Environmental Engineering

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Learning Objectives

- describe toxicological pathways relevant to chemical exposures;
- compare and contrast acute and chronic exposures;
- develop dose-response relationships that can be used to define the relative toxicities of different chemicals;
- determine LOAEL, NOAEL, and RfD values, based upon a dose-response curve for non-carcinogens;
- compare and contrast common source and propagated disease epidemics;
- differentiate between cross-sectional, case-control, and cohor t studies;
- explain how the different public health measures for control of infectious disease are employed;
- understand how the 13 different factors responsible for disease dissemination collectively affect disease emergence and reemergence.

11.1 Introduction

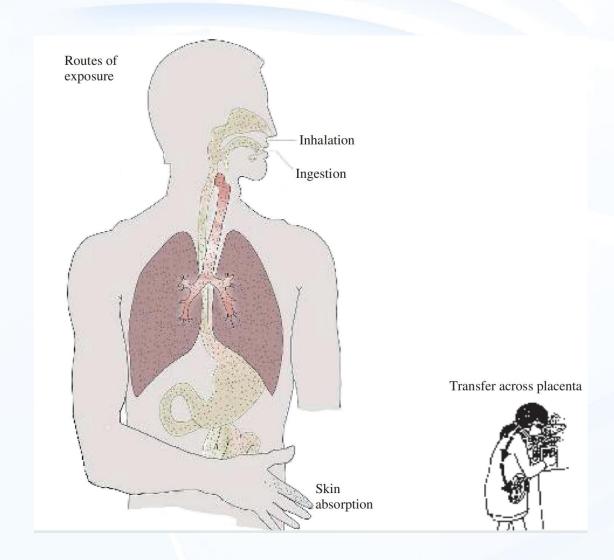
• Environmental public health is concerned with the human and ecological consequences of exposure to potentially harmful physical, thermal, chemical, or biological constituents of manmade and natural environments.

Table II.I Physical, thermal, chemical, and biological constituents of natural and anthropogenic environments that may be potentially harmful.

Physical	Thermal	Chemical	Biological
Explosives	Excess heat	Pesticides	Infectious bacteria
Corrosives	Excess cold	Toxins produced by biological organisms	Infectious virus
Oxidants		Pharmaceuticals	Infectious protozoa
		Disinfection by-products	Infectious fungi
			Infectious helminths

11.1 Introduction

• Chemical and biological exposures can occur via ingestion摄入 (eating and/or drinking), inhalation吸入 (breathing), dermal absorption皮肤吸收 (through the skin), as well as placental transfer in utero胎盘吸收.



11.1 Introduction

- For the purposes of this chapter, we define disease as any condition that impairs the normal function of an organism. To comprehend diseases and the mechanisms by which they are spread, it is necessary to understand two complementary fields:
- 1 **Toxicology**毒理学 the study of the adverse effects of biological and chemical agents on living organisms.
- 2 **Epidemiology** 流行病学 the investigative methodology used to study the nature, cause, control, and determinants of disease transmission and distribution.
- These two fields work together, with toxicology focused on developing **dose-response relationships** and studying mechanisms of action following exposure to toxic substances, while epidemiology is concerned with the occurrence and etiology of disease.

11.2 Toxicology

- Paracelsus, a Swiss chemist and physician in the late 1400s and early 1500s, is widely attributed to have stated: "All things are poison and nothing is without poison; only the dose makes a thing not a poison."
- Whether it be table salt (NaCl) or sodium cyanide (NaCN), can be considered a poison if it is administered in a dose sufficient to produce a toxic effect. For something relatively innocuous, such as table salt, the lethal dose necessary to kill 50% of the adult humans exposed to it (defined as the LD₅₀ 半数致死剂量) is approximately 2,400 mg/kg, while formore highly toxic sodium cyanide, the LD₅₀ is much lower at 10 mg/kg. For chemicals such as table salt and sodium cyanide, comparisons of LD₅₀ values or other toxicological endpoints provide a straightforward mechanism to relate the potential hazards associated with a particular material.

11.2 Toxicology

- Toxicology is dedicated to the quantitative evaluation of the lethal and sub-lethal effects of exposure to biological and chemical agents. In environmental systems, we generally deal with chronic low-dose exposures over extended periods of time. However, acute high-dose exposures can occur as a result of industrial accidents and work-place activities. Acute responses occur within a short period of time after a single exposure to a biological or chemical agent, while chronic responses occur as a result of prolonged exposure over months or years.
- A poison is any biological or chemical agent that can elicit a deleterious response in a biological system.
- A toxicant is a toxic substance produced by anthropogenic activities, while a toxin is a toxic substance produced by living organisms

11.2 Toxicology

• Toxicologists classify toxic substances using a number of hierarchies that are based upon chemical class, the exposure route, or the organ systems affected by a particular substance.

• The third classification system, and the one generally preferred by toxicologists, categorizes toxic

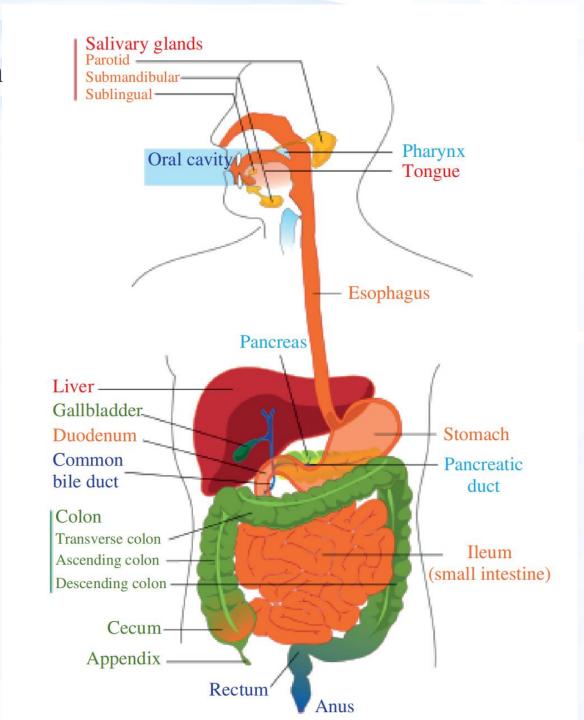
substances based upon their target organs.

 Table 11.3
 Organ systems affected by toxic substances.

