*

Hair	0.1–0.6 DW	22
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Table 30.2 (continued) Molybdenum Concentrations in Field Collections of Selected Species of Animals and Plants (Values shown are in mg Mo/kg [ppm Mo] fresh weight [FW], dry weight [DW], or ash weight [AW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Cattle, cows, <i>Bos</i> spp.		
Normal		
Blood	0.06 FW	2
Milk	0.07 (0.02–0.2) FW	2, 4
Liver	0.7–2 FW; 2.9–5.4 DW	2, 11, 23
Kidney	0.3 FW; 1.3–2.7 DW	2, 23
Muscle	0.1 FW; 0.5 DW	2, 23
Feces	1.1–2.1 DW	23
Elevated or poisoned		
Blood	0.6–0.8 FW	2
Kidney	21 FW	11
Rumen contents	21–28 DW	24
Horse, <i>Equus caballus</i>		
Liver	3–85 DW	21
Human, <i>Homo sapiens</i>		
Liver	0.5–1.0 FW; 3.2 DW	21, 25
Liver cortex	0.9 FW	21, 25
Kidney	0.2–0.3 FW; 1.6 DW	21, 25
Kidney cortex	0.2 FW	21, 25
Adrenal	0.7 FW	21, 25
Amnion	3.5 FW	21, 25
Chorion	0.6 FW	21, 25
Spleen	0.2 DW	21, 25
Lung	0.15 DW	21, 25
Brain	0.14 DW	21, 25
Muscle	0.14 DW	21, 25
Hair	0.06 (0.02–0.13) DW	21, 25
Blood	<0.005–0.1 FW	21, 25
Mule deer, <i>Odocoileus hemionus</i> ; liver		
Molybdenum mining area	1.0 FW	26
Control site	0.6 FW	26
Healthy	1.3 FW	26
Sheep, <i>Ovis aries</i>		
Wool	0.2 (0.03–0.6) DW	21
Liver		
Normal diet		
Adults	2–4 DW	21
Newborn lambs	2–4 DW	21
High molybdenum diet		
Adults	25–30 DW	21
Newborns	12–20 DW	21
Milk		
Grazing on low molybdenum (<1 mg Mo/kg) pasture	<0.01 FW	21
Grazing on high molybdenum (13 mg Mo/kg) pasture	>1 FW	21
Grazing on high molybdenum (25 mg Mo/kg) pasture, and given high sulfate (23 g/daily) for 3 days	0.1 FW	21
As above, without sulfate administration	1 FW	21
Rat, <i>Rattus</i> sp.		
Liver	2 DW	21
Kidney	1 DW	21
Spleen	0.5 DW	21
Lung	0.4 DW	21
Brain	0.2 DW	21
Muscle	0.06 DW	21

Table 30.2 (continued) Molybdenum Concentrations in Field Collections of Selected Species of Animals and Plants (Values shown are in mg Mo/kg [ppm Mo] fresh weight [FW], dry weight [DW], or ash weight [AW].)

Taxonomic Group, Organism, Tissue, and Other Variables	Concentration ^a (mg/kg)	Reference ^b
Hump-backed dolphin, <i>Sousa chinensis</i> ; Hong Kong		
Stomach contents		
Whole decapod crustaceans	<0.9 – 17.2 DW	29
Whole fishes	<0.9–16.4 DW	29
Diet, all sources	3.3 DW	29
Liver	0.8 DW; Max. 1.6 DW	29
Kidney	0.09 DW; Max. 0.8 DW	29
Blubber	0.3 DW; Max. 1.2 DW	29
Mole, <i>Talpa europaea</i> ; Finland; 1986–87; liver		
Adults	1.7 DW	28
Juveniles	1.5 DW	28
Wildlife, 9 species		
From areas of high environmental molybdenum levels		
Liver	0.1–4 DW	20
Kidney	0.3–3 DW	20

^a Concentrations are listed as means, minimum–maximum (in parentheses), and maximum (Max.).

^b 1, Smith et al. 1987; 2, Penumarthy and Oehme 1978; 3, Elseewi and Page 1984; 4, Friberg et al. 1975; 5, Kubota et al. 1967; 6, Shacklette et al. 1978; 7, Garmo et al. 1986; 8, Schalscha et al. 1987; 9, Pierzynski and Jacobs 1986; 10, Eisler 1981; 11, Schroeder et al. 1970; 12, Colborn 1982; 13, Livingston and Thompson 1971; 14, Hall et al. 1978; 15, Brooks and Rumsby 1965; 16, Prange and Kremling 1985; 17, Papadopoulou et al. 1981; 18, Rao 1984; 19, Ward 1973; 20, Kienholz 1977; 21, Underwood 1971; 22, Flynn et al. 1976; 23, Kume et al. 1984; 24, Sas 1987; 25, Friberg and Lener 1986; 26, King et al. 1984; 27, Franson et al. 1995; 28, Pankakoski et al. 1993; 29, Parsons 1998.

30.4 EFFECTS

30.4.1 General

Trace quantities of molybdenum are beneficial and perhaps essential for normal growth and development of plants and animals. In mammals, molybdenum can protect against poisoning by copper, mercury, and probably other metals, and may have anticarcinogenic properties. For all organisms, the interpretation of molybdenum residues depends on knowledge of molybdenum, copper, and inorganic sulfate concentrations in diet and in tissues. Some molybdenum compounds have insecticidal properties at low concentrations and have been proposed as selective termite control agents.

Aquatic flora and fauna seem to be comparatively resistant to molybdenum salts. Adverse effects on growth and survival were usually noted only at water concentrations of 50 mg Mo/L and higher. However, one study with newly fertilized eggs of rainbow trout produced an LC50 (28 day) value of 0.79 mg Mo/L compared to an LC50 (96 h) value of 500 mg/L for adults. Also, bioconcentration of molybdenum by selected species of algae and invertebrates (up to 20 g/kg dry weight) poses questions on risk to higher trophic level organisms.

In birds, adverse effects of molybdenum have been reported on growth at dietary concentrations of 200 to 300 mg/kg, on reproduction at 500 mg/kg, and on survival at 6000 mg/kg. In mammals, cattle are especially sensitive to molybdenum poisoning, followed by sheep, under conditions of copper and inorganic sulfate deficiency. Cattle were adversely affected when grazing pastures with a copper:molybdenum ratio <3, when fed low copper diets containing 2 to 20 mg Mo/kg diet, or when total daily intake approaches 141 mg molybdenum. Cattle usually die at doses of 10 mg Mo/kg body weight. Other mammals, including horses, pigs, rodents, and ruminant and nonruminant

nant wildlife, are comparatively tolerant to molybdenum. Deer, for example, are at least 10 times more resistant than domestic ruminants to molybdenum. No adverse effects in deer were noted at dietary levels of 1000 mg/kg after 8 days, slight effects at 2500 mg/kg after 25 days, and reduction in food intake and diarrhea at 5000 mg/kg diet after 15 days.

30.4.2 Terrestrial Plants

In a major literature review, Gupta and Lipsett (1981) concluded that molybdenum was essential for plant growth due to its role in the fixation of nitrogen by bacteria using the enzymes nitrogenase and nitrate reductase, and that plants readily accumulated MoO_4^{2-} except under conditions of low pH, high sulfate, and low phosphate, and in some highly organic soils. Molybdenum deficiency has been recorded in a variety of crops worldwide, but there is an extremely narrow range between adequacy and deficiency. In lettuce (*Lactuca sativa*), for example, adverse effects were noted at 0.06 mg/kg (dry weight) in plants, but sufficiency was attained at 0.08 to 0.14 mg/kg. A similar case is made for *Brassica* spp. (i.e., Brussels sprouts, cabbage, and cauliflower) (Gupta and Lipsett 1981). In certain species, such as beets (*Beta vulgaris*) and corn (*Zea mays*), the ratio between deficiency and sufficiency may differ by more than 10 times (Gupta and Lipsett 1981).

Okra (*Abelmoschus esculentus*), grown in soils supplemented with molybdenum at 1, 2, or 3 mg/kg, as sodium molybdate, showed increasing growth and yields when compared to nonsupplemented soils. Fruiting occurred earlier and persisted longer with increasing molybdenum concentration (Singh and Mourya 1983). The cashew (*Anacardium occidentale*) — one of the most valuable plantation crops in India — developed yellow-leaf spots accompanied by low molybdenum levels and excess manganese in low pH soils; in extreme cases the tree was defoliated (Subbaiah et al. 1986). The disorder was corrected by foliar spraying of molybdenum salts or by liming the soil. A similar case was reported for Florida citrus in the 1950s, which was shown to be due to molybdenum deficiency (Subbaiah et al. 1986).

Soils amended with sewage sludge containing 12 to 39 mg Mo/kg dry weight (soil contained 2 mg Mo/kg dry weight at start and 4.8 to 6 mg/kg after treatment) were planted with corn and bromegrass (*Bromus inermis*). A lime-treated sludge increased molybdenum concentrations in plant tissues after several years of sludge application; maximum values recorded were 1.9 mg Mo/kg dry weight in bromegrass and 3.7 in corn (Soon and Bates 1985). No toxicity of molybdenum has yet been observed in field-grown crops, although forages containing 10 to 20 mg/kg dry weight are considered toxic to cattle and sheep (Soon and Bates 1985).

30.4.3 Terrestrial Invertebrates

Sodium molybdate and other molybdenum compounds in toxic baits have potential for termite control (Brill et al. 1987). Baits containing 1000 mg Mo/kg were fatal to 99% of the termite *Reticulitermes flavipes* in 48 days. After 8 to 10 days, termites became steel-gray in color, but appeared otherwise normal. Mortality began only after day 16. Termites did not avoid the poisoned bait, even at concentrations of 5000 mg Mo/kg. Yoshimura et al. (1987) reported similar results with another species of termite; sodium molybdate killed 100% of the workers in a colony of *Copotermes formosanus* within 24 h after eating filter paper treated with a 5% solution. Some other species of insects — including fire ants (*Solenopsis* sp.) and various species of beetles and cockroaches — were not affected when exposed to baits containing 5000 mg Mo/kg for 48 days (Brill et al. 1987).

30.4.4 Aquatic Organisms

Aquatic plants are comparatively resistant to molybdenum. In sensitive species, adverse effects were evident on growth at 50 mg/L and on development at 108 mg/L (Table 30.3). Bioconcentration of molybdenum from the medium by certain freshwater algae can result in residues up to 20 g/kg

dry weight without apparent damage ([Table 30.3](#)). The implications of this phenomenon for waterfowl and other species that consume molybdenum-laden algae need to be explored.

Molybdenum is considered essential for aquatic plant growth, but the concentrations required are not known with certainty and are considered lower than those for any other essential element (Schroeder et al. 1970; Henry and Tundisi 1982). Molybdenum starvation restricts nitrogen fixation in algae, thereby limiting photosynthetic production during depleted conditions. Blue-green alga (*Anabaena oscillaroides*) cultured in molybdenum-deficient media containing 0.004 to 0.005 µg Mo/L rapidly depleted molybdenum in the medium; this ability was lost at higher concentrations of added molybdenum, when *Anabaena* began to accumulate the element (Steeg et al. 1986). The addition of tungstate to molybdenum-deficient media enhances dinitrogenase inactivation, resulting in inhibited algal growth. This process is reversed at molybdenum levels of 0.005 to 0.04 µg/L (Steeg et al. 1986). On the other hand, algal growth was significantly enhanced when vanadium (V) was present at 12.5 µg/L, although higher concentrations of V were growth inhibitory in 7 days (Vaishampayan 1983). Algal uptake of molybdenum is rapid during the first 2 h, and slower thereafter. The sequential biological reduction of hexavalent to pentavalent to trivalent molybdenum occurs intracellularly in green algae (Sakaguchi et al. 1981). Uptake is greater in freshwater than in seawater, greater at increased doses, and greater at reduced algal densities (Sakaguchi et al. 1981); it is also greater at elevated temperatures (Penot and Videau 1975).

Molybdenum occurs naturally in seawater as molybdate ion, MoO_4^{2-} , at about 10 µg/L (Abbott 1977). Despite the high concentrations of dissolved molybdenum in offshore seawater, phytoplankton from offshore locales contain extremely low molybdenum residues, almost typical of molybdenum-deficient terrestrial plants (Howarth and Cole 1985). This phenomenon is attributed to the high concentrations of sulfate in seawater; sulfate inhibits molybdate assimilation by phytoplankton, making it less available in seawater than in freshwater. As one result, nitrogen fixation and nitrate assimilation — processes that require molybdenum — may require greater energy expenditure in marine than in freshwaters and may explain, in part, why marine ecosystems are usually nitrogen-limited and lakes are not (Howarth and Cole 1985). Experimentally increasing the ratio of sulfate to molybdate inhibits molybdate uptake by marine algae, slows nitrogen fixation rates, and slows the growth of organisms that use nitrate as a nitrogen source (Howarth and Cole 1985).

Limited data suggested that aquatic invertebrates were very resistant to molybdenum. Adverse effects were observed on survival at >60 mg Mo/L and on growth at >1000 mg Mo/L ([Table 30.3](#)). Bioconcentration factors were low, but depending on initial dose, measured residues (mg/kg fresh weight) were as high as 16 in amphipods, and were 3 in clams, 18 in crayfish muscle, and 32 in crayfish carapace (Short et al. 1971). The host organisms seemed unaffected under these molybdenum burdens, but effects on upper trophic level consumers were not clear. Tailings from a pilot molybdenum mine on the North American Pacific coast were acutely lethal at concentrations of >61,000 mg tailings solids/L seawater to larvae of the mussel *Mytilus edulis*, and to adults of the amphipod *Rhepoxynius abronius* and the euphausiid *Euphausia pacifica*. Acute sublethal effects were observed at >277,000 mg/L (Mitchell et al. 1986). All species of invertebrates tested in this preliminary study were more sensitive than juvenile coho salmon, *Oncorhynchus kisutch* (Mitchell et al. 1986). In another study, zooplankton exposed to molybdenum mine tailings <8 µm in diameter at high sublethal concentrations ingested and excreted these particles (Anderson and Mackas 1986). The lowest tailing concentration tested at which a deleterious effect was observed was 100 mg/L for depression of respiration in the copepod *Calanus marshallae*, and 560 mg/L for increased mortality in copepods and the euphausiid *Euphausia pacifica*; concentrations of molybdenum mine tailings were always <15 mg/L at 0.5 km downstream from a molybdenum tailings outfall (Anderson and Mackas 1986).

Freshwater and marine fishes were — with one exception — extremely resistant to molybdenum. LC50 (96 h) values ranged between 70 mg/L and <3000 mg/L ([Table 30.3](#)). The exception was newly fertilized eggs of rainbow trout exposed for 28 days through day 4 posthatch; the LC50 (28 day) value was only 0.79 mg/L (Birge et al. 1980), suggesting that additional research is needed

on the sensitivity of early life stages to molybdenum. In general, molybdenum was more toxic to teleosts in freshwater than in seawater, and more toxic to younger fish than to older fish. In rainbow trout, it bioconcentrated up to 16 mg/kg fresh weight in liver, 18 in spleen, 7 in muscle, 6 in gill, and 2 in gastrointestinal tract (Table 30.3) (Short et al. 1971). Environmental levels of molybdenum as molybdate measured in the Mo mining areas of Colorado were not considered harmful to rainbow trout (McConnell 1977). Molybdenum enrichment of Castle Lake, California (a high mountain lake in which molybdenum was determined to be the limiting micronutrient), coupled with favorable environmental conditions, led to record high yields of trout. The addition of 16 kg sodium molybdate, or 6.4 kg molybdenum, to Castle Lake in July 1963 was followed by larger standing crops of zooplankton and bottom fauna, which probably promoted survival of the 1965 year class and resulted in record yields to the angler of rainbow trout and brook trout (*Salvelinus fontinalis*) in 1967 (Cordone and Nicola 1970). Enrichment of molybdenum-deficient waters to improve angler success merits additional research.

Table 30.3 Molybdenum Effects on Selected Species of Aquatic Organisms

Organism, Mo Concentration, and Other Variables	Effect	Reference ^a
AQUATIC PLANTS		
Blue-green alga, <i>Anabaena oscillarioides</i>		
0.005 µg/L	Bioconcentration factor (BCF) of 3300 in 60 min	1
0.073 µg/L	BCF of 550 in 60 min	1
25 µg/L	BCF of 7–24 in 60 min	1
Green alga, <i>Chlorella vulgaris</i>		
10 mg/L	Residues of about 20,000 mg/kg dry weight in 20 h. Dead (heat-killed) <i>Chlorella</i> contained 4902 mg/kg dry weight in 1 h vs. 3264 mg/kg in live cells	2
20 mg/L	Normal growth in 96 h	2
50 mg/L	Reduced growth in 96 h	2
Euglena, <i>Euglena gracilis</i>		
5.4 mg/L	Normal growth and reproduction	3
96 mg/L	No abnormal cells in 48 h	3
108 mg/L	Abnormal development, cells forming clusters. Culture is photosensitive with blue color	3
>960 mg/L	No growth	3
Freshwater alga, <i>Nitella flexilis</i>		
0.014 µg/L	BCF of 628 in 25 days	4
3.3 mg/L	BCF of 39 in 24 days; elevated residues of 130 mg/kg fresh weight	4
Blue-green alga, <i>Nostoc muscorum</i>		
17.7 µg/L	Required for growth	5
INVERTEBRATES		
Amphipod, <i>Allorchestes compressa</i>		
60 mg/L	No deaths (= LC0) in 96 h	6
247 mg/L	50% dead (= LC50) in 96 h	6
450 mg/L	97% dead (= LC97) in 96 h	6
Starfish, <i>Asterias rubens</i>		
127 mg/L	LC50 (24 h) at pH 5.8	7
254 mg/L	LC50 (24 h) at pH 8.2	7
Copepod, <i>Calanus marshallae</i>		
20 mg/L	Minor increase in oxygen consumption in 24 h	8
100 mg/L	Decreased oxygen consumption in 24 h	8
560 mg/L	LC50 (19 days)	8
Green crab, <i>Carcinus maenas</i>		
1018 mg/L	LC50 (48 h)	7

Table 30.3 (continued) Molybdenum Effects on Selected Species of Aquatic Organisms

Organism, Mo Concentration, and Other Variables	Effect	Reference ^a
American oyster, <i>Crassostrea virginica</i> 1375 mg/L	Reduction of 50% in shell growth in 96 h	9
Hermit crab, <i>Eupagurus bernhardus</i> 100 mg/L	LC0 (50 days)	7
222 mg/L	LC50 (48 h)	7
Euphausiid, <i>Euphausia pacifica</i> 560 mg/L	LC50 (112 h)	8
Amphipod, <i>Gammarus</i> sp. 3.3 mg/L	BCF of 4.8 in whole animal in 24 days	4
Lake periphyton 0.014 µg/L	BCF of 3570 in 24 days	4
Clam, <i>Margaretifera margaretifera</i> 3.3 mg/L	Maximum BCF values in 15–24 days were 1.8 in shell, 0.9 in soft parts, and 0.3 in muscle	4
Mysid shrimp, <i>Mysidopsis bahia</i> 1205 mg/L	LC50 (96 h)	9
Mussel, <i>Mytilus edulis</i> , larvae 147 mg/L	Development reduced 50% in 48 h, based on survival and abnormalities	10
Crayfish, <i>Pacifastacus leniusculus</i> 3.3 mg/L	BCF in 24 days of 5.7 for muscle and 9.8 for carapace	4
Pink shrimp, <i>Penaeus duorarum</i> 1909 mg/L	LC50 (96 h)	9
Pullet-shell (clam), <i>Venerupis pallustra</i> 381 mg/L	LC50 (24 h)	7
FISH		
Flannelmouth sucker, <i>Catostomus latipinnis</i> ; larvae; age 12–13 days; molybdenum as sodium molybdate >2800 mg Mo/L	LC50 (48 h)	15
1940 (95% CI = 1680–2370) mg Mo/L	LC50 (96 h)	15
Sheepshead minnow, <i>Cyprinodon variegatus</i> 3057 mg/L	LC50 (96 h)	9
Bluegill, <i>Lepomis macrochirus</i> 1320 mg/L	LC50 (96 h)	11
Rainbow trout, <i>Oncorhynchus mykiss</i> Embryos and larvae exposed for 28 days starting at fertilization through 4 days posthatch 28 µg/L	LC1 (28 days)	12
125 µg/L	LC10 (28 days)	12
790 (610–990) µg/L	LC50 (28 days)	12
17.0–18.5 mg/L, exposed continuously for 1 year from eyed eggs to juvenile stage	No significant effect on survival, growth, or blood hematocrit	10, 11
500 mg/L	LC25 (96 h), mean length 20 mm	11
800 mg/L	LC50 (96 h), mean length 20 mm	11
1320 mg/L	LC50 (96 h), mean length 55 mm	11
Steelhead trout, <i>Oncorhynchus mykiss</i> 0.014 µg/L	Max. BCF of 1143 in liver and gastrointestinal tract after chronic exposure	4
3.3 mg/L	Max. BCF in 24 days of 5.4 in spleen, 4.5 in liver, 2.3 in muscle, 1.8 in gill, and 0.6 in gastrointestinal tract	4
Coho salmon, <i>Oncorhynchus kisutch</i> >1000 mg/L	LC50 (96 h); fry	13

Table 30.3 (continued) Molybdenum Effects on Selected Species of Aquatic Organisms

Organism, Mo Concentration, and Other Variables	Effect	Reference ^a
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
Juveniles exposed to 193 µg Mo/L, as sodium molybdate, for 90 days	No accumulation; whole-body content of <0.7 mg Mo/kg DW	14
More than 1000 mg/L	LC50 (96 h); fry	13
Fathead minnow, <i>Pimephales promelas</i>		
70 mg/L	LC50 (96 h), soft water	11
360 mg/L	LC50 (96 h), hard water	11

^a 1, Steeg et al. 1986; 2, Sakaguchi et al. 1981; 3, Colmano 1973; 4, Short et al. 1971; 5, Vaishampayan 1983; 6, Ahsanullah 1982; 7, Abbott 1977; 8, Anderson and Mackas 1986; 9, Knothe and Van Riper 1988; 10, Morgan et al. 1986; 11, McConnell 1977; 12, Birge et al. 1980; 13, Hamilton and Buhl 1990; 14, Hamilton and Wiedmeyer 1990; 15, Hamilton and Buhl 1997.

30.4.5 Birds

Data are missing on the effects of molybdenum on avian wildlife under controlled conditions. All studies conducted with birds have been restricted to domestic poultry. Signs of molybdenum deficiency in domestic chickens included loss of feathers, lowered tissue molybdenum concentrations, reduced xanthine dehydrogenase activity in various organs, decreased uric acid excretion, disorders in ossification of long bones, and changes in joint cartilage that led to complete immobility. Signs were eliminated when diets were supplemented with molybdenum at concentrations of 0.2 to 2.5 mg/kg (Reid et al. 1956; Friberg and Lener 1986). Efforts to produce a molybdenum deficiency syndrome in birds and mammals by feeding diets low in molybdenum have been unsuccessful (Friberg et al. 1975). Thus, it has been necessary to introduce a compound with a known property of inhibiting molybdenum, namely wolframate (Na_2WO_4), a tungsten compound. Wolframate increases molybdenum excretion, leading to molybdenum deficiency in rats and chickens. With this technique it has been possible to produce an assumed molybdenum deficiency in chicks consisting of reduced weight gain and sometimes death (Friberg et al. 1975). Dietary requirements to maintain normal growth in rats and chicks were probably less than 1 mg Mo/kg food, and thus substantially less than that of any other trace element recognized as essential (Mills and Breamer 1980). In fact, birds may require molybdenum at concentrations up to 6 mg/kg in their diets for optimal growth (Kienholz 1977). Dietary molybdenum counteracts adverse effects in chicks on growth and survival induced by hexavalent chromium. Chicks fed 900 mg chromium/kg ration for 4 weeks showed significantly depressed growth, 25% mortality, and elevated liver chromium. However, diet supplementation to 150 mg Mo/kg resulted in normal growth and liver chromium values, and no deaths (Chung et al. 1985).

Early studies with chicks and turkey poult showed that the addition of only 13 to 25 µg Mo/kg — as molybdate or molybdic acid — to basal diets containing 1.0 to 1.5 mg Mo/kg resulted in a growth advantage of 14 to 19% in 4 weeks over that in unsupplemented groups (Reid et al. 1956, 1957). Roosters given daily dietary supplements of 100 or 400 µg molybdenum per bird for 4 weeks to basal diets containing 0.51 mg Mo/kg had reduced serum uric acid values when compared to those of controls. The significance of this finding is not clear (Karring et al. 1981). Birds are relatively resistant to molybdenum. For example, day-old chicks fed diets containing 20% molybdenum mine tailings for 23 days were unaffected, and those fed diets containing 40% molybdenum mine tailings showed only a slight reduction in body weight during the same period (Kienholz 1977). Dietary levels of 200 mg Mo/kg ration results in minor growth inhibition of chicks; and at 300 mg/kg feed, the growth of turkey poult was reduced (Underwood 1971). Dietary supplements of 500 mg Mo/kg ration produced a slight decrease in growth rate of chicks after 4 weeks; hens, however, laid 15% fewer eggs than controls, and all eggs contained embryolethal concentrations of 16 to 20 mg Mo/kg (Friberg et al. 1975). At dietary supplements of 1000 mg

Mo/kg, egg production was reduced 50% in domestic chickens (Friberg et al. 1975). Dietary loadings of 2000 mg/kg induced severe growth depression and a 100-fold increase in molybdenum content in tibia (Underwood 1971) and an 80% reduction in egg production (Friberg et al. 1975). At 4000 mg/kg diet, severe anemia was reported in chickens (Underwood 1971). Mortality of chicks fed 6000 mg Mo/kg diet for 4 weeks was 33%; at 8000 mg Mo/kg diet for 4 weeks, 61% of the chicks died and survivors weighed only 16% as much as the controls (Friberg et al. 1975). Chicks, unlike mammals, did not experience molybdenum reduction in tissues after sulfate administration — although sulfate markedly reduced the signs of Mo toxicity (Underwood 1971).

30.4.6 Mammals

Almost all studies conducted to date on molybdenum effects under controlled conditions have been on livestock, especially cattle and sheep. Molybdenum is beneficial and perhaps essential to adequate mammalian nutrition. Moreover, it can protect against poisoning by copper or mercury, and may be useful in controlling cancer. Evidence of functional roles for molybdenum in the enzymes xanthine oxidase, aldehyde oxidase, and sulfite oxidase suggests that molybdenum is an essential trace nutrient for animals (Underwood 1971; Earl and Vish 1979; Mills and Breamer 1980). Signs of molybdenum deficiency include decreased intestinal and liver xanthine oxidase activity (Mills and Breamer 1980). Molybdenum prevents damage to the liver in sheep receiving excess copper; accumulations of copper and molybdenum in kidney were present in a biologically unavailable form and of negligible physiological significance (Van Ryssen et al. 1982). Dietary supplements of 70 mg molybdenum per day for a restricted period is recommended for reduction of liver Cu in sheep, provided dietary Cu levels are simultaneously reduced (Van Ryssen et al. 1986). Molybdenum, as sodium molybdate, protects against acute inorganic mercury toxicity in rats by altering the metabolism of cysteine-containing proteins in the cytoplasm of liver and kidney, resulting in lowered mercury content in these organs (Yamane and Koizumi 1982; Koizumi and Yamane 1984). Anticarcinogenic properties of molybdenum in rats have been reported, although the mechanisms of action are unknown. In one study, 2 or 20 mg Mo/L in drinking water significantly inhibited cancer of the esophagus and forestomach experimentally induced by *N*-nitrososarcosine ethyl ester (Luo et al. 1983). In another study with virgin female rats, 10 mg Mo/L in drinking water reduced by half the number of mammary carcinomas experimentally induced by *N*-nitroso-*N*-methylurea (Wei et al. 1985). Additional research seems warranted on the role of molybdenum in cancer inhibition.

Molybdenosis has been produced experimentally in many species of mammals, including cattle, sheep, rabbits, and guinea pigs (Friberg et al. 1975). Signs of molybdenum poisoning vary greatly among species, but generally include the following: copper deficiency, especially in serum; reduced food intake and growth rate; liver and kidney pathology; diarrhea and dark-colored feces; anemia; dull, wiry, and depigmented hair; reproductive impairment, including delayed puberty, female infertility, testicular degeneration, and abnormal or delayed estrus cycle; decreased milk production; joint and connective tissue lesions; bone abnormalities; and loosening and loss of teeth (Underwood 1971; Dollahite et al. 1972; Friberg et al. 1975; Erdman et al. 1978; Penumopathy and Oehme 1978; Ward 1978; Chappell et al. 1979; Mills and Breamer 1980; Alary et al. 1981; Baldwin et al. 1981; Friberg and Lener 1986; Van Ryssen et al. 1986; Phillippe et al. 1987a). These authorities also agree on three additional points:

- Early signs of molybdenosis are often irreversible, especially in young animals
- The severity of the signs depends on the level of molybdenum intake relative to that of copper and inorganic sulfate
- If afflicted animals are not removed promptly from molybdenum-contaminated diets and given copper sulfate therapy, death may result.

Molybdenum poisoning in ruminants, or teart disease, has been known since the mid-1800s and affects only ruminants of special pastures. Degree of teartness varies from field to field and season to season, and is usually proportional to the molybdenum content in herbage. Molybdenum levels in typical teart pastures range from 10 to 100 mg/kg dry weight compared to normal levels of 3 to 5 mg/kg (Friberg and Lener 1986). If herbage contains more than 12 mg Mo/kg dry weight, problems should be expected in cattle, and to a lesser extent in sheep (Friberg et al. 1975). In situations where cattle are accidentally exposed to high molybdenum levels, the administration of copper sulfate should result in molybdenum excretion, up to 50% in 10 days (Penumarthy and Oehme 1978). Aside from cattle and sheep, all evidence indicates that other mammals are comparatively tolerant of high dietary intakes of molybdenum, including horses, pigs, small laboratory animals, and mammalian wildlife (Underwood 1971; Buck 1978; Chappell et al. 1979; Friberg and Lener 1986; Osman and Sykes 1989; [Table 30.4](#)). Cattle excrete molybdenum primarily through feces, but other (more tolerant) species such as pigs, rats, and humans, rapidly excrete molybdenum through urine, and this may account, in part, for the comparative sensitivity of cattle to molybdenum (Underwood 1971). Cattle normally excrete about 67% of all administered MoO_3 in feces and urine in 7 days; guinea pigs excreted 100% in urine in 8 days; and swine excreted 75% in urine in 5 days (Penumarthy and Oehme 1978). Cattle are adversely affected when:

- They graze copper-deficient pastures containing 2 to 20 mg/kg molybdenum, and the copper to molybdenum ratio is less than 3
- They are fed low copper diets containing 5 mg (or more) Mo/kg dry weight
- The total daily intake approaches 141 mg molybdenum
- The body weight residues exceed (a fatal) 10 mg Mo/kg ([Table 30.4](#)).

It is clear that both the form of molybdenum administered and the route of exposure affect molybdenum metabolism and survival ([Table 30.4](#)). By comparison, adverse effects (some deaths) were noted at 250 mg Mo/kg body weight (BW) (in guinea pigs), at 50 mg/kg BW in domestic cats (central nervous system impairment), at 10 mg/L drinking water in mice (survival), at 10 to 15 mg total daily intake in humans (high incidence of gout-like disease), and at 3 mg/m³ air in humans for 5 years (respiratory difficulties), or 6 to 19 mg/m³ in humans for 4 years ([Table 30.4](#)).

In newborn lambs from ewes that consumed high-molybdenum diets during pregnancy, demyelination of the central nervous system was severe, accompanied by low copper contents in the liver (Earl and Vish 1979). Sheep are more tolerant than cattle to molybdenum poisoning due, in part, to a lower turnover of ceruloplasmin, a copper-transporting enzyme that is inhibited by molybdenum. However, this characteristic makes sheep more sensitive than cattle to copper poisoning (Ward 1978). For example, chronic copper poisoning in sheep in several districts in Norway is probably due to molybdenum-deficient forages rather than to excess copper intake (Froslie et al. 1983). Swayback is a spastic paralysis in lambs born of ewes that were copper deficient during pregnancy (Todd 1976). In northern Ireland, where cases have been reported, pastures were not copper deficient, and swayback was due to an imbalance of copper, molybdenum, and sulfur. Very severely affected lambs were paralyzed in all limbs and died shortly after birth because they were unable to stand and suckle. Lambs less severely affected developed signs in about 2 weeks, but usually only the hind limbs were affected. Brain and spinal cord lesions were present, resulting in demyelination of spinal cord and cavitation of brain tissues; lesions were irreversible, but death might have been avoided with adequate copper therapy (Todd 1976).

Horses are generally considered to be tolerant of dietary copper deficiencies and of copper and molybdenum excesses that affected ruminants. Yet molybdenum accumulated in equine liver and has been implicated as a possible contributory factor in bone disorders in foals and yearlings grazing pastures containing 5 to 25 mg Mo/kg (Cymbaluk et al. 1981; Strickland et al. 1987). Cattle and horses are highly susceptible to pyrrolizidine alkaloids, an ingredient in certain poisonous plants such as tansy ragwort (*Senecio jacobaea*). Signs of poisoning included elevated copper levels in

liver followed by fatal hemolytic crisis. Sheep are more resistant to alkaloids than equines or bovines, and sheep grazing has been recommended as a means of controlling tansy ragwort. However, dietary supplements of 10 mg Mo/kg increased the susceptibility of sheep to tansy ragwort intoxication, despite the observed increase in copper excretion (White et al. 1984).

In rodents, molybdenum is neither teratogenic nor embryocidal to golden hamsters at doses up to 100 mg/kg body weight, and has no measurable effect on fertility or gestation of female rats given similar high doses (Earl and Vlish 1979). Voluntary rejection of high-molybdenum diets by rats results in anorexia. This phenomenon implies sensory, probably olfactory, recognition of molybdate in combination with other dietary constituents to form compounds with a characteristic odor detectable by rats (Underwood 1971). The ability to reject high-molybdenum diets requires a learning or conditioning period because it is lacking or weak with freshly prepared diets and extends to a discrimination between a toxic (high molybdenum) and nontoxic (high molybdenum plus sulfate) diet. Rats may associate a gastrointestinal disturbance with a sensory attribute of diets containing toxic levels of molybdenum (Underwood 1971).

Data on molybdenum effects on mammalian wildlife are scarce, although those available strongly suggest that domestic livestock are at far greater risk (Osman and Sykes 1989) ([Table 30.4](#)). Studies with mule deer (*Odocoileus hemionus*) showed that this species was at least an order of magnitude more tolerant to high levels of dietary molybdenum than were domestic ruminants, and at least as resistant as swine, horses, and rabbits (Nagy et al. 1975; Ward and Nagy 1976; Ward 1978; Chappell et al. 1979). Female mule deer showed no visible effects after 33 days on diets containing up to 200 mg Mo/kg feed, or after 8 days at 1000 mg/kg. Only slight effects — some reduction in food intake and some animals with diarrhea — were observed at diets of 2500 mg/kg for 25 days. At feeding levels of 5000 and 7000 mg/kg for periods of 3 to 15 days, signs were more pronounced; however, recovery began almost immediately after transfer to uncontaminated feed. Signs of copper deficiency and of molybdenosis are very similar, and careful diagnosis is necessary to ensure use of the correct remedial action. For example, some populations of Alaskan moose (*Alces alces gigas*) showed faulty hoof keratinization and decreased reproductive rates, but this was attributed to copper-deficient browse growing on low copper soils, and not to increased molybdenum levels in herbage (Flynn et al. 1977). In another case, a high proportion of white-tailed deer (*Odocoileus virginianus*) feeding near uranium-mine spoil deposits in several Texas counties — areas in which extreme molybdenosis has been documented in grazing cattle — had antlers that were stunted, twisted, and broadened or knobby at the tips (King et al. 1984). However, the copper levels in liver of these deer were similar to those of deer in a control area — 16.7 mg/kg fresh weight vs. 18.0 — and only 1 of 19 deer examined from the mining district had a detectable molybdenum concentration in liver (0.7 mg/kg fresh weight) vs. none in any control sample. On the basis of low contents of copper in soils and vegetation, it was concluded that white-tailed deer examined were experiencing copper deficiency (hypocuprosis), with signs similar to molybdenosis (King et al. 1984).

In humans, molybdenum is low at birth, increases until age 20 years, and declines thereafter (Goyer 1986). Although conclusive evidence that molybdenum is required by humans is lacking, there is general agreement that it should be considered as one of the essential trace elements. The absence of any documented deficiencies in man indicates that the required level is much less than the average daily intake of 180 µg molybdenum in the United States (Chappell et al. 1979). Human discomfort has been reported in workers from copper–molybdenum mines, and in those eating food products containing 10 to 15 mg Mo/kg and <10 mg copper/kg and grown on soils containing elevated molybdenum of 77 mg/kg and 39 mg copper/kg. Symptoms included general weakness, fatigue, headache, irritability, lack of appetite, epigastric pain, pain in joints and muscles, weight loss, red and moist skin, tremors of the hands, sweating, dizziness (Friberg et al. 1975), renal xanthine calculi, uric acid disturbances (Schroeder et al. 1970), and increased serum ceruloplasmin (Friberg and Lener 1986). The typical human adult contains only 9 mg molybdenum, primarily in liver, kidney, adrenal, and omentum (Goyer 1986). Most of the ingested molybdenum is easily

absorbed from the GI tract and excreted within hours or days in urine, mostly as molybdate; excesses may be excreted also by the bile, particularly as hexavalent molybdenum (Friberg et al. 1975; Goyer 1986; Friberg and Lener 1986). At high dietary levels, molybdenum reportedly prevents dental caries (Schroeder et al. 1970), but this requires verification.

Table 30.4 Molybdenum Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects (Reference) ^a
CATTLE, COWS, <i>Bos</i> spp.	
Near steelworks, 20 kg Mo as MoO_3 emitted daily in gaseous form; fallout deposits ~2 mg/m ² monthly, corresponding to a pasture Mo content from 2–20 mg Mo/kg dry weight (DW). Pasture had slight Cu deficiency of natural origin, with copper:Mo ratio in pastures <3	About 40% of 5000 grazing cows with signs of molybdenosis. No signs of poisoning before steelworks began operations. Signs evident almost immediately in first grazing season; most pronounced in younger animals closest to source. Remedial actions included copper glycine and installation of additional emission filters at the steel-works (1)
Low dietary Mo (<5 mg Mo/kg), adequate copper	Growth and fertilization rate normal; liver copper >70 mg/kg DW; 63% of embryos developed normally (2)
Fed diets containing 5 mg Mo/kg DW and 4 mg copper/kg DW for 84 weeks	Reduced food intake and efficiency of food use, altered iron metabolism, clinical signs of copper deficiency. Onset of puberty delayed 10 weeks, decreased conception rate (fertility 12–33% vs. 57–80% in controls), disrupted estrus cycle (67% were anestrus vs. 7% in controls), and other signs consistent with decreased releases of luteinizing hormones associated with altered ovarian secretion (3, 4)
High dietary Mo (15–20 mg Mo/kg), copper deficient	Growth and fertilization normal; liver copper 10 mg/kg DW; only 16% of embryos developed normally (2)
Fed diets of normal copper and high Mo (30 mg/kg feed)	Blood Mo level of 0.6–0.8 mg/L (5)
Diets containing 40 mg Mo/kg and 6 mg copper/kg fed to lactating cows for 9 weeks	Reduction of 30% in milk yield; rapid decline in plasma copper; milk Mo levels of 1.6 mg/L; growth reduction in nursing calves (6)
Fed diets of 60 mg Mo/kg DW	Low liver copper, intestinal disturbances, brittle bones prone to fracture (7)
Dairy herd fed pelleted feed containing 140 mg Mo/kg FW and up to 10 mg copper/kg FW	Molybdenosis. Contaminated magnesium oxide (12,200 mg Mo/kg) added to ration at 1% was the source of the excess Mo (8)
Drinking water with Mo as ammonium molybdate. Basal diet with 13 mg copper/kg and 2900 mg sulfur/kg	In 5-week-old calves, there was no effect on liver or plasma copper levels (9)
1 or 10 mg Mo/L in drinking water for 21 days	Copper liver burden reduced to 201 mg/kg DW vs. 346 in controls; copper in plasma elevated to 1100 µg/L vs. 690 in controls. No effect on growth, or food and water consumption (9)
50 mg Mo/L in drinking water for 21 days	Normal milk Mo level of 0.06 mg/L (5)
Total daily intake of 100 mg Mo	Anorexia, diarrhea, and weight loss in Swiss beef cattle (10)
Total daily intake of 141 mg Mo	Milk Mo level of 0.37 mg/L (5)
Total daily intake of 500 mg Mo	Signs of molybdenum poisoning (7)
Total daily intake of 1360 mg Mo daily as soluble molybdate	Lethal dose (11)
10 mg Mo/kg BW	
GUINEA PIG, <i>Cavia</i> sp.	
Chronic exposure, daily dose in mg Mo/animal	
25, as MoO_3	75% mortality (12)
200, as calcium molybdate	25% mortality (12)
Air concentrations of 28–285 mg Mo/m ³	Hexavalent Mo compounds absorbed appreciably, but not disulfide compounds (10, 13)
Dose, in mg Mo/kg BW, various administration routes	
80	LD0 (12)
250	Some deaths (11)
400	LD75 (4 days) (12)
800	LD100 (4 months) (12)

Table 30.4 (continued) Molybdenum Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects (Reference)^a
DOMESTIC RUMINANTS	
Pastures containing 10–20 mg Mo/kg DW	“Risk” zone for molybdenosis (12)
Pastures containing 20–100 mg Mo/kg DW	“Teart” disease characterized by anemia, poor growth, diarrhea; prolonged exposure resulted in joint deformities and death (13)
HORSES, PONIES, <i>Equus</i> sp.	
Feeding on teart pastures with elevated Mo content	No effect (5)
Given single oral dose of radio Mo-99, as molybdate, or about 20–28 mg	Mo-99 appeared rapidly in plasma as molybdate, but quickly cleared with Tb 1/2 of 7–10 h (14)
Fed diets containing 20 mg Mo/kg DW for 4.5 months; diet supplemented with sulfur for 1 month at 1.2 g/kg feed	Animals remained healthy. No decline in total plasma copper or increase in plasma insoluble copper (14)
Fed diets containing up to 107 mg Mo/kg for 14 days	Increasing dietary Mo resulted in decreasing copper retention due to increasing excretion of copper in feces; up to 1.45 g Mo/kg BW absorbed and retained with no obvious adverse effects (15)
DOMESTIC CAT, <i>Felis domesticus</i>	
Intravenous injection, in mg Mo/kg BW	
25	Increased arterial blood pressure (12)
50	Central nervous system impairment (12)
HUMAN, <i>Homo sapiens</i>	
Drinking water, in µg/L	
50	No effect (11)
200	Increased urinary excretion, normal serum Mo levels, no change in copper metabolism (11)
Total intake, in mg Mo daily	
0.18	Average intake in U.S. (11)
0.5–1	Increased urinary copper excretion (11)
10	Increase in blood and urine Mo levels, increases in serum ceruloplasmin, increased xanthine oxidase activity (11)
10–15	Increased uric acid, decreased copper excretion, high incidence of gout-like disease (11)
Atmospheric concentrations, in mg Mo/m ³ air	
1–3; 5-year exposure	Respiratory difficulties (12)
6–19; 4-year exposure	Respiratory difficulties (12)
MOUSE, <i>Mus</i> spp.	
10 mg Mo/L in drinking water of breeding mice	Decrease in survival of F ₂ and F ₃ generations (16)
SHEEP, <i>Ovis</i> spp.	
Molybdenum-deficient diet of 0.03 mg/kg	High incidence of renal xanthine calculi (5)
Adequate diet of 0.4 mg Mo/kg, due to resowing of pasture and lime treatment	Zero incidence of renal calculi (5)
Content of pasture 0.4–1.5 mg Mo/kg DW	Mo concentrations, in mg/kg FW, were 0.0–0.03 in plasma, 2.0–2.4 in liver, and 0.4–0.5 in kidney. No lameness or connective tissue lesions (17)
2.4 mg Mo/kg diet in lambs	Significantly enhanced growth when compared to sheep fed 0.36 mg Mo/kg diet; growth associated with increased cellulose digestibility by rumen biota (5)
Grazing pastures treated 3 times with 420 g Mo/ha: at start, and weeks 45 and 72. Mo content of pasture usually 5.5–12.5 mg/kg DW	Mo concentrations, in mg/kg FW, were 1.7–2.4 in plasma, 6.0–6.4 in liver, and 6.9–8.1 in kidney. Lameness and connective tissue lesions in most sheep (17)

Table 30.4 (continued) Molybdenum Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects (Reference)^a
Given diets of high copper (82 mg/kg) and sulfur (3.8 g/kg), and Mo at 20, 40, or 60 mg/kg for 193 days	Liver damage due to copper at low Mo (20 mg/kg) diets; at 40 and 60 mg Mo/kg, both metals accumulated in kidney cortex but no evidence of liver histopathology or kidney damage (18)
Breeding ewes fed diets of normal Cu, high Mo (30 mg/kg feed)	Blood Mo level of 2.4–3.4 mg/L (5)
Diets of 50 mg Mo/kg	Avoidance by lambs; may be learned olfactory recognition (19)
Lambs grazing on soils where copper:Mo ratio is <0.4	Swayback observed in 15–39% (10)
Ram lambs fed diets of adequate sulfate and copper (7.7 mg/kg DW). Copper to Mo ratios of 5.5, 5.3, 1.1, or 0.7 for 105 days	No significant measurable effects at ratios of 5.5 and 5.3. Secondary Cu deficiency (molybdenosis) at 1.1 ratio evident in blood and plasma, and in liver at 0.7 (20)
Lambs fed daily intake of 8 mg Mo, 36.3 mg Cu, and 3.7 g S for 125 days	No effect on growth of food intake; significant increases in levels of kidney cortex copper, liver Mo, and plasma copper; major differences in responses among breeds tested (21)
Total intake raised from 0.4 mg daily to 96 mg daily	Blood Mo level of 4.95 mg/L (5)
Fed 75 mg Cu daily for 50 days, followed by 140 mg Mo and 4 g S daily for 13 days with no added Cu	Molybdenosis within 8 days (22)
As above, but 70 mg Mo daily at day 13 for 34 days	40% reduction in liver copper (22)
WHITE RABBIT, <i>Oryctolagus</i> spp.	
Dietary Mo concentrations, in mg Mo/kg ration 100; lifetime exposure	Reduced growth, hair loss, dermatosis, anemia, skeletal and joint deformities, decreased thyroxin (11)
500; 12 weeks	No obvious effects (12)
1000; 12 weeks	Some growth retardation (12)
2000–4000	Many deaths of weanlings in about 37 days, and of adults in 53 days. Survivors were anorexic, diarrheic, anemic, and had front-leg abnormalities; successful recovery after copper therapy (12)
5000	Thyroid dysfunction (11)
RAT, <i>Rattus</i> spp.	
Drinking water, in mg Mo/L 10; exposure for 3 years	Disrupted calcium metabolism (29). Increased sensitivity to cold stress, elevated tissue residues of 50–60 mg Mo/kg DW (23, 24)
20; 30 weeks exposure	No effect on growth or organ histology (25)
50; lifetime exposure	Some growth retardation (11)
1000; lifetime exposure	No severe signs observed in breeding adults. Resultant pups, however, maintained on this regimen were stunted, rough haired, sterile (males), and hyperactive (11)
Dose, in mg Mo per animal daily for up to 232 days	LD25 to LD50 for hexavalent Mo compounds (12)
10	LD50 for calcium molybdate (12)
100	LD50 for MoO ₃ (12)
125	LD50 for ammonium molybdate (12)
333	
Atmospheric concentrations, in mg Mo/m ³ 64; 2 h	Outwardly normal, some microscopic damage due to MoO ₃ exposure (12)
Up to 5000 ammonium paramolybdate, 12,000 Mo dioxide, 15,000 Mo trioxide, or 30,000 metallic molybdenum; exposure for 1 h	At 4 weeks postexposure, there were no adverse effects except for irritation of upper respiratory passage (12)
Feeding levels, in mg Mo/kg diet	

Table 30.4 (continued) Molybdenum Effects on Selected Species of Mammals

Species, Dose, and Other Variables	Effects (Reference)^a
50	Diet avoidance (19). In low sulfate diets and 5 weeks exposure, rats had reduced growth and mandibular exostoses (10)
80; copper deficient	Inhibited growth and reduced survival (5, 26)
80; 35 mg CuSO ₄ /kg	No measurable effects (5, 26)
100; lifetime exposure	Appetite loss, weight loss, reduced growth, anemia, mandibular exostoses, bone deformities, liver and kidney histopathology, increased liver copper residues, male sterility (11)
400	After 5 weeks, growth depression, anemia, mandibular exostoses; some deaths at lifetime exposures (12)
500 or 800	No deaths in 6 weeks; growth retardation and anemia (12)
500 or 1000; 77 mg Cu/kg	Poor growth (5, 26)
5000	Lethal in 2 weeks (11, 12)
Dose, in mg Mo/kg BW	
0.00002–0.001	50% excretion (Tb 1/2) in 60–113 h for kidney, liver, spleen, small intestine, and skin (10)
0.003	Tb 1/2 in 47 h (10)
>0.003	Tb 1/2 in 3 h when administered subcutaneously, 6 h for intragastric application (10)
4.5, intravenous injection	Biliary excretion of Mo ⁺⁶ compounds was more rapid than Mo ⁺⁵ compounds (27)
100	When inhaled as MoO ₃ , irritating to eyes and mucous membranes and eventually lethal. Repeated oral administration leads to histopathology of liver and kidney (13)
100–150	Lethal (11)
114	All recovered after intraperitoneal injection of sodium molybdate (12)
117	All dead within a few hours after intraperitoneal injection of sodium molybdate (12)
500; daily	Tolerated when given as disulfide (13)
500; 28 days	Reduced growth, disrupted blood and enzyme chemistry, histopathology of liver and kidney; partly reversed by 20% protein diet (28)

DOMESTIC PIG, *Sus* sp.

Fed diets containing 1000 mg Mo/kg for 3 months No effect (5)

^a 1, Alary et al. 1981; 2, O'Gorman et al. 1987; 3, Phillippe et al. 1987a; 4, Phillippe et al. 1987b; 5, Underwood 1971; 6, Wittenberg and Devlin 1987; 7, Penumarthi and Oehme 1978; 8, Lloyd et al. 1976; 9, Kincaid 1980; 10, Friberg and Lener 1986; 11, Chappell et al. 1979; 12, Friberg et al. 1975; 13, Goyer 1986; 14, Strickland et al. 1987; 15, Cymbaluk et al. 1981; 16, Earl and Vish 1979; 17, Pitt et al. 1980; 18, Van Ryssen et al. 1982; 19, White et al. 1984; 20, Robinson et al. 1987; 21, Harrison et al. 1987; 22, Van Ryssen et al. 1986; 23, Winston et al. 1973; 24, Winston et al. 1976; 25, Luo et al. 1983; 26, Underwood 1979; 27, Lener and Bibr 1979; 28, Bandyopadhyay et al. 1981; 29, Solomons et al. 1973.

30.5 RECOMMENDATIONS

Although molybdenum is generally recognized as an essential trace metal for plants and animals, and may reduce the incidence and severity of carcinomas in rats (Luo et al. 1983; Wei et al. 1985) and dental caries in humans (Shamberger 1979), there is no direct evidence of molybdenum deficiency being detrimental to animal health. The minimum daily molybdenum requirements in diets are not yet established due to problems in preparing molybdenum-free rations (Chappell et al. 1979). As a consequence, no regulatory agency recognizes molybdenum as safe and necessary, and molybdenum cannot be legally incorporated into animal feeds (Penumarthi and Oehme 1978).

The richest natural sources of molybdenum (i.e., 1.1 to 4.7 mg Mo/kg fresh weight) are plants unusually high in purines such as legumes and whole grains (Schroeder et al. 1970), followed by leafy vegetables, liver, and kidney (Shamberger 1979). The poorest sources are fruits, sugars, oils, and fat (Schroeder et al. 1970).

The greatest economic importance of molybdenosis is associated with subclinical manifestations of copper deficiency resulting from forages containing a low copper:molybdenum ratio. Unfortunately, these conditions are often difficult to diagnose accurately, and animal response to copper may be difficult to demonstrate (Ward 1978). One recommended treatment for afflicted cattle is 2 g daily of copper sulfate to cows and 1 g daily to young stock, or intravenous injection of 200 to 300 mg copper sulfate daily for several days (Underwood 1971).

The animals most sensitive to molybdenum insult are domestic ruminants, especially cattle. Diets containing more than 15 mg Mo/kg dry weight and with a low copper:molybdenum ratio, or drinking water levels more than 10 mg Mo/L were frequently associated with molybdenosis in cattle (Table 30.5). By contrast, adverse effects were documented in birds at dietary levels more than 200 mg Mo/kg ration, in ruminant wildlife at dietary levels greater than 2500 mg Mo/kg, and in aquatic organisms — with one exception — at more than 50 mg Mo/L (Table 30.5). The exception was newly fertilized eggs of rainbow trout, which were about 21 times more sensitive to molybdenum than were zygotes approximately one third through embryonic development, and about 90 times more sensitive than adult fish (Table 30.5).

Proposed criteria for human health protection include drinking water concentrations less than 50 µg Mo/L, and daily dietary intakes less than 7 µg Mo/kg food — based on a 70-kg adult (Table 30.5). Molybdenum concentrations in blood of “healthy” people averaged 14.7 µg Mo/L, distributed between the plasma and erythrocytes. Anemic people had significantly lower blood molybdenum levels. In leukemia patients, molybdenum levels increased significantly in whole blood and erythrocytes but not in plasma (Shamberger 1979). Additional work is recommended on the use of blood in fish and wildlife as an indicator of molybdenum stress and metabolism (Eisler 1989).

Increasing problems associated with marginal mineral deficiencies and unfavorable mineral interaction — as has been the case in the older agricultural areas of northern Europe — can be anticipated as pasture and forage production becomes more intensive (Ward 1978). Research has been recommended in areas having a high molybdenum content in soils and vegetation, and also in noncontaminated areas where consumption habits favor a high molybdenum intake and an imbalance in relation to other dietary constituents of importance, such as copper (Friberg et al. 1975). In some parts of the world where molybdenum has been substituted for lime, the soils have become more acidic, thus making them difficult to farm. Liming under these conditions may elevate soil molybdenum from levels previously considered safe, to levels potentially hazardous to grazing animals through high-molybdenum herbage (Gupta and Lipsett 1981). The addition of molybdenum fertilizers to sheep pastures resulted in small increments in molybdenum content with negligible risk of induced copper deficiency. But it would be unwise to apply molybdenum fertilizers to temperate grasslands grazed by animals of low initial copper status, as judged by growth retardation of lambs from pastures supplemented with molybdenum (Suttle 1983a).

Table 30.5 Proposed Molybdenum Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
TERRESTRIAL PLANTS		
Okra, <i>Abelmoschus esculentus</i>		
Increased growth	3 mg/kg soil	1
Lettuce, <i>Lactuca sativa</i>		
Molybdenum deficiency	~0.06 mg/kg dry weight (DW) plant	2
Molybdenum sufficiency	More than 0.08 mg/kg DW	2

Table 30.5 (continued) Proposed Molybdenum Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
Corn, <i>Zea mays</i> No adverse effect	3.7 mg/kg DW plant	3
Agricultural soils, Bangladesh Deficiency	<0.1 mg/kg DW surface soil	38
TERRESTRIAL INVERTEBRATES		
Toxic baits Termites	~1000 mg/kg	4
Other insect species	>5000 mg/kg	4
AQUATIC LIFE		
Algae Deficiency levels	<0.005–17.7 µg/L	5, 6
High bioconcentration	>0.014 µg/L	7
Growth reduction	>50 mg/L	8
Invertebrates Reduced survival	>60 mg/L	9
Fish Adults High bioconcentration	>0.014 µg/L	7
Reduced survival	>70 mg/L	10
Eggs Newly fertilized	>0.79 mg/L	11
Reduced survival	<28 µg/L	11
No adverse effects Eyed Adverse effects	>17.0 mg/L	10, 12
BIRDS		
Molybdenum deficiency	13–200 µg/kg diet	13–15
Normal growth	~1.0 mg/kg diet	16
Optimal growth	6.0 mg/kg diet	17
Growth reduction	200–300 mg/kg diet	18
Reproductive impairment	500 mg/kg diet	19
Reduced survival	6000 mg/kg diet	19
MAMMALS		
Cattle, cows (<i>Bos</i> spp.) Forage Healthy pasture	3–5 mg/kg DW	18
Possibility of molybdenosis	10–20 mg/kg DW	19
Probability of molybdenosis	20–100 mg/kg DW	18, 19
Toxic	15–30 mg/kg DW	20
Maximum tolerable level	6 mg/kg DW	20, 21
Recommended	0.1–0.5 mg/kg DW	22
Ratio of copper to molybdenum in diet Molybdenosis probable	<0.4	23
Critical	<2.0	20
Critical	>20.0	22
Optimal for growth and reproduction	6.1–10.1	22, 23
Drinking Water Safe level	<10 mg/L	24
Minimum toxic concentration for calves	10–50 mg/L	24
Guinea pig, <i>Cavia</i> sp.		

Table 30.5 (continued) Proposed Molybdenum Criteria for the Protection of Living Resources and Human Health

Resource, Criterion, and Other Variables	Concentration	Reference ^a
No effect on survival	80 mg/kg BW	19
Cat, <i>Felis domesticus</i>		
Adverse nonlethal effects	25–50 mg/kg BW	19
Mule deer, <i>Odocoileus hemionus</i>		
No effect	200–1000 mg/kg diet	25–28
Reduction in food intake	2500 mg/kg diet	25–28
Nonlethal adverse effects	5000–7000 mg/kg diet	25–28
Sheep, <i>Ovis</i> sp.		
Forage, recommended	<0.5 mg/kg DW	22
Rat, <i>Rattus</i> sp.		
Minimum daily need	0.5 µg	29
Disrupted calcium metabolism, elevated tissue residues	10 mg/L drinking water	30–32
Cancer inhibition	2–20 mg/L drinking water	33, 34
Food avoidance	50 mg/kg diet	35
HUMAN HEALTH		
Total daily intake, 70-kg adult		
Minimal need	120 µg	29
Average range	100–500 µg	18, 19, 28, 29, 36, 37
Maximum	10–15 mg	28
In molybdenum mining areas	>1 mg	19
From food		
United States	170 µg	28
United States	335 (210–460) µg	19
Former Soviet Union		
Children	159 µg	19
Adults	353 µg	19
United Kingdom	128 (110–1000) µg	19
From drinking water	<5 µg	28
No effect level	<500 µg daily	28
Adverse effects		
Biochemical	0.5–10 mg daily	28
Clinical	10–15 mg daily	28
Drinking water		
Safe level	<50 µg/L	28
Irrigation water		
Safe level	<10 µg/L	28
Air		
Maximum permissible concentration		
Former Soviet Union	6 mg/m ³	3
United States, 8 h daily, 5 days weekly	9.5–10 mg/m ³	15, 36
Blood		
“Normal”	14.7 µg/L	37

^a 1, Singh and Mourya 1983; 2, Gupta and Lipsett 1981; 3, Soon and Bates 1985; 4, Brill et al. 1987; 5, Vaishampayan 1983; 6, Steeg et al. 1986; 7, Short et al. 1971; 8, Sakaguchi et al. 1981; 9, Ahsanullah 1982; 10, McConnell 1977; 11, Birge et al. 1980; 12, Morgan et al. 1986; 13, Reid et al. 1956; 14, Reid et al. 1957; 15, Friberg and Lener 1986; 16, Mills and Bremner 1980; 17, Kienholz 1977; 18, Underwood 1971; 19, Friberg et al. 1975; 20, Schalscha et al. 1987; 21, Kume et al. 1984; 22, Garmo et al. 1986; 23, Baldwin et al. 1981; 24, Kincaid 1980; 25, Nagy et al. 1975; 26, Ward and Nagy 1976; 27, Ward 1978; 28, Chappell et al. 1979; 29, Schroeder et al. 1970; 30, Solomons et al. 1973; 31, Winston et al. 1973; 32, Winston et al. 1976; 33, Luo et al. 1983; 34, Wei et al. 1985; 35, White et al. 1984; 36, Goyer 1986; 37, Shamberger 1979; 38, Miah 1999.

30.6 SUMMARY

The element molybdenum (Mo) is found in all living organisms and is considered to be an essential or beneficial micronutrient. However, molybdenum poisoning of ruminants has been reported in at least 15 states and 8 foreign countries. Molybdenum is used primarily in the manufacture of steel alloys. Its residues tend to be elevated in plants and soils near molybdenum mining and reclamation sites, fossil-fuel power plants, and molybdenum disposal areas. Concentrations of molybdenum are usually lower in fish and wildlife than in terrestrial macrophytes.

Aquatic organisms are comparatively resistant to molybdenum salts: adverse effects on growth and survival usually appeared only at water concentrations >50 mg Mo/L. But in one study, 50% of newly fertilized eggs of rainbow trout (*Oncorhynchus mykiss*) died in 28 days at only 0.79 mg Mo/L. High bioconcentration of molybdenum by certain species of aquatic algae and invertebrates — up to 20 g Mo/kg dry weight — has been recorded without apparent harm to the accumulator. However, hazard potential to upper trophic organisms (such as waterfowl) that may feed on bioconcentrators is not clear. Data on molybdenum effects are missing for avian wildlife and are inadequate for mammalian wildlife. In domestic birds, adverse effects on growth have been reported at dietary molybdenum concentrations of 200 mg Mo/kg, on reproduction at 500 mg/kg, and on survival at 6000 mg/kg.

Molybdenum chemistry is complex and inadequately known. Its toxicological properties in mammals are governed to a remarkable extent through interaction with copper and sulfur; residues of molybdenum alone are not sufficient to diagnose molybdenum poisoning. Domestic ruminants, especially cattle, are especially sensitive to molybdenum poisoning when copper and inorganic sulfate are deficient. Cattle are adversely affected — and die if not removed — when grazing on pastures where the ratio of copper to molybdenum is <3 , or if they are fed low copper diets containing molybdenum at 2 to 20 mg/kg diet; death usually occurs when tissue residues exceed 10 mg/kg body weight. The resistance of other species of mammals tested, including domestic livestock, small laboratory animals, and wildlife, was at least tenfold higher than that of cattle. Mule deer (*Odocoileus hemionus*), for example, showed no adverse effects at dietary levels of 1000 mg/kg.

Additional research is needed in several fields, including:

- The role of molybdenum on inhibition of carcinomas and dental caries
- The establishment of minimum, optimal, and upper daily requirements of molybdenum in aquatic and wildlife species of concern
- The improvement in diagnostic abilities to distinguish molybdenum poisoning from copper deficiency
- The determination of sensitivity of early developmental stages of fishes to molybdenum insult.

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CHAPTER 31

Selenium

31.1 INTRODUCTION

Selenium poisoning is an ancient and well-documented disease (Rosenfeld and Beath 1964). Signs of it were reported among domestic livestock by Marco Polo in western China near the borders of Turkestan and Tibet in about the year 1295; among livestock, chickens, and children in Colombia, South America, by Father Pedro Simon in 1560; among human adults in Irapuato, Mexico, in about 1764; and among horses of the U.S. Cavalry in South Dakota in 1857 and again in 1893 (Rosenfeld and Beath 1964). In 1907/08, more than 15,000 sheep died in a region north of Medicine Bow, Wyoming, after grazing on seleniferous plants. The incidents have continued, and recent technical literature abounds with isolated examples of selenosis among domestic animals and wildlife.

Selenium (Se) was first identified as an element in 1817 by the Swedish chemist Berzelius. It is now firmly established that selenium is beneficial or essential in amounts from trace to $\mu\text{g/kg}$ (ppb) concentrations for humans and some plants and animals, but toxic at some concentrations present in the environment (Rosenfeld and Beath 1964). Selenium deficiency was reported among cattle grazing in the Florida Everglades, which showed evidence of anemia, slow growth, and reduced fertility (Morris et al. 1984). Selenium deficiency has been demonstrated in Atlantic salmon, *Salmo salar* (Lorentzen et al. 1994), in various species of deer in Florida and Washington (Hein et al. 1994; McDowell et al. 1995), and in free-ranging ungulates in Washington state, including moose (*Alces alces*) and bighorn sheep (*Ovis canadensis*) (Hein et al. 1994). Conversely, calves of Indian buffaloes died of selenium poisoning after eating rice husks grown in naturally seleniferous soils (Prasad et al. 1982). Adverse effects of excess selenium are reported on reproduction of cattle, monkeys, sheep, swine, rats, and hamsters, including fetal and maternal death, and a dramatic increase in developmental abnormalities (Domingo 1994). Severe reproductive and developmental abnormalities were observed in aquatic birds nesting at selenium-contaminated irrigation drainwater ponds in the San Joaquin Valley, California (Ohlendorf et al. 1986, 1986a, 1987, 1989, 1990; Hoffman et al. 1988; Schuler et al. 1990; Besser et al. 1993; Lemly 1996b). Accumulation of more than 8 mg Se/kg dry weight in fish gonads is the probable cause of reduced reproduction and subsequent species disappearances in Belews Lake, North Carolina, and the endangered razorback sucker (*Xyrauchen texanus*) from the Green River, Utah, in 1991 (Cumbie and Van Horn 1978; Hamilton and Waddell 1994; Waddell and May 1995).

Selenium has been the subject of many reviews (Rosenfeld and Beath 1964; Frost 1972; Sandholm 1973; Zingaro and Cooper 1974; Frost and Ingvoldstad 1975; Anonymous 1975; National Academy of Sciences [NAS] 1976; Harr 1978; U.S. Environmental Protection Agency [USEPA] 1980, 1987; Lo and Sandi 1980; Shamberger 1981; Wilber 1980, 1983; Fishbein 1977, 1983; National Research Council [NRC] 1983; Reddy and Massaro 1983; Eisler 1985; Lemly and Smith

1987; Ohlendorf 1989; Hodson 1990; Goede 1993; Lemly 1993, 1996a, 1996b; Heinz 1996; U.S. Public Health Service [USPHS] 1996). These authorities agree that selenium is widely distributed in nature, being especially abundant with sulfide minerals of various metals, such as iron, lead, and copper. The major source of environmental selenium is the weathering of natural rock. The amount of selenium entering the atmosphere as a result of anthropogenic activities is estimated to be 3500 metric tons annually, of which most is attributed to combustion of coal and the irrigation of high-selenium soils for crop production. However, aside from highly localized contamination, the contribution of selenium by human activities is small in comparison with that attributable to natural sources. Collectively, all authorities agree that selenium may favorably or adversely affect growth, survival, and reproduction of algae and higher plants, bacteria and yeasts, crustaceans, molluscs, insects, fish, birds, and mammals (including humans). Most acknowledge that sensitivity to selenium and its compounds is extremely variable in all classes of organisms and, except for some instances of selenium deficiency or of selenosis, metabolic pathways and modes of action are imperfectly understood. For example, selenium indicator plants can accumulate selenium to concentrations of thousands of parts per million (mg/kg) without ill effects. In these plants, selenium promotes growth; whereas in crop plants, accumulations as low as 25 to 50 mg/kg may be toxic. Thus, plants and waters high in selenium are considered potentially hazardous to livestock and to aquatic life and other natural resources in seleniferous zones.

31.2 ENVIRONMENTAL CHEMISTRY

Selenium is characterized by an atomic weight of 78.96, an atomic number of 34, a melting point of 271°C, a boiling point of 685°C, and a density of 4.26 to 4.79. Chemical properties, uses, and environmental persistence of selenium were documented by a number of researchers whose works constitute the major source material for this section: Rosenfeld and Beath (1964); Bowen (1966); Lakin (1973); Stadtman (1974, 1977); Frost and Ingvoldstad (1975); Chau et al. (1976); Harr (1978); Wilber (1980, 1983); Zieve and Peterson (1981); Robberecht and Von Grieken (1982); Cappon and Smith (1982); Nriagu and Wong (1983); Eisler (1985); USPHS (1996).

There was general agreement on four points.

1. Selenium chemistry is complex, and additional research is warranted on chemical and biochemical transformations among valence states, allotropic forms, and isomers of selenium.
2. Selenium metabolism and degradation are significantly modified by interaction with heavy metals, agricultural chemicals, microorganisms, and a variety of physicochemical factors.
3. Anthropogenic activities (including fossil fuel combustion and metal smelting) and naturally seleniferous areas pose the greatest hazards to fish and wildlife.
4. Selenium deficiency is not as well documented as selenium poisoning, but may be equally significant.

Selenium chemistry is complex (Rosenfeld and Beath 1964; Harr 1978; Wilber 1983; Porcella et al. 1991; Wiedmeyer and May 1993; Besser et al. 1994; USPHS 1996). In nature, selenium exists: as six stable isotopes (Se-74, -76, -77, -78, -80, and -82), of which Se-80 and -78 are the most common, accounting for 50% and 23.5%, respectively; in three allotropic forms; and in five valence states. Changes in the valence state of selenium from -2 (hydrogen selenide) through 0 (elemental selenium), +2 (selenium dioxide), +4 (selenite), and +6 (selenate) are associated with its geologic distribution, redistribution, and use. Soluble selenates occur in alkaline soils, are slowly reduced to selenites, and are then readily taken up by plants and converted into organoselenium compounds, including selenomethionine, selenocysteine, dimethyl selenide, and dimethyl diselenide. In drinking water, selenates represent the dominant chemical species. Selenites are less soluble than the corresponding selenates and are easily reduced to elemental selenium. In seawater, selenites are the dominant chemical species under some conditions (Cappon and Smith 1981). Selenium dioxide is formed by combustion of elemental selenium present in fossil fuels or rubbish.

Selenium is the most strongly enriched element in coal, being present as an organoselenium compound, a chelated species, or as an adsorbed element. On combustion of fossil fuels, the sulfur dioxide formed reduces the selenium to elemental selenium. Elemental selenium is insoluble and largely unavailable to the biosphere, although it is still capable of satisfying metabolic nutritional requirements. Hydrogen selenide is highly toxic (at 1 to 4 µg/L in air), unstable, acidic, and irritative. Selenides of mercury, silver, copper, and cadmium are very insoluble, although their insolubility may be the basis for the reported detoxification of methylmercury by dietary selenite, and for the decreased heavy metal toxicity associated with selenite. Metallic selenides are thus biologically important in sequestering both Se and heavy metals in a largely unavailable form.

In areas of acid or neutral soils, the amount of biologically available selenium should steadily decline. The decline may be accelerated by active agricultural or industrial practices. In dry areas, with alkaline soils and oxidizing conditions, elemental selenium and selenides in rocks and volcanic soils may oxidize sufficiently to maintain the availability of biologically active selenium. Concentrations of selenium in water are a function of selenium levels in the drainage system and of water pH. In Colorado, for example, streams with pH 6.1 to 6.9 usually contain <1 µg Se/L, but those with pH 7.8 to 8.2 may contain 270 to 400 µg/L (Lakin 1973). Selenium volatilizes from soils at rates that are modified by temperature, moisture, time, season of year, concentration of water-soluble selenium, and microbiological activity. Conversion of inorganic and organic selenium compounds to volatile selenium compounds (such as dimethyl selenide, dimethyl diselenide, and an unidentified compound) by microorganisms has been observed in lake sediments of the Sudbury area of Ontario. This conversion may have been effected by pure cultures of *Aeromonas*, *Flavobacterium*, *Pseudomonas*, or an unidentified fungus, all of which are found in methylated lake sediments. Production of volatile selenium is temperature dependent. Compared with the amount of $(CH_3)_2Se$ produced at an incubation temperature of 20°C, 25% less was produced at 10°C and 90% less at 4°C. Details of selenium reduction and oxidation by microorganisms are not clear. One suggested mechanism for selenite reduction in certain microorganisms involves attachment to a carrier protein and transformation from selenite to elemental selenium, which in turn may be oxidized to selenite by the action of *Bacillus* spp., as one example. It is apparent that much additional research on this problem is warranted. It now appears that selenates and selenites are absorbed by plants, reduced, and then incorporated in amino acid synthesis. The biological availability of selenium is higher in plant foods than in foods of animal origin (Lo and Sandi 1980). The net effect of soil, plant, and animal metabolism is to convert selenium to inert and insoluble forms such as elemental selenium, metallic selenides, and complexes of selenite with ferric oxides.

Selenium was used in the early 1900s as a pesticide to control plant pests, and is still used sparingly to control pests of greenhouse chrysanthemums and carnations (Rosenfeld and Beath 1964). It has been used to control cotton pests (in Trinidad), mites and spiders that attack citrus, and mites that damage apples. Although no insect-resistant strains have developed, the use of selenium pesticides has been discontinued, owing to their stability in soils and resultant contamination of food crops, their high price, and their proven toxicity to mammals and birds (Rosenfeld and Beath 1964; Eisler 1985). In Canada and France, sodium selenite applied to the soil to discourage deer from browsing conifer seedlings when deer numbers were high was unsuccessful and should be avoided (Jobidon and Prevost 1994). Selenium shampoos, which contain about 1% selenium sulfide, are still used to control dandruff in humans and dermatitis and mange in dogs. Selenium is used extensively in the manufacture and production of glass, pigments, rubber, metal alloys, textiles, petroleum products, medical therapeutic agents, and photographic emulsions (Eisler 1985).

