Environmental Toxicology (ET)

Course: ES 535

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Dose Response Relationship

- The dose – response relationship provides an estimation of the relationship between the dose of a chemical agent and incidence of effects in a population.
- The dose is the actual amount of a chemical that enters the body. The dose received may be due to either acute (short) or chronic (long-term) exposure.
- Approaches to characterizing dose – response relationships: include effect levels: such as lethal dose 50 (LD 50), lethal concentration 50 (LC 50), effective dose 50 (ED 50), No observed adverse effect levels (NOAELs), margins of safety.

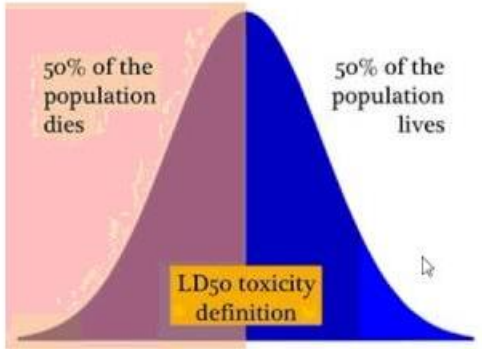
Dose Response Relationship

- In toxicology, the lethal dose (LD) is an indication of the lethal toxicity of a given substance or type of radiation
- Because resistance varies from one individual to another, the "lethal dose" represents a dose (usually recorded as dose per kilogram of subject body weight) at which a given percentage of subjects will die
- LD50 (abbreviation for "lethal dose, 50%"), LC50 (lethal concentration, 50%) of a toxin, radiation, or pathogen is the dose required to kill half the members of a tested population after a specified test duration.
- A lower LD50 is indicative of increased toxicity.

Toxicity

Lethal Dose-50% (LD_{50})

- Lethal dose 50% (LD_{50})-dose that is lethal to 50% of a population of test animals
  - Reported by mg of toxicant/kg of body weight
  - Smaller the LD_{50}=more toxicity of chemical
  - Greater the LD_{50}=less toxicity of chemical



Limitations

- As a measure of toxicity, lethal dose is somewhat unreliable and results may vary greatly between testing facilities due to factors such as the

✓ genetic characteristics of the sample population,

✓animal species tested,

✓environmental factors and

✓mode of administration

- There can be wide variability between species as well; what is relatively safe for rats may very well be extremely toxic for humans (cf. paracetamol toxicity), and vice versa.
- For example, chocolate, comparatively harmless to humans, is known to be toxic to many animals.
- When used to test venom from venomous creatures, such as snakes, LD50 results may be misleading due to the physiological differences between mice, rats, and humans.
- Many venomous snakes are specialized predators of mice, and their venom may be adapted specifically to incapacitate mice; and mongooses may be exceptionally resistant. While most mammals have a very similar physiology, LD50 results may or may not have equal bearing upon every mammal species, including humans.

Toxic Action of Pollutants

- A pollutant can elicit adverse effects on the living processes of an organism when present at a sufficiently high concentration or concentration high enough to elicit physiological responses in organisms, potentially causing toxicity.
- To exert damage to an exposed organism, a pollutant must first enter the host and reach its target site.
- A complex pathway exists between the time of initial toxicant exposure and the manifestation of damage by the organism.
- **Focus on**: general ways in which environmental pollutants exert their actions on plants, animals, and humans.

Plants: Sources, Composition, Uptake

Sources of pollution:

- Anthropogenic: atmospheric pollution: motor vehicles, industrial activities, power generation, brick kilns (mainly in dry season in BD), construction activities, dust, and etc.
- About 58% of the fine particle concentration in Dhaka to the brick kiln industry, 10.4% to vehicles and 15.3% to dusts (CASE project, 2014)

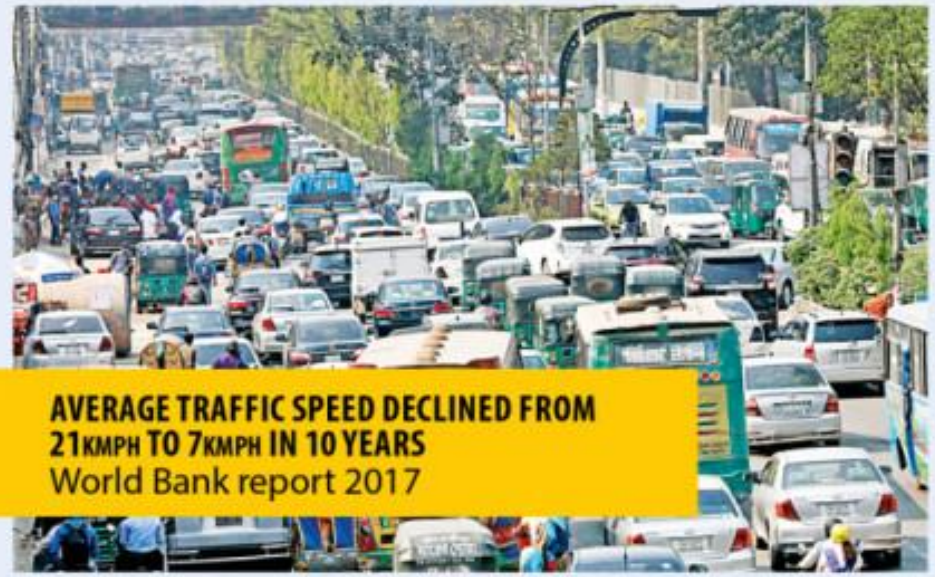
Composition:

- CO (vehicles), SO_x (industries, power generation), PM, SOx,& VOC's (brick kilns), peroxyacetyl nitrate (PAN), and other photochemical oxidants

Pollutant uptake:

- Terrestrial plants: exposed: Two main ways: One is exposure of forage (vegetation) to air pollutants; another is uptake of toxicants by roots growing in contaminated soils

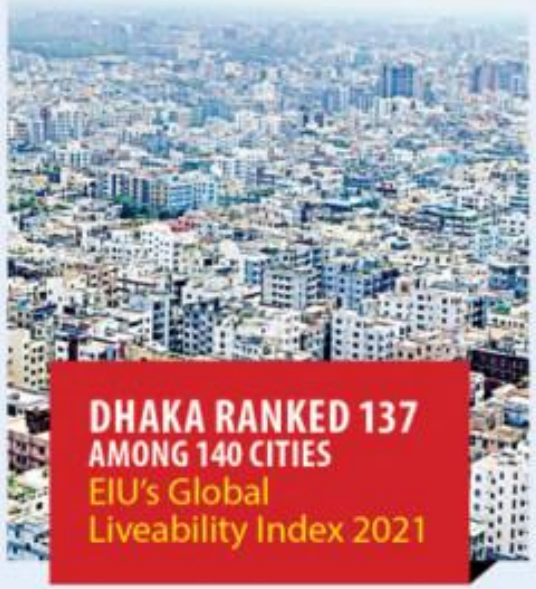
LIVING IN DHAKA



AVERAGE TRAFFIC SPEED DECLINED FROM 21KMPH TO 7KMPH IN 10 YEARS
World Bank report 2017

Water supplied to 57 areas was polluted because of faulty pipes
Wasa report in 2019

SECOND WORST CITY
World Air Quality Report 2021



DHAKA RANKED 137 AMONG 140 CITIES
EIU's Global Liveability Index 2021

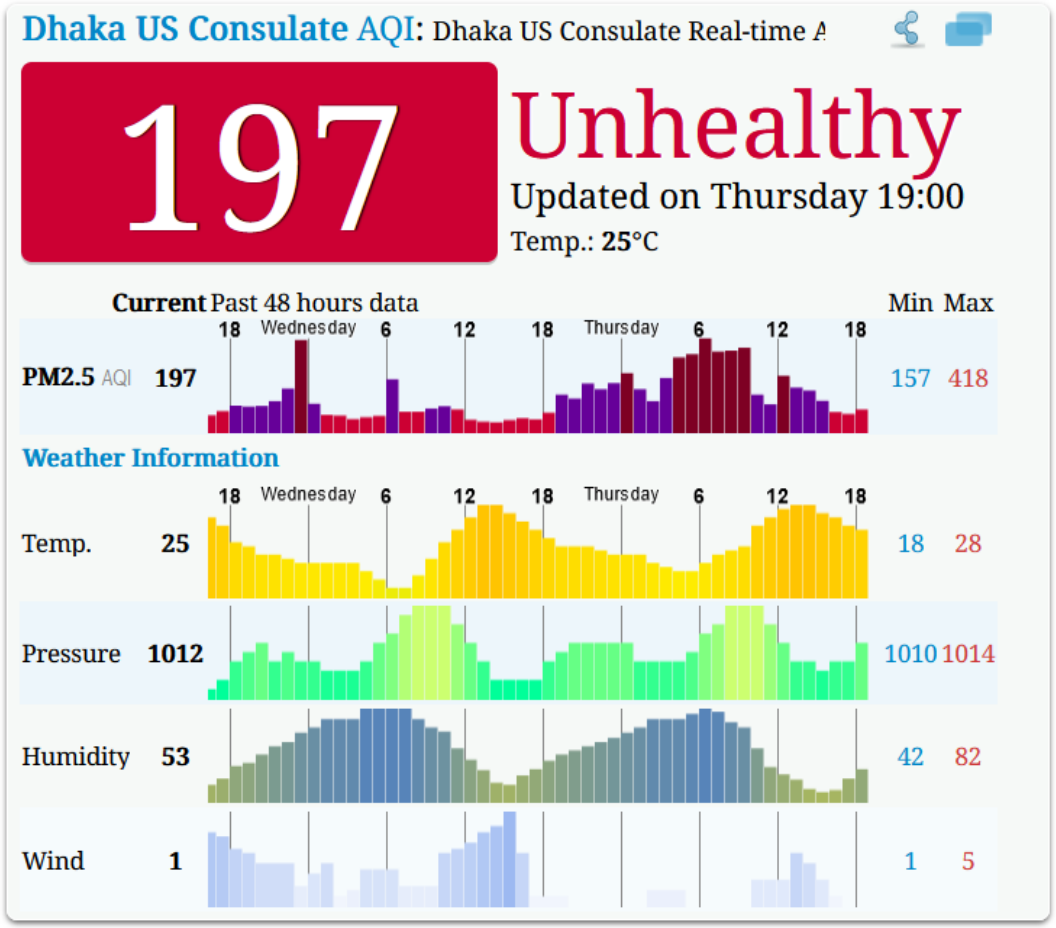
DHAKA NOISIEST CITY IN THE WORLD
United Nations Environment Programme Report