Classification	Target organ		Example toxic substances
hepatotoxins	liver	Transport of toxic substances by the bloodstream enables the liver to be directly damaged. As the function of the liver is to metabolize materials, it is potentially subject to attack not only by the substance itself, but also by toxic metabolites produced by the liver.	Carbon tetrachloride, chloroform, trichloroethylene, DDT, heavy metals
nephrotoxins	kidney	The primary function of the kidneys is to filter blood, such that wastes are removed and ultimately excreted in urine. Toxic substances that attack the kidneys can alter the flow of urine and cause severe poisoning, due to the buildup of the body's waste products.	Heavy metals, chlorinated hydrocarbons
neurotoxins	nervous system	Neurotoxins act on nerve cells and typically do so by interacting with and affecting membrane proteins.	Animal venoms, saxitoxin, botulinum toxin
hematotoxins	blood system	Some hematotoxins alter the ability of the body to form the platelets necessary for blood clotting. Other hematotoxins affect the ability of blood to transport oxygen.	Carbon monoxide, nitrate

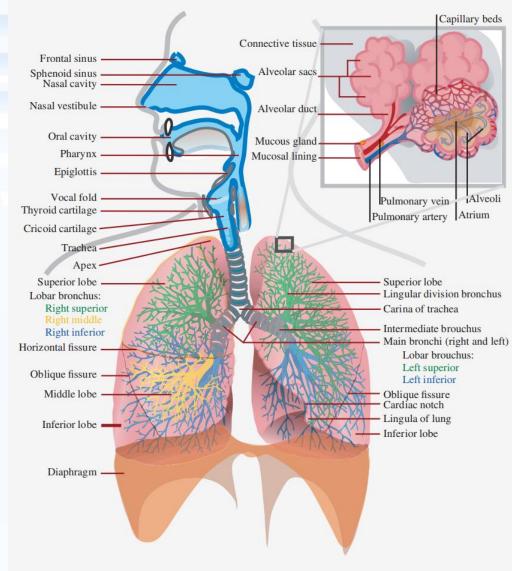
- 11.2 Toxicology
- 11.2.1 Exposure
- Exposures to toxic substances occur via **ingestion** (eating and/or drinking), **inhalation** (breathing), **dermal absorption** (through the skin), as well as placental **transfer in utero**.
- Depending upon the chemical nature of the substance, it can be stored internally in lipids, eliminated from the body via excretion, or transformed into a different material.
- Metabolic breakdown of toxic substances generally produces metabolites with lower toxicity than the starting material; however, in some cases, more toxic byproducts are produced.

- 11.2 Toxicology
- 11.2.1 Exposure
- 11.2.1.1 Ingestion 摄入
- The human gastrointestinal tract extends from the mouth to the anus and incorporates the mouth, pharynx, esophagus, stomach, small intestine, large intestine, and anus.
- The majority of nutrient and toxic substance absorption occurs in the stomach and upper portions of the small intestine 小肠.



- 11.2 Toxicology
- 11.2.1 Exposure
- 11.2.1.2 Inhalation 吸入
- As shown in Figure 11.3, the human respiratory system consists of three regions: nasopharyngeal 鼻咽部(nose, pharynx咽, larynx喉), tracheobronchial 气管支气管部 (trachea气管, bronchi支气管), and pulmonary 肺部 (alveolar sacs肺泡囊).
- Any materials that deposit within the mucous membrane粘膜 are trapped, and are eventually either coughed up or swallowed, whereupon they are subject to digestion. In contrast, materials that reach the alveolar sacs are often retained. These retained materials can potentially be absorbed into the bloodstream.

Respiratory

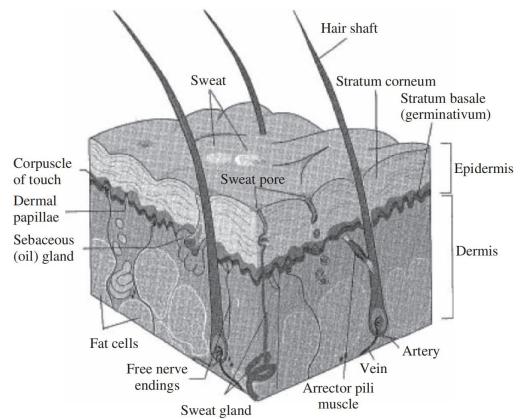


A complete, schematic view of the human respiratory system with their parts and functions.

Latin

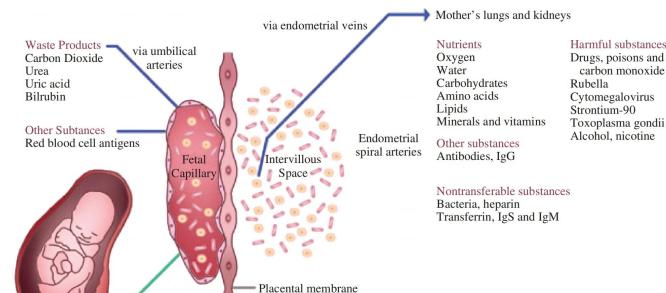
systema respiratorium

- 11.2 Toxicology
- 11.2.1 Exposure
- 11.2.1.3 Dermal Absorption
- Dermal absorption is the transport of chemicals from the outer surface of the skin, into the skin, and ultimately into the bloodstream.
- Because skin contains significant quantities of lipids, it is highly effective at excluding water and water-soluble materials. However, some of these materials can be absorbed through hair follicles 毛囊and sweat glands汗腺. In contrast, hydrophobic (fat-soluble) materials such as petroleum products and chlorinated organic solvents are readily absorbed by the skin and can be transferred to blood vessels present in the dermis, or to the underlying subcutaneous layer.