Domestic consumption of selenium in 1981 exceeded 453,000 kg. About 50% was used in electronic and copier components, 22% in glass manufacturing, 20% in chemicals and pigments, and 8% miscellaneous (Cleveland et al. 1993). In 1987, world production of selenium was about 1.4 million kg (USPHS 1996). In 1986, 46% of the global selenium produced was used in the semiconductor and photoelectric industries; 27% in the glass industry to counter coloration impurities from iron; 14% in pigments; and 13% in medicine, in antidandruff shampoos, as catalysts in

pharmaceutical preparations, in nutritional feed additives for poultry and livestock, and in pesticide formulations (USPHS 1996).

Air and surface waters generally contain nonhazardous concentrations of selenium. Significant increases of selenium in specific areas are attributed exclusively to industrial sources, and to leaching of groundwater from seleniferous soils. In the United States, about 4.6 million kg selenium are released annually into the environment: 33% from combustion of fossil fuels, 59% from industrial losses, and 8% from municipal wastes. Of the total, about 25% is in the form of atmospheric emissions, and the rest in ash. Mining and smelting of copper–nickel ores at Sudbury, Ontario, Canada, alone releases about 2 metric tons selenium to the environment daily, and probably represents the greatest point source of selenium release in the world. In 1977, 680,000 kg selenium was produced at Sudbury, but only about 10% was recovered, suggesting that about 90% was lost to the environment. Of the amount lost, perhaps 50 metric tons were dispensed into the atmosphere, probably as selenium dioxide (airborne Se levels 1 to 3 km from Sudbury were as high as $6.0 \mu\text{g}/\text{m}^3$). The rest was probably associated with mine tailings, wastewater, and scoria, and is a local source of selenium contamination, most notably in lakes. The present annual rates of selenium accumulation in lake sediments in the Sudbury area range from 0.3 to $12.0 \text{ mg}/\text{m}^2$. These deposition rates exceed those of pre-colonial times by factors of 3 to 18, and are among the highest recorded in North America (Nriagu and Wong 1983).

Selenium is a serious hazard to livestock and probably to people in a wide semiarid belt that extends from inside Canada southward across the United States into Mexico (NRC 1983). Selenium tends to be present in large amounts in areas where the soils have been derived from Cretaceous rocks. Total selenium in such soils averages about 5 mg/kg, but is sometimes as high as 80 mg/kg. Lack of rainfall has prevented the solution of the selenium minerals and the removal of their salts in drainage waters. In some areas, modern fertilization practices and the buildup of sulfates in the soil due to acid precipitation partly lessen the availability of selenium to plants and forage crops. In the United States, highly seleniferous natural areas (200 to 300 $\mu\text{g}/\text{kg}$ in forage) are most abundant in the Rocky Mountain and High Central Plains areas. Areas with lower concentrations (20 to 30 $\mu\text{g}/\text{kg}$) in forage are typical in the Pacific Northwest and the Southeast. However, huge variations are not uncommon from one specific location to another. Among plants, primary and secondary selenium accumulators are almost always implicated in cases of acute or chronic selenium poisoning of livestock. Primary selenium accumulator plants, such as various species of *Astragalus*, *Oenopsis*, *Stanelya*, *Zylorrhiza*, and *Machaeranthera*, may require 1 to 50 mg Se/kg in either soil or water for growth, and may contain 100 to 10,000 mg Se/kg as a glutamyl dipeptide or selenocystanthionine. Secondary accumulator plants (representative genera: *Aster*, *Gutierrezia*, *Atriplex*, *Grindelia*, *Castillaja*, and *Comandra*) grow in either seleniferous or nonseleniferous soils and may contain 25 to 100 mg Se/kg. Nonaccumulator plants growing on seleniferous soils contain 1 to 25 mg Se/kg fresh weight. Meat and eggs of domestic animals may contain 8 to 9 mg Se/kg in seleniferous areas, compared with 0.01 to 1.0 mg/kg in nonseleniferous areas. Tissues from animals maintained on high-Se feeds generally contain 3 to 5 mg Se/kg fresh weight vs. up to 20 mg/kg in animals dying of selenium poisoning (Harr 1978).

Selenium is nutritionally important as an essential trace element, but is harmful at slightly higher concentrations. Although normal selenium dietary levels required to ensure human health range from 0.04 to 0.1 mg/kg, toxicity may occur if food contains as little as 4.0 mg/kg. Minimum selenium concentrations required are usually higher in livestock than in humans. In areas with highly seleniferous soils, excess selenium is adsorbed onto a variety of plants and grains and can be fatal to grazing livestock. There is general agreement, however, that selenium inadequacy can be of greater concern to health than selenium toxicity. Selenium has a comparatively short effectual biological life in various species of organisms for which data are available. Studies with radio-selenium-75 indicated that its biological half-life is 10 to 64 days: 10 in pheasants, 13 in guppies and voles, 15 in ants, 27 in eels, 28 in leeches, and 64 in earthworms (Wilber 1983). Many investigators concluded that the greatest current and direct use of selenium is in the transportation of grains grown in seleniferous areas to selenium-deficient areas as animal and human food.

31.3 CONCENTRATIONS IN FIELD COLLECTIONS

Selenium concentrations in nonbiological materials extend over several orders of magnitude (Table 31.1; Lemly 1996b). In terrestrial materials, concentrations in excess of 5 mg Se/kg are routinely recorded in meteorites, copper–nickel ores, coal and other fossil fuels, lake sediments in the vicinity of a nickel–copper smeltery, and in sediments of flyash settling ponds. Water concentrations exceeding 50 µg Se/L have been documented in groundwater, especially in areas with seleniferous soils, in sewage wastes, in irrigation drain water, and in water of flyash settling ponds. Selenium concentrations in air samples were >0.5 µg/m³ in the vicinity of selenium production plants, and these were at least 500 times higher than in a control area (Table 31.1).

Table 31.1 Selenium Concentrations in Nonbiological Materials

Sample and Unit of Concentration	Concentration	Reference ^a
TERRESTRIAL (mg/kg)		
Earth's crust	0.05	1
Soils	0.2	2
Limestones	0.08	2
Sandstones	Up to 0.05	2
Shales	0.6	2
Chondrites	8.0	2
Ocean sediments	0.34–4.8	3
Coal	3.4 (0.5–10.7)	4, 5, 15
Fossil fuels	1–10	6
Petroleum	500–1650	15
Lake sediments		
NY, Lake George	0.22	7
Great Lakes	0.35–0.75	8
Freshwater lakes, Canada	0.2–14.5	9
AQUATIC (µg/L)		
Drinking water		
Worldwide	0.12–0.44	10
Groundwater		
Nebraska, U.S.	<1–480	10
Argentina	48–67	10
Australia	0.008–0.33	10
France	<5–75	10
Israel	0.9–27	10
Italy	<0.002–1.9	10
Sewage waters		
United States		
Raw sewage	280	4
Primary effluent	45	4
Secondary effluent	50	4
Worldwide		
Japan	480–700	2
United States	10–280	2
Former Soviet Union	1.8–2.7	2
Germany	1.5	2
River waters		
Japan	0.03–0.09	11
Germany	0.015	2
Amazon River	0.021	2
United States		
Ohio River	<0.01	10
Mississippi River	0.14	10

Table 31.1 (continued) Selenium Concentrations in Nonbiological Materials

Sample and Unit of Concentration	Concentration	Reference ^a
Michigan	0.8–10	10
Nebraska	<1–20	10
Colorado River	30	10
Lake waters		
Sweden	0.04–0.21	11
United States	0.04–1.4	4
Great Lakes	0.001–0.036	8
Seawater		
Worldwide	0.009–0.045	1, 2
Worldwide	0.09–0.45	12, 15
Worldwide	0.09–<6.0	4
Israel, Dead Sea	0.8	10
Japan	0.04–0.08	10
AIR ($\mu\text{g}/\text{m}^3$)		
Near Se industrial plant	0.7	4
Control area	0.001	4
Near Sudbury (Canada) smelter Max.	6.0	11
United States	Usually <0.01	15
INTEGRATED STUDIES ($\mu\text{g}/\text{kg}$ or $\mu\text{g}/\text{L}$)		
California		
Rainwater	0.05	10
Lake water	0.018	10
Seawater	0.058–0.08	10
Irrigation drain water		
Subsurface	300–1400	13
Surface	300	13
Vicinity of nickel–copper smelter, Sudbury, Ontario		
Lake waters	0.1–0.4	11
Lake sediments	2000–6000	11
Lake sediments 240 km south of Sudbury	1000–3000	11
Cu–Ni ores	20,000–80,000	11
Flyash ponds		
Sediment	14,000	14
Water	350	14

^a 1, Frost and Ingvaldstad 1975; 2, Ebens and Shacklette 1982; 3, de Goeij et al. 1974; 4, NAS 1976; 5, Kuhn et al. 1980; 6, Harr 1978; 7, Heit et al. 1980; 8, Adams and Johnson 1977; 9, Speyer 1980; 10, Robberecht and Von Grieken 1982; 11, Nriagu and Wong 1983; 12, Whittle et al. 1977; 13, Ohlendorf et al. 1986; 14, Furr et al. 1979; 15, USPHS 1996.

As a result of natural and anthropogenic processes, comparatively high concentrations of selenium in nonbiological materials may offer protection or pose significant risks to fish and wildlife. In Finland, for example, agricultural fertilizers were supplemented with 6 to 16 mg Se/kg beginning in 1985. In Finnish lakes, selenium concentrations have increased in sediments and fish muscle from this activity and from atmospheric fallout, but no adverse biological effects were observed (Wang et al. 1995). In Sweden, selenium treatment raised the lake water concentrations from 3 μg Se/L at the start to 5 μg /L. This treatment lowered mercury concentrations in mercury-contaminated northern pike (*Esox lucius*) and yellow perch (*Perca flavescens*) in treated Swedish lakes by 60 to 85% (Paulsson and Lundbergh 1991). Selenium is normally present in surface waters at about 0.1 to 0.3 $\mu\text{g}/\text{L}$. However, at 1 to 5 $\mu\text{g}/\text{L}$, it can biomagnify in aquatic food chains and pose a concentrated dietary source of selenium that is toxic to fish and wildlife (Lemly 1993c, 1996a).

Selenium concentrations in representative species of freshwater, marine, and terrestrial flora and fauna are listed in [Table 31.2](#). Additional information on body and tissue burdens of selenium was given by Birkner (1978), Jenkins (1980), Lo and Sandi (1980), Eisler (1981, 1985), and Wilber (1983). It is emphasized that selenium concentrations in all organisms tended to be significantly higher when collected from locales having certain characteristics: highly seleniferous soils or sediments (de Goeij et al. 1974; Birkner 1978; Speyer 1980; Wilber 1983); high human population densities (Beal 1974); heavy accumulations of selenium-laden wastes, such as effluents from systems used to collect flyash scrubber sludge or bottom ash (Cumbie and Van Horn 1978; Sorensen et al. 1982, 1984); and selenium-contaminated subsurface irrigation drainwater (Ohlendorf et al. 1986, 1987; Presser and Ohlendorf 1987; Schuler et al. 1990; Lemly 1993c; Hothem and Welsh 1994). Accumulation, transfer, and release of selenium by aquatic biota may affect the speciation and toxicity of dissolved selenium in aquatic environments (Besser et al. 1994). Depletion of dissolved selenite and increased concentrations of organoselenium compounds occur during seasonal peaks in phytoplankton abundance in freshwater and marine systems. For example, green algae (*Chlamydomonas reinhardtii*) previously exposed to inorganic radioselenium-75 produced increased concentrations of organoselenium species during population blooms and crashes (Besser et al. 1994).

Among terrestrial plants, selenium accumulations in species of *Aster*, *Astragalus*, and several other genera are sometimes spectacularly high ([Table 31.2](#)). *Astragalus* is the most widely distributed. About 24 of its more than 200 species are selenium accumulators that require selenium to grow well. The highest reported concentration in plants was 15,000 mg Se/kg DW, in loco weed (*Astragalus racemosus*) (Wilber 1983). Consumption of these and other selenium-accumulating forage plants by livestock has induced illness and death from selenium poisoning. Even at much lower concentrations, selenium may harm animals that eat considerable amounts of the forage. Plants that accumulate selenium tend to be deeper rooted than the grasses and survive more severe aridity, thus remaining as the principal forage for grazing in time of drought (Wilber 1983). There is little danger to human health of selenium toxicity from consuming game that foraged in high-selenium environments (Medeiros et al. 1993).

Selenium levels in freshwater biota are relatively low compared with those in their marine counterparts. In freshwater organisms, about 36% of the total selenium was present as selenate, and the rest as selenite and selenide. In marine samples, only 24% of the total selenium was present as selenate (Cappon and Smith 1982). The implications of this difference are not now understood, but have relevance in the ability of selenium to complex and detoxify various potentially toxic heavy metals, such as mercury and cadmium. In a nationwide monitoring of selenium and other contaminants in freshwater fishes, selenium ranged from 0.05 to 2.9 mg/kg FW whole fish and averaged about 0.6 mg/kg. Stations where concentrations in fish exceeded 0.82 mg/kg (>85th percentile) were in three areas: Atlantic coastal streams, Mississippi River system, and California ([Table 31.2](#)) (May and McKinney 1981). Among fish from Atlantic coastal streams, those from the Delaware River near Camden, New Jersey, had elevated whole-body concentrations (i.e., >1.0 and <3.0 mg Se/kg FW), which were attributed to the industrialized character of the river. In the Big Horn and Yellowstone Rivers, high selenium concentrations in fish may result from geologic sources of the element, including coal, phosphate, and sedimentary rock. Fish from the South Platte River near Denver, Colorado, may receive selenium from industrial effluents, or from natural and anthropogenic activities associated with the removal of deposits of coal, barite, and sulfur (May and McKinney 1981). These same trends persisted in more recent nationwide monitoring of freshwater fishes, with selenium concentrations usually highest in whole fish from stations in Utah, Nevada, Texas, California, Hawaii, and in arid locations of the western United States ([Table 31.2](#); Schmitt and Brumbaugh 1990). In California, where selenium was elevated in fish from the San Joaquin River, it was speculated that Selocide, a selenium-containing pesticide registered for use on citrus fruits in the 1960s, may have been a source, although contaminated irrigation drainwater was considered a more likely possibility (Ohlendorf et al. 1986). Of seven species of fishes analyzed

from the San Joaquin Valley, California, in 1986/1987, mosquitofish (*Gambusia affinis*) had the highest concentrations (11.1 mg Se/kg DW whole body); these fish were collected from canals and sloughs in the Grasslands Water District that received large inflows of subsurface agricultural drainage water (Saiki et al. 1991, 1992). Selenium persisted in the biota of the Grasslands drainage regions for at least 1 year after the switch to uncontaminated drainage water (Hothem and Welsh 1994).

Selenium bioconcentrates and biomagnifies in aquatic food chains from invertebrates to birds (Rusk 1991; Saiki et al. 1993). Maximum selenium concentrations reported in Cibola Lake in the lower Colorado River Valley in 1989/90 were 5.0 µg/L in water, and — in mg Se/kg DW — 3.3 in sediments, 1.2 in aquatic plants (*Myriophyllum*, *Ceratophyllum*), 4.6 in crayfish (*Procambarus clarkii*), and 9.2 in bluegills (*Lepomis macrochirus*) (Welsh 1992). Diet is the primary source of selenium to fish, as judged by radioiselenium-75 uptake studies in Canadian oligotrophic lakes (Harrison et al. 1990). Hatchery-reared smolts and adults of silver salmon (*Oncorhynchus kisutch*) had less selenium in livers than did wild fish, and this could account for the higher survival and better health of wild fish (Felton et al. 1990).

Belews Lake in North Carolina was contaminated with selenium during the 1970s from coal-fired power plant wastewater, causing mortality and reproductive failure in the fish population (Lemly 1993a, 1993c). Selenium concentrations in fish tissues were as high as 125 mg Se/kg DW and were as much as 100 times higher than those from nearby reference sites. There was a positive relation between tissue selenium concentrations and frequency of developmental malformations for largemouth bass and bluegill over the range 1 to 80 mg Se/kg DW tissue and 0% to 70% deformities. In 1992, selenium residues had declined to less than 20 mg/kg DW, but were still 5 to 18 times higher than those in reference lakes, and deformity frequency was 7 times higher (Lemly 1993a). Alterations in zooplankton species densities and dominance — but not diversity — were observed in Belews Lake between 1970 (uncontaminated), 1976/77 (selenium contamination), and 1984 to 1986. Observed changes are attributed to the dominance of planktivorous fishes (Marcogliese et al. 1992).

All reported selenium levels in tissues of marine invertebrates and plants were less than 2 mg Se/kg on a fresh weight (FW) basis, or 12 mg/kg dry weight (DW). In marine algae, most of the selenium accumulated was associated with proteins and may represent a form of storage prior to detoxification (Boisson et al. 1995). Higher levels are routinely recorded in liver and kidney tissues of marine and coastal vertebrates, including teleosts, birds, and mammals. Livers from adult seals were comparatively rich in selenium (Table 31.2); however, high concentrations in liver of maternal California sea lions were not reflected in the livers of newborn pups (Martin et al. 1976). In marine mammals, selenium concentrations are positively correlated with increasing age (Teigen et al. 1993; Mackey et al. 1996) and with increasing mercury residues in piscivorous mammals (Reijnders 1980; Wren 1984; Leonzio et al. 1992; Teigen et al. 1993). The mercury:selenium ratio was close to 1.0 in tissues of marine mammals at mercury concentrations >15 mg Hg/kg FW (Skaare et al. 1994). Increasing mercury concentrations in tissues of marine teleosts are also positively correlated with selenium (Ganther et al. 1972; Leonzio et al. 1982), although the evidence is conflicting (Tamura et al. 1975; Speyer 1980; Maher 1983). Selenium varies seasonally in crustaceans (Zafiroopoulos and Grimanis 1977). In general, concentrations of selenium in various tissues are usually higher in older than in younger organisms. Among marine vertebrates, selenium increases were especially pronounced among the older specimens of predatory, long-lived species (Eisler 1984).

Selenium concentrations in avian tissues are modified by the age, condition, and diet of the organism, the presence of other metals, and other variables. Fish-eating birds had the highest selenium concentrations in livers, and herbivorous species the lowest; omnivores were intermediate (Mora and Anderson 1995). Selenium concentrations were elevated in livers of molting birds compared to nonmolting conspecifics (Jenny et al. 1990), elevated in feathers of older terns and egrets when compared to younger stages (Burger et al. 1994), and elevated in tissues of marine birds that consume invertebrate prey animals with elevated selenium burdens (Goede et al. 1993).

Selenium concentrations in tissues of shorebirds were positively correlated with concentrations of copper, zinc (Wenzel and Gabrielsen 1995), and iron (Goede and Wolterbeek 1994). Feathers have been proposed as indicators of selenium exposure. However, variability in selenium concentrations in whole feathers is considerable (Goede 1991) (Table 31.2). In shorebirds, for example, the highest selenium concentrations are found in wing feathers, specifically in the outer primaries, notably primary 8. Moreover, within the vane of a single feather, the highest selenium concentrations are in the tip and the lowest at the basis. All of these differences need to be considered before feathers are routinely used as indicators of selenium exposure (Goede 1991).

Subsurface agricultural drainage waters from the western San Joaquin Valley, California, had elevated selenium concentrations, as selenate. In 1978, these drainage waters were diverted to Kesterson Reservoir, a pond system within the Kesterson National Wildlife Refuge (KNWR), with diversion complete by 1982. In 1983, aquatic birds at KNWR had unusual rates of death and developmental abnormalities attributed to selenium (Presser and Ohlendorf 1987). In 1984/85, selenium-induced recruitment failure was observed at KNWR in American avocets (*Recurvirostra americana*) and black-necked stilts (*Himantopus mexicanus*); unlike a nearby reference area, chicks at KNWR of either species did not survive to fledging (Williams et al. 1989). Selenium concentrations in livers of diving ducks from San Francisco Bay in 1982 were similar to those of dabbling ducks in the nearby San Joaquin Valley where reproduction was severely impaired (Ohlendorf et al. 1986b). Mean concentrations of selenium in kidneys of seven species of coastal birds collected from the highly industrialized Corpus Christi, Texas, area usually varied between 1.7 and 5.6 mg Se/kg FW, but were 10.2 mg/kg FW in one bird. According to White et al. (1980), selenium concentrations of this magnitude may be sufficient to impair reproduction in shorebirds. Barn swallows (*Hirundo rustica*) nesting at a selenium-contaminated lake in Texas had elevated concentrations of selenium in eggs and tissues when compared to conspecifics at a reference site. However, nest success of barn swallows was significantly higher at the contaminated site; development was normal at both sites (King et al. 1994).

Table 31.2 Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
MARINE		
Algae and macrophytes		
Whole	0.04–0.24 DW	1–3
Edible seaweeds, whole	0.16–0.39 DW; 0.047 FW	4
Molluscs		
American oyster, <i>Crassostrea virginica</i> Redwood Creek, San Francisco, CA		
Mantle	4.8 DW	5
Digestive gland	8.8 DW	5
Kidney	4.7 DW	5
Tomales Bay, CA		
Mantle	2.2 DW	5
Digestive gland	6.4 DW	5
Kidney	2.5 DW	5
Transferred from Redwood Creek to Tomales Bay for 56 days		
Mantle	3.5 DW	5
Digestive gland	6.5 DW	5
Kidney	3.8 DW	5
Bivalve molluscs		
Shell	0.03–0.06 DW	6
Soft parts	0.1–0.9 FW; 1.3–9.9 DW	2, 6–10

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Muscle	1.1–2.3 DW	11
Viscera	1.6–2.5 DW	11
Edible flesh, 3 species		
Total Se	0.22 (0.16–0.31) FW	12
As selenate	0.05 FW	12
As selenite and selenide	0.17 FW	12
Common mussel, <i>Mytilus edulis</i>		
Gills	2.0–16.0 DW	13
Viscera	Up to 5.0 DW	13
Mussel, <i>Mytilus galloprovincialis</i>		
Gills	7.0 DW	14
Soft parts	6.0 DW	14
Mantle	5.2 DW	14
Viscera	3.2 DW	14
Muscle	1.9 DW	14
Shell	<0.05 DW	14
Echinoderms		
Whole, 7 species	0.8–4.4 DW	15
Crustaceans		
Digestive system, 3 species	3.0–3.5 DW	11
Edible tissues sold for human consumption, 17 species	0.2–2.0 FW	4, 8, 10
Edible tissues, 2 species		
Total Se	0.21 FW	12
As selenate	0.05 FW	12
As selenite and selenide	0.16 FW	12
Muscle, 5 species	2.4–4.4 DW	11
Soft tissues, 2 species	2.0–2.8 DW	11
Copepods, whole	1.8–3.4 DW	3, 16
Euphausiid, <i>Meganyctiphanes norvegica</i>		
Viscera	11.7 DW	17
Eyes	7.8 DW	17
Muscle	1.8 DW	17
Exoskeleton	0.8 DW	17
Shrimp, <i>Lysmata seticaudata</i>		
Viscera	7.0 DW	14
Eyes	4.8 DW	14
Whole	2.6 DW	14
Muscle	1.9 DW	14
Exoskeleton	1.5 DW	14
Molts	0.3 DW	14
Sharks		
Muscle	0.2–0.8 FW	18
Fishes		
Digestive system, 4 species	1.0–2.4 DW	11
Liver		
2 species	2.6–6.6 DW	19
74 species	0.6–5.0 FW	8, 10, 20
13 species	5.0–30.0 FW	8
Meals, 3 species	1.0–4.0 DW	21
Muscle		
4 species	0.5–1.5 DW	11
182 species	0.1–2.0 FW	4, 8, 10, 19, 22, 23

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
5 species, Total Se	0.4 (0.2–0.6) FW	12
As selenate	0.1 FW	12
As selenite and selenide	0.3 FW	12
Whole, 21 species	0.3–2.0 FW	8, 23, 24
Japanese tunas, 4 species		
Liver	10.0–15.0 FW	25
White muscle	0.5–1.3 FW	25
Red muscle	3.5–9.1 FW	25
Snapper, <i>Chrysophrys auratus</i> ; Australia; 1976; muscle	Max. 0.85 FW	73
Black marlin, <i>Makaira indica</i>		
Muscle	0.4–4.3 FW	26
Liver	1.4–13.5 FW	26
Blue marlin, <i>Makaira nigricans</i>		
Kidney	23.0 FW	27
Blood	1.0 FW	27
Gill	1.0 FW	27
Muscle		
Total Se	3.3 (2.5–4.1) FW	12
As selenate	0.2 (0.09–0.3) FW	12
As selenite and selenide	3.1 (2.4–3.8) FW	12
Striped bass, <i>Morone saxatilis</i>		
Muscle	0.3 FW	28
Liver	0.6 FW	28
Tuna, canned	1.9–2.9 FW	29
Swordfish, <i>Xiphias gladius</i>		
Muscle	0.3–1.3 FW	30
Birds		
Kidney, 12 species	1.2–5.6 FW	31, 32
Liver; 5 species; Baja California; 1986	0.7–5.1 (0.2–7.3) FW	101
Western grebe, <i>Aechmophorus occidentalis</i> ; Puget Sound, Washington; 1986; liver	7.6–9.3 (2.2–24.0) DW	109
Great Skua, <i>Catharacta skua</i>		
Kidney	32.8 (13.3–89.1) DW	37
Liver	19.7 (6.7–34.6) DW	37
Oystercatcher, <i>Haematopus ostralegus</i>		
Kidney	12.7 (2.3–17.5) DW	37
Liver	12.8 (5.0–20.5) DW	37
Herring gull, <i>Larus argentatus</i>		
Kidney	14.1 (8.6–19.4) DW	37
Liver	7.9 (6.9–9.3) DW	37
Eggs; Long Island, New York; 1989–94	1.0–2.1 DW	102
Franklin's gull, <i>Larus pipixcan</i> ; Minnesota; 1994		
Feathers, males vs. females	0.5 DW vs. 0.6 DW	103
Eggs	3.0 DW	103
Diet (earthworms)	4.9 DW	103
Brown pelican, <i>Pelecanus occidentalis</i>		
Egg	0.19–0.38 FW	36
Liver	1.0–4.2 FW	36
White-faced ibis, <i>Plegadis chihi</i>		
Egg	0.3–1.1 FW	33
Wedge-tailed shearwater, <i>Puffinus pacificus</i>		
Egg	1.1–1.3 FW	35
Black skimmer, <i>Rynchops niger</i> ; breast feathers; New York	1.2–1.3 DW	104

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Seabirds		
Liver, 11 species	Means 17–107 DW	128
Most tissues, 3 species	Max. 2–34 DW	128
Seabirds; northern Norway; summer, 1992–93		
Kittiwake, <i>Rissa tridactyla</i> ; adults vs. fledglings		
Feather	1.8 FW vs. 1.3 FW	96
Liver	16.9 DW vs. 8.9 DW	96
Common guillemot, <i>Uria aalge</i>		
Feather	2.6 FW	96
Gonad	21.9 DW	96
Kidney	43.7 DW	96
Liver	17.6 DW	96
Brunnich's guillemot, <i>Uria lomvia</i>		
Feather	2.7 FW	96
Gonad	12.2 DW	96
Kidney	15.6 DW	96
Liver	17.6 DW	96
Shorebirds		
New Jersey, Cape May; 3 species; feathers; 1991–92	1.3–6.2 DW	106
Pacific coast; U.S.; 1984–85; livers		
Dunlin, <i>Calidris alpina</i>	12.9 (7.0–20.2) DW	105
Long-billed dowitcher, <i>Limnodromus scolopaceus</i>	11.1 (5.5–15.3) DW	105
Black-bellied plover, <i>Pluvialis squatoriora</i>	9.4 (5.8–29.9) DW	105
Texas; 1984; mercury-contaminated bay vs. reference site; eggs less shell		
Forster's tern, <i>Sterna forsteri</i>	0.71 FW vs. 0.68 FW	108
Black skimmer, <i>Rynchops niger</i>	0.8 FW vs. 0.3 FW	108
Sooty tern, <i>Sterna fuscata</i>		
Egg	1.1–1.4 FW	35
Common tern, <i>Sterna hirundo</i> ; feathers; Massachusetts; May–June		
Adults		
Age 2–3 years	1.3 DW	107
Age 9–10 years	2.1 DW	107
Age 16–21 years	2.4 DW	107
Fledglings, age 20–23 days	0.8 DW	107
Royal tern, <i>Sterna maxima</i>		
Egg	0.4–2.1 FW	34
Red-footed booby, <i>Sula sula</i>		
Egg	0.8–0.9 FW	35
Mammals		
Alaska; liver		
Bowhead whale, <i>Balaena mysticetus</i>	0.5–1.2 FW	85
Beluga whale, <i>Delphinapterus leucas</i>	4–75 FW; usually <20.0 FW	85
Bearded seal, <i>Erignathus barbatus</i>	0.5–5.3 FW	85
Ringed seal, <i>Phoca hispida</i>	1.2–5.7 FW	85
Minke whale, <i>Balaenoptera rostrata</i> ; Antarctic Ocean; 1990–91; urine	1.5 FW	84
Pilot whale, <i>Globicephala macrorhynchus</i>		
Blubber	0.8–1.4 FW	38
Liver	22.8–61.6 FW	38
Kidney	3.0–10.0 FW	38

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Italy; 1987–89; found stranded Striped dolphin, <i>Stenella coeruleoalba</i>		
Brain	9 (5–36) DW	88
Kidney	25 (50–101) DW	88
Liver	106 (2–960) DW	88
Muscle	(10–55) DW	88
Bottle-nosed dolphin, <i>Tursiops truncatus</i>		
Brain	4.9 (3.3–5.2) DW	88
Kidney	53 (21–186) DW	88
Liver	139 (2–2400) DW	88
Muscle	Max. 48 DW	88
Saimaa ringed seal, <i>Phoca hispida saimensis</i>		
Muscle	0.2–2.8 FW	23
Liver	29.0–170.0 FW	23
Kidney	0.3–3.0 FW	23
Blubber	0.06–0.11 FW	23
Harbor seal, <i>Phoca vitulina</i>		
Juveniles		
Kidney	0.6 (0.0–1.3) FW	39
Liver	2.8 (2.6–6.5) FW	39
Brain	1.1 (0.0–7.4) FW	39
Adults		
Kidney	3.5 (1.9–7.3) FW	39
Liver	109.0 (Max. 409.0) FW	39
Brain	3.7 (1.5–8.2) FW	39
Norway, 1989–90		
Brain, 4 species	<0.01 FW	86
Grey seal, <i>Halichoerus grypus</i>		
Kidney	Max. 4.1 FW	86
Liver	Max. 21.8 FW	86
Ringed seal, <i>Phoca hispida</i>		
Kidney	Max. 5.7 FW	86
Liver	Max. 3.7 FW	86
Harp seal, <i>Phoca groenlandica</i>		
Kidney	Max. 7.2 FW	86
Liver	Max. 3.4 FW	86
Harbor seal, <i>Phoca vitulina</i>		
Kidney	Max. 7.7 FW	86
Liver	Max. 7.8 FW	86
Harbor porpoise, <i>Phocaena phocoena</i> ; Norway; 1989–90; ages 1–5 years		
Kidney	0.6–8.6 FW	87
Liver	0.7–14.2 FW	87
Seals		
Liver, 4 species	6.1–170.0 FW	23, 40, 41
California sea lion, <i>Zalophus californianus</i>		
Mothers with normal pups		
Liver	260.0 DW	42
Kidney	22.0 DW	42
Normal pups		
Liver	4.1 DW	42
Kidney	6.1 DW	42

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Mothers with premature pups		
Liver	79.0 DW	42
Kidney	12.0 DW	42
Pups born prematurely		
Liver	2.9 DW	42
Kidney	3.7 DW	42
FRESHWATER		
Algae and higher plants		
Algae, whole	<2.0 DW	43
Higher plants	0.1 DW	44
Aquatic mosses	0.8 DW	44
Filamentous algae		
Se-contaminated area	35.2 (12–68) DW	57
Control area	<0.5 DW	57
Rooted plants		
Se-contaminated area	52.1 (18–79) DW	57
Control area	0.4 DW	57
Molluscs		
Mussels, 3 species, NY state		
Soft parts	2.0–4.0 DW	71
Asiatic clam, <i>Corbicula fluminea</i>		
Whole, Florida	0.7 FW	45
Arthropoda		
Zooplankton	0.8–3.9 DW	46
Plankton		
Se-contaminated area	85 (58–124) DW	57
Control site	2 (1.4–2.9) DW	57
Insects		
Se-contaminated area	20–218 DW	57
Control site	1.1–3.0 DW	57
Mayfly, <i>Hexagenia</i> sp.	0.3–0.5 FW	45
Fishes		
California		
San Joaquin River; whole		
1984–85; 5 species	Max. 23.0 DW	75
1986; 5 species	Max. 11.0 DW	75
1986–87; 7 species; whole		
Sacramento River	Max. 2.1 DW	76
San Francisco Bay	Max. 3.3 DW	76
San Joaquin River	Max. 11.1 DW	76
Reservoirs receiving ash pond effluent		
Bluegill, <i>Lepomis macrochirus</i> ; ovary	Max. 12.0 FW	89
Largemouth bass, <i>Micropterus salmoides</i> ; ovary	Max. 7.0 FW	89
Common carp, <i>Cyprinus carpio</i>		
Whole	1.0 (0.7–1.4) DW	47
Liver	3.6 (2.2–5.2) DW	47
Bluegill, <i>Lepomis macrochirus</i>		
From water containing <5 µg Se/L		
White muscle	0.04 FW	48
Liver	0.7 FW	48
Spleen	1.6 FW	48
Erythrocytes	0.04 FW	48
Heart	1.0 FW	48

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
From water containing 22.6 µg Se/L		
White muscle	3.1 FW	48
Liver	11.2 FW	48
Spleen	17.7 FW	48
Erythrocytes	7.2 FW	48
Heart	12.8 FW	48
Upper Mississippi River		
Whole	1.2 (0.7–1.4) DW	47
California, San Joaquin Valley, 1988		
Carcass		
Males	2.0 (1.5–3.1) DW	80
Females	1.9 (1.2–3.0) DW	80
Gonads		
Males	3.8 (3.2–4.1) DW	80
Females	3.2 (2.3–4.3) DW	80
Largemouth bass, <i>Micropterus salmoides</i>		
From water containing <5 µg Se/L		
White muscle	0.05 FW	48
Liver	0.8 FW	48
Spleen	1.8 FW	48
Erythrocytes	0.07 FW	48
Heart	1.2 FW	48
From water containing 22.6 µg Se/L		
White muscle	1.7 FW	48
Liver	10.2 FW	48
Spleen	16.6 FW	48
Erythrocytes	8.0 FW	48
Heart	12.0 FW	48
Colorado River Valley; Cibola Lake, 1989–90		
Liver	8.4–18.0 DW	81
Muscle	4.5–5.9 DW	81
Ovary	5.4–7.8 DW	81
Apalachicola River, Florida		
Whole		
Females	0.3–0.4 FW	45
Males	0.3–0.5 FW	45
Juveniles	0.3–0.5 FW	45
Eggs	0.7–1.0 FW	45
Striped bass, <i>Morone saxatilis</i> ; California; whole; juveniles		
San Joaquin River		
1984	6.5 DW	74
1985	4.1 DW	74
1986	3.5 DW	74
San Joaquin Valley vs. San Francisco estuary; 1986	Max. 7.9 DW vs. Max. 3.3 DW	74
Channel catfish, <i>Ictalurus punctatus</i>		
Apalachicola River, Florida		
Whole		
Females	1.1–0.3 FW	45
Males	0.2–0.3 FW	45
Juveniles	0.4–0.6 FW	45
Eggs	0.8–2.1 FW	45
Threadfin shad, <i>Dorosoma petenense</i>		
Whole	0.3–0.5 FW	45

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Green sunfish, <i>Lepomis cyanellus</i>		
From water containing 13 µg Se/L		
Liver	7.0–21.4 FW	49
Muscle	2.3–12.9 FW	49
From control site		
Liver	1.3 FW	49
Muscle	1.3 FW	49
Trout, 2 species, Wyoming		
From water containing 12.3–13.3 µg Se/L		
Liver	50.0–70.0 FW	50
Muscle	<2.0 FW	50
Skin	Max. 4.8 FW	50
Mosquitofish, <i>Gambusia affinis</i> , whole		
From Se-contaminated irrigation drainwater pond	170 (65–360) DW	57, 77
Control site	1.3 (1.2–1.4) DW	57
Coho salmon, <i>Oncorhynchus kisutch</i>		
Muscle	0.7–1.0 DW	51
Liver	3.8 DW	51
Adults, liver		
Ocean caught	8.8 DW; 1.7 FW	79
Estuary caught	8.1 DW; 1.6 FW	79
Hatchery return	7.6 DW; 1.6 FW	79
Farmed fish	4.8 DW; 1.0 FW	79
Smolts, liver		
Hatchery reared	2.0 DW; 0.4 FW	79
Naturally reared	3.6 DW; 0.7 FW	79
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
Muscle	1.6 DW	51
Razorback sucker, <i>Xyrauchen texanus</i> ; Green River, Utah		
Eggs		
1988	4.9 DW	82
1991	28.0 DW	82
1992	3.7–10.2 DW	82
Milt, 1992	<1.1–6.7 DW	82
Fry, 1992	2.2 DW; 0.54 FW	82
Muscle, 1992		
Females	4.4–32.0 DW	82
Males	3.6–26.0 DW	82
Maximum concentrations	11.5–54.1 DW	83
Fish		
Muscle		
25 species	0.0–0.5 FW	52–56
18 species	0.5–1.0 FW	53–55
3 species	1.0–2.0 FW	55, 58
3 species		
Total Se	0.25 (0.15–0.34) FW	12
As selenate	0.09 FW	12
As selenate and selenide	0.16 FW	12
10 species, Western Lake Erie	0.4–1.5 FW; 1.8–8.1 DW	46
Liver		
17 species	0.0–0.5 FW	59
7 species	0.5–1.0 FW	59
4 species	0.6–5.0 FW	10

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Whole		
Nationwide, U.S.		
1972	0.60 (0.57–0.64) FW	60
1973	0.46 (0.42–0.49) FW	60
1976–77	0.58 (0.53–0.62) FW	60
1978–79	0.48 FW	78
1980–81	0.46 FW	78
1984–85	0.42 FW	78
1976–84	Max. 2.3–3.6 FW	78
5 species	0.5–1.9 FW	61
4 species	0.2–0.3 DW	56
6 species	0.0–0.5 FW	62
12 species	0.5–1.0 FW	62
6 species	1.0–2.0 FW	62
6 species	2.1–6.0 FW	62
Amphibians		
Southern toad, <i>Bufo terrestris</i> ; adults; whole		
From coal ash settling basins vs. reference site (sediments 4.4 mg Se/kg DW vs. 0.1 mg/kg)	17.4 DW vs. 2.1 DW	130
Transferred from reference site to settling basin for 7–12 weeks	2.1 DW vs. 3.5–5.5 DW	130
Bullfrog, <i>Rana catesbeiana</i> ; tadpoles; South Carolina; 1997		
With digestive tract		
Body	9.7 DW; 1.9 FW	131
Tail	11.5 DW; 1.8 FW	131
Whole	9.3 DW; 1.9 FW	131
Without digestive tract		
Body without gut	10.0 DW	131
Tail	12.6 DW	131
Whole	6.7 DW	131
Digestive tract		
	18.2 DW	131
Various species, liver	0.7–4.7 FW	43
Reptiles		
Water snake, <i>Natrix</i> sp.		
Whole, Florida	0.3–0.5 FW	45
Birds		
Little green heron, <i>Butorides virescens</i> ; Apalachicola River, Florida; whole	0.1–0.5 FW	45
California		
Aquatic birds; 4 species; 1985–88; Grasslands area; livers; North Grasslands vs. South Grasslands (more Se-contaminated area)		
1985	Max. 14 DW vs. Max. 25 DW	97
1987	Max. 10 DW vs. Max. 24 DW	97
1988	Max. 12 DW vs. Max. 14 DW	97
Grasslands drainage area (Se-contaminated prior to 1985); 1986 vs. 1987; eggs		
Mallard, <i>Anas platyrhynchos</i>	6 DW vs. 20 DW	98
Cinnamon teal, <i>Anas cyanoptera</i>	0.2 DW vs. 12 DW	98
Gadwall, <i>Anas strepera</i>	5.3 DW vs. 8 DW	98
Near Salton Sea; 1985; eggs		
Black-crowned night heron, <i>Nycticorax nycticorax</i>	1.1 (0.9–1.4) FW	99
Great egret, <i>Casmerodius albus</i>	0.6 (0.5–0.8) FW	99

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
San Francisco Bay, 1982		
Greater scaup, <i>Aythya marila</i> ; liver	19 (7–31) DW	100
Surf scoter, <i>Melanitta perspicillata</i> ; liver	34 (16–59) DW	100
From Kesterson National Wildlife Refuge (KNWR), California, nesting on Se-contaminated irrigation drainwater ponds — 1983		
American coot, <i>Fulica americana</i>		
Liver	37 (21–63) DW	57
Egg	54 (34–110) DW	57
Ducks, <i>Anas</i> spp.		
Liver	28.6 (19–43) DW	57
Egg	9.9 (2.2–46) DW	57
Black-necked stilt, <i>Himantopus mexicanus</i>		
Egg	32.7 (12–74) DW	57
American avocet, <i>Recurvirostra americana</i>		
Egg	9.1 DW	57
Eared grebe, <i>Podiceps nigricollis</i>		
Liver	130.0 DW	57
Egg	81.4 (72–110) DW	57
From Volta Wildlife Area, California, control site — 1983		
American coot		
Liver	5.0 (4.4–5.6) DW	57
Ducks, 2 species		
Liver	4.1 (3.9–4.4) DW	57
Black-necked stilt		
Liver	6.1 DW	57
KNWR vs. reference site; 1983–85		
Diets	>50 DW vs. <2 DW	125
Livers		
Adults, 8 species	26–101 DW vs. 3–11 DW	125
Juveniles, 5 species	21–95 DW vs. 2–4 DW	125
Canada; eastern section; from freezer archives; total Se		
Common loon, <i>Gavia immer</i>		
Kidney	15 DW	129
Liver	15 DW	129
Muscle	2.8 DW	129
Common merganser, <i>Mergus merganser</i>		
Kidney	8.5 DW	129
Liver	9.7 DW	129
Muscle	1.8 DW	129
Willet, <i>Catoptrophorus semipalmatus</i> ; 1986; south Texas; liver	2.8–8.3 DW	110
China; feathers; 1992		
Heron; chicks; 2 species	1.0–2.0 DW	111
Egrets; chicks; 3 species	1.2–2.8 DW	111
Common loon, <i>Gavia immer</i>		
Egg	0.4 (0.3–0.7) FW	63
Red-breasted merganser, <i>Mergus serrator</i>		
Egg	0.47–1.0 FW	72
Mallard, <i>Anas platyrhynchos</i>		
Egg	0.28–0.81 FW	72
Flamingo, <i>Phoenicopterus ruber</i> ; feather; France; 1988		
Adults	7.1 (1.6–33.0) FW	112
Juveniles	0.8 FW; Max. 2.3 FW	112

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
White-faced ibis, <i>Plegadis chihi</i> ; Carson Lake, Nevada; 1985–86		
Eggs	1.9–5.4 DW	113
Livers	9.6 (5–27) DW	113
Eared grebe, <i>Podiceps nigricollis</i> ; Stewart Lake, North Dakota; 1991; eggs	4.5 (2.9–6.5) DW; no deformities	114
TERRESTRIAL		
Fungi	<2.0 DW	43
Macrophytes		
Western wheat grass, <i>Agropyron smithii</i> , South Dakota, plant top	0.0–8.4 DW	43
Little bluestem, <i>Andropogon scoparius</i> , plant top	0.0–6.0 DW	43
Asparagus, <i>Asparagus officinale</i> , western U.S.	2.7–11.0 DW	43
Aster, whole		
<i>Aster caeruleus</i>	560.0 DW	43
<i>A. commutatus</i>	Max. 590.0 DW	43
<i>A. multiflora</i>	Max. 320.0 DW	43
<i>A. occidentalis</i>	284.0 DW	43
Milk vetch, <i>Astragalus argillosus</i>		
Top	385.0 DW	43
Root	27.0 DW	43
<i>A. beatii</i>		
Top	1963.0 DW	43
Root	6.0 DW	43
<i>A. bisulcatus</i>		
Top	Max. 10,239.0 DW	43
Seed	305.1 DW	43
<i>A. confertiflorus</i>		
Top	1372.0 DW	43
<i>A. crotalariae</i>		
Top	2000.0 DW	43
Root	45.0 DW	43
Loco weed, <i>Astragalus</i> spp.		
	Max. 46,000.0 AW;	43
	Max. 6000.0 DW	
Saltbush, <i>Atriplex</i> spp.	300.0–1734.0 DW	43
Oats, <i>Avena sativa</i>	2.0–15.0 DW	43
Buffalo grass, <i>Bouteloua dactyloides</i>	2.7 (0.0–12.0) DW	43
Indian paint brush, <i>Castilleja</i> spp.	0.0–1812.0 DW	43
Gumweed, <i>Grindelia squarrosa</i>	38 (0.0–2160) DW	43
Broomweeds		
<i>Gutierrezia</i> spp.	Max. 723.0 DW	43
<i>Haplopappus</i> spp.	Max. 4800.0 DW	43
Tobacco, <i>Nicotiana tabacum</i>		
Leaf	5.8 DW	43
Stem	44.2 DW	43
Rice, <i>Oryza sativa</i>		
Grain	0.09–0.11 FW	43
Pear, <i>Pyrus communis</i>		
Fruit	0.02 FW	43
Rye, <i>Secale cereale</i>		
Potato, <i>Solanum tuberosum</i>		
Tuber	0.2–0.9 DW	43

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Wheat, <i>Triticum aestivum</i>		
Grain	1.1–35.0 DW	43
Stem and leaf	17.0 DW	43
Root	36.0 DW	43
Corn, <i>Zea mays</i>		
Grain	1.0–20.0 DW	43
Grape, <i>Vitis</i> sp.		
Raisin	<0.001 FW	43
Annelids		
Earthworms, whole		
From normal soil	2.2 FW	64
From selenite-enriched soil	7.5 FW	64
From soil amended with sewage sludge		
Whole	15.0–22.4 DW	65
Casts	0.6–0.7 DW	65
From control field		
Whole	22.1 DW	65
Casts	0.6 DW	65
Arthropods		
Sow bug, <i>Porcellio</i> sp.	0.9 FW	43
Crane fly, larva, <i>Tipula</i> sp.	0.9 FW	43
"Fly larvae," whole, from <i>Astragalus</i> plant with 1800 mg Se/kg	20.0 FW	43
Birds		
Cattle egret, <i>Bubulcus ibis</i> ; juveniles; 1989–91; feathers		
New York	1.3 DW	115
Delaware	1.6 DW	115
Puerto Rico	1.3 DW	115
Cairo, Egypt	0.3 DW	115
Aswan, Egypt	1.0 DW	115
Barn swallow, <i>Hirundo rustica</i> ; 1986–87; Martin Lake, Texas (selenium-contaminated) vs. reference site		
Eggs	Max. 12 DW vs. Max. 4.5 DW	116
Kidneys	Max. 14 DW vs. Max. 5.8 DW	116
Wood stork, <i>Mycteria americana</i> ; feathers		
Florida, juveniles, 1991	1.8 DW	117
Costa Rica		
Adults, 1992	3.4 DW	117
Juveniles		
1990	2.2 DW	117
1992	1.5 DW	117
House sparrow, <i>Passer domesticus</i>		
Whole	0.6 DW	66
Ring-necked pheasant, <i>Phasianus colchicus</i>		
Whole	0.6 DW	66
Common blackbird, <i>Turdus merula</i>		
Whole	2.1 DW	66
Mammals		
California; San Francisco Bay; 1989; livers		
California vole, <i>Microtus californicus</i>	0.5–1.6 DW	90
House mouse, <i>Mus musculus</i>	1.5–4.8 DW	90
Deer mouse, <i>Peromyscus maniculatus</i>	2.3–3.5 DW	90

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
California; Kesterson National Wildlife Refuge vs. control site; May 1984; liver		
California vole, <i>Microtus californicus</i>	Max. 250.0 DW vs. Max. 1.4 DW	120
House mouse, <i>Mus musculus</i>	Max. 41.0 DW vs. Max. 3.7 DW	120
Desert cottontail, <i>Sylvilagus audubonii</i>	Max. 3.3 DW vs. Max. 0.1 DW	120
South Dakota; various species; muscle	0.2–1.1 FW	95
Washington State; 1992–93; blood		
Moose, <i>Alces alces</i>	0.015 (0.01–0.02) FW	94
Elk, <i>Cervus elaphus</i>	0.04–0.16 FW; Max. 0.49 FW	94
Mule deer, <i>Odocoileus hemionus</i>	0.08 (0.06–0.15) FW	94
California bighorn sheep, <i>Ovis canadensis californiana</i>	0.09 (0.04–0.13) FW	94
Livestock	>0.1 FW (adequate selenium)	94
Wyoming; muscle; animals had access to forage grown on medium up to 5.0 mg/L water-soluble selenium) to high (>10 mg Se/L)		
American bison, <i>Bison bison</i>	0.5 FW; 1.7 DW	95
Cattle, <i>Bos</i> sp.	0.1 FW; 0.5 DW	95
Elk, <i>Cervus elaphus</i>	0.4 FW; 1.6 DW	95
Mule deer	0.6 FW; 2.5 DW	95
Common beaver, <i>Castor canadensis</i>		
Liver	0.2 FW	67
Kidney	0.9 FW	67
Intestine	0.04 FW	67
Muscle	0.09 FW	67
Human, <i>Homo sapiens</i>		
Fetus, United States		
Most tissues	<0.4 FW	118
Thyroid, blood	<1.0 FW	118
Liver	2.8 FW	118
Adults, United States		
Urine	0.002–0.113 FW	118
Milk	0.007–0.053 FW	118
Semen	0.016–0.131 FW	118
Erythrocytes	0.02–0.52 FW	118
Whole blood	0.08–0.3 FW	118
Nails	0.08–3.8 FW	118
Hair	0.6 FW	118
Pancreas, kidney	0.6–0.9 FW	118
Liver	0.6–1.7 FW	118
Diet		
Fruits and vegetables	Usually <0.03 FW	118
Grains and cereals	0.03–1.4 FW	118
Brazil nuts	14.7 (0.2–253.0) FW	118
Dairy products	0.01–0.1 FW	118
Meat and poultry		
Muscle	0.1–0.5 FW	118
Organ meats	0.4–2.3 FW	118
Seafood	0.2–3.4 FW	118

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
River otter, <i>Lutra canadensis</i>		
Liver	2.1 FW	67
Kidney	1.9 FW	67
Intestine	1.1 FW	67
Muscle	0.2 FW	67
Woodchuck, <i>Marmota monax</i>		
From flyash landfill vicinity		
Adults		
Liver	2.2–10.7 DW	68
Lung	1.4–4.4 DW	68
Juveniles		
Liver	3.9–6.4 DW	68
Lung	2.1–2.8 DW	68
From control area		
Adults		
Liver	0.4 DW	68
Lung	0.4 DW	68
Juveniles		
Liver	0.2–0.4 DW	68
Lung	0.2 DW	68
Field vole, <i>Microtus agrestis</i>		
Whole	0.5 DW	66
Mule deer, <i>Odocoileus hemionus</i> ; California; whole blood; 1981–88		
Winter	0.07 FW	91
Spring	0.05 FW	91
Summer	0.09 FW	91
Fall	0.02 FW	91
Range	0.02–0.17 FW	91
Most deer	<0.1 FW (Se-deficient)	92
White-tailed deer, <i>Odocoileus virginianus</i>		
Muscle	0.16 (0.05–0.49) DW	69
Southern Florida; 1984–88		
Heart	0.37 (0.01–1.0) DW	93
Kidney	3.7 (1.2–11.3) DW	93
Liver	0.7 (0.1–4.3) DW	93
Serum	0.05 (0.01–0.5) FW	93
Raccoon, <i>Procyon lotor</i>		
Liver	1.8 FW	67
Kidney	1.9 FW	67
Muscle	0.2 FW	67
Norway rat, <i>Rattus norvegicus</i>		
Whole	0.4 DW	66
Rock squirrel, <i>Spermophilus variegatus</i>		
Kidney	8.9–53.0 DW; Max. 90.0 DW	70
Mole, <i>Talpa europaea</i>		
Whole	2.6 DW	66

INTEGRATED STUDIES

California; Kesterson NWR vs. control site; 1984–85; liver

Gopher snake, <i>Pituophis melanoleucus</i>	11.1 (8.2–32.0) DW vs. 2.1 (1.3–3.6) DW	121
Bullfrog, <i>Rana catesbeiana</i>	45.0 DW vs. 6.2 DW	121

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
California; Kesterson NWR vs. control site; August 1983; maximum values recorded		
Water	0.3 FW vs. 0.0005 FW	124
Sediments	8.8 DW vs. not detectable (ND)	124
Detritus	80 DW vs. 2 DW	124
Algae	330 DW vs. <2 DW	124
Rooted plants	300 DW vs. <1 DW	124
Aquatic insects	290 DW vs. <3 DW	124
Mosquitofish	290 DW vs. ND	124
California; San Joaquin River; 1987; maximum concentrations recorded		
Water	0.025 FW	122
Sediments	3 DW	122
Invertebrates	14 DW	122
Fishes	17 DW	122
Greenland; 1975–91		
Bivalve molluscs; 3 species; soft parts	0.2–0.9 FW	127
Crustaceans; 6 species; whole	0.2–3.2 FW	127
Fish; 5 species		
Liver	0.3–0.9 FW	127
Muscle	<0.2–0.7 FW	127
Seabirds; 9 species		
Kidney	3.7–17.6 FW	127
Liver	1.9–14.1 FW	127
Muscle	0.5–4.4 FW	127
Seals; 2 species		
Kidney	2.6–4.2 FW	127
Liver	1.0–7.6 FW	127
Muscle	0.2–0.4 FW	127
Whales; 4 species		
Kidney	1.5–6.3 FW	127
Liver	1.7–5.0 FW	127
Muscle	Max. 0.2 FW	127
Skin	Max. 47.9 FW	127
Polar bear, <i>Ursus maritimus</i>		
Kidney	6.0–11.6 FW	127
Liver	3.1–9.1 FW	127
Muscle	<0.2–1.3 FW	127
Norway; 1990–91; near Russian nickel smelter vs. reference site; liver		
Willow ptarmigan, <i>Lagopus lagopus</i>	0.9 DW vs. 0.5 DW	119
Blue hare, <i>Lepus timidus</i>	Max. 1.8 DW vs. Max. 0.6 DW	119
Common shrew, <i>Sorex araneus</i>	Max. 4.6 DW vs. 4.5 DW	119
Grey-sided vole, <i>Clethrionomys rufocaninus</i>	Max. 1.8 DW vs. no data	119
Texas; shoalgrass community; Lower Laguna Madre; 1986–87		
Sediments	2.8 (0.5–4.5) DW	123
Shoalgrass, <i>Halodule wrightii</i> ; rhizomes	Not detected	123
Grass shrimp, <i>Palaeomonetes</i> sp.; whole	1.2 (0.7–1.8) DW	123
Brown shrimp, <i>Penaeus aztecus</i> ; whole	1.8 (0.6–3.2) DW	123
Blue crab, <i>Callinectes sapidus</i> ; whole except legs, carapace, and abdomen	1.3 (0.4–3.9) DW	123
Pinfish, <i>Lagodon rhomboides</i> ; whole	1.4 (0.8–2.2) DW	123

Table 31.2 (continued) Selenium Concentrations in Field Populations of Selected Species of Flora and Fauna (Values shown are in mg total Se/kg [ppm] fresh weight [FW], dry weight [DW], or ash weight [AW]. Hyphenated numbers show range, and single numbers the mean; where both appear, the range is in parentheses.)

Ecosystem, Taxonomic Group, Organism, Tissue, Location, and Other Variables	Concentration (ppm)	Reference ^a
Lower Colorado River Valley; 1985–91		
Sediments	1.2 (0.3–3.9) DW	126
Crayfish	3.5 (1.5–3.9) DW	126
Marsh birds, livers		
Rails, 3 species	13.1–26.0 DW	126
Others, 7 species	2.6–8.5 DW	126

^a 1, Chau and Riley 1970; 2, Lunde 1970; 3, Tijoe et al. 1977; 4, Noda et al. 1979; 5, Okazaki and Panietz 1981; 6, Bertine and Goldberg 1972; 7, Karbe et al. 1977; 8, Hall et al. 1978; 9, Fukai et al. 1978; 10, Luten et al. 1980; 11, Maher 1983; 12, Cappon and Smith 1982; 13, Stump et al. 1979; 14, Fowler and Benayoun 1976c; 15, Papadopoulou et al. 1976; 16, Zafiroopoulos and Grimanis 1977; 17, Fowler and Benayoun 1976a; 18, Glover 1979; 19, Grimanis et al. 1978; 20, de Goeij et al. 1974; 21, Kifer and Payne 1968; 22, Bebbington et al. 1977; 23, Kari and Kauranen 1978; 24, United Nations 1979; 25, Tamura et al. 1975; 26, MacKay et al. 1975; 27, Schultz and Ito 1979; 28, Heit 1979; 29, Ganther et al. 1982; 30, Freeman et al. 1978; 31, Turner et al. 1978; 32, White et al. 1980; 33, King et al. 1980; 34, King et al. 1983; 35, Ohlendorf and Harrison 1986; 36, Blus et al. 1977; 37, Hutton 1981; 38, Stoneburner 1978; 39, Reijnders 1980; 40, Smith and Armstrong 1978; 41, van de Ven et al. 1979; 42, Martin et al. 1976; 43, Jenkins 1980; 44, Rossi et al. 1976; 45, Winger et al. 1984; 46, Adams and Johnson 1977; 47, Wiener et al. 1984; 48, Lemly 1982b; 49, Sorensen et al. 1984; 50, Kaiser et al. 1979; 51, Rancitelli et al. 1968; 52, Utne and Bligh 1971; 53, Willford 1971; 54, Tong et al. 1971; 55, Pakkala et al. 1972; 56, Rossi et al. 1976; 57, Ohlendorf et al. 1986; 58, Schroeder et al. 1970; 59, Lucas et al. 1970; 60, May and McKinney 1981; 61, Pratt et al. 1972; 62, Walsh et al. 1977; 63, Haseltine et al. 1983; 64, Birkner 1978; 65, Helmke et al. 1979; 66, Nielsen and Gissel-Nielsen 1975; 67, Wren 1984; 68, Fleming et al. 1979; 69, Ullrey et al. 1981; 70, Sharma and Shupe 1977; 71, Heit et al. 1980; 72, Haseltine et al., 1981; 73, Chvojka et al. 1990; 74, Saiki and Palawski 1990; 75, Saiki et al. 1992; 76, Saiki et al. 1991; 77, Saiki 1987; 78, Schmitt and Brumbaugh 1990; 79, Felton et al. 1990; 80, Nakamoto and Hassler 1992; 81, Welsh 1992; 82, Hamilton and Waddell 1994; 83, Waddell and May 1995; 84, Hasunuma et al. 1993; 85, Mackey et al. 1996; 86, Skaare et al. 1994; 87, Teigen et al. 1993; 88, Leonzio et al. 1992; 89, Baumann and Gillespie 1986; 90, Clark et al. 1992; 91, Dierenfeld and Jessup 1990; 92, Oliver et al. 1990b; 93, McDowell et al. 1995; 94, Hein et al. 1994; 95, Medeiros et al. 1993; 96, Wenzel and Gabrielsen 1995; 97, Paveglio et al. 1992; 98, Hothem and Welsh 1994; 99, Ohlendorf and Marois 1990; 100, Ohlendorf et al. 1986b; 101, Mora and Anderson 1995; 102, Burger and Gochfeld 1995; 103, Burger and Gochfeld 1996; 104, Burger and Gochfeld 1992; 105, Custer and Meyers 1990; 106, Burger et al. 1993b; 107, Burger et al. 1994; 108, King et al. 1991; 109, Henny et al. 1990; 110, Custer and Mitchell 1991; 111, Burger and Gochfeld 1993; 112, Amiard-Triquet et al. 1991; 113, Henny and Herron 1989; 114, Olson and Welsh 1993; 115, Burger et al. 1992; 116, King et al. 1994; 117, Burger et al. 1993a; 118, USPHS 1996; 119, Kalas et al. 1995; 120, Clark 1987; 121, Ohlendorf et al. 1988; 122, Saiki et al. 1993; 123, Custer and Mitchell 1993; 124, Saiki and Lowe 1987; 125, Ohlendorf et al. 1990; 126, Rusk 1991; 127, Dietz et al. 1996; 128, Kim et al. 1998; 129, Scheuhammer et al. 1998; 130, Hopkins et al. 1998; 131, Burger and Snodgrass 1998.

31.4 DEFICIENCY AND PROTECTIVE EFFECTS

Selenium is an essential nutrient for most plants and animals. It constitutes an integral part of the enzyme glutathione peroxidase and may have a role in other biologically active compounds, especially Vitamin E and the enzyme formic dehydrogenase. Some animals require selenium-containing amino acids (*viz.* selenocysteine, selenocystine, selenomethionine, selenocystathione, selenium-methylselenocysteine, and selenium-methylselenomethionine), but reportedly are incapable of producing them. Selenium also forms part of certain proteins, including cytochrome c, hemoglobin, myoglobin, myosin, and various ribonucleoproteins (Rosenfeld and Beath 1964; Eisler 1985; USPHS 1996).

The availability of selenium to plants may be lessened by modern agricultural practices, eventually contributing to selenium deficiency in animal consumers. For example, fertilizers containing nitrogen, sulfur, and phosphorus all influence selenium uptake by plants through different

modes of action, the net effect being a reduction in selenium uptake (Frost and Ingvoldstad 1975). The buildup of sulfur (as sulfates) in the soil — due to acid rain, fertilizers, and other sources — interferes with selenium accumulation by crops (Frost and Ingvoldstad 1975). In addition, high dietary levels of various heavy metals (including copper, zinc, silver, and mercury) contribute to selenium deficiency in animals (Frost and Ingvoldstad 1975; Harr 1978), presumably as a result of selenium binding with the metal into biologically unavailable forms (Harr 1978; Kaiser et al. 1979).

Clinical selenium deficiency in ruminants is expressed as white muscle disease, lethargy, impaired reproduction, weight loss and reduced growth, shedding, decreased immune response, decreased erythrocyte glutathione peroxidase, and sudden death (Knox et al. 1987; Flueck and Flueck-Smith 1990). Selenium deficiency — as judged by blood concentrations <0.1 mg Se/L — has been documented in California among domestic cattle, mule deer (*Odocoileus hemionus*), pronghorn antelope (*Antilocapra americana*), elk (*Cervus elaphus*), and bighorn sheep (*Ovis canadensis*) (Oliver et al. 1990a). More than 95% of black-tailed deer (*Odocoileus hemionus columbianus*) in northern California had inadequate blood selenium levels (37 µg/kg whole blood FW), as judged by recommended levels for cattle (>40 µg/kg) and sheep (>50 µg/kg) (Flueck 1994). Selenium deficiency in red deer was reversed with subcutaneous injection of 50 mg Se/mL as barium selenate at 2 mL per 50 kg body weight (Knox et al. 1987). Selenium boluses calibrated to release 1.0 mg selenium daily, given orally to selenium-deficient adult female black-tailed deer, effectively raised whole blood levels to 121 µg Se/kg FW. These selenium-supplemented females produced fawns with increased survival (0.83 fawns/female) when compared to untreated does (0.32 fawns/female) (Flueck 1994). Supplementation of selenium-deficient mule deer does with intraruminal selenium pellets can triple fawn survivability (Oliver et al. 1990a). Some feral animals selectively prefer plants with comparatively elevated selenium content. The black rhinoceros (*Diceros bicornis*) in Kenya, for example, prefers 10 of 103 plants ingested; preferred vegetation contained 3.0 to 6.3 µg Se/kg FW vs. 1.8 to 2.7 µg/kg FW in nonpreferred plants (Ghebremeshel et al. 1991).

There is a general consensus that selenium deficiency in livestock is increasing in many countries, resulting in a need for added selenium in the food. Selenium deficiency is considered by some researchers to constitute a greater threat to health than selenium poisoning. Studies with animals and humans have suggested that selenium deficiency, in part, underlies susceptibility to cancer, arthritis, hypertension, heart disease, and possibly periodontal disease and cataracts (Frost and Ingvoldstad 1975; Shamberger 1981; Robberecht and Von Grieken 1982). These linkages have not yet been demonstrated conclusively. For example, eye lens cataract was induced in 10-day-old male rats by selenate, selenite, selenomethionine, and selenocystine, presumably through interference with glutathione metabolism (Ostadalova and Babicky 1980). On the other hand, adverse effects of selenium inadequacy have been clearly documented for a wide variety of organisms, including bacteria, protozoans, Atlantic salmon, rainbow trout, Japanese quail, ducks, poultry, rats, dogs, horses, domestic sheep, bighorn sheep, swine, cattle, antelopes, gazelles, deer, monkeys, and humans (Jensen 1968; Frost and Ingvoldstad 1975; Jones and Stadtman 1975; Fishbein 1977; Harr 1978; Kaiser et al. 1979; Hilton et al. 1980; Shamberger 1981; Bovee and O'Brien 1982; Robberecht and Von Grieken 1982; NRC 1983; Levander 1983, 1984; Knox et al. 1987; Morris et al. 1984; Flueck and Smith-Flueck 1990; Oliver et al. 1990a; USPHS 1996). Selenium deficiency, whether induced experimentally by use of low-selenium feeds supplemented with alpha-tocopherol or by chronic ingestion of low-selenium diets, has caused a number of maladies:

- High embryonic mortality in cattle and sheep
- Anemia in cattle
- Poor growth and reproduction in sheep and rats
- Reduced viability of newly hatched quail

- Nutritional myopathy (white muscle disease) in sheep, swine, and cattle
- Hepatic necrosis and lameness in dogs, horses, and breeding bulls
- Hair loss and sterility in rat offspring
- Spermatozoan abnormalities in rats

Deficiencies were usually prevented or reversed by supplements with sodium selenate or selenite at 100 µg Se/kg ration, or 20 µg Se/kg body weight administered parenterally.

The protective action of selenium against the adverse or lethal effects induced by mercury, cadmium, arsenic, thallium, copper, zinc, silver, and various pesticides is well documented for a wide variety of plant and animal species (Hill 1976; Wilber 1985; Eisler 1985; USPHS 1996). Among marine organisms, for example, selenium protects against toxic levels of mercury in algae (Gotsis 1982), shrimp (Lucu and Skreblin 1982), crabs and oysters (Glickstein 1978), fish (Sheline and Schmidt-Nielsen 1977), and mammals (Koeman et al. 1975). Similar observations have been recorded for copper and marine algae (Gotsis 1982); cadmium and freshwater snails (Wilber 1983), marine crabs (Bjerragaard 1982), earthworms (Helmke et al. 1979; Beyer et al. 1982), and rats (Harr 1978); mercury or methylmercury and rats (Cappon and Smith 1982), eggs of lake trout (Klaverkamp et al. 1983b), freshwater teleosts (Kim et al. 1975, 1977) and (temporarily) Japanese quail (El-Bergearmi et al. 1977, 1982; Beijer and Jernelov 1978); and arsenic and freshwater and marine teleosts (Luten et al. 1980; Orvini et al. 1980). Not all tests were conclusive. Studies with some species of freshwater teleosts demonstrated negligible antagonism of selenium against mercury (Klaverkamp et al. 1983a) or cadmium (Duncan and Klaverkamp 1983). Selenium reportedly protects mammals and poikilotherms against poisoning by thallium, the herbicide paraquat, cadmium, mercury, lead, arsenic, and copper (Wilber 1983; USPHS 1996). Selenium also protects against fatal biological agents. Juvenile chinook salmon (*Oncorhynchus tshawytscha*) naturally infected with *Renibacterium salmoninarum*, the causative agent of bacterial kidney disease, were protected when diets were supplemented with 2.5 mg Se/kg DW ration and Vitamin E (Thorarinsson et al. 1994).

Reasons to account for the antagonism of selenium and heavy metals (here, mercury is used as an example) include the dietary source and chemical form of selenium, influence of sulfur, biological translocation of selenium or mercury to less-critical body parts, and chemical linkage of selenium to mercury on a linear basis. The exact mode of interaction is probably complex and has not yet been resolved. In regard to diet, selenium of animal origin and in the form of selenate is less effective than selenium from plant and inorganic sources in preventing methylmercury neurotoxicity in experimental animals (Cappon and Smith 1982). Disruption of sulfur metabolism by selenium, the sulfur being replaced by seleno-amino acids and other cell constituents containing selenium in living organisms, is one probable cause of selenosis. It is conceivable that Se–Hg compounds formed within the organism would be sufficiently nonreactive biologically to interfere with sulfur kinetics, presumably –SH groups (Koeman et al. 1975; Beijer and Jernelov 1978; Cappon and Smith 1982; Gotsis 1982). Differential redistribution of selenium or mercury to less-critical body parts may partly account for observed antagonisms. Pretreatment of marine minnows with selenium protects against mercury poisoning and causes a marked redistribution of mercury among organs, presumably to noncritical body parts, and this transfer may partly account for the observed Se–Hg antagonisms in that species (Sheline and Schmidt-Nielsen 1977). Some investigators have reported that selenium results in increased mercury accumulations. Increased retention of mercury and other metals may lead to a higher level of biomagnification in the food chain and higher body burden in the individual, which might counteract the positive effect of decreased intoxication (Beijer and Jernelov 1978). Extensive research is under way on the chemical linkage of selenium and mercury. In marine mammals and humans, selenium and mercury concentrations are closely related, almost linearly in a 1:1 molar ratio, but this relation blurs in teleosts in which selenium is in abundance, and fails in birds (Koeman et al. 1975; Beijer and Jernelov 1978; Orvini et al. 1980; Cappon and Smith 1982).

31.5 LETHAL EFFECTS

31.5.1 Aquatic Organisms

Among representative species of aquatic organisms, death was observed at water concentrations between 60 and 600 µg Se/L; early life history stages that were subjected to comparatively lengthy exposures accounted for most of these data (Hamilton and Wiedmeyer 1990; Cleveland et al. 1993; Table 31.3). Sensitive species of fishes had reduced survival after extended exposure to 10 to 47 µg Se/L. Adult bluegills (*Lepomis macrochirus*), for example, had reduced survival after exposure to 10 µg Se/L for 1 year; those exposed to 30 µg Se/L all died (Hermanutz et al. 1992). Adult bluegills exposed for 60 days to 10 µg Se/L as selenite, plus 33.3 mg Se/kg ration as seleno-L-methionine, were normal but produced fry with reduced survival (Coyle et al. 1993). Exposure for 1 year to 25 µg/L caused reduced survival and reproduction of perch and grass carp (Crane et al. 1992). Mortality of 35% occurred at 47 µg Se/L, as selenite, in chinook salmon exposed for 90 days at the yolk-sac stage; 70% died at 100 µg/L (Lemly et al. 1993). Survival was reduced in chinook salmon fingerlings when their diets contained >9.6 mg Se/kg ration (Hamilton et al. 1990; Lemly et al. 1993).

Latent mortality after exposure to comparatively high selenium concentrations has been documented, but not extensively. For example, all embryos of the zebrafish (*Brachydanio rerio*) survived exposure to 3000 µg Se/L during development, but more than 90% of the resultant larvae died soon after hatching. At 1000 µg/L, survival was similar to that in controls (Niimi and LaHam 1975). It has been suggested (USEPA 1980) that selenite is more toxic than selenate and is preferentially concentrated over selenate by mussels, *Mytilus galloprovincialis* (Measures and Burton 1980). Selenite is generally more toxic to early life history stages, and effects are most pronounced at elevated temperatures (Klaverkamp et al. 1983a). Also, selenium salts may be converted to methylated forms by microorganisms, and these are readily accumulated by aquatic vertebrates (Klaverkamp et al. 1983a). Among freshwater algae species, it has been demonstrated that selenite, selenate, selenomethionine, and selenopurine are all toxic, but that sulfur, as sulfate, has a significant protective role against selenium toxicity (Kumar and Prakash 1971). Numerous additional chemical compounds and mixtures probably protect against selenium toxicity, much as selenium protects against toxic effects of mercury salts and other chemicals, but data are sparse on selenium protective agents.

More than 60 years ago, Ellis et al. (1937) recorded a long list of signs of selenium poisoning in teleosts: loss of equilibrium, lethargy, contraction of dermal chromatophores, loss of coordination, muscle spasms, protruding eyes, swollen abdomen, liver degeneration, reduction in blood hemoglobin and erythrocyte number, and increase in white blood cells. Sorensen et al. (1984) observed most of these signs in selenium-poisoned green sunfish (*Lepomis cyanellus*), together with elevated liver selenium concentrations, reduced blood hematocrit, enlarged liver, histopathology of kidney and heart, swollen gill lamellae with extensive cellular vacuolization, and necrotic and degenerating ovarian follicles. Other signs of selenosis in freshwater fishes include loss of osmotic control and liver histopathology (Hodson 1990).

Table 31.3 Toxicity of Selenium Salts to Aquatic Biota (Values shown are in µg/L [ppb] in medium fatal to 50% of the organisms during exposure for various intervals.)