- 11.2 Toxicology
- 11.2.1 Exposure
- 11.2.1.4 Placental Transfer 胎盘转运
- The potential in utero exposure of fetuses to environmental chemical pollutants is a particularly challenging and politically sensitive area of research. Although it is well established that chemicals present within a pregnant mother's bloodstream can cross the placenta (a complex tissue attached to the wall of the mother's womb and to the baby through the umbilical cord) and enter the bloodstream of the fetus.

via umbilical vein



11.2 Toxicology

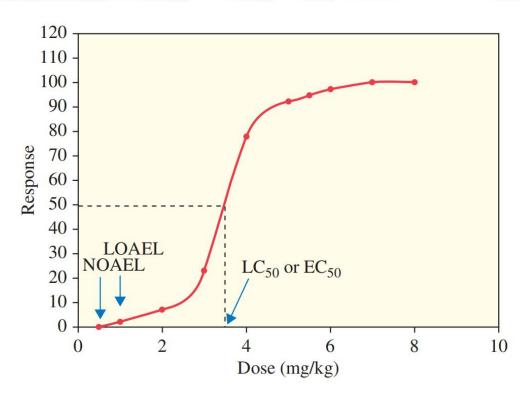
- To quantify the effects of a toxic substance, a toxicologist develops a dose-response curve that correlates a measured biological response to the chemical dose required to elicit that response.
- For acute exposures, the response may be organ injury, coma, or death, while chronic exposures typically result in mutagenic or carcinogenic responses. Dose refers to the actual amount of a toxic substance that is received by a target organism.
- There are four principal mechanisms by which a biological consequence occurs:
 - 1 Disruption or destruction of cellular structures.
 - 2 Direct chemical combination with a cellular constituent.
 - 3 Effects on enzyme activity.
 - 4 Secondary actions that occur as a result of the presence of a pollutant.

11.2 Toxicology

- Depending on which type of adverse effect is observed, toxic substances are placed into two general categories: non-carcinogens and carcinogens.
- Mutagens致突变物 are toxic substances that elicit alterations to DNA. Mutagens, unfortunately, alter DNA such that the genetic code is no longer precisely retained or transmitted. These changes can cause cell death, cancer, reproductive failures, or birth defects in offspring.
- Carcinogens致癌物质 are a specific class of mutagen that causes cancer. Carcinogens promote the growth of tumors by attacking or altering the DNA retained within a cell.
- The US EPA has defined five categories (A through E) to describe how likely a given chemical is a carcinogen. These categories are as follows:
- A. Human carcinogen. There is sufficient evidence from epidemiological studies to establish a causal association between exposure to the toxic substance and cancer.
 - B. Probable human carcinogen.
- C. Possible human carcinogen. There is limited evidence of carcinogenicity in animals and an absence of information regarding humans
 - D. Not classified. There is inadequate human and animal evidence of carcinogenicity.
 - E. Evidence of noncarcinogenicity.

11.2 Toxicology

- The central reason to conduct dose-response testing is to identify the nature of health damage caused by a substance and the range of doses over which such damage occurs. An example dose-response curve is illustrated in Figure 11.6. In this figure, the dose is represented on the x-axis in terms of the mass of contaminant dose per mass of test organism (body weight).
- When the dose is represented on a log-scale, such curves often exhibit a sigmoid shape with a flat portion at low dosages.
- Once the threshold is exceeded, however, there is a sharp increase in the measured response until, at some point, the maximal response is reached and the curve flattens out. The threshold is defined as the lowest dose at which a particular response is measurable.
- The simplest response to measure in toxicology tests is mortality and, as explained previously, the LD₅₀ is the median lethal dose that results in death in 50% of the test organism population. For these chronic exposures, toxicological endpoints other than death are of interest, and they are represented in terms of EC_{50} values (the effective concentration that affects 50% of the population) or other effective concentrations (i.e., EC_{10} , EC_{90}).



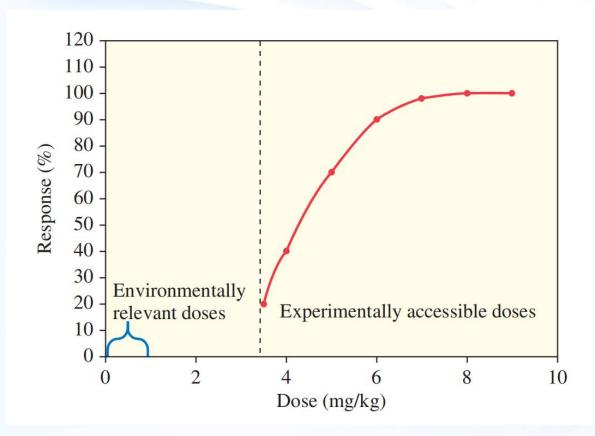
11.2 Toxicology

- Determination of LD and EC values reveals that not all individuals exposed in the same way to the same dose of a substance respond similarly. Some individuals are severely affected by the toxic substance at a particular dosage, while others are completely unaffected.
- Potentially susceptible populations潜在敏感人群 include the elderly, small children, fetuses, and immunocompromised individuals. Full evaluation of the toxicity of a given chemical requires consideration of its toxicity to susceptible populations.
- As noted previously, for ethical reasons toxicity testing is generally not performed on humans, and animal models are employed instead. One problem faced by the toxicology field is that each animal species may respond differently to a given potential toxicant.

11.2 Toxicology

11.2.2 Dose and Response

• An additional challenge associated with the development of dose-response tests is that the doses employed in animal studies are generally much higher than the actual doses that would be encountered in normal environmental settings. For this reason, extrapolation from the high-dose region to the low-dose region is often required. Such extrapolation is not without its challenges, however, since a number of assumptions must be made as to the shape of the dose-response curve in the low-dose region.



11.2 Toxicology

11.2.2 Dose and Response

- For **carcinogens**, a linear-extrapolation in the low-dose region is used since it is assumed that exposure to any amount of a carcinogen will increase an individual's likelihood of cancer.
- This linear extrapolation 线性外推法 results from fits to the collected dose-response data using what is known as a linearized multistage model. This conservative model overemphasizes risk and thus is highly protective of human health. The slope斜率 of the dose-response curve in the low-dose region is defined as the potency factor效价因子 (PF) or slope factor (SF) for a particular carcinogen.

$$PF = \frac{Incremental lifetime cancer risk}{Chronic daily intake}$$
 (11.1)

• The numerator defines the lifetime cancer risk and the denominator is the lifetime weight averaged dose or chronic daily intake慢性日摄入量 (CDI). The CDI typically has units of mg/kg-day and is defined as follows:

$$CDI = \frac{\text{Average daily dose (mg/day)}}{\text{Body weight (kg)}}$$
 (11.2)

11.2 Toxicology

11.2.2 Dose and Response

• In addition, the exposure is then averaged over an assumed 75-year lifetime. US EPA-recommended values for the daily intake parameters, an individual frequency of exposure to a given matrix, and body weights are found in Table 11.6.

Table 11.6 US EPA recommended exposure factors.

Exposure pathway	- To the state of		Exposure Duration (years)	Body Weight (kg)	
Ingestion of potable water	1.04 L (adult > 21 years) 0.33 L (child 3–6 years)	350	30	80 (adult > 21 years) 18.6 (child 3–6 years)	
Ingestion of soil and dust	50 mg (adult > 21 years) 100 mg (child 1–6 years)	350	24 5	80 (adult > 21 years) 18.6 (child 3–6 years)	
Inhalation of contaminants	21.2 m ³ (adult >21 years, <61) 18.1 m ³ (adult 61 – 70 years) 10.1 m ³ (child 3 – 6 years)	350	30	80 (adult > 21 years) 18.6 (child 3–6 years)	

11.2 Toxicology

- For non-carcinogens, a threshold dose, below which no toxic effects are observed, is typically assumed. Unfortunately, because of the high costs associated with dose-response assessment, the actual threshold dose is often challenging to accurately determine.
- NOAEL No observed adverse effect level. In other words, the highest administered dose at which no adverse effects were measured. This dose often approximates the threshold dose below which no effects are observed.
- LOAEL Lowest observed adverse effect level. In other words, the lowest administered dose at which adverse effects were measured.
- The NOAEL can then be used to determine what is known as the reference dose (RfD). The RfD is simply calculated by dividing the NOAEL (or sometimes the LOAEL) by an appropriate uncertainty factor.

Table 11.8 Guidelines for uncertainty factors.

Uncertainty factor	Guideline
1-10	When a NOAEL from a human study is used (account for interspecies diversity).
100	When a LOAEL from a human study is used, incorporating a factor of 10 to account for lack of NOAEL and a factor of 10 for intraspecies diversity; or when a NOAEL from an animal study is used, incorporating a factor of 10 to account for interspecies diversity and a factor of 10 for intraspecies diversity.
1000	When a LOAEL from an animal study is used; incorporates factors of 10 each for lack of NOEAL, interspecies diversity, intraspecies diversity.
1-10	Additional uncertainty factors, ranging from 1 to 10, may be incorporated on a case-by-case basis to account for database deficiencies.

11.2 Toxicology

- 11.2.2 Dose and Response
- Similar to what was done with carcinogens, it is possible to evaluate the hazard associated with exposure to non-carcinogens. This process is done through the calculation of Hazard Quotients (HQ)危害商数 that relate the average daily dose of a contaminant to the RfD:

$$HQ = \frac{\text{Average daily dose over period of exposure}}{\text{RfD}} \quad (11.4)$$

• If the hazard quotient for any particular exposure is less than 1.0, there is little risk of toxicity. In contrast, hazard quotient values that exceed 1.0 suggest there is a potential risk.

11.2 Toxi	cology					
Exercises	•					
1.Chemical	and biological exp	posures can occur via	,		,	, as well as
		ve categories (A through				
		C		E		<u>.</u>
3	are toxi	c substances that elicit	t alterations to DNA	Mutagens,	unfortunately, a	alter DNA such that the genetic code is no
longer preca	isely retained or tr	ansmitted. These chang	ges can cause cell de	ath, cancer, r	eproductive fail	ures, or birth defects in offspring.
4	are a spec	cific class of mutagen	that causes cancer. C	Carcinogens 1	promote the gro	wth of tumors by attacking or altering the
DNA retain	ed within a cell.					
5	is the me	edian lethal dose that	results in death in	50% of the	test organism 1	population.For these chronic exposures
toxicologic	al endpoints other	than death are of inte	rest, and they are re	presented in	terms of	(the effective concentration tha
affects 50%	of the population).				
6 the highe	r the PF, the	carcinogenic a	compound is.			
7.Potentiall	y susceptible popu	lations include	,	,	, and	Full evaluation of the toxicity of a
		deration of its toxicity				
8.The nume	erator defines the l	ifetime cancer risk and	the denominator is t	the		
9.the toxico	logist usually can	determine the following	ng parameters when o	describing do	se-response cur	ves for non-carcinogens:
	•		O 1	•	-	t which no adverse effects were measured
1		the threshold dose belo	· · · · · · · · · · · · · · · · · · ·	•		
	* *					at which adverse effects were measured.
			,			

11.3 Epidemiology

- Epidemiology流行病学 is the methodology used to detect the cause or source of diseases that produce pain, injury, illness, disability, or death in human populations or groups. Epidemiology characterizes the factors determining the frequency and distribution of disease and death in human populations, and is one of the foundations of public health and preventative medicine.
- An epidemiologist characterizes the time, place, and person aspects of disease by examining the risk factors that impact, influence, provoke, and affect disease distribution in a population. By studying these factors, an epidemiologist is able to determine the needs of disease control programs, develop preventative programs and health services planning activities, and establish patterns of endemic diseases, epidemics, and pandemics 地方病、流行病和大流行病.

11.3 Epidemiology

- 11.3.1 Incidence, prevalence, and epidemics
- Incidence发病率 is the extent that people within a population who do not have a disease will develop the disease during a specific time period. In other words, incidence defines the number of new cases of a disease in a population over a specific period of time. A related term is prevalence患病率, which is the number of people within a population who have a certain disease at a given point in time.
- The typical prevalence of a disease within a given population or geographic area is described as the endemic 地方病 level of disease. Depending on environmental and social conditions, some regions exhibit higher levels of endemic disease. As an example, although it is endemic in both regions, malaria generally exhibits a higher endemicity in Sub-Saharan Africa than it does in South America. Within any particular region, some portions of the population may exhibit hyperendemic levels高流行水平 of disease. These higher levels of prevalence are typically associated with distinct populations, such as might be found in a hospital, nursing home, or other institution. A holoendemic disease 全流行病 is one that is highly prevalent and is commonly acquired early in life. Prior to the advent of widespread immunization in the USA, chickenpox 水痘was considered a holoendemic disease.
- Epidemics, or outbreaks, can arise within local populations either due to contamination by a single source or via person-to-person propagation through a community.
- Widespread epidemics that traverse national borders and affect multiple countries, continents, and the globe are known as pandemics. AIDS, cholera, and tuberculosis pandemics afflict the world in the early part of the 21st century.