Medium, Taxonomic Group, and Species	Exposure Interval (hours [h], days [d], or life cycle [LC])	LC50 (µg/L)	Reference ^a
FRESHWATER			
Algae			
<i>Anabaena variabilis</i>	96 h	15,000–17,000	1
<i>Anacyclis nidulans</i>	96 h	30,000–40,000	1
<i>Oedogonium cardiacum</i>	48 h	<100	2

Table 31.3 (continued) Toxicity of Selenium Salts to Aquatic Biota (Values shown are in µg/L [ppb] in medium fatal to 50% of the organisms during exposure for various intervals.)

Medium, Taxonomic Group, and Species	Exposure Interval (hours [h], days [d], or life cycle [LC])	LC50 (µg/L)	Reference ^a
Coelenterates			
<i>Hydra</i> sp.			
Selenite	96 h	1700	17
Selenate	96 h	7300	17
Molluscs			
Snail, <i>Physa</i> sp.	96 h	24,000	3
Snail, <i>Physa</i> sp.	48 h	>10,000	2
Insects			
Mosquito larvae, <i>Culex fatigans</i>	48 h	<3100	2
Midge, <i>Tanytarsus dissimilis</i>	96 h	42,400	4
Crustaceans			
Daphnid, <i>Ceriodaphnia affinis</i>	96 h	480–720	17
Cladoceran, <i>Daphnia magna</i>			
Selenite	48 h	700	18
Selenate	48 h	2560	18
Selenite	MATC ^b	110–237	17
Selenate	MATC ^b	1730–2310	17
<i>D. magna</i>	96 h	710	5
<i>D. magna</i>	14 d	430	5
<i>D. magna</i>	28 d	240	4
Scud, <i>Hyallecta azteca</i>	96 h	760	6
<i>H. azteca</i>	96 h	340	7
<i>H. azteca</i>	14 d	70	5
Cladoceran, <i>Daphnia pulex</i>	96 h	3870	3
<i>D. pulex</i>	LC	600–800	4
Amphibians			
South African clawed frog, <i>Xenopus laevis</i>			
Embryo	27 h	20,000	8
Embryo	61 h	10,000	8
Embryo	96 h	4000	8
Embryo	113 h	2000	8
Tadpole	3 d	8000	8
Tadpole	5 d	2600	8
Tadpole	7 d	1500	8
Fishes			
Goldfish, <i>Carassius auratus</i>	96 h	26,100	9
<i>C. auratus</i>	14 d	6300	9
White sucker, <i>Catostomus commersoni</i>	48 h	48,600	10
<i>C. commersoni</i>	96 h	31,400	10
Common carp, <i>Cyprinus carpio</i>	24 h	72,000	11
<i>C. carpio</i>	96 h	35,000	12
Northern pike, <i>Esox lucius</i>	75 h	11,100	13
Mosquitofish, <i>Gambusia affinis</i>	48 h	>6000	2
<i>G. affinis</i>	96 h	12,600	3
Green River, Utah; 3 endangered species (Colorado squawfish, <i>Ptychocheilus lucius</i> ; razorback sucker, <i>Xyrauchen texanus</i> ; bonytail, <i>Gila elegans</i>); fry and juveniles			
Selenite	96 h	18,000 (14,000–22,000)	19
Selenate	96 h	97,000 (75,000–129,000)	19
Channel catfish, <i>Ictalurus punctatus</i>	96 h	13,600	9
Flagfish, <i>Jordanella floridae</i>	96 h	6500	9

Table 31.3 (continued) Toxicity of Selenium Salts to Aquatic Biota (Values shown are in µg/L [ppb] in medium fatal to 50% of the organisms during exposure for various intervals.)

Medium, Taxonomic Group, and Species	Exposure Interval (hours [h], days [d], or life cycle [LC])	LC50 (µg/L)	Reference ^a
Bluegill, <i>Lepomis macrochirus</i>			
Seleno[DL]methionine	96 h	13	18
Seleno[L]methionine	96 h	13	18
Selenite	96 h	7800–13,000	18
Selenate	96 h	98,000	18
Striped bass, <i>Morone saxatilis</i> , fingerlings			
Seleno[L]methionine	96 h	4	18
Selenite	96 h	1000	18
Selenate	96 h	39,000	18
Coho salmon, <i>Oncorhynchus kisutch</i>			
Fry	43 d	160	6
Yellow perch, <i>Perca flavescens</i>	10 d	4800	13
Fathead minnow, <i>Pimephales promelas</i>			
Fry	96 h	2100	9
Juvenile	96 h	5200	9
Adult	96 h	620–12,500	4–6
Adult	9 d	2100	9
Adult	48 d	1100	6
Selenite	MTAC ^b	83–153	17
Selenate	MTAC ^b	390–820	17
Rainbow trout, <i>Oncorhynchus mykiss</i>			
<i>O. mykiss</i>	96 h	4200–12,500	4, 6, 12, 14
<i>O. mykiss</i>	9 d	5400–7000	14
Selenite	MTAC ^b	60–130	17
Selenate	MTAC ^b	2200–3800	17
Chinook salmon, <i>Oncorhynchus tshawytscha</i> , fry			
Selenite	96 h	13,800	18
Selenate	96 h	115,000	18
Colorado squawfish, <i>Ptychocheilus lucius</i>			
Larva, selenite	96 h	12,800	20
Larva, selenate	96 h	24,600	20
Juveniles, selenite	96 h	27,900	20
Juveniles, selenate	96 h	77,500	20
Brook trout, <i>Salvelinus fontinalis</i>	96 h	10,200	9
MARINE			
Molluscs			
Pacific oyster, <i>Crassostrea gigas</i>			
Larvae	48 h	>10,000	15
Crustaceans			
Copepod, <i>Acartia clausi</i>	96 h	1740	4
Copepod, <i>A. tonsa</i>	96 h	800	4
Blue crab, <i>Callinectes sapidus</i>	96 h	4600	16
Dungeness crab, <i>Cancer magister</i>			
Larvae	96 h	1040	15
Mysid shrimp, <i>Mysidopsis bahia</i>			
Adult	96 h	1500	16
Juvenile	96 h	600	4
Egg	LC	27–143	4
Brown shrimp, <i>Penaeus aztecus</i>	96 h	1200	16

Table 31.3 (continued) Toxicity of Selenium Salts to Aquatic Biota (Values shown are in µg/L [ppb] in medium fatal to 50% of the organisms during exposure for various intervals.)

Medium, Taxonomic Group, and Species	Exposure Interval (hours [h], days [d], or life cycle [LC])	LC50 (µg/L)	Reference ^a
Fish			
Fourspine stickleback, <i>Apeltes quadratus</i>	96 h	17,350	4
Sheepshead minnow, <i>Cyprinodon variegatus</i>			
Adult	96 h	7400–67,100	4
Egg through juvenile	MATC ^b	470–970	17
Pinfish, <i>Lagodon rhomboides</i>	96 h	4400	16
Haddock, <i>Melanogrammus aeglefinus</i>			
Larvae	96 h	600	4
Atlantic silverside, <i>Menidia menidia</i>	96 h	9725	4
Striped bass, <i>Morone saxatilis</i>			
Selenite	96 h	1600	17
Selenate	96 h	9800	17
Summer flounder, <i>Paralichthys dentatus</i>			
Larvae	96 h	3500	4
Winter flounder, <i>Pleuronectes americanus</i>			
Larvae	96 h	4250–15,100	4

^a 1, Kumar and Prakash 1971; 2, Nassos et al. 1981; 3, Reading 1979; 4, USEPA 1980; 5, Halter et al. 1980; 6, Adams 1976; 7, Murphy 1971; 8, Browne and Dumont 1979; 9, Cardwell et al. 1976; 10, Duncan and Klaverkamp 1983; 11, Sato et al. 1980; 12, Spehar et al. 1982; 13, Klaverkamp et al. 1983a; 14, Hodson et al. 1980; 15, Glickstein 1978; 16, Ward et al. 1981; 17, USEPA 1987; 18, Lemly et al. 1993; 19, Hamilton 1995; 20, Buhl and Hamilton 1995.

^b MATC = maximum acceptable toxicant concentration. Lower value in each MATC pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, and metabolism during chronic exposure. Higher value indicates lowest concentration tested producing a measurable effect.

31.5.2 Mammals and Birds

“The element selenium can be traced in an orderly sequence from its origin in the Earth’s crust to specific geological formation, to distribution of specific genera and groups of plants which require the element for their growth, to the accumulation in vegetation, and to its subsequent toxicity to birds or mammals that consume the seleniferous foods” (Rosenfeld and Beath 1964). Selenosis in warm-blooded organisms is modified by numerous factors, including method of administration, chemical form of selenium, dietary composition, and age and needs of the organism. Concurrent ingestion of minerals and rough or high protein feeds reduces selenium toxicity, and exposure by diet is less toxic than exposure parenterally or by inhalation. Many compounds are known to prevent or reduce toxic effects of subacute and chronic selenosis in pigs, beef cattle, and other warm-blooded organisms. A partial list includes arsenic, strychnine sulfate, tungsten, germanium, antimony, beet pectin, high-fat diets, ACTH injections, sulfate, increased dietary proteins, lactalbumin, ovalbumin, wheat protein, dried brewer’s yeast, desiccated liver, linseed oil meal, glucosamine, hemocysteine, creatine, methionine, and choline. Not all of these compounds afforded equal protection against various selenium formulations. The reasons for the difference are not clear, but it appears that the subject of selenoprotective agents warrants additional research effort. Selenium poisoning in livestock, discussed here, was largely extracted from reviews by Rosenfeld and Beath (1964), Frost (1972), Fishbein (1977), Harr (1978), Shamberger (1981), NRC (1983), Wilber (1983), and USPHS (1996).

In livestock, there are three basic types of selenium poisoning:

- Acute, resulting from consumption (usually in a single feeding) of a sufficient quantity of highly seleniferous weeds
- “Blind staggers,” from consumption of moderately toxic amounts of seleniferous weeds over an extended period of time
- “Alkali disease,” caused by the consumption of moderately seleniferous grains and forage grasses over a period of several weeks to months

Acute poisoning is associated with plant materials containing 400 to 800 mg Se/kg: sheep died when fed amounts of plant material ranging from 8 to 16 g/kg BW, or about 3.2 to 12.8 mg Se/kg BW. The minimum lethal dose of Se administered orally as selenite (mg Se per kg body weight) ranged from 3.3 for horses and mules, to 11 for cattle, and 15 for swine. Other modes of administration were more toxic; for example, 2 and 1.2 mg Se/kg BW given subcutaneously killed swine in 4 h and 5 days, respectively; and 1.5 to 6.0 mg Se/kg BW given intravenously or intraperitoneally to rats and rabbits were fatal. Accidental toxicosis of sheep and cattle from overtreatment with commercial mixtures of Se salts and Vitamin E are also documented for Australia and New Zealand. Acute Se poisoning in domestic livestock is characterized by abnormal movements, lowered head, drooped ears, diarrhea, elevated temperature, rapid pulse, labored breathing, bloating with abdominal pain, increased urination, and dilated pupils. Before death, which is due to respiratory failure, there is complete prostration and lethargy. Duration of illness extends from a few hours to several days, depending on the toxicity of plant material ingested. In these cases, selenium is distributed by the circulatory system to all body organs, the concentrations being highest in liver, blood, kidney, spleen, and brain, and lowest in muscle, skin, hair, and bone. Elimination is primarily in the urine; smaller quantities are excreted with the feces, breath, perspiration, and bile. Postmortem examinations indicate many pathological changes in the heart, lungs, rumen, liver, kidney, and other organs. No effective treatment is known for counteracting toxic effects of large amounts of ingested selenium.

Chronic selenosis in mammals may be induced by dietary exposure to natural selenite, selenate, or seleniferous feedstuffs at dietary concentrations between 1 mg/kg (rat) and 44 mg/kg (horse), or from water containing 0.5 to 2.0 mg Se/L. Cattle fed 0.5 mg Se/kg BW three times weekly lost their appetite; sheep fed up to 75 mg selenite daily developed myocardial degeneration and fibrosis, pulmonary congestion, and edema. The minimum toxic concentration of selenium in lifetime exposure of rats (a comparatively sensitive species) fed Se-deficient diets fortified with selenium was 0.35 mg Se/kg diet, as judged by changes in liver chemistry; and 0.75 mg Se/kg diet, as judged by longevity, and histological changes in heart, kidney, and spleen. These concentrations are 10 times the nutritional threshold for selenium, and about 25% of the minimum lifetime exposure to selenium in natural feedstuffs that produces similar effects under the same experimental conditions. Signs of chronic selenosis include skin lesions, lymph channel inflammation, loss of hair and nails, anemia, enlarged organs (spleen, pancreas, liver), fatigue, lassitude, and dizziness. “Blind staggers” is characterized by anorexia, emaciation, and sudden collapse, followed by death. Typically, the upper intestinal tract is ulcerated. In “alkali disease” in cattle, hogs, and horses that had eaten seleniferous grains, the signs were deformation and sloughing of the hooves, hair loss, lassitude, erosion of the articular cartilages, reduced conception, increased reabsorption of fetuses, and degeneration of heart, kidney, and liver. It is likely that selenium displaces sulfur in keratin, resulting in structural changes in hair, nails, and hooves (Fishbein 1977).

Elevated selenium concentrations were measured in tissues and diet of two captive California sea lions (*Zalophus californianus*) that died shortly after performing at a show in 1988. Selenium concentrations, in mg/kg FW, were 49 and 88 in liver, 42 and 47 in kidney, and 5.1 and 5.2 in blood. Selenium concentrations in their fish diet was 2.5 mg/kg FW, and in thawed fish fluids 45 mg/kg FW (Alexander et al. 1990).

Fatal chronic selenosis in aquatic birds is characterized by low body weight or emaciation, liver necrosis, enlarged kidneys (up to 40% heavier than normal), and more than 66 mg Se/kg DW liver

(Albers et al. 1996). Selenomethionine was the most toxic form of selenium tested against mallards (Lemly et al. 1994). Mallard ducklings fed 8 mg Se/kg ration as selenomethionine for 120 days had hepatotoxicity as adults; 10 mg/kg ration for 120 days inhibited reproduction; 15 mg/kg ration for 28 days inhibited growth; and 60 mg/kg ration for 60 days was fatal to all ducklings (Lemly et al. 1994) (Table 31.4). All fatal cases of selenomethionine-induced poisoning in mallards were characterized by histologic lesions of the liver, pancreas, spleen, and lymph nodes, and severe atrophy and degeneration of fat (Green and Albers 1997).

Table 31.4 Selenium Effects on Birds

Species, Dose, and Other Variables	Effect	Reference ^a
MALLARD, <i>Anas platyrhynchos</i>		
Adults given drinking water containing 0, 0.5, or 3.5 mg Se/L as sodium selenite, or 2.2 mg Se/L as selenomethionine for 12 weeks	Selenomethionine group had altered immune function, altered serum enzyme activities, and elevated concentrations of selenium in liver (4 times control values) and breast muscle (14 times). Sodium selenite-treated birds had normal immune function and selenium tissue burdens; however, serum enzyme activity was disrupted in the 3.5 mg/L group	1
Breeding adults fed diets for 100 days containing 0, 1, 2, 4, 8, or 16 mg Se/kg fresh weight (FW) ration as seleno-DL-methionine, or 16 mg Se/kg ration as seleno-DL-cysteine	Adults normal. Impaired reproduction (reduced survival of ducklings, increased developmental abnormalities) for selenomethionine occurs between 4 and 8 mg/kg ration; selenocysteine did not impair reproduction at 16 mg Se/kg ration	2
Breeding adults fed diets containing 0, 1, 5, 10, 25, or 100 mg Se/kg ration as sodium selenite for as long as 12 weeks, or 10 mg Se/kg ration as seleno-DL-methionine for as long as 12 weeks	Sodium selenite groups had normal growth, survival, and reproduction at 10 mg/kg ration and lower; growth and reproduction inhibited in the 25- and 100-mg/kg groups. Selenomethionine birds produced fewer ducklings with a high incidence of developmental abnormalities; surviving ducklings had impaired growth	3
Breeding adults fed diets containing 0, 3.5, or 7 mg Se/kg ration as seleno-DL-methionine for as long as 21.8 weeks. Ducklings produced received the same treatment as their parents for 14 days, then killed	No deaths or histopathology in any group. Dose-dependent decrease in adult growth, duckling weight, and hatching success; dose-dependent increase in selenium concentrations in adult liver, eggs, and duckling liver	4
Adults and resultant ducklings fed diets supplemented with up to 400 mg As (as sodium arsenate)/kg ration and zero or 10 mg Se (as seleno-DL-methionine)/kg ration	Arsenic or selenium at dose levels and forms given adversely affect mallard reproduction and duckling growth and survival. In mixtures, arsenic reduced selenium accumulation in liver and eggs and alleviated adverse affects of selenium on hatching success and embryo deformities	5
Day-old mallard ducklings fed diets for 2 weeks containing 0, 15, or 30 mg Se/kg ration in a 75% wheat diet (22% protein). Selenium given as seleno-DL-methionine, seleno-L-methionine, or selenized yeast	All forms of selenium caused significant increases in plasma and hepatic glutathione peroxidase activities. Seleno-L-methionine at 30 mg/kg ration was the most toxic form, resulting in high mortality (64%), impairing growth more than 50% in survivors, and the greatest increase in the ratio of oxidized to reduced hepatic glutathione. When the basal diet was a commercial duck feed (22% protein), survival was not adversely affected and oxidative effects were less pronounced	6
Adult males fed diets containing 0.2 (control), 1, 2, 4, 8, 16, or 32 mg Se/kg ration as selenomethionine for 14 weeks	Plasma glutathione peroxidase activity increased at 2 mg/kg ration and greater; altered liver enzyme activity in 8 mg/kg ration and higher; dose-dependent increase in liver selenium, reaching 29 mg Se/kg FW in the 32-mg/kg group; the high-dose group had decreased survival, altered blood chemistry, and hepatotoxicity	7
Adults fed diets 6 weeks before egg laying through day 7 of incubation containing either sodium selenite — at 1, 5, 10, or 25 mg Se/kg ration — or selenomethionine at 10 or 16 mg Se/kg ration	The 25 mg/kg group of sodium selenite had 42% fewer eggs than controls that hatched, more birth defects (4.2%), and decreased embryo weights. Developmental abnormalities in the selenomethionine groups were 13.1% in the 10-mg/kg group and 68.0% in the 16-mg/kg group	8

Table 31.4 (continued) Selenium Effects on Birds

Species, Dose, and Other Variables	Effect	Reference^a
Ducklings fed diets containing 0, 10, 20, 40, or 80 mg Se/kg ration as selenomethionine or sodium selenite from hatching to age 6 weeks	At 80 mg/kg ration, all ducklings were dead in the selenomethionine group and 98% were dead in the selenite group. At 40 mg/kg ration, 25% were dead in the selenomethionine group and 13% in the selenite group. Survival was normal in other groups. Growth was decreased at 20 mg/kg ration and higher — regardless of chemical form — due to decreases in food consumption. The 10-mg/kg selenite group had significantly heavier livers than controls	9
Adult males fed diets containing 0, 10, 20, 40, or 80 mg Se/kg ration as seleno-DL-methionine for 16 weeks	All dead at 80 mg/kg ration. Survival reduced, growth impaired, and molt delayed at 40 mg/kg ration. Dose-dependent increase in tissue selenium concentrations. Dead birds had consistent histologic lesions in the liver, kidneys, and organs of the immune system	10, 13
Adults males given a choice between a control diet or diets with 5, 10, or 20 mg Se/kg ration as selenomethionine	Mallards avoided diets containing 10 or 20 mg Se/kg; avoidance may not be due to aversion to the taste of selenium	11
Adult males were fed diets supplemented with 0, 10, 20, 40, or 80 mg Se/kg ration as selenomethionine for 16-week exposure that began in November. Survivors were fed untreated diets for 4 more weeks	No deaths in controls or 10-mg/kg group, 25% dead in the 20-mg/kg group, 95% in the 40-mg/kg group, and 100% in the high-dose group. Body weights depressed in the 20-, 40-, and 80-mg/kg groups; but after 4 weeks on untreated diet, the 20-mg/kg group was the same as controls	12
Mallards fed diet containing 0 or 15 mg Se/kg ration as seleno-DL-methionine for 21 weeks, untreated food for 12 weeks, followed by 100 mg Se/kg ration for 5 weeks for both groups	No difference between groups in survival (85%), weight loss in survivors (40%), or liver burdens (35–40 mg Se/kg FW)	14
Adults fed diet containing 10 mg Se/kg ration as selenomethionine for 6 weeks followed by 6 weeks on untreated diet	Equilibrium reached in liver in 7.8 days and in muscle in 81 days with half-time persistence of 19 days in liver and 30 days in muscle	15
Fed diet with 15 mg Se/kg ration as selenomethionine for 21 weeks during winter, ending with onset of reproductive season	Selenium group had elevated concentrations in eggs, decreased survival, and higher incidence of deformed embryos. Reproduction and survival normal after 2 weeks on an uncontaminated diet	16
Ducklings fed diets for 4 weeks containing 15 or 60 mg Se/kg ration as selenomethionine, with and without 1000 mg boron/kg ration	Severe adverse effects of 60 mg Se/kg ration on survival, growth, and liver histology; effects exacerbated by the addition of boron	17
Females that had just initiated egg laying were fed diet containing 20 mg Se/kg ration as selenomethionine for 20 days, then an untreated diet for 20 days	Selenium concentrations in eggs reached a maximum of 20 mg Se/kg FW in about 2 weeks on the treated diet. Concentrations fell to less than 5 mg/kg FW after 10 days on the untreated diet	18
Ducklings fed diet containing 22% protein and 60 mg Se/kg ration as selenomethionine for 4 weeks	Selenium-induced reduction in growth and survival, and increase in liver histopathology. Effects exacerbated at 7% and 44% protein. Effects alleviated by addition of 200 mg As/kg ration as sodium arsenite, and partially alleviated by methionine dietary supplement	19, 20
AMERICAN KESTREL, <i>Falco sparverius</i>		
Adults fed diets for 11 weeks containing 5 or 9 mg Se/kg DW ration as seleno-L-methionine or naturally incorporated selenium (mammals from Kesterson National Wildlife Refuge, California)	All birds seemed normal during the study. Maximal Se concentrations in blood were measured at week 5 in the seleno-L-methionine groups: 4.3 mg Se/kg DW (low Se group) and 8.4 mg Se/kg DW (high Se group) vs. 1.6 mg/kg in controls. Excreta Se levels were 5.8 and 1.8 mg/kg DW in the low and high seleno-L-methionine groups, respectively, vs. 1.4 in controls. All treatment groups had reduction of Se concentration in excreta, but not in blood, to baseline values 4 weeks after treatment ended	22

Table 31.4 (continued) Selenium Effects on Birds

Species, Dose, and Other Variables	Effect	Reference ^a
EASTERN SCREECH-OWL, <i>Otus asio</i>		
Breeding adults fed diets containing 0, 4.4, or 13.2 mg Se/kg ration as seleno-DL-methionine for 3 months (equivalent to 0, 10, and 30 mg seleno-DL-methionine/kg ration)	Growth and reproduction inhibited at high dose. No malformed nestlings at low dose, but femur lengths were shorter than controls. Altered liver biochemistry of nestlings from parents fed low dose	21
^a 1, Fairbrother and Fowles 1990; 2, Heinz et al. 1989; 3, Heinz et al. 1987; 4, Stanley et al. 1996; 5, Stanley et al. 1994; 6, Hoffman et al. 1996; 7, Hoffman et al. 1991a; 8, Hoffman and Heinz 1988; 9, Heinz et al. 1988; 10, Albers et al. 1996; 11, Heinz and Sanderson 1990; 12, Heinz and Fitzgerald 1993a; 13, Green and Albers 1997; 14, Heinz 1993b; 15, Heinz et al. 1990; 16, Heinz and Fitzgerald 1993b; 17, Hoffman et al. 1991b; 18, Heinz 1993a; 19, Hoffman et al. 1992a; 20, Hoffman et al. 1992b; 21, Wiemeyer and Hoffman 1996; 22, Yamamoto et al. 1998.		

31.6 SUBLETHAL AND LATENT EFFECTS

Results of laboratory studies and field investigations with fish, mammals, and birds have led to general agreement that elevated concentrations of selenium in diet or water were associated with reproductive abnormalities, including congenital malformations, selective bioaccumulation by the organism, and growth retardation. Not as extensively documented, but nevertheless important, are reports of selenium-induced chromosomal aberrations, intestinal lesions, shifts in species composition of freshwater algal communities, swimming impairment of protozoans, and behavioral modifications.

31.6.1 Aquatic Organisms

Adverse effects on reproduction are among the most insidious effects of selenium in freshwater ecosystems. Adult bluegills exposed to 2.5 µg Se/L as sodium selenite for 319 days in an experimental stream ecosystem produced fry with a high incidence of edema, lordosis, and hemorrhaging (Coyle et al. 1993). Fathead minnows (*Pimephales promelas*) held in ecosystems containing 10 or 30 µg Se/L for 1 year produced a high incidence of malformed progeny with humped backs, missing scales, and malformations of the jaw, head, operculum, snout, and mandible. The frequency of malformations in the controls was 0.3%; in the 10- and 30-µg/L groups, these frequencies were 8% and 29.8%, respectively (Hermanutz 1992). Selenium concentrations in whole fathead minnows from the 10-µg Se/L group were 3.9 mg/kg FW vs. 0.3 in the controls (Schultz and Hermanutz 1990). Mosquitofish reproduction was inhibited when whole-body selenium concentrations were >100 mg Se/kg DW vs. normal reproduction in a reference area at 1.5 mg Se/kg DW whole body (Saiki and Ogle 1995).

In green sunfish from a lake in North Carolina receiving selenium (as flyash wastes from a coal-fired power station), reproduction failed and the population declined markedly. In these fish, selenium levels were elevated in liver (up to 21.4 mg/kg FW) and other tissues; kidney, heart, liver, and gill showed histopathology; and blood chemistry was altered. Ovaries of fish had numerous necrotic and ruptured egg follicles that may have contributed to the population extinction (Sorensen et al. 1984). It is probable that selenium uptake by plankton (containing 41 to 97 mg/kg DW) from lake water (9 to 12 µg/L) introduced selenium to the food chain, where it ultimately reached elevated levels in fish through biomagnification (Cumbie and Van Horn 1978). In laboratory tests, however, eggs of common carp hatched normally when incubated in media containing 5000 µg Se/L (Huckabee and Griffith 1974), as did eggs of lake trout (*Salvelinus namaycush*) at 10,000 µg Se/L (Klavertkamp et al. 1983b). In frogs (*Xenopus laevis*), cranial and vertebral deformities and lowered survival were documented during development in water with concentrations of 2000 µg Se/L or higher (Browne and Dumont 1979).

Reduced growth of freshwater fishes was associated with tissue concentrations of 3.6 to 6.7 mg Se/kg DW (Hamilton and Wiedmeyer 1990), and dietary concentrations between 5.3 and 25 mg Se/kg DW ration (Hamilton et al. 1990; Cleveland et al. 1993; Lemly et al. 1993). Toxic sublethal effects of selenium in aquatic systems were more pronounced for organoselenium compounds than inorganic compounds and more pronounced for inorganic selenite than inorganic selenate compounds (USEPA 1987; Hamilton and Buhl 1990; Chapman 1992; Boisson et al. 1995) (Table 31.3). In salmon, younger stages were more sensitive than older stages (Hamilton and Buhl 1990; Chapman 1992). Adverse effects of selenium stress to freshwater fishes were reduced with increasing water hardness (Hamilton and Buhl 1990; Hamilton et al. 1990), and fishes were more sensitive to selenium stress under conditions of reduced temperature and photoperiod (Lemly 1993c).

At water concentrations of 47 to 53 µg/L, selenium was associated with anemia and reduced hatch of rainbow trout (Hodson et al. 1980), growth retardation of freshwater green algae (Hutchinson and Stokes 1975; Klaverkamp et al. 1983a), and shifts in species composition of freshwater algal communities (Patrick 1978). At 250 µg Se/L, growth was reduced in rainbow trout fry after exposure for 21 days (Adams 1976), and goldfish demonstrated an avoidance response after 48 h (Weir and Hine 1970). At water concentrations of 7930 to 11,000 µg Se/L, growth was inhibited in freshwater and marine algae (Patrick 1978; USEPA 1980), and swimming rate was reduced in the protozoan *Tetrahymena pyriformis* (Bovee and O'Brien 1982). Eggs of channel catfish exposed to certain metals (including cadmium, mercury, and copper) produced an increased percentage of albino fry; however, eggs exposed to 250 µg Se/L produced fry with normal pigmentation (Westernman and Birge 1978).

A significant number of chromosomal aberrations were induced in the edible goby (*Boleophthalmus dussumieri*) by selenium after intramuscular and water exposures (Krishnaja and Rege 1982). Intramuscular injections as low as 0.1 mg Se/kg BW, or 3200 µg/L in the water column, were associated with a marked enhancement of polyploid cells 76 to 96 h postadministration. Some deaths were recorded at higher test concentrations. Selenite was more effective than selenate in inducing chromosomal aberrations. The authors concluded that a relatively narrow range of selenium concentrations leads to a mutagenic rather than lethal effect.

Accumulation of selenium by aquatic organisms is highly variable. In short-term (48-h) laboratory tests at water concentrations of 0.015 to 3.3 µg Se/L, Nassos et al. (1980) reported biological concentration factors (BCFs) of 460 for mosquitofish to 32,000 for a freshwater gastropod. Values were intermediate for daphnids (2100), plankton (2600), and *Fundulus kansae* (3300), the freshwater killifish. High BCFs (>680) were recorded for freshwater diatoms subjected to maximum concentrations of 40 µg Se/L (Patrick 1978). Livers from rainbow trout and brown trout may contain from 50 to 70 mg Se/kg FW during lifetime exposure in seleniferous (12.3 to 13.3 µg/L) water, and have BCF values of 3759 to 5691 (Kaiser et al. 1979). BCF values were 361 to 390 for skin, and about 180 for muscle (Kaiser et al. 1979). In short-term exposures, most of the selenium was probably adsorbed to the body surface (Fowler and Benayoun 1976c), and then rapidly lost on transfer to selenium-free media (Browne and Dumont 1979). In longer exposures, the BCF values in aquatic organisms were lower after immersion in high ambient selenium concentrations over extended periods. Thus, marine crabs exposed to a water concentration of 250 µg Se/L for 29 days accumulated selenium over water concentration level by a factor of 25 for carapace, and 3.8 for gill; accumulations in muscle and hepatopancreas were negligible. Cadmium in solution enhanced selenium uptake (Bjerragaard 1982). Exposure of common carp to 1000 µg Se/L for 85 days resulted in a whole-body BCF of 6; additional studies of 7 weeks exposure plus 7 weeks postexposure at concentrations between 500 and 5000 µg Se/L (Sato et al. 1980) yielded a BCF range of 0.6 (5000 µg/L) to 1.8 (500 µg/L). Highest BCF values in carp were 50 for kidney and 80 for liver after exposure of the fish to 100 µg Se/L for 7 weeks plus 7 weeks in selenium-free media. For carp, selenium tended to accumulate in kidney, liver, gill, gall bladder, heart, bone, and muscle, in that general order (Sato et al. 1980). Studies with freshwater organisms collected from a farm pond

contaminated by flyash with high selenium levels (Furr et al. 1979), and with marine bivalves and nereid worms held for 4 months in seawater flowing through coal flyash containing 6200 µg Se/L (Ryther et al. 1979), showed that accumulation was slight. Contrasted to this are the observations of Cherry et al. (1976) and Ohlendorf et al. (1986). Cherry and co-workers collected mosquitofish from a drainage system that received high coal flyash concentrations at one end and thermal discharges at the other. Mosquitofish contained up to 9.0 mg Se/kg whole-body fresh weight. Of 40 elements examined, only selenium, zinc, and calcium were accumulated in excess of the levels measured in the water. Ohlendorf et al. found mean residues of 172 mg/kg DW (range 110 to 280 mg/kg) in whole mosquitofish from irrigation drainwater ponds contaminated by about 300 µg Se/L; based on a wet/dry factor of 4, the BCF for whole mosquitofish was >91.

Selenium accumulation is modified by water temperature, age of the organism, organ or tissue specificity, mode of administration, chemical species, and other factors. In freshwater fishes, selenium concentrations in tissues increased with increasing exposure (Hamilton and Wiedmeyer 1990) and increasing dose (Hamilton and Wiedmeyer 1990; Cleveland et al. 1993), and decreased with increasing water hardness (Hamilton and Wiedmeyer 1990). Food chain accumulation of selenium can severely affect reproductive success of bluegills (Coyle et al. 1993). Bluegills tend to accumulate inorganic selenium compounds through the diet, and organoselenium compounds through the medium as well as the diet (Besser et al. 1993). Dietary selenite accumulates in liver and gonads, and selenomethionine in muscle and whole fish (Gillespie et al. 1988; Lorentzen et al. 1994).

Diet is the major route of selenium intake by mussels (*Mytilus edulis*). Studies with radio selenium-75 demonstrated that selenium efficiency was 28 to 34% from the diet and 0.03% from the medium (Wang et al. 1996). Authors concluded that 96% of the selenium in mussels is obtained from ingested food under conditions typical of coastal waters (Wang et al. 1996). In the marine mussel *Mytilus galloprovincialis*, an increase in water temperature from 13 to 29°C doubled the bioconcentration factor (BCF) in 13 days (Fowler and Benayoun 1976b). Mussels preferentially accumulated selenite over selenate (Fowler and Benayoun 1976b); however, mussels did not reach a steady state in 63 days (Fowler and Benayoun 1976c), indicating that selenium kinetics in some species are difficult to elucidate in short-term studies. Accumulation rates were higher in small than in large mussels (Fowler and Benayoun 1976b), as they were in freshwater teleosts (Furr et al. 1979). However, the reverse was documented for marine mammals and teleosts (Eisler 1984). When selenium was available from both the diet and the medium, concentrations were highest in liver, kidney, and gills of teleosts (Sorensen et al. 1982; Furr et al. 1979; Kaiser et al. 1979), exoskeleton of crustaceans (Fowler and Benayoun 1976c; Bjerragaard 1982), and visceral mass and gills of molluscs (Fowler and Benayoun 1976c). When selenium was administered in food to marine shrimps, concentrations were highest in viscera and exoskeleton, suggesting that ingested selenium is readily translocated from internal to external tissues (Fowler and Benayoun 1976c). Concentrations of selenium in crustaceans usually were higher in fecal pellets than in the diet; fecal pellets may represent a possible biological mechanism for downward vertical transport of selenium in the sea (Fowler and Benayoun 1976a), as well as in freshwater environments.

The time for 50% excretion of accumulated selenium was found to range from 13 to 181 days in various species of marine and freshwater fauna. Biological half-life of selenium accumulated from the medium was estimated at 28 days for carp (Sato et al. 1980), 37 days for the marine euphausiid crustacean *Meganctiphanes norvegica* (Fowler and Benayoun 1976a), 63 to 81 days for the marine mussel *Mytilus galloprovincialis* (Fowler and Benayoun 1976b), 58 to 60 days for the marine shrimp *Lysmata caudata* (Fowler and Benayoun 1976b), and, as reviewed by Stadtman (1974, 1977), 13 days for guppies, 27 days for eels, and 28 days for leeches. Studies by Lemly (1982a) with bluegills and largemouth bass showed elevated tissue levels after exposure to 10 µg Se/L for 120 days. Time for 50% excretion in 30-day elimination trials was about 15 days from

gill and erythrocytes; however, there was essentially no elimination from spleen, liver, kidney, or muscle. It appears that research is needed on preferential tissue retention of selenium and its implications for biochemical and metabolic transport mechanisms. Urine is a major excretory route for selenium in marine mammals. Urine of minke whales (*Balaenoptera acutorostrata*) contains 1.5 mg Se/L, or about 30 times more selenium than human urine (Hasunuma et al. 1993). There are at least five selenium components in urine of minke whales, including trimethylselenium ion; the significance of this observation is imperfectly understood (Hasunuma et al. 1993).

31.6.2 Terrestrial Invertebrates

Concentrations of selenium decreased in whole earthworms from 22.4 to 15.0 mg/kg (dry weight) as the rate of sludge application increased from 15 to 60 metric tons/ha. Concentrations of selenium in soil and sludge were 0.3 and 0.5 mg/kg dry weight, respectively (Helmke et al. 1979). Other studies indicated that some metals, notably cadmium, decreased in worms living in soils amended with sewage sludge but that selenium concentrations were not affected (Beyer et al. 1982). The biological half-life of selenium in earthworms is estimated to be 64 days, a period consistent with values of 10 to 81 days documented for ants, birds, mammals, and aquatic biota (Stadtman 1974, 1977).

31.6.3 Birds

Embryos of the domestic chicken (*Gallus domesticus*) are extremely sensitive to selenium. The hatchability of eggs is reduced by concentrations of selenium in feeds (6 to 9 mg/kg) that were too low to produce poisoning in other avian species. Dietary selenium excess was associated with decreased egg weight, decreased egg production and hatchability, anemia, elevated kidney selenium residues in chicks, and a high incidence of grossly deformed embryos with missing or distorted eyes, beaks, wings and feet (Ort and Latshaw 1978; Harr 1979). Similar results were observed by El-Bergarmi et al. (1977) in Japanese quail at 6 and 12 mg/kg dietary selenite. Ohlendorf et al. (1986) reported severe reproductive effects in ducks (*Anas* spp.), American coot (*Fulica americana*), and other species of aquatic birds nesting at irrigation drainwater ponds in the San Joaquin Valley, California. Water in these ponds contained abnormally high concentrations of about 300 µg Se/L, but low or nondetectable levels of silver, chromium, arsenic, cadmium, mercury, lead, and zinc. Of 347 nests examined from this site, about 40% had at least one dead embryo, and about 20% had at least one embryo or chick with obvious external anomalies, including missing or abnormal beaks, eyes, wings, legs, or feet. In addition, brain, heart, liver, and skeletal anomalies were recorded. Concentrations of selenium (mg/kg, dry weight) were 2 to 110 in eggs and 19 to 130 in livers of birds, 12 to 79 in plants, 23 to 200 in invertebrates, and 110 to 280 in fish from the ponds, or 7 to 130 times those found at a nearby control area. It was concluded that selenium was the probable cause of poor reproduction and developmental abnormalities in the aquatic nesting birds, due to interference with their reproductive processes. The concentrations of selenium in breast muscle of coots were sufficiently high (up to 11.0 mg Se/kg FW) to induce state agencies to post the area, advising against the consumption of more than one meal per week of this species, or of any coots by children or pregnant women (Ohlendorf et al. 1986).

Selenomethionine is the predominant form of selenium in commercial grains (Heinz et al. 1989), usually as seleno-L-methionine (Heinz et al. 1996). Selenomethionine is more teratogenic and embryotoxic to avian waterfowl than inorganic forms of selenium tested (Heinz and Fitzgerald 1993b; Heinz et al. 1996; Hoffman et al. 1996) (Table 31.4), possibly due to higher uptake of organoselenium (Hoffman and Heinz 1988). Blood selenium concentrations in American kestrels (*Falco sparverius*) seemed to reflect dietary concentrations of seleno-L-methionine (Yamamoto

et al. 1998). Embryotoxic and teratogenic effects of selenomethionine were observed in mallards at dietary concentrations exceeding 4 mg Se/kg FW ration in the laboratory, causing effects similar to those found in field studies (Heinz et al. 1987, 1989; Hoffman and Heinz 1988). Excess dietary selenium, as seleno-DL-methionine has a more pronounced effect on hepatic glutathione metabolism and lipid peroxidation than selenite (Hoffman et al. 1989), and may enhance selenium accumulation (Moksnes 1983; Hoffman et al. 1989). In aquatic birds, developmental malformations were associated with lipid peroxidation in livers. Selenomethionine causes lipid peroxidation in livers of aquatic birds, and this is consistent with the observation that selenomethionine is the primary causative agent of selenium-induced embryonic mortality and overt teratogenesis in waterfowl at Kesterson Reservoir (Hoffman et al. 1988). Dietary selenomethionine effects were modified by salts of boron (Hoffman et al. 1991b; Stanley et al. 1996), arsenic (Hoffman et al. 1992a; Stanley et al. 1994), and protein composition (Hoffman et al. 1992b, 1996), with significant interactions between mixtures.

31.6.4 Mammals

Pregnant long-tailed macaques (*Macaca fascicularis*) given L-selenomethionine for 30 days at doses of 25, 150, or 300 µg Se/kg body weight daily showed dose-dependent increases in erythrocyte and plasma selenium, glutathione peroxidase activities, hair and fecal selenium, and urinary selenium excretion. Adverse effects, including body weight loss, were associated with daily doses of 150 and 300 µg Se/kg BW and concentrations of erythrocyte selenium >2.3 mg/L, plasma selenium >2.8 mg/L, and hair selenium >27 mg/kg FW (Hawkes et al. 1992). Young adult female mice (*Mus* sp.) given intraperitoneal injections of sodium selenate or selenomethionine (in each case, three injections of 2 mg Se/kg BW at 2-day intervals) had altered blood composition 24 days after the last injection. Both forms of selenium induced a transient, marked decrease in the number of circulating leukocytes (a condition known as leukopenia) following serial injections. Leukopenia was more extensive and of greater duration for selenomethionine-treated mice (Hogan 1998).

Harr (1978) and NRC (1983) summarized nonlethal effects of selenium on mammals, including reproductive anomalies. Selenosis caused congenital malformations in rats, mice, swine, and cattle. In general, young born to females with selenosis were emaciated and unable to nurse. Mice given selenium in drinking water reproduced normally for three generations, but litters were fewer and smaller when compared to controls, pups were runts with high mortality before weaning, and most survivors were infertile.

In rats, selenium did not induce cirrhosis or neoplasia; however, intestinal lesions were observed among those fed diets containing 0.8 to 1.0 mg Se/kg ration during lifetime exposure. The threshold requirement for optimal rat nutrition under similar conditions is about 0.08 mg Se/kg ration, again demonstrating the relatively narrow range separating selenium deficiency from selenium poisoning. Absorption of oral radioselenite by rats was as high as 95 to 100%. A single dose of radioselenite concentrated, in descending order of accumulation, in pancreas, intestine, erythrocytes, liver, kidney, and testes; tissue distributions from chronic exposure were similar. As expected, levels of selenium in poisoned rats were highest in liver and kidney. Rats, and probably other mammals, can regulate dietary selenium accumulations. Dietary concentrations in excess of 54 to 84 µg/kg ration were usually excreted in urine (Harr 1978; NRC 1983). Urine is the major excretory route for selenium. In urine of selenium-challenged rats, the trimethylselenium ion — a metabolic product of selenite or selenoamino acid, such as selenomethionine — is dominant (Hasunuma et al. 1993). However, when selenium intake exceeded 1000 µg/kg ration, pulmonary excretion was active (Harr 1978; NRC 1983). Excretion of selenium in feces, bile, saliva, and hair appears to be relatively constant, regardless of the amount of exposure. Yonemoto et al. (1983) demonstrated that some selenotoxic effects in mice, including abortion and maternal death, were prevented by prior treatment with Vitamin E, but exacerbated by reduced glutathione. The mechanisms for these interactions are unknown, and merit additional research.

31.7 RECOMMENDATIONS

All investigators appear to agree on four points:

1. Insufficient selenium in the diet may have harmful and sometimes fatal consequences.
2. Exposure to grossly elevated levels of selenium in the diet or water is inevitably fatal over time to terrestrial and aquatic organisms.
3. There is a comparatively narrow concentration range separating effects of selenium deficiency from those of selenosis.
4. Additional fundamental and basic research is required on selenium metabolism, physiology, recycling, interactions with other compounds or formulations, and chemical speciation in order to elucidate its nutritive role as well as its toxic effects.

Accordingly, the proposed selenium criteria shown in [Table 31.5](#) for prevention of selenium deficiency and for protection of aquatic life, livestock, crops, and human health, should be viewed as guidelines, pending acquisition of additional, more definitive, data.

Table 31.5 Proposed Criteria for Prevention of Selenium Deficiency and for Protection Against Selenosis (Values are in mg of selenium/kg fresh weight [FW] or dry weight [DW].)

Criterion	Selenium Concentration	Reference ^a
PREVENTION OF SELENIUM DEFICIENCY		
Rainbow trout (water levels of 0.4 µg Se/L)		
Diet	>70 µg/kg FW	1
Diet	150–380 µg/kg DW	26
Poultry		
Diet	>30–50 µg/kg FW	2
Dietary supplement allowed		
Chickens, ducks	100 µg/kg DW ration as sodium selenate or selenite	37
Turkeys	200 µg/kg DW ration as sodium selenate or selenite	37
Rats		
Diet	>54–84 µg/kg FW	3
Livestock		
Diet	>20 µg/kg FW	2
Dietary supplement allowed		
Cattle, sheep, adult swine	100 µg/kg DW ration as sodium selenate or selenite	37
Weanling swine	300 µg/kg DW ration as sodium selenate or selenite	37
Forage, grazing sheep and cattle	>100 µg/kg DW	4
Blood	>40–80 µg/L FW	17
White-tailed deer		
Heart	>150 µg/kg DW	17
Kidney	>3000 µg/kg DW	17
Liver	>250 µg/kg DW	17
Serum	>30 µg/L FW	17
Humans		
Diet	40–200 µg/kg FW	3, 5
Daily intake		
Recommended		
Females	55 µg (= 1.0 µg/kg BW daily)	18, 40
Males	70 µg (= 1.0 µg/kg BW daily)	18, 40
Children	0.004 µg/kg BW	18
Maximum	500 µg	40

Table 31.5 (continued) Proposed Criteria for Prevention of Selenium Deficiency and for Protection Against Selenosis (Values are in mg of selenium/kg fresh weight [FW] or dry weight [DW].)

Criterion	Selenium Concentration	Reference ^a
Drinking water		
Bottled water	<10 µg/L FW	18
Assuming water is sole selenium source, 2 L daily	20 µg/L FW	6
PROTECTION AGAINST SELENOSIS		
Crop protection		
Irrigation water	<50 µg/L	5, 12
Aquatic life protection		
Freshwater		
Total dissolved	Average 4-day concentration not to exceed 5 µg acid-soluble Se/L more than once every 3 years; average 1-h concentration not to exceed 20 µg/L more than once every 3 years	7, 18–20
Total recoverable ^b	After filtration through 0.45-µ filter, <2 µg total Se/L, sometimes <1 µg/L for organoselenium compounds	27
Waterborne selenium	<2 µg/L	42
Adverse effects on fish reproduction possible	>2 µg inorganic Se/L; >1 µg organic Se/L; sometimes, <1 µg organic Se/L	42
Fish		
Diet		
Freshwater fishes		
Acceptable	<3000 µg/kg DW ration	42
Lethal	>6500–54,000 µg/kg DW feed	42
Growth reduction	>5000–20,000 µg/kg DW feed	42
Kidney damage	>11,000 µg/kg DW feed	42
Juvenile chinook salmon		
Adverse effects	>3000–5000 µg total Se/kg DW	21
Safe	<3000 µg total Se/kg DW	21
Rainbow trout, safe	<3000 µg/kg DW	26
Tissue residues, acceptable		
Whole body	<12,000 µg/kg DW	22
Gonads	<8000–<10,000 µg/kg DW	23, 25, 27
Carcass or ovaries, bluegills	<6000 µg/kg FW	24
Freshwater and anadromous fishes		
Whole body	<4000 µg/kg DW	27, 42
Liver	<12,000 µg/kg DW	27, 42
Muscle	<8000 µg/kg DW	27, 42
Ovaries and eggs	<10,000 µg/kg DW	42
Great Lakes		
Water	<10 µg/L	8, 18
Saltwater		
Total dissolved	Average 4-day concentration not to exceed 71 µg acid-soluble Se/L more than once every 3 years and 1-h concentration does not exceed 300 µg/L more than once every 3 years	7, 18
Birds		
Diet		
Mallard		
Maximum tolerated	<10,000 µg/kg DW	31
Reproduction inhibited	7000–11,000 µg/kg DW, as selenomethionine	33, 34, 41, 42
Malformed embryos	16,000 µg/kg DW, as selenomethionine	34

Table 31.5 (continued) Proposed Criteria for Prevention of Selenium Deficiency and for Protection Against Selenosis (Values are in mg of selenium/kg fresh weight [FW] or dry weight [DW].)

Criterion	Selenium Concentration	Reference ^a
Fatal	10,000–20,000 µg/kg, as selenomethionine	33
Water		
Sensitive fish-eating species	<0.8–<1.9 µg dissolved Se/L	28
Mallard	<2.1 µg dissolved Se/L	28
Aquatic birds, most species		
Minimal hazard	<2.3 µg dissolved Se/L	29
Hazardous	3–20 µg dissolved Se/L	29
Maximum allowable	<10.0 µg dissolved Se/L	29
Tissues		
Eggs		
Reproductive impairment		
Unlikely	<2000 µg/kg DW; <3000–<3300 µg/kg FW	27, 31, 35, 41
Possible	>1000 µg/kg FW	30
Probable	>5000 µg/kg FW; >15,000 µg/kg DW	30, 35
Liver		
Acceptable	<3000 µg/kg FW	41
Acceptable	<5200–<10,000 µg/kg DW	27, 31
Adverse effects	>10,000 µg/kg FW	41
Poisoned	>66,000 µg/kg DW	32
Lethal	>20,000 µg/kg FW	41
Mammals (non-humans)		
Livestock protection		
Drinking water	<50 µg/L FW	5, 9
Diet (total)	<2000 µg/kg DW	10
Diet (natural)	<4000 µg/kg DW	5, 39
Feeds (natural)	<2000 µg/kg DW	11
Forage (natural)	<5000 µg/kg DW	11
Tissues		
Blood		
Adequate	80 µg/L FW	17
Toxic	>3000 µg/L FW	17, 36
Kidney		
Toxic	>3000–6000 µg/kg FW	36
Liver		
Toxic	>12,000–15,000 µg/kg FW	36
Monkeys		
Adverse effects		
Erythrocytes	>2300 µg/kg FW	38
Hair	>27,000 µg/kg FW	38
Plasma	>2800 µg/L FW	38
Drinking water		
River otter	<0.7 µg dissolved Se/L	28
Bats and shrews	<0.9 µg dissolved Se/L	28
Mink	<1.1 µg dissolved Se/L	28
Human health protection		
Seafood	Not to exceed 2000 µg/kg FW	13
Drinking water		
Most states	<10 µg/L FW	18
Minnesota	<20 µg/L FW	18
International	<10 µg/L FW	18
Maximum permissible ^c	<50 µg/L FW	18
Health advisory, chronic		
Child	<31 µg/L FW	18
Adult	<107 µg/L FW	18

Table 31.5 (continued) Proposed Criteria for Prevention of Selenium Deficiency and for Protection Against Selenosis (Values are in mg of selenium/kg fresh weight [FW] or dry weight [DW].)

Criterion	Selenium Concentration	Reference ^a
Food (natural)	<5000 µg/kg FW; <850 µg daily	5, 18
Milk or water	<500 µg/L FW	5
Daily intake (all sources)		
Adults		
Safe	<200 µg	4
Safe, chronic ^d	<5 µg/kg BW (= <350 µg for a 70-kg adult)	18
Normal	60–250 µg	14
Maximum tolerable level	<500 µg	15
Infants	4–<35 µg	14
Children		
Age 1–3	20–<80 µg	15
Age 4–6	30–<120 µg	15
Age 7–11+	50–<200 µg	15
Air		
Japan	<100 µg/m ³	16
Russia	<100 µg/m ³	16
United States	Usually <200 µg/m ³ ; some states 2–<5 µg/m ³	16, 18

^a 1, Hilton et al. 1980; 2, Fishbein 1977; 3, Harr 1978; 4, Shamberger 1981; 5, Wilber 1983; 6, Robberecht and Von Grieken 1982; 7, USEPA 1987; 8, Wong et al. 1980; 9, NAS 1973; 10, NRC 1983; 11, Frost 1972; 12, Birkner 1978; 13, Bebbington et al. 1977; 14, Lo and Sandi 1980; 15, Levander 1984; 16, NAS 1976; 17, Oliver et al. 1990; 18, USPHS 1996; 19, Allen and Wilson 1990; 20, Coyle et al. 1993; 21, Hamilton et al. 1990; 22, Saiki et al. 1992; 23, Waddell and May 1995; 24, Gillespie 1986; 25, Lemly 1993c; 26, Lorentzen et al. 1994; 27, Lemly 1993b; 28, Peterson and Nebeker 1991; 29, Skorupa and Ohlendorf 1991; 30, Heinz et al. 1989; 31, Wiemeyer and Hoffman 1996; 32, Albers et al. 1996; 33, Heinz and Fitzgerald 1993a; 34, Heinz and Fitzgerald 1993b; 35, Ohlendorf et al. 1986a; 36, Alexander et al. 1990; 37, U.S. Food and Drug Administration 1993; 38, Hawkes et al. 1992; 39, Hoffman et al. 1989; 40, Medeiros et al. 1993; 41, Heinz 1996; 42, Lemly 1996b.

^b High potential for biomagnification in aquatic food chains, dietary toxicity, and reproductive toxicity.

^c Based on a NOAEL (no observable adverse effect level) of 400 µg Se daily, equivalent to 5.7 µg/kg BW daily for a 70-kg person.

^d Based on a NOAEL of 15 µg/kg BW daily for dermal effects and an uncertainty factor of 3 to account for sensitive individuals (USPHS 1996).

Regarding selenium deficiency, it appears that diets containing 50 to 100 µg Se/kg ration provide adequate protection to humans and to various species of fish, small laboratory mammals, and livestock (Table 31.5). Factors contributing to selenium deficiency in crops include increasing use of agricultural fertilizers and increasing atmospheric fallout of sulfur. Furthermore, foliar applications of selenate, although efficient in raising selenium levels in plants, have only short-term value (Frost and Ingvoldstad 1975). There is a general consensus that selenium deficiency in livestock in many countries is increasing, resulting in a need for added selenium in the food chain.

Recommendations for protection of freshwater aquatic life include acid-soluble total selenium concentrations in the water of less than 5 µg/L on a daily average, or 20 µg/L at any time (Table 31.5). These values are higher for saltwater life: 71 µg/L daily average, 300 µg/L at any time. The concentration range of 5 to 20 µg/L recommended for protection of freshwater aquatic life is below the range of 60 to 600 µg/L that is fatal to various sensitive species of marine and freshwater fauna, and in this respect affords an adequate measure of protection. It is also below the range (47 to 53 µg/L) that has been associated with growth inhibition of freshwater algae, anemia and reduced hatch in rainbow trout, and shifts in species composition of freshwater algal communities. But studies by Cumbie and Van Horn (1978) and Sorensen et al. (1984) showed that water concentrations of 9 to 12 µg Se/L were associated with reduced reproduction of freshwater fishes, and their results strongly indicated that some downward modification of the selenium freshwater aquatic life protection criterion may be appropriate. Furthermore, high bioconcentration

and accumulation of selenium from the water column by numerous species of algae, fish, and invertebrates is well documented at levels between 0.015 and 3.3 µg Se/L, which is substantially below the recommended range of 5 to 20 µg/L in freshwater. The significance of selenium residues in aquatic biota in terms of bioavailability and selenium receptor sites is imperfectly understood, and it appears that much additional research is warranted on formulating suitable models of selenium biogeochemistry and pharmacokinetics in aquatic environments (Hodson 1990; Bowie and Grieb 1991; Hermanutz et al. 1992).

Resource managers and aquatic biologists need data on selenium concentrations in water, food-chain organisms, and fish and wildlife tissues in order to adequately assess the overall selenium status and health of aquatic ecosystems (Lemly 1993b). Because selenium is depurated rapidly in aquatic birds, resource managers should be concerned primarily about current exposure in nature and not previous exposures (Heinz 1993b). The potential for food-chain biomagnification and reproductive impairment in fish and birds is the most sensitive biological response for estimating ecosystem-level impacts of selenium contamination (Baumann and Gillespie 1986; Lemly 1996a), and these are best reflected in selenium concentrations in gravid ovaries and eggs of adult fish and aquatic bird populations (Ohlendorf et al. 1986a; Lemly 1993b). More research is recommended on biomarkers of selenium exposure and effect (USPHS 1996).

Field studies demonstrated that migratory waterfowl were heavily and adversely affected while nesting at selenium-contaminated irrigation drainwater ponds in California, where food chain organisms contained between 12,000 and 280,000 µg Se/kg. The source and fate of selenium in irrigation drainwater ponds are largely unknown; they must be determined so that alternate technologies for selenium control can be implemented to protect waterfowl in that geographical region.

Livestock appear to be protected against selenosis provided that their diets contain less than 4000 µg Se/kg of natural (i.e., nonsupplemented) selenium (Table 31.5). This concentration is somewhat higher than levels reported for rats (Wilber 1983). Minimum toxic concentrations of selenium in lifetime exposure of rats given diets containing natural selenium were 1400 µg/kg ration as judged by evidence of liver changes, and 3000 µg/kg ration as estimated from longevity and histological changes in heart, kidney, and spleen. These values were only 350 and 750 µg/kg ration, respectively, when rat diets contained purified, rather than natural, selenium. This relationship emphasizes that accidental poisoning of livestock, and presumably fish and wildlife, may occur when soils are deliberately supplemented with purified selenium, or when soils or aquifers are contaminated as a result of faulty waste disposal practices. Although the concentration of <50 µg Se/L for livestock drinking water and irrigation water for crop protection is inconsistent with that of <35 µg Se/L for aquatic life protection, neither livestock nor crops appear threatened at the higher level. Since many waterways that abut agricultural lands or areas of high anthropogenic loadings of selenium contain valuable and desirable aquatic species, it would appear that some downward modification of the current livestock drinking water concentration of selenium is necessary. Selenium is a proven teratogen in fishes and birds, but this has not been established in mammals (USPHS 1996). More research is needed on possible teratogenic effects of organoseelenium compounds in mammals.

Acute lethal doses for livestock species ranged from 3300 µg Se/kg body weight for horses and mules to 15,000 µg/kg for swine; appetite loss in cattle was noted at 500 µg/kg. For humans, the maximum tolerance level is usually set at 500 µg Se daily (Lo and Sandi 1980), and the "safe" level at 200 µg/day (Shamberger 1981). Selenium dietary levels for humans should not exceed 5000 µg/kg ration; however, recommended maximum dietary levels in other mammals ranged from 1000 µg/kg for rats to 4000 µg/kg for horses. For all species, including humans, there is a tendency to list selenium dosage levels in terms of "natural" and "supplemented" levels, with the tacit understanding that "natural" levels are about one fourth as toxic as "supplemented" values. Given the complexities of selenium metabolism and speciation, it appears that greater precision and clarity are necessary in formulating selenium criteria if these criteria are to become administratively enforced standards through passage of appropriate legislation.

Aerosol concentrations in excess of 4.0 µg Se/m³ are potentially harmful to human health (Harr 1978). Concentrations in excess of this value (6.0 µg Se/m³) were regularly encountered in the vicinity of the smeltery at Sudbury, Ontario, Canada (Nriagu and Wong 1983). It is not now known whether respiration rates of wildlife, particularly birds, are comparable to those of humans, whether selenium absorption energetics are similar, or whether wildlife species that frequent point sources of air contaminated by high selenium levels for protracted periods are at greater risk than humans. Until additional and more conclusive data become available, aerosol concentrations of less than 4.0 µg Se/m³ are recommended for the protection of sensitive wildlife species.

31.8 SUMMARY

Most authorities agree on five points.

1. Selenium deficiency is not as well documented as selenosis, but may be equally significant.
2. Selenium released as a result of anthropogenic activities (including fossil fuel combustion and metal smelting), as well as that in naturally seleniferous areas, poses the greatest threat of poisoning to fish and wildlife.
3. Additional research is required on chemical and biological transformations among valence states, allotropic forms, and isomers of selenium.
4. Metabolism and degradation of selenium are both significantly modified by interaction with various heavy metals, agricultural chemicals, microorganisms, and numerous physicochemical factors; and until these interactions are resolved, it will be difficult to meaningfully interpret selenium residues in various tissues.
5. Documented biological responses to selenium deficiency or to selenosis vary widely, even among closely related taxonomic groups.

It is generally agreed that selenium deficiency can be prevented in fish, small laboratory mammals, and livestock by feeding diets containing 50 to 100 µg Se/kg. The concentration range of total acid-soluble selenium currently recommended for aquatic life protection — 5 µg/L in freshwater to 71 µg/L in marine waters — is below the range of 60 to 600 µg/L that is fatal to sensitive aquatic species. In freshwater, it is also below the range of 47 to 53 µg/L associated with growth inhibition of freshwater algae, anemia and reduced hatching in trout, and shifts in species composition of freshwater algae communities. Accordingly, current recommendations for selenium with respect to aquatic life appear to afford an adequate measure of protection. However, some studies have shown that water concentrations of 9 to 12 µg Se/L are associated with inhibited reproduction of certain freshwater teleosts, suggesting that selenium criteria for protection of freshwater life should be revised downward. Also, high bioconcentration and accumulation of selenium from water by numerous species of algae, fish, and invertebrates is well documented at levels of 0.015 to 3.3 µg Se/L, which are substantially below the recommended range of 5 to 71 µg Se/L. The significance of selenium residues in aquatic biota is still unclear, and more research appears to be needed on selenium pharmacokinetics in aquatic environments.

Aerosol concentrations exceeding 4.0 µg Se/m³ are considered potentially harmful to human health. However, no comparable database for birds and other wildlife species is available at this time. Selenium poisoning in livestock is prevented if diets do not exceed 5.0 mg Se/kg natural forage, or 2.0 mg Se/kg in feeds supplemented with purified selenium. Minimum toxic concentrations of selenium in the rat (a sensitive species) fed diets containing natural selenium were 1400 µg Se/kg as judged by evidence of liver changes, and 3000 µg Se/kg as estimated from longevity and histopathology. These values were only 350 and 750 µg/kg, respectively, when diets low in natural selenium were fortified with purified selenium. The evidence is incomplete for migratory waterfowl and other birds, but diets containing more than 3.0 mg Se/kg are demonstrably harmful, as are total selenium concentrations in excess of 5 mg/kg FW in eggs and 10 mg/kg DW in livers.

31.9 LITERATURE CITED

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CHAPTER 32

Radiation

32.1 INTRODUCTION

Life on Earth has evolved under the ubiquitous presence of environmental solar, X-ray, gamma, and charged-particle radiation. On a global basis, radiation from natural sources is a far more important contributor to radiation dose to living organisms than radiation from anthropogenic sources (Aarkrog 1990). However, ionizing radiation can harm biological systems (Aarkrog 1990; Nozaki 1991; Severa and Bar 1991), and this harm can be expressed (1) in a range of syndromes from prompt lethality to reduced vigor, shortened life span, and diminished reproductive rate by the irradiated organism and (2) by the genetic transmission of radiation-altered genes that are most commonly recessive and almost always disadvantageous to their carriers (Bowen et al. 1971). Direct effects of radiation were documented in lampreys in 1896 — soon after H. Becquerel discovered radioactivity — and in brine shrimp (*Artemia* sp.) in 1923 (Whicker and Schultz 1982a). Genetic effects of ionizing radiation, and thus X-rays, as a mutagenic agent were first documented in 1927 in fruit flies, *Drosophila melanogaster* (Evans 1990). The discovery of radioactivity of nuclear particles and the discovery of uranium fission resulted in a great upsurge of nuclear research. During and shortly after World War II, nuclear reactors, testing of nuclear weapons, and use of radionuclides as tracers in almost all scientific and technical fields were developed rapidly (Severa and Bar 1991). Environmental radiation from anthropogenic sources caused serious concerns beginning in the early 1940s when fission of uranium and transuranic nuclei became possible in reactors and in explosions of nuclear weapons (Aarkrog 1990). The first nuclear explosion resulted from a 19-kiloton (TNT-equivalent) source in New Mexico in July 1945 (Whicker and Schultz 1982a). On August 6, 1945, about 75,000 people were killed when the United States Army Air Corps dropped a uranium nuclear bomb on Hiroshima, Japan; on August 9, 1945, about 78,000 Japanese were killed and more than 100,000 injured when a plutonium nuclear bomb was detonated at Nagasaki (Kudo et al. 1991). The former Soviet Union detonated its first nuclear device in August 1949; and in 1952, the United Kingdom exploded a device in Australia (Whicker and Schultz 1982a). Since 1960, nuclear devices have also been detonated by France, India, Pakistan, The People's Republic of China, and possibly others. Nuclear devices have been developed that can release energy in the megaton range. The first such device was detonated by the United States in 1954 at Bikini Atoll and accidentally contaminated Japanese fishermen and Marshall Island natives. Between 1945 and 1973, an estimated 963 nuclear tests were conducted by The People's Republic of China, France, the former Soviet Union, the United Kingdom, and the United States; 47% of them were atmospheric and 53% subsurface (Whicker and Schultz 1982a).

Today, the most important environmentally damaging anthropogenic radiation comes from atmospheric testing of nuclear weapons conducted 20 to 30 years ago, authorized discharges to the sea from nuclear reprocessing plants, and from the Chernobyl accident in 1986 (Aarkrog 1990).

By the year 2000, the United States will have an estimated 40,000 tons of spent nuclear fuel stored at some 70 sites and awaiting disposal. By 2035, after all existing nuclear plants have completed 40 years of operation, about 85,000 metric tons will be awaiting disposal (Slovic et al. 1991).

Ecological and toxicological information on radiation is especially voluminous, and the reader is strongly advised to consult several of the reviews listed below.*

32.2 PHYSICAL PROPERTIES OF RADIATION

32.2.1 General

Radiation is usually defined as the emission and propagation of energy through space in the form of waves and subatomic particles (Weast 1985; Kiefer 1990). For regulatory purposes in the United States, radiation is narrowly defined as α , β , γ , or X-rays; neutrons; and high-energy electrons, protons, or other atomic particles; but not radio-waves nor visible, infrared, or ultraviolet light (U.S. Code of Federal Regulations [USCFR] 1990). Readers may wish to consult the glossary at the end of this chapter.

In current atomic theory, all elementary forms of matter consist of small units called atoms. All atoms of the same element have the same size and weight. Atoms of different elements differ in size and weight. Atoms of the same or different elements may unite to form compound substances called molecules. Each atom consists of a central nucleus and several negatively charged electrons in a cloud around the nucleus. The nucleus is composed of positively charged particles called protons, and particles without charge called neutrons. Electrons are arranged in successive energy levels around the nucleus, and the extranuclear electronic structure of the atom is characteristic of the element. Electrons in the inner shells are tightly bound to the nucleus but can be altered by high-energy waves and particles (Weast 1985). Atoms are classified chemically into 92 naturally occurring elements and another dozen or so artificial elements based on the number of protons in their nucleus (= the atomic number) (Rose et al. 1990; Severa and Bar 1991). Atoms of the same element may occur as isotopes that differ in the number of neutrons accompanying the protons in the nucleus. The sum of the number of protons and neutrons in the nucleus is called the mass number (see Glossary), and is indicated by a superscript that precedes the chemical symbol of the element. For example, three isotopes of hydrogen (one proton) are denoted as ^1H (no neutrons), ^2H (1 neutron, also known as deuterium), and ^3H (2 neutrons, also known as tritium). A nuclide is an elemental form distinguished from others by its atomic and mass numbers. Some nuclides, such as ^{238}U and ^{137}Cs , are radioactive and spontaneously decay to a different nuclide with the emission of characteristic energy particles or electromagnetic waves; isomers of a given nuclide that differ in energy content are metastable (i.e., ^{115m}Cd) and characterized, in part, by the half-life of the isomer (Rose et al. 1990; Severa and Bar 1991).

Chemical forms with at least one radioactive atomic nucleus are radioactive substances. The capability of atomic nuclei to undergo spontaneous nuclear transformation is called radioactivity. Nuclear transformations are accompanied by emission of nuclear radiation (Severa and Bar 1991). The average number of nuclei that disintegrate per unit time (= activity) is directly proportional to the total number of radioactive nuclei. The time for 50% of the original nuclei to disintegrate (= half-life or Tb 1/2) is equal to $\ln 2/\text{decay constant}$ for that element (Kiefer 1990). Radiations

* National Academy of Sciences [NAS] 1957, 1971; Glasstone 1958; Schultz and Klement 1963; Nelson and Evans 1969; Nelson 1971; Polikarpov 1973; Cushing 1976; Nelson 1976; International Atomic Energy Agency [IAEA] 1976, 1992; International Commission on Radiological Protection [ICRP] 1977, 1991a, 1991b; Luckey 1980; Whicker and Schultz 1982a, 1982b; League of Women Voters [LWV] 1985; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR] 1988; Becker 1990; Kiefer 1990; Majumdar et al. 1990; Brisbin 1991; Kershaw and Woodhead 1991; Sankaranarayanan 1991a, 1991b, 1991c; National Council on Radiation Protection and Measurements [NCRP] 1991; Severa and Bar 1991; Eisler 1994; Talmage and Meyers-Schone 1995.

that have sufficient energy to interact with matter to produce charged particles are called ionizing radiations (Hobbs and McClellan 1986; UNSCEAR 1988). Radiation injury is related to the production of ions inside the cell. Ionizing radiations include electromagnetic radiation such as gamma (γ) and X-rays and particulate or corpuscular radiation such as alpha (α) particles, beta (β) particles, electrons, positrons, and neutrons. Ionizing radiation may be produced from manufactured devices such as X-ray tubes or from the disintegration of radioactive nuclides. Some nuclides occur naturally, but others may be produced artificially, for example, in nuclear reactors. The basic reaction of ionizing radiation with molecules is either ionization or excitation. In ionization, an orbital electron is ejected from the molecule and forms an ion pair. Directly ionizing particles are charged and possess the energy to produce ionizations along their path from impulses imparted to orbital electrons via electrical forces between the charged particles and electrons. In excitation, an electron is raised to a higher energy level. Indirectly ionizing radiations are not charged and penetrate a medium until they collide with elements of the atom and liberate energetically charged ionizing particles.

32.2.2 Electromagnetic Spectrum

The electromagnetic spectrum is defined as the ordered array of known electromagnetic radiations, including cosmic rays; gamma rays; X-rays; ultraviolet, visible, and infrared radiations; and radio-waves (Weast 1985). The energy transfer by electromagnetic waves can be described by discrete processes with elementary units called photons (Kiefer 1990). Their energy, E, is given by $E = hv$, where h is Planck's constant and v the frequency. Because velocity C, wavelength λ , and frequency v are related ($C = \lambda v$), $E = hc/\lambda$ (Kiefer 1990). The relationships between E, v, and λ for parts of the total spectrum of the electromagnetic waves are shown in Figure 32.1. The high-energy radiation that enters the Earth's atmosphere from outer space is known as primary cosmic rays. On interaction with the nuclei of atoms in the air, secondary cosmic rays and a variety of reaction products (cosmogenic nuclides) such as ^3H , ^7Be , ^{10}Be , ^{14}C , ^{22}Na , and ^{24}Na are produced (UNSCEAR 1988).

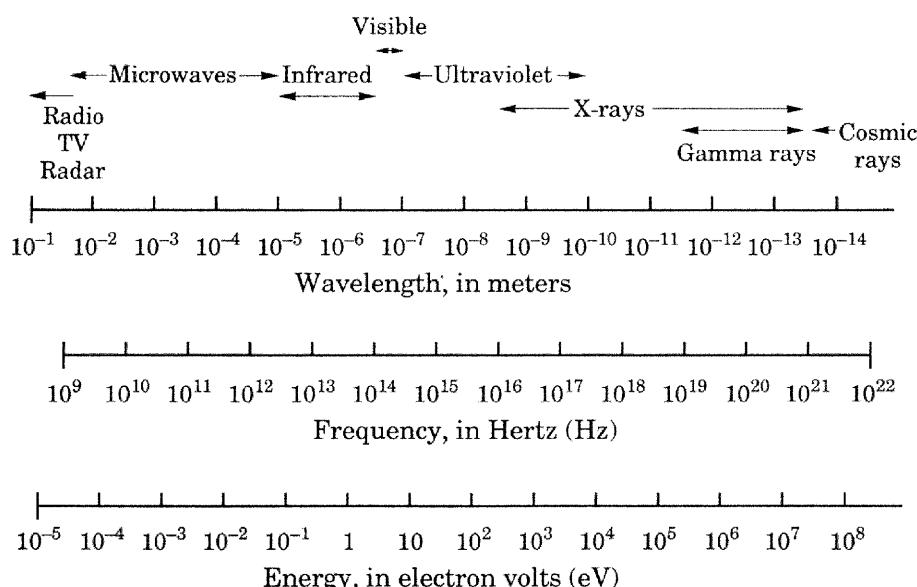


Figure 32.1 The spectrum of electromagnetic waves, showing the relationship between wavelength, frequency, and energy. (Modified from Kiefer, J. 1990. *Biological Radiation Effects*. Springer-Verlag, Berlin. 444 pp.)