11.3 Epidemiology

11.3.2 Epidemiology triangle

• Four interrelated factors contribute to outbreaks of infectious disease:

1 the host;

2 an agent or disease-causing organism;

3 the environmental circumstances needed for a disease to thrive, survive, and spread;

4 time.

The inter-relationship between these factors is often described in terms of the epidemiology triangle.

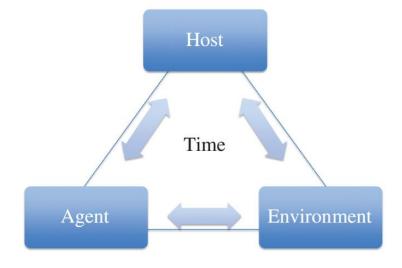
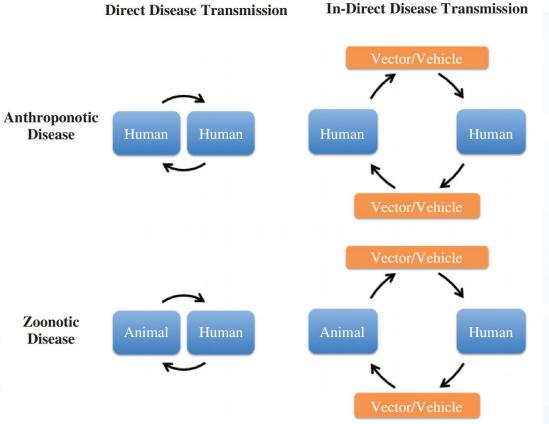


Figure 11.10 Epidemiological triangle. Source: P. Vikesland.

11.3 Epidemiology

11.3.3 Infectious disease transmission concepts

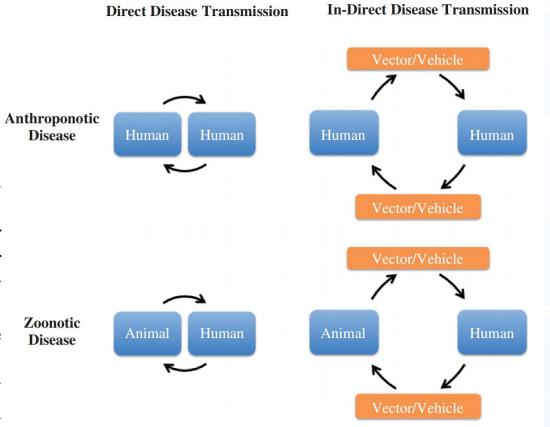
- A disease reservoir is an animate or inanimate medium in which infectious organisms live and multiply. Potential reservoirs include humans, animals, plants, soils, and inanimate organic matter (feces or food). Infectious organisms reproduce in the reservoir in a manner that facilitates disease transmission to a susceptible host. A living reservoir is generally referred to as a host宿主.
- A carrier 携带者contains, spreads, or harbors infectious organisms, but does not show obvious signs of clinical disease. Carriers serve as a potential source of infection and disease transmission to others (both humans and animals).
- Infectious diseases can be transmitted either directly (organism-to-organism) or indirectly (organism to intermediate to organism). Direct transmission is the immediate transfer of the agent from a host/reservoir to a susceptible host via physical contact (skin-to-skin contact, kissing, sexual intercourse). In contrast, indirect transmission involves an intermediate vector or vehicle that facilitates disease agent transfer from an infected organism to a susceptible host, resulting in disease. Some infectious diseases are solely the provenance of humankind and are referred to as anthroponotic diseases; diseases that afflict both humans and animals are described as zoonotic diseases.



11.3 Epidemiology

11.3.3 Infectious disease transmission concepts

- A vector病媒 is any living nonhuman carrier of disease that transports and serves the process of disease transmission. Typically vectors are insects (fly, flea, mosquito) or small animals (mouse, rat, other rodents, birds). A vector spreads an infectious agent from an infected human or animal to other susceptible humans or animals through its waste products, bite, or bodily fluids, or indirectly through food contamination.
- A vehicle载体 is a non-living carrier of disease. Air, water, and food are common vehicles for disease
- Airborne diseases are spread when aerosol droplets or particles of dust carry the pathogen to the host and enable its transmission. Airborne diseases can be spread by sneezing, coughing, or via the simple act of talking.
- Waterborne diseases are spread when a pathogen is present in drinking water, swimming pools, streams, or lakes used for swimming or other types of body contact.
- Foodborne diseases are spread when a pathogen or a toxic compound produced by a pathogen is present in food that is consumed. Foodborne diseases are classified in one of two categories: food poisonings and food infections.



11.3 Epidemiology

11.3.4 Disease epidemics

- Epidemics are often classified either as common source共源 or propagated 传播(host-to-host). In a common source epidemic, exposure of a disease to a group of persons arises from a singlesource that all persons in the group had a chance to encounter.
- Examples of common source epidemics are food and water contamination events that occur when there is a breakdown in the sanitation processes used to protect public health.
- Propagated epidemics occur via the direct or indirect transmission of a communicable disease from one individual to another within a susceptible population.
- Common source and propagated epidemics can be differentiated from one another by the relative shapes of their epidemic curves. A common source epidemic exhibits a rapid rise in the epidemic curve, followed by a rapid fall that is generally attributable to discovery of the common source and its sanitation or removal. In contrast, propagated epidemics are generally slower to rise and slower to fall, since they are passed between members of the community.

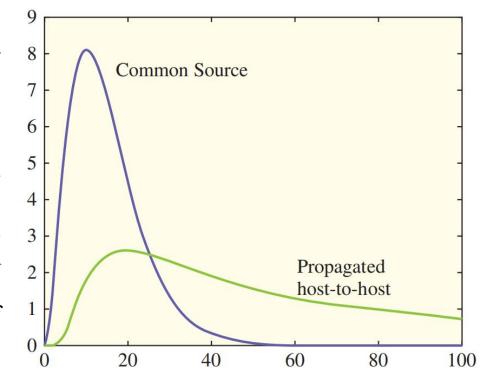


Figure 11.14 Comparison of common source and propagated outbreaks of infectious disease. Y-axis: # of cases, X-axis: time.

- 11.3 Epidemiology
- 11.3.5 Mortality and morbidity
- Mortality致死率 is the incidence of death in a population and can be quantitatively defined as the ratio of the number of deaths during a specific period of time relative to the number of people at risk of dying:

where 'multiplier' is typically either 100, which then makes the ratio a percentage, or is 1,000 to reflect the number of deaths on a 1,000 person basis.

11.3 Epidemiology

11.3.5 Mortality and morbidity

- Morbidity发病率 is the magnitude of illness, injury, or disability in a defined population and is quantitatively described using incidence and prevalence rates. The overall health of a population is generally better defined in terms of morbidity statistics rather than mortality statistics, since many diseases that affect health often have low mortality.
- As shown in Table 11.10, the major causes of illness in high income countries are often quite different from the major causes of death, and there are also major differences between high income countries and low income countries.

ntal public health									
	HIGH INCOME COUNTRIES				LOW INCOME COUNTRIES				
of	Causes of death ^a	Number of deaths per 100,000	Causes of infectious disease ^b	Number of reported cases	Causes of death ^a	Number of deaths per 100,000	Causes of infectious disease ^b	Number of reported cases	
a	Ischaemic heart disease	119	Mumps	136,000	Lower respiratory infections	98	Malaria	59,600,000	
i S	Stroke	69	Tuberculosis	129,000	HIV-AIDS	70	Tuberculosis	1,250,000	
ıg	Trachea, bronchus,	51	Pertussis	61,200	Diarrhoeal diseases	69	Cholera	177,000	
ne	lung cancers				Stroke	56	Measles	76,500	
1S of	Alzheimers and other dementias	48	Rubella	8,540	Ischaemic heart disease	47	Leprosy	35,200	
ın	COPD	32	Measles	6,540	Prematurity	43	Rubella	18,200	
ıy		32	Leprosy	297	Malaria	38	Pertussis	7,310	
ve					Tuberculosis	32	Tetanus	5,230	
	Colon rectum	27	Tetanus	293	Malnutrition	32			
or	cancers				Birth asphyxia and	30			
ne	Diabetes mellitus	21			birth trauma				
nt	Hypertensive heart disease	20							

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11.3 Epidemiology

- 11.3.6 Epidemiological study types
- There are three classic epidemiological study types: cross-sectional, case-control, and cohort studies横断面研究、病例对照研究和队列研究.
- These three types differ with respect to their temporal nature, with cross-sectional studies occurring at a single point in time, case-control studies being retrospective (i.e., looking backwards in time), and cohort studies being prospective (i.e., looking forwards in time).
- A cross-sectional study determines the prevalence and distribution of disease within a population at a particular point in time. A challenge associated with cross-sectional studies is that because all of the data are collected at the same time, it is impossible to establish causality between disease prevalence and possible risk factors.
- In a case-control study, people who have an illness (cases) are compared with others who do not have an illness (controls) with respect to past exposures and risk factors. Such studies are useful for diseases that are relatively rare, since they can establish exactly what risk factors are most likely responsible for the development of disease within a particular population. Unfortunately, as was the case with cross-sectional studies, a case-control study has no causality; cases and controls often differ in terms of their characteristics.
- In a cohort study, two groups or cohorts with different exposures/risk factors are monitored over time for certain health outcomes. In general, cohort studies are prospective, but they can be retrospective if necessary criteria to truly define the cohorts can be applied. The exposures can be observed (observational cohort study) or controlled (experimental).

11.3 Epidemiology

11.3.7 Incidence and attack rates

- Incidence was previously defined as the number of new cases of a disease that came into existence within a certain period of time for a specified unit of population. The incidence rate 发病率 provides an estimate of the risk or the probability of getting a disease within a certain time period. Higher incidence rates indicate an increased risk of getting a disease following an exposure. Comparison of incidence rates enables evaluation of the time, person, and place aspects of disease transmission.
- Time if the incidence rate for a particular disease is reliably higher during a specific time of year, the risk of developing the disease goes up at that time. This phenomenon is illustrated by the higher incidence rate of influenza in winter

months relative to the summer.

- Person if incidence rates are consistently higher among individuals with a specific lifestyle factor, the risk of getting the disease goes up amongst that group. For example, the incidence rate of lung cancer is higher amongst smokers versus non-smokers.
- Place if the incidence rate is consistently higher among people who live in a certain place, the risk goes up for developing that disease if one lives in the area. For example, the incidence rate of malaria is higher in sub-Saharan Africa than in South America, and one thus has a greater risk of malaria infection in Africa.

11.3 Epidemiology

11.3.7 Incidence and attack rates

- The duration of common source disease epidemics is often very short and, under these conditions, a special type of incidence rate, known as an attack rate发作率, is defined.
- As defined mathematically, attack rates are the same as incidence rates, but in practice they are only used to analyze epidemics in which a small select population is exposed to a disease or an injury-causing event, such as food poisoning or chemical exposures.

11.3 Epidemiology

11.3.8 Prevalence Rates

- Prevalence is the number of cases of disease at a particular time in relation to the size of the population from which this number is drawn. We can define the prevalence rate 流行率as the incidence rate multiplied by the average duration of disease.
- Two types of prevalence rates are generally reported: period prevalence and point prevalence.

11.3 Epidemiology

Exercises

1.Two type	es of prevalence ra	tes are generall	y reported:	and		
2.There are	e three classic epid	emiological stu	ıdy types:	,	, and	
3.Epidemic	es are often classif	ied either as	or			
4.Four inte	rrelated factors co	ntribute to outb	reaks of infectious	s disease:		
1 1	. 2	.3	. 4			

11.4 Agents of infectious disease

• The infectious microbial agents of greatest concern are prions, viruses, bacteria, protozoa, and fungi.

11.4.1 Prions 朊病毒

- Prions are infectious extracellular proteins that are known to cause a variety of diseases in animals. Among the different prion-associated diseases are scrapie in sheep, bovine spongiform encephalophathy (BSE of 'mad cow disease') in cattle, and kuru and Creutzfeldt-Jakob disease羊瘙痒症、牛海绵状脑病(BSE,即"疯牛病")、克鲁氏病和克雷氏病 in humans.
- Prions cause disease by modifying the normal proteins in a host cell, such that they become misfolded. This misfolding causes the proteins to lose their normal function, to become more resistant to protease attack, and to become insoluble.

- 11.4 Agents of infectious disease
- 11.4.2 Viruses 病毒
- Viruses are common disease agents but, because they lack internal structure and cannot replicate by themselves, they are not considered to be living cells.
- Either DNA or RNA (but not both) can serve as the nucleic acid, and viruses are often described as being either a DNA virus or a RNA virus.