32.2.3 Radionuclides

Radioactive nuclides contain atoms that disintegrate by emission of subatomic particles and gamma or X-ray photons (Weast 1985; Hobbs and McClellan 1986; Kiefer 1990; Rose et al. 1990). In alpha decay, a helium nucleus of two protons and two neutrons is emitted and reduces the mass number by 4 and the atomic number by 2. In beta decay, an electron — produced by the disintegration of a neutron into a proton, an electron, and an antineutrino — is emitted from the nucleus and increases the atomic number by 1 without changing the mass number. Sometimes, a positron together with a neutrino is emitted. And sometimes an electron may be captured from the K (outermost) shell of the atom; the resultant electron hole in the K shell is filled by electrons from outer orbits and causes the emission of X-rays. Alpha and beta decay generally leave the resultant daughter nuclei in an excited state that is deactivated by emission of γ photons. Although γ emission accompanies most decays, it is not always detected, especially not with light β emitters such as ^3H , ^{14}C , ^{32}P , and ^{35}S . The half-life of individual radionuclides can be measured (i.e., the time during which half the atoms of the radionuclide spontaneously decay to a daughter nuclide). Another form of nuclear breakdown is fission, in which the nucleus breaks into two nuclides of approximately half the parent's size (Rose et al. 1990). The symbol, mass number, atomic number, half-life, and decay mode of all radionuclides mentioned herein are listed in [Table 32.1](#).

Table 32.1 Selected Radionuclides: Symbol, Mass Number, Atomic Number, Half-Life, and Decay Mode

Nuclide	Symbol	Mass Number	Atomic Number	Half-life ^a	Major Decay Mode ^b
Hydrogen-3	^3H	3	1	12.26 y	β^-
Beryllium-7	^7Be	7	4	53.3 d	EC
Beryllium-10	^{10}Be	10	4	1,600,000 y	β^-
Carbon-14	^{14}C	14	6	5730 y	β^-
Sodium-22	^{22}Na	22	11	2.6 y	β^+ , EC
Sodium-24	^{24}Na	24	11	15 h	β^-
Phosphorus-32	^{32}P	32	15	14.3 d	β^-
Sulfur-35	^{35}S	35	16	87 d	β^-
Argon-39	^{39}Ar	39	18	261 y	β^-
Potassium-40	^{40}K	40	19	1,250,000,000 y	β^- , β^+ , EC
Potassium-42	^{42}K	42	19	12.4 h	β^-
Calcium-45	^{45}Ca	45	20	164 d	β^-
Chromium-51	^{51}Cr	51	24	28 d	EC
Manganese-54	^{54}Mn	54	25	312 d	EC
Manganese-56	^{56}Mn	56	25	2.6 h	β^-
Iron-55	^{55}Fe	55	26	2.7 y	EC
Iron-59	^{59}Fe	59	26	45 d	β^-
Cobalt-57	^{57}Co	57	27	271 d	EC
Cobalt-58	^{58}Co	58	27	71 d	β^+ , EC
Cobalt-60	^{60}Co	60	27	5.3 y	β^-
Nickel-63	^{63}Ni	63	28	100 y	β^-
Nickel-65	^{65}Ni	65	28	2.5 h	β^-
Copper-64	^{64}Cu	64	29	12.7 h	β^- , β^+ , EC
Zinc-65	^{65}Zn	65	30	244 d	β^+ , EC
Selenium-75	^{75}Se	75	34	118 d	EC
Krypton-85	^{85}Kr	85	36	10.72 y	β^-
Rubidium-86	^{86}Rb	86	37	18.6 d	β^-
Rubidium-87	^{87}Rb	87	37	49,000,000,000 y	β^-
Strontium-85	^{85}Sr	85	38	64.8 d	EC
Strontium-89	^{89}Sr	89	38	50.5 d	β^-
Strontium-90	^{90}Sr	90	38	29 y	β^-

Table 32.1 (continued) Selected Radionuclides: Symbol, Mass Number, Atomic Number, Half-Life, and Decay Mode

Nuclide	Symbol	Mass Number	Atomic Number	Half-life ^a	Major Decay Mode ^b
Yttrium-90	⁹⁰ Y	90	39	64 h	β^-
Yttrium-91	⁹¹ Y	91	39	59 d	β^-
Zirconium-95	⁹⁵ Zr	95	40	65 d	β^-
Niobium-95	⁹⁵ Nb	95	41	35 d	β^-
Molybdenum-99	⁹⁹ Mo	99	42	66 h	β^-
Technetium-99	⁹⁹ Tc	99	43	213,000 y	β^-
Technetium-99m	^{99m} Tc	99	43	6 h	IT
Ruthenium-103	¹⁰³ Ru	103	44	40 d	β^-
Ruthenium-106	¹⁰⁶ Ru	106	44	373 d	β^-
Rhodium-106	¹⁰⁶ Rh	106	45	29.8 s	β^-
Palladium-109	¹⁰⁹ Pd	109	46	14 h	β^-
Silver-108m	^{108m} Ag	108	47	130 y	EC, IT
Silver-110m	^{110m} Ag	110	47	250 d	β^- , IT
Silver-110	¹¹⁰ Ag	110	47	24.6 s	β^-
Silver-111	¹¹¹ Ag	111	47	7.5 d	β^-
Silver-113	¹¹³ Ag	113	47	5.3 h	β^-
Cadmium-109	¹⁰⁹ Cd	109	48	462 d	EC
Cadmium-113m	^{113m} Cd	113	48	13.7 y	β^-
Cadmium-115m	^{115m} Cd	115	48	44.6 d	β^-
Cadmium-115	¹¹⁵ Cd	115	48	54 h	β^-
Tin-123	¹²³ Sn	123	50	129 d	β^-
Tin-126	¹²⁶ Sn	126	50	100,000 y	β^-
Antimony-124	¹²⁴ Sb	124	51	60 d	β^-
Antimony-125	¹²⁵ Sb	125	51	2.7 y	β^-
Antimony-127	¹²⁷ Sb	127	51	3.8 d	β^-
Tellurium-127m	^{127m} Te	127	52	109 d	IT, β^-
Tellurium-129m	^{129m} Te	129	52	33 d	IT, β^-
Tellurium-129	¹²⁹ Te	129	52	69.5 m	β^-
Tellurium-132	¹³² Te	132	52	78.2 h	β^-
Iodine-125	¹²⁵ I	125	53	60 d	β^- , EC
Iodine-129	¹²⁹ I	129	53	16,000,000 y	β^-
Iodine-130	¹³⁰ I	130	53	12.4 h	β^-
Iodine-131	¹³¹ I	131	53	8 d	β^-
Xenon-131	¹³¹ Xe	131	54	11.9 d	IT
Xenon-133	¹³³ Xe	133	54	5.3 d	β^-
Xenon-135	¹³⁵ Xe	135	54	9.1 h	β^-
Cesium-134	¹³⁴ Cs	134	55	2.06 y	β^-
Cesium-135	¹³⁵ Cs	135	55	3,000,000 y	β^-
Cesium-137	¹³⁷ Cs	137	55	30.2 y	β^-
Barium-140	¹⁴⁰ Ba	140	56	12.8 d	β^-
Lanthanum-140	¹⁴⁰ La	140	57	40 h	β^-
Cerium-141	¹⁴¹ Ce	141	58	33 d	β^-
Cerium-143	¹⁴³ Ce	143	58	33 h	β^-
Cerium-144	¹⁴⁴ Ce	144	58	284 d	β^-
Praseodymium-143	¹⁴³ Pr	143	59	13.6 d	β^-
Praseodymium-144	¹⁴⁴ Pr	144	59	7.2 m	IT
Praseodymium-147	¹⁴⁷ Pr	147	59	13.4 m	β^-
Neodymium-147	¹⁴⁷ Nd	147	60	11 d	β^-
Promethium-147	¹⁴⁷ Pm	147	61	2.6 y	β^-
Samarium-143	¹⁴³ Sm	143	62	8.8 m	β^+ , EC
Samarium-151	¹⁵¹ Sm	151	62	90 y	β^-
Europium-152	¹⁵² Eu	152	63	13.4 y	EC, β^-
Europium-155	¹⁵⁵ Eu	155	63	15.2 d	β^-
Tungsten-181	¹⁸¹ W	181	74	121 d	EC

Table 32.1 (continued) Selected Radionuclides: Symbol, Mass Number, Atomic Number, Half-Life, and Decay Mode

Nuclide	Symbol	Mass Number	Atomic Number	Half-life ^a	Major Decay Mode ^b
Tungsten-185	¹⁸⁵ W	185	74	75 d	β^-
Tungsten-187	¹⁸⁷ W	187	74	24 h	β^-
Gold-198	¹⁹⁸ Au	198	79	2.7 d	β^-
Mercury-203	²⁰³ Hg	203	80	47 d	β^-
Mercury-206	²⁰⁶ Hg	206	80	8.1 m	β^-
Thallium-206	²⁰⁶ Tl	206	81	4.3 m	β^-
Thallium-207	²⁰⁷ Tl	207	81	4.8 m	β^-
Thallium-208	²⁰⁸ Tl	208	81	3 m	β^-
Thallium-210	²¹⁰ Tl	210	81	1.3 m	β^-
Lead-210	²¹⁰ Pb	210	82	22.3 y	β^-
Lead-211	²¹¹ Pb	211	82	36.1 m	β^-
Lead-212	²¹² Pb	212	82	10.6 h	β^-
Lead-214	²¹⁴ Pb	214	82	26.8 m	β^-
Bismuth-210	²¹⁰ Bi	210	83	5.0 d	β^-
Bismuth-211	²¹¹ Bi	211	83	2.2 m	α
Bismuth-212	²¹² Bi	212	83	1.0 h	β^-, α
Bismuth-214	²¹⁴ Bi	214	83	19.9 m	β^-
Bismuth-215	²¹⁵ Bi	215	83	7.4 m	β^-
Polonium-210	²¹⁰ Po	210	84	138.4 d	α
Polonium-211	²¹¹ Po	211	84	0.52 s	α
Polonium-212	²¹² Po	212	84	0.0000003 s	α
Polonium-214	²¹⁴ Po	214	84	0.000163 s	α
Polonium-215	²¹⁵ Po	215	84	0.00178 s	α
Polonium-216	²¹⁶ Po	216	84	0.15 s	α
Polonium-218	²¹⁸ Po	218	84	3.1 m	α
Astatine-215	²¹⁵ At	215	85	0.0001 s	α
Astatine-218	²¹⁸ At	218	85	1.6 s	α
Astatine-219	²¹⁹ At	219	85	0.9 m	α
Radon-218	²¹⁸ Rn	218	86	0.0356 s	α
Radon-219	²¹⁹ Rn	219	86	3.96 s	α
Radon-220	²²⁰ Rn	220	86	56 s	α
Radon-222	²²² Rn	222	86	3.8 d	α
Francium-223	²²³ Fr	223	87	21.8 m	β^-
Radium-223	²²³ Ra	223	88	11.4 d	α
Radium-224	²²⁴ Ra	224	88	3.7 d	α
Radium-226	²²⁶ Ra	226	88	1620 y	α
Radium-228	²²⁸ Ra	228	88	5.75 y	β^-
Actinium-227	²²⁷ Ac	227	89	21.8 y	β^-
Actinium-228	²²⁸ Ac	228	89	6.13 h	β^-
Thorium-227	²²⁷ Th	227	90	18.8 d	α
Thorium-228	²²⁸ Th	228	90	1.91 y	α
Thorium-230	²³⁰ Th	230	90	75,400 y	α
Thorium-231	²³¹ Th	231	90	25.6 h	β^-
Thorium-232	²³² Th	232	90	14,000,000,000 y	α
Thorium-234	²³⁴ Th	234	90	24 d	β^-
Protactinium-231	²³¹ Pa	231	91	32,700 y	α
Protactinium-234	²³⁴ Pa	234	91	6.7 h	β^-
Protactinium-234m	^{234m} Pa	234	91	1.17 m	β^-, IT
Uranium-233	²³³ U	233	92	160,000 y	α
Uranium-234	²³⁴ U	234	92	245,000 y	α
Uranium-235	²³⁵ U	235	92	710,000,000 y	α
Uranium-236	²³⁶ U	236	92	23,400,000 y	α
Uranium-238	²³⁸ U	238	92	4,470,000,000 y	α
Neptunium-235	²³⁵ Np	235	93	1.08 y	EC

Table 32.1 (continued) Selected Radionuclides: Symbol, Mass Number, Atomic Number, Half-Life, and Decay Mode

Nuclide	Symbol	Mass Number	Atomic Number	Half-life ^a	Major Decay Mode ^b
Neptunium-237	^{237}Np	237	93	2,140,000 y	α
Neptunium-239	^{239}Np	239	93	2.35 d	β^-
Neptunium-241	^{241}Np	241	93	13.9 m	β^-
Plutonium-238	^{238}Pu	238	94	87.7 y	α
Plutonium-239	^{239}Pu	239	94	24,110 y	α
Plutonium-240	^{240}Pu	240	94	6537 y	α
Plutonium-241	^{241}Pu	241	94	14.4 y	β^-
Plutonium-242	^{242}Pu	242	94	376,000 y	α
Plutonium-244	^{244}Pu	244	94	82,000,000 y	α
Americium-241	^{241}Am	241	95	458 y	α
Americium-243	^{243}Am	243	95	7370 y	α
Curium-241	^{241}Cm	241	96	33 d	EC
Curium-242	^{242}Cm	242	96	463 d	α
Curium-243	^{243}Cm	243	96	28.5 y	α
Curium-244	^{244}Cm	244	96	18.1 y	α
Curium-247	^{247}Cm	247	96	15,600,000 y	α
Curium-248	^{248}Cm	248	96	340,000 y	α
Curium-250	^{250}Cm	250	96	7400 y	SF
Californium-252	^{252}Cf	252	98	2.6 y	α , SF

^a s = seconds; m = minutes; h = hours; d = days; y = years

^b Observed modes of decay for all radioactive species: α = particle emission; β^- = beta emission, β^+ = positron emission; EC = electron capture resulting in X-ray emission; IT = isomeric transition from higher to lower energy state; SF = spontaneous fission.

Modified from Whicker and Schultz 1982a, 1982b; Weast 1985; Kiefer 1990; Severa and Bar 1991.

Four general groups of radionuclides are distinguished:

1. A long half-life group (i.e., Tb 1/2 > 10⁹ years) of elements, including ^{238}U , ^{235}U , ^{232}Th , ^{40}K , ^{87}Rb , and ^{143}Sm , formed about 4.5 billion years ago
2. Shorter-lived daughters of U and Th such as Ra and Rn that form as a result of the decay of their long-lived parents
3. Nuclides (i.e., ^{14}C and ^3H) formed by continuing natural nuclear transformations driven by cosmic rays, natural sources of neutrons, or energetic particles that are formed in the upper atmosphere by cosmic rays
4. Nuclides formed as a result of nuclear weapons tests, nuclear reactor operations, and other human activities. Important members of this group include ^{90}Sr , ^{137}Cs , ^{14}C , and ^3H ; note that many members of the third group — such as ^{14}C and ^3H — are also formed in this fourth fashion (Rose et al. 1990).

Radioactive decay usually does not immediately lead to a stable end product, but to other unstable nuclei that form a decay series (Kiefer 1990). The most important examples of unstable nuclei are started by very heavy, naturally occurring nuclei. Because the mass number changes only with α decay, all members of a series can be classified according to their mass numbers (see the uranium-238 decay series in Figure 32.2). A total of three natural decay series — formed at the birth of our planet — are named after their parent isotope: ^{232}Th , ^{235}U , and ^{238}U (Figure 32.3). Several shorter decay series also exist. For example, ^{90}Sr decays with a Tb 1/2 of 28 years by β emission to ^{90}Y , which in turn disintegrates (β emission) with a Tb 1/2 of 64 h to the stable ^{90}Zr (Kiefer 1990). Other examples of known radionuclides since the Earth's origin include ^{40}K and ^{87}Rb . In hazard assessments, all members of a decay series must be considered.

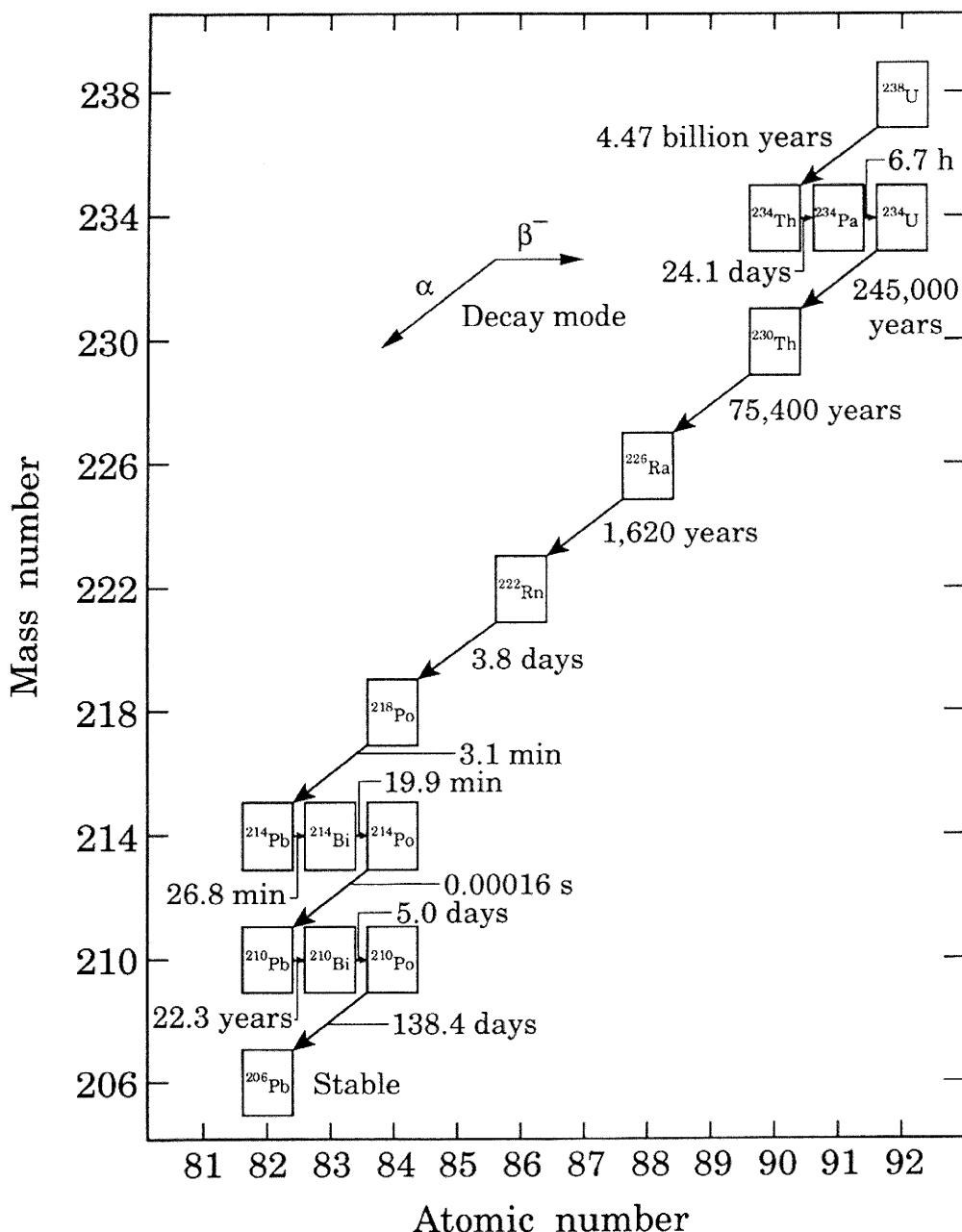


Figure 32.2 The principal uranium-238 decay series, indicating major decay mode and physical half-time of persistence. (Modified from Cecil, L.D. and T.F. Gesell. 1992. Sampling and analysis for radon-222 dissolved in ground water and surface water. *Environ. Monitor. Assess.* 20:55-66.)

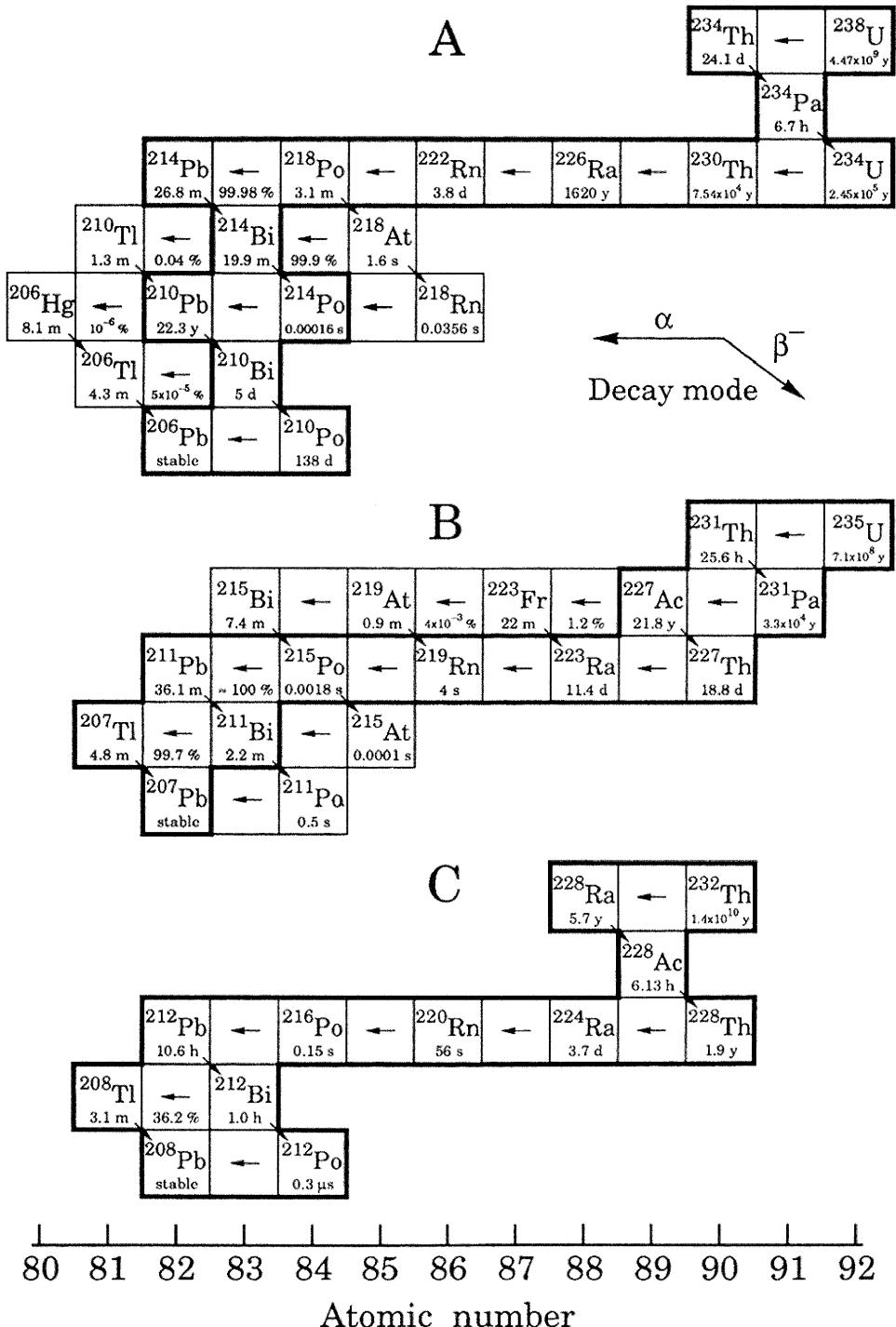


Figure 32.3 The three still-existing natural decay series. **A.** Uranium-238; **B.** Uranium-235; and **C.** Thorium-232. (Modified from Holtzman 1969; LWV 1985; UNSCEAR 1988; Kiefer 1990; Rose et al. 1990). Principal decay products occur within the heavy borders outlined.

32.2.4 Linear Energy Transfer

The deposition of energy in an exposed body is mediated almost exclusively by charged particles. These particles cause ionizations but lose energy with each ionization until they reach the end of their range. Depending on the type of particle, the ionizations are more or less closely spaced and described by the energy loss of a traversing particle. The linear energy transfer (LET) is defined as the amount of locally absorbed energy per unit length; that is, only the energy fraction that leads to ionizations or excitations in the considered site is counted (Kiefer 1990; ICRP 1991a). Because radiation effects are dependent on the nature of the radiation, a weighting factor is used to modify the absorbed dose and to define the dose equivalent. This factor — now called the Radiation Weighting Factor — is a function of LET. Approximate weighting values range from 1 (X-rays, electrons, gamma rays) to 10 (neutrons, protons, singly charged particles of rest mass greater than one atomic mass of unknown energy), and to 20 (alpha particles and multiply charged particles of unknown energy) (ICRP 1977; Whicker and Schultz 1982a; Hobbs and McClellan 1986; Severa and Bar 1991). The relation between radiation type and energy to weighting factors is shown in [Table 32.2](#).

Table 32.2 Radiation Weighting Factors for Various Types of Ionizing Radiations

Radiation Type and Energy Range	Radiation Weighting Factor
X-rays, gamma rays, beta particles, electrons, muons; all energies	1
Neutrons	
10 keV	5
10 keV–100 keV	10
>100 keV–2 MeV	20
>2 MeV–20 MeV	10
>20 MeV	5
Protons	5
Alpha particles, fission fragments, heavy nuclei	20

Data from International Commission on Radiological Protection 1991a.

32.2.5 New Units of Measurement

A variety of units have been used for the assessment of exposures to ionizing radiation. The current international standard terminology is shown in [Table 32.3](#). This chapter uses the new terminology exclusively; this frequently necessitated data transformation of units from early published accounts into the currently accepted international terminology.

Table 32.3 New Units for Use with Radiation and Radioactivity

Variable	Old Unit	New Unit	Old Unit in Terms of New Unit
Activity	Curie (Ci) = 3.7×10^{10} disintegrations per s (dps)	Becquerel (Bq) = 1 dps	1 Ci = 3.7×10^{10} Bq
Exposure	Roentgen (R) = 2.58×10^{-4} Coulombs/kg	Coulomb/kg (C/kg)	1 R = 2.58×10^{-4} C/kg
Absorbed dose	Rad = 100 erg/g	Gray (Gy) = 1 J/kg	1 Rad = 0.01 Gy
Dose equivalent	Rem = damage effects of 1 R	Sievert (Sv) = 1 J/kg	1 Rem = 0.01 Sv

Note: See Glossary (Section 32.11).

Data from International Commission on Radiological Protection [ICRP] 1977, 1991a; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR] 1988.

32.3 SOURCES AND USES

32.3.1 General

Most external exposure of living organisms to radiation is from naturally occurring electromagnetic waves, and most internal exposure from naturally occurring radionuclides, such as potassium-40. Natural radiation doses vary significantly with altitude, radionuclide concentrations in the biogeophysical environment, and uptake kinetics. The major source of global anthropogenic radioactivity is fallout from military atmospheric weapons testing; locally, radiation levels tend to be elevated near nuclear power production facilities, nuclear fuel reprocessing plants, and nuclear waste disposal sites. Dispersion of radioactive materials is governed by a variety of physical, chemical, and biological vectors, including winds, water currents, plankton, and avian and terrestrial wildlife.

32.3.2 Natural Radioactivity

Exposure to natural sources of radiation is unavoidable. Externally, individuals receive cosmic rays, terrestrial X-rays, and gamma radiation. Internally, naturally occurring radionuclides of Pb, Po, Bi, Ra, Rn, K, C, H, U, and Th contribute to the natural radiation dose from inhalation and ingestion. Potassium-40 is the most abundant radionuclide in foods and in all tissues. The mean effective human dose equivalent from natural radiations is 2.4 milliSieverts (mSv). This value includes the lung dose from radon daughter products and is about 20% higher than a 1982 estimate that did not take lung dose into account ([Table 32.4](#)).

Table 32.4 Annual Effective Dose Equivalent to Humans from Natural Sources of Ionizing Radiation

Source of Radiation	Dose Equivalents (mSv)
Cosmic rays	
Ionizing component	0.30
Neutron component	0.06
Cosmogenic radionuclides (mainly ^{3}H and ^{14}C)	0.02
Primordial radionuclides	
Potassium-40	0.33
Rubidium-87	0.01
Uranium-238 series	1.34
Thorium-232 series	0.34
Total	2.4

Data from Whicker and Schultz 1982a; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR] 1988; Aarkrog 1990.

The dose of natural radiation that an organism receives depends on height above sea level, amount and type of radionuclides in the soil of its neighborhood, and the amount taken up from air, water, and food (ICRP 1977; Whicker and Schultz 1982a; Hobbs and McClellan 1986; UNSCEAR 1988; Aarkrog 1990; Kiefer 1990; Nozaki 1991). Natural radiations in various ecosystems result in radiation dose equivalents that usually range between <0.005 and 2.07 mSv annually ([Figure 32.4](#)). Radiation doses are substantially higher at typically elevated local sites ([Table 32.5](#)), such as Denver, and sometimes exceed 17 mSv annually in mountainous regions of Brazil and the former Soviet Union (Whicker and Schultz 1982a).

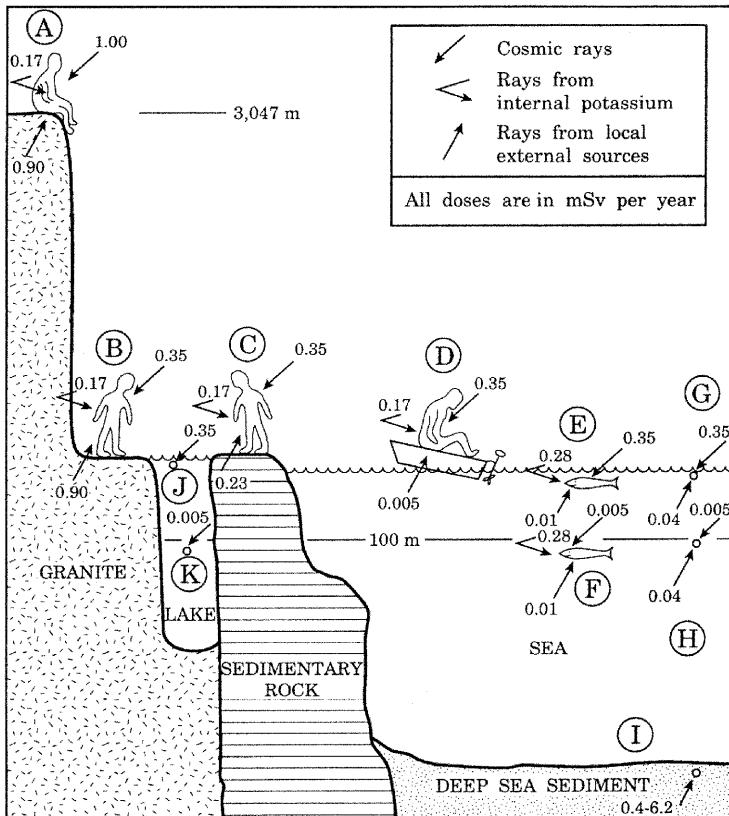


Figure 32.4 Natural radiations in selected radiological domains. (Modified from Folsom, T.R. and J.H. Harley. 1957. Comparisons of some natural radiations received by selected organisms. Pages 28-33 in National Academy of Sciences. The Effects of Atomic Radiation on Oceanography and Fisheries. Publ. No. 551, Natl. Acad. Sci.-Natl. Res. Coun., Washington, D.C.) **A.** Human over granite at 3047 m (10,000 feet) elevation above sea level; total annual dose equivalent of 2.07 mSv (cosmic rays 1.00, granite 0.90, internal emitters 0.17). **B.** Human over granite at sea surface; total annual dose of 1.42 mSv. **C.** Human over sedimentary rock at sea level; total annual dose of 0.75 mSv. **D.** Human over sea; total annual dose of 0.525 mSv. **E.** Large fish in sea near surface; total annual dose of 0.64 mSv. **F.** Large fish in sea at depth of 100 m; total annual dose of 0.295 mSv. **G.** Microorganism in water >100 m deep in sea; total annual dose of 0.045 mSv. **H.** Microorganism in water near sea surface; total annual dose of 0.045 mSv. **I.** Microorganism buried in deep sea sediments; total annual dose between 0.4 and 6.2 mSv. **J.** Microorganism near freshwater surface; total annual dose of 0.35 mSv. **K.** Microorganism 100 m deep in a freshwater lake; total annual dose of 0.005 mSv.

32.3.3 Anthropogenic Radioactivity

Nuclear explosions and nuclear power production are the major sources of anthropogenic activity in the environment. But radionuclide use in medicine, industry, agriculture, education, and production and transport, use, and disposal from these activities present opportunities for wastes to enter the environment (Whicker and Schultz 1982a; [Table 32.6](#)). Radiation was used as early as 1902 in the treatment of diseases, including enlarged thymus, tinea capitis, acne, and cancers of childhood and adolescence (Bowden et al. 1990). The use of X-rays by physicians and dentists represents the largest source of annual dose equivalent of the U.S. population to artificial radiation: 0.78 to 1.01 mSv to bone marrow and 0.016 mSv to the upper GI tract; radiopharmaceuticals contribute an additional 0.14 mSv or a yearly total mean dose of 0.94 to 1.17 mSv to bone marrow (Hobbs and McClellan 1986).

Table 32.5 Annual Whole-Body Radiation Doses to Humans from Various Sources

Source of Radiation	Dose (mSv)
Natural external background	
Denver, Colorado	1.65
Washington state, mean	0.88
United States, average	0.84
Hanford, Washington	0.59
Average medical dose per capita, United States	0.36
Average internal dose from natural radioactivity, United States	0.25
Global weapons fallout	0.05
Consumer product radiation (TV, smoke detector, and other sources)	0.02
Total	1.27–2.33

Data from Gray, R.H., R.E. Jaquish, P.J. Mitchell, and W.H. Rickard. 1989. Environmental monitoring at Hanford, Washington, USA: a brief site history and summary of recent results. *Environ. Manage.* 13:563–572.

Table 32.6 Sources and Applications of Atomic Energy

Source and Output	Application
Nuclear reactor	
Steam, electricity	Electric power (stationary or portable plants), desalination, propulsion of submarines and surface ships
Heat, electricity, neutrons	Spacecraft and satellite power, spacecraft propulsion, research and special materials production
Nuclear explosives, kinetic energy	Military and civilian applications: large-scale earth moving, subsurface excavation, mineral extraction from underground
Encapsulated radioisotopes	
Electricity	Marine navigation aids, unmanned weather stations, spacecraft project power, artificial human organs
Beta and gamma radiation	Food preservation, polymerization, sterilization of medical supplies, thickness gauges
Radionuclides, beta and gamma radiation	Medical uses, tracers in scientific research, measures of manufacturing processes

Data from Joseph, A.B., P.F. Gustafson, I.R. Russell, E.A. Schuert, H.L. Volchok, and A. Tamplin. 1971. Sources of radioactivity and their characteristics. Pages 6–41 in *National Academy of Sciences. Radioactivity in the Marine Environment*. Natl. Acad. Sci., Panel on Radioactivity in the Marine Environment, Washington, D.C.

Atmospheric testing of nuclear weapons is an important human source of environmental radiation (Hobbs and McClellan 1986; UNSCEAR 1988; Aarkrog 1990) (Table 32.7). The first test explosion of a nuclear weapon took place in 1945. Atmospheric tests by the United States, the former Soviet Union, and the United Kingdom continued until they were banned in 1963. France and The People's Republic of China continued to conduct limited atmospheric tests, although no atmospheric nuclear explosions have taken place since 1980. Large nuclear explosions in the atmosphere carry most of the radioactive material into the stratosphere where it remains for 1 to 5 years, depending on the altitude and latitude. Fallout can occur years after an explosion injected material into the atmosphere. Smaller explosions carry the radioactive material only into the troposphere, and fallout occurs within days or weeks. Fallout was highest in the temperate regions and in the northern hemisphere where most of the testing was done. The most abundant radionuclides from atmospheric tests to date are $^{14}\text{C} > ^{137}\text{Cs} > ^{95}\text{Zr} > ^{90}\text{Sr} > ^{106}\text{Ru} > ^{144}\text{Ce} > ^3\text{H}$. Of the many radionuclides produced in nuclear and thermonuclear explosions, the primary contributors to human radiation exposure include ^{14}C , $^{89+90}\text{Sr}$, ^{95}Zr , ^{106}Ru , ^{131}I , ^{137}Cs , ^{141}Ce , and ^{144}Ce . Isotopes of plutonium and americium — although present in quantity — are not significant contributors

Table 32.7 Annual Effective Dose Equivalent from Nuclear Weapons Testing to Humans in the North Temperate Zone

Nuclide	Dose (mSv ^a)
³ H	0.05
¹⁴ C	2.6
⁹⁰ Sr	0.18
⁹⁵ Zr	0.29
¹⁰⁶ Ru	0.14
¹³¹ I	0.05
¹³⁷ Cs	0.88
¹⁴⁴ Ce	0.09
Pu and Am nuclides	0.09
Other nuclides	0.08
Total	4.45 ^b

^a External, 24%; inhalation, 5%; ingestion, 71%.

^b Equivalent to 1.85 times the natural background dose.

Data from Aarkrog, A. 1990. Environmental radiation and radiation releases. *Inter. Jour. Radiation Biol.* 57:619-631.

because of their low solubility. The primary dose from fallout radiation is through external gamma radiation, assimilation through the food chain, or beta radiation of the skin.

Radioisotope thermoelectric generators (RTGs) are sometimes used as power sources for space systems. In April 1964, a United States RTG navigational satellite, SNAP 9A, reentered the atmosphere and burned up at high altitude over the Mozambique Channel, releasing 629 trillion becquerels (TBq), equivalent to 17,000 Ci, of ²³⁸Pu and 0.48 TBq of ²³⁹Pu (Whicker and Schultz 1982a; Richmond 1989). In January 1978, a Soviet RTG satellite, Kosmos 954, reentered the atmosphere over Canada and spread radionuclides across parts of that country (Richmond 1989). The amount of radioactive materials in space applications is expected to increase (Richmond 1989).

Significant amounts of radioactivity are present in the Great Lakes basin, which has numerous nuclear reactors and uranium-mine waste areas (Joshi 1991). The prevailing low levels of artificially produced radionuclides, arising largely from previous fallout (Table 32.8), provide small doses of radiation to residents who consume lake water. Radionuclides enter the Great Lakes ecosystem from natural and anthropogenic processes. The main natural processes that introduce radioactivity are the weathering of rocks, which contain uranium- and thorium-series radionuclides, and fallout of cosmic ray-produced radionuclides such as ³H, ⁷Be, and ¹⁴C. Anthropogenic radioactivity is created, for example, by uranium mining, milling, and fuel fabrication; releases of artificially

Table 32.8 Estimated Fallout of ⁹⁰Sr and ¹³⁷Cs over the Great Lakes, 1954–1983, in Cumulative Millions of Bq/km²

Great Lake	Cesium-137	Strontium-90	Total
Superior	2429	1491	3920
Michigan	2738	1680	4418
Huron	2670	1638	4308
Erie	2859	1754	4613
Ontario	2773	1701	4474
Total	13,469	8264	21,733

Data from Joshi, S.R. 1991. Radioactivity in the Great Lakes. *Sci. Total Environ.* 100:61-104.

produced radionuclides through nuclear power reactors and nuclear fuel processing plants; medical uses of radioisotopes; and coal-fired electrical generating plants (Joshi 1991).

Production of power from nuclear reactors involves uranium mining, fuel fabrication, the reactor operations, and storage of wastes. All of these processes may expose humans and the environment to radiation (Hobbs and McClellan 1986). Uranium production in the United States was 12,300 tons U₃O₈ in 1977, primarily from western states, Texas, and Florida (Whicker and Schultz 1982a). Mining from deep shafts or open pits is the preferred method of uranium extraction, although in Florida it is produced as a by-product of phosphate mining. Mines disperse radionuclides of uranium, thorium, and radium, which are associated with dust particles, and radon, which emanates from ore as a gas and decays to create a series of radioactive daughters. Groundwater also contains radionuclides of the uranium series. As many as 18 uranium mills were in operation, located close to major mining centers in the western states. Collectively, these mills process or processed about 30,000 tons of ore daily and use acid or alkali leach methods to extract 90 to 95% of the uranium from ore. Uranium is barreled at the mill for shipment as uranium oxide or as salt concentrates (yellowcake) that contain 70 to 90% U₃O₈ by weight. Residues of the uranium extraction process are usually pumped as a slurry to liquid-retention impoundments; about 0.55 TBq of ²³⁰Th and ²²⁶Ra enter tailings each day from milling operations. Radium-226 produces gaseous ²²²Rn; daughters of ²²²Rn, such as ²¹⁰Pb, expose the surrounding biota to measurable radiation. Purification of yellowcake to UF₆ (uranium hexafluoride) and its enrichment to ²³⁵U causes a loss of about 0.55 TBq annually. Nuclear reactor fuel contains about 3% ²³⁵U. A nuclear explosion in a nuclear reactor is highly unlikely because the nuclear fuel suitable for weapons must contain >90% ²³⁵U. Following enrichment, UF₆ is hydrolyzed to uranyl fluoride, converted to ammonium diuranate, and calcined to the dioxide UO₂. Uranium dioxide pellets at one time were prepared by as many as ten commercial fuel fabrication plants and subsequently transported to nuclear reactors (Whicker and Schultz 1982a). In the current light-water-cooled reactors, the most abundant radionuclides in the reactor effluents under normal conditions are ³H, ⁵⁸Co, ⁶⁰Co, ⁸⁵Kr, ⁸⁵Sr, ⁹⁰Sr, ¹³⁰I, ¹³¹I, ¹³¹Xe, ¹³³Xe, ¹³⁴Cs, ¹³⁷Cs, and ¹⁴⁰Ba (Hobbs and McClellan 1986). Gaseous and volatile radionuclides, such as ⁸⁵Kr, ¹³¹Xe, and ¹³³Xe, contribute to the external gamma dose, whereas the others contribute to the dose externally by surface deposition and internally by way of the food chain. The mean dose from environmental releases of all radionuclides from nuclear reactors in the United States is <0.01 mSv/year (Hobbs and McClellan 1986). Nuclear fission follows the capture of a neutron by an atom of fissionable material, such as ²³⁵U or ²³⁹Pu. The fission releases 1 to 3 neutrons and, if additional fissionable material is present in sufficient quantity and in the right configuration, a chain reaction occurs (Hobbs and McClellan 1986). Radionuclides formed per megaton of fission include fission products (⁸⁹Sr, ⁹⁰Sr, ⁹⁵Zr, ¹⁰³Ru, ¹⁰⁶Ru, ¹³¹I, ¹³⁷Cs, ¹⁴⁴Ce) and activation products in air (³H, ¹⁴C, ³⁹Ar) and soil (²⁴Na, ³²P, ⁴²K, ⁴⁵Ca, ⁵⁵Fe, ⁵⁹Fe) (Whicker and Schultz 1982a). Fission-product radionuclides of potential biological importance include ⁹⁰Sr, ¹³⁷Cs, ¹³¹I, ¹²⁹I, ¹⁴⁴Ce, ¹⁰³Ru, ¹⁰⁶Ru, ⁹⁵Zr, ¹⁴⁰Ba, ⁹¹Y, ¹⁴³Ce, ¹⁴⁷Nd (Kahn 1971; Whicker and Schultz 1982a), and others (Table 32.9).

Most of the world's supply of uranium consists of about 0.7% ²³⁵U and 99% ²³⁸U. In theory, about 2.27 kg of ²³⁵U can release energy equivalent to 20,000 tons of TNT (Hobbs and McClellan 1986). ²³⁸U and ²³²Th can be converted into fissionable material following neutron capture. Radionuclides of biological significance produced by neutron activation in nuclear reactors include ³H, ¹⁴C, ²⁴Na, ³²P, ³⁵S, ⁴⁵Ca, ⁵⁴Mn, ⁵⁵Fe, ⁵⁷⁺⁵⁸⁺⁶⁰Co, ⁶⁵Zn, ²³⁹Pu, ²³⁹Np, ²⁴¹Am, and ²⁴²Cm (Whicker and Schultz 1982a). Nuclear energy can also be released by fusion of smaller nuclei into larger nuclei that is accompanied by a decrease in mass (Hobbs and McClellan 1986). Fusion reactors — which do not yet exist — require very high temperatures of several million degrees; no fission products are produced in the fusion process (Whicker and Schultz 1982a).

Radioactive wastes are usually stored in underground tanks or in temporary storage at reactor sites for recycling or disposal (Whicker and Schultz 1982a). For low-level wastes, containment and isolation are the preferred disposal options, including burial, hydraulic injection into deep geological strata, and ocean disposal (Table 32.10). Options for the disposal of high-level wastes include

Table 32.9 Fission Products per kg ^{235}U Reactor Charge at 100 Days Cooling

Product	Grams	Trillions of becquerels per kg ^{235}U	
		Beta	Gamma
Short-lived ^a	15.93	7217	6002
Long-lived ^b	16.61	698	755
Inactive fission products	230.00	—	—
Total	262.54	8045	6757

^a ^{90}Y , ^{106}Rh , ^{144}Ce , ^{95}Zr , ^{95}Nb , ^{91}Y , ^{89}Sr , ^{103}Ru , ^{141}Ce , ^{137}Ba , ^{106}Ru , ^{143}Pr , ^{140}Ba , ^{140}La , ^{131}I .^b ^{137}Cs , ^{90}Sr , ^{144}Pr , ^{129}Te .

Modified from Renn, C.E. 1957. Physical and chemical properties of wastes produced by atomic power industry. Pages 26-27 in National Academy of Sciences. The Effects of Atomic Radiation on Oceanography and Fisheries. Publ. No. 551, NAS-Natl. Res. Coun., Washington, D.C.

Table 32.10 Radioactive Waste Disposal at Sea

Disposer and Other Variables	Quantity (trillions of becquerels [TBq])	Reference ^a
UNITED STATES		
Atlantic Ocean, 1951–60 vs. 1961–67	2939 vs. 2	1
Pacific Ocean, 1951–60 vs. 1961–67	527 vs. 16	1
UNITED KINGDOM		
1951–67, alpha vs. beta	123 vs. 1631	1
Sellafield, alpha (primarily Pu and Am)		
1968–70	50–61	2
1971 vs. 1972	99 vs. 143	2
1973 vs. 1974	181 vs. 17	2
Sellafield reprocessing plant ^b		
1980 vs. 1981	5145 vs. 4451	3
1982 vs. 1983	4005 vs. 3112	3
1984 vs. 1985	1835 vs. 646	3
EUROPE		
Germany, Netherlands, Belgium, France; 1961; alpha vs. beta plus gamma	6 vs. 220	1
France, Cap de la Hague reprocessing plant ^c		
1980 vs. 1981	503 vs. 455	3
1982 vs. 1983	694 vs. 683	3
1984 vs. 1985	670 vs. 674	3

^a 1, Joseph et al. 1971; 2, Hetherington et al. 1976; 3, UNSCEAR 1988.^b Effluent composition primarily ^{137}Cs and ^{241}Pu .^c Effluent composition primarily ^{106}Ru and ^{125}Sb .

retrievable surface storage and entombment in deep geological strata; many risks are associated with these options, and more suitable alternative disposals are needed. Spent nuclear fuel elements are usually stored for about 3 months to allow the decay of shorter-lived radionuclides before reprocessing or disposal. Reprocessing involves extractions to separate uranium and plutonium from the fission products into UF_6 and plutonium dioxide. Longer-lived fission products, such as ^{90}Sr and ^{137}Cs , are sometimes chemically separated and encapsulated for storage or disposal. Fuel reprocessing tends to release measurable quantities of various radionuclides that are detected in fish, wildlife, and food for humans (Whicker and Schultz 1982a). Liquid discharges from the Sellafield reprocessing plant (Table 32.10) have been reduced by a factor of more than 100 since

the mid-1970s (Aarkrog 1990). Human populations that consume higher than average quantities of marine fish and shellfish from the Sellafield area theoretically receive about 3.5 mSv annually from radioactivity associated with nuclear power production. Human populations in the vicinity of nuclear power production discharging directly into the marine environment — except for Sellafield — generally receive <0.05 mSv annually from this source (Aarkrog 1990).

Radioactive transuranic elements with atomic numbers that are greater than 92 have been introduced into the environment since the 1940s from atmospheric testing of nuclear weapons, discharges of nuclear wastes, and nuclear fuel reprocessing (Noshkin et al. 1971; Hetherington et al. 1976; Sibley and Stohr 1990; Morse and Choppin 1991). Transuranic isotopes with half-lives of more than 10,000 years (i.e., ^{247}Cm , ^{248}Cm , ^{239}Pu , ^{242}Pu , ^{244}Pu , ^{237}Np) will persist over geologically significant time periods. Transuranics at detectable but considered nonhazardous levels to biota are now widely dispersed throughout the environment in most waters, soils, sediments, and living organisms including humans. Of current primary concern are ^{244}Cm , ^{241}Am , $^{238+239+240+241}\text{Pu}$, and ^{237}Np — especially ^{241}Am , which is increasing globally as a result of ^{241}Pu decay (Sibley and Stohr 1990; Morse and Choppin 1991). However, the estimated peak dose received from Pu and Am radioisotopes seems to be decreasing in the vicinity of the Sellafield nuclear fuel reprocessor (Table 32.11). Miscellaneous exposures include radiations from television sets, luminous dial watches, smoke detectors, electron microscopes, building materials, and air travel (Hobbs and McClellan 1986). Most of the exposure in building materials is due to naturally occurring radionuclides. Similarly, air travel increases radiation exposure of travelers from increased exposure to cosmic radiations. Cigarette smokers may receive dose-equivalent rates up to 3 times higher than nonsmokers because of inhalation of ^{210}Po and ^{210}Pb from the cigarette. Some of the lung dose is also received from radionuclides released during combustion of fossil fuels, which contain small quantities of naturally occurring radionuclides (Hobbs and McClellan 1986).

Table 32.11 Theoretical Peak Dose, in microsieverts per year, Received from Plutonium and Americium by Three Human Populations

Population	Year		
	1973	1987	2000
Average person near Sellafield nuclear fuel reprocessor	24	4	2
Critical group, mainly agricultural workers	35	20	16
Heavy consumers of Irish Sea fish and shellfish in local fishing communities	—	250	55–90

Data from McKay, W.A. and N.J. Pattenden. 1990. The transfer of radionuclides from sea to land via the air: a review. *Jour. Environ. Radioactiv.* 12:49-77.

32.3.4 Dispersion

Radioactive materials are cycled throughout the environment by a variety of physical, chemical, and biological vectors. Dispersion through the atmosphere is governed by the magnitude, frequency, and direction of the wind. In the hydrosphere, transport is modified by water depth, motion, temperature, winds, tides, and groundwater (Whicker and Schultz 1982b). Deposition from the atmosphere is a function of particle size, precipitation, and dry deposition. Small radioactive particles may be elevated into the airstream from the ground surface; resuspension is a function of disturbances by wind at the soil surface, atmospheric variables (i.e., velocity, turbulence, density, viscosity), and soil-ground variables such as texture, cohesiveness, moisture content, density, vegetation cover, ground surface roughness, and topography (Whicker and Schultz 1982b). Only 1 kg of the original 15 kg Pu was fissioned from the dropping of the plutonium nuclear bomb on Nagasaki, Japan, on August 9, 1945 (Kudo et al. 1991). The remaining 14 kg Pu escaped into the environment. Local fallout accounted for about 37 g or 0.26% of the total global fallout; the highest $^{239+240}\text{Pu}$ concentration measured was 64 Bq/kg soil about 2.8 km from ground zero (Kudo et al. 1991).

Biological agents can also transport radioactive wastes. Birds, especially waterfowl, disperse accumulated radiocesium and other radionuclides along their migratory flyways (Brisbin 1991). Native mammalian herbivores and their predators that have come in contact with radioactivity in food or soils disperse the material in their feces, urine, or regurgitated pellets (O'Farrell and Gilbert 1975). For example, the black-tailed jackrabbit (*Lepus californicus*) in the vicinity of radioactive waste-disposal trenches dispersed radioactive fecal pellets over an area of 15 km². Elevated radioactivity readings were recorded in jackrabbits and in their predators, including feces of coyotes (*Canis latrans*) and bones of hawks (O'Farrell and Gilbert 1975).

Biological transport of trace elements and radionuclides in the sea is provided mainly through phytoplankton and zooplankton because of their (1) ability to accumulate these elements to high levels, (2) diurnal vertical migration, and (3) production of detritus in the form of fecal pellets, molts, and carcasses (Lowman et al. 1971). Considerations related to biomass, feeding rates, conversion efficiencies, migratory habits of zooplankton, and the chemical properties of trace elements suggest that the major downward transport of these elements and radionuclides is through gravitational action on fecal pellets, molts, and carcasses; direct biological transport accounts for <10% of the total downward movement. In estuarine and near-shore regions, the bottom sediments and their associated epiphyton often significantly influence the distribution of added radionuclides. Large populations of sessile filter feeders may drastically increase the rate of sedimentation of added trace elements and radionuclides (Table 32.12).

Table 32.12 Time Required to Transport Selected Radionuclides Added into Marine Waters at Surface out of the Upper Mixed Layer by Biological Transport (Processes include diurnal vertical migration, fecal pellets, and sinking of dead matter.)

Radionuclide	Time required to transport radionuclides (years)		
	Eastern North Pacific	Coastal Areas	Upwelling Areas
⁵⁴ Mn	74	7	3
⁵⁵⁺⁵⁹ Fe	7.2	0.7	0.3
⁵⁷⁺⁵⁸⁺⁶⁰ Co	220	20	8.8
⁶⁵ Zn	12	1.1	0.5
⁹⁵ Zr	5.4	0.5	0.2
²¹⁰ Pb	7.3	0.7	0.3

Data from Lowman, F.G., T.R. Rice, and F.A. Richards. 1971. Accumulation and redistribution of radionuclides by marine organisms. Pages 161-199 in *National Academy of Sciences. Radioactivity in the Marine Environment*. Natl. Acad. Sci., panel on radioactivity in the marine environment. Washington, D.C.

In some coastal areas, some of the radionuclides discharged into coastal waters from industrial establishments are recycled via the air/sea interface back onto land (McKay and Pattenden 1990). At the sea surface, aerosol is generated by bubble bursting and wave shearing. The aerosol is advected to land by onshore winds and deposited in coastal regions. Sea-to-land transfer has been documented from the vicinity of nuclear fuel reprocessing facilities in England, Scotland, and France; however, the sea-to-land transfer pathway was only about 8% of that from the seafood pathway (McKay and Pattenden 1990). The solubility of different radionuclides at the sediment/seawater interface is variable. Plutonium solubility, for example, depends on pH, Eh, ionic strength, complexing ions, organic chelators, living accumulator organisms, and oxidation state (Mo and Lowman 1976). The oceanic distributions of many nuclides are strongly controlled by interactions with particulate matter (Nozaki 1991). Thorium is an extreme case; the high reactivity of this element accounts for its residence of only a few decades in the ocean from which it is removed largely by vertical transport in association with settling particulate matter. ²¹⁰Pb and ²³¹Pa are also particle-reactive but to a lesser extent than Th. Their oceanic mean residence time is about 100 years.

The mean oceanic residence time of ^{227}Ac and Ra isotopes is about 1000 years because of particulate scavenging; these nuclides are supplied by insoluble parents in underlying sediments and are released to overlying waters by porewater diffusion. ^{228}Ra can serve as a novel tracer in ocean circulation for about 30 years; ^{227}Ac can be used for about 100 years. The distribution of ^{226}Ra is largely governed by biogeochemical cycling, much like dissolved silica (Nozaki 1991).

32.4 RADIONUCLIDE CONCENTRATIONS IN FIELD COLLECTIONS

32.4.1 General

The wide dispersion of anthropogenic radiocontaminants has significantly altered natural background levels of radioactivity in many parts of the globe. Radionuclide concentrations in selected abiotic materials and living organisms were usually elevated in samples from the vicinity of human nuclear activities, especially atmospheric military tests. Radionuclide concentrations in organisms were significantly modified by the organism's age, sex, diet, metabolism, trophic level, proximity to point source, and many other biological, chemical, and physical variables, as discussed later. Additional and more detailed data on environmental radionuclide concentrations and isotopic composition and levels of radioactive wastes discharged into the biosphere from nuclear plants and other anthropogenic activities are given in Schultz and Klement (1963), Nelson and Evans (1969), Nelson (1971), IAEA (1976), Whicker and Schultz (1982a, 1982b), and UNSCEAR (1988).

32.4.2 Abiotic Materials

Radionuclide concentrations in selected nonliving materials (Table 32.13) show that concentrations are elevated in samples from the site of repeated nuclear detonations, near nuclear fuel reprocessing and waste facilities, and from locations receiving radioactive fallout from atmospheric military tests. Rocks, especially granite, had high levels of naturally occurring radionuclides such as ^{40}K . Concentrations were usually low or negligible in drinking water and cow's milk for human consumption. Nuclear-weapons testing has resulted in large environmental releases of radionuclides. Between 1961 and 1966, for example, the Republic of Korea received fallout from nuclear tests by the former Soviet Union in 1961 and by the United States in 1962 and from three explosions by The People's Republic of China (Bai 1969). The highest levels of total combined β and γ activity in various Korean samples during 1962 to 1964, in Bq/L or Bq/kg, were: 0.0002 in air, 133 in water, 1572 in milk, 2023 in rain, 16,428 in plants, and 99,345 in soils (Bai 1969).

Water in the Great Lakes in 1981 contained measurable concentrations of ^{137}Cs , ^3H , and ^{90}Sr , and detectable — but extremely low — concentrations of ^{241}Am , ^{113m}Cd , ^{144}Ce , ^{210}Pb , $^{239+240}\text{Pu}$, ^{226}Ra , ^{125}Sb , and ^{228}Th (Joshi 1991). Radiocesium-137 in water from the Hudson River estuary, New York, decreased tenfold between 1964 and 1970, but the ^{137}Cs content in fish and in sediments remained relatively constant (Wrenn et al. 1971). The effluent from the United Kingdom's Atomic Energy Agency Sellafield facility on the Cumberland Coast of the Irish Sea contained ^{90}Sr and ^{137}Cs , which are soluble in seawater and tend to remain in solution, and ^{106}Ru , ^{144}Ce , and $^{95}\text{Zr}/^{95}\text{Nb}$, which are relatively insoluble in seawater and coprecipitate or adsorb on free inorganic and organic surfaces (Pentreath et al. 1971).

Soils in the vicinity of an English nuclear fuel reprocessing facility in the period 1979 to 1985 contained as much as 42 times more ^{241}Am , 12 times more ^{137}Cs , 13 times more ^{90}Sr , and 87 times more $^{239+240}\text{Pu}$ than soils from a reference site (Curtis et al. 1991). In the United States, radiological trends in abiotic materials were difficult to interpret. For example, one nationwide monitoring program for radionuclide concentrations in air, drinking water, milk, groundwater, and precipitation (Table 32.13) was not consistent in the selection of measured radionuclides, frequency of sampling, and types of samples analyzed.

Table 32.13 Radionuclide Concentrations in Field Collections of Selected Abiotic Materials
 (Concentrations are in becquerels per kilogram fresh weight [FW], or dry weight [DW].)

Material, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
COMMON ROCK TYPES		
Shale, limestone, sandstone, basalt		
⁴⁰ K	63–518 DW	2
²³² Th	4–48 DW	2
²³⁸ U	6–44 DW	2
Granite vs. beach sands		
⁴⁰ K	1184 DW vs. 100 DW	2
²³² Th	74 DW vs. 25 DW	2
²³⁸ U	62 DW vs. 37 DW	2
DRINKING WATER		
Mol, Belgium, 1983, near former nuclear fuel reprocessing plant closed in 1974, ¹²⁹ I	Max. 0.000082 FW	3
United States, nationwide		
1977 vs. 1981		
²³⁸ Pu	Max. 0.00004 FW vs. Max. 0.0004 FW	1, 4
²³⁹ Pu	Max. 0.0004 FW vs. Max. 0.0003 FW	1, 4
²³⁴ U	Max. 0.093 vs. Max. 2.19 FW	1, 4
²³⁵ U	Max. 0.0026 FW vs. Max. 0.027 FW	1, 4
²³⁸ U	Max. 0.067 FW vs. Max. 0.562 FW	1, 4
1988		
¹³¹ I	Max. 0.011 FW	5
²³⁸ Pu	Max. 0.002 FW	6
²³⁹⁺²⁴⁰ Pu	Max. 0.0003 FW	6
²²⁶ Ra	Usually <0.007 FW; Max. 0.24 FW	6
⁹⁰ Sr	Max. 0.018 FW	6
²³⁴ U	Max. 0.090 FW	6
²³⁵ U	Max. 0.007 FW	6
²³⁸ U	Max. 0.183 FW	6
1989, ¹³¹ I	Max. 0.022 FW	7
1990, ¹³¹ I	Max. 0.022 FW	8
FRESHWATER		
Vicinity of nuclear weapons tests and operation of nuclear reactors, maximum values		
¹⁴¹ Ce	0.08 FW	2
¹⁴⁴ Ce	0.41 FW	2
¹³⁷ Cs	0.18 FW	2
¹³¹ I	5.2 FW	2
⁵⁴ Mn	0.05 FW	2
¹⁰³ Ru	0.25 FW	2
¹⁰⁶ Ru	1.1 FW	2
⁸⁹ Sr	1.9 FW	2
⁹⁰ Sr	0.66 FW	2
⁹⁵ Zr/ ⁹⁵ Nb	2.4 FW	2
Typical maximum concentrations		
³ H	0.6 FW	2
⁴⁰ K	0.2 FW	2
²¹⁰ Pb	0.01 FW	2
²¹⁰ Po	0.008 FW	2
²²⁶ Ra	0.11 FW	2
⁸⁷ Rb	0.00007 FW	2
²²² Rn	6.7 FW	2

Table 32.13 (continued) Radionuclide Concentrations in Field Collections of Selected Abiotic Materials
 (Concentrations are in becquerels per kilogram fresh weight [FW], or dry weight [DW].)

Material, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
²³² Th	0.0002 FW	2
²³⁴ U	0.12 FW	2
²³⁵ U	0.002 FW	2
²³⁸ U	0.06 FW	2
GROUNDWATER		
United States, nationwide, ²²² Rn, 1981 vs. 1982	Usually <10 FW; Max. 388 FW vs. Max. 90 FW	1, 9
LAKEWATER		
Canada 1984–87, ²²⁶ Ra		
Near uranium tailings area, dissolved vs. total	0.12 FW vs. 0.56 FW	10
Control site, dissolved vs. total	0.012 FW vs. 0.009 FW	10
Great Lakes, 1973 vs. 1981		
¹³⁷ Cs	0.003 FW vs. 0.0006–0.002 FW	11
³ H	12.6 FW vs. 6.7–13.5 FW	11
⁹⁰ Sr	0.019–0.047 FW vs. 0.016–0.024 FW	11
MILK, (COW) PASTEURIZED		
Mol, Belgium, 1983, near former nuclear fuel reprocessing plant, ¹²⁹ I	Max. 0.0005 FW	3
United States, nationwide		
1975 vs. 1977		
¹⁴ C	17.7–18.8 FW vs. — ^b	12
¹³⁷ Cs	Max. 1.07 FW vs. Max. 1.04 FW	4, 12
¹²⁹ I	— ^b vs. ND ^c	4
¹³¹ I	ND vs. Max. 0.59 FW	4, 12
⁸⁹ Sr	ND vs. Max. 0.22 FW	4, 12
⁹⁰ Sr	Max. 0.17 FW vs. Max. 0.27 FW	4, 12
1978 vs. 1981		
¹³⁷ Cs	Max. 0.92 FW vs. Max. 0.66 FW	9, 13
¹³¹ I	Max. 0.29 FW vs. Max. 0.48 FW	9, 13
⁸⁹ Sr	Max. 0.15 FW vs. Max. 0.07 FW	9, 13
⁹⁰ Sr	Max. 0.32 FW vs. Max. 0.14 FW	9, 13
1982 vs. 1988		
¹³⁷ Cs	Max. 0.67 FW vs. Max. 0.70 FW	1, 15, 16
¹³¹ I	Max. 0.25 FW vs. Max. 0.48 FW	1, 15, 16
⁸⁹ Sr	Max. 0.07 FW vs. 0.007–0.09 FW	1, 16
⁹⁰ Sr	Max. 0.13 FW vs. Max. 0.07 FW	1, 16
1983, ¹⁴ C	16.1–17.5 FW	14
1989 vs. 1990		
¹³⁷ Cs	Max. 0.78 FW vs. Max. 0.67 FW	5, 7, 8, 14, 17–19
¹³¹ I	Max. 0.66 FW vs. Max. 0.48 FW	5, 7, 8, 14, 17–19
⁸⁹ Sr	Max. 0.11 FW vs. — ^b	5, 14, 17, 18
⁹⁰ Sr	Max. 0.18 FW vs. — ^b	5, 14, 17, 18
PRECIPITATION		
United States, nationwide		
1978		
²³⁸ Pu	Max. 0.0004 FW	13
²³⁹ Pu	Max. 0.0006 FW	13
²³⁴ U	Max. 0.004 FW	13
²³⁵ U	Max. 0.0001 FW	13
²³⁸ U	Max. 0.003 FW	13

Table 32.13 (continued) Radionuclide Concentrations in Field Collections of Selected Abiotic Materials
 (Concentrations are in becquerels per kilogram fresh weight [FW], or dry weight [DW].)

Material, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
1987 vs. 1988		
²³⁸ Pu	Max. 0.0007 vs. Max. 0.001 FW	5, 15
²³⁹⁺²⁴⁰ Pu	Max. 0.0003 FW vs. Max. 0.0005 FW	5, 15
²³⁴ U	Max. 0.013 FW vs. Max. 0.002 FW	5, 15
²³⁵ U	Max. 0.0004 FW vs. Max. 0.0003 FW	5, 15
²³⁸ U	Max. 0.0026 FW vs. Max. 0.002 FW	5, 15
SEAWATER		
Major fallout radionuclides in surface seawater, typical concentrations		
¹⁴ C	0.0004–0.001 FW	2
¹³⁷ Cs	0.005–0.04 FW	2
³ H	0.3–1.8 FW	2
⁹⁰ Sr	0.003–0.026 FW	2
²³⁹ Pu	0.000004–0.00005 FW	2
Natural radionuclides in surface seawater, typical concentrations		
³ H	0.022–0.111 FW	2
¹⁴ C	0.007 FW	2
⁴⁰ K	11.8 FW	2
²¹⁰ Pb	<0.0003 FW	2
²¹⁰ Po	0.0002–0.001 FW	2
²²⁶ Ra	0.0016 FW	2
²²⁸ Ra	0.00004–0.004 FW	2
⁸⁷ Rb	0.107 FW	2
²²⁸ Th	0.00007–0.0001 FW	2
²³⁰ Th	<0.00005 FW	2
²³² Th	<0.00003 FW	2
²³⁴ U	0.048 FW	2
²³⁵ U	<0.002 FW	2
²³⁸ U	0.044 FW	2
SEDIMENTS		
Deep Ocean		
²³² Th	1–74 DW	2
²³⁸ U	5–37 DW	2
Hanford, Washington, 1973, plutonium processing waste pond		
²⁴¹ Am	2627 DW	20
²³⁸ Pu	4144 DW	20
²³⁹⁺²⁴⁰ Pu	4477 DW	20
Hudson River estuary, 1970, ¹³⁷ Cs, bottom sediments vs. suspended sediments	75 DW vs. 152 DW	21
SOILS		
Belgium, Mol, near former nuclear fuel reprocessing plant, 1983, ¹²⁹ I	Max. 0.2 DW	3
Tennessee, 1974, ¹³⁷ Cs; 12–22 cm depth; accidentally contaminated in 1944 vs. control site	Usually near 185,000 DW, Max. 740,000 DW vs. <222 DW	22
WATER, VARIOUS LOCATIONS		
Hanford, Washington; plutonium processing waste ponds		
²⁴¹ Am	0.04 FW	20
²³⁸ Pu	0.0003 FW	20
²³⁹⁺²⁴⁰ Pu	0.00007 FW	20

Table 32.13 (continued) Radionuclide Concentrations in Field Collections of Selected Abiotic Materials
 (Concentrations are in becquerels per kilogram fresh weight [FW], or dry weight [DW].)

Material, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
Hudson River estuary, 1970, ^{137}Cs , dissolved vs. suspended	0.01 FW vs. 0.005 FW	21
Italy, 1971, nuclear power station		
^{60}Co	Max. 0.06 FW	23
^{137}Cs	Max. 0.33 FW	23

^a 1, U.S. Environmental Protection Agency (USEPA) 1982b; 2, International Atomic Energy Agency (IAEA) 1976; 3, Handl et al. 1990; 4, USEPA 1977; 5, USEPA 1989c; 6, USEPA 1990a; 7, USEPA 1990c; 8, USEPA 1991; 9, USEPA 1982a; 10, Clulow et al. 1991; 11, Joshi 1991; 12, USEPA 1975; 13, USEPA 1979; 14, USEPA 1990a; 15, USEPA 1989a; 16, USEPA 1989b; 17, USEPA 1989d; 18, USEPA 1990b; 19, USEPA 1990d; 20, Emery et al. 1976; 21, Wrenn et al. 1971; 22, Dahlman and Voris 1976; 23, Smedile and Queirazza 1976.

^b — = no data.

^c ND = not detectable.

32.4.3 Aquatic Ecosystems

Field studies indicate that effects of radiation on marine ecosystems cannot be demonstrated at prevailing dose rates (Templeton et al. 1971). Two major periods of worldwide fallout occurred in Arctic ecosystems. The first and most sustained occurred from 1953 to 1959, and the second from 1961 to 1964, reflecting the atmospheric nuclear-weapons test regimes of Great Britain, the former Soviet Union, and the United States (Hanson 1976). Military accidents created localized radiocontamination of the Arctic environment. In one case, a B-52 aircraft from the U.S. Air Force crashed on the ice in northwestern Greenland in January 1968. Plutonium from the nuclear weapons onboard contaminated the benthos (Figure 32.5). The $^{239+240}\text{Pu}$ concentrations in various environmental samples declined at a much faster rate than the physical half-life of ^{239}Pu (24,000 years), suggesting that Pu becomes increasingly unavailable to the benthos over time as a result of dispersion from the epicenter and a dilution effect (Aarkrog 1990).

In marine environments, the major portion of the background dose rate in plankton and fish arises from the incorporated activity of natural alpha emitters, such as ^{210}Po , and from ^{40}K ; in molluscs, crustaceans, and benthos, the gamma radiation from the seabed provides the major background dose (IAEA 1976). The situation is similar in freshwater environments, although water containing appreciable levels of ^{222}Rn and its daughter radionuclides may exert an additional burden, especially to phytoplankton. Artificial radionuclides that contribute significantly to background concentrations of marine organisms include ^{239}Pu and ^{90}Sr ; of freshwater organisms, ^{137}Cs and ^{90}Sr (IAEA 1976). The total natural radiation received by a marine flounder (*Pleuronectes platessa*) in the Irish Sea consisted of 63% from radiations from seabed sediments, 16% from ^{40}K in seawater, 15% from internal ^{40}K , and 6% from cosmic radiation (Templeton et al. 1971). The estimated dose rates in aquatic environments from natural background are as high as 3.5 mGy annually and of the same order as those in most terrestrial environments. By 1976, the estimated dose rates from global fallout had declined to the same range as natural dose rates, although environments receiving radioactive wastes had variable responses (IAEA 1976).

Muscle of largemouth bass (*Micropterus salmoides*) collected from lakes in South Carolina in May and June of 1993 contained 109 to 4607 Bq $^{137}\text{Cs}/\text{kg DW}$. Increasing concentrations of ^{137}Cs were correlated with increasing DNA damage (Sugg et al. 1995). Increasing levels of ^{137}Cs in the muscle of fish in Minnesota between 1954 and 1966 reflect fallout from atmospheric nuclear testing. The effective half-time for ^{137}Cs in these lakes, as judged from small fish, is about 30 months (Gustafson 1969). In game fish from Colorado, ^{137}Cs in muscle was up to 7 times higher in 1968 than in 1965; higher in fish in mountain lakes than in fish from reservoirs in the plains, foothills, lakes, and rivers; and highest in trout from alpine lakes and reservoirs (Nelson and Whicker 1969).

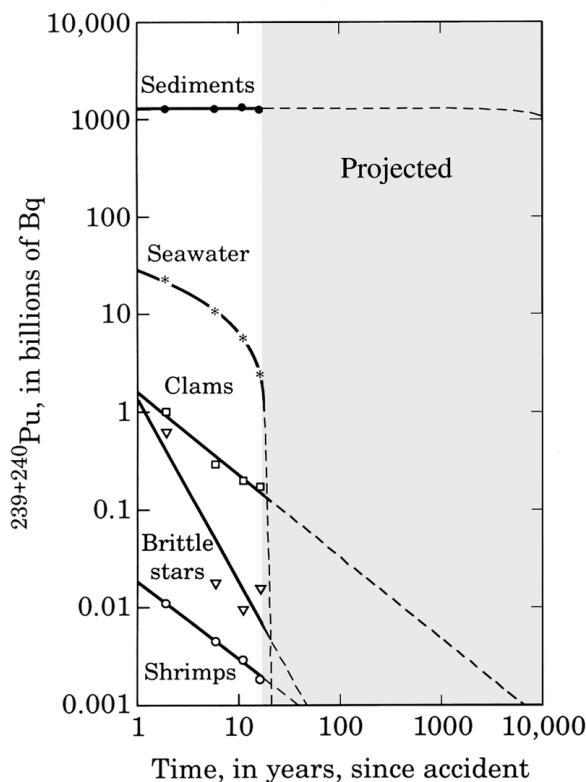


Figure 32.5 Plutonium-239+240 in environmental samples at Thule, Greenland, between 1970 and 1984, after a military accident in 1968. (Modified from Aarkrog, A. 1990. Environmental radiation and radiation releases. *Inter. Jour. Radiation Biol.* 57:619-631.) Within the contaminated area of $3.2 \times 10^9 \text{ m}^2$, the fresh weight biomass of shrimps was $0.11 \times 10^9 \text{ kg}$; of brittle star echinoderms $0.06 \times 10^9 \text{ kg}$; and of clam (*Macoma balthica*) soft parts $0.32 \times 10^9 \text{ kg}$. The seawater mass was $3 \times 10^{14} \text{ kg}$, and the dry weight of the upper 15-cm sediment layer was $3 \times 10^{11} \text{ kg}$.

In 1966, ^{137}Cs levels in trout from Colorado alpine lakes were 8 to 18 times higher than mean levels in muscle of deer from Colorado during the same period, and 20 to 300 times higher than domestic meat products (Nelson and Whicker 1969). Radionuclides in livers of tunas from southern California during the period 1964 to 1970 originated mainly from weapons tests in 1961/62, although ^{65}Zn may have reached southern California waters from nuclear reactors in Hanford (Washington) and from French or Chinese nuclear tests (Folsom et al. 1971).

Many variables are known to modify radionuclide concentrations in biota. In general, lower trophic levels of aquatic organisms are likely to have greater concentrations of radionuclides than higher trophic levels (Bowen et al. 1971). However, radionuclide concentrations in biota are modified significantly by the organism's age, size, sex, tissue, season of collection, and other variables — and these have to be acknowledged when integrating radiological analyses. For example, older *Fucus vesiculosus* had higher radioactivity concentrations than younger algae; concentrations of ^{60}Co and ^{54}Mn were highest in older parts of plants during spring and summer; and ^{137}Cs and ^{40}K were highest in receptacles and new vegetative fronds (Carlson and Erlandsson 1991). Changes in concentrations of ^{60}Co and ^{137}Cs in freshwater plankton from the discharge canal of an Italian

nuclear power station seem to reflect changes in water concentrations of these isotopes; changes were lowest in winter and highest in summer (Smedile and Queirazza 1976). Marine bivalve molluscs and algae from Connecticut in 1960 and 1961 had the highest levels of gross beta radioactivity in spring and summer and the lowest in winter ([Table 32.14](#)) (Hatfield et al. 1963); natural ^{40}K probably accounted for most of the beta radioactivity. Similar seasonal variations in gross beta radioactivity in other species of marine algae and molluscs were documented, suggesting a correspondence with periods of dormancy and activity (Hatfield et al. 1963). Although fat in the liver of crabs accounted for 47% of the fresh weight (74% on a dry weight basis), the gross beta activity of the fat fraction amounted to <0.5% of the total radioactivity, suggesting that radiological liver analyses be compared on the basis of nonfat solids (Chakravarti and Eisler 1961). In mosquitofish (*Gambusia holbrooki*) from some locations in a ^{137}Cs -contaminated reservoir, males contained higher ^{137}Cs concentrations than females, and smaller females contained more ^{137}Cs than larger females (Newman and Brisbin 1990). Strontium-90 concentrations in the carapace bone of turtles from five southwestern states in 1970 were used as indicators of ^{90}Sr fallout. However, older turtles tended to have lower concentrations of ^{90}Sr and concentrations differed geographically. Concentrations were highest in Georgia and increasingly lower in Tennessee, Mississippi, Arkansas, and Florida ([Table 32.14](#)) (Holcomb et al. 1971).

Consumption of shellfish represents a negligible radiological risk to humans (Crowley et al. 1990), although bivalve molluscs seem to be effective accumulators of radioisotopes. After the Chinese nuclear tests in May and December 1966, concentrations of ^{144}Ce , ^{103}Ru , ^{95}Zr , ^{95}Nb , ^{140}Ba , and ^{140}La in three species of bivalves in the Neuse River, North Carolina, increased suddenly (Wolfe and Schelske 1969). In 1973, Pacific oysters (*Crassostrea gigas*) from the discharge canal of a nuclear power plant in Humboldt Bay, California, rapidly accumulated ^{54}Mn , ^{60}Co , ^{65}Zn , and ^{137}Cs within 30 min of release. Isotope uptake correlated positively with particulates in the water, including living microorganisms, organic detritus, inorganic materials, and especially resuspended bottom sediments (Harrison et al. 1976). Although concentrations of cesium and plutonium in mussels (*Mytilus edulis*) from most Irish estuaries are essentially the same as global fallout levels, concentrations were elevated in mussels from the northeast coast (Crowley et al. 1990).

32.4.4 Birds

Television and newspaper reporters attributed radionuclides to a decline in bird numbers at the Ravenglass estuary, England, particularly of the black-headed gull (*Larus ridibundus*), although the concentrations of radionuclides in the avian diet, body tissues, and general environment were at least 1000 times too low to have had any effect ([Table 32.14](#)) (Lowe 1991). Although oystercatchers (*Haematopus ostralegus*) and shelducks (*Tadorna tadorna*) had the highest concentrations of ^{137}Cs in their tissues, the breeding success and population size of these birds were not affected. Black-headed gulls had less radiocontamination than other birds at Ravenglass, but their population continued to decline. The most likely cause was a combination of an uncontrolled fox population, a severe outbreak of myxomatosis in rabbits (normal fox prey), and a drought — all in the same year (Lowe 1991). Nesting success of birds was unaffected in the vicinity of nuclear power plants. For example, nesting barn swallows (*Hirundo rustica*) near radioactive leaching ponds had normal nesting success despite their consumption of arthropods from the pond and use of contaminated mud for nest construction (Millard and Whicker 1990; [Table 32.14](#)). Adult swallows received a total internal dose rate of 219 $\mu\text{Gy/day}$, mostly (72%) from ^{24}Na ; daily dose rates for eggs and nestlings during the nesting season were 840 μGy and 2200 μGy . The total dose to eggs and nestlings (54 mGy) and adults (450 mGy) had no measurable effect on survival and was below accumulated doses reported to cause death of passerines (Millard and Whicker 1990).

Strontium-90 behaves much like calcium in the biological environment. In birds, ⁹⁰Sr is expected to occur in bone and in the calcium-rich eggshell. In one case, a positive relation was demonstrated between reactor releases of ⁹⁰Sr to the Columbia River and ⁹⁰Sr concentrations in reed canary grass (*Phalaris arundinacea*) and eggshells of the Canada goose (*Branta canadensis moffitti*) (Rickard and Price 1990).

No human health problem is anticipated from consumption of ruffed grouse (*Bonasa umbellus*) contaminated with ²²⁶Ra in Canada or American coot (*Fulica americana*) contaminated with ¹³⁷Cs in Washington state. Tissues of ruffed grouse collected near discharged uranium tailings in Canada in 1987/88 did not contain grossly elevated levels of ²²⁶Ra over controls; consumption of grouse by humans did not present a radiological health problem (Clulow et al. 1992). Based on ¹³⁷Cs alone, humans who consume a single contaminated American coot captured at Hanford, Washington, would receive about 1.1% of the annual radiation protection dose of 1.70 mSv for individuals and populations in uncontrolled areas (Cadwell et al. 1979).

32.4.5 Mammals

Diets in Denmark contained elevated loadings of ¹³⁷Cs in 1964 because of the intensive atmospheric nuclear test series by the United States and the former Soviet Union in 1961 and 1962. Total ¹³⁷Cs intake declined in the Danish population from 72 Bq/kg BW in 1964 to <2 in 1985, but rose to about 13 in 1986 from the effects of debris from Chernobyl on dietary ¹³⁷Cs during the first year after the accident (Aarkrog 1990). The estimated dose equivalent from ¹³⁷Cs to human consumers of fish from the Great Lakes is about 0.01 µSv/kg fresh weight (FW) muscle from fish in Lakes Erie and Ontario, and 0.06 to 0.07 µSv/kg from fish in Lakes Superior and Huron (Joshi 1991). The guide for the protection of the general public from radiation is <5 mSv annually, and consumption of fish containing a dose equivalent greater than 0.02 µSv/kg fish flesh is not recommended (Joshi 1991). Some Scandinavians now receive a dose equivalent of about 5 mSv/year from intake of radio cesium in the diet (Johanson 1990). In Finland, uptake of radionuclides by humans in Finnish Lapland and in other areas with an arctic climate is attributed to ecological factors and to a high amount of local fallout. For example, reindeer-herding Finnish Lapps contained about 50 times more ¹³⁷Cs and 10 times more ⁵⁵Fe than other Finns during 1961 to 1967. For ¹³⁷Cs, this disparity is attributed mainly to the reliance by Finns on reindeer meat — which contains high levels of ¹³⁷Cs as a result of reindeer feeding on lichens — and secondarily, on freshwater fish and cow's milk (Miettinen 1969).

In the United States, the estimated annual whole-body human radiation dose equivalent is 1.61 mSv, mostly from natural sources (0.85 mSv) and medical sources (0.70 mSv), but also from fallout (0.03 mSv), miscellaneous sources (0.02 mSv), occupational hazards (0.008 mSv), and nuclear power (0.0001 mSv) (League of Women Voters [LWV] 1985). Radiation doses to people living near the Hanford nuclear industrial and research site in the state of Washington are well below existing regulatory standards. Only trace amounts of radionuclides from Hanford have been detected in the offsite environment (Gray et al. 1989). In December 1984, radon levels up to 130 times greater than considered safe under the current guideline for underground uranium miners were discovered in human residences in eastern Pennsylvania, New Jersey, and New York. About 25% of all residences in ten states exceeded the action level for radon of 0.185 Bq/L air (Cross 1990; Oge and Dickson 1990). The significance of this observation to avian and terrestrial wildlife merits investigation.

As a result of nuclear weapons testing, mandibles of Columbian black-tailed deer (*Odocoileus hemionus columbianus*) from California increased from <9 Bq ⁹⁰Sr/kg ash weight (AW) to >204 Bq/kg AW between 1952 and 1960 (Table 32.14) (Schultz and Longhurst 1963). Age and season affected strontium kinetics in male mule deer (*Odocoileus hemionus hemionus*) during the period of antler

growth; these variables did not affect strontium kinetics in females (Schreckhise and Whicker 1976). The concentrations of ^{90}Sr in forage of mule deer were higher in summer than in winter, and the differences were of sufficient magnitude to account for the ^{90}Sr variations in mule deer antlers (Farris et al. 1969); ^{137}Cs concentrations were similar in the forage and flesh of the white-tailed deer (*Odocoileus virginianus*) (Cummings et al. 1971). Levels of iodine-129 in thyroids of mule deer and pronghorns (*Antilocapra americana*) increased with proximity to nuclear fuel reprocessing plants in Colorado, Idaho, New Mexico, and Wyoming during 1972 to 1976, although levels were considered of no consequence to the health of the animals (Markham et al. 1983).

Radium-226, a bone-seeking α emitter with a half-life of 1600 years, may cause tissue damage and possibly subsequent osteosarcoma. Elevated ^{226}Ra concentrations have been reported in tissues of the common beaver (*Castor canadensis*) from the Serpent River watershed, Canada, the recipient of uranium tailings during 1984 to 1987 (Table 32.14). Measurable levels of ^{226}Ra were also found in feces of snowshoe hares (*Lepus americanus*) from this area and in black cutworms (*Agrotis ipsilon*) eaten by herring gulls (*Larus argentatus*) on the tailings (Clulow et al. 1991). Maximum levels in tissues of beavers from this watershed were <5 Bq $^{232}\text{Th}/\text{kg}$ dry weight (DW) in all tissues, 15 Bq $^{228}\text{Th}/\text{kg}$ DW bone, <5 Bq $^{228}\text{Th}/\text{kg}$ DW muscle and liver, 70 to 160 Bq $^{210}\text{Po}/\text{kg}$ DW bone, 11 to 75 Bq $^{210}\text{Po}/\text{kg}$ DW muscle, and 35 to 65 Bq $^{210}\text{Po}/\text{kg}$ DW liver. Consumption of these beavers would not be hazardous to human health. In the worst case, humans who consume substantial (71 kg) amounts of the flesh of beavers from the Serpent River drainage system would receive <10% of the annual limits set by Canadian regulatory authorities (Clulow et al. 1991).

Cesium-137 levels in grey seals (*Halichoerus grypus*) in 1987 seem to reflect ^{137}Cs levels in their fish diet, but there is no biomagnification of ^{137}Cs and other radionuclides. An estimated 29% of the ^{137}Cs in the diets of grey seals is from the Chernobyl accident and 71% from the nuclear facility at Sellafield, United Kingdom. The dose to grey seals from their diet is about 36 mSv annually and higher than the permissible dose limit of 5 mSv/year allowed the general public, but below the current limit for radiation workers of 50 mSv/year (S.S. Anderson et al. 1990).

The weekly dose rates from internal radionuclides were markedly different in muskrats (*Ondatra zibethicus*) and cotton rats (*Sigmodon hispidus*) collected at Oak Ridge, Tennessee, in August 1960 (20 to 1112 mSv for muskrats vs. 3 mSv for cotton rats). The difference is probably due to differences in diets and habitats (Kaye and Dunaway 1963). Foxes and wildcats contain 2 to 16 times more ^{137}Cs than their prey organisms, such as rats and rabbits (Jenkins et al. 1969), suggesting food-chain magnification. The biological half-time of ^{137}Cs is about 30 days in foxes, dogs, and pigs but about 60 days in humans (Jenkins et al. 1969). Jackrabbits (*Lepus californicus*) in 1958, one year after contamination at the Nevada test site, averaged 1908 Bq $^{90}\text{Sr}/\text{kg}$ AW bone within a 160-km radius from ground zero. In 1961, the average for the same population was only 984 Bq $^{90}\text{Sr}/\text{kg}$ AW bone, and the few higher values were restricted to older animals (Neel and Larson 1963). The authors concluded that ^{90}Sr from fallout in jackrabbits is at its maximum at an early time after contamination and that biological availability is later reduced by natural (unspecified) mechanisms. Jackrabbits at the Nevada test site also contained certain neutron activation products, including isotopes of Co, Mn, and W (Romney et al. 1971).

Radionuclide concentrations in sheep and cattle grazing near a nuclear fuel reprocessing facility amounted to a small fraction of the recommended limits. ^{241}Am , ^{137}Cs , and $^{239+240}\text{Pu}$ in the bone, liver, lung, and muscle of beef cattle were quite low from the vicinity of a nuclear fuel reprocessing facility in England between September and December 1986 and practically indistinguishable from control samples. Maximum concentrations, in Bq/kg FW, were 0.0015 $^{239+240}\text{Pu}$ in lung, 0.019 ^{241}Am in liver, and 3.1 ^{137}Cs in muscle (Curtis et al. 1991). Levels of ^{129}I were elevated in thyroids of cows near Mol, Belgium, in 1978 in the vicinity of a nuclear reprocessing plant closed in 1974 (Table 32.14) (Handl et al. 1990).

**Table 32.14 Radionuclide Concentrations in Field Collections of Selected Living Organisms
(Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)**

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
TERRESTRIAL PLANTS		
Sweet potato, <i>Ipomoea batatas</i> , Nagasaki, Japan, 1945, postatomic detonation		
¹³⁷ Cs	0.09 DW	1
²³⁹⁺²⁴⁰ Pu	0.01 DW	1
Lichens, various species, Alaska and Greenland		
²³⁸ Pu		
1971 vs. 1972	0.4 DW vs. 0.9 DW	2
1973	0.4 DW	2
²³⁹⁺²⁴⁰ Pu		
1971 vs. 1972	7.4 DW vs. 10.3 DW	2
1973 vs. 1974	5.4 DW vs. 9.6 DW	2
Reed canarygrass, <i>Phalaris arundinacea</i> , Columbia River Washington, 1985–87, near reactor, ⁹⁰ Sr	Max. 1480–1850 DW	3
Largetooth aspen, <i>Populus grandidentata</i> , ²²⁶ Ra		
Near uranium tailing plant vs. control site		
Leaves	53 DW vs. 4 DW	4
Stems	99 DW vs. 5 DW	4
Elliot Lake, Canada, 1984–87 vs. control site		
Leaves	252 DW vs. 46 DW	5
Stems	223 DW vs. 4 DW	5
Trembling aspen, <i>Populus tremuloides</i> , ²²⁶ Ra		
Near uranium tailings plant vs. control site		
Leaves	42 DW vs. 11–15 DW	4
Stems	69 DW vs. 3–11 DW	4
Vegetation		
Belgium, near former nuclear fuel reprocessing plant, 1983, ¹²⁹ I	Max. 0.09 FW	6
California, deer forage plants, three spp., 1968–69, ¹³⁷ Cs	414–514 DW	7
Colorado, mule deer diet, all plants, ⁹⁰ Sr		
1962–63 vs. 1963–64	2242 AW vs. 4499 AW	8
1964–65 vs. 1965–66	3492 AW vs. 2257 AW	8
Colorado, mule deer diet, 8 species of forage plants, ⁹⁰ Sr, 1963–64 vs. 1964–65	1258–17,412 AW vs. 828–16,620 AW	8
Finland, reindeer forage plants, 1961, Lapland		
Lichen, <i>Cladonia alpestris</i>		
¹³⁷ Cs	466,200 AW	11
⁹⁰ Sr	53,428 AW	11
Lichen mixture		
¹³⁷ Cs	133,200 AW	11
⁹⁰ Sr	19,980 AW	11
Other forage plants		
¹³⁷ Cs	962–8800 AW	11
⁹⁰ Sr	266–1924 AW	11
Florida, April 1969, ¹³⁷ Cs	Max. 0.65 DW	12
Georgia, deer browse, 29 species, 1965–66		
¹⁴⁴ Ce	Max. 373 DW	13
⁶⁰ Co	Max. 15 DW	13
¹³⁷ Cs	Max. 104 DW	13
⁵⁴ Mn	Max. 118 DW	13
¹⁰⁶ Ru	Max. 226 DW	13
¹²⁵ Sb	Max. 56 DW	13

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
⁹⁰ Sr	Max. 377 DW; Max. 2005 AW	13
⁹⁵ Zr	Max. 63 DW	13
⁶⁵ Zn	Max. 22 DW	13
Tennessee, 1974, ¹³⁷ Cs, from soil accidentally contaminated in 1944		
Roots	Usually ~3700 DW; Max. 111,000 DW	14
Trees	74–5920 DW	14
Ground vegetation	592–3996 DW	14
Ginger, <i>Zingiber officinale</i> , root, Nagasaki, Japan, 1945, postatomic detonation		
¹³⁷ Cs	0.07 DW	1
²³⁹⁺²⁴⁰ Pu	0.04 DW	1
AQUATIC PLANTS		
Algae, decomposing; Hanford, Washington, 1973; plutonium processing pond		
²⁴¹ Am	9472 DW	15
²³⁸ Pu	36,482 DW	15
²³⁹⁺²⁴⁰ Pu	22,755 DW	15
Algae and macrophytes, ¹³⁷ Cs, Hudson River, 1970	1.5–5.6 FW	16
Algae, South Carolina, 1971–72, reactor discharge, ¹³⁷ Cs	12,284 DW	17
Brown algae, <i>Fucus vesiculosus</i>		
Ireland, 1985–86, ²³⁹⁺²⁴⁰ Pu, northeast coast vs. western seaboard	3.2 DW vs. 0.09 DW	18
Sweden, 1984, vicinity of nuclear plant		
⁵⁸ Co	20–23 DW	19
⁶⁰ Co	1700–2003 DW	19
¹³⁷ Cs	7–16 DW	19
⁴⁰ K	735–966 DW	19
⁵⁴ Mn	36–60 DW	19
⁶⁵ Zn	90–144 DW	19
Seaweed, <i>Porphyra</i> sp., 1974, Cumbrian coast, U.K., <2 km from beach		
²⁴¹ Am	458 FW	20
²⁴² Cm	18 FW	20
²³⁸ Pu	37 FW	20
²³⁹⁺²⁴⁰ Pu	162 FW	20
Sea lettuce, <i>Ulva lactuca</i> , whole, Connecticut, 1960, gross beta activity		
May	5402–6253 AW	21
August	5291–8066 AW	21
December	2183–3700 AW	21
AQUATIC INVERTEBRATES		
Clams, 15 species, freshwater, 1960, Tennessee River, near Oak Ridge, ⁹⁰ Sr, shell	15–921 AW	23
Connecticut, 1960, gross beta activity		
American oyster, <i>Crassostrea virginica</i> , soft parts		
May	2553–3589 AW	21
August	2775–4551 AW	21
December	851–1850 AW	21

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Mussel, <i>Mytilus edulis</i> , soft parts, August vs. December	3256–4551 AW vs. 3034–3108 AW	21
Crabs, Hudson River, 1970, ¹³⁷ Cs	0.6 FW	16
Crustaceans, marine; fallout radionuclides, typical values		
^{110m} Ag	37.0 FW	24
⁶⁰ Co	24.1 FW	24
⁵⁴ Mn	2.2 FW	24
⁶⁵ Zn	2.6 FW	24
Crustaceans, marine; natural radionuclides, typical values		
¹⁴ C	22.2 FW	24
³ H	0.1 FW	24
⁴⁰ K	92.5 FW	24
²¹⁰ Pb	2.2 FW	24
²¹⁰ Po	37.0 FW	24
⁸⁷ Rb	1.5 FW	24
Molluscs, bivalves, Hudson River, 1970, ¹³⁷ Cs, soft parts	3 FW	16
Molluscs, freshwater; fallout radionuclides, typical values		
¹⁴ C	4–11 FW	24
³ H	0.1–159 FW	24
⁵⁴ Mn	4–518 FW	24
Molluscs, marine; fallout radionuclides, typical values		
¹⁴¹⁺¹⁴⁴ Ce	5–1813 FW	24
⁵⁷ Co	2–16 FW	24
⁶⁰ Co	1–26 FW	24
¹³⁷ Cs	5–25 FW	24
⁵⁵ Fe	14–5180 FW	24
⁵⁴ Mn	2–222 FW	24
⁶³ Ni	1–555 FW	24
²³⁹ Pu	Max. 0.02 FW	24
¹⁰³⁺¹⁰⁶ Ru	1–518 FW	24
^{110m} Ag	0.1–155 FW	24
⁶⁵ Zn	0.7–425 FW	24
⁹⁵ Zr/ ⁹⁵ Nb	3–925 FW	24
Molluscs, marine; natural radionuclides		
¹⁴ C	18 FW	24
³ H	0.1 FW	24
⁴⁰ K	107 FW	24
²¹⁰ Pb	0.3 FW	24
²¹⁰ Po	25 FW	24
⁸⁷ Rb	2 FW	24
Mussel, <i>Mytilus edulis</i> , soft parts		
Irish coastal waters, August 1988		
¹³⁴ Cs	<0.7 DW	18
¹³⁷ Cs	Usually <3 DW; Max. 9 DW	18
⁴⁰ K	182–355 DW	18
²³⁸ Pu	Usually <0.003 DW; Max. 0.21 DW	18
²³⁹⁺²⁴⁰ Pu	Usually <0.035 DW; Max. 1 DW	18
England, 1986–87, near nuclear plant		
^{110m} Ag	13 FW	25
²⁴¹ Am	9–15 FW	25
¹⁴⁴ Ce	6 FW	25

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
⁶⁰ Co	3–7 FW	25
¹³⁴ Cs	11 FW	25
¹³⁷ Cs	5–31 FW	25
⁴⁰ K	25–188 FW	25
⁹⁵ Nb	3–106 FW	25
¹⁰³ Ru	4–169 FW	25
¹⁰⁶ Ru	64–151 FW	25
⁹⁵ Zr	3–36 FW	25
Plankton, ¹³⁷ Cs, Hudson River, 1970	2 FW	16
Plankton, Italy, 1971, near nuclear power station		
⁶⁰ Co	Max. 203 FW	26
¹³⁷ Cs	Max. 1113 FW	26
Plankton, marine; fallout radionuclides, typical values		
¹⁴¹⁺¹⁴⁴ Ce	14–17,760 FW	24
⁵⁷ Co	85 FW	24
⁶⁰ Co	11–592 FW	24
¹³⁷ Cs	18–1332 FW	24
¹⁵⁵ Eu	14 FW	24
⁵⁴ Mn	196 FW	24
⁶³ Ni	4–14 FW	24
¹⁴⁷ Pm	122 FW	24
¹⁰³⁺¹⁰⁶ Ru	11–1110 FW	24
¹²⁵ Sb	33 FW	24
⁹⁰ Sr	0.7–12 FW	24
⁹⁵ Zr/ ⁹⁵ Nb	74–29,600 FW	24
Plankton, marine; natural radionuclides, typical values		
¹⁴ C	11 FW	24
³ H	0.1 FW	24
⁴⁰ K	92 FW	24
²¹⁰ Pb	9–25 FW	24
²¹⁰ Po	22–62 FW	24
²²⁶ Ra	0.7 FW	24
²²⁸ Th	0.4–2 FW	24
²³⁴ U	0.7–2 FW	24
²³⁵ U	0.02–0.07 FW	24
²³⁸ U	0.7–2 FW	24
Polychaete annelid worms, marine; England, 1984–86; near nuclear plant vs. control location		
<i>Arenicola marina</i>		
¹³⁷ Cs	132–321 FW vs. 3 FW	25
⁴⁰ K	162–307 FW vs. 90 FW	25
²³⁸ Pu	14–16 FW vs. <0.05 FW	25
²³⁹⁺²⁴⁰ Pu	60–72 FW vs. 0.01 FW	25
<i>Nereis diversicolor</i>		
¹³⁷ Cs	41–358 FW vs. 6 FW	25
⁴⁰ K	23–148 FW vs. 134 FW	25
²³⁸ Pu	6–11 FW vs. <0.02 FW	25
²³⁹⁺²⁴⁰ Pu	25–48 FW vs. 0.03 FW	25
Clam, <i>Rangia cuneata</i> , Neuse River, North Carolina, 1965–67, soft parts; before Chinese nuclear tests in May and December 1966 vs. posttest		
¹⁴⁴ Ce	5.3 FW vs. 7.2 FW	27, 28
¹³⁷ Cs	1.0 FW vs. 1.6 FW	27, 28

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
⁵⁵ Fe	0.12 FW vs. 0.75 FW	27, 28
⁵⁴ Mn	2.5 FW vs. 2.7 FW	27, 28
¹⁰⁶ Ru	2.1 FW vs. 2.7 FW	27, 28
⁶⁵ Zn	0.4 FW vs. 0.8 FW	27, 28
Sea urchin, <i>Strongylocentrotus purpuratus</i> , 1966		
²¹⁰ Pb	Max. 2 AW	29
²¹⁰ Po	Max. 7 AW	29
FISH		
Goldfish, <i>Carassius auratus</i> from plutonium processing waste pond, Hanford, Washington, 1973		
²⁴¹ Am, whole vs. muscle	399 DW vs. 14 DW	15
²³⁸⁺²³⁹⁺²⁴⁰ Pu, whole vs. muscle	351 DW vs. 10 DW	15
Colorado, 1965–66, ¹³⁷ Cs, muscle, maximum values		
Cutthroat trout, <i>Oncorhynchus clarkii</i>	59 FW	30
Rainbow trout, <i>Oncorhynchus mykiss</i>	117 FW	30
Sockeye (kokanee) salmon, <i>Oncorhynchus nerka</i>	8 FW	30
Brook trout, <i>Salvelinus fontinalis</i>	215 FW	30
Lake trout, <i>Salvelinus namaycush</i>	25 FW	30
Brown trout, <i>Salmo trutta</i>	121 FW	30
Columbia River, Washington; near nuclear facility, 1961, ²³⁹ Np, muscle		
Chiselmouth, <i>Acrocheilus alutaceus</i>	Max. 14,900 FW	31
Bridgelip sucker, <i>Catostomus columbianus</i>	Max. 5600 FW	31
Largescale sucker, <i>Catostomus macrocheilus</i>	Max. 3600 FW	31
Mountain whitefish, <i>Prosopium williamsoni</i>	Max. 18,800 FW	31
Freshwater fish, whole body, fallout radionuclides, typical values		
¹⁴ C	4–7 FW	24
¹³⁷ Cs	1–973 FW	24
⁵⁵ Fe	1–3 FW	24
³ H	0.1–159 FW	24
⁵⁴ Mn	11 FW	24
⁸⁵ Sr	0.04–0.4 FW	24
⁸⁹ Sr	0.2–40 FW	24
⁹⁰ Sr	0.04–177 FW	24
⁹⁵ Zr/ ⁹⁵ Nb	2.2–2.6 FW	24
Freshwater fish, 1963–64, ²¹⁰ Pb, bone vs. soft tissues	2.5 AW vs. 0.2 AW	29
Freshwater fish, whole body, ¹³⁷ Cs; Red Lakes, Minnesota		
1954–57	0.7–2.4 FW	32
1959–62	3–12 FW	32
1963–66	8–22 FW	32
Freshwater fish, typical maximum concentrations, whole body		
³ H	0.5 FW	24
⁴⁰ K	130 FW	24
⁸⁷ Rb	8 FW	24
²³⁸ U	0.1 FW	24

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
²³⁴ U	0.2 FW	24
²²⁶ Ra	129 FW	24
²¹⁰ Pb (bone)	3 FW	24
²¹⁰ Po (liver)	18 FW	24
²³² Th	0.05 FW	24
²³⁵ U	0.004 FW	24
Mosquitofish, <i>Gambusia holbrooki</i> , ¹³⁷ Cs, April 1987; from South Carolina reservoir contaminated with ¹³⁷ Cs between 1961 and 1964, whole body	Max. 2230 FW	33
Hudson River, 1970, ¹³⁷ Cs		
Atlantic sturgeon, <i>Acipenser oxyrinchus</i> , muscle	0.6 FW	16
American eel, <i>Anguilla rostrata</i> , muscle	1.3 FW	16
Mummichog, <i>Fundulus heteroclitus</i> , whole	2.0 FW	16
Catfish, <i>Ictalurus</i> sp., muscle	1.9 FW	16
White perch, <i>Morone americana</i> , muscle vs. whole body	0.8 FW vs. 0.8 FW	16
Striped bass, <i>Morone saxatilis</i> , muscle	0.9 FW	16
Yellow perch, <i>Perca flavescens</i> , muscle	1.5 FW	16
Italy, 1971, near nuclear power station, whole fish, various species		
⁶⁰ Co	Max. 9 DW	26
¹³⁷ Cs	Max. 104 DW	26
Lake Ontario, ¹³⁷ Cs, 1981		
Common carp, <i>Cyprinus carpio</i> , bone vs. other tissues	5 FW vs. <5 FW	34
Northern pike, <i>Esox lucius</i>		
Bone, liver	5 FW	34
Roe	15 FW	34
Other tissues	<5 FW	34
Coho salmon, <i>Oncorhynchus kisutch</i>		
GI tract	5 FW	34
Liver	13 FW	34
Other tissues	<5 FW	34
Largemouth bass, <i>Micropterus salmoides</i> , South Carolina, reactor discharge, 1971–72, ¹³⁷ Cs, whole	3677 DW	17
<i>Micropterus salmoides</i> , South Carolina, muscle, 5 lakes; May–June 1993, ¹³⁷ Cs	109–4607 DW	60
Marine fishes, whole body, fallout radionuclides, typical values		
^{110m} Ag	2–3 FW	24
^{141–144} Ce	2–1036 FW	24
⁶⁰ Co	1–13 FW	24
¹³⁷ Cs	2–3 FW	24
⁵⁵ Fe		
Gonad	8140–10,360 FW	24
Liver	59,940–68,820 FW	24
Muscle	37–3922 FW	24
⁵⁴ Mn	0.07–2 FW	24
²³⁹ Pu	Max. 0.005 FW	24
¹⁰³⁺¹⁰⁶ Ru	2–244 FW	24
⁹⁵ Zr/ ⁹⁵ Nb	1–277 FW	24
⁶⁵ Zn	2–7 FW	24

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Marine fishes, whole body, natural radionuclides, typical values		
¹⁴ C	15 FW	24
³ H	0.1 FW	24
⁴⁰ K	92 FW	24
²¹⁰ Pb	5 FW	24
²¹⁰ Po	33 FW	24
²²⁶ Ra	0.2 FW	24
⁸⁷ Rb	1 FW	24
²³⁴ U	1 FW	24
²³⁵ U	0.05 FW	24
²³⁸ U	1 FW	24
Golden shiner, <i>Notemigonus crysoleucas</i> , whole, ¹³⁷ Cs, Hudson River estuary		
1966 vs. 1968	0.9 FW vs. 0.8 FW	16
1969 vs. 1970	0.7 FW vs. 0.5 FW	16
Oceanic fishes, 1962–64, bone vs. soft parts		
²¹⁰ Pb	10 AW vs. 0.06 AW	29
²¹⁰ Po	12 AW vs. 0.1 AW	29
²²⁶ Ra	2 AW vs. 0.06 AW	29
Plaice, <i>Pleuronectes platessa</i> , near nuclear facility, England		
1968 vs. 1969, ¹³⁷ Cs		
Gut contents	44–181 FW vs. 126–266 FW	35
Muscle	26–70 FW vs. 89–152 FW	35
1968, gut contents		
¹⁴⁴ Ce	880–1150 FW	35
¹⁰⁶ Ru	1343–5143 FW	35
⁹⁵ Zr/ ⁹⁵ Nb	3122–5794 FW	35
Albacore, <i>Thunnus alalunga</i> , southern California near San Diego, liver		
Summer 1964 vs. summer 1965		
^{110m} Ag	3 FW vs. 4 FW	36
⁶⁰ Co	7 FW vs. 7 FW	36
⁴⁰ K	71 FW vs. 72 FW	36
⁵⁴ Mn	39 FW vs. 22 FW	36
⁶⁵ Zn	46 FW vs. 14 FW	36
Summer 1968 vs. summer 1970		
⁶⁰ Co	2 FW vs. 2 FW	36
⁴⁰ K	81 FW vs. 78 FW	36
⁵⁴ Mn	2 FW vs. 0.6 FW	36
⁶⁵ Zn	25 FW vs. 9 FW	36
Yellowfin tuna, <i>Thunnus albacares</i> , 1968, near San Diego, liver		
⁶⁰ Co	1 FW	36
⁴⁰ K	93 FW	36
⁵⁴ Mn	1 FW	36
⁶⁵ Zn	3 FW	36
Tunas, 1970–71, Hawaii, liver		
^{108m} Ag	0.03–2 FW	36
^{110m} Ag	0.01–7 FW	36
⁶⁰ Co	0.9–3 FW	36
⁴⁰ K	68–83 FW	36
⁶⁵ Zn	5–27 FW	36

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
REPTILES		
Snakes, two species (<i>Elaphe obsoleta</i> , <i>Nerodia taxispilota</i>), Aiken, South Carolina; whole animal, ¹³⁷ Cs		
Site contaminated with ¹³⁷ Cs between 1961 and 1970, <i>Elaphe</i> vs. <i>Nerodia</i>		
1972	6037 FW vs. 7629 FW	58
1976	592 FW vs. 1333 FW	58
1980	296 FW vs. 1037 FW	58
<37 FW		58
Uncontaminated site, both species, 1972–80		
Snakes, 19 species, whole, vicinity of Aiken, South Carolina, March 1971–November 1972, ¹³⁴⁺¹³⁷ Cs		
Near reactor effluent stream	4870 FW, Max. 38,200 FW	9
Near reactor cooling reservoir	1025 FW, Max. 5159 FW	9
Uncontaminated habitats	92 FW	9
Slider turtle, <i>Trachemys scripta</i> , from radioactive reservoirs, Aiken, South Carolina, whole body		
High-level waste pond vs. low-level waste pond		
¹³⁷ Cs	3020 FW vs. 1002 FW	37
⁹⁰ Sr	94,030 FW vs. 2236 FW	37
Control sites		
¹³⁷ Cs	0.001 FW	37
⁹⁰ Sr	0.2 FW	37
Turtles, southeastern U.S., 1970, ⁹⁰ Sr, exoskeleton		
Snapping turtle, <i>Chelydra serpentina</i>	784 (284–1283) AW	38
Gopher tortoise, <i>Gopherus polyphemus</i>	4765 AW	38
Common mud turtle, <i>Kinosternon subrubrum</i>	1309 (569–2904) AW	38
Missouri slider, <i>Trachymys floridana hoyi</i>	1761 AW	38
Peninsula cooter, <i>Pseudemys floridana peninsularis</i>	33 (ND–48) AW	38
Pond slider, <i>Pseudemys scripta</i>	777 (188–2190) AW	38
Loggerhead musk turtle, <i>Sternotherus minor</i>	24 (ND–48) AW	38
Common musk turtle, <i>Sternotherus odoratus</i>	525 (52–999) AW	38
Common box turtle, <i>Terrapene carolina</i>	1087 (48–2856) AW	38
BIRDS		
Wood duck, <i>Aix sponsa</i> ; 1991–92; from abandoned (in 1964) reactor cooling reservoir; eggs, ¹³⁷ Cs		
Whole egg	113 FW	59
Albumin	1096 DW	59
Shell vs. yolk	132 DW vs. 98 DW	59
Ruffed grouse, <i>Bonasa umbellus</i> ; near uranium tailings discharge, Canada, Elliot Lake, 1987–88, ²²⁶ Ra		
Bone vs. gut contents	10–28 DW vs. 7–22 DW	4
Liver vs. muscle	5–12 DW vs. 1.5–1.9 DW	4
Canada goose, <i>Branta canadensis moffitti</i> ; Columbia River, Washington, 1985–87, near reactor; eggshell, ⁹⁰ Sr	18–60 DW	39

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
American coot, <i>Fulica americana</i> ; Hanford, Washington, June 1974–January 1977		
¹³⁷ Cs (Hanford vs. control ponds)		
Bone	7400 vs. 37 DW	40
Gut contents	125,800 vs. 29 DW	40
Liver	16,280 vs. 26 DW	40
Muscle	21,090 vs. 0.7 DW	40
⁹⁰ Sr (Hanford only)		
Bone	96 DW	40
Gut contents	159 DW	40
Liver	18 DW	40
Muscle	10 DW	40
Barn swallow, <i>Hirundo rustica</i> ; Idaho, 1976–77, nesting near radioactive leaching ponds		
Whole adults		
¹⁴⁰ Ba	800 FW	41
¹³⁴ Cs	1300 FW	41
¹³⁷ Cs	6400 FW	41
⁵¹ Cr	16,100 FW	41
⁶⁰ Co	1480 FW	41
¹³¹ I, whole vs. thyroid	5500 FW vs. 3,330,000 FW	41
²⁴ Na	8600 FW	41
⁷⁵ Se	5000 FW	41
⁶⁵ Zn	5900 FW	41
Nests		
¹⁴⁰ Ba	1200 DW	41
¹³⁴ Cs	13,800 DW	41
¹³⁷ Cs	92,000 DW	41
¹⁴¹ Ce	1200 DW	41
¹⁴⁴ Ce	4000 DW	41
⁵¹ Cr	230,000 DW	41
¹³¹ I	800 DW	41
⁶⁵ Zn	1800 DW	41
Massachusetts, 1973–75, 15 passerine species, trapped near nuclear power station, whole body		
Common bobwhite, <i>Colinus virginianus</i>		
¹³⁷ Cs	Max. 73 FW	42
¹³¹ I	Max. 6 FW	42
⁴⁰ K	Max. 131 FW	42
⁹⁵ Zr– ⁹⁵ Nb	Max. 4 FW	42
Bluejay, <i>Cyanocitta cristata</i>		
¹³⁷ Cs	28 FW; Max. 65 FW	42
¹³¹ I	1 FW; Max. 9 FW	42
⁴⁰ K	96 FW; Max. 181 FW	42
⁹⁵ Zr– ⁹⁰ Nb	2 FW; Max. 6 FW	42
13 species		
¹³⁷ Cs	Max. 82 FW	42
¹³¹ I	Max. 18 FW	42
⁴⁰ K	Max. 268 FW	42
⁹⁵ Zr– ⁹⁵ Nb	Max. 40 FW	42
United Kingdom, Ravenglass estuary, 1980–84, near nuclear plant		
Mallard, <i>Anas platyrhynchos</i>		
¹³⁴ Cs, muscle	87 FW	25
¹³⁷ Cs, muscle vs. liver	167 FW vs. 126 FW	25

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
²³⁹⁺²⁴⁰ Pu, liver	3.4 FW	25
²³⁸ Pu, liver	1.1 FW	25
Greylag goose, <i>Anser anser</i>		
¹³⁷ Cs, muscle vs. liver	58 FW vs. 28 FW	25
²³⁸ Pu, muscle vs. liver	0.03 FW vs. 3 FW	25
²³⁹⁺²⁴⁰ Pu, muscle vs. liver	0.1 FW vs. 13 FW	25
Carrion crow, <i>Corvus corone</i>		
¹³⁷ Cs, Ravenglass vs. control location		
Muscle	162 FW vs. 17 FW	25
Liver	131 FW vs. 8 FW	25
Lesser black-backed gull, <i>Larus marinus</i>		
¹³⁷ Cs, muscle vs. liver	158 FW vs. 163 FW	25
²³⁹⁺²⁴⁰ Pu, muscle vs. liver	0.1 FW vs. 5 FW	25
Black-headed gull, <i>Larus ridibundus</i> , whole chick		
¹³⁴ Cs	0.8 FW	25
¹³⁷ Cs	25 FW	25
²³⁸ Pu	0.1 FW	25
²³⁹⁺²⁴⁰ Pu	0.5 FW	25
Oystercatcher, <i>Haematopus ostralegus</i> , Ravenglass vs. control location		
¹³⁷ Cs		
Muscle	613 FW vs. 22 FW	25
Liver	463 FW vs. 20 FW	25
²³⁸ Pu		
Muscle	0.2 FW vs. <0.01 FW	25
Liver	1.8 FW vs. 0.04 FW	25
²³⁹⁺²⁴⁰ Pu		
Muscle	0.5 FW vs. 0.04 FW	25
Liver	4.1 FW vs. 0.09 FW	25
Bar-tailed godwit, <i>Limosa lapponica lapponica</i>		
¹³⁷ Cs, muscle vs. liver	478 FW vs. 510 FW	25
²³⁸ Pu, muscle vs. liver	<0.02 FW vs. 0.2 FW	25
²³⁹⁺²⁴⁰ Pu, muscle vs. liver	0.03 FW vs. 0.9 FW	25
Merganser, <i>Mergus serrator</i>		
¹³⁴ Cs, muscle vs. liver	8 FW vs. 13 FW	25
¹³⁷ Cs, muscle vs. liver	144 FW vs. 251 FW	25
²³⁸ Pu, muscle vs. liver	<0.01 FW vs. <0.04 FW	25
²³⁹⁺²⁴⁰ Pu, muscle vs. liver	0.02 FW vs. <0.04 FW	25
Curlew, <i>Numenius arquata</i>		
¹³⁷ Cs, Ravenglass vs. control location		
Muscle	140 FW vs. 49 FW	25
Liver	104 FW vs. 99 FW	25
²³⁸ Pu, Ravenglass vs. control location		
Muscle	0.09 FW vs. <0.02 FW	25
Liver	0.14 FW vs. <0.05 FW	25
²³⁹⁺²⁴⁰ Pu, Ravenglass vs. control location		
Muscle	0.09 FW vs. <0.02 FW	25
Liver	0.14 FW vs. <0.05 FW	25

MARINE MAMMALS

Bearded seal, *Erignathus barbatus*; Alaska, 1963

Bone		
²¹⁰ Pb	Max. 2.7 AW	29
²²⁶ Ra	2.4 AW	29

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Soft tissues, ²¹⁰ Pb	Max. 0.2 AW	29
Grey seal, <i>Halichoerus grypus</i> , North Sea and northeast Atlantic Ocean, 1987		
Females, milk vs. muscle		
²⁴¹ Am	<0.0002 FW vs. <0.0005 FW	43
¹³⁴ Cs	0.6 (0.4–0.7) FW vs. <0.002 FW	43
¹³⁷ Cs	2.9 (1.1–4.8) FW vs. 14.3 FW	43
⁴⁰ K	107 (67–215) FW vs. 0.2 FW	43
²³⁸ Pu	<0.0002 FW vs. <0.0005 FW	43
²³⁹⁺²⁴⁰ Pu	<0.0002 FW vs. <0.0005 FW	43
Pup, muscle vs. liver		
²⁴¹ Am	<0.0003 FW vs. <0.0003 FW	43
¹³⁴ Cs	Max. 0.003 FW vs. Max. 0.001 FW	43
¹³⁷ Cs	Max. 0.03 FW vs. Max. 0.02 FW	43
⁴⁰ K	Max. 0.2 FW vs. Max. 0.2 FW	43
²³⁸ Pu	Max. 0.0005 FW vs. Max. 0.001 FW	43
²³⁹⁺²⁴⁰ Pu	Max. 0.002 FW vs. Max. 0.004 FW	43
Spotted seal, <i>Phoca largha</i> ; Alaska, 1963, bone vs. soft tissues		
²¹⁰ Pb	2 AW vs. 0.1 AW	29
²²⁶ Ra	3 AW vs. No Data	29
Sperm whale, <i>Physeter macrocephalus</i> ; Alaska, 1965, bone vs. soft tissue		
²¹⁰ Pb	135 AW vs. 0.37 AW	29
²¹⁰ Po	114 AW vs. 23 AW	29
TERRESTRIAL MAMMALS		
Cattle, <i>Bos</i> sp.		
Nevada, 1973, grazing for 3 years in area contaminated in 1957 with transuranic radionuclides		
²⁴¹ Am		
Bone vs. liver	Max. 1 FW vs. Max. 0.6 FW	44
Lymph nodes vs. lungs	Max. 24 FW vs. Max. 2 FW	44
Other tissues	<0.6 FW	44
²³⁸ Pu		
Lungs, lymph nodes	Max. 3 FW	44
Testes	Max. 0.8 FW	44
Other tissues	<0.6 FW	44
²³⁹⁺²⁴⁰ Pu		
Bone vs. liver	Max. 3 FW vs. Max. 34 FW	44
Lungs vs. lymph nodes	Max. 34 FW vs. Max. 85 FW	44
Muscle vs. other tissues	Max. 7 FW vs. <1.2 FW	44
Europe, ¹²⁹ I, thyroids		
1978		
Belgium vs. Germany	0.017–3.7 FW vs. Max. 0.03 FW	6
Italy vs. Netherlands	Max. 0.05 FW vs. Max. 0.03 FW	6
1979, Netherlands		
1980, Netherlands	Max. 0.07 FW	6
1981, Germany	0.07–0.6 FW	6
Max. 0.02 FW		6
Common beaver, <i>Castor canadensis</i> ; Canada, 1984–87, adults, ²²⁶ Ra; from watershed containing uranium tailings vs. control site		
Bone	115 DW vs. 20 DW	5
Gut contents	62 DW vs. 9 DW	5

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Kidney	9 DW vs. 2 DW	5
Liver	2.7 DW vs. 1.4 DW	5
Muscle	2.9 DW vs. 1.0 DW	5
Georgia and South Carolina, 1964–66, ¹³⁷ Cs, whole organism		
Domestic dog, <i>Canis familiaris</i>	23 FW	45
Coyote, <i>Canis latrans</i>	26 FW	45
Bobcat, <i>Lynx rufus</i>	117–561 FW	45
Cotton rat, <i>Sigmodon hispidus</i>	16–29 FW	45
Eastern cottontail, <i>Sylvilagus floridanus</i>	19–35 FW	45
Gray fox, <i>Urocyon cinereoargentatus</i>	34–169 FW	45
Red fox, <i>Vulpes fulva</i>	23–60 FW	45
Humans, <i>Homo sapiens</i> ; Denmark, ¹³⁷ Cs, annual dietary loading		
1964	71.9 FW	46
1985	1.4 FW	46
1986–87	12.6 FW	46
Black-tailed jack rabbit, <i>Lepus californicus</i> ; Nevada test site, bone, ⁹⁰ Sr		
1952–66	74–476 AW	47
1958 (1-year postdetonation), ground zero vs. 32–700 km distant	373 AW vs. 88–198 AW	48
1959, ground zero	329 AW	48
1959, 32 km vs. 120–700 km	466 AW vs. 95–222 AW	48
1961, within 160 km of ground zero	143 AW	48
Mule deer, <i>Odocoileus hemionus</i> ; 1961–65, Colorado, femur, ⁹⁰ Sr		
1961–62 vs. 1962–63	Max. 215 AW vs. Max. 528 AW	8
1963–64 vs. 1964–65	Max. 777 AW vs. Max. 637 AW	8
Black-tailed deer, <i>Odocoileus hemionus columbianus</i> ; California		
Muscle vs. rumen contents, 1968–69, ¹³⁷ Cs		
Summer	37 DW vs. 48 DW	7
Fall	33 DW vs. 37 DW	7
Winter	48 DW vs. 67 DW	7
Mendocino County, California, mandible, yearlings, ⁹⁰ Sr		
1952–53 vs. 1954	3–11 AW vs. 26–34 AW	49
1955 vs. 1956	29–124 AW vs. 112 AW	49
1957 vs. 1958	87–239 AW vs. 134–228 AW	49
1959 vs. 1960	243–533 AW vs. 204–332 AW	49
White-tailed deer, <i>Odocoileus virginianus</i>		
Georgia, 1965–66		
¹³⁷ Cs		
Heart vs. kidney	127 FW vs. 149 FW	13
Liver vs. lung	70 FW vs. 73 FW	13
Muscle vs. spleen	126 FW vs. 126 FW	13
Tongue	172 FW	13
⁹⁰ Sr, mandible		
Age 1.5 years	940 AW	13
Age 2.5 years	828 AW	13
Age 3.5 years	799 AW	13
Southeastern United States		
¹³⁷ Cs, muscle, 1967–71		
Alluvial region (LA, MS, FL, SC, NC)	85 (9–650) FW	50
Lower Coastal Plain (SC, GA, FL, VA, NC)	1036 (9–5658) FW	50

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Mountain region (WV, KY, MD, NC, TN, GA)	78 (9–401) FW	50
Piedmont region (GA, SC, AL)	105 (9–383) FW	50
Upper Coastal Plain region (MD, NC, GA, VA, MS, LA, AK)	154 (9–1752) FW	50
⁹⁰ Sr, bone, 1969		
Lower Coastal Plain	1172 (376–1766) FW	50
Mountain region	499 (148–888) FW	50
Piedmont region	471 (263–683) FW	50
Muskrat, <i>Ondatra zibethicus</i> ; August 1960, Oak Ridge, Tennessee, from settling basin for radioactive wastes, single most radioactive animal		
Brain vs. eyes		
⁶⁰ Co	10,545 DW vs. 39,960 DW	51
¹³⁷ Cs	392,200 DW vs. 640,100 DW	51
⁶⁵ Zn	21,016 DW vs. 36,593 DW	51
Femur		
⁶⁰ Co	5920 DW	51
¹³⁷ Cs	121,360 DW	51
⁹⁰ Sr	7,030,000 DW	51
⁶⁵ Zn	28,601 DW	51
Kidney vs. spleen		
⁶⁰ Co	279,720 DW vs. 47,730 DW	51
¹³⁷ Cs	954,600 DW vs. 799,200 DW	51
Liver		
⁶⁰ Co	156,880 DW	51
¹³⁷ Cs	629,000 DW	51
⁶⁵ Zn	78,440 DW	51
Muscle		
⁶⁰ Co	8103 DW	51
¹³⁴ Cs	13,949 DW	51
¹³⁷ Cs	1,265,400 DW	51
⁶⁵ Zn	19,610 DW	51
Teeth		
¹³⁷ Cs	64,010 DW	51
⁹⁰ Sr	9,916,000 DW	51
⁶⁵ Zn	25,789 DW	51
Pelt		
⁶⁰ Co	15,022 DW	51
¹³⁷ Cs	204,980 DW	51
⁹⁰ Sr	37,000 DW	51
⁶⁵ Zn	26,196 DW	51
Domestic sheep, <i>Ovis aries</i>		
Near nuclear fuel reprocessing facility vs. control site, England, 1983		
Bone		
²⁴¹ Am	1 FW vs. 0.003 FW	52
²³⁹⁺²⁴⁰ Pu	0.6 FW vs. 0.002 FW	52
Liver		
²⁴¹ Am	1 FW vs. 0.002 FW	52
¹³⁷ Cs	8 FW vs. 0.2 FW	52
²³⁹⁺²⁴⁰ Pu	2 FW vs. 0.008 FW	52
Lung		
²⁴¹ Am	0.3 FW vs. 0.003 FW	52
²³⁹⁺²⁴⁰ Pu	0.4 FW vs. 0.002 FW	52

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Muscle		
²⁴¹ Am	0.03 FW vs. 0.0005 FW	52
¹³⁷ Cs	49 FW vs. 0.2 FW	52
²³⁹⁺²⁴⁰ Pu	0.007 FW vs. 0.0008 FW	52
Near nuclear fuel reprocessing plant, England, winter 1986–87		
²⁴¹ Am	0.03–0.7 FW vs. 0.03–0.8 FW	53
Bone vs. liver	0.009–0.1 FW vs. 0.002–0.03 FW	53
Lung vs. muscle	0.27–4 FW	53
Whole sheep		
¹³⁷ Cs	1.3–14 FW vs. 1.8–30 FW	53
Bone vs. liver	1.5–16 FW vs. 4.6–42 FW	53
Lung vs. muscle	159–748 FW	53
²³⁹⁺²⁴⁰ Pu		
Bone vs. liver	0.024–0.2 FW vs. 0.07–0.9 FW	53
Lung vs. muscle	0.005–0.02 FW vs. 0.0005–0.005 FW	53
Whole sheep	0.02–2 FW	53
Serbia, 1988, wildlife		
Roe deer, <i>Capreolus</i> sp.; bone vs. muscle		
¹³⁷ Cs	ND vs. 0.2 AW	54
⁴⁰ K	23 AW vs. 39 AW	54
⁹⁰ Sr	6 AW vs. 0.6 AW	54
Fallow deer, <i>Dama</i> sp.; bone vs. muscle		
¹³⁷ Cs	ND vs. 0.1 AW	54
⁴⁰ K	8 AW vs. 45 AW	54
⁹⁰ Sr	10 AW vs. 0.3 AW	54
Wild hare, <i>Lepus</i> sp.; bone vs. muscle		
¹³⁷ Cs	ND vs. 0.1 AW	54
⁴⁰ K	26 AW vs. 52 AW	54
⁹⁰ Sr	18 AW vs. ND	54
Wild boar, <i>Sus scrofa</i> ; bone vs. muscle		
¹³⁷ Cs	ND vs. 0.4 AW	54
⁴⁰ K	21 AW vs. 56 AW	54
⁹⁰ Sr	34 AW vs. 2 AW	54
Common shrew, <i>Sorex araneus</i> ; 1988, England, muscle; shrews from mineral soils vs. peaty soils		
¹³⁴ Cs	7 FW vs. 16 FW	55
¹³⁷ Cs	58 FW vs. 161 FW	55

INTEGRATED STUDIES

Brazil, site of radiological accident in September 1987 at Goiania wherein ¹³⁷Cs was deposited on soil for 3 weeks before remedial action.

Rainwater runoff contaminated the waterways

3 weeks postaccident, up to 12 km from accident area, ¹³⁷Cs

Fish muscle Max. 200 FW

Sediments Max. 1300 DW

Surface waters and suspended particulates <1 FW

10 months postaccident, up to 80 km downstream, ¹³⁷Cs

Fish muscle

Pike, *Hoplias* sp. 14 FW

56

56

56

56

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
Piranha, <i>Seerasalmus</i> sp.	10 FW	56
Sediments	100 DW	56
Water hyacinth, <i>Eichhornia</i> sp.	Max. 0.4 FW	56
Great Lakes, ¹³⁷ Cs, 1981		
Aquatic plants vs. clams	1.4 FW vs. 0.3 FW	34
Fish vs. plankton	1.5 FW vs. 0.1 FW	34
Sediments vs. water	24 FW vs. 0.0007 FW	34
Irish Sea and North Sea, 1983, invertebrates vs. fish		
²⁴¹ Am	Max. 75 FW vs. Max. 0.05 FW	57
²⁴² Cm	Max. 2 FW vs. Max. 0.0003 FW	57
²⁴³⁺²⁴⁴ Cm	Max. 0.5 FW vs. 0.0003 FW	57
²³⁸ Pu	14 FW vs. 0.01 FW	57
²³⁹⁺²⁴⁰ Pu	54 FW vs. 0.04 FW	57
²⁴¹ Pu, invertebrates only	Max. 1000 FW	57
Japan, Nagasaki, 1945 post atomic detonation		
Fish vs. snail		
¹³⁷ Cs	0.01 DW vs. 0.02 DW	1
²³⁹⁺²⁴⁰ Pu	0.03 DW vs. 0.03 DW	1
South Carolina, watershed of a former reactor effluent stream, ¹³⁷ Cs, 1971 vs. 1981		
Plants	14,000–19,000 DW vs. 2600–9600 DW	10
Arthropods	9600–16,000 DW vs. 700–3300 DW	10
South Carolina; reactor cooling impoundment accidentally contaminated in 1961–64 with ¹³⁷ Cs, ⁹⁰ Sr, and various transuramics; samples collected September 1983–February 1984		
¹³⁷ Cs		
Water vs. sediments	0.76 FW vs. Max. near 40,000 DW	22
Aquatic macrophytes vs. benthic invertebrates	Max. near 30,000 DW vs. 930–14,000 DW	22
Fish muscle	2100–8000 FW; 21,000 DW	22
Turtle muscle	2100 FW	22
Waterfowl muscle	3100 FW; 15,000 DW	22
⁹⁰ Sr		
Water vs. sediments	0.14 FW vs. Max. near 400 DW	22
Aquatic macrophytes vs. benthic invertebrates	Max. 2600 DW vs. 42–7900 DW	22
Fish bone ash vs. fish muscle	12,000–23,000 DW vs. 86–470 DW	22
Turtle shell and bone ash	12,000 DW	22
Waterfowl muscle vs. waterfowl bone ash	14 DW vs. 420 DW	22
²³⁸ Pu		
Water vs. sediments	0.0000034 FW vs. Max. 10 DW	22
Aquatic macrophytes vs. fish muscle	Max. 0.5 DW vs. 0.004 DW	22
Turtle shell ash vs. waterfowl bone ash	0.1 DW vs. 100 DW	22
Waterfowl muscle	0.013 DW	22
²³⁹⁺²⁴⁰ Pu		
Water	0.0000088 FW	22
Sediments	Max. near 85 DW	22
Aquatic macrophytes	Max. near 1.2 DW	22
Turtle shell ash	ND	22
Waterfowl muscle	0.008 DW	22
²⁴¹ Am		
Water vs. sediments	0.000023 FW vs. Max. 40 DW	22
Turtle shell ash vs. waterfowl muscle	ND vs. 0.015 DW	22

Table 32.14 (continued) Radionuclide Concentrations in Field Collections of Selected Living Organisms (Concentrations are in becquerels per kilogram fresh weight [FW], dry weight [DW], or ash weight [AW].)

Ecosystem, Organism, Radionuclide, and Other Variables	Concentration (Bq/kg ^a)	Reference ^b
²⁴⁴ Cm		
Water vs. sediments	0.00064 FW vs. Max. 18 DW	22
Fish liver vs. turtle shell ash	11 DW vs. 0.2 DW	22
Waterfowl muscle	0.071 DW	22

^a Values originally expressed in strontium units (1 nCi ⁹⁰Sr/g calcium AW) were transformed to Bq/kg AW by a multiplication factor of 98.4.

^b 1, Kudo et al. 1991; 2, Hanson 1976; 3, Rickard and Price 1990; 4, Clulow et al. 1992; 5, Clulow et al. 1991; 6, Handl et al. 1990; 7, Book 1969; 8, Farris et al. 1969; 9, Brisbin et al. 1974; 10, Brisbin et al. 1989; 11, Miettinen 1969; 12, Cummings et al. 1971; 13, Plummer et al. 1969; 14, Dahlman and Voris 1976; 15, Emery et al. 1976; 16, Wrenn et al. 1971; 17, Shure and Gottschalk 1976; 18, Crowley et al. 1990; 19, Carlson and Erlandsson 1991; 20, Hetherington et al. 1976; 21, Hatfield et al. 1963; 22, Whicker et al. 1990; 23, Nelson 1963; 24, IAEA 1976; 25, Lowe 1991; 26, Smedile and Queirazza 1976; 27, Wolfe and Schelske 1969; 28, Wolfe and Jennings 1971; 29, Holtzman 1969; 30, Nelson and Whicker 1969; 31, Poston et al. 1990; 32, Gustafson 1969; 33, Newman and Brisbin 1990; 34, Joshi 1991; 35, Pentreath et al. 1971; 36, Folsom et al. 1971; 37, Lamb et al. 1991; 38, Holcomb et al. 1971; 39, Rickard and Price 1990; 40, Cadwell et al. 1979; 41, Millard and Whicker 1990; 42, Levy et al. 1976; 43, S. S. Anderson et al. 1990; 44, Gilbert et al. 1989; 45, Jenkins et al. 1969; 46, Aarkrog 1990; 47, Romney et al. 1971; 48, Neel and Larson 1963; 49, Schultz and Longhurst 1963; 50, Jenkins and Fendley 1971; 51, Kaye and Dunaway 1963; 52, Curtis et al. 1991; 53, Ham et al. 1989; 54, Veskovac and Djuric 1990; 55, Lowe and Horrill 1991; 56, Godoy et al. 1991; 57, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; 58, Bagshaw and Brisbin 1984; 59, Colwell et al. 1996; 60, Sugg et al. 1995.

^c ND = not detectable.

32.5 CASE HISTORIES

Military weapons tests conducted at the Pacific Proving Grounds in the 1940s and 1950s resulted in greatly elevated local concentrations of radionuclides, and an accident at the Chernobyl nuclear power plant in the former Soviet Union in 1986 resulted in comparatively low concentrations of radionuclides dispersed over a wide geographical area. Both cases are briefly reviewed.

32.5.1 Pacific Proving Grounds

The first artificial, large-scale introduction of radionuclides into a marine environment was at Bikini Atoll in 1946. In succeeding years through 1958, Bikini and Eniwetok became the Pacific Proving Grounds where 59 nuclear and thermonuclear devices were detonated between 1946 and 1958 (Welander 1969; Templeton et al. 1971; Bair et al. 1979) (Table 32.15). Gross radiation injury to marine organisms has not been documented, possibly because seriously injured individuals do not survive and the more subtle injuries are difficult to detect. On land, the roof rat (*Rattus rattus*) survived heavy initial radiation by remaining in deep burrows. Terrestrial vegetation was heavily damaged by heat and blast, although regrowth occurred in 6 months. The land-dwelling hermit crab (*Coenobita* sp.) and coconut crab (*Birgus latro*) were subjected to higher levels of chronic radiation from internally deposited radionuclides than any other atoll organism studied. Levels remained constant in *Coenobita* at 166,000 Bq ⁹⁰Sr/kg skeleton and 16,835 Bq ¹³⁷Cs/kg muscle over 2 years; *Birgus* contained 25,900 Bq ⁹⁰Sr/kg skeleton and 3700 Bq ¹³⁷Cs/kg muscle over 10 years (Templeton et al. 1971). A survey in August 1964 at Eniwetok and Bikini Atolls (Welander 1969) (Table 32.15) showed that general levels of radioactivity were comparatively elevated and highest in soils and increasingly lower in aquatic invertebrates, groundwater, shorebirds, plants, rats, zooplankton, algae, fish, sediments, seawater, and seabirds. Cobalt-60 was found in all samples

of animals, plants, water, sediments, and soils and was the major radionuclide in the marine environment; on land, cesium-137 and ⁹⁰Sr predominated. All samples contained traces of ⁵⁴Mn; ¹⁰⁶Ru and ¹²⁵Sb were detected in groundwater and soil and trace concentrations in animals and plants. Trace amounts of ²⁰⁷Bi and ¹⁴⁴Ce were usually detected in algae, soils, and land plants. Iron-55 was comparatively high in vertebrates, and ²³⁹Pu was found in the soil and in the skin of rats and birds (Welander 1969).

**Table 32.15 Radionuclide Concentrations in Selected Samples from the Pacific Proving Grounds
(Concentrations are in becquerels/kg fresh weight [FW] or dry weight [DW].)**

Location, Sample, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
BIKINI ATOLL		
Samples with highest concentrations, August 1964		
²⁰⁷ Bi, sediments	Max. 6660 DW	1
¹⁴⁴ Ce, marine algae	Max. 1739 DW	1
¹³⁷ Cs, land invertebrates	Max. 14,060 DW	1
⁵⁷ Co, sediments	Max. 3400 DW	1
⁶⁰ Co, marine invertebrates	Max. 35,150 DW	1
⁵⁴ Mn, sediments	Max. 962 DW	1
¹⁰⁶ Ru, sediments	Max. 10,360 DW	1
¹²⁵ Sb, groundwater	Max. 12,950 DW	1
Seawater, 1972, ⁵⁵ Fe	Max. 0.025 FW	2
Sediments		
1958 vs. 1972, ⁵⁵ Fe	Max. 777,000 DW vs. 11,100 DW	2
August 1964, ground zero		
²⁰⁷ Bi	6660 DW	1
⁵⁷ Co	3404 DW	1
⁶⁰ Co	9620 DW	1
⁵⁴ Mn	962 DW	1
¹⁰⁶ Ru	10,360 DW	1
¹²⁵ Sb	3663 DW	1
ENIWETOK ATOLL, AUGUST 1964		
Whole marine algae vs. whole marine fishes		
²⁰⁷ Bi	181 DW vs. 74 DW	1
¹⁴⁴ Ce	814 DW vs. nondetectable (ND)	1
¹³⁷ Cs	52 DW vs. 21 DW	1
⁶⁰ Co	355 DW vs. 888 DW	1
⁵⁴ Mn	48 DW vs. 70 DW	1
¹⁰⁶ Ru	96 DW vs. ND	1
¹²⁵ Sb	34 DW vs. ND	1
Terrestrial invertebrates vs. terrestrial vegetation		
²⁰⁷ Bi	6 DW vs. 10 DW	1
¹⁴⁴ Ce	5 DW vs. 888 DW	1
¹³⁷ Cs	No data vs. 12,580 DW	1
⁶⁰ Co	888 DW vs. 141 DW	1
⁵⁴ Mn	281 DW vs. 296 DW	1
¹⁰⁶ Ru	15 DW vs. 19 DW	1
¹²⁵ Sb	ND vs. 8 DW	1
Seabirds (whole) vs. shorebirds (whole)		
²⁰⁷ Bi	ND vs. ND	1
⁵⁷ Co	12 DW vs. ND	1
⁶⁰ Co	340 DW vs. 4810 DW	1
¹³⁷ Cs	ND vs. 4440 DW	1
⁵⁴ Mn	81 DW vs. ND	1
¹⁰⁶ Ru, ¹²⁵ Sb	ND vs. ND	1

Table 32.15 (continued) Radionuclide Concentrations in Selected Samples from the Pacific Proving Grounds (Concentrations are in becquerels/kg fresh weight [FW] or dry weight [DW].)

Location, Sample, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
Roof rat, <i>Rattus rattus</i> ; whole		
²⁰⁷ Bi	5 DW	1
¹⁴⁴ Ce	362 DW	1
⁶⁰ Co	888 DW	1
¹³⁷ Cs	19,980 DW	1
⁵⁴ Mn	1 DW	1
¹⁰⁶ Ru, ¹²⁵ Sb	ND	1
Samples with highest concentrations		
²⁰⁷ Bi, marine plankton	Max. 333 DW	1
¹⁴⁴ Ce, soils	Max. 2109 DW	1
¹³⁷ Cs, rats	Max. 19,980 DW	1
⁵⁷ Co, sediments	Max. 740 DW	1
⁶⁰ Co, marine invertebrates	Max. 6290 DW	1
⁵⁴ Mn, land plants	Max. 296 DW	1
¹⁰⁶ Ru, soils	Max. 4440 DW	1
¹²⁵ Sb, soils	Max. 703 DW	1
Soils vs. sediments		
²⁰⁷ Bi	20 DW vs. 218 DW	1
¹⁴⁴ Ce	2109 DW vs. No Data	1
¹³⁷ Cs	2072 DW vs. 814 DW	1
⁵⁷ Co	No Data vs. 740 DW	1
⁶⁰ Co	2849 DW vs. 1073 DW	1
⁵⁴ Mn	44 DW vs. 148 DW	1
¹⁰⁶ Ru	4440 DW vs. 3700 DW	1
¹²⁵ Sb	703 DW vs. 407 DW	1
ENIWETOK ATOLL, RUNIT ISLAND		
(8 nuclear detonations between 1948 and 1958)		
Roof rat, whole		
Immediate vicinity of detonations; 1967 vs. 1973		
¹³⁷ Cs		
Bone	21,978 DW vs. 81,363 DW	3
Intestine	137,344 DW vs. No Data	3
Kidney	189,958 DW vs. 126,799 DW	3
Liver	83,657 DW vs. 83,583 DW	3
Muscle	137,122 DW vs. 156,880 DW	3
Skin	13,209 DW vs. 77,256 DW	3
⁶⁰ Co		
200 m vs. 2460 m; 1967		
Bone	185 DW vs. ND	3
Intestine	8251 DW vs. No Data	3
Kidney	110,223 DW vs. 333 DW	3
Muscle	499 DW vs. 266 DW	3
Skin	259 DW vs. ND	3
Soils		
¹³⁷ Cs, 1967		
Ground zero vs. 200 m	1258 DW vs. 399 DW	3
1030 m vs. 2460 m	88 DW vs. 18 DW	3
¹³⁷ Cs, 1971		
Ground zero vs. 200 m	4736 DW vs. 403 DW	3
1030 m	44 DW	3
⁶⁰ Co, 1967		
Ground zero vs. 200 m	1221 DW vs. 66 DW	3
1030 m	25 DW	3

Table 32.15 (continued) Radionuclide Concentrations in Selected Samples from the Pacific Proving Grounds (Concentrations are in becquerels/kg fresh weight [FW] or dry weight [DW].)

Location, Sample, Radionuclide, and Other Variables	Concentration (Bq/kg or Bq/L)	Reference ^a
^{60}Co , 1971		
Ground zero vs. 200 m	1110 DW vs. 133 DW	3
1030 m vs. 2460 m	40 DW vs. 4 DW	3
1973, 2460 m		
^{137}Cs	11 DW	3
^{60}Co	52 DW	3
Terrestrial vegetation		
Ground zero, 1967 vs. 1971		
^{137}Cs	16,199–93,380 DW vs. 34,780–94,239 DW	3
^{60}Co	Max. 1221 DW vs. Max. 2775 DW	3
1030 m, 1967 vs. 1971		
^{137}Cs	296–2035 DW vs. 333–1961 DW	3
^{60}Co	Max. 14 DW vs. Max. 48 DW	3

^a 1, Welander 1969; 2, Schell 1976; 3, Bastian and Jackson 1976.

32.5.2 Chernobyl

32.5.2.1 General

Several accidents in nuclear facilities have been extensively analyzed and reported. The three most widely publicized accidents were at Windscale (now known as Sellafield), United Kingdom, in 1957; Three Mile Island, Pennsylvania, in 1979; and Chernobyl, Ukraine, in 1986 (UNSCEAR 1988; Severa and Bar 1991; Eisler 1995). From the accident at Windscale about 750 trillion (T)Bq ^{131}I , 22 TBq ^{137}Cs , 3 TBq ^{89}Sr , and 0.33 TBq ^{90}Sr were released and twice the amount of noble gases that were released at Chernobyl, but 2000 times less ^{131}I and ^{137}Cs . From the Three Mile Island accident, about 2% as much noble gases and 50,000 times less ^{131}I than from the Chernobyl accident were released. The most abundant released radionuclides at Three Mile Island were ^{133}Xe , ^{135}Xe , and ^{131}I , but the collective dose equivalent to the population during the first post-accident days was <1% of the dose accumulated from natural background radiation in a year.