11.4 Agents of infectious disease

11.4.3 Bacteria

- Bacteria are single-celled prokaryotic organisms. In a prokaryotic cell there are no cellular compartments, and the DNA of the cell resides directly within the cytoplasm. Even without internal structures, bacteria are able to carry on all of the essential functions of life. Current estimates suggest that there are millions, and possibly billions, of different types of bacteria. Most of these types are harmless, and only a select few are human pathogens.
- Bacterial diversity arises from differences in their metabolic characteristics and their structural morphologies. Bacterial metabolism, the food sources on which bacteria thrive and the methods by which they produce energy.

11.4 Agents of infectious disease

11.4.4 Protozoa

- Protozoa are unicellular, eukaryotic organisms that do not possess a cell well but do possess a nucleus. Protozoa can be differentiated from algae due to their lack of chlorophyll, and from fungi by their subcellular differentiation, motility, and lack of a cell wall.
 - Amoebae变形虫
 - Ciliates 纤毛虫
 - Flagellates 鞭毛虫
 - Sporozoa 孢子虫
- Malaria 疟疾 is an important disease caused by a protozoan

11.4 Agents of infectious disease

11.4.5 Fungi

- Fungi are eukaryotic and possess a cell wall.
- Some fungi elicit immune responses that can result in an allergic reaction following exposure to specific fungal antigens.
- Fungi also cause disease through the production of fungal exotoxins known as mycotoxins霉菌毒素.
- A third mechanism by which fungi cause disease is via fungal infections on or in the body. These types of infections are known as mycoses真菌病 (singular: mycosis) and can be superficial, subcutaneous, or systemic浅表性、皮下性或全身性.

- 11.4 Agents of infectious disease
- 11.4.6 Exotoxins versus endotoxins 外毒素与内毒素
- Exotoxins are heat-labile proteins嗜热蛋白质 that are actively excreted by some types of gram-positive and gram-negative bacteria革兰氏阳性和革兰氏阴性. These compounds generally exhibit highly specific modes of action, due to their association with specific cell receptors. There are three general types of exotoxins: A-B toxins, cytolytic toxins细胞溶解性毒素, and superantigen toxins超抗原毒素.
- Endotoxins are generally much less toxic than exotoxins.
- The mode of action of an endotoxin is usually quite general, resulting in fever, diarrhea, and vomiting. In contrast, exotoxins are often quite specific, since they bind to specific cell receptors to elicit a toxic response. It is this specificity that enables much smaller doses of exotoxins to elicit a toxic effect.

- 11.5 Public health and engineering measures for control of disease
- 11.5.1 Controls directed against disease reservoirs 疾病库
- Many infectious diseases are harbored by animal reservoirs.
- Elimination can be achieved via immunization for diseases treatable using available vaccines. Alternately, for diseases of health concern for which no vaccines are available, elimination can be achieved via the destruction of infected animals.
- For diseases in which the reservoir is a wild animal, it is much more challenging, if not impossible, to eradicate the disease completely.
- For this particular disease, it is possible to control its spread by immunizing the domestic animal populations, but disease eradication is unattainable, since it would require the capture and destruction of all of the wild animal reservoirs.
- For diseases in which the reservoir is an insect, it is possible to achieve effective control by eliminating the reservoir using chemical or other means of control

11.5 Public health and engineering measures for control of disease

For diseases that do not have an asymptomatic phase, control can be achieved by immunization, quarantine, and surveillance. These three control strategies are discussed in the following sections.

11.5.2 Immunization 免疫

- Immunization is the purposeful stimulation of immunity to infectious disease in a given individual. This stimulation of immunity is achieved either by purposely exposing an individual to a controlled dose of non-infective antigen that induces production of antibodies against the disease, or by injection of antibodies derived from an individual who already has immunity. The former approach is known as vaccination, while the latter results in passive immunity. In general, vaccination is used to prevent the spread of infectious disease, while antibody injection is used as a therapeutic approach to control active disease.
- An important aspect of immunization programs is that it is generally not necessary to achieve 100% immunization to control disease. The reason for this has to do with the concept of **herd immunity**群体 免疫. The more infectious a disease agent, the greater the required proportion of immune individuals in a population to prevent disease epidemics.

11.5 Public health and engineering measures for control of disease

For diseases that do not have an asymptomatic phase, control can be achieved by immunization, quarantine, and surveillance. These three control strategies are discussed in the following sections.

11.5.3 Quarantine 检疫

- Quarantine and isolation 检疫与隔离 are used to prevent the spread of highly infectious diseases. Quarantine strictly applies to those who have been potentially exposed to an infectious disease, while isolation applies to those who are known to be suffering from the disease.
- Because of the limits that quarantine and isolation place on individual liberties, the quarantine period is generally only as long as necessary to protect the public. This period must be sufficient to:
 - 1 provide therapeutic health care; and
 - 2 ensure that quarantined individuals cannot infect others.
- By international convention, there are six diseases that require quarantine: smallpox天花, cholera,霍乱 plague鼠疫, yellow fever黄热病, typhoid fever伤寒, and relapsing fever复发性热病. In addition, highly infectious diseases such as viral hemorrhagic fevers 病毒性出血热are also often quarantined.

11.5 Public health and engineering measures for control of disease

For diseases that do not have an asymptomatic phase, control can be achieved by immunization, quarantine, and surveillance. These three control strategies are discussed in the following sections.

11.5.4 Surveillance 监测

- Surveillance is a passive monitoring system used to observe, recognize, and report diseases as they occur.
- The way that this system works in the US is that doctors are instructed to look for the particular symptoms of a disease and report their observations to local and state health departments. The local and state health departments then forward this data to the US Centers for Disease Control and Prevention (CDC).
- One challenge associated with disease surveillance programs is their reliance on initial reporting by doctors.

11.5 Public health and engineering measures for control of disease

11.5.5 Controls directed against pathogen transmission

- Engineering and public health controls have been developed to minimize pathogen transmission. In the case of foodborne and waterborne diseases, significant progress was made over the course of the 20th century through the institution of public health procedures that either prevent contamination of these vehicles or that destroy the pathogen in the vehicle.
- Examples of controls include the use of drinking water purification and the widespread implementation of wastewater treatment throughout the developed world. These have collectively led to dramatic reductions in the prevalence of infectious diseases such as typhoid fever and cholera. Similarly, milk pasteurization 巴氏消毒法 has helped to control bovine tuberculosis.

11.5.6 Pathogen eradication 根除病原体

- To date, only two diseases smallpox天花 and rinderpest牛瘟 have been eradicated.
- As a result of these intensive efforts, the last naturally occurring smallpox infection occurred in 1975. At the present time, there are only two known repositories for smallpox: the Centers for Disease Control and Prevention (CDC) in the United States and the State Research Center of Virology and Biotechnology VECTOR in Koltsovo, Russia.

11.5 Public health and engineering measures for control of disease

Exercises

1. For diseases that do not have an asymptomatic phase, control can be achieved by	,	,
and .		

11.6 Emergent and reemergent infectious diseases

- Infectious diseases are of global health concern because their worldwide distribution can change dramatically and rapidly, due to alterations to the pathogen, the environment, or the host population that collectively contribute to the rapid spread of newly emergent diseases, as well as reemergent diseases that had previously been controlled.
- The factors that affect disease emergence are:
 - 1 Microbial adaptation and change.
 - 2 Human susceptibility to infection.
 - 3 Climate and weather.
 - 4 Changing ecosystems.
 - 5 Human demographics and behavior.
 - 6 Economic development and land use.
 - 7 International travel and commerce.
 - 8 Technology and industry.
 - 9 Breakdown of public health measures.
 - 10 Poverty and social inequality.
 - 11 War and famine.
 - 12 Lack of political will.
 - 13 Intent to harm.

11.6 Emergent and reemergent infectious diseases

11.6.1 Microbial adaptation and change

• Horizontal gene transfer 横向基因转移and viral mutations collectively result in antimicrobial drug resistance, which hinders the use of many once viable pharmaceutical treatments.

11.6.2 Human susceptibility to infection

- The human body has many defense mechanisms that restrict the capacity for a pathogen to cause disease.
- Should the skin, mucous membranes, or intestinal epithelium be breached, the human body has additional non-specific (innate) and specific (adaptive) defense mechanisms.
- The capacity for the specific and non-specific defense mechanisms to protect against disease can be altered by a number of different factors. Amongst these are genetic polymorphisms and malnutrition.

11.6.3 Climate and weather

• As described by the epidemiological triangle, the physical environment influences the host, the disease agent, and the transmission of agents between hosts. Accordingly, changes in the physical environment have potentially important effects on the dissemination of infectious disease.

11.6 Emergent and reemergent infectious diseases

11.6.4 Changing ecosystems

- Changes in ecosystems alter the capacity for pathogens to interact with humans. Transmission of many vehicle-borne and vector-borne diseases is influenced by ecosystem changes.
- Changes in ecological conditions may alter human exposures to vectors, may increase the vector distribution and density, or may alter the longevity, activity, and habitat of the vector.

11.6.5 Economic development and land use

• As the world's human population grows and people transition from rural to urban lifestyles, there is often the concomitant consumption of natural resources, deforestation, and dam building. Each of these activities has both intended and unintended impacts on the environment that can, in turn, alter the number of interactions between human and animal reservoirs.

11.6 Emergent and reemergent infectious diseases

11.6.6 Human demographics人口 and behavior

- As of 2011, approximately 7 billion people inhabit the earth, and it has been projected that its population will exceed 9.3 billion by 2050. Concomitant with this growth has been a transfer of people from rural areas to urban settings, such that over 50% of the world's people now live in cities. Explosive growth in the human population and the greater number of interpersonal contacts that occur as a result of urban living have collectively enhanced the opportunity for pathogens to be transferred from one human to another.
- In these and other developing countries, the transition from a rural to an urban lifestyle is complicated by the lack of adequate water and sanitation infrastructure.
- Coupled with increases in population and urban living are increases in the numbers of immunocompromised 免疫力低下peoples and those that engage in high-risk behaviors.
- The immunocompromised population has steadily increased across the world, due to advances in medicine, science, and technology.

11.6 Emergent and reemergent infectious diseases

11.6.7 Technology and industry

- Numerous technological and industrial advances such as antibiotics, organ transplants, and food pasteurization have significantly improved people's lives, added years to life expectancy, and led to the control of many historically prevalent diseases. These technological advances, however, come with a price, since they have enabled some novel previously unknown disease agents to emerge.
- Advances in health care have significantly improved the survival of previously vulnerable populations, but have simultaneously led to increases in the total number of hospital-based (nosocomial) infections and the further development of antimicrobial drug resistance.

11.6.8 International travel and commerce

- Increased international travel and the expansion of global trade have enhanced the potential for rapid disease agent and vector dissemination.
- As these fruits and vegetables travel from their countries of origin, the cross-border transmission of infectious agents becomes increasingly possible.

11.6 Emergent and reemergent infectious diseases

11.6.9 Breakdown of public health measures

• Across the world, far too many infectious diseases are spread due to a lack of proper sanitation. As noted previously, many infectious diseases are spread via fecal contamination of waters used for drinking or other daily uses. Simply improving sanitation practices would significantly decrease the prevalence of infectious disease worldwide.

11.6.10 Poverty and social inequality

- Poverty and social inequality are major factors in disease emergence. Many diseases predominantly afflict the poor, due to chronic malnutrition, lack of access to clean water and sanitation, poor housing conditions, and limited funds to pay for out-of-pocket expenditures.
- Developing countries chronically underfund health care relative to the developed world and, thus, they suffer from inadequate and erratic supplies of drugs and high transportation costs. Each of these factors results in poor patient compliance to doctor-initiated care, and the resultant emergence of antimicrobial resistance.

11.6 Emergent and reemergent infectious diseases

11.6.11 War and famine

• In many cases, these "complex humanitarian emergencies" displace people and force them to live in squalid refugee camps with little to no access to medical care, protection from vectors, or adequate sanitation.

11.6.12 Lack of political will

• Diseases move rapidly around the world as a result of technology and economic independence.

11.6.13 Intent to harm

- Biological weapons
- Smallpox was used as a biological weapon during the French and Indian Wars (1754–1767) in colonial North America.
- In the 20th century, Germany and Japan tested biological weapons during World War I and World War II, respectively and, during the Cold War, both the Soviet Union and the USA developed and tested biological weapons.

Thanks!