The most serious accident of a nuclear reactor occurred on April 26, 1986, at one of the four units at Chernobyl when at least 3,000,000 TBq were released from the fuel during the accident (Table 32.16). The accident happened while a test was conducted during a normal scheduled shutdown and is attributed mainly to human error: "...the operators deliberately and in violation of rules, withdrew most control rods from the core and switched off some important safety systems..." (UNSCEAR 1988). The first power peak reached 100 times the nominal power within 4 seconds. Energy released in the fuel by the power excursion suddenly ruptured part of the fuel into minute pieces. Small, hot fuel particles caused a steam explosion. After 2 or 3 seconds, another explosion occurred, and hot pieces of the reactor were ejected. The damage to the reactor allowed air to enter, causing combustion of the graphite (UNSCEAR 1988). About 25% of the released radioactive materials escaped during the first day of the accident; the rest, during the next 9 days (UNSCEAR 1988). The initial explosions and heat from the fire carried some of the radioactive materials to an altitude of 1500 m where they were transported by prevailing winds (Figure 32.6) and caused widespread radioactive contamination of Europe and the former Soviet Union, initially with ^{131}I , ^{134}Cs , and ^{137}Cs (Smith and Clark 1986; Anspaugh et al. 1988; Clark and Smith 1988; UNSCEAR 1988; Aarkrog 1990; Johanson 1990; Brittain et al. 1991; Palo et al. 1991). Long-range

Table 32.16 Selected Fission Products in the Chernobyl Reactor Core, and Their Estimated Escape into the Environment

Radionuclide	Trillions of becquerels (TBq)	
	In Core	Escaped ^a
⁸⁵ Kr	33,000	33,000
¹³³ Xe	1,700,000	1,700,000
¹³¹ I	1,300,000	260,000
¹³² Te	320,000	48,000
¹³⁴ Cs	190,000	19,000
¹³⁷ Cs	290,000	37,700
⁹⁹ Mo	4,800,000	110,400
⁹⁵ Zr	4,400,000	140,800
¹⁰³ Ru	4,100,000	118,900
¹⁰⁶ Ru	2,000,000	58,000
¹⁴⁰ Ba	2,900,000	162,400
¹⁴¹ Ce	4,400,000	101,200
¹⁴⁴ Ce	3,200,000	89,600
⁸⁹ Sr	2,000,000	80,000
⁹⁰ Sr	200,000	8000
²³⁹ Np	140,000	4200
²³⁸ Pu	1000	30
²³⁹ Pu	850	25
²⁴⁰ Pu	1200	36
²⁴¹ Pu	170,000	5100
²⁴² Cm	26,000	780

^a Aarkrog (1990) estimates escapement of 100,000 TBq of ¹³⁷Cs; 50,000 TBq of ¹³⁴Cs; and 35,000 TBq of ¹⁰⁶Ru. Aarkrog (1990) also includes the following radionuclides in the Chernobyl escapement: 1500 TBq of ¹¹⁰Ag, 3000 TBq of ¹²⁵Sb, 6 TBq of ²⁴¹Am, and 6 TBq of ²⁴³⁺²⁴⁴Cm. Data from Severa, J. and J. Bar. 1991. *Handbook of Radioactive Contamination and Decontamination*. Studies in Environmental Science 47. Elsevier, New York. 363 pp.

atmospheric transport spread the radioactive materials through the northern hemisphere where it was first detected in Japan on May 2, in China on May 4, in India on May 5, and in Canada and the United States on May 5–6 1986 (UNSCEAR 1988). Airborne activity was also detected in Turkey, Kuwait, Monaco, and Israel in early May. No airborne activity from Chernobyl has been reported south of the equator (UNSCEAR 1988). Among the reactors now operating in the former Soviet Union are 13 identical to the one in Chernobyl, Ukraine, including units in Chernobyl, Leningrad, Kursk, and Smolensk (Mufson 1992).

Effective dose equivalents from the Chernobyl accident in various regions of the world were highest in southeastern Europe (1.2 mSv), northern Europe (0.97 mSv), and Central Europe (0.93 mSv) (Table 32.17). In the first year after the accident, whole-body effective dose equivalents were highest in Bulgaria, Austria, Greece, and Romania (0.5 to 0.8 mSv); Finland, Yugoslavia, Czechoslovakia, Italy (0.3 to 0.5 mSv); Switzerland, Poland, U.S.S.R., Hungary, Norway, Germany, and Turkey (0.2 to 0.3 mSv); and elsewhere (<0.2 mSv) (UNSCEAR 1988). Thyroid dose equivalents were significantly higher than whole-body effective dose equivalents because of significant amounts of ¹³¹I in the released materials. Thyroid dose equivalents were as high as 25 mSv to infants in Bulgaria, 20 mSv in Greece, and 20 mSv in Romania; the adult thyroid dose equivalents were usually 80% lower than the infant dose equivalents (UNSCEAR 1988).

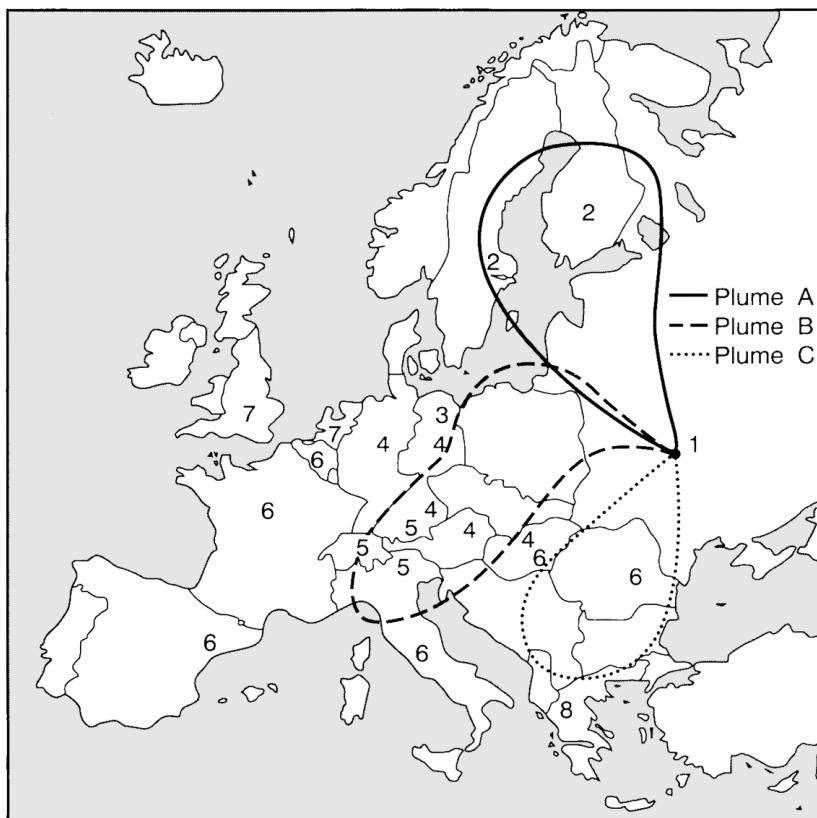


Figure 32.6 Chernobyl air plume behavior and reported initial arrival times of detectable radioactivity. Plume **A** originated from Chernobyl on April 26, 1986; Plume **B** on April 27–28; and Plume **C** on April 29–30. The numbers indicate initial arrival times: **1**, April 26; **2**, April 27; **3**, April 28; **4**, April 29; **5**, April 30; **6**, May 1; **7**, May 2; and **8**, May 3. (From United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 1988. Sources, *Effects and Risks of Ionizing Radiation*. United Nations, New York. 647 pp.)

Table 32.17 Regional Total Effective Human Dose Equivalent Commitment from the Chernobyl Accident

Region	Effective Dose Equivalent (mSv)
Southeastern Europe	1.2
Northern Europe	0.97
Central Europe	0.93
Former Soviet Union	0.81
Southwest Asia, West Europe	>0.1–<0.2
North Africa, Greenland, East Africa, Central Africa, South Asia, West Africa	>0.01–<0.1
East Asia, Southwest Europe, Southeast Asia, North America, Caribbean, South America, Central America	<0.01

Data from United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 1988. Sources, *Effects and Risks of Ionizing Radiation*. United Nations, New York. 647 pp.; Aarkrog, A. 1990. Environmental radiation and radiation releases. *Inter. Jour. Radiation Biol.* 57:619–631.

32.5.2.2 Local Effects

At Chernobyl, at least 115 humans received acute bone-marrow doses of greater than 1 Gy, as judged by lymphocyte aberrations (UNSCEAR 1988). The death toll within 3 months of the accident was at least 30 individuals, usually from groups receiving more than 4 Gy and including the reactor's operating staff and the fire-fighting crew. Local residents were evacuated from a 30-km exclusion zone around the reactor because of increasing radiation levels. More than 115,000 people, including 27,000 children, were evacuated from the Kiev region, Byelorussia, and the Ukraine. Tens of thousands of cattle were also removed from the contaminated area, and consumption of locally produced milk and other foods was banned. Agricultural activities were halted and a large-scale decontamination effort was undertaken (UNSCEAR 1988). The radiological effect of the accident to individual risk was insignificant outside a limited local region, either because contamination levels were generally low or because remedial actions to ban the consumption of highly contaminated foodstuffs prevented high exposures (UNSCEAR 1988).

Acute biological effects of the Chernobyl accident on local natural resources were documented by Sokolov et al. (1990). They concluded that the most sensitive ecosystems affected at Chernobyl were the soil fauna and pine forest communities and that the bulk of the terrestrial vertebrate community was not adversely affected by released ionizing radiation. Pine forests seemed to be the most sensitive ecosystem. One stand of 400 ha of *Pinus silvestris* died and probably received a dose of 80 to 100 Gy; other stands experienced heavy mortality of 10- to 12-year-old trees and up to 95% necrotization of young shoots. These pines received an estimated dose of 8 to 10 Gy. Abnormal top shoots developed in some *Pinus*, and these probably received 3 to 4 Gy. In contrast, leafed trees such as birch, oak, and aspen in the Chernobyl Atomic Power Station zone survived undamaged, probably because they are about 10 times more radioresistant than pines. There was no increase in the mutation rate of the spiderwort, (*Arabidopsis thaliana*) a radiosensitive plant, suggesting that the dose rate was less than 0.05 Gy/h in the Chernobyl locale.

Populations of soil mites were reduced in the Chernobyl area, but no population showed a catastrophic drop in numbers. By 1987, soil microfauna — even in the most heavily contaminated plots — were comparable to controls. Flies (*Drosophila* spp.) from various distances from the accident site and bred in the laboratory had higher incidences of dominant lethal mutations (14.7%, estimated dose of 0.8 mGy/h) at sites nearest the accident than controls (4.3%). Fish populations seemed unaffected in July/August 1987, and no grossly deformed individuals were found. However, ¹³⁴⁺¹³⁷Cs levels were elevated in young fishes. The most heavily contaminated teleost in May 1987 was the carp (*Carassius carassius*). But carp showed no evidence of mutagenesis, as judged by incidence of chromosomal aberrations in cells from the corneal epithelium of carp as far as 60 km from Chernobyl (Sokolov et al. 1990).

The most contaminated water body in the Chernobyl emergency zone was the Chernobyl cooling pond ecosystem (Kryshev 1995). On May 30, 1986, the total amount of radioactivity in the water of this system was estimated at 806 TBq, and in sediments 5657 TBq. In water, ¹³¹I contributed about 31% of the total radioactivity, ¹⁴⁰Ba-¹⁴⁰La 25%, ⁹⁵Zr-⁹⁵Nb 15%, ¹³⁴Cs and ¹³⁷Cs 11%, ¹⁴¹Ce and ¹⁴⁴Ce 10%, ¹⁰³Ru and ¹⁰⁶Ru 7%, and ⁹⁰Sr <1%. The distribution pattern in sediments was significantly different: about 41% of the total radioactivity was contributed by ⁹⁵Zr-⁹⁵Nb, 27% by ¹⁴¹Ce and ¹⁴⁴Ce, 16% by ¹⁰³Ru and ¹⁰⁶Ru, 12% by ¹⁴⁰Ba-¹⁴⁰La, 3% by ¹³⁴Cs and ¹³⁷Cs, 1% by ⁹⁰Sr, and 0.5% by ¹³¹I. Concentrations of radioactivity in water, sediments, and biota declined between 1986 and 1990, as judged by ¹³⁷Cs concentrations (Kryshev 1995). Cesium-137 concentrations in the Chernobyl cooling pond ecosystem declined in water from 210 Bq/L in 1986 to 14 Bq/L in 1990; for bottom sediments, these values were 170,000 Bq/kg FW in 1986 and 140,000 Bq/kg FW in 1990; for algae, 90,000 Bq/kg FW in 1986 to 19,000 Bq/kg FW in 1990; and for muscle of five species of fishes, ¹³⁷Cs concentrations ranged from 30,000 to 180,00 Bq/kg FW in 1986, and from

8000 to 80,000 Bq/kg FW in 1990 (Kryshev 1995). Silver carp (*Hypophthalmichthys molitrix*) born in 1989 from parents reared in Chernobyl cooling pond waters had a marked increase of 17 to 26% above controls in reproductive system anomalies in 1989 to 1992 (Makeyeva et al. 1995). Anomalies included degenerative changes in oocytes, spermatogonia, and spermatocytes, and the appearance of bisexual and sterile fish. The gonadal abnormalities are attributed to the high radiation dose of 7 to 10 Gy received by the parent fish during gonad formation and the continuing exposure of 0.2 Gy annually to this generation (Makeyeva et al. 1995). Silver carp from this ecosystem also had a dose-dependent decrease in hormonal control over Na^+ , K^+ -pump in erythrocytes, with increased passive permeability of the erythrocyte membrane to radioactive analogues of sodium and potassium (Kotelevtsev et al. 1996).

Several rodent species compose the most widely distributed and numerous mammals in the Chernobyl vicinity. It was estimated that about 90% of rodents died in an area that received 60 Gy and 50% in areas that received 6 to 60 Gy. Rodent populations seemed normal in spring 1987, and this was attributed to migration from adjacent nonpolluted areas. The most sensitive small mammal was the bank vole (*Clethrionomys glareolus*), which experienced embryonic mortality of 34%. The house mouse (*Mus musculus*) was one of the more radioresistant species. *Mus* from plots receiving 0.6 to 1 mG/h did not show signs of radiation sickness, were fertile with normal sperm, bred actively, and produced normal young. Some chromosomal aberrations were evident, namely, an increased frequency of reciprocal translocations (Sokolov et al. 1990). New data on the house mouse suggests that fertility was dramatically reduced in the 30-km zone around the Chernobyl nuclear power plant station in 1986/87 and that survivors had high frequencies of abnormal spermatozoa heads and dominant lethal mutations (Pomerantseva et al. 1996). Dose rates from soil to the house mouse between 1986 and 1993 ranged from 0.0002 to 2 mGy/h, and these were positively correlated with the frequency of reciprocal translocations in mouse spermatocytes. The frequency of mice heterozygous for recessive lethal mutations decreased over time after the accident (Pomerantseva et al. 1996).

During the early period after the accident, there was no evidence of increasing mortality, decline in fecundity, or migration of vertebrates as a result of the direct action of ionizing radiation. The numbers and distribution of wildlife species were somewhat affected by the death of the pine stand, the evacuation of people, the termination of cultivation of soils (the crop of 1986 remained standing), and the evacuation of domestic livestock. There were no recorded changes in survival or species composition of game animals and birds. In fact, because humans had evacuated and hunting pressure was negligible, many game species, including foxes, hares, deer, moose, wolves, and waterfowl, moved into the zone in fall 1986 to winter 1987 from the adjacent areas in a 50- to 60-km radius (Sokolov et al. 1990).

In 1991, 5 years after the accident, a female root vole (*Microtus oeconomus*) with an abnormal karyotype (reciprocal translocation) was found within the 30-km radius of the Chernobyl nuclear power plant. These chromosomal aberrations were probably inherited and did not affect the viability of vole populations (Nadzhafova et al. 1994). In 1994/95, the diversity and abundance of the small mammal population (12 species of rodents) at the most radioactive sites at Chernobyl were the same as reference sites (Baker et al. 1996). Rodents from the most radioactive areas did not show gross morphological features other than enlargement of the spleen. There were no gross chromosomal arrangements, as judged by examination of the karyotypes. Also observed within the most heavily contaminated site were red fox (*Vulpes vulpes*), gray wolf (*Canis lupus*), moose (*Alces alces*), river otter (*Lutra lutra*), roe deer (*Capreolus capreolus*), Russian wild boar (*Sus scrofa*), brown hare (*Lepus europaeus*), and feral dogs (Baker et al. 1996).

32.5.2.3 Nonlocal Effects

The partial meltdown of the 1000-megawatt reactor at Chernobyl on April 26, 1986, released large amounts of radionuclides into the environment — especially ^{131}I , ^{137}Cs , and ^{134}Cs — and

resulted in widely dispersed and deposited radioactive material in Europe and throughout the northern hemisphere (UNSCEAR 1988; Palo et al. 1991) (Table 32.18). Transuranics and to some extent ⁹⁰Sr were deposited closer to the accident site than more volatile radionuclides such as radiocesium; accordingly, radiological problems changed quantitatively and qualitatively with increasing distance from the accident site (Aarkrog 1990).

Soil and Vegetation. The radiocesium fallout in Sweden was among the highest in western Europe — exceeding 60,000 Bq/m² on Sweden's Baltic coast — and involved mainly upland pastures and forests (Johanson 1990; Brittain et al. 1991; Palo et al. 1991). In Norway, radiocesium deposition from the Chernobyl accident ranged from <5000 to >200,000 Bq/m² and greatly exceeded the deposition from prior nuclear weapons tests (Hove et al. 1990a). In Italy, heavy rainfall coincident with the passage of the Chernobyl radioactive cloud caused high local deposition of radionuclides in the soil, grass, and plants (Battiston et al. 1991). The Chernobyl plume reached Greece on May 1, 1986. A total of 14 gamma emitters were identified in the soil and vegetation in May 1986, and three (¹³⁴Cs, ¹³⁷Cs, ¹³¹I) were also detected in the milk of free-grazing animals in the area (Assimakopoulos et al. 1989). Radiocesium-134 and ¹³⁷Cs intake by humans in Germany during the period 1986/87 was mainly from rye, wheat, milk, and beef (Cloon and Aumann 1990). In the United Kingdom, elevated concentrations of radionuclides of iodine, cesium, ruthenium, and others were measured in the air and rainwater from May 2–5, 1986 (Smith and Clark 1986). The background activity concentrations were about 3 times normal levels in early May, and those of ¹³¹I approached the derived emergency reference level (DERL) of drinking water of 5 mSv ¹³¹I (equivalent to a thyroid dose of 50 mSv); however, ¹³¹I levels were not elevated in foodstuffs or cow's milk (Smith and Clark 1986). Syria — 1800 km from Chernobyl — had measurable atmospheric concentrations of ¹³⁷Cs and ¹³¹I and near-detection limit concentrations of ¹⁴⁴Ce, ¹³⁴Cs, ¹⁴⁰La, and ¹⁰⁶Ru (Othman 1990). The maximum ¹³¹I thyroid dose equivalent received by Syrians was 116 µSv in adults and 210 µSv in children. One year later, these values were 25 µSv in adults and 70 µSv in a 10-year-old.

The amount of fallout radioactivity deposited on plant surfaces depends on the exposed surface area, the developmental season of the plants, and the external morphology. Mosses, which have a relatively large surface area, showed the highest concentrations of radiocesium (Table 32.18). In northern Sweden, most of the radiocesium fallout was deposited on plant surfaces in the forest ecosystem and was readily incorporated into living systems because of browsing by herbivores and cesium's chemical similarity to potassium (Palo et al. 1991). Forest plants seemed to show less decrease than agricultural crops in ¹³⁷Cs activity over time (Bothmer et al. 1990). For example, the effective retention half-time of ¹³⁷Cs from Chernobyl was 10 to 20 days in herbaceous plants and 180 days in chestnut trees, *Castanea* spp. (Tonelli et al. 1990). The radioactive fallout from the Chernobyl accident also resulted in high ¹³⁷Cs levels in Swedish pasture grass and other forage, although levels in grain were relatively low (Andersson et al. 1990). Radiocesium isotopes were still easily measurable in grass silage harvested in June 1986 and used as fodder for dairy cows in 1988 (Voors and Van Weers 1991). The rejection of the first harvests of radiocesium-contaminated perennial pasture and in particular of rye grass (*Lolium perenne*) does not constitute a safe practice because later harvests — even 1 year after the contamination of the field — may contain very high values, as in Greece (Douka and Xenoulis 1991).

Aquatic Life. After Chernobyl, the consumption of freshwater fishes by Europeans declined, fish license sales dropped by 25%, and the sale of fish from radiocesium-contaminated lakes was prohibited (Brittain et al. 1991). Many remedial measures have been attempted to reduce radiocesium loadings in fishes, but none have been effective to date (Hakanson and Andersson 1992).

Radiocesium concentrations in muscle of fishes from the southern Baltic Sea increased 3 to 4 times after Chernobyl (Grzybowska 1989), and ¹³⁴⁺¹³⁷Cs and ¹⁰⁶Ru in fishes from the Danube River increased by a factor of 5. However, these levels posed negligible risk to human consumers

(Conkic et al. 1990). Chernobyl radioactivity, in particular ^{141}Ce and ^{144}Ce , entering the Mediterranean as a single pulse, was rapidly removed from surface waters and transported to 200 m in a few days, primarily in fecal pellets of grazing zooplankton (Fowler et al. 1987). Bioconcentration factors (BCF) of ^{137}Cs in fishes from Lake Paijanne, Finland — a comparatively contaminated area — ranged between 1250 and 3800; the highest BCF values were measured in the predatory northern pike (*Esox lucius*) a full 3 years after the Chernobyl accident; consumption of these fishes was prohibited (Korhonen 1990).

After the Chernobyl accident, radiocesium isotopes were also elevated in trees and lichens bordering an alpine lake in Scandinavia and in lake sediments, invertebrates, and fishes (Table 32.18). Radiocesium levels in muscle of resident brown trout (*Salmo trutta*) remained elevated for at least 2 years (Brittain et al. 1991). People consuming food near this alpine lake derived about 90% of their effective dose equivalent from the consumption of freshwater fish, reindeer meat, and milk. The average effective dose equivalent of this group during the next 50 years is estimated at 6 to 9 mSv with a changed diet and 8 to 12 mSv without any dietary changes (Brittain et al. 1991).

Wildlife. Reindeer (*Rangifer tarandus*) — also known as caribou in North America — are recognized as a key species in the transfer of radioactivity from the environment to humans because (1) the transfer factor of radioactivity from reindeer feed to reindeer muscle is high, (2) lichens — which constitute a substantial portion of the reindeer diet — are efficient accumulators of strontium, cesium, and actinide radioisotopes, and (3) reindeer feed is not significantly supplemented with grain or other feeds low in contamination (Jones et al. 1989; Rissanen and Rahola 1989; 1990; Eikelmann et al. 1990; Skogland and Espelien 1990). During 1986/87, about 75% of all reindeer meat produced in Sweden was unfit for human consumption because ^{137}Cs exceeded 300 Bq/kg FW. In May 1987, the maximum permissible level of ^{137}Cs in Swedish reindeer, game, and freshwater fish was raised to 1500 Bq/kg FW; however, about 25% of slaughtered reindeer in 1987 to 1989 still exceeded this limit (Ahman et al. 1990b). Concentrations in excess of 100,000 Bq $^{134+137}\text{Cs}/\text{kg}$ FW lichens have been recorded in the most contaminated areas and in the 1986/87 season was reflected in reindeer muscle concentrations >50,000 Bq/kg FW from the most contaminated areas of central Norway (Roed et al. 1991). Norwegian reindeer containing 60,000 to 70,000 Bq $^{137}\text{Cs}/\text{kg}$ FW in muscle receive an estimated yearly dose of 500 mSv (Jones 1990). The maximum radiation dose to reindeer in Sweden after the Chernobyl accident was about 200 mSv/year, with a daily dose rate of about 1 mSv during the winter period of maximum tissue concentrations (Jones et al. 1989). In general, reindeer calves had higher ^{137}Cs levels in muscle than adult females (4700 vs. 2700 Bq/kg FW) during September 1988, suggesting translocation to the fetus (Eikelmann et al. 1990). Two reindeer herds in Norway that were heavily contaminated with radiocesium had a 25% decline in survival of calves; survival was normal in a herd with low exposure (Skogland and Espelien 1990). Several compounds inhibit uptake and reduce retention of ^{137}Cs in reindeer muscle from contaminated diets, but the mechanisms of the action are largely unknown. These compounds include:

- Zeolite — a group of tectosilicate minerals — when fed at 25 to 50 g daily (Ahman et al. 1990a)
- Ammonium hexacyanoferrate — also known as Prussian Blue or Giese salt — at 0.3 to 1.5 g daily (Hove et al. 1990b; Mathiesen et al. 1990; Staalund et al. 1990)
- Bentonite — a montmorillonite clay — when fed at 2% of diet (Ahman et al. 1990a)
- High intakes of potassium (Ahman et al. 1990a)

Much additional work seems needed on chemical and other processes that hasten excretion and prevent uptake and accumulation of radionuclides in livestock and wildlife. Reindeer herding is the most important occupation in Finnish Lapland and portions of Sweden (Rissanen and Rahola

1989). Swedish Lapland reindeer herders have experienced a variety of sociocultural problems as a result of the Chernobyl accident. The variability of contamination has been compounded by the variability of expert statements about risk, the change in national limits of Bq concentrations set for meat marketability, and the variability of the compensation policy for slaughtered reindeer. These concerns may result in fewer Lapps becoming herders and a general decline in reindeer husbandry (Beach 1990).

Caribou in northern Quebec contained up to 1129 Bq $^{137}\text{Cs}/\text{kg}$ muscle FW in 1986/87, but only 10 to 15% of this amount originated from Chernobyl; the remainder is attributed to fallout from earlier atmospheric nuclear tests (Crete et al. 1990). The maximum concentration of ^{137}Cs in meat of caribou (*Rangifer tarandus granti*) from the Alaskan Porcupine herd after the Chernobyl accident did not exceed 232 Bq/kg FW, and this is substantially below the recommended level of 2260 Bq $^{137}\text{Cs}/\text{kg}$ FW (Allaye-Chan et al. 1990). Radiocesium transfer in an Alaskan lichen-reindeer-wolf (*Canis lupus*) food chain has been estimated. If reindeer forage contained 100 Bq/kg DW in lichens and 5 Bq/kg DW in vascular plants, the maximum winter concentrations — at an effective half-life of 8.2 years in lichens and 2.0 years in vascular plants — were estimated at 20 Bq/kg FW in reindeer-caribou skeletal muscle and 24 Bq/kg FW in wolf muscle (Holleman et al. 1990).

The radioactive body burden of exposed reindeer and the character of chromosomal aberrations — which was different in exposed and nonexposed reindeer — indicated a genetic effect of radiation from the Chernobyl accident (Roed et al. 1991). Chromosomal aberrations in Norwegian female reindeer positively correlated with increasing radiocesium concentrations in flesh (Skogland and Espelien 1990). The frequency of chromosomal aberrations in reindeer calves from central Norway were greatest in those born in 1987 when tissue loadings were equivalent to fetal doses of 70 to 80 mSv and lower in 1988 (50 to 60 mSv) and 1989 (40 to 50 mSv), strongly suggesting a dose-dependent induction (Roed et al. 1991). Mutagenicity tests have also been used successfully with feral rodents to evaluate the biological effects of the radiation exposure from the Chernobyl accident. Increased mutagenicity in mice (*Mus musculus domesticus*) was evident, as judged by tests of the bone-marrow micronucleus at 6 months and 1 year after the accident. Rodents with increased chromosomal aberrations also had ^{137}Cs burdens that were 70% higher 6 months after the accident and 55% higher after 1 year, but elevated radiocesium body burdens alone were not sufficient to account for the increase in mutagenicity (Cristaldi et al. 1990). In bank voles, however, mutagenicity (micronucleated polychromatic erythrocytes) correlated well with the ^{137}Cs content in muscle and in the soil of the collection locale (Cristaldi et al. 1991). The estimated daily absorbed doses (4.2 to 39.4 μGy) were far lower than those required to produce the same effect in the laboratory (Cristaldi et al. 1991).

For many households in Sweden, moose (*Alces alces*) are an important source of meat (Palo et al. 1991). Radiocesium concentrations in the foreleg muscle of moose in Sweden during 1987/88 were highest in autumn when the daily dietary intake of the animals was about 25,000 Bq ^{137}Cs and lowest during the rest of the year when the mean daily intake was about 800 Bq (Bothmer et al. 1990). Cesium-137 levels in moose flesh did not decrease significantly for about 2 years after the Chernobyl accident (Johanson 1990). The selection of food by moose is paramount to the uptake of environmental contaminants and the changes in tissue levels over time. Increased foraging on highly contaminated plant species, such as bilberry (*Vaccinium myrtillus*), aquatic plants, and mushrooms, might account for the increased ^{137}Cs radioactivity in moose (Palo et al. 1991). Habitat is a useful indicator of ^{137}Cs radioactivity in moose muscle; radioactivity was highest in moose captured in swamp and marsh habitats and lowest in farmlands (Nelin 1995). For reasons that are not yet clear, transfer coefficients of ^{137}Cs from diet to muscle were about the same in moose (0.03) and beef cattle (0.02), but were significantly higher in sheep (0.24) (Bothmer et al. 1990).

The songthrush (*Turdus philomelas*) collected in Spain in November 1986 had elevated concentrations of ^{134}Cs , ^{137}Cs , and ^{90}Sr . The contamination probably occurred in central and northern Europe before the birds' migration to Spain (Baeza et al. 1991). Spaniards who ate songthrushes

contaminated with radiocesium isotopes usually received about 58 $\mu\text{Sv}/\text{year}$, which is well below current international guidelines (Baeza et al. 1991). Consumption of game or wildlife in Great Britain after the Chernobyl accident probably also does not exceed the annual limits of intake (ALI) based on $^{134+137}\text{Cs}$ concentrations in game and the numbers of animals that can be eaten in 1 year before ALI is exceeded (Lowe and Horrill 1991). For example, a person who eats hares containing 3114 Bq $^{134+137}\text{Cs}/\text{kg FW}$ in muscle would have to consume 99 hares before exceeding the ALI. For the consumption of red grouse (3022 Bq/kg), this number is 441 grouse; and for the consumption of woodcock (55 Bq/kg), it is 45,455 woodcocks (Lowe and Horrill 1991). Rabbits (*Oryctolagus* sp.) from northeastern Italy that were fed Chernobyl-contaminated alfalfa meal (1215 Bq $^{134+137}\text{Cs}/\text{kg diet}$) had a maximum of 156 Bq/kg muscle FW of $^{134+137}\text{Cs}$, a value much lower than the current Italian guideline of 370 Bq/kg FW for milk and children's food and 600 Bq/kg FW for other food (Battiston et al. 1991). More than 85% of the ingested radiocesium was excreted by rabbits in their feces and urine; about 3% was retained (Battiston et al. 1991).

Cesium radioactivity in tissues and organs of the wolverine (*Gulo gulo*), lynx (*Felis lynx*), and Arctic fox (*Alopex lagopus*) in central Norway after the Chernobyl accident was highly variable. In general, cesium-137 levels were substantially lower in these carnivores than in lower trophic levels (Ekker et al. 1990), suggesting little or no food-chain biomagnification, and at variance with results of studies of the omnivore and herbivore food chain.

Domestic Animals. Radiocesium isotopes from the Chernobyl accident transferred easily to grazing farm animals (Hove et al. 1990a). Both ^{134}Cs and ^{137}Cs were rapidly distributed throughout the soft tissues after dietary ingestion and were most highly concentrated in muscle (Book 1969; Van Den Hoek 1989). Radiocesium activity in milk and flesh of Norwegian sheep and goats increased three- to fivefold 2 years after the accident and coincided with an abundant growth and availability of fungal fruit bodies with $^{134+137}\text{Cs}$ levels as much as 100 times greater than green vegetation (Hove et al. 1990a). In cattle, coefficients of radiocesium transfer from diet to muscle were about 2.5% in adults and 16% in calves. The higher value in calves was probably due to a high availability of cesium from the gastrointestinal tract and to daily uptake of potassium in growing animal muscle (Daburon et al. 1989). There was no correlation between the retention of ^{137}Cs and the pregnancy stage in cattle (Calamosca et al. 1990). Radiocesium concentrations in pork in Czechoslovakia did not decline between 1986 and 1987 because the feed of pigs during this period contained milk by-products contaminated with $^{134+137}\text{Cs}$ (Kliment 1991).

Sheep farming is the main form of husbandry in the uplands of west Cumbria and north Wales, a region that received high levels of radiocesium fallout during the Chernobyl accident. Afterwards, typical vegetation activity concentrations were ~6000 Bq/kg (down to ~1000 Bq/kg in January 1989). But sheep muscle concentrations exceeded 1000 Bq $^{137}\text{Cs}/\text{kg FW}$, which is the United Kingdom's dietary limit for human health protection (Crout et al. 1991). Contaminated lambs — which usually had higher concentrations of ^{137}Cs than ewes — that were removed to lowland pastures (<50 Bq/kg vegetation) rapidly excreted radiocesium in feces and urine, and cesium body burdens had an effective half-life of 11 days. This practice should not significantly increase radiocesium levels in the soil and vegetation of lowland pastures (Crout et al. 1991). The absorption and retention of radiocesium by suckling lambs is highly efficient, about 66%. Fecal excretion was an important pathway after the termination of ^{137}Cs ingestion. In weaned animals, the absorption of added ionic cesium was about twice that of cesium fallout after the accident at Chernobyl (Moss et al. 1989). Silver-110m was also detected in the brains and livers of ewes and lambs in the United Kingdom. The transfer of $^{110\text{m}}\text{Ag}$ was associated with perennial rye grass harvested soon after deposition in 1986. Silver-110m was taken up to a greater extent than ^{137}Cs in liver; but unlike ^{137}Cs , the $^{110\text{m}}\text{Ag}$ was not readily translocated to other tissues. Other than cesium isotopes and ^{131}I , $^{110\text{m}}\text{Ag}$ was the only detected nuclide in sheep tissues (Beresford 1989).

Atmospheric deposition of ^{137}Cs from Chernobyl to vegetation and eventually to the milk of sheep, cows, and goats on contaminated silage was reported in Italy, the Netherlands, Japan, and the United Kingdom (Book 1969; Belli et al. 1989; Pearce et al. 1989; Voors and Van Weers 1989; Aii et al. 1990; Monte 1990). The effective half-life of ^{137}Cs was 6.7 days in pasture grass and 13.6 days in milk (Spezzano and Giacomelli 1991). The average transfer coefficient of $^{134+137}\text{Cs}$ from Chernobyl from a 70% grass silage diet to milk of Dutch dairy cows was about 0.25%/liter/day (Voors and Van Weers 1991). In goats (*Capra* sp.), about 12% of orally administered ^{137}Cs was collected in milk within 7 days after dosing (Book 1969).

Iodine-131 was one of the most hazardous radionuclides released in the Chernobyl accident because it is easily transferred through the pasture-animal-milk pathway and rapidly concentrated in the thyroid gland to an extent unparalleled by any other organ. Because of its high specific activity, ^{131}I can transmit a high dose of radiation to the thyroid (Ionannides and Pakou 1991). Iodine-131 levels of 618,000 Bq/kg FW sheep thyroids from northwestern Greece on July 3, 1986, are similar to maximal ^{131}I concentrations in sheep thyroids in Tennessee in 1957 after global atmospheric fallout from military weapons tests and in London after the Windscale accident (Ionannides and Pakou 1991). Iodine-131 has an effective whole-body half-life of about 24 h and is rapidly excreted from sheep and cows (Assimakopoulos et al. 1989). The effective half-life of ^{131}I in pasture grass was 3.9 days and 5 days in cow's milk (Spezzano and Giacomelli 1991). The transfer coefficients of ^{131}I from vegetation to cow's milk was 0.007% day/L milk. This value was 57 times higher (0.4) in sheep (Monte 1990), but the mechanism to account for this large interspecies difference is not clear.

Table 32.18 Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
ALASKA AND YUKON TERRITORIES		
Barren-ground caribou (<i>Rangifer tarandus granti</i>); porcupine herd; March–November 1987; ^{137}Cs		
Feces	Max. 802 DW	1
Muscle	133 (26–232) FW	1
Rumen contents	Max. 538 DW	1
ALBANIA		
^{137}Cs ; May 2–19, 1986		
Air	Max. 1.8 Bq/m ³	2
Milk vs. wheat flour	Max. 380 FW vs. Max. 236 FW	2
^{131}I ; cow's milk; May 2–19, 1986	Max. 3500 FW	2
CANADA		
Caribou, <i>Rangifer tarandus</i> ; northern Quebec; 1986 (post-Chernobyl)–1987; muscle; ^{137}Cs		
CZECHOSLOVAKIA		
$^{134+137}\text{Cs}$; 1986 (post-Chernobyl)		
Barley, <i>Hordeum vulgare</i>	7 DW	4
Cow, <i>Bos</i> sp., milk		
May	42 FW	4
July	10 FW	4
December	7 DW	4
Wheat, <i>Triticum</i> sp.	16 DW	4
$^{134+137}\text{Cs}$; domestic pig, <i>Sus</i> sp.; muscle; July 1986 vs. July 1987	15–22 FW vs. 22 FW	4

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
DANUBE RIVER, HUNGARY-YUGOSLAVIA		
Water; 1986; post-Chernobyl		
¹³⁴ Cs	0.015 FW	5
¹³⁷ Cs	0.096 FW	5
¹⁰³ Ru	0.070 FW	5
Fish, various species; 1986 (post-Chernobyl) vs. 1987		
¹³⁴ Cs	8 FW vs. 4 FW	5
¹³⁷ Cs	13 FW vs. 12 FW	5
¹⁰³ Ru	1 FW vs. <1 FW	5
¹⁰⁶ Ru	4 FW vs. 3 FW	5
Sediments; 1986 (post-Chernobyl) vs. 1988		
¹³⁴ Cs	500 DW vs. 80 DW	5
¹³⁷ Cs	750 DW vs. 200 DW	5
Algae; 1986 (post-Chernobyl) vs. 1988		
¹³⁴ Cs	275 FW vs. 25 FW	5
¹³⁷ Cs	625 FW vs. 100 FW	5
FINLAND		
Finnish Lapland; ¹³⁷ Cs; 1979–84 vs. 1986 (post-Chernobyl)		
Arboreal lichens	120 DW vs. 590 DW	7
Ground lichens	230 DW vs. 900 DW	7
Birch, <i>Betula</i> sp.	68 DW vs. 51 DW	7
Horsetails, <i>Equisetum</i> sp.	203 DW vs. 280 DW	7
Bilberry, <i>Vaccinium</i> sp.	120 DW vs. 590 DW	7
Lichens; ¹³⁷ Cs		
From reindeer herding areas; 1986 (post-Chernobyl) vs. 1987	900 DW vs. 800 DW	8
Isolated areas; 1986 (post-Chernobyl)–1987	3000–10,000 DW	8
Gulf of Finland; ¹³⁷ Cs		
Seawater		
1985 (pre-Chernobyl) vs. 1986 (post-Chernobyl)	0.01 FW vs. 1.05 FW	53
1987 vs. 1990	0.23 FW vs. 0.05 FW	53
Bottom sediments		
1985 vs. 1986	1.2 FW vs. 40.0 FW	53
1987 vs. 1990	19.0 FW vs. 5.0 FW	53
Algae, whole		
1985 vs. 1986	3.9 FW vs. 175.0 FW	53
1987 vs. 1990	30.0 FW vs. 14.0 FW	53
Fish, 2 species, whole		
1985 (pre-Chernobyl)	1.4–3.5 FW	53
1986 (post-Chernobyl)	22.0–54.0 FW	53
1987	60.0–120.0 FW	53
1990	36.0–116.0 FW	53
Lake Paijanne (estimated ¹³⁷ Cs Chernobyl loading of 20,000 Bq/m ²); ¹³⁷ Cs; whole fish; three species (northern pike, <i>Esox lucius</i> ; yellow perch, <i>Perca flavescens</i> ; roach, <i>Rutilus rutilus</i>)		
1986; pre-Chernobyl vs. post-Chernobyl	580 FW vs. 1250 FW	6
1987	1000–2000 FW	6
1988	160–2000 FW	6
Reindeer, <i>Rangifer tarandus</i> ; muscle; ¹³⁷ Cs		
1964–65 (following nuclear tests) vs. 1985–86 (pre-Chernobyl)	Max. 2500–2600 FW vs. 300 FW	7, 8
1986–87 vs. 1987–88	720 FW, Max. 16,000 FW vs. 640 FW, Max. 9000 FW	8

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
FRANCE		
Cows, fed hay (harvested post-Chernobyl) diet containing 5500 $^{134+137}\text{Cs}/\text{kg}$ for mean daily intake of 15,900 Bq	A plateau was observed in milk after 15 days and in meat after 50–60 days; radiocaesium transfer coefficients from diet were 1.1% for milk and 2.0–2.7% for meat	9
Calves fed $^{134+137}\text{Cs}$ -contaminated milk from birth to age 80 days	Transfer coefficient from milk to meat was 16%	9
GERMANY		
Soils; June 24, 1986		
^{134}Cs	Max. 602 Bq/m ² DW	10
^{137}Cs	Max. 1545 Bq/m ² DW	10
^{103}Ru	Max. 808 Bq/m ² DW	10
Pasture vegetation; May 1986		
^{134}Cs	20 FW	10
^{137}Cs	40 FW	10
^{131}I	75 FW	10
Cow; milk; May 1986		
^{134}Cs	140 FW	10
^{137}Cs	250 FW	10
^{131}I	250 FW	10
^{103}Ru	250 FW	10
Human, <i>Homo sapiens</i>		
Intake per person		
^{134}Cs ; 1986 vs. 1987	354 Bq vs. 8 Bq	10
^{137}Cs ; 1986 vs. 1987	728 Bq vs. 37 Bq	10
Whole-body dose (Bonn and vicinity); 1986 vs. 1987	0.0147 mSv (0.008 from ^{137}Cs , 0.0067 from ^{134}Cs) vs. 0.00056 mSv (0.0004 from ^{137}Cs , 0.00016 from ^{134}Cs)	10
Thyroid, ^{129}I	Negligible	11
GREECE		
Alfalfa, <i>Medicago sativa</i> ; June 1986		
^{134}Cs	2303 DW	12
^{137}Cs	4551 DW	12
^{103}Ru	358 DW	12
^{106}Ru	1075 DW	12
Lichen, <i>Ramalina fraxinea</i> vs. moss, <i>Homalothecium sericum</i> ; 1986 (post-Chernobyl); after decay of short-lived radionuclides		
^{134}Cs	426 FW vs. 1121 FW	13
^{137}Cs	951 FW vs. 2612 FW	13
^{40}K	222 FW vs. 278 FW	13
^{103}Ru	63 FW vs. 115 FW	13
^{106}Ru	436 FW vs. 1365 FW	13
Rye grass, <i>Lolium perenne</i> ; June 1986		
^{134}Cs	3518 DW	12
^{137}Cs	7090 DW	12
^{103}Ru	708 DW	12
^{106}Ru	1747 DW	12
Plants, various; measured about 4 months post-Chernobyl; ^{137}Cs ; values represent about 9% of initial Chernobyl radioactivity		
Aromatic plants; 11 species	22–11,344 FW; 26–22,000 DW	13
Cereals; 4 species	11–2257 FW; 11–2775 DW	13

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
Fruit-bearing trees; 7 species	85–1572 FW; 122–2116 DW	13
Fungi; 4 species	103–5553 FW; 214–11,418 DW	13
Marine algae; 4 species	85–139 FW; 529–917 DW	13
Mosses and lichens; 6 species	1184–9413 FW; 1110–18,847 DW	13
Vegetables; 18 species	18–244 FW; 18–299 DW	13
Northern Greece; May 1986; ¹³¹ I		
Grasses	Max. 1500 FW	14
Milk; cow vs. domestic sheep, <i>Ovis aries</i>	Max. 300 FW vs. Max. 800 FW	14
Domestic sheep; thyroid; ¹³¹ I; maximum values; 1986		
June 27 vs. July 2	4000 FW vs. 15,600 FW	15
July 3 vs. July 5	618,000 FW vs. 9000 FW	15
July 29 vs. August 20	8500 FW vs. 600 FW	15
ITALY		
Honey bee, <i>Apis</i> spp.; honey; May 10, 1986		
¹³⁴ Cs	Max. 171 FW	16
¹³⁷ Cs	Max. 363 FW	16
¹³¹ I	Max. 1051 FW	16
¹⁰³ Ru	Max. 575 FW	16
Cow		
Fed diets contaminated with Chernobyl ¹³⁷ Cs for 8 months before slaughter		
Female vs. fetus		
Amniotic fluid	Max. 82 FW vs. — ^b	17
Blood	Max. 13 FW vs. Max. 44 FW	17
Muscle	Max. 179 FW vs. Max. 126 FW	17
Kidney	Max. 232 FW vs. Max. 139 FW	17
Liver	Max. 163 FW vs. Max. 115 FW	17
Placenta	Max. 93 FW vs. — ^b	17
Rodent, <i>Mus musculus domesticus</i> ; carcass less internal organs; ¹³⁷ Cs		
October–November 1981 vs. May 1986	5 DW vs. 43 DW	18
October–November 1986 vs. May 1987	20 DW vs. 18 DW	18
Northwest Saluggia, May 1986		
¹³⁷ Cs, pasture grass vs. cow's milk	8000 DW vs. 180 FW	19
¹³¹ I, pasture grass vs. cow's milk	12,000 DW vs. 870 FW	19
Rabbit, <i>Oryctolagus</i> sp.; fed Chernobyl-contaminated alfalfa meal diet containing, in Bq/kg FW, 856 ¹³⁷ Cs, 369 ¹³⁴ Cs, and 540 ⁴⁰ K; or normal diet (112 ¹³⁷ Cs, 41 ¹³⁴ Cs, 503 ⁴⁰ K) for various intervals		
Control diet		
Whole animal	16 ¹³⁷ Cs FW, 7 ¹³⁴ Cs FW, 87 ⁴⁰ K FW	20
Muscle	22 ¹³⁷ Cs FW, 8 ¹³⁴ Cs FW, 117 ⁴⁰ K FW	20
21 days on contaminated diet followed by 21 days on control diet		
Whole animal	20 ¹³⁷ Cs FW, 9 ¹³⁴ Cs FW, 79 ⁴⁰ K FW	20
Muscle	31 ¹³⁷ Cs FW, 128 ¹³⁴ Cs FW, 117 ⁴⁰ K FW	20
42 days on contaminated diet		
Whole animal	81 ¹³⁷ Cs FW, 32 ¹³⁴ Cs FW, 85 ⁴⁰ K FW	20
Muscle	112 ¹³⁷ Cs FW, 44 ¹³⁴ Cs FW, 124 ⁴⁰ K FW	20
JAPAN		
¹³⁷ Cs		
Milk; cow; May 1986	Max. 0.6 FW	21
Soil; estimated deposition from Chernobyl	180 Bq/m ² DW	21

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
¹³⁴⁺¹³⁷ Cs; humans, children; estimated internal dose through milk consumption		
1986	0.0006 mSv	21
1987	0.0003 mSv	21
1988	0.0001 mSv	21
¹³¹ I, grass vs. cow's milk		
May 10–11, 1986	65 FW vs. 4.3 FW	22
May 30, 1986	14 FW vs. ND ^c	22
MONACO		
Air, Bq/m ³ , April 26, 1986; Monaco vs. Chernobyl (former Soviet Union)		
¹³⁴ Cs	8.2 vs. 53	50
¹³⁷ Cs	1.6 vs. 120	50
¹⁰³ Ru	3.5 vs. 280	50
¹³¹ I	4.6 vs. 750	50
¹⁰⁶ Ru	3.0 vs. 110	50
¹⁴⁰ Ba	9.8 vs. 420	50
⁹⁹ Mo	3.8 vs. 490	50
¹⁴¹ Ce	3.7 vs. 190	50
¹⁴⁴ Ce	2.5 vs. 110	50
⁹⁵ Zr	1.2 vs. 590	50
Marine copepods, 3 species; May 6, 1986; whole organism vs. fecal pellets		
¹⁰³ Ru	280 DW vs. 16,000 DW	49
¹⁰⁶ Ru	70 DW vs. 5800 DW	49
¹³⁴ Cs	22 DW vs. 3400 DW	49
¹³⁷ Cs	34 DW vs. 6300 DW	49
¹⁴¹ Ce	20 DW vs. 900 DW	49
¹⁴⁴ Ce	100 DW vs. 2500 DW	49
Mussel, <i>Mytilus galloprovincialis</i> ; soft parts; May 6 vs. August 14, 1986		
¹⁰³ Ru	480 FW vs. 9.6 FW	51
¹⁰⁶ Ru	121 FW vs. 11.2 FW	51
¹³¹ I	84 FW vs. <2 FW	51
¹³⁴ Cs	6 FW vs. 0.1 FW	51
¹³⁷ Cs	5.2 FW vs. 0.3 FW	51
NETHERLANDS		
¹³⁴ Cs; grass silage; 1986 (post-Chernobyl) vs. 1987	Max. 50 DW vs. 2 DW	23
¹³⁷ Cs; grass silage; 1986 (post-Chernobyl) vs. 1987	Max. 172 DW vs. 9 DW	23
¹³⁷ Cs-contaminated roughage fed to lactating cows		
10.3 Bq ¹³⁷ Cs/kg FW; grass	1.0–1.6 FW milk	24
173–180 Bq ¹³⁷ Cs/kg FW; grass silage	12–28 FW milk	24
260–271 Bq ¹³⁷ Cs/kg DW; grass	5.4–6.2 FW milk	24
⁴⁰ K; grass silage; 1986 vs. 1987	910 DW vs. 1028 DW	23
NORWAY		
Alpine lake and vicinity; ¹³⁴⁺¹³⁷ Cs		
Dwarf birch, <i>Betula nana</i> ; leaves; August 1986	4000 FW	25
Lichens; August 1986	60,000 FW	25
Willow, <i>Salix</i> spp.; leaves; September 1980 vs. August 1986	<50 FW vs. 600 FW	25
Lake sediment; upper 10 cm; July–August 1986	1050 FW	25

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
Aquatic organisms; July–August 1986		
Cladoceran, <i>Bosmina longispina</i> , whole	5300 FW	25
Amphipod, <i>Gammarus lacustris</i> , whole	6700 FW	25
Mayfly, <i>Siphlonurus lacustris</i> , whole	2800 FW	25
Stonefly, 2 spp., whole	1300–4120 FW	25
Minnow, <i>Phoxinus phoxinus</i> , whole	8800 FW	25
Brown trout, <i>Salmo trutta</i>		
Muscle		
1985 (pre-Chernobyl) vs. June 1986	<100 FW vs. 300 FW	25
August 1986 vs. June 1988	7000 FW vs. 4000 FW	25
Eggs vs. milt; July–August 1986	1740–3600 FW vs. 1300 FW	25
Dovrefjell, May 1986 vs. August 1990		
Earthworms (<i>Lumbricus rubellus</i> , <i>Allobophora caliginosa</i>), whole	121 FW vs. 74 FW	52
Eurasian woodcock, <i>Scolopax rusticola</i> , breast muscle	737 FW vs. 53 FW	52
Litter	14,400 DW vs. 2900 DW	52
Mushroom, <i>Lactarius</i> spp.; post-Chernobyl; ¹³⁴⁺¹³⁷ Cs	Max. 445,000 FW	26
Reindeer; muscle; ¹³⁴⁺¹³⁷ Cs		
1986; post-Chernobyl	10,000–50,000 FW	27
January 1987 vs. September 1988	Max. 56,000 FW vs. Max. 13,900 FW	28
Reindeer; 2 groups of adult females were fed lichen diets containing 45,000 Bq ¹³⁴⁺¹³⁷ Cs/kg ration for 35 days; one group received daily oral administration of 250 mg ammonium hexacyanoferrate (Giese salt)	Both groups accumulated 400 Bq/kg FW daily in muscle. Retention time of Cs isotopes was 25 days without Giese salt and only 7–10 days when treated with Giese salt	29
POLAND		
Freshwater fish; 4 species; muscle; January 1987; ¹³⁴⁺¹³⁷ Cs	4.5–6.1 FW	30
Southern Baltic Sea, ¹³⁴⁺¹³⁷ Cs; pre-Chernobyl (1982–February 1986) vs. post-Chernobyl (June 1986–July 1987)		
Water	(13.8–19.8) Bq/m ³ vs. (59–100) Bq/m ³	30
Atlantic cod, <i>Gadus morhua</i> ; muscle	(1.4–2.3) FW vs. (5.0–7.4) FW	30
Flounder, <i>Pleuronectes flesus</i> ; muscle	(1.1–4.5) FW vs. (3.4–6.7) FW	30
SPAIN		
Songthrush, <i>Turdus philomelos</i> ; edible tissues; November 1986 vs. November 1987		
¹³⁴ Cs	Max. 90 DW for adults and young vs. Max. 7 DW for adults and 5 DW for young	31
¹³⁷ Cs	Max. 208 DW vs. Max. 27 DW for adults and 22 for young	31
⁹⁰ Sr	Max. 23 DW vs. Max. 7 DW	31
SWEDEN		
Moose, <i>Alces alces</i> ; central Sweden; muscle; ¹³⁷ Cs		
September 1986; adults vs. calves	300 FW vs. 500 FW	32
1986; all age groups	20–3000 FW	33
September 1987; adults vs. calves	201 FW vs. 401 FW	32
1987, all age groups	Max. 1600 FW	34
September 1988, adults vs. calves	640 FW vs. 1300 FW	32
1988, all age groups	Max. 2500 FW	34
1991, all age groups; May–September; various habitats	Mean 478 FW; Max. 1060 FW; highest in swamps and marshes and lowest in farmlands	54

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
Moose dietary plants; 1986 (post-Chernobyl)–1988; ^{137}Cs		
Birch, <i>Betula</i> spp.; leaves	1200 DW	34
Heather, <i>Calluna vulgaris</i> ; whole	13,000–32,000 DW	34, 35
Sedge, <i>Carex</i> spp.; whole	12,000 DW	35
Hair grass, <i>Deschampia flexuosa</i> ; whole	1900 DW	34
Fireweed, <i>Epilobium angustifolium</i> ; whole	400 DW	34
Grasses, various species; blades	2500 DW	34
Buckbean, <i>Menyanthes trifoliata</i> ; whole	3800 DW	34
Pine, <i>Pinus sylvestris</i> ; shoots	2500 DW	34
Aspen, <i>Populus tremula</i> ; leaves	700 DW	34
Willow, <i>Solix</i> spp.; leaves	300 DW	34
Mountain ash, <i>Sorbus aucuparia</i> ; leaves	1300 DW	34
Bilberry, <i>Vaccinium myrtillus</i> ; leaves		
July 1986	2000 FW; 4000 DW	32, 34
July 1987 vs. July 1988	1138 FW vs. 600 FW	32
Bog whortleberry, <i>Vaccinium uliginosum</i> ; foliage	5900 DW	34
Cowberry, <i>Vaccinium vitis-idaea</i> ; foliage	7500 DW	34
Cow's milk; ^{137}Cs ; July 1986 vs. 1987	Usually <250 FW, Max. 375 FW vs. usually <70 FW, Max. 120 FW	36
Lichen, <i>Bryoria fuscescens</i> ; ^{137}Cs ; June 4, 1986	34,000–120,000 DW	35
Roe deer, <i>Capreolus</i> sp.; muscle; ^{137}Cs ; 1986 (post-Chernobyl)	20–12,000 FW	33
Lichen, <i>Cladina</i> spp.; ^{137}Cs ; 1986 (post-Chernobyl)	Max. 40,000 DW	35
Bank vole, <i>Clethrionomys glareolus</i> ; collected from soil containing various concentrations of $^{134+137}\text{Cs}$; voles analyzed less skull and digestive organs		
1800 Bq/m ² soil (control)	Voles had 9 Bq $^{134}\text{Cs}/\text{kg}$ FW and 39 of ^{137}Cs ; mutation frequency of 1.3; total irradiation of 0.0042 mGy daily	37
22,000 Bq/m ² soil	In Bq/kg FW, voles had 279 ^{134}Cs and 1031 ^{137}Cs ; mutation frequency was 1.5; daily dose rate of 0.0088 mGy	37
90,000 Bq/m ² soil	Voles had 1356 Bq $^{134}\text{Cs}/\text{kg}$ FW and 5119 of ^{137}Cs ; mutation frequency 1.9; daily dose of 0.0268 mGy	37
145,000 Bq/m ² soil	Voles had 2151 Bq $^{134}\text{Cs}/\text{kg}$ FW and 7784 ^{137}Cs ; mutation frequency 2.6; daily dose of 0.0394 mGy	37
Buckbean, <i>Menyanthes trifoliata</i> ; foliage; ^{137}Cs ; 1985 vs. 1987	1800 DW vs. 3880 DW	35
Reindeer dietary lichens; ^{137}Cs ; April 1986	Usually 40,000–60,000 DW; Max. 120,000 DW	38
Reindeer		
Moved in November 1986 from a highly contaminated area (>20,000 Bq $^{137}\text{Cs}/\text{m}^2$) to a less-contaminated area (<3000 Bq/m ²) of natural pasture	^{137}Cs content in muscle declined from 12,000 FW in November to about 3000 FW in April	39
Reindeer; muscle; ^{137}Cs ; 1986 (post-Chernobyl)	100–40,000 FW	33
Rodents and insectivores; July–August 1986; ^{137}Cs		
Control site, soil	1800 Bq/m ²	40
Bank vole; whole less skull, stomach, viscera	39 FW	40
Common shrew, <i>Sorex araneus</i> ; whole less skull, stomach, viscera	48 FW	40
Site 2, soil	22,000 Bq/m ²	40
Bank vole vs. common shrew	676 FW vs. 751 FW	40
Site 3, soil	90,000 Bq/m ²	40
Bank vole vs. common shrew	5119 FW vs. 3233 FW	40
Site 4, soil	145,000 Bq/m ²	40
Bank vole vs. common shrew	7993 FW vs. 6289 FW	40

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
SYRIA		
¹³⁷ Cs; air; May 7–10, 1986	0.12 Bq/m ³	41
¹³¹ I; May 7–10, 1986; air vs. goat's milk	4 Bq/m ³ vs. 55 FW	41
UNITED KINGDOM		
Upland pastures		
Moss, <i>Sphagnum</i> sp.; September 1986		
^{110m} Ag	202 DW	42
¹⁴⁴ Ce	202 DW	42
¹³⁴ Cs	8226 DW	42
¹³⁷ Cs	17,315 DW	42
¹⁰⁶ Ru	1893 DW	42
¹²⁵ Sb	294 DW	42
Vegetation; ¹³⁴⁺¹³⁷ Cs; June 1986 vs. January 1989	About 6000 DW vs. 1000 DW	43
Marine molluscs; 7 species; near nuclear plant; 1984 (pre-Chernobyl) vs. 1986 (post-Chernobyl)		
^{110m} Ag	<77 FW vs. 13–77 FW	44
⁶⁰ Co	<29 FW vs. 16–32 FW	44
¹³⁴ Cs	<14 FW vs. 37–388 FW	44
¹³⁷ Cs	<139 FW vs. 31–836 FW	44
⁴⁰ K	<59 FW vs. 57–61 FW	44
²³⁸ Pu	<27 FW vs. 11–22 FW	44
²³⁹⁺²⁴⁰ Pu	<107 FW vs. 19–89 FW	44
¹⁰⁶ Ru	<632 FW vs. 124–1648 FW	44
¹²⁵ Sb	ND vs. 29 FW	44
European oystercatcher, <i>Haematopus ostralegas</i> ; near nuclear reactor; June 1986; egg contents vs. egg shells		
¹³⁴ Cs	4 FW vs. — ^b	44
¹³⁷ Cs	18 FW vs. 6 FW	44
²³⁸ Pu	0.2 FW vs. 1.1 FW	44
²³⁹⁺²⁴⁰ Pu	0.05 FW vs. 4.6 FW	44
Red grouse, <i>Lagopus lagopus</i> ; muscle; November 1986–February 1987		
¹³⁴ Cs; cock vs. hen	325 FW vs. 602 FW	45
¹³⁷ Cs; cock vs. hen	962 FW vs. 1684 FW	45
Black-headed gull, <i>Larus ridibundus ridibundus</i> ; near nuclear reactor; 1980 vs. June 1986		
Egg contents		
¹³⁴ Cs	ND vs. 22 FW	44
¹³⁷ Cs	10 FW vs. 43 FW	44
²³⁸ Pu	0.02 FW vs. 0.01 FW	44
²³⁹⁺²⁴⁰ Pu	0.05 FW vs. 0.04 FW	44
Egg shells		
¹³⁴ Cs	— ^b vs. 7 FW	44
¹³⁷ Cs	— ^b vs. 16 FW	44
²³⁸ Pu	<0.17 FW vs. 0.4	44
²³⁹⁺²⁴⁰ Pu	0.6 FW vs. 1.6 FW	44
Woodcock, <i>Scolopax rusticola</i> ; muscle; November 1986–February 1987		
¹³⁴ Cs	13 FW	45
¹³⁷ Cs	42 FW	45
Black grouse, <i>Tetrao tetrix</i> ; ¹³⁷ Cs, November 1986–February 1987; diet vs. muscle	167 FW vs. 270 FW	45
Cow's milk; May 5–8, 1986		
¹³⁷ Cs	Max. 150 FW	46
¹³¹ I	Max. 127 FW	46

Table 32.18 (continued) Radionuclide Concentrations in Biotic and Abiotic Materials from Various Geographic Locales Before or After the Chernobyl Nuclear Accident on April 26, 1986 (All concentrations are in Bq/kg fresh weight [FW], or dry weight [DW], unless noted otherwise.)

Locale, Radionuclide, Sample, and Other Variables	Concentration	Reference ^a
Roe deer, <i>Capreolus capreolus</i> ; ¹³⁷ Cs; muscle; November 1986–February 1987		
Calves	711 FW	45
Hinds	375–586 FW	45
Stags	1564 FW	45
Red deer, <i>Cervus elephas</i> ; muscle; November 1986–February 1987		
¹³⁴ Cs; calf vs. hind	186 FW vs. 112 FW	45
¹³⁷ Cs; calf vs. hind	535 FW vs. 311 FW	45
Brown hare, <i>Lepus capensis</i> ; ¹³⁷ Cs; female; November 1986–February 1987; diet vs. muscle	198 FW vs. 656 FW	45
Blue hare, <i>Lepus timidus</i> ; ¹³⁷ Cs; November 1986–February 1987		
Males; diet vs. muscle	808 FW vs. 1677 FW	45
Females; diet vs. muscle	577 FW vs. 1440 FW	45
Rabbit, <i>Oryctolagus</i> sp.; muscle; male; November 1986–February 1987		
¹³⁴ Cs	6 FW	45
¹³⁷ Cs	15 FW	45
Domestic sheep		
Muscle; ¹³⁷ Cs; September 1986 vs. July 1987	1500 FW vs. 1170 FW	42
Liver; ^{110m} Ag; ewes vs. lambs		
September 1986	34 FW vs. 17 FW	47
July 1987	55 FW vs. <8 FW	47
Diet (rye grass and vegetation); ^{110m} Ag; 1986 vs. 1987	32 DW vs. 10–30 DW	47
Lambs fed a milk replacement diet containing 950 Bq ¹³⁷ Cs/kg ration for 21 days. After weaning, lambs were fed silage contaminated with fallout radiocesium plus ionic ¹³⁴ CsCl for 3 weeks	Absorption during the first 21 days was about 90%, equivalent to 975 Bq ¹³⁷ Cs/kg BW. During the silage feeding period, uptake of ionic ¹³⁴ Cs was about twice that of fallout ¹³⁴ Cs present in silage	48
Red fox, <i>Vulpes vulpes</i> ; muscle; November 1986–February 1987; vixen		
¹³⁴ Cs	176 FW	45
¹³⁷ Cs	461–643 FW	45

^a 1, Allaye-Chan et al. 1990; 2, Kedhi 1990; 3, Crete et al. 1990; 4, Kliment 1991; 5, Conkic et al. 1990; 6, Korhonen 1990; 7, Rissanen and Rahola 1989; 8, Rissanen and Rahola 1990; 9, Daburon et al. 1989; 10, Clooth and Aumann 1990; 11, Handl et al. 1990; 12, Douka and Xenoulis 1991; 13, Sawidis 1988; 14, Assimakopoulos et al. 1989; 15, Ionannides and Pakou 1991; 16, Tonelli et al. 1990; 17, Calamosca et al. 1990; 18, Cristaldi et al. 1990; 19, Spezzano and Giacomelli 1991; 20, Battiston et al. 1991; 21, Imanaka and Koide 1990; 22, Aii et al. 1990; 23, Voors and Van Weers 1991; 24, Vreman et al. 1989; 25, Brittain et al. 1991; 26, Hove et al. 1990a; 27, Skogland and Espelien 1990; 28, Eikelmann et al. 1990; 29, Mathiesen et al. 1990; 30, Grzybowska 1989; 31, Baeza et al. 1991; 32, Palo et al. 1991; 33, Johanson 1990; 34, Bothmer et al. 1990; 35, Eriksson 1990; 36, Johanson et al. 1989; 37, Cristaldi et al. 1991; 38, Jones 1990; 39, Jones et al. 1989; 40, Mascanzoni et al. 1990; 41, Othman 1990; 42, Coughtrey et al. 1989; 43, Crout et al. 1991; 44, Lowe 1991; 45, Lowe and Horrill 1991; 46, Clark and Smith 1988; 47, Beresford 1989; 48, Moss et al. 1989; 49, Fowler et al. 1987; 50, Whitehead et al. 1988b; 51, Whitehead et al. 1988a; 52, Kalas et al. 1994; 53, Kryshev 1995; 54, Nelin 1995.

^b — = no data.

^c ND = not detectable.

32.6 EFFECTS: NONIONIZING RADIATIONS

Living organisms are constantly exposed to nonionizing electromagnetic radiations, including ultraviolet (UV), visible, infrared, radio, and other low-energy radiations that form an integral part of the biosphere. Emissions from anthropogenic sources such as radios, microwave ovens, television

communications, and radar have significantly altered the character of our natural electromagnetic field (Garaj-Vrhovac et al. 1990). Although the primary focus of this review is on ionizing radiations, it would be misleading to assume that low-energy electromagnetic waves cannot elicit significant biological responses. For example, behavioral and biochemical changes are reported in rats, monkeys, rabbits, and other laboratory animals after exposure to nonionizing electromagnetic radiations. The severity of the effect is associated with the type and duration of the radiation and various physicochemical variables (Ghandi 1990). Selected examples follow.

Ultraviolet radiation should be considered a plausible factor contributing to amphibian malformations in field settings (Ankley et al. 1998). Ultraviolet radiation is linked to teratogenesis, growth inhibition, and DNA photodamage in larvae of the South African clawed frog, *Xenopus laevis* (Bruggeman et al. 1998). About 50% of newly fertilized eggs of the northern leopard frog (*Rana pipiens*) exposed to UV radiation for 24 h developed hindlimb malformations, such as missing limb segments, missing or reduced digits, and missing or malformed femurs (Ankley et al. 1998). The higher-energy portion of the ultraviolet spectrum (UV-B) was lethal to embryos of Canadian frogs, with death occurring in as little as 30 min; the lower-energy portion (UV-A) was not harmful to eggs or larvae at exposures twice that of ambient levels (Grant and Licht 1995). Exposure to solar radiation — even at low elevations — is lethal to amphibian eggs of species with relatively poor capacity to repair UV-damaged DNA (Blaustein et al. 1994, 1996). Increased UV-B radiation in the environment due to decreasing ozone levels has been suggested as a factor in the worldwide decline of sensitive species of amphibians (Blaustein et al. 1994; Ankley et al. 1998). However, UV-B radiation was not implicated in the decline of the endangered green and golden bell frog (*Litoria aurea*) in Australia (van de Mortel and Buttemer 1996).

UV radiation in mammals causes the aging of skin, making it wrinkled and leathery (Kligman and Kligman 1990). Dermatologists of the late 19th century described the devastating effects of sunlight on the skin of farmers and sailors when compared with indoor workers. Photoaged skin has a variety of neoplasms, deep furrows, extensive sagging, and profound structural alterations that are quite different from those in protected, intrinsically aged skin (Kligman and Kligman 1990). Similar results were documented for the skin of guinea pigs (Davidson et al. 1991) and rodents (Ananthaswamy and Pierceall 1990; Ronai et al. 1990) after exposure to UV radiation. UV radiation causes eye cancer in cattle (Anderson and Badzioch 1991), interferes with wound healing in guinea pig skin (Davidson et al. 1991), is a potent damaging agent of DNA and a known inducer of skin cancer in experimental animals (Ronai et al. 1990), and interferes with an immune defense mechanism that normally protects against skin cancer (Ananthaswamy and Pierceall 1990). Aquatic organisms exposed to UV radiation show disrupted orientation, decreased motility, and reduced pigmentation in *Peridinium gatunense*, a freshwater alga (Hader et al. 1990). Effects were similar in several species of marine algae (Lesser and Shick 1990; Hader and Hader 1991; Shick et al. 1991). Increased lipid peroxidation rates and a shortening of the life-span after UV exposure were reported in the rotifer *Asplanchna brightwelli* (Sawada et al. 1990). Cells of the goldfish (*Carassius auratus*) were damaged, presumably by DNA impairment, from UV exposure (Yasuhira et al. 1991).

Visible radiation adversely affected survival and growth of embryos of the chinook salmon (*Oncorhynchus tshawytscha*) (Eisler 1961), the chloroplast structure in the symbiotic marine dinoflagellate *Symbiodinium* sp. (Lesser and Shick 1990), and *in vitro* growth of cultured mammalian cells (Karu 1990). Infrared radiation contributes significantly to skin photoaging, producing severe elastosis; the epidermis and the dermis were capable of self-restoration when the exogenous injury ceased (Kligman and Kligman 1990).

Investigations of the cellular effects of radiofrequency radiation provide evidence of damage to various types of avian and mammalian cells. These effects involve radiofrequency interactions with cell membranes, especially the plasma membrane. Effects include alterations in membrane cation transport, Na^+/K^+ -ATPase activity, protein kinase activity, neutrophil precursor membrane receptors, firing rates and resting potentials of neurons, brain cell metabolism, DNA and RNA synthesis in glioma cells, and mitogenic effects on human lymphocytes (Cleary 1990).

Microwaves inhibit thymidine incorporation by DNA blockage in cultured cells of the Chinese hamster; irradiated cells had a higher frequency of chromosome lesions (Garaj-Vrhovac et al. 1990). Microwaves induce teratogenic effects in mice when the intensity of exposure places a thermal burden on the dams and fetuses, resulting in a reduction in fetal body mass and an increased number of resorptions (O'Connor 1990).

Extremely low frequency (ELF) electromagnetic fields — similar to fields that emanate from electrical appliances and the electrical power distribution network, usually <300 Hz — are used therapeutically in the healing of human nonunion bone fractures, in the promotion of nerve regeneration, and in the acceleration of wound healing (Anderson 1990). ELF electric and magnetic fields produce biological effects, usually subtle, and are of low hazard in short-term exposure. These effects include altered neuronal excitability, neurochemical changes, altered hormone levels, and changes in behavioral responses. For example, electric field perception has been reported in humans, mice, pigs, monkeys, pigeons, chickens, and insects; altered cardiovascular responses in dogs and chickens; and altered growth rate of chicks. No deleterious effects of ELF fields on mammalian reproduction and development or on carcinogenesis and mutagenesis have been documented (Anderson 1990). In the vicinity of a powerful radar station, some birds avoided nesting (flycatchers, *Myiarchus* spp.), and the percent of nesting boxes occupied by other species (tit, *Parus* spp.) increased significantly with increasing distance from the radar station (Liepa and Balodis 1994). ELF fields had no effect on the growth of bone in chicks (Coulton and Barker 1991). However, adult newts (*Notophthalmus viridescens*), regenerating amputated forelimbs, had grossly abnormal forelimbs 12% of the time when exposed for 30 days to ELF fields of the type reported to facilitate healing of human bone fractures (Landesman and Douglas 1990). Additional studies are recommended on the biological effects of nonionizing radiations on fishery and wildlife resources, especially on ELF radiations.

32.7 EFFECTS: IONIZING RADIATIONS

32.7.1 General

High acute doses of ionizing radiation produce adverse biological effects at every organizational level: molecular, cellular, tissue–organ, whole animal, population, community, and ecosystem (ICRP 1977; Whicker and Schultz 1982b; LWV 1985; Hobbs and McClellan 1986; UNSCEAR 1988; Kiefer 1990; Severa and Bar 1991). Typical adverse effects of ionizing radiation include:

- Cell death (McLean 1973; LWV 1985; Kiefer 1990)
- Decreased life expectancy (Lorenz et al. 1954; Brown 1966; Hobbs and McClellan 1986; Kiefer 1990; Rose 1992)
- Increased frequency of malignant tumors (Lorenz et al. 1954; ICRP 1977; Hobbs and McClellan 1986; UNSCEAR 1988; Hopewell 1990; Kim et al. 1990; Little 1990; Nagasawa et al. 1990; Raabe et al. 1990; Fry 1991)
- Inhibited reproduction (ICRP 1977; Barendson 1990; Kiefer 1990; Rose 1992)
- Increased frequency of gene mutations (ICRP 1977; Whicker and Schultz 1982b; Hobbs and McClellan 1986; Abrahamson 1990; Evans 1990; Kiefer 1990; Thacker 1990; Sankaranarayanan 1991a; 1991b; Rose 1992; Macdonald and Laverock 1998)
- Leukemia (ICRP 1977; Kiefer 1990)
- Altered blood–brain barrier function (Trnovec et al. 1990)
- Reduced growth and altered behavior (Rose 1992)

Species within kingdoms have a wide variation in sensitivity, and sometimes at low radiation exposures the response is considered beneficial (Luckey 1980; Rose 1992). Overall, the lowest

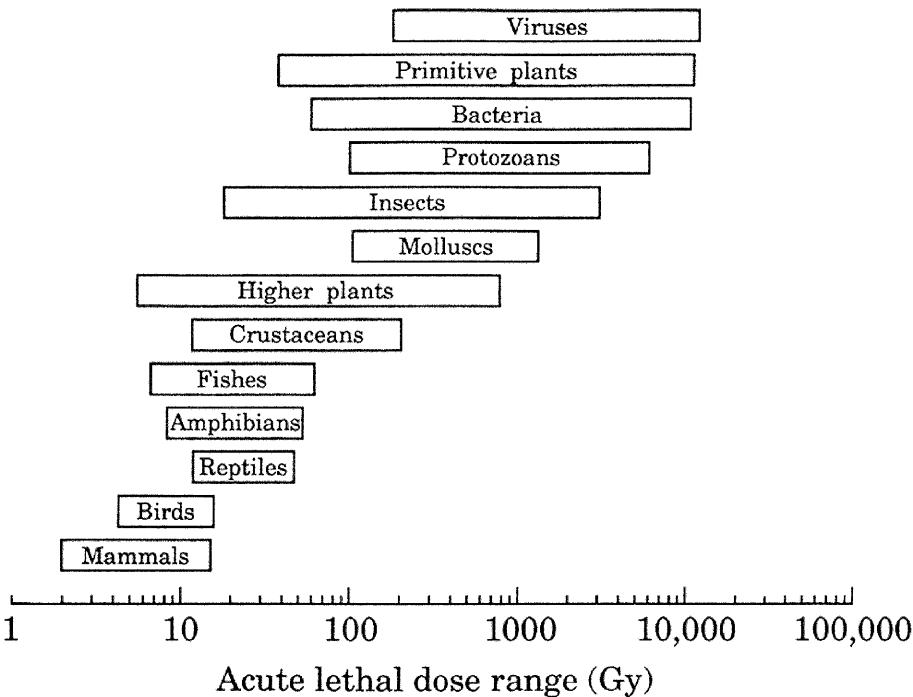


Figure 32.7 Acute radiation dose range fatal to 50% (30 days postexposure) of various taxonomic groups. (Modified from Whicker, F.W. and V. Schultz. 1982b. *Radioecology: Nuclear Energy and the Environment*. Vol. II. CRC Press LLC, Boca Raton, FL. 228 pp.; Hinton, T.G. and D.E. Scott. 1990. Radioecological techniques for herpetology, with an emphasis on freshwater turtles. Pages 267-287 in J.W. Gibbons (ed.). *Life History and Ecology of the Slider Turtle*. Smithsonian Instit. Press, Washington, D.C.)

dose rate at which harmful effects of chronic irradiation have been reliably observed in sensitive species is about 1 Gy/year; this value for acute radiation exposures is about 0.01 Gy (Rose 1992).

In general, the primitive organisms are the most radioresistant taxonomic groups, and the more advanced complex organisms — such as mammals — are the most radiosensitive (Figure 32.7). The early effects of exposure to ionizing radiation result primarily from cell death; cells that frequently undergo mitosis are the most radiosensitive, and cells that do not divide are the most radioresistant. Thus, embryos and fetuses are particularly susceptible to ionizing radiation, and very young animals are consistently more radiosensitive than adults (McLean 1973; Hobbs and McClellan 1986). In addition to the evolutionary position and cell mitotic index, many extrinsic and intrinsic factors modify the response of a living organism to a given dose of radiation. Abiotic variables include the type and energy of radiation, exposure rate, length of exposure, total exposure and absorbed dose, dose rate, spatial distribution of dose, season, temperature, day length, and environmental chemicals. Biotic variables include the species, type of cell or tissue, metabolism, sex, nutritional status, sensitizing or protective substances, competition, parasitism, and predation (Whicker and Schultz 1982b; Hobbs and McClellan 1986; UNSCEAR 1988; Kiefer 1990).

Radiosensitivity of cells is related directly to their reproductive capacity and indirectly to their degree of differentiation (Hobbs and McClellan 1986). Early adverse effects of exposure to ionizing radiation are due mainly to the killing of cells. Cell death may result from the loss of reproductive integrity, that is, when after irradiation a cell fails to pass through more than one or two mitoses. Reproductive death is important in rapidly dividing tissues such as bone marrow, skin, gut lining, and germinal epithelium. When the whole animal is exposed to a large dose of ionizing radiation,

some tissues are more prone to damage than others. Death rates of mammalian reproductive cells from ionizing radiations are modified by variations in the linear energy transfer of the radiation, the stage in the cell cycle, cell culture conditions, and sensitizing and protecting compounds (Barendsen 1990). The chemical form of the main stage of the acute radiation syndrome depends on the size and distribution of the absorbed dose. It is determined mainly by damage to blood platelets and other blood-forming organs at 4 to 5 Gy, to epithelial cells lining the small intestine at 5 to 30 Gy, and to brain damage at >30 Gy; death usually occurs within 48 h at >30 Gy (McLean 1973).

Cellular DNA is extremely sensitive to ionizing radiation, although other cell constituents may approach DNA in sensitivity (IAEA 1976; Billen 1990; Kiefer 1990; Lett 1990; Lucke-Huhle et al. 1990; Woloschak et al. 1990a; Shadley et al. 1991). Radiation-induced mutations are explainable on the basis of chromatin and DNA organization in cells and the biophysical properties of ionizing radiation (Sankaranarayanan 1991b). Based on studies of spontaneous and radiation-induced mutations in the mouse (Sankaranarayanan 1991a), more than 67% of the ionizing radiation-induced mutations are lethal, and almost all mutations, including enzyme activity variants, dominant visibles, and dominant skeletal mutations, are lethal. These findings are consistent with the view that most radiation-induced mutations in germ cells of mice are due to DNA deletions (Sankaranarayanan 1991a).

Experimental animal data clearly demonstrate that ionizing radiation at relatively high doses and delivered at high dose rates is mutagenic (Hobbs and McClellan 1986). However, radiation-induced genetic damage in the offspring of exposed parents has not been credibly established in any study with humans (Abrahamson 1990). In one human population — the ethnically isolated Swedish reindeer-breeding Lapps — elevated concentrations of fallout products have been ingested via the lichen–reindeer–human food chain since the 1950s. However, from 1961 to 1984, no increased incidence of genetic damage was evident in Lapps (Wiklund et al. 1990).

Radiation is carcinogenic. The frequency of death from cancer of the thyroid, breast, lung, esophagus, stomach, and bladder was higher in Japanese survivors of the atomic bomb than in nonexposed individuals, and carcinogenesis seems to be the primary latent effect of ionizing radiation. The minimal latent period of most cancers was <15 years and depended on an individual's age at exposure and site of cancer. The relation of radiation-induced cancers to low doses and the shape of the dose-response curve (linear or nonlinear), the existence of a threshold, and the influence of dose rate and exposure period have to be determined (Hobbs and McClellan 1986).

Radioactive materials that gain entry to the body, typically through ingestion or inhalation, exert effects that are governed by their physical and chemical characteristics which, in turn, influence their distribution and retention inside the body. The effective half-life includes both physical and biologic half-times. In addition, the type of radiation (i.e., α , β , γ) and its retention and distribution kinetics govern the radiation dose pattern. In general, the radiation dose from internal emitters is a function of the effective half-time, energy released in the tissue, initial amount of introduced radioactivity, and mass of the organ (Hobbs and McClellan 1986). Retention of radionuclides by living organisms is quite variable and modified by numerous biologic and abiotic variables. For example, ^{137}Cs retention in selected animals varies significantly with the body weight, diet, and metabolism of an organism ([Figure 32.8](#)). The time for 50% persistence of ^{137}Cs ranges between 30 and 430 days in ectotherms, and it was longer at lower temperatures and shortest in summer and under conditions of inadequate nutrition (Hinton and Scott 1990). In mammals, the ^{137}Cs biological half-life was between 6 and 43 days in rodents, dogs, mule deer, reindeer, and monkeys. In humans, this value ranged from 60 to 160 days. The biological half-life of ^{90}Sr ranges from 122 to 6000 days in ectotherms and is longer at colder temperatures and under laboratory conditions. In mammals and under conditions of chronic intake, the ^{90}Sr biological half-life was 533 days in rat, 750 days in humans, and at least 848 days in beagles (Hinton and Scott 1990).

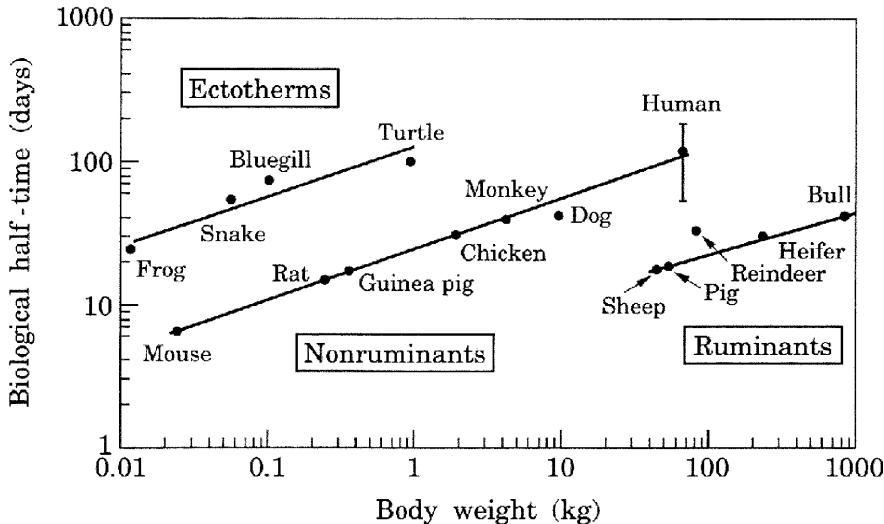


Figure 32.8 Relation between diet, metabolism, and body weight with half-time retention of longest-lived component of cesium-137. Data are shown for selected ruminant and nonruminant mammals (Richmond 1989) and ectotherms (Hinton and Scott 1990).

32.7.2 Terrestrial Plants and Invertebrates

Radiosensitive terrestrial plants exposed to single doses of ionizing radiation had reduced growth at 0.5 to 1.0 Gy and reduced survival at 3.0 to 4.1 Gy (Table 32.19). Chronic exposures of 0.2 to 0.65 Gy/day adversely affected sensitive forest ecosystems (Table 32.19). Chronic gamma irradiation of 131 Gy/year and higher of mixed forest ecosystems caused the disappearance of trees and shrubs and subsequent erosion of the soil (Poinsot-Balaguer et al. 1991). The radiation sensitivity of five plant communities suggested that pine forests were the most sensitive and that deciduous evergreen forests, tropical rainforests, herbaceous rock outcrop communities, and abandoned cropland were increasingly less sensitive (McCormick 1969). Neutrons were 3 to 4 times more effective than gamma rays in root growth inhibition (Witherspoon 1969). Altitude affects the response of vegetation to ionizing radiation. Peas (*Pisum sativum*) in gardens 2225 to 3750 m above mean sea level and exposed to 0, 5, 10, or 50 Gy had reduced growth from all treatments at increasing altitudes; however, a dose-response growth curve was evident only at <3049 m altitude (Osburn 1963). Seeds of tobacco (*Nicotiana tabacum*) exposed to cosmic rays aboard a spacecraft had a higher mutation rate than controls; effects occurred at total doses as low as 0.1 to 0.2 Gy (Gaubin et al. 1990), but this needs verification.

Sometimes, irradiation prevents the usual colonizing vegetation from becoming established (Poinsot-Balaguer et al. 1991). Germination and survival of shrub seedlings have been much slower at nuclear test sites than at non-disturbed sites (Romney et al. 1971). The return to its original state of the perennial shrub vegetation takes decades on a radiation-disturbed site, although native annual species and grasses have grown abundantly within 12 months. Transplanting of shrubs into radiation-disturbed areas has been largely unsuccessful because of intense browsing by rabbits and other small mammals (Romney et al. 1971). A nuclear detonation damages terrestrial vegetation by heat, blast, or radiation. Plant injury from thermal or ionizing radiation at an above-ground detonation site varied with stem rigidity and stability of the substratum, although radiation effects are ordinarily masked by damage from blasts. A typical nuclear detonation at the Nevada test site — an airburst of a 20- to 40-kiloton yield — denuded a zone of desert within a 0.8-km radius of shrub vegetation. Recovery at the Nevada site seemed complete within 4 years, suggesting little relation between

fatal injury, morphological aberration in vegetation, and ionizing radiation from nuclear detonations (Shields and Wells 1963). A northern Wisconsin forest experimentally subjected to a ^{137}Cs radiation source for 5 months showed several trends (Zavitkovski and Rudolph 1971):

1. Herbaceous and shrub species with a spreading form of growth are more radioresistant than upright forms.
2. Larger pine and oak trees are more radioresistant than smaller trees.
3. Perennial plants with shielded buds and vigorous asexual reproduction are relatively radioresistant.
4. Plants adapted to extreme habitats, such as old fields and granite rock outcrops, and plants typical of early successional stages are relatively radioresistant.
5. All plants are more radiosensitive during the growing season than during the dormant season.
6. Reproductive stages are always more radiosensitive than vegetative stages.

The recovery of vegetation in a tropical rainforest in Puerto Rico — after plants were deliberately subjected to lethal doses of gamma radiation — closely resembled secondary succession after other types of disturbances, such as mechanical stripping and treatment with the Picloram herbicide (Jordan 1969).

Table 32.19 Radiation Effects on Selected Terrestrial Plants

Species, Dose, and Other Variables	Effect	Reference ^a
Tropical rainforest tree, <i>Dacryodes excelsa</i> , 4–280 Gy per year	Growth stimulation	1
Deciduous evergreen forest		
40 Gy yearly	Minor effects	2
100 Gy yearly	Severe sublethal effects	2
350 Gy yearly	Lethal	2
Deciduous plants, 13 species		
4–15 Gy, single fast neutron doses	Shoot growth inhibited by >85%	3
60–85 Gy, single gamma radiation dose	Shoot growth inhibited by >85%	3
Forest ecosystem, northern Wisconsin, experimentally exposed to a ^{137}Cs point source for 5 months during a growing season. Distance from source (meters) and daily exposure (Gy)		
5 m, 15 Gy	No vegetation	4
5–10 m, 5–15 Gy	Lower plants present	4
10–15 m, 1.5 Gy	Resistant trees and shrubs present	4
10–15 m, 2.5–5.0 Gy	Some growth	4
20–30 m, 0.65–1.5 Gy	Resistant angiosperm trees	4
30–50 m, 0.2–0.65 Gy	Angiosperm trees present	4
50 m, 0.2 Gy	Original northern forest	4
Herbaceous rock outcrop community		
90 Gy yearly	Minor effects	2
400 Gy yearly	Severe sublethal effects	2
1000 Gy yearly	Lethal	2
Queensland mango, <i>Mangifera indica</i> , fruit irradiated postharvest, single dose, 250 or 750 Gy	At 250 Gy, skin and pulp color inhibited 50% due to irradiation-induced suppression of chlorophyll breakdown and reduction in carotenoid production. At 750 Gy, fruit respiration increased for 3–5 days, but no effect on fruit firmness	5
Mixed oak forest, southern France, experimentally irradiated for 18 years by a ^{137}Cs source at dose rates between 0.3 and 116 mGy/h, equivalent to a yearly rate between 2.6 and 1016 Gy	At 60–100 mGy/h (525–876 Gy yearly), all trees, shrubs, and litter were absent; low overall insect density; soil deficient in carbon, nitrogen, and water. At 15 mGy/h (131 Gy yearly), woody plants were present, but visibly abnormal	6

Table 32.19 (continued) Radiation Effects on Selected Terrestrial Plants

Species, Dose, and Other Variables	Effect	Reference^a
Tobacco, <i>Nicotiana tabacum</i> , 55 Gy per year	Growth stimulation	1
Pine forest		
1–10 Gy yearly	Minor effects	2
20 Gy yearly	Severe sublethal effects	2
30 Gy yearly	Lethal	2
Slash pine, <i>Pinus elliottii</i> , acute single exposure of 3 Gy	50% dead 1–4 months after exposure; no other deaths in 2 years	2
Sugar pine, <i>Pinus lambertiana</i> , acute single exposure of 4.1 Gy	LD50 (30 days postexposure)	1
Longleaf pine, <i>Pinus palustris</i>		
0.5 Gy, single dose	Growth inhibition	1
8 Gy, acute single exposure	50% of trees <5 years old died in 1–4 months; others survived for at least 2 years	2
>28 Gy, acute single exposure	Fatal to 50% of trees >5 years old in 1–4 months; no other deaths in 2 years	2
Winter wheat, <i>Triticum aestivum</i> , acute single exposure of 1.0 Gy	Growth inhibition	1
Tropical rainforest		
70 Gy yearly	Minor effects	2
350 Gy yearly	Severe sublethal effects	2
400 Gy yearly	Lethal	2
Vegetation, abandoned crop land		
50 Gy yearly	Minor effects	2
450 Gy yearly	Severe sublethal effects	2
1500 Gy yearly	Lethal	2
Bean, <i>Vicia faba</i> , 58–100 Gy per year	Growth stimulation	1

^a **1**, Rose 1992; **2**, McCormick 1969; **3**, Witherspoon 1969; **4**, Zavitokovski and Rudolph 1971; **5**, Boag et al. 1990; **6**, Poinsat-Balaguer et al. 1991.

Hormesis — the beneficial physiological stimulation by low doses of a potentially harmful agent — is documented for ionizing radiation and many species of terrestrial plants and invertebrates (Luckey 1980). Radiation hormesis in plants includes increased germination, growth, survival, and yield. Some species of terrestrial invertebrates had increased fecundity, growth, survival, disease resistance, and longevity after exposure to low sublethal doses of ionizing radiation (Luckey 1980). The growth and development of some terrestrial invertebrates are stimulated at comparatively high sublethal acute doses (i.e., 2 Gy in silkworm, *Bombyx mori*), but survival is reduced at 10 Gy. In all cases, younger stages were the most sensitive (Table 32.20). Cockroaches (*Blaberus giganteus*) adapted to the dark reportedly can visually detect radiation sources as low as 0.001 mGy (Rose 1992). However, the mechanisms are not understood.

Following the successful application of radiation to sterilize male screw-worm flies (*Cochliomyia hominivorax*), various insect pests became the target of similar techniques throughout the world (Al-Izzi et al. 1990). The technique has suppressed populations of the Mediterranean fruitfly (*Ceratitis capitata*), a major pest of fruits, although results have not been as spectacular as with the screw-worm fly (McInnes and Wong 1990). The pestiferous Caribbean fruitfly (*Anastrepha suspensa*), heavily parasitized by a beetle, became sterile after acute exposures to ionizing radiation, although beetles remained fecund. Mass rearing and inundative release of the radioresistant beetle parasite is now considered an option for control of the Caribbean fruitfly (Table 32.20).

Table 32.20 Radiation Effects on Selected Terrestrial Invertebrates

Species, Dose, and Other Variables	Effect	Reference ^a
Caribbean fruitfly, <i>Anastrepha suspensa</i> ; larvae, heavily parasitized by the hymenopteron <i>Diachasmimorpha longicaudata</i> , exposed to single acute exposures of 10–70 Gy	50% of control flies developed into adults vs. 25% at 10 Gy, and <1% at 30 Gy. At 40 Gy and higher, no adults were recovered but parasite development was the same at all doses	1
Silkworm, <i>Bombyx mori</i> ; eggs, acute single exposure of 2, 5, or 10 Gy	At 2 Gy, an average increase of 23% in larval mass, cocoon shell weight, and silk production; no stimulatory effect at 5 Gy; at 10 Gy, larval development inhibited	2
Mediterranean fruitfly, <i>Ceratitis capitata</i> ; females, acute single exposure of 150–155 Gy	Inhibited oviposition	3
Moth, <i>Ectomyelois ceratoniae</i> ; male pupae, age 3 or 5 days, acute single exposure of 50–500 Gy	Younger pupae were more sensitive than older pupae. Only 3% of pupae developed into adults at 500 Gy. At >250 Gy, progeny development reduced 50%. Normal fecundity at 100–250 Gy when mated with control females	4
Leafmining fly, <i>Liriomyza trifolii</i> ; immature stages, on artificially infested bean seedlings; acute single exposure of 25–2000 Gy	All dead at >750 Gy; 80% dead at 250 Gy; eggs and prepupae were the most sensitive stages; no phytotoxic effects	5

^a 1, Sivinski and Smittle 1990; 2, Yusifov et al. 1990; 3, McInnes and Wong 1990; 4, Al-Izzi et al. 1990; 5, Yathom et al. 1990.

32.7.3 Aquatic Organisms

Among aquatic organisms, it is generally acknowledged that primitive forms are more radioreistant than complex vertebrates and that older organisms are more resistant than the young (Donaldson and Foster 1957; Bonham and Welander 1963; Templeton et al. 1971) (Table 32.21). Developing eggs and young of some freshwater fish species are among the most sensitive tested aquatic organisms. Death was observed at acute doses of 0.3 to 0.6 Gy, and minor effects on physiology or metabolism were observed at chronic daily dose rates of 0.01 Gy (Bonham and Welander 1963; Templeton et al. 1971; IAEA 1976) (Table 32.21). Radiosensitivity correlated positively with the metabolic rate of the dividing cell, which accounts for the radioresistance of dormant eggs of aquatic invertebrates and the general sensitivity of early embryonic stages of all aquatic species (Donaldson and Foster 1957) (Table 32.21).

Adverse effects on the fecundity of sensitive aquatic vertebrates were detected at dose rates as low as 0.4 mGy/h; adverse effects on fecundity of resistant species were measured only at dose rates greater than 1.0 mGy/h. Thus, deleterious effects in populations of aquatic vertebrates are probably not detected until the 0.4 to 1.0-mGy/h dose rate is exceeded (NCRP 1991). Organisms, such as estuarine organisms, that are exposed to variable physicochemical conditions are more radioresistant than those in buffered environments, and this may be due to a higher degree of genetic polymorphism in species of fluctuating environment (IAEA 1976). Dose-effect estimates for the induction of chromosomal aberrations in polychaete annelid worms were dependent on cell stage at time of irradiation (S.L. Anderson et al. 1990). For reproduction, dose-effect estimates were dependent on potential for regeneration of gonadal tissue (S.L. Anderson et al. 1990).

Radiation causes dominant lethal mutations in the medaka (*Oryzias latipes*) (Shima and Shimada 1991). Mosquitofish (*Gambusia* spp.) from radionuclide-contaminated ponds in South Carolina differed from conspecifics in reference ponds, as judged by the frequency of DNA markers, and this is consistent with the hypothesis that these DNA markers may originate from genetic elements that provide a selective advantage in contaminated habitats (Theodorakis et al. 1998). Ionizing radiation at low-level chronic exposure reportedly has no deleterious genetic effects on aquatic populations because exposure is compensated by density-dependent responses in fecundity (IAEA 1976). However, this needs verification.

Table 32.21. Radiation Effects on Selected Aquatic Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Reference ^a
ALGAE		
Diatom, <i>Nitzchia closterium</i> ; acute single exposure of 100 Gy	Lethal	1
Euglena, <i>Euglena gracilis</i> ; acute single exposure of 550 Gy	Tolerated	1
Freshwater algae, 7 species, held in water containing 1110 Bq $^{226}\text{Ra}/\text{L}$ for as long as 14 days	After 24 h, 4 species (<i>Ankistrodesmus falcatus</i> , <i>Chlorella vulgaris</i> , <i>Coelastrum cambricum</i> , <i>Scenedesmus obliquus</i>) had decreased oxygen production by 22–37%; after 14 days, no effect on growth or protein content	2
Various species, single acute exposure 80–1000 Gy 250–6000 Gy	LD50, 45 days, postexposure LD100, 45 days after single exposure	3 3
PROTOZOANS		
Various species, acute single exposure 100–300 Gy 180–12,500 Gy	LD50, up to 40 days postexposure LD100, up to 40 days postexposure	3 3
COELENTERATES		
Sea anemone, <i>Anthopleura xanthogrammica</i> ; 0.2 Gy, acute single exposure	Tentacles withdrawn	1
Jellyfish, <i>Aurelia aurita</i> ; acute single exposure 50–150 Gy 50–400 Gy	No deaths in 60 days Dose-dependent increase in developmental abnormalities and abnormal budding rates and patterns	4 4
100 Gy	Metamorphosis and budding inhibited; reduction in pulsation rate	4
150 Gy	Inhibited reproduction	4
200 Gy	60% died in 60 days	4
400 Gy	90% died in 30 days	4
MOLLUSCS		
Water snail, <i>Physa heterostropha</i> ; exposure of 2.4–5.5 Gy daily for 1 year	Increased growth rate	1
Various species, acute single exposure 50–200 Gy 100–500 Gy	LD50, up to 2 years postexposure LD100, up to 2 years postexposure	3 3
CRUSTACEANS		
Brine shrimp, <i>Artemia salina</i> ; acute single exposure 0.004 Gy 0.1–9 Gy	No adverse effects on development of cysts Decreased development when exposed as cysts	5 5
4.5–9 Gy	LD50, nauplii, 20–25 days postexposure	6
130 Gy	LD50, adults, 25 days after exposure	6
486–2084 Gy	Dose-dependent delay in development of eggs	7
3000 Gy	LD50, cysts	5
Blue crab, <i>Callinectes sapidus</i> ; continuous exposure to 0.76 Gy daily for 1 year	Increased growth rate	1

Table 32.21. (continued) Radiation Effects on Selected Aquatic Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Reference ^a
Shore crab, <i>Carcinus maenas</i>		
Americium-241, dose unknown	After 8 days, bioconcentration factors (BCF) were 145 in whole crab, 960 in gills, and 240 in exoskeleton; 50% elimination in 45 days	8
Plutonium-237, dose unknown	After 8 days, BCF values were 75 in whole crab, 340 in gills, and 70 in exoskeleton; 50% elimination in 55 days	8
Daphnid, <i>Daphnia pulex</i> ; daily exposure to 8.2–17.8 Gy for 1 year	Increased growth rate	1
Various species, single acute exposure		
5–900 Gy	LD50, up to 80 days postexposure	3
50–800 Gy	LD100, up to 80 days postexposure	3
ANNELIDS		
Polychaete, <i>Neanthes arenaceodentata</i> ; acute single exposure		
1–4 Gy	Adverse effects on reproduction	9
2–100 Gy	Significant increase in frequency of chromosomal aberrations	9
>100 Gy	Decreased life span	9
>500 Gy	Death	9
FISH		
Common carp, <i>Cyprinus carpio</i>		
Adults, 3 Gy, acute single exposure	No effect on growth	1
Fertilized eggs, exposed through hatch		
144 million Bq ²³⁸ Pu/L	Increased abnormalities	10
277 million Bq ²³⁸ Pu/L	Decreased hatch	10
44 million Bq ²³² U/L	Increased abnormalities	10
815 million Bq ²³² U/L	Decreased hatch	10
Anchovy, <i>Engraulis</i> sp.; fertilized eggs, ⁹⁰ Sr– ⁹⁰ Y, continuous exposure		
7.4 Bq/L	Increased developmental abnormalities	10
740 Bq/L	Decreased hatch, retarded growth rate	10
Fish, various species, acute single exposure		
6–30 Gy	LD50, up to 460 days postexposure	3
3.7–200 Gy	LD100, up to 460 days postexposure	3
Pinfish, <i>Lagodon rhomboides</i> ; exposure to 0.197 Gy daily for 1 year	Increased growth rate	1
Bluegill, <i>Lepomis macrochirus</i> ; acute single exposure of 10, 20, or 30 Gy		
Marine teleosts, 6 species, 10–55 Gy, acute single exposure	At 20 and 30 Gy, serum proteins were reduced more than 50% within 24 h; damage to the GI capillary system and injury to the gastroepithelium accounted for the excessive protein loss	12
Silver salmon, <i>Oncorhynchus kisutch</i> ; acute single exposure	LD50	11
Early embryonic stages, 0.3–0.6 Gy	LD50 at hatch	13
Later embryonic stages, 9.2–18.7 Gy	LD50 at hatch	13
Rainbow trout, <i>Oncorhynchus mykiss</i>		
Embryos, acute single exposure		
0.6 Gy, 1-cell stage	LD50 by end of yolk resorption	10
0.8 Gy, 1-cell stage	LD50 at hatch	3
3.1 Gy, 32-cell stage	LD50 by end of yolk resorption	10
4.1 Gy, early eyed stage	LD50 by end of yolk resorption	3

Table 32.21. (continued) Radiation Effects on Selected Aquatic Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Reference ^a
4.6 Gy, 32-cell stage	LD50 by hatch	3
9.0 Gy, late eyed stage	LD50 by end of yolk resorption	3
Embryos held in water containing 370 million Bq/L of ³ H from immediately after fertilization through hatching	No effect on hatching abnormalities	10
Embryos held in water containing 37 million Bq/L of ³ H from 6 h after fertilization through hatch	Suppressed immune response of fry	10
Immature, single acute exposure of 0.2 Gy	Growth stimulation	1
Juveniles exposed for 27 days to radioneptunium isotopes and analyzed 2–15 days postexposure	Maximum BCF values were 8.7 for whole fish, 1.1 for skin, and 0.34 for muscle	14
Yearlings, force-fed 185,000, 1.85 million, or 18.5 million Bq ⁹⁰ Sr– ⁹⁰ Y/kg BW daily for 21 weeks	At highest dose, adverse effects on growth (week 12) and survival (week 15); survivors had leucopenia and gut histopathology, and concentrations of 9.2 billion Bq/kg FW in bone and 9.99 million Bq/kg FW in muscle. Residues in the 1.85-million group were 1.04 billion Bq/kg in bone and 2.96 million Bq/kg in muscle. For the 185,000 group, these values were 77.7 million Bq/kg in bone and 74,000 Bq/kg in muscle	11, 15
Yearlings force-fed 370,000, 3.7 million, or 37 million Bq ⁶⁵ Zn/kg BW daily for 17 weeks, or 370 million Bq ⁶⁵ Zn/kg BW daily for 10 weeks	Adverse effects on growth, survival, or gut histology at any dose; leucopenia evident at week 10 at the highest dose. Residues, in Bq/kg FW, in the 37 million group at 17 weeks were 148 million in bone and 12.9 million in muscle	11, 15
Yearlings force-fed 222,000, 2.2 million, or 22.2 million Bq ³² P/kg BW daily for as long as 25 weeks	At highest dose tested, adverse effects on growth, survival, and gut histology between day 17 and 77. In the intermediate 2.2-million group, adverse effects on growth at 17 weeks; residues (Bq/kg FW) were 66.6 million in bone and 8.5 million in muscle. The 220,000 group had no adverse effects in 25 weeks on growth, survival, or tissue alterations	11
Gametes of adults, single acute exposure of 0.5–1.0 Gy	50% reduction in fecundity	3
Adults, single acute exposure of 15 Gy	LD50	3
Chinook salmon, <i>Oncorhynchus tshawytscha</i>		
0.0004 Gy/h, eggs, 81-day exposure, total dose of 0.78 Gy	Significant adverse effects on survival and development	21
0.005 Gy daily, continuous exposure from egg fertilization through yolk sac absorption; total dose of 0.35 Gy	No adverse effects on growth and survival or on numbers of returning adults after seaward migration	22
0.028 Gy daily, continuous exposure from egg fertilization through yolk sac absorption; total dose of 1.99 Gy	No adverse effects observed prior to seaward migration	22
0.2 Gy, single acute exposure	Growth increase	1
10 Gy, eyed eggs, single acute exposure	LD50	3
12.5–25 Gy, fingerlings, single acute exposure	LD50	3
Medaka, <i>Oryzias latipes</i> ; adult males receiving single acute exposure of 0.64, 4.75, or 9.5 Gy	Dose-dependent increase in total mutations in sperm, spermatids, and spermatogonia	16
Sea lamprey, <i>Petromyzon marinus</i> ; males captured during spawning run, single acute exposure		
20 Gy	LD50, 45 days postexposure; survivors sterile	17
30 Gy	All died before spawning	17

Table 32.21. (continued) Radiation Effects on Selected Aquatic Organisms

Taxonomic Group, Organism, Dose, and Other Variables	Effect	Reference ^a
Fathead minnow, <i>Pimephales promelas</i> ; developing eggs, continuous exposure 4440 Bq ^{144}Ce – ^{144}Pr /L 9.6 million Bq ^{238}Pu /L 48.1 million Bq ^{238}Pu /L 7.4 million Bq ^{232}U /L 18.5 million Bq ^{232}U /L	No effect on embryonic development or hatch Increased abnormalities Decreased hatch Increased abnormalities Decreased hatch Increased mortality of embryos and fry	10 10 10 10 10 10
Atlantic salmon, <i>Salmo salar</i> ; fertilized eggs, continuous immersion in 92.5 Bq ^{137}Cs /L or 185 Bq ^{90}Sr /L	Increased mortality of embryos and fry	10
Brown trout, <i>Salmo trutta</i> Fertilized eggs continuously immersed in water containing 3.7 million Bq/L of ^{90}Sr – ^{90}Y through hatch Juveniles held in water containing 30,000 Bq ^{110m}Ag /L for 57 days, then transferred to uncontaminated media for 28 days	No effect on hatch or developmental abnormalities At day 57, whole trout contained 105,000 Bq ^{110m}Ag /kg FW; about 70% was in liver. No detectable radioactivity after depuration for 28 days	10 18
Juveniles fed diet containing 3,343,000 Bq ^{110m}Ag /kg for 1 week (5 times weekly), then 269,000–296,000 Bq ^{110m}Ag /kg diet between weeks 2 and 5. Depuration for 28 days	At end of exposure, whole trout contained 27,400 Bq ^{110m}Ag /kg, equivalent to 11.7% of ingested radioactivity; liver accounted for 63%. No detectable radioactivity after depuration for 28 days	19
INTEGRATED STUDY		
Artificial stream simulating outfall from Czechoslovakian nuclear power plant, 28-day exposure, ^{90}Sr Water Sediments Alga, <i>Cladophora glomerata</i> Snail, <i>Planorbis corneus</i> , shell vs. soft parts Common carp, <i>Cyprinus carpio</i> Bone Muscle Scales Uncontaminated site Water Common carp, internal organs vs. scales	894 Bq/L 1589–2288 Bq/kg FW Max. 22,106 Bq/kg FW 760,588 Bq/kg FW vs. 27,468 Bq/kg FW 29,144 Bq/kg FW 580 Bq/kg FW 13,101 Bq/kg FW 0.002–0.005 Bq/L 0.1–0.5 Bq/kg FW vs. 1.5–9.3 Bq/kg FW	20 20 20 20 20 20 20 20 20

^a 1, Rose 1992; 2, Havlik and Robertson 1971; 3, Donaldson and Foster 1957; 4, Prokopchak et al. 1990; 5, Gaubin et al. 1990; 6, Engel and Davis 1976; 7, Su et al. 1990; 8, Guary and Fowler 1990; 9, S. L. Anderson et al. 1990; 10, Whicker and Schultz 1982b; 11, Templeton et al. 1971; 12, Ulrickson 1971; 13, Bonham and Welander 1963; 14, Poston et al. 1990; 15, IAEA 1976; 16, Shima and Shimada 1991; 17, Hanson 1990; 18, Garnier et al. 1990; 19, Garnier and Baudin 1990; 20, Stanek et al. 1990; 21, National Council on Radiation Protection and Measurements (NCRP) 1991; 22, Donaldson and Bonham 1970.

Accumulation of radionuclides from water by aquatic organisms varies substantially with ecosystem, radionuclide, and trophic level (Tables 32.22, 32.23, 32.24, respectively); with numerous biological, chemical, and physical variables; and with proximity to sources of radiation (Bowen et al. 1971; Lowman et al. 1971; Templeton et al. 1971; Mo and Lowman 1976; Shure and Gottschalk 1976; Whicker and Schultz 1982b; Becker 1990; Poston et al. 1990; Joshi 1991). Accumulated radionuclides within embryos of the scorpionfish (*Scorpaena porcus*) and turbot (*Scophthalmus maeoticus*) increased the frequency of nuclear disruptions in these species; ^{90}Sr – ^{90}Y and ^{91}Y had greater cytogenetic effects than other radionuclides tested (Polikarpov 1973). In the absence of site-specific data, the U.S. Nuclear Regulatory Commission recommends the use of

Table 32.22 Concentration Factors for Cesium-137 and Strontium-90 in Aquatic Organisms

Radionuclide and Ecosystem	Molluscs, Whole	Crustaceans, Whole	Fish, Muscle
CESIUM-137			
Freshwater	600	4000	3000
Marine	8	23	15
STRONTIUM-90			
Freshwater	600	200	200
Marine	1	3	0.1

Note: Concentration factors given in Bq per gram fresh weight sample/Bq per mL medium

Data from Whicker, F.W. and V. Schultz. 1982a. *Radioecology: Nuclear Energy and the Environment*. Vol. I. CRC Press LLC, Boca Raton, FL. 212 pp.

Table 32.23 Approximate Maximum Concentration Factors for Selected Transuranics in Marine Sediments, Macroalgae, and Fish

Transuranic Nuclide	Concentration Factor		
	Sediments	Macroalgae	Fish
Neptunium	1000	5000	10
Plutonium	100,000	2000	40
Americium, curium, berkelium, californium	2,000,000	8000	50

Note: Concentration factors given in Bq per gram fresh weight sample/Bq per mL water.

Data from Morse, J.W. and G.R. Choppin. 1991. The chemistry of transuranic elements in natural waters. *Rev. Aquat. Sci.* 4:1-22.

listed concentration ratios — the concentration of the element in the organism (in mg/kg FW) divided by the concentration in the medium (in mg/L) — for various elements in marine and freshwater fishes and invertebrates (Whicker and Schultz 1982b). However, the Commission clearly indicates that these values are only approximations.

After more than 400 atmospheric nuclear test explosions and the fallout from Chernobyl, ¹³⁷Cs became the most frequently released nuclear fission product throughout central Europe (Jandl et al. 1991). Cesium behaves like potassium: it has a ubiquitous distribution inside the body, especially in soft tissues. In the gastropod *Helix pomatia*, the biological half-time after a single 24-h dietary dose was 2.5 days for the short-lived component and 28.5 days for the long-lived component (Jandl et al. 1991). Concentration factors (CF) of ¹³⁷Cs in muscle (ratio of Bq/kg FW muscle:Bq/L filtered seawater) of marine fishes from the North Sea between 1978 and 1985 ranged from a low of 39 in the plaice (*Pleuronectes platessa*) to a high of 150 in the whiting (*Merlangius merlangius*); CF values were intermediate in the haddock (*Melanogrammus aeglefinus*; CF of 58) and Atlantic cod (*Gadus morhua*; CF of 92). These data seem to support the use of a CF of 100 for ¹³⁷Cs in muscle of marine fishes in generalized assessments, although some adjustment is necessary when particular species, such as whiting, form the bulk of a consumer's diet (Steele 1990). In the Great Lakes, the maximum CF values of ¹³⁷Cs range from 1000 to 10,000 in algae, amphipods, and fishes, and from 100 to 1000 in zooplankton (Joshi 1991). Maximum concentration factors of ¹³⁷Cs in a contaminated creek in South Carolina were 4243 in suspended particulates, 938 in detritus, 4496 in algae and macrophytes, 997 in omnivores, 1292 in primary carnivores, and 1334 to 2595 in top carnivores, such as redbreast sunfish (*Lepomis auritus*), largemouth bass (*Micropterus salmoides*), and water

Table 32.24 Maximum Concentration Factors Reported for Selected Elements in Marine Organisms at Various Trophic Levels

Element	Algae	Grazers	Predators
Ag	1000	20,000	3000
Cd	6000	2,000,000	10,000
Ce	4500	300	12
Co	1000	10,000	50,000
Cr	600	300,000	3900
Cs	50	15	10
Fe	70,000	300,000	30,000
I	7000	70	10
Mo	200	175	200
Mn	20,000	60,000	100,000
Ni	1000	10,000	80
Pb	3,000,000	2,000,000	200,000
Ru	1000	16	10
Sr	90	85	5
Ti	30,000	20,000	3000
Zn	3000	100,000	20,000
Zr	20,000	30,000	40,000

Note: Concentration factors given in Bq per gram fresh weight tissue/Bq per mL seawater.

Data from Bowen, V.T., J.S. Olsen, C.L. Osterberg, and J. Ravera. 1971. Ecological interactions of marine radioactivity. Pages 200-222 in National Academy of Sciences. *Radioactivity in the Marine Environment*. Natl. Acad. Sci., Panel on Radioactivity in the Marine Environment. Washington, D.C.

snakes (*Natrix spp.*) (Shure and Gottschalk 1976). Cesium uptake by oligochaete worms (*Limnodrilus hoffmeisteri*) is inhibited by low temperatures, potassium concentrations >1 mg/L, and the presence of bacteria (*Escherichia coli*) that compete with the worms for ¹³⁷Cs (Steger and Goodnight 1976).

Atmospheric fallout from nuclear testing is the main pathway by which transuranic nuclides, such as Np, Pu, Cm, and Am, enter the aquatic environment (Guary and Fowler 1990). In general, transuranics are strongly partitioned onto particulates. Living organisms are less enriched than particulate matter by as much as 1000 times, and concentration factors by marine biota are similar for transuranics beyond neptunium (Morse and Choppin 1991). The uptake of ²⁴¹Am and ²⁴⁴Cm from contaminated sediments by a freshwater amphipod (*Hyalella sp.*) and oligochaete (*Tubifex sp.*) is reported, presumably by way of adsorption, and this is considered the principal uptake pathway by benthic organisms in freshwater and marine ecosystems (Sibley and Stohr 1990). Transuranics ingested with food by various crabs were initially excreted with feces; the remaining transuranics entered a soluble radionuclide pool within the animal that was slowly excreted. Decapod crustaceans assimilate and retain 10 to 40% of the transuranic nuclides in their diets. Initially, absorbed radionuclides accumulate in the hepatopancreas but are then translocated to other tissues, particularly to tissues of the exoskeleton. Accordingly, molting strongly influences elimination in crustaceans (Guary and Fowler 1990). Neptunium isotopes have a higher potential for environmental transport in aquatic systems and groundwater than other actinides tested. Laboratory studies with ²³⁵Np and ²³⁷Np, for example, show concentration factors between 275 and 973 in a green alga (*Selenastrum capricornutum*); between 32 and 72 in a daphnid (*Daphnia magna*); 2 in an amphipod (*Gammarus sp.*); and in juvenile rainbow trout, 8.7 in carcass, 1.1 in skin, and 0.3 in muscle over a 96-h period (Poston et al. 1990). When the much higher biological effectiveness of alpha vs. beta or gamma radiation is considered, plutonium isotopes may contribute more artificial radiation dose equivalent to marine invertebrates than either ⁹⁰Sr or ¹³⁷Cs. Concentration factors of

^{239}Pu and marine organisms ranged from 300 to 100,000 in seaweeds, 250 to 690 in molluscs, 760 to 1020 in echinoderms, 2100 in sponges, and as much as 4100 in worms (Noshkin et al. 1971). Concentration factors of $^{239+240}\text{Pu}$ in Lake Michigan ranged between 1 and 10 in predatory salmonids, between 10 and 300 in nonpredatory fish, between 900 and 1200 in amphipods and shrimp, about 200 in zooplankton, and about 6000 in algae (Joshi 1991).

Iodine-131 (half-life of 8 days) may cause deleterious effects in marine teleosts — although ^{131}I concentrations in tissues were not detectable. In one case, coral reef fishes from Eniwetok Atoll collected as long as 8 months after a nuclear explosion had thyroid necroalteration, suggesting a thyrotoxic level of ^{131}I in the environment. Laboratory studies with teleosts injected with ^{131}I showed similar signs of histopathology. Herbivorous fishes and species that habitually consumed bivalve molluscs were the most severely affected (Gorbman and James 1963).

Strontrium-90 is an anthropogenic radionuclide in liquid effluents from some European nuclear power plants. Algae and sediments are the most important accumulators of ^{90}Sr , although levels in gastropods and fish bone and scales are also elevated, suggesting piscine uptake through gills and skin (Stanek et al. 1990). Fish tend to accumulate calcium more than strontium, even when Ca levels in food and water were low. Gill tissue was the most and gut the least discriminatory against Sr. Strontium assimilation was linked to the Sr:Ca ratio in food and water, amounts of Ca derived from each source, and biological discrimination against Sr relative to Ca (Ophel and Judd 1976). The ability of organisms to discriminate between strontium radioisotopes is also documented. In one case, ^{85}Sr was taken up rapidly in bluegill (*Lepomis macrochirus*) muscle and blood and quickly exchanged with stable strontium. However, ^{90}Sr was retained longer than 35 days in these tissues (Reed and Nelson 1969).

Ruthenium-106 appeared in clams from North Carolina within 2 weeks after the third and fifth Chinese nuclear tests in 1965 to 1967. Its retention was resolved into two rate functions with apparent effective half-lives of 40 days and 7 days (Wolfe and Jennings 1971). Iron-55 is a neutron-activation product produced in large quantities from ferrous materials in the immediate vicinity of a nuclear detonation. Concentration factors of ^{55}Fe and plankton in Bikini Atoll ranged from 15,000 to 25,000 (Schell 1976). Silver-110m has been detected in marine organisms after atmospheric weapon tests in the Pacific, in fishes from the Rhone River after the Chernobyl accident, and in fishes near reactor-waste outfalls (Garnier et al. 1990). Silver-110m is depurated rapidly by brown trout (*Salmo trutta*) after high intake exposures via the water or diet (Garnier et al. 1990; Garnier and Baudin 1990). Radiotungsten is produced in quantity by certain types of nuclear devices. In one case, tungsten was the most abundant radionuclide in the environment, accounting for about 90% of the total fallout activity 167 days after the detonation (Reed and Martinedes 1971). Tungsten-181 tended to concentrate in the hepatopancreas and gut of the crayfish (*Cambarus longulus longirostris*). Whole-body elimination consisted of two components: a rapid 1-day component and a second slower component with a biological half-time of 12.2 days (Reed and Martinedes 1971). Benthic organisms take up limited amounts of heavy metals and radionuclides associated with bottom sediments and recycle them to benthic and pelagic food webs. For example, polychaete worms (*Nereis diversicolor*) in contact with ^{65}Zn -contaminated sediments for 5 days lost 50% of accumulated ^{65}Zn in about 19 days on transfer to uncontaminated sediments (Renfro and Benayoun 1976).

32.7.4 Amphibians and Reptiles

Radiation adversely affects limb regeneration of amphibians, alters DNA metabolism, and increases the frequency of chromosomal aberrations and liver lesions (Table 32.25). In some species of amphibians and reptiles, as in many mammals, mortality rates after acute exposure to radiation do not stabilize within 30 days — effectively invalidating the conventional LD50 (30-day postexposure) value. In the rough-skinned newt (*Taricha granulosa*), for example, the minimal LD50 dose at 200 days after irradiation was 2.5 Gy, compared with 350 Gy at 30 days (Willis and

Table 32.25 Radiation Effects on Selected Amphibians and Reptiles

Species, Dose, and Other Variables	Effect	Reference ^a
Leopard lizard, <i>Crotaphytus wislizenii</i> ; chronic field exposure of 0.04–0.06 Gy daily (4–5 Sv yearly) for 3–6 years	No female reproduction in years 3 and 4. In year 5, males were sterile and females had complete regression of ovaries, undeveloped oviductal walls, and hypertrophied fat bodies. In year 6, 75% of females lacked ovaries and 25% had normal ovaries with signs of recent egg deposition; males appeared normal	1
Mud puppy, <i>Necturus maculosus</i> ; 1.1 Gy, single acute exposure	LD50, 30 days postexposure	2
Salamander, <i>Necturus</i> sp.; 0.8 Gy, single acute exposure	LD50, 200 days postexposure	3
Newt, <i>Notophthalmus viridescens</i> ; adults, single acute exposure of 20 Gy, one limb shielded; or 22 Gy, whole body, no limbs shielded	Forelimb regeneration completely suppressed when limbs to be amputated were irradiated directly. Irradiated limbs had severe and protracted inflammation, with total resorption of the affected limbs in 85% of the cases. Shielded limbs subsequently amputated had delays — but not suppression — in rate of forelimb regeneration and skin graft rejection	4
Frog, <i>Rana</i> sp., single acute exposure 7.0–7.2 Gy	LD50, 730 days after exposure	3
7.8 Gy	LD50, 150 days after exposure	3
Snakes, 2 species, 3–4 Gy, single acute exposure	LD50, 90 days after exposure	3
Rough-skinned newt, <i>Taricha granulosa</i> ; single acute exposure 2.5 Gy	LD50, 200 days after exposure; skin lesions and depigmentation	5
>6.5 Gy	Progressive anemia over 6-week postirradiation period; reduction in erythrocyte numbers and weight of spleen	5
80 Gy	LD50, 100 days after exposure	5
350 Gy	LD50, 30 days after exposure	5
Turtles, 4 species, <8–15 Sv, single acute exposure	LD50, 120 days postexposure	3
Slider turtle, <i>Trachemys scripta</i> ; inhabiting a radioactive reservoir, in Aiken, South Carolina. Radionuclide concentrations, in Bq/kg, whole-body fresh weight, (FW) were 1002 for 137Cs and 550 for 90Sr. For controls, these values were 2 for 137Cs and 260 for 90Sr	Contaminated turtles, when compared with controls, had greater variation in DNA content of red blood cell nuclei, suggesting genetic damage. The biological half-life of 137Cs in soft tissues was 64 days; for 90Sr in shell and bone, it was 364 days	6
Spiny tailed lizard, <i>Uromastix hardwickii</i> ; single acute exposure, held for up to 14 days after irradiation 2.25 Gy	No lesions in liver	7
4.5 Gy	No liver lesions, but swollen hepatocytes, increases in bile pigmentation, and altered cytoplasmic degranulation; normal after 14 days	7
9.0 Gy	Some liver lesions, but all livers normal 14 days postexposure	7
Lizard, <i>Uta</i> sp.; 10–22 Gy, single acute exposure	LD50, 30 days postexposure	3

^a 1, Turner et al. 1971; 2, Rose 1992; 3, Hinton and Scott 1990; 4, Sicard and Lombard 1990; 5, Willis and Lappenbusch 1976; 6, Lamb et al. 1991; 7, Gupta and Umadevi 1990.

Lappenbusch 1976). Low temperatures seem to prolong the survival of amphibians exposed to ionizing radiation. The survival was greater of leopard frogs (*Rana pipiens*) held at low temperatures

(5 to 6°C) after total-body exposure to lethal doses of X-rays than of frogs held at higher temperatures. Prolonged survival at low temperatures was due to a prolongation of the latent period rather than to appreciable recovery (Patt and Swift 1948).

The South African clawed frog (*Xenopus laevis*) has been suggested as a bioindicator of radioactive contamination because of the greater radiosensitivity of amphibians than fishes, the ease of maintaining *Xenopus* in the laboratory, and the sensitivity of the *Xenopus* liver to radioactive contamination — including ⁴⁵Ca, which does not accumulate in the liver (Giannetti et al. 1990). *Xenopus* oocytes exposed to X-rays showed single- and double-strand breaks in DNA and oxidative-type base lesions at a frequency between 85 and 95%. *Xenopus* oocytes repaired X-ray induced damage in plasmid DNA; however, some X-ray lesions can stimulate homologous recombination in these cells (Sweigert and Carroll 1990). Slider turtles (*Trachemys scripta*) in a radioactive reservoir show evidence of genetic damage, and this was attributed to long-term exposure to low concentrations of long-lived radionuclides, including ¹³⁷Cs and ⁹⁰Sr (Lamb et al. 1991). Natural populations of toads (*Bufo valliceps*) reportedly can survive genetically damaging doses of ionizing radiation without impairment of population integrity (Whicker and Schultz 1982b). Toads and many other species share a high attrition on the large numbers of young produced each generation, and this provides an agency for intensive selection. Also under this regime, recessive mutants are eliminated as they are exposed through inbreeding in future generations (Whicker and Schultz 1982b). Sterility in field collections of the leopard lizard (*Crotaphytus wislizenii*) and the whip-tail lizard (*Cnemidophorus tigris*) was reported after long-term exposure of 3 to 5 years to various doses of gamma radiation (i.e., 4 to 5 Sv annually in *Crotaphytus* and 2.0 to 2.5 Sv annually in *Cnemidophorus*) (Turner et al. 1971). However, a third species of lizard in the study area (side-blotched uta, *Uta stansburiana*) reproduced normally (Turner et al. 1971).

The retention of selected isotopes by amphibians and reptiles is quite variable. For example, whole-body retention of ¹³¹I after intraperitoneal injection in the rough-skinned newt showed two distinct loss components with biological half-lives of 2 and 210 days. The slower component accounted for 26% of the administered activity; thyroid contained 78% of the total ¹³¹I and clearly accounted for the long-term component (Willis and Valett 1971). However, similar studies with ¹³¹I and the leopard frog showed three distinct loss components (0.1 day; 1.4 to 2.9 days; 44.3 to 69.4 days); loss of each component was greater at 25°C than at 10°C. Also, the fast component probably represented plasma clearance through urinary excretion (Willis and Valett 1971).

32.7.5 Birds

Among birds, as in most other tested species, there is a direct relation between dose and mortality at single high doses of ionizing radiations (Whicker and Schultz 1982b; [Table 32.26](#)). For any given total dose, the survival of a bird is higher if the dose is delivered at a lower rate or over a longer period of time and suggests that biological repair processes compensate for radiation-induced cellular and tissue damage over a prolonged period or at a comparatively low dose rate (Brisbin 1991). Nestling bluebirds (*Sialia sialis*) were more resistant to gamma radiation than young domestic chickens (*Gallus* sp.), and nestling great crested flycatchers (*Myiarchus crinitus*) were more sensitive than bluebirds (Willard 1963). Passerine nestlings are more resistant to radiation stress than adults of larger-bodied precocial species (Brisbin 1991). But the comparatively resistant passerine nestlings frequently show a disproportional disturbance in radiation-induced growth, resulting in a reduction of overall survival. For example, if feather growth is stunted, death results from the inability to escape predators because of impaired flight (Brisbin 1991).

Free-living, resident bird populations in the vicinity of sites contaminated with low levels of ionizing radiations generally have negligible genotoxic effects (George et al. 1991). However, 14% of mallards (*Anas platyrhynchos*) from an abandoned South Carolina reactor cooling reservoir heavily contaminated with ¹³⁷Cs (mallards contained an average of 2520 Bq ¹³⁷Cs/kg whole-body FW) had abnormal chromosome numbers and unusual variability in the concentration of erythrocyte

DNA (George et al. 1991). Contaminated waterfowl rapidly eliminate accumulated radionuclides, suggesting inconsequential long-term damage to the birds and little hazard to human consumers of waterfowl flesh (Halford et al. 1983). This conclusion was from a study wherein mallards were held for 68 to 145 days on liquid radioactive waste ponds in southeastern Idaho and then transferred to an uncontaminated environment for 51 days. The biological half-life in mallards under these conditions was 10 days for ^{131}I and ^{134}Cs , 11 days for ^{137}Cs , 22 days for ^{140}Ba , 26 days for ^{75}Se , 32 days for ^{58}Co , 67 days for ^{60}Co and ^{65}Zn , and 86 days for ^{51}Cr . At the time of removal from the waste ponds, radionuclide concentrations were highest in gut, then feather, liver, and muscle, in that order. After 51 days in a radionuclide-free environment, decreasing order of radionuclide concentrations was feather, liver, muscle, and gut (Halford et al. 1983).

Zinc-65 in trace amounts is accumulated by migratory waterfowl in the Pacific flyway of North America from ^{65}Zn discharged into the Columbia River from water-cooled reactors at Hanford, Washington (Curnow 1971). The retention of ^{65}Zn in mallards was affected by sex and season, but not by the age of the duck. Biological retention of ^{65}Zn was greater in males (Tb 1/2 of 34.7 days) than in females (29.8 days), and greater in October (38 days) than in the spring (32 days). Egg production accounted for the elimination of 25% of the ^{65}Zn and feather molt of 2% to 8% (Curnow 1971). Retention of ^{60}Co and ^{137}Cs — but not ^{109}Cd — in the common bobwhite (*Colinus virginianus*) after either acute or chronic exposure to contaminated food is similar. The biological half-life in bobwhites during exposure for 21 days was 8 days of ^{109}Cd , 11 days of ^{137}Cs , and 13 days of ^{60}Co . When radioisotopes were administered during a single 4-h feeding, Tb 1/2 values were 3 days of ^{109}Cd , 10 days of ^{137}Cs , and 15 days of ^{60}Co (Anderson et al. 1976). The biological half-life of ^{137}Cs in avian tissues is about 6.0 days in domestic chickens (Andersson et al. 1990); 6.7 days in the bluejay (*Cyanocitta cristata*) (Levy et al. 1976); 5.6 days in the American wood duck (*Aix sponsa*); and 11.7 days in mallards (Cadwell et al. 1979). Domestic poultry, when compared with mammals, seem to accumulate a higher fraction of the daily ingested $^{137}\text{Cs}/\text{kg}$ muscle, but levels were effectively reduced by feeding an uncontaminated ration for at least 10 days prior to slaughter (Andersson et al. 1990).

Table 32.26 Radiation Effects on Selected Birds

Species, Dose, and Other Variables	Effect	Reference ^a
Green-winged teal, <i>Anas carolinensis</i> ; 4.8 Gy, single acute exposure	LD50, 30 days postexposure	1
Northern shoveler, <i>Anas clypeata</i> ; 8.9 Gy, single acute exposure	LD50, 30 days postexposure	1
Blue-winged teal, <i>Anas discors</i> ; 7.2 Gy, single acute exposure	LD50, 30 days postexposure	1
Birds		
Eggs, passerine species, single acute exposure, 5–10 Gy	LD100	2
Nestlings, various species, 1 Gy daily	Growth retardation	3
Common quail, <i>Coturnix coturnix</i> ; fertilized eggs, exposed first 9 days of incubation, single acute exposure		
5 Gy	Negligible effect on survival	4
7 Gy	Mortality >50%	4
9 Gy	All dead before hatch	4
Domestic chicken, <i>Gallus</i> sp.		
Single acute exposure		
Eggs of broilers exposed to 0.05–2.1 Gy before incubation	No adverse effects on embryonic development at 1.6 Gy and lower; at 2.1 Gy, adverse effects on development, survival, and body weight of hatched chicks	5
Chicks, age 15 days		
2.1 Gy	Reversible changes in blood chemistry within 60 days; no deaths	6
6.6 Gy	Irreversible and permanent damage to red blood cells, hemoglobin, and hematocrit; all dead within 7 days	6

Table 32.26 (continued) Radiation Effects on Selected Birds

Species, Dose, and Other Variables	Effect	Reference ^a
Dietary exposure		
Laying hens fed diet containing 400 Bq $^{137}\text{Cs}/\text{kg}$ ration for 4 weeks	Of total ^{137}Cs ingested, 3% was distributed in egg contents (29–33 Bq/kg egg; 2 Bq egg); 9% in muscle (171 Bq/kg FW); and 81% in excreta	7
Broiler chickens fed diets containing 400 Bq $^{137}\text{Cs}/\text{kg}$ ration for 40 days; some diets contained up to 5% bentonite	Feeding with bentonite reduced ^{137}Cs concentration in muscle by 32% from 155 to 105 Bq/kg FW	7
Black-headed gull, <i>Larus ridibundus ridibundus</i> ; eggs, 9.6 Gy over 20 days	LD50	3
Great crested flycatcher, <i>Myiarchus crinitus</i> ; nestlings, single acute exposure >8 Gy	All dead by fledging	8
Eastern bluebird, <i>Sialia sialis</i> , single acute exposure		
Nestlings, age 2 days		
3 Gy	Reduced growth after 16 days	8
3–5 Gy	Reduced growth and shorter primary feathers at fledging	8
4–12 Gy	Developed normally and fledged successfully	2
5–6 Gy	LD50, nestling to fledgling	8
25 Gy	LD50, 16 days postexposure	8
30 Gy	All dead 4 days postexposure	2, 8
Fertilized eggs, 6 Gy	All dead before hatch	2
European starling, <i>Sturnus vulgaris</i> ; >2 Gy, single exposure	Fatal	9
Tree swallow, <i>Tachycineta bicolor</i>		
0.006 mGy/h during breeding season, equivalent to annual dose of about 50 mSv	No adverse effects on breeding performance of adults or growth performance of nestlings	10
0.9–4.5 Gy, single acute exposure, nestlings	Adverse effects on growth, survival, or both	2
1.0 Gy daily, chronic	Reduced hatch, depressed growth	2
House wren, <i>Troglodytes aedon</i> ; fledglings, 0.9 Gy, single acute exposure	Growth reduction	9

^a 1, Hinton and Scott 1990; 2, Millard and Whicker 1990; 3, Lowe 1991; 4, Wetherbee 1966; 5, Zakaria 1991; 6, Malhotra et al. 1990; 7, Andersson et al. 1990; 8, Willard 1963; 9, Rose 1992; 10, Zach et al. 1993.

32.7.6 Mammals

The mammalian sensitivity to acute and chronic exposures of ionizing radiation, ability to retain selected radionuclides, and effect of biological and abiotic variables on these parameters are briefly summarized in Table 32.27. These data clearly indicate a dose-dependent effect of radiation on growth, survival, organ development, mutagenicity, fatal neoplasms, kidney failure, skeletal development, behavior, and all other investigated parameters. In general, fetuses and embryos were most sensitive to ionizing radiation, and acute or chronic exposures between 0.011 and 0.022 Gy were demonstrably harmful to mice, rats, and guinea pigs.

Table 32.27 Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference ^a
Short-tailed shrew, <i>Blarina brevicauda</i> ; 7.8 Gy, single acute exposure	LD50, 30 days postexposure	1
Cow, <i>Bos</i> sp.		
Oral intake of 0.89 Bq ^{129}I , whole animal	Thyroid contained 0.97 Bq $^{129}\text{I}/\text{kg}$ fresh weight (FW) vs. <0.0012 Bq/kg FW for all other tissues	2
Fed 6.4 Bq ^{129}I daily for 8 days	After 8 days, 22% of total dose of 51.2 Bq was in thyroid; after 63 days, thyroid contained 1 Bq/kg FW and other tissues <0.01 Bq/kg FW	3

Table 32.27 (continued) Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Dog, <i>Canis familiaris</i>		
Beagle embryos age 55 days, or pups 2 days old, given single acute exposure of 0.16, 0.83, or 1.25 Gy	Dose-dependent increase in immature dysplastic glomeruli and other signs of progressive renal failure	4
Beagles, prenatal and early neonatal stages, given single acute dose of 0.2–1.0 Gy, then observed over 11-year life span	Irradiation at all ages was associated with increased risk of: decreased fertility; inhibited growth and development; lower brain weight; and increase in fatal neoplasms	5
Beagle embryos or pups. As above, 2.24–3.57 Gy	Reduction in total number of nephrons and progressive renal failure	4
Beagles, 17–20 months old, single intravenous injection of 200–440,000 Bq ^{226}Ra /kg body weight (BW)	Dose-dependent increase in skeletal malignancies in 36% of dogs during lifetime	6
Beagles, age 5 years, given single injection of ^{226}Ra , in Bq/kg BW, of 39,000, 116,000, or 329,000. Injected ^{226}Ra solutions also contained ^{210}Po , ^{210}Pb , and ^{210}Bi	At lowest dose of 39 kBq/kg BW, kidney was normal, death after 2032 days. At intermediate dose, death in 1210 days; at high dose, death in 581 days. Tubular degeneration and necrosis of kidney at 116 and 329 kBq	7
Beagles, age 7 years, single injection of ^{226}Ra (no contaminating ^{210}Po , ^{210}Pb , or ^{210}Bi) at 45,000 Bq/kg BW, or 122,000 Bq ^{210}Po /kg BW	No kidney damage with ^{226}Ra , but kidney damage with ^{210}Po	7
Beagles, age 7 years given single injection of 1,629,000 Bq ^{226}Ra /kg BW, equivalent to 1.89 Gy (from ^{210}Po contaminants), or 4,831,000 Bq ^{226}Ra /kg BW = 5.15 Gy from ^{210}Po	At low dose, all dead after 516 days; at high dose, all dead in 266 days. Death was from renal failure	7
Guinea pig, <i>Cavia</i> sp.; chronically irradiated daily during 8-h exposure. Daily dose, in Gy		
0.000	Mean survival time of 1372 days	8
0.001	50% dead in 1457 days	8
0.011	50% dead in 1224 days	8
0.022	50% dead in 978 days; anemia	8
0.044	50% dead in 653 days; anemia	8
0.088	50% dead in 187 days; anemia	8
Monkey, <i>Cebus apella</i> ; 1 Gy, whole body, single acute exposure	Leucocyte reduction in 6 days; blood chemistry normal after 90 days	9
Chinese hamster, <i>Cricetus</i> sp.; ovary cells, single acute dose ranging between 0.005 and 0.06 Gy	Increased frequency of sister chromatid exchange at 0.005 Gy; increased numbers of chromosomal aberrations at >0.02 Gy; no significant increase in cell death	10
Syrian hamster, <i>Cricetus</i> sp.; 0.12–2 Gy, single acute exposure	Genes modifying cytoskeletal development adversely affected at all doses within 3 h by both high LET (neutrons) and low LET (gamma rays, X-rays) radiations	11
Human, <i>Homo sapiens</i>		
Developing forebrain, 0.18–0.55 Gy (estimated dose to prenatally exposed Japanese atomic bomb survivors)	Seizures in childhood; reduced school performance at least through age 11 years; some cases of severe mental retardation by age 17 years	12
Fetus, 1 Sv, 8–15 weeks of gestation	40% probability of severe mental retardation; IQ score lowered 30 points	13
Sperm chromosomes, 0.23, 0.45, 0.91, or 1.82 Gy, single acute exposure	Chromosomal aberrations increased linearly from 6.1% at 0.23 Gy to 62% at 1.82 Gy	14
Thyroid, single acute exposure		
0.065 Gy	Minimum dose for induction of thyroid carcinoma	15
3–5 Gy	5% increase in thyroid malignancies 20 years after exposure, with tumors appearing 4–5 years after exposure	16

Table 32.27 (continued) Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference^a
7–10 Gy	Linear dose relation to thyroid cancer, and pathology in adjacent parathyroid and salivary glands	16
Whole body		
Single brief exposure		
0.05–0.11 Sv	Doubles rate of cancers	17
0.15 Sv	Temporary sterility, males	13
0.18–0.29 Sv	Doubles rate of pregnancy complications	17
0.5–2.0 Sv	Opacity of lens; depression of hematopoiesis	13
0.68–1.10 Sv	Doubles rate of F1 generation mortality	17
1 Sv, adults	1% probability of hereditary effects; 4% probability of fatal cancer in occupational workers	13
2.5–6.0 Sv	Sterility, females	13
3.5–6.0 Sv	Permanent sterility, males	13
5.0 Sv	Cataracts	13
<1 Gy	Survival almost certain	18
1–2 Gy	Survival probable	18
1–2 Gy	About 5% mortality in several months from infection and hemorrhage	19
2–5 Gy	Survival possible	18
2–7.5 Gy	Hematopoietic syndrome characterized by bone marrow damage, anemia, lowered immune response, hemorrhage, and sometimes death	20
3–5 Gy	Death in 30–60 days, bone marrow damage	13
5–10 Gy	100% adversely affected within weeks with bone marrow abnormalities; about 45% mortality	19
5–15 Gy	Death in 10–20 days; GI tract and lung damage	13
5–20 Gy	Survival improbable	18
7.5–30 Gy	Gastrointestinal damage: nausea, vomiting, anorexia, diarrhea, lethargy, weight loss, dehydration, exhaustion, and death	20
10–15 Gy	All adversely affected with intestinal problems within 30 min; 95% dead in 2 weeks from enterocolitis shock	19
>15 Gy	Death in 1–5 days; nervous system damage	13
>50 Gy	All dead in 48 h, usually from cerebral edema	19
Annual dose rate or protracted annual exposure for many years		
>0.1 Sv	Lens opacity	13
>0.15 Sv	Cataracts	13
>0.2 Sv	Sterility, females	13
0.4 Sv	Temporary sterility, males; hematopoiesis depression	13
2.0 Sv	Permanent sterility, males	13
Rhesus monkey, <i>Macaca mulatta</i>		
Females, single acute dose of 0.25–6.5 Gy, observed over a 17-year postexposure period	At doses >2 Gy, 53% developed endometriosis (abnormal uterine growth) vs. 26% in controls; irradiated monkeys weighed 43% less than controls, 35% were anorexic, 89% had abnormal uterine anatomy, and histopathology in most tissues exceed 50% frequency	21
Exposed to single brief whole-body proton irradiation (protons in the energy range encountered by astronauts) ranging between 0.25 and 12 Gy and observed for 24 years until death	Dose-dependent life shortening of at least 40 months at doses >4.5 Gy; mean life shortening was 200–500 monkey days per Gy (equivalent to 500–1250 human days). Brain cancer first observed in 8 Gy group after 13 months. Monkeys receiving 3–8 Gy had a	22

Table 32.27 (continued) Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Mammals	significantly higher proportion of cancer deaths than those receiving 0.25–2.8 Gy. Latent period for cancer in animals receiving 4–8 Gy ranged from 13 months to 20 years	
10 species, 2.8–8.05 Gy, single acute exposure	LD50, 30 days after exposure	23
Various species, bioconcentration factors (BCF) of selected radionuclides		
⁶⁰ Co		
Herbivores	Whole body BCF of 0.3	24
Caribou, <i>Rangifer tarandus</i>		
Bone vs. kidney	BCF of 0.5 vs. 0.4	24
Liver vs. muscle	BCF of 0.9 vs. 0.02	24
¹³⁴⁺¹³⁷ Cs		
Herbivores	Whole body BCF of 0.3–2.0	24
Omnivores	Whole body BCF of 1.2–2.0	24
Carnivores	Whole body BCF of 3.8–7.0	24
¹³¹ I		
Herbivores	Whole body BCF of 0.05	24
Omnivores	Whole body BCF of 0.2	24
Carnivores	Whole body BCF of 0.1	24
⁹⁰ Sr, caribou, muscle vs. bone	BCF of 0.02 vs. 7.0	24
Various species, biological half-life of selected radionuclides		
²⁴¹ Am		
Bone	27.4 years	25
Gonads	>27.4 years	25
Kidney, liver	11 years	25
Muscle	4 years	25
Serum	5 days	25
¹³⁷ Cs, kidney, liver, and muscle	30–50 days	25
²³⁸⁺²³⁹⁺²⁴⁰ Pu		
Bone	49 years	25
Gonads	>49 years	25
Kidney, liver	19 years	25
Muscle	5.5 years	25
Serum	5 days	25
Singing vole, <i>Microtus miurus</i> ; 8.46 Gy, single acute dose	LD50, 30 days after exposure	26
Creeping vole, <i>Microtus oregoni</i> ; 6.51 Gy, single acute dose	LD50, 30 days after exposure; sensitivity may be associated with low chromosome complement	26
Meadow vole, <i>Microtus pennsylvanicus</i> ; single brief exposure		
7.04 (6.35–7.98) Gy, irradiated in November	LD50, 30 days after exposure; irradiated voles released into environment	27
7.67 (7.01–8.39) Gy, irradiated in May	LD50, 30 days after exposure; irradiated voles released into environment	27
8.44 (8.17–8.77) Gy	LD50, 30 days after exposure; irradiated voles held in laboratory	7
Pine vole, <i>Microtus pinetorum</i> ; single brief exposure		
7 Gy	None dead 30 days after exposure; weight normal	28
8.8 Gy, males	LD50, 30 days after exposure; weight loss in survivors	28
10.0 Gy, females	LD50, 30 days postexposure; weight loss in survivors	28

Table 32.27 (continued) Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference^a
House mouse, <i>Mus musculus</i> ; single brief exposure		
7.5–8.8 Gy	LD50, 30 days postexposure	26, 29
7.8, 8.1, 8.3, or 9.8 Gy	LD50, 30 days after exposure; 4 different strains	1
Mouse, <i>Mus sp.</i>		
Intraperitoneal injection		
Single injection of 850 Bq $^{227}\text{Ac}/\text{kg}$ BW alone or in combination with ^{227}Th at 18,500, 74,000, or 185,000 Bq/kg BW	The highest bone cancer incidence was observed at the highest doses of ^{227}Th . The addition of ^{227}Ac resulted in an additional osteosarcoma incidence only at 18,500 Bq $^{227}\text{Th}/\text{kg}$ BW	30
Single injection of ^{241}Am at concentrations — in Bq/kg BW — of 0.02, 0.06, 0.19, 0.37, or 1.2	Survival time decreased from 594 days for controls and 0.02 group to 135 days in the 1.2 group; increased frequency of tumors in bone, liver and lymph	31
Adult males, 84 days old, given 2–64 Bq $^{224}\text{Ra}/\text{mouse}$, either as single injection, or 8 injections at 3.5-day intervals over 4 weeks; observed for 24 months	No difference in single or multiple injection effects. No effect at 16 Bq and lower. At 32 and 64 Bq, reduction in bone growth and osteonecrosis of mandible ("radium jaw")	32
Oocytes given single exposures of 0.1, 0.15, or 0.25 Gy; immature oocytes examined 8–12 weeks later	Controls had 100% survival and zero chromosome aberrations; the 0.1 Gy group had 30% survival and 2% chromosome aberrations; 0.15 Gy group had 17% survival and 6% chromosome aberrations; 0.25 Gy group had 5% survival and 23% chromosomal aberrations	33
Whole body, single brief exposure		
1 Gy	Acute exposure may extend life span	34
1.35 Gy	Doubles mutation rate of spermatogonia	17
7.6 Gy	LD50, 30 days postexposure	35
9.5 Gy	LD100, 30 days postexposure	35
10.0 Gy, adult males, 16–20 weeks old, observed for 7 days	At 90 min after irradiation, locomotor activity was suppressed and remained depressed; at 4 days, body weight decreased; at day 7, offensive aggressive behavior	20
12.5 Gy	LD100, days 3–7 postexposure	35
0.12–2.5 Sv	Doubles rate of heritable translocations in males	17
0.25–2.5 Sv	Doubles rate of congenital malformations in females	17
0.4–1.0 Sv	Doubles frequency of dominant lethal mutations	17
0.5–1.0 Sv	Doubles rate of heritable translocations in females	17
0.8–2.5 Sv	Doubles rate of congenital malformations in males	17
1.5–3.0 Sv	Doubles rate of recessive lethal mutations	17
Chronic exposure, daily dose over 8-h period, in Gy		
0.0	Mean survival time of 703 days	8
0.001	Mean survival of 761 days	8
0.011	Mean survival time of 684 days; 50% weight gain over controls	8
0.022	50% dead in 630 days	8
0.044	50% dead in 591 days	8
0.088	50% dead in 488 days	8
Total yearly dose, chronic exposure, 16 Gy (about 0.044 Gy daily)	Tolerated	34
Domestic ferret, <i>Mustela putorius</i> ; 2, 4, or 6 Gy; single brief exposure; adult males	All doses depressed locomotion; vomiting in 22 min at 2 Gy, 13 min at 4 Gy, and 11 min at 6 Gy. Various substituted benzamides reduced vomiting	36

Table 32.27 (continued) Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference^a
Marsh rice rat, <i>Oryzomys palustris</i> ; 5.25 Gy, single acute exposure	LD50, 30 days after exposure; this species was the most sensitive of the 10 rodent species tested	1
Domestic sheep, <i>Ovis aries</i>		
Ewes fed hay containing 9000 Bq ¹³⁷ Cs/kg DW for 50–60 days, then 40 days on uncontaminated hay; some diets contained 30 or 60 g of vermiculite daily, or 2 g of ammonium ferricyanoferrate (AFCF) daily	Maximum levels of ¹³⁷ Cs were reached in 10 days in milk and 35–40 days in muscle. Radionuclide transfer to milk and meat was reduced 2.5 times at daily intakes of 30 g vermiculite, and 8 times at 60 g vermiculite or 2 g AFCF	37
Ewes given oral dose of 74,000 Bq ¹³⁷ Cs, observed for 76 days	At 76 days, only 26% of ¹³⁷ Cs remained; tissue concentrations, in Bq ¹³⁷ Cs/kg FW, were: 77,000 in salivary gland; 42,000 in muscle; 24,000–36,000 in pancreas, liver, and kidney; 14,000–17,000 in spleen and lung; and <8000 in other tissues	38
Lambs fed 21 kg of vegetation containing 16,600 Bq of ²³⁸⁺²³⁹⁺²⁴⁰ Pu and 14,400 Bq of ²⁴¹ Am over a 14-day period, followed by 4 days on uncontaminated hay	Of the Pu ingested, 46% was in liver, 30% in bone, 12% in muscle, and 2% in lung; for ²⁴¹ Am, these values were 19% in liver, 15% in bone, 6% in meat, and 0.5% in lungs	39
Lamb given single intravenous injection of 23 Bq ²³⁸ Pu plus 27 Bq ²⁴¹ Am and held for 11 days	Liver retained up to 44% of the injected ²³⁸ Pu and 28% of the ²⁴¹ Am; bone had 21% of the ²³⁸ Pu and 20% of the ²⁴¹ Am	39
Great basin pocket mice, <i>Perognathus parvus</i> ; 8.56 Gy, single exposure	LD50, 30 days after exposure; hair loss within 7 days	26
White-footed mice, <i>Peromyscus leucopus</i> ; whole body, single brief exposure		
9.5 Gy, both sexes irradiated	No reproduction	40
9.5 Gy, males only irradiated	91% of pairs successful in producing young	40
9.5 Gy, females only irradiated	40% of pairs reproduced successfully	40
10.7 Gy	LD50, 30 days postexposure; this species was the most radioresistant of 10 species of rodents tested	1
Deer mice, <i>Peromyscus maniculatus</i> ; 9.19 Gy, single brief exposure	LD50, 30 days after irradiation	26
Old-field mouse, <i>Peromyscus polionotus</i> ; 11.25 Gy, single exposure	LD50, 30 days after exposure	29
Norway rat, <i>Rattus norvegicus</i> ; 8.67 Gy, single exposure	LD50, 30 days postexposure	1
Laboratory white rat, <i>Rattus</i> spp.		
0.001, 0.01, or 0.1 Gy; single acute whole-body exposure; adult males; killed up to 180 days after exposure	Fertility reduction was zero in the low-dose group, 25% at 0.01 Gy, and 66% at 0.1 Gy. Primary sites of damage were tubuli of the testes and spermatogonia. The high-dose group also had altered serum hormone chemistry after 30 days that persisted for 180 days	41
Pregnant rats given single, brief exposure to 0.25, 0.5, 0.75, or 1 Gy on gestational day 15; fetuses examined 24 h after irradiation	No effect at 0.5 Gy and lower on cerebral mantle of developing brain; however, dose-related increase in pyknotic cells and macrophages in cortical mantle of fetus for all doses	42
Pregnant females exposed on day 15 of gestation to 0.75 Gy; fetuses examined 1–3 months after birth	Rats irradiated <i>in utero</i> had impaired gait, slower motor behavior, difficulty in learning motor tasks, reduced growth rate, and reduced thickness of cerebral cortex	43
<1 Gy, whole body, single exposure	No brain pathology	44
2 Gy, whole body, single exposure	Brain pathology	44
Adult males conditioned to avoid electric shock by pressing a lever were subjected to various whole-body acute exposures		
1.5 Gy daily for 5 consecutive days (total 7.5 Gy)	No significant change in performance over 8 weeks	45

Table 32.27 (continued) Radiation Effects on Selected Mammals

Species, Dose, and Other Variables	Effect	Reference^a
4.5 Gy, single exposure	No effect on performance for at least 6 weeks	45
7.5 Gy, single exposure	Significantly decreased response rate over the first 4 weeks; performance normal during weeks 5–6; 9% reduction in body weight	45
9.5 Gy, single exposure	LD100, 30 days postexposure	45
Single local dose of 5–20 Gy to various salivary glands	Dose-dependent decrease in salivary flow rate and sodium composition of saliva; at 10 Gy and higher, changes were irreversible	46
25 Gy, single whole-body exposure	50% dead 30–60 days postirradiation from fatal stomach damage; significant liver damage in survivors	47
Eastern harvest mouse, <i>Reithrodontomys humulis</i> ; 9.5 Gy, single exposure	LD50, 30 days after exposure	1
Rodents, single brief exposure		
3.8–13.3 Gy, 13 species	LD50, 30 days postexposure; females more sensitive than males	48
4–8 Gy, 5 species	Dead rodents had histopathology of lymph nodes, thymus, bone marrow, liver, lung, and gonads; male survivors had atrophied testes	26
5.3–10.7 Gy, 10 species	Range of LD50 values (30 days after exposure); survivors showed conjunctivitis, ataxia, diarrhea, passiveness, cessation of feeding, aggressiveness, and graying of pelage	1
Squirrel monkey, <i>Saimiri</i> spp.; fetuses, 80–90 days postconception; given 0.1 or 1.0 Gy, single acute exposure; young observed from birth to age 2 years	No effect on behavior at 0.1 Gy. At 1 Gy, emotional stability and vision impaired at age 30 days, learning impaired at 1 year; normal at 2 years	44
Cotton rat, <i>Sigmodon hispidus</i>		
Females given 5, 7.5, 9, 10.5, or 12 Gy whole body once a month for 4 months, then released into a 0.4-ha impoundment with unirradiated males and females for 15 days	Survival was 91% at 5 Gy and 25% at 12 Gy; intermediate doses had intermediate survival	49
9.58 Gy, single brief exposure	LD50, 30 days after exposure	1
11.2 Gy, single acute exposure, adult females	LD50, 30 days after exposure	49
11.3 Gy, single exposure, adult females	LD50, 15 days postexposure	49
Eastern chipmunk, <i>Tamias striatus</i>		
2–4 Gy, single exposure	Irreversible injury throughout life, but life span was increased	50
Given single exposure of 2 or 4 Gy, then released into environment	Irradiated chipmunks had consistently smaller home ranges and moved shorter distances than did controls	51
Iodine-131, half-time release rate from thyroid; females vs. males		
Summer	2.3 h vs. 263 h	52
Spring	156 h vs. 217 h	52
Autumn	126 h vs. 129 h	52

^a 1, Dunaway et al. 1969; 2, Handl et al. 1990; 3, Handl and Pfau 1989; 4, Jaenke and Angleton 1990; 5, Benjamin et al. 1990; 6, Lloyd et al. 1991; 7, Bruenger et al. 1990; 8, Lorenz et al. 1954; 9, Egami et al. 1991; 10, Nagasawa et al. 1990; 11, Woloschak et al. 1990a; 12, Mole 1990; 13, ICRP 1991a; 14, Kamiguchi et al. 1990; 15, Kim et al. 1990; 16, Refetoff 1990; 17, Sankaranarayanan 1991c; 18, McLean 1973; 19, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; 20, Maier and Landauer 1990; 21, Fanton and Golden 1991; 22, Wood 1991; 23, Hobbs and McClellan 1986; 24, Kitchings et al. 1976; 25, Gilbert et al. 1989; 26, O'Farrell 1969; 27, Iverson and Turner 1976; 28, Dunaway et al. 1971; 29, Golley and Gentry 1969; 30, Muller et al. 1990; 31, Schoeters et al. 1991; 32, Robins 1990; 33, Straume et al. 1991; 34, Rose 1992; 35, Cronkite et al. 1955; 36, King and Landauer 1990; 37, Daburon et al. 1991; 38, Vandecasteele et al. 1989; 39, Ham et al. 1989; 40, Di Gregorio et al. 1971; 41, Canfi et al. 1990; 42, Norton and Kimler 1990; 43, Norton et al. 1991; 44, Mole 1990; 45, Mele et al. 1990; 46, Vissink et al. 1990; 47, Geraci et al. 1991; 48, Whicker and Schultz 1982b; 49, Pelton and Provost 1969; 50, Thompson et al. 1990; 51, Snyder et al. 1976; 52, Kodrich and Tryon 1971.

32.7.6.1 Survival

Survival time is inversely related to dose in whole-body, acute exposures to ionizing radiation (Figure 32.9). In general, hematopoietic organs are most sensitive, and the gastrointestinal tract and central nervous system are next most sensitive (UNSCEAR 1988). Body weight is an important modifier, and heavier mammals are usually most sensitive to radiation (Figure 32.10). Feral rodent populations are at risk from ionizing radiation through the reduction in numbers from direct kill and indirectly from the radiation-caused diminution of reproduction (Di Gregorio et al. 1971).

Low doses of ionizing radiation are beneficial to many species of mammals. Effects of radiation hormesis include increased survival and longevity, lowered sterility, increased fecundity, and accelerated wound healing (Luckey 1980). Low doses of gamma irradiation cause irreversible injury to the eastern chipmunk (*Tamias striatus*), although the life-span was significantly longer (Thompson et al. 1990). Acquired radioresistance after exposure to a low dose of ionizing radiation has been described in rats, mice, and yeast (Yonezawa et al. 1990). In mice, for example, low doses of X-irradiation (not higher than 0.15 Gy) enhanced 30-day survival if given 2 months prior to a dose of 7.5 Gy. The low-dose exposure seems to stimulate the recovery of blood-forming stem cells after the second irradiation and favors a decrease in the incidence of bone-marrow death. The exact mechanisms of radiation hormesis are unknown because effects are not related to and not predictable from the high-dose exposure (Yonezawa et al. 1990).

Irradiated small mammals released into the environment had a lower survival rate than laboratory populations, suggesting that the extrapolation from laboratory results may overestimate the radioresistance of free-ranging voles and other small animals because of the general level of stress in the population (Iverson and Turner 1976). The opposite was observed in eastern chipmunks given high sublethal doses of X-rays. Chipmunks had an overall reduction in mobility when they were released

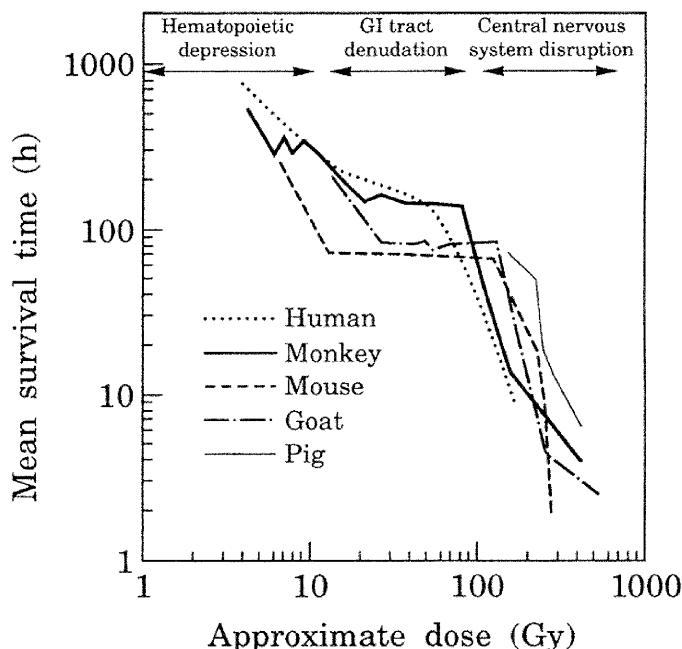


Figure 32.9 Survival time and associated mode of death of selected mammals after whole-body doses of gamma radiation. (Modified from Hobbs, C.H. and R.O. McClellan. 1986. Toxic effects of radiation and radioactive materials. Pages 669-705 in C.D. Klaassen, M.O. Amdur, and J. Doull [eds.]. *Casarett and Doull's Toxicology. Third Edition*. Macmillan, New York; United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR]. 1988. Sources, Effects and Risks of Ionizing Radiation. United Nations, New York. 647 pp.)

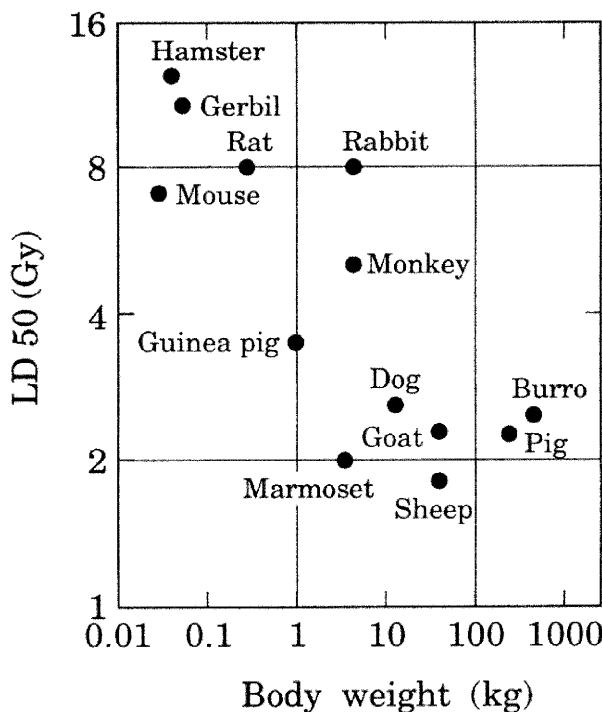


Figure 32.10 Relation between body weight and radiation-induced LD₅₀ (30 days postexposure) for selected mammals. (Modified from United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR]. 1988. Sources, *Effects and Risks of Ionizing Radiation*. United Nations, New York. 647 pp.)

into the environment and a higher survival rate than controls (Snyder et al. 1976), possibly because of increased predation on the more mobile controls.

32.7.6.2 Carcinogenicity

The risk of the induction of cancer is a recognized somatic effect of low doses of ionizing radiation, as judged by epidemiological studies of Japanese survivors of U.S. nuclear bombs (Coggle and Williams 1990) and of Marshall Islanders, underground miners, and radium watch dial workers (Bowden et al. 1990). However, Yoshimoto et al. (1990), in a study on the occurrence of malignant tumors in Japanese children <10 years old and born between 1946 and 1982 to survivors of the atomic bombings in 1945, found no statistically significant increase in malignant tumors in the children of parents exposed to >0.01 Sv whole-body radiation (mean gonadal exposure of 0.43 Sv) at the time of the atomic bombings when compared to a suitable control group. Nutritional status is important when treating malignant tumors. Unlike tumors of nonanemic individuals, tumors in anemic mice and humans frequently do not respond satisfactorily to radiotherapy (McCormack et al. 1990).

Ionizing radiation induces basal cell carcinomas in skin and is active in the initiation of malignant tumors and in the progression of benign to malignant tumors (Bowden et al. 1990). Skin has been widely used in studies of carcinogens because of its accessibility and the visibility of its tumors. All data on experimental radiogenic skin cancer in mice are on a relatively narrow and well-defined response curve. However, mouse skin is about 100 times more sensitive than human skin (Coggle and Williams 1990), strongly suggesting that appropriate animal models are necessary in the extrapolation of results to other species.

Thyroidal cancer in dogs and sheep has been induced with repeated administrations of ^{131}I , although single injections of ^{131}I failed to induce thyroid cancer in adult animals except in some strains of laboratory rodents (Walinder 1990). Humans with a prior history of ^{131}I and other radiation exposure in childhood are at a significantly higher risk of thyroid carcinogenesis, and females are at higher risk than males. The minimum latent period in humans is about 4 years, and neoplastic lesions may develop as late as 40 years after irradiation (Kim et al. 1990). Historically, the human thyroid received radiation from irradiation of the scalp for epilation (up to 0.5 Gy), thymus (up to 5 Gy), tonsils and adenoids (8 Gy), and facial acne (15 Gy). Higher doses of external irradiation (up to 50 Gy) were used from 1920 to 1940 for the treatment of hyperthyroidism in adults and are still used for the treatment of cervical malignancies in people of all ages (Refetoff 1990).

Radium-induced bone malignancies after exposure to ^{226}Ra are similar in beagles and humans, and the tibia in dogs is especially sensitive (Lloyd et al. 1991). “Radium jaw” has been described in humans as a late effect of accidental ingestion or therapeutic administration of long-lived radium isotopes, such as ^{226}Ra and ^{228}Ra , and is characterized by bone tumors, spontaneous fractures, and osteosclerosis (Robins 1990). However, the short-lived ^{224}Ra (T_b 1/2 of 3.6 days) produces similar effects in mice, suggesting that the events that trigger radium-induced bone disorders occur within days of incorporation, although the consequence is a late effect (Robins 1990).

Aerosol exposures of mice, rats, dogs, and hamsters to radon and its decay products resulted in lifetime shortening, pulmonary emphysema, pulmonary fibrosis, and respiratory tract carcinoma. Damage to the skin and kidney was also reported, but the lung seems to be the primary affected organ (Cross 1990). Small mammals and birds that live in burrows containing radon-rich soils (9900 Bq/m³ of ^{222}Rn) are expected to have an additional 17 lung cancers per 1000 animals than animals not similarly exposed. However, tumors have not been widely reported in these species (Macdonald and Laverock 1998). Radon and ^{222}Rn daughters have caused problems in miners who work underground in uranium mines. These miners had an excessive incidence of disease of the respiratory system, including lung cancer. The problem is related to the emanation of radon into the mines and the decay of the radon, the short-lived radioactive daughters (^{216}Po , ^{214}Pb , ^{214}Bi , ^{214}Po) that attach to dust particles, eventually resulting in alpha radiation exposure of the respiratory airways (Hobbs and McClellan 1986). A similar pattern was evident in rats exposed to ^{239}Pu . Rats exposed to $^{239}\text{PuO}_2$ aerosol of about 3700 Bq/lungs and examined 8 to 18 months after exposure had a very high frequency (as much as 80%) of malignant pulmonary neoplasms; genetic mutations were evident in 46% of the radiation-induced tumors (Stegelmeier et al. 1991).

The incidence of ovarian tumors in mice, guinea pigs, and rabbits increased after 3 years of chronic irradiation at doses as low as 1.1 mGy daily (Lorenz et al. 1954). Unlike other tumors, the induction of ovarian tumors depended on a minimum total dose and seemed to be independent of a daily dose (Lorenz et al. 1954). Radiation-induced neoplastic transformation of hamster cells may be associated initially with changes in expression of the genes modifying cytoskeletal elements (Woloschak et al. 1990b).

32.7.6.3 Mutagenicity

In general, ionizing radiation has produced mutations in every plant and animal species studied. Some genetic risks are associated with exposures, but the risk of inducing a dominant genetic disease is quite small because radiation-induced mutations are primarily recessive and usually lethal (Sankaranarayanan 1991c). Residents living near the site of extensive mining and milling of uranium operations in Texas have an increased frequency of chromosomal aberrations and a reduced DNA repair capacity; uranium-238 was much higher in these areas when compared to reference sites, possibly as a result of leaching into the groundwater (McConnell et al. 1998). The genetic doubling dose of radiation is the amount of acute or chronic radiation that doubles the naturally occurring spontaneous mutation rate each generation. For mice, the estimated genetic doubling dose equivalent

is 1.35 Sv from acute exposures and 4.0 Sv from chronic exposures to radiation (Neel and Lewis 1990). For protection from radiation, the estimated genetic risks to humans have largely been based on data from mice (Straume et al. 1991). Studies of children of Japanese survivors of nuclear bomb explosions showed that the genetic doubling dose equivalent of acute gonadal radiation is about 2.0 Sv (1.69 to 2.23); from chronic radiation, this value is about 4.0 Sv (Neel and Lewis 1990). Based on results of the study of Japanese survivors of the nuclear explosions, Yoshimoto et al. (1990) and Sankaranarayanan (1991c) concluded that there was no increase in the spontaneous mutation rate after parents were exposed. The high doubling dose of about 4 Sv estimated from these data is another way of stating that, relative to the assumed spontaneous rates, the rate of induction of mutations leading to the measured effects is too small (Sankaranarayanan 1991c). The transmission of radiation-induced genetic effects to offspring has not yet been demonstrated in any human population (Straume et al. 1991).

Specific point mutations were identified in ^{239}Pu -induced preneoplastic lesions and malignant neoplasms in the lungs of rats (Stegelmeier et al. 1991). Mice exposed to a single whole-body dose of 3 Gy produced a radiation-induced mutation that simultaneously generated distinct alleles of the limb deformity and agouti (grizzled fur color) loci, two developmentally important — but not adjoining — regions on a single chromosome. This phenomenon was probably associated with DNA breaks caused by inversion of a segment in another chromosome (Woychik et al. 1990). The plasma membrane in immature oocytes of mice is the hypersensitive lethal target in producing radiation-induced genetic damage (Straume et al. 1991).

32.7.6.4 Organ and Tissue Damage

In the abdomen, the kidneys are one of the most sensitive organs to serious or fatal radiation-induced damage (Jaenke and Angleton 1990). The relatively high incidence of kidney disease among mature beagles injected with ^{226}Ra and its accompanying ^{210}Bi and ^{210}Po resulted from alpha irradiation of the kidneys by the substantial amount of ^{210}Po that was in the injected solution (Bruenger et al. 1990). Hepatic injury induced by ionizing radiation can be a life-threatening complication. The main responses of the liver to acute radiation exposure include enlargement, dilation of blood vessels, fluid accumulation, and histopathology (Geraci et al. 1991). Damaging effects of ionizing radiation on the fetal cerebral cortex has been recognized for many years (Norton and Kimler 1990). The deleterious effects of ionizing radiation on the developing brain are prolonged and progressive. Doses <2 Gy of gamma radiation are harmful to the developing brain; and in humans, mental retardation may occur from doses as low as 0.2 Gy between week 8 and 15 of gestation (Norton et al. 1991).

Irradiated white-footed mice (*Peromyscus leucopus*) frequently had atrophied gonads, degenerating fetuses in the uterus, and greying hair (Di Gregorio et al. 1971). High sublethal doses (7 Gy) of radiation to the pine vole (*Microtus pinetorum*) caused pelage graying, wherein unpigmented hair from damaged follicles replaces molted pigmented hair. Pelage graying may decrease survival from increased predation (Dunaway et al. 1971), although this needs verification.

Human sperm chromosomes retain a high fertilizing ability after a high dose of X-irradiation, although mammalian spermatozoa have little capacity to repair DNA damage induced by radiation (Kamiguchi et al. 1990). Radiation-induced death of lymphoid cells in rats is associated with damage to the cell itself but may also be due to secretions from irradiation-activated natural killer cells that induce pycnosis and interphase death in lymphoid cells (Eidus et al. 1990).

32.7.6.5 Behavior

Numerous behavioral measures have been evaluated for their usefulness in providing a sensitive index of exposure to ionizing radiation. Radiation-related mental retardation is the most likely type of behavioral abnormality in humans; sensitivity peaked between 8 and 15 weeks of conception

and at doses >0.4 Gy (UNSCEAR 1988). No specific mechanism for the production of mental retardation has been established, although proposed mechanisms include the loss of cells, migration of neurons, and failure of synaptogenesis (Norton and Kimler 1990). In studies with rats, operant responses decreased (maintained by positive reinforcement such as food or water) at sublethal radiation doses (3.0 to 6.75 Gy) under various schedules of reinforcement (Mele et al. 1990). Disrupted operant responses under shock avoidance at >LD100 levels are reported in pigs and rhesus monkeys (Mele et al. 1990).

32.7.6.6 Absorption and Assimilation

The absorption, bioavailability, and retention of radionuclides in mammals are modified by:

- The age, sex, species, and diet of the organism
- Season of collection
- The chemical form of the radionuclide in tissue and blood
- Residence time in the digestive tract
- Preferential accumulation by selected organs and tissues
- Other variables (Kitchings et al. 1976; Whicker and Schultz 1982a, 1982b; Richmond 1989; Desmet et al. 1991; Harrison 1991).

Assimilation fractions of various elements recommended by the International Commission on Radiological Protection are presented in detail by Whicker and Schultz (1982b).

Many radionuclides preferentially accumulate in certain organs or tissues, but the critical organ is different for different radionuclides: liver for ^{54}Mn , erythrocytes and spleen for ^{55}Fe , liver and kidney for cobalt nuclides, liver and prostate for ^{65}Zn , skeletal muscle for ^{137}Cs , and GI tract for ^{95}Zr (Whicker and Schultz 1982a). The persistence of radionuclides in mammals varies with the chemical form, kinetics, species, and other variables. For example, the time for 50% persistence of selected radionuclides in whole-animal studies ranges from 19 h to 14 days of ^{134}Cs ; 4 to 35 days of ^{137}Cs ; 5 to 12 h of the short-lived component of ^{60}Co , and 5 to 21 days of the long-lived component; 25 to 593 days of ^{90}Sr ; and 4 to 26 days of ^{131}I (Kitchings et al. 1976; Whicker and Schultz 1982b).

Some radionuclides act antagonistically when administered together. The combined incorporation of ^{227}Ac and ^{227}Th at levels tested in mice shows a lower biological effect than the sums of the effects of the components administered singly. The less-than-additive effect is in good agreement with experiments with the incorporation of a mixture of β emitters, in which the effects are also less-than-additive (Muller et al. 1990). Uptake and retention characteristics of essential biological nutrients (i.e., H, C, P, I, K, Ca, Mn, Fe, Co, Zn) are largely controlled by biological processes (Whicker and Schultz 1982a). For example, ^{131}I , regardless of route of administration, is rapidly absorbed into the bloodstream and concentrated in the thyroid. Ionizing radiation associated with high levels of ^{131}I destroys the thyroid, affecting the thyroid hormone production (Hobbs and McClellan 1986).

Alkali metals (K, Rb, Cs) behave similarly and sometimes one is accumulated preferentially when another is deficient. A similar case is made for Sr and Ca (Whicker and Schultz 1982a). The most important alkali metal isotope is ^{137}Cs because of its long physical half-life (30 years) and its abundance as a fission product in fallout from nuclear weapons and in the inventory of a nuclear reactor or a fuel-reprocessing plant. Cesium behaves much like potassium. It is rapidly absorbed into the bloodstream and distributed throughout the active tissues of the body, especially muscle. The β and γ radiation from the decay of ^{137}Cs and its daughter, ^{137}Ba , result in essentially whole-body irradiation that harms bone marrow (Hobbs and McClellan 1986).

Because ^{226}Ra and ^{90}Sr are metabolic analogs of calcium, they are deposited in the skeleton. Both isotopes are associated with bone cancers (Hobbs and McClellan 1986). In pregnant rats, the total amount of ^{226}Ra transferred from the dam to the 8 to 10 fetuses in a litter was low after a single

injection and did not exceed 0.3% of the maternal content. The retained whole-body burden in dams was 53% at the first, 48% at the second, and 44% at the third pregnancy, mostly in the skeletal system (Kshirsagar 1990). The rare earths (i.e., ^{144}Ce , ^{152}Eu , ^{140}La , ^{147}Pr , ^{151}Sm) are usually not effectively absorbed from the GI tract, and elimination is rapid (Palumbo 1963). Cerium-144 is one of the more biologically hazardous radionuclides in this group because of its half-life (285 days) and the energetic β emissions from it and its daughter, ^{144}Pr (Hobbs and McClellan 1986).

The greatest uncertainty in dose estimates from the ingestion of long-lived alpha emitters is the values used for their fractional absorption from the GI tract (Harrison 1991). For transuranic elements, the fraction of the ingested material that was assimilated by the whole organism was always <0.01% and usually nearer 0.003% (Whicker and Schultz 1982b). The major hazard of plutonium nuclides to terrestrial organisms comes from inhalation; uptake by plants is low, and further uptake by humans through the gut is low (Noshkin et al. 1971). Americium-241 is an artificial, toxic bone-seeking radionuclide produced through beta decay of ^{241}Pu (Schoeters et al. 1991). Because of its long half-life, its high-energy alpha irradiation, and its accumulation in the liver and skeleton, consideration should be given to ^{241}Am in risk estimates of latent effects, such as induction of liver cancers, bone cancers, and leukemias. In comparison with ^{226}Ra , ^{241}Am is 20 times more effective in reducing life-span in mice and 13 times more effective in the rate of death from bone cancer (Schoeters et al. 1991).

Although radon has long been known as a health hazard to miners in the uranium industry, it was only in the 1980s that radon contamination of buildings was recognized as widely distributed over the Earth. However, years of exposure are required before a health problem develops (Majumdar et al. 1990). Exposure to radon-decay products can be expressed in two different ways: the amount of inhaled decay products (taking into account their potential to emit radiation energy) or the product of the time during which the decay products were inhaled and their concentration in the inhaled air. The potential alpha energy of the inhaled decay products may be expressed in joules (J). The potential alpha energy concentrations in air is expressed in joules per cubic meter; for radon in equilibrium with its decay product, this corresponds to 3700 Bq/m³ (UNSCEAR 1988).

Rodents dosed with tungsten-185 excreted 80% in 24 h; bone was the major retention site; the half-time persistence ranged from 5.7 days in femurs of mice to 86 days in femurs of rats; some components in the bone of rats persisted with a half-time >3 years (Reed and Martinedes 1971). Niobium-95 is produced directly by nuclear fission and indirectly by decay of ^{95}Zr . Routine discharges of ^{95}Nb from a nuclear fuel reprocessing plant in the United Kingdom in 1970 contributed about 5% of the bone-marrow dose to a 10-year-old child living in the vicinity (Harrison et al. 1990). Gastrointestinal absorption of ^{95}Nb by adult guinea pigs was about 1.1%, and supports the values of 1% absorption in adults and 2% in infants now used to calculate percentage absorption of niobium isotopes by humans (Harrison et al. 1990).

32.8 PROPOSED CRITERIA AND RECOMMENDATIONS

For the protection from radiation, effects of radiation have been characterized as stochastic or nonstochastic. The probability of a stochastic effect — and not its severity — varies as a function of dose in the absence of a threshold (i.e., hereditary effects or carcinogenesis). The probability and severity of nonstochastic effects vary with dose, and a threshold for the dose exists (i.e., cataract of lens, nonmalignant damage to the skin, cell depletion in the bone marrow causing hematological deficiencies, gonadal cell damage leading to impairment of fertility, or pneumotis and pulmonary fibrosis following lung irradiation) (ICRP 1977; Hobbs and McClellan 1986; UNSCEAR 1988). The prevention of nonstochastic effects is achieved by setting dose-equivalent limits at sufficiently low levels so that no threshold dose is reached, not even after exposure for the whole of a lifetime or for the total period of a working life (ICRP 1977, 1991a, 1991b). Guides for the protection from radiation are also predicated on the effective half-life of each isotope, the critical organ, the fraction

that reaches the critical organ by ingestion and inhalation, and the maximum tolerable whole-body burdens, as judged by radionuclide concentrations in air, water, and diet (Palumbo 1963).

At present, no radiological criteria or standards have been recommended or established for the protection of fish, wildlife, or other natural resources. All radiological criteria now promulgated or proposed are directed toward the protection of human health. It is generally assumed that humans are comparatively radiosensitive and that guides will probably also protect sensitive natural resources (UNSCEAR 1988; ICRP 1991a, 1991b; NCRP 1991; IAEA 1992; Zach et al. 1993), although this needs verification. Numerous radiological criteria now exist for the protection of human health ([Table 32.28](#)). Most authorities agree that some adverse effects to humans are likely under the following conditions:

- >5 mSv whole-body exposure of women during the first 2 months of pregnancy
- >50 mSv whole-body exposure in any single year or >2000 mSv in a lifetime
- An annual inhalation intake by a 60-kg individual — in Bq/kg BW — that exceeds 0.67 ^{232}Th , 3.3 ^{241}Am , 3.3 ^{239}Pu , 16 ^{252}Cf , 33 ^{235}U , 1666 ^{90}Sr , 16,666 ^{60}Co , or 166,666 ^{32}P
- An annual ingestion intake by a 60-kg individual — in Bq/kg BW — that exceeds 3333 ^{129}I , 16,666 ^{125}I , 16,666 ^{131}I , or 66,666 ^{137}Cs
- A total annual intake from all sources — in Bq/kg BW by a 60-kg person — that exceeds 66 ^{210}Pb , 166 ^{210}Po , 333 ^{226}Ra , 666 ^{230}Th , 833 ^{228}Th , or 1333 ^{238}U (see [Table 32.28](#)).

Astronauts between 25 and 55 years of age usually receive an average career dose of 2.0 Sv (1.0 to 3.0 Sv in females; 1.5 to 4.0 Sv in males); theoretically, this may cause a life shortening of 2000 to 3000 days (Wood 1991). Other environmental variables also result in life shortening and include cigarette smoking (2250 days), coal mining (1100 days), and being 30% overweight (1300 days); thus, models that assess the harm of a single variable — such as radiation — on life expectancy must incorporate all known data and their interacting effects (Wood 1991).

Environmental dose-response models and animal epidemiological data are most frequently used to assess the risk from ionizing radiation. In its ideal form, a risk assessment should clearly present the rationale for an estimate of risk and should include the recognition of the roles of assumptions, approximations, data, theories, models, and deductions in arriving at an inference and a discussion of the involved uncertainties (Cothorn et al. 1990). It now seems clear that current risk assessments of ionizing radiation hazards to all living organisms — not just humans — require additional data and reinterpretation of existing data. Specifically, more effort is needed in the following areas:

1. Measurement of concentrations of naturally occurring radionuclides and natural background doses in the environment as a baseline for studies on radiation effects (Templeton et al. 1971)
2. Refinement of models of radionuclide transfer in food chains to aid in the assessment of radioactive releases from nuclear reactors and other point sources, including possible biomagnification by trophic components and turnover rates by receptor organisms (Kitchings et al. 1976)
3. Continuance of protracted exposure studies to measure carcinogenesis in animal and human cell lines and the role of secondary factors — especially chemical agents — in radiation carcinogenesis (Little 1990)
4. Research on radiation-induced recessive lethal mutations — the predominant type of radiation-induced mutation — and dominant mutation systems (Sankaranarayanan 1991c)
5. Initiation of long-term studies to establish sensitive indicators of radiation stress on individuals and communities, including effects on growth and reproduction (Templeton et al. 1971)
6. Clarification of the role of enzymes and proteins in repair of radiation-damaged cellular DNA and of mechanisms of enzymatic reactions leading to altered nucleotide sequences (Hagen 1990)
7. Reinterpretation of low-level chronic irradiation effects on developing embryos under rigorously controlled conditions (Templeton et al. 1971)
8. Resolution of mathematical shape(s) of radiation dose-response curve(s) (Hobbs and McClellan 1986).

Table 32.28 Recommended Radiological Criteria for the Protection of Human Health

Criterion and Other Variables	Concentration or Dose	Reference^a
AIR		
United States; radon-222		
Average	<0.0555 Bq (<1.5 pCi)/L or <55 Bq/m ³	1
Acceptable	<0.148 Bq (<4.0 pCi)/L	1, 2
Allowable emission discharge	<0.74 Bq (<20 pCi)/m ² per sec; should not increase the radon-222 concentration in air at or above any location outside the disposal site by >0.0185 Bq (>0.5 pCi)/L or >18 Bq (>500 pCi)/m ³	3
Unacceptable	>0.185 Bq (>5 pCi)/L	2
ASTRONAUTS		
Age 25–55 years; expected whole-body career dose; females vs. males	1.0–3.0 Sv (100–300 rem) vs. 1.5–4.0 Sv (150–400 rem)	4
Adverse effects expected; lifetime exposure	>2.0 Sv (>200 rem)	4
CANCER RISK AND BIRTH DEFECTS		
Projected 0.04% increase in cancers; 0.01% increase in birth defects	0.11 mSv (0.011 rem) whole-body maximum per year; 0.69 mSv (0.069 rem) whole body over 30 years; or 1.00 mSv (0.1 rem) bone marrow over 30 years	5
Projected 0.18% increase in cancers; 0.07% increase in birth defects	0.51 mSv (0.05 rem) whole-body maximum per year; 3.30 mSv (0.33 rem) whole body over 30 years; or 4.60 mSv (0.46 rem) bone marrow over 30 years	5
Projected 0.92% increase in cancers; 0.38% increase in birth defects	3.03 mSv (0.3 rem) whole-body maximum per year; 19.0 mSv (1.9 rem) whole body over 30 years; or 23.0 mSv (2.3 rem) bone marrow over 30 years	5
Projected 4.4% increase in cancers; 1.8% increase in birth defects	20.1 mSv (2.0 rem) whole-body maximum per year; 91.0 mSv (9.1 rem) whole body over 30 years; or 110.0 mSv (11 rem) bone marrow over 30 years	5
DIET		
All foods; maximum recommended values		
Adults, Italy	600 Bq (16,200 pCi) cesium-134+137/kg fresh weight (FW)	6
Children, Italy	370 Bq (10,000 pCi) cesium-134+137/kg FW	6
Sweden, pre-Chernobyl	300 Bq (8100 pCi) cesium-134+137/kg FW	6
Caribou; muscle; North America	<2260 Bq (<61,000 pCi) cesium-137/kg FW	8
Fish; Great Lakes; muscle	Dose of <0.02 µSv (0.00002 rem)/kg FW fish flesh equivalent to consumers	9
Fish; Sweden	<1500 Bq (<40,500 pCi) cesium-137/kg FW	10
Fraction of ingested dose absorbed; recommended maximum; selected isotopes		
Americium, curium, neptunium, plutonium, thorium	<0.05%	11
Americium, plutonium	<0.1%	12
Californium, and higher mass radionuclides	<0.1%	11
Uranium	<5.0%	11
Milk; maximum values		
Italy	370 Bq (10,000 pCi) cesium-134+137/L	6
Japan	370 Bq (10,000 pCi) cesium-137/L	13
Sweden	300 Bq (8100 pCi) cesium-137/L	14
Meat and fish; Sweden; maximum values	1500 Bq (40,500 pCi) cesium-137/kg FW	14

Table 32.28 (continued) Recommended Radiological Criteria for the Protection of Human Health

Criterion and Other Variables	Concentration or Dose	Reference^a
Reindeer meat, game, animal meat, fish, berries, mushrooms; Sweden; post-Chernobyl; maximum values	1500 Bq (40,500 pCi) cesium-137/kg FW	15
Sheep, muscle	<1000 Bq (<27,000 pCi) cesium-134+137/kg FW	16
Sheep, muscle	<1000 Bq (<27,000 pCi) cesium-137/kg FW	17
DRINKING WATER		
Natural radioactivity; maximum allowed		
Radium-226+228	0.185 Bq (5 pCi)/L	18
Gross alpha	0.555 Bq (15 pCi)/L	18
Artificial radioactivity; maximum allowed		
Gross beta	1.85 Bq (50 pCi)/L	18
Tritium (Hydrogen-3)	740 Bq (20,000 pCi)/L	18
Strontium-90	0.296 Bq (8 pCi)/L	18
Great Lakes; maximum dose to consumers	10 µSv (0.001 rem)/year	9
GENERAL PUBLIC		
Annual effective dose ^b	<1 mSv (<0.1 rem)	19, 29
Cesium-137; total intake		
Sweden	<50,000 Bq (<1,350,000 pCi)/year, equivalent to <1 mSv (<0.1 rem)	15
North America	<300,666 Bq (<8,100,000 pCi)/year	8
United Kingdom	<400,000 Bq (<10,800,000 pCi)/year, equivalent to <5 mSv (0.5 rem)	20
Maximum permissible dose		
Eye lens	<15 mSv (<1.5 rem)/year	19
Skin	<50 mSv (<5 rem)/year	19
Whole body		
Individual, except students and pregnant women	<5 mSv (<0.5 rem)/year	9, 21–23
Students	<1 mSv (<0.1 rem)/year	21
Pregnant women	<5 mSv (<0.5 rem) during the first 2 months of pregnancy	22
Population dose limits, genetic or somatic	<1.7 mSv (<0.17 rem) yearly average	21
GROUNDWATER		
Maximum allowed		
Radium-226+228	0.185 Bq (5 pCi)/L	3
Alpha emitting radionuclides — including radium-226+228, but excluding radon isotopes	0.555 Bq (15 pCi)/L	3
Total beta and gamma radiation	Total annual whole-body dose equivalent, or dose to any internal organ, <0.04 mSv (<0.004 rem), based on individual consumption of 2 L daily of drinking water from a groundwater source	3
RADIOACTIVE WASTES		
Dose limits from spent nuclear fuel or transuranic radioactive wastes		
Whole body	<0.25 mSv (<0.025 rem)/year	3, 24
Thyroid	<0.75 mSv (<0.075 rem)/year	3, 24
Any other critical organ	<0.25 mSv (<0.025 rem)/year	3, 24
Stored for 10,000 years; maximum cumulative release allowed to the accessible environment per 1000 metric tons of heavy metal during storage		
Americium-241	3.7 trillion (T) Bq (100 TpCi)	3
Americium-243	3.7 TBq (100 TpCi)	3

Table 32.28 (continued) Recommended Radiological Criteria for the Protection of Human Health

Criterion and Other Variables	Concentration or Dose	Reference^a
Any alpha emitter with physical half-life >20 years	3.7 TBq (100 TpCi)	3
Any non-alpha emitter radionuclide with physical half-life >20 years	37.0 TBq (1000 TpCi)	3
Carbon-14	3.7 TBq (100 TpCi)	3
Cesium-135	37.0 TBq (1000 TpCi)	3
Cesium-137	37.0 TBq (1000 TpCi)	3
Iodine-129	3.7 TBq (100 TpCi)	3
Neptunium-237	3.7 TBq (100 TpCi)	3
Plutonium-238	3.7 TBq (100 TpCi)	3
Plutonium-239	3.7 TBq (100 TpCi)	3
Plutonium-240	3.7 TBq (100 TpCi)	3
Plutonium-242	3.7 TBq (100 TpCi)	3
Radium-226	3.7 TBq (100 TpCi)	3
Strontium-90	37.0 TBq (1000 TpCi)	3
Thorium-230	0.37 TBq (10 TpCi)	3
Thorium-232	0.37 TBq (10 TpCi)	3
Tin-126	37.0 TBq (1000 TpCi)	3
Uranium-233	3.7 TBq (100 TpCi)	3
Uranium-234	3.7 TBq (100 TpCi)	3
Uranium-235	3.7 TBq (100 TpCi)	3
Uranium-236	3.7 TBq (100 TpCi)	3
Uranium-238	3.7 TBq (100 TpCi)	3
Uranium by-product materials; maximum discharge rates allowed into water		
Radium-226+228	0.185 Bq (5 pCi)/L	24
Gross alpha particle activity, excluding radon and uranium isotopes	0.555 Bq (15 pCi)/L	24
Wastes from uranium fuel cycle entering the environment per billion watts/year of electrical energy produced by the fuel cycle; maximum allowed		
Krypton-85	1.85 TBq (50 TpCi)	24
Iodine-129	185 million Bq (5 billion pCi)	24
Plutonium-239 and other alpha emitting transuranics with Tb 1/2 >1 year	2.69 million Bq (72.6 million pCi)	24

OCCUPATIONAL WORKERS**Annual Limit of Intake^b**

Inhalation vs. oral		
Americium-241	200 Bq (5400 pCi) vs. 50,000 Bq	25
Californium-252	1000 Bq (27,000 pCi) vs. 200,000 Bq	25
Cesium-137	6 million Bq (162 million pCi) vs. 4 million Bq	25
Cobalt-60	1 million Bq (27 million pCi) vs. 7 million Bq	25
Hydrogen-3	3 billion Bq (81 billion pCi) vs. 3 billion Bq	25
Iodine-125	2 million Bq (54 million pCi) vs. 1 million Bq	25
Iodine-129	300,000 Bq (8,100,000 pCi) vs. 200,000 Bq	25
Iodine-131	2 million Bq (54 million pCi) vs. 1 million Bq	25
Phosphorus-32	10 million Bq (270 million pCi) vs. 20 million Bq	25
Plutonium-239	200 Bq (5400 pCi) vs. 200,000 Bq	25
Polonium-210	20,000 Bq (540,000 pCi) vs. 100,000 Bq	25
Radium-226	20,000 Bq (540,000 pCi) vs. 70,000 Bq	25
Strontium-90	0.1 million Bq (2.7 million pCi) vs. 1.0 million Bq	25
Thorium-232	40 Bq (1000 pCi) vs. 30,000 Bq	25
Uranium-235	2000 Bq (54,000 pCi) vs. 500,000 Bq	25
Total intake from all sources; Canada		
Lead-210	<4000 Bq (<108,000 pCi)	26, 27
Polonium-210	<10,000 Bq (<270,000 pCi)	26, 27

Table 32.28 (continued) Recommended Radiological Criteria for the Protection of Human Health

Criterion and Other Variables	Concentration or Dose	Reference ^a
Radium-226	<20,000 Bq (<540,000 pCi)	26, 27
Thorium-228	<50,000 Bq (<1.35 million pCi)	26, 27
Thorium-230	<40,000 Bq (<1.08 million pCi)	26, 27
Thorium-232	<7000 Bq (<189,000 pCi)	26, 27
Uranium-238	<80,000 Bq (<2.1 million pCi)	26, 27
Effective dose ^b		
Average annual	20 mSv (2 rem), not to exceed 50 mSv (5 rem)	28
5-year maximum	<100 mSv (<10 rem), not to exceed 50 mSv (5 rem) in any year	28
Maximum permissible dose		
Whole body	50 mSv (5 rem) in any one year	21, 22, 29
Long-term accumulation to age N years	(N–18) × 50 mSv (5 rem)	21
Skin	150 mSv (15 rem) in any one year	21
Hands	750 mSv (75 rem) in any one year; not to exceed 250 mSv (25 rem) in 3 months	21
Forearms	300 mSv (30 rem) in any one year; not to exceed 100 mSv (10 rem) in 3 months	21
Skin and hands	500 mSv (50 rem) annually	19, 28
Other organs	150 mSv (15 rem) in any one year; not to exceed 50 mSv (5 rem) in 3 months	21
Pregnant women	5 mSv (0.5 rem) in gestation period	21
Eye lens	150 mSv (15 rem) annually	19, 28
SOIL		
Radium-226; maximum allowed	<185 Bq (<5000 pCi)/kg over background in top 15 cm; <555 Bq (<15,000 pCi)/kg in soils at depth >15 cm	3
Total gamma; maximum allowed	<0.2 µSv (<0.00002 rem)/h over background	3

^a 1, Gangopadhyay and Majumdar 1990; 2, Oge and Dickson 1990; 3, United States Code of Federal Regulations (USCFR) 1990; 4, Wood 1991; 5, Bair et al. 1979; 6, Battiston et al. 1991; 7, Andersson et al. 1990; 8, Allaye-Chan et al. 1990; 9, Joshi 1991; 10, Hakanson and Andersson 1992; 11, Harrison 1991; 12, Gilbert et al. 1989; 13, Aii et al. 1990; 14, Johanson et al. 1989; 15, Johanson 1990; 16, Moss et al. 1989; 17, Crout et al. 1991; 18, Rose et al. 1990; 19, International Commission on Radiological Protection (ICRP) 1991a; 20, Lowe and Horrill 1991; 21, Hobbs and McClellan 1986; 22, ICRP 1977; 23, Gray et al. 1989; 24, USCFR 1991; 25, Kiefer 1990; 26, Clulow et al. 1991; 27, Clulow et al. 1992; 28, ICRP 1991b; 29, National Council on Radiation Protection and Measurements (NCRP) 1991.

^b The Annual Limit of Intake (ALI) for any radionuclide is obtained by dividing the annual average effective dose limit (20 mSv) by the committed effective dose (E) resulting from the intake of 1 Bq of that radionuclide. ALI data for individual radionuclides are given in ICRP (1991b).

32.9 SUMMARY

This chapter is a selective review and synthesis of the voluminous technical literature on radiation and radionuclides in the environment, notably on fish, wildlife, invertebrates, and other natural resources. The subtopics include the physical and biological properties of the electromagnetic spectrum and of charged particles; radiation sources and uses; concentrations of radionuclides in field collections of abiotic materials and living organisms; lethal and sublethal effects, including effects on survival, growth, reproduction, behavior, metabolism, carcinogenicity, and mutagenicity; a synopsis of two case histories involving massive releases of radionuclides into the biosphere (military weapons tests at the Pacific Proving Grounds, and the Chernobyl nuclear reactor accident); current radiological criteria proposed for the protection of human health and natural resources; and recommendations for additional research. A glossary is included.

Nuclear explosions and nuclear power production are the major sources of human radioactivity in the environment. Other sources include radionuclide use in medicine, industry, agriculture,

education, and production; transport and disposal from these activities present opportunities for wastes to enter the environment. Dispersion of radioactive materials is governed by a variety of biogeochemical factors, including winds, water currents, and biological vectors. Living organisms normally receive most of their external exposure to radiation from naturally occurring electromagnetic waves and their internal exposure from naturally occurring radionuclides such as potassium-40. Radiation exposure doses from natural sources of radiation are significantly modified by altitude, amount and type of radionuclides in the immediate vicinity, and route of exposure.

Radionuclide concentrations in representative field collections of biota tend to be elevated in the vicinity of nuclear fuel reprocessing, nuclear power production, and nuclear waste facilities; in locations receiving radioactive fallout from nuclear accidents and atmospheric nuclear tests; and near sites of repeated nuclear detonations. Radionuclide concentrations in field collections of living organisms vary significantly with organism age, size, sex, tissue, diet, and metabolism; season of collection; proximity to point source; and other biological, chemical, and physical variables. To date, no extinction of any animal population has been linked to high background concentrations of radioactivity.

The accident at the Chernobyl, Ukraine, nuclear reactor on April 26, 1986, contaminated much of the northern hemisphere, especially Europe, by releasing large amounts of radiocesium-137 and other radionuclides into the environment. In the immediate vicinity of Chernobyl; at least 30 people died, more than 115,000 others were evacuated, and the consumption of locally produced milk and other foods was banned because of radiocontamination. The most sensitive local ecosystems were the soil fauna and pine forest communities. Elsewhere, fallout from Chernobyl measurably contaminated freshwater, marine, and terrestrial ecosystems, including flesh and milk of domestic livestock. Reindeer (*Rangifer tarandus*) calves in Norway showed an increasing frequency of chromosomal aberrations that seemed to correlate with cesium-137 tissue concentrations; tissue concentrations, in turn, were related to cesium-137 in lichens, an efficient absorber of airborne particles containing radiocesium and the main food source of reindeer during winter. A pattern similar to that of reindeer was documented in moose (*Alces*) in Scandinavia.

A dose- and dose-rate dependent radiation effect on growth, survival, organ development, mutagenicity, fatal neoplasms, and other parameters exists for almost all organisms tested under laboratory conditions. Some discoveries suggest that low acute exposures of ionizing radiation may extend the life-span of certain species, although adverse genetic effects may occur under these conditions. In living organisms, the sensitivity to radiation is governed by ontogeny and phylogeny. Thus, rapidly dividing cells, characteristic of embryos and fetuses, are most radiosensitive and evolutionarily advanced organisms such as mammals are more radiosensitive than primitive organisms. Between species within each taxonomic grouping are large variations in sensitivity to acute and chronic exposures of ionizing radiation and in ability to retain selected radionuclides; these processes are modified by numerous biological and abiotic variables.

Radiosensitive terrestrial plants are adversely affected at single exposures of 0.5 to 1.0 Gy and at chronic daily exposures of 0.2 to 0.65 Gy. Terrestrial insects are comparatively resistant to ionizing radiation; some species show growth stimulation and development at acute doses of 2 Gy — a demonstrably harmful dose for many species of vertebrates. Among aquatic organisms, the developing eggs and young of freshwater fish are among the most sensitive tested organisms; death was observed at acute doses of 0.3 to 0.6 Gy and adverse effects on physiology and metabolism at chronic daily exposure rates of 0.01 Gy. The ability of aquatic organisms to concentrate radionuclides from the medium varies substantially with ecosystem, trophic level, radionuclide, proximity to radiation point source, and many other biological, chemical, and physical modifiers. In amphibians, radiation adversely affects limb regeneration, alters DNA metabolism, causes sterility, and increases the frequency of chromosomal aberrations. Mortality patterns in some species of amphibians begin to stabilize about 200 days after exposure to a single acute dose of ionizing radiation and cannot be evaluated satisfactorily in the typical 30-day postexposure period. In birds,

adverse effects on growth were noted at chronic daily exposures as low as 0.9 to 1.0 Gy, and on survival and metabolism at single exposures to 2.1 Gy. Genotoxic effects were associated with whole-body loadings of 2520 becquerels (Bq) of cesium-137/kg in mallards (*Anas platyrhynchos*). The radionuclide retention in birds was modified by sex, season, and reproductive state. In mammals, embryos and fetuses of sensitive species were adversely affected at acute doses of 0.011 to 0.022 Gy. Humans exposed as fetuses to 0.18 to 0.55 Gy scored significantly lower on tests of intelligence.

No radiological criteria now exist for the protection of fish, wildlife, or other sensitive natural resources. All current guides for protection from radiation target human health and are predicated on the assumption that protection of comparatively radiosensitive humans confers a high degree of protection to other life forms. Most authorities agree that significant harmful effects to humans occur under the following conditions:

- Exposure of the whole body of women during the first 2 months of pregnancy to >5 millisieverts (mSv)
- Exposure of the whole body to >50 mSv in any single year or to >2000 mSv in a lifetime
- Annual inhalation intake by a 60-kg individual, in Bq/kg body weight (BW), of more than 0.7 of thorium-232, 3.3 of americium-241, 3.3 of plutonium-239, 16 of californium-252, 33 of uranium-235, 1670 of strontium-90, 16,670 of cobalt-60, or 166,670 of phosphorus-32
- Annual ingestion intake by a 60-kg individual, in Bq/kg BW, of more than 3330 of iodine-129, 16,670 of iodine-125, 16,670 of iodine-131, or 66,670 of cesium-137
- Total annual intake, in Bq/kg BW, from all sources by a 60-kg person exceeds 66 of lead-210, 166 of polonium-210, 333 of radium-226, 670 of thorium-230, 830 of thorium-228, or 1330 of uranium-238.

Current risk assessments of ionizing radiation hazards to living organisms require additional data and reinterpretation of existing data. Specifically, more effort seems needed in eight areas:

1. Establishing a baseline for studies on radiation through measurement of naturally occurring radionuclides and natural background radiation doses
2. Refining radionuclide food-chain transfer models
3. Measuring the role of chemical agents in radiation-induced carcinogenesis
4. Accelerating research on radiation-induced lethal mutations
5. Initiating long-term studies to establish sensitive indicators of radiation stress on individuals and ecosystems
6. Clarifying the role of enzymes and proteins in repair of radiation-damaged cellular DNA
7. Reinterpreting embryotoxic effects of low level chronic irradiation
8. Resolving the mathematical shapes of radiation dose-response curves.

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32.11 GLOSSARY*

- Actinides:** Elements of atomic numbers 89 to 103 (Ac, Th, Pa, U, Np, Pu, Am, Cm, Bk, Cf, Es, Fm, Md, No, Lw).
- Activity:** The activity of a radioactive material is the number of nuclear disintegrations per unit time. Up to 1977, the accepted unit of activity was the curie (Ci), equivalent to 37 billion disintegrations/s, a number that approximated the activity of 1 g radium-226. The present unit of activity is the becquerel (Bq), equivalent to 1 disintegration/s.
- Alpha (α) particles:** An α particle is composed of two protons and two neutrons, with a charge of +2; essentially, it is a helium nucleus without orbital electrons. Alpha particles usually originate from the nuclear decay of radionuclides of atomic number >82, and are detected in samples containing U, Th, or Ra. Alpha particles react strongly with matter and consequently produce large numbers of ions per unit

length of their paths. As a result, they are not very penetrating and will traverse only a few centimeters of air. Alpha particles are unable to penetrate clothing or the outer layer of skin; however, when internally deposited, α particles are often more damaging than most other types of radiations because comparatively large amounts of energy are transferred within a very small volume of tissue. Alpha particle absorption involves ionization and orbital electron excitation. Ionization occurs whenever the α particle is sufficiently near an electron to pull it from its orbit. The α particle also loses kinetic energy by exciting orbital electrons with interactions that are insufficient to cause ionization.

Atom: The smallest part of an element that has all the properties of that element. An atom consists of one or more protons and neutrons (in the nucleus) and one or more electrons.

Atomic number: The number of electrons outside the nucleus of a neutral (nonionized) atom and the number of protons in the nucleus.

Becquerel (Bq): The presently accepted unit of activity is the becquerel, equivalent to 1 disintegration/s. About 0.037 Bq = 1 picocurie.

Beta (β) particles: Beta particles are electrons that are spontaneously ejected from the nuclei of radioactive atoms during the decay process. They may either be positively or negatively charged. A positively charged beta (β^+), called a *positron*, is less frequently encountered than its negative counterpart, the *negatron* (β^-). The *neutrino*, a small particle, accompanies beta emission. The neutrino has very little mass and is electrically neutral; however, neutrinos conduct a variable part of the energy of transformation and account for the variability in kinetic energies of beta particles emitted from a given radionuclide. Positrons (β^+) are emitted by many of the naturally and artificially produced radionuclides; they are considerably more penetrating than α particles, but less penetrating than X-rays and γ rays. Beta particles interact with other electrons as well as nuclei in the travel medium. The ultimate fate of a beta particle depends on its charge. Negatrons, after their kinetic energy is spent, combine with a positively charged ion or become free electrons. Positrons also dissipate kinetic energy through ionization and excitation; the collision of positrons and electrons causes annihilation and release of energy equal to the sums of their particle masses.

Breeder reactor: A nuclear chain reactor in which transmutation produces a greater number of fissionable atoms than the number of consumed parent atoms.

Cosmic rays: Highly penetrating radiations that originate in outer space.

Curie (Ci): The Ci is equal to that quantity of radioactive material producing 37 billion nuclear transformations/s. One millicurie (mCi) = 0.001 Ci; 1 microcurie (μ Ci) = 1 millionth of a Ci; 1 picocurie (pCi) = 1 millionth of a millionth Ci = 0.037 disintegrations/s. About 27 pCi = 1 becquerel (Bq).

Decay: Diminution of a radioactive substance because of nuclear emission of α or β particles or of γ rays.

Decay product: A nuclide resulting from the radioactive disintegration of a radionuclide and found as the result of successive transformations in a radioactive series. A decay product may be either radioactive or stable.

Effective dose equivalent: The weighted sum, in sieverts (Sv), of the radiation dose equivalents in the most radiosensitive organs and tissues, including gonads, active bone marrow, bone surface cells, and the lung.

Electron: An electron is a negatively charged particle with a diameter of 10^{-12} cm. Every atom consists of one nucleus and one or more electrons. Cathode rays and negatrons are electrons.

Electron-volt (eV): Energy acquired by any charged particle that carries unit electronic charge when it falls through a potential difference of 1 volt. One eV = 1.602×10^{-19} joule.

Fission: The splitting of an atomic nucleus into two fragments that usually releases neutrons and γ rays. Fission may occur spontaneously or may be induced by capture of bombarding particles. Primary fission products usually decay by β particle emission to radioactive daughter products. The chain reaction that may result in controlled burning of nuclear fuel or in an uncontrolled nuclear weapons explosion results from the release of 2 or 3 neutrons/fission. Neutrons cause additional fissile nuclei in the vicinity to fission, producing still more neutrons, in turn producing still more fissions. The speed of the chain reaction is governed by the density and geometry of fissile nuclei and of materials that slow or capture the neutrons. In nuclear reactors, neutron-absorbing rods are inserted to various depths into the reactor core. A nuclear explosion is not physically possible in a reactor because of fuel density, geometry, and other factors.

Fusion: A nuclear reaction in which smaller atomic nuclei or particles combine to form larger ones with the release of energy from mass transformation.

Gamma (γ) rays: Gamma rays have electromagnetic wave energy that is similar to but higher than the energy of X-rays. Gamma rays are highly penetrating, being able to traverse several cm of lead. See **Photons**.

Genetically significant dose (GSD): A radiation dose that, if received by every member of the population, would produce the same total genetic injury to the population as the actual doses received by the various individuals.

Gray (Gy): $1 \text{ Gy} = 1 \text{ joule/kg} = 100 \text{ rad}$.

Half-life: The average time in which half the atoms in a sample of a radioactive element decay.

Hertz (Hz): A measure of frequency equal to 1 cycle/s.

Indirectly ionizing particles: Uncharged particles such as neutrons or photons that directly liberate ionizing particles or initiate nuclear transformations.

Ion: An atomic particle, atom, or chemical radical with either a negative or positive electric charge.

Ionization: The process by which neutral atoms become either positively or negatively electrically charged by the loss or gain of electrons.

Isomer: One of two or more radionuclides having the same mass number and the same atomic number, but with different energies and radioactive properties for measurable durations.

Isotope: One of several radionuclides of the same element (i.e., with the same number of protons in their nuclei) with different numbers of neutrons and different energy contents. A single element may have many isotopes. Uranium, for example, may appear naturally as ^{234}U (142 neutrons), ^{235}U (143 neutrons), or ^{238}U (146 neutrons); however, each uranium isotope has 92 protons.

Joule (J): $1 \text{ J} = 10^7 \text{ ergs}$.

Latent period: Period of seeming inactivity between time of exposure of tissue to an acute radiation dose and the onset of the final stage of radiation sickness.

Linear energy transfer (LET): A function of the capacity of the radiation to produce ionization. LET is the rate at which charged particles transfer their energies to the atoms in a medium and a function of the energy and velocity of the charged particle. See **Radiation dose**.

Linear hypothesis: The assumption that any radiation causes biological damage in direct proportion of dose to effect.

Mass number: The total number of neutrons and protons in the nucleus of the element, and equal to the sum of the atomic number and the number of neutrons.

Meson: Particles of mass that are intermediate between the masses of the electron and proton.

Neutrinos: Neutrinos and antineutrinos are formed whenever a positron particle is created in a radioactive decay; they are highly penetrating.

Neutrons: Neutrons are electrically neutral particles that consist of an electron and a proton and are not affected by the electrostatic forces of the atom's nucleus or orbital electrons. Because they have no charge, neutrons readily penetrate the atom and may cause a nuclear transformation. Neutrons are produced in the atmosphere by cosmic ray interactions and combine with nitrogen and other gases to form carbon-14, tritium, and other radionuclides. A free neutron has a lifetime of about 19 minutes, after which it spontaneously decays to a proton, a β particle, and a neutrino. A high-energy neutron that encounters biological material is apt to collide with a proton with sufficient force to dislodge the proton from the molecule. The recoil proton may then have sufficient energy to cause secondary damage through ionization and excitation of atoms and molecules along its path.

Nucleus: The dense central core of the atom in which most of the mass and all of the positive charge is concentrated. The charge on the nucleus distinguishes one element from another.

Photons: X-rays and gamma (γ) rays, collectively termed photons, are electromagnetic waves with shorter wavelengths than other members of the electromagnetic spectrum such as visible radiation, infrared radiation, and radiowaves. X- and γ photons have identical properties, behavior, and effects. Gamma rays originate from atomic nuclei, but X-rays arise from the electron shells. All photons travel at the speed of light, but energy is inversely proportional to wavelength. The energy of a photon directly influences its ability to penetrate matter. Many types of nuclear transformations are accompanied by γ ray emission. For example, α and β decay of many radionuclides is frequently accompanied by γ photons. When a parent radionuclide decays to a daughter nuclide, the nucleus of the daughter frequently contains excess energy and is unstable; stability is usually achieved through release of one or more γ photons, a process called *isometric transition*. The daughter nucleus decays from one energy state to another without a change in atomic number or weight.

The most probable fate of a photon with an energy higher than the binding energy of an encountered electron is photoelectric absorption, in which the photon transfers its energy to the electron and photon existence ends. As with ionization from any process, secondary radiations initiated by the photoelectron produce additional excitation of orbital electrons.

Planck's constant (**h):** A universal constant of nature that relates the energy of a photon of radiation to the frequency of the emitting oscillator. Its numerical value is about 6.626×10^{-27} ergs/s.

Positron: A positively charged particle of mass equal to an electron. Positrons are created either by the radioactive decay of unstable nuclei or by collision with photons.

Proton: A positively charged subatomic particle with a mass of 1.67252×10^{-24} g that is slightly less than the mass of a neutron but about 1836 times greater than the mass of an electron. Protons are identical to hydrogen nuclei; their charge and mass make them potent ionizers.

Radiation: The emission and propagation of energy through space or through a material medium in the form of waves. The term also includes subatomic particles, such as α , β , and cosmic rays and electromagnetic radiation.

Radiation absorbed dose (rad): Radiation-induced damage to biological tissue results from the absorption of energy in or around the tissue. The amount of energy absorbed in a given volume of tissue is related to the types and numbers of radiations and the interactions between radiations and tissue atoms and molecules. The fundamental unit of the radiation absorbed dose is the rad; 1 rad = 100 erg (absorbed)/g material. In the latest nomenclature, 100 rad = 1 gray (Gy).

Radiation dose: The term "radiation dose" can mean several things, including absorbed dose, dose equivalent, or effective dose equivalent. The absorbed dose of radiation is the imparted energy per unit mass of the irradiated material. Until 1977, the rad was the unit of absorbed dose, wherein 1 rad = 0.01 Joule/kg. The present unit of absorbed dose is the gray (Gy), equivalent to 1 Joule/kg. Thus, 1 rad = 0.01 Joule/kg = 0.01 Gy. Different types of radiation have different Relative Biological Effectiveness (RBE). The RBE of one type of radiation in relation to a reference type of radiation (usually X or γ) is the inverse ratio of the absorbed doses of the two radiations needed to cause the same degree of the biological effect for which the RBE is given. Regulatory agencies have recommended certain values of RBE for radiation protection, and absorbed doses of various radiations are multiplied by these values to arrive at radioprotective doses. The unit of this weighted absorbed dose is the roentgen equivalent man (rem). The dose equivalent is the product of the absorbed dose and a quality factor (Q), and its unit is the rem. The quality factor is a function of the capacity to produce ionization, expressed as the linear energy transfer (LET). A Q value is assigned to each type of radiation: 1 to X-rays, γ rays, and β particles; 10 to fast neutrons; and 20 to α particles and heavy particles. The new unit of the effective dose equivalent is the sievert (Sv), replacing rem, where 1 Sv = 100 rem. In addition to absorbed dose and dose equivalent, there is also the exposure. Exposure is the total electrical charge of ions of one sign produced in air by electrons liberated by X- or gamma rays per unit mass of irradiated air. The unit of exposure is Coulomb/kg, but the old unit, the roentgen (R) is still in use. One roentgen = 2.58×10^{-4} Coulomb/kg.

Radioactivity: The process of spontaneous disintegration by a parent radionuclide, which releases one or more radiations and forms a daughter nuclide. When half the radioactivity remains, that time interval is designated the half-life (T_b 1/2). The T_b 1/2 value gives some insight into the behavior of a radionuclide and into its potential hazards.

Radionuclide: An atom that is distinguished by its nucleus composition (number of protons, number of neutrons, energy content), atomic number, mass number, and atomic mass.

Relative biological effectiveness (RBE): The biological effectiveness of any type of ionizing radiation in producing a specific damage (i.e., leukemia, anemia, carcinogenicity). See **Radiation dose**.

Roentgen (R): $1 R = 2.58 \times 10^{-4}$ Coulombs/kg air = production by X- or γ rays of one electrostatic unit of charge per cm³ of dry air at 0°C and 760 mmHg = 0.87 rad in air.

Roentgen equivalent man (rem): The amount of ionizing radiation of any type that produces the same damage to humans as 1 roentgen of radiation. One rem = 1 roentgen equivalent physical (rep)/relative biological effectiveness (RBE). In the latest nomenclature, 100 rem = 1 Sievert (Sv).

Roentgen equivalent physical (rep): One rep is equivalent to the amount of ionizing radiation of any type that results in the absorption of energy of 93 ergs/g, and is approximately equal to 1 roentgen of X-radiation in soft tissue.

Shell: Extranuclear electrons are arranged in orbits at various distances from the nucleus in a series of concentric spheres called shells. In order of increasing distance from the nucleus, the shells are designated the K, L, M, N, O, P, and Q shells; the number of electrons that each shell can contain is limited.

Sievert (Sv): New unit of dose equivalent. One Sv = 100 rem = 1 J/kg. See **Radiation dose**.

Specific activity: The ratio between activity (in number of disintegrations/min) and the mass (in grams) of material giving rise to the activity. Biological hazards of radionuclides are directly related to their specific activity and are expressed in Bq/kg mass.

Threshold hypothesis: A radiation-dose-consequence hypothesis that holds that biological radiation effects will occur only above some minimum dose.

Transmutation: A nuclear change that produces a new element from an old one.

Transuranic elements: Elements of atomic number >92. All are radioactive and produced artificially; all are members of the actinide group.

X-rays: See **Photons**.

*From Whicker and Schultz 1982a; League of Women Voters (LWV) 1985; Weast 1985; Hobbs and McClellan 1986; United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1988; U.S. Code of Federal Regulations (USCFR) 1990; Eisler 1994.

CHAPTER 33

Cumulative Index to Chemicals and Species

33.1 INTRODUCTION

Indices are presented of biologically active compounds or substances, and common and scientific names of all living species listed in the three-volume *Handbook of Chemical Risk Assessment* series.

33.2 INDEX TO CHEMICALS

All chemicals, chemical trade names, and other substances with known biological properties listed in the *Handbook of Chemical Risk Assessment* series — a total of about 1600 — are presented in [Table 33.1](#).

33.3 INDEX TO SPECIES

Taxonomic nomenclatures for plants and animals are under constant revision. In the *Handbook of Chemical Risk Assessment* series, the author elected to conform as much as possible to the systems and spellings used by Scott and Wasser (1980) for plants, Swain and Swain (1948) for insects, Turgeon et al. (1988) for aquatic molluscs, Williams et al. (1989) for decapod crustaceans, Pratt (1935) and Hyman (1940, 1951a, 1951b, 1955) for miscellaneous invertebrates, Robins et al. (1991) for fishes, Ditmars (1966) for reptiles, Edwards (1974) and Howard and Moore (1991) for birds, and Nowak and Paradiso (1983) for mammals. Individual species are arranged alphabetically by scientific and common names ([Table 33.2](#)). In total, about 2300 species of animals and plants were cited, of which only 23 (1.0%) were listed in at least 20 chapters. The most widely cited species include:

- One species of plant (corn, *Zea mays*)
- Two species of invertebrates (freshwater crustacean, *Daphnia magna*; American oyster, *Crassostrea virginica*)
- Seven species of teleosts (channel catfish, *Ictalurus punctatus*; bluegill, *Lepomis macrochirus*; coho salmon, *Oncorhynchus kisutch*; rainbow trout, *Oncorhynchus mykiss*; fathead minnow, *Pimephales promelas*; brook trout, *Salvelinus fontinalis*; lake trout, *Salvelinus namaycush*)

- Three species of birds (mallard, *Anas platyrhynchos*; domestic chicken, *Gallus* sp.; Japanese quail, *Coturnix japonica*)
- Ten species of mammals (cow, *Bos* spp.; domestic dog, *Canis familiaris*; guinea pig, *Cavia* spp.; domestic cat, *Felis domesticus*; human, *Homo sapiens*; hamster, *Cricetus* spp.; domestic mouse, *Mus* spp.; domestic sheep, *Ovis aries*; laboratory white rat, *Rattus* spp.; domestic pig, *Sus* spp.).

It is probable that these species are not representative of unusually sensitive or endangered species, but they can be considered appropriate sentinel organisms for many species of free-living wildlife.

33.4 SUMMARY

An index is provided to the common and scientific names of approximately 2300 biological species listed in the *Handbook of Chemical Risk Assessment* series. A similar index is shown for the approximately 1600 chemicals, chemical trade names, and other substances with known biological properties.

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Table 33.1 Chemical and Trade Names of Substances Listed in the *Handbook of Chemical Risk Assessment Series*

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