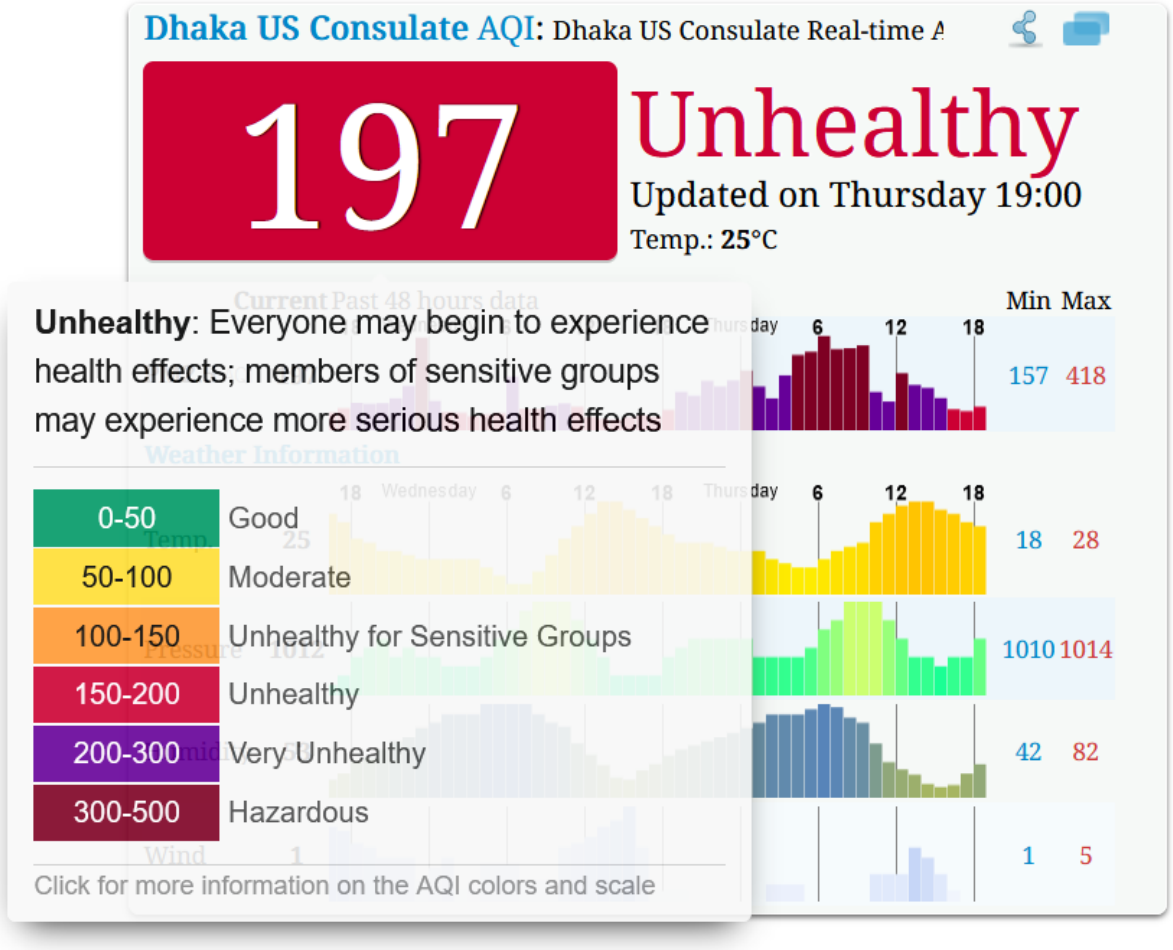
FALLING GROUNDWATER LEVEL

1980	9 metres
1990	22.5 metres
2000	41.5 metres
2020	74 metres

SOURCE: BWDB

Dhaka Air Quality





Daily Air Quality Index Report (AQI): Date_ 08/02/2023 (DoE)

LOCATION	AQI	CATEGORY	RANGE
Dhaka[b]	170	UNHEALTHY	166-174
Chittagong[c]	181	UNHEALTHY	179-183
Gazipur[c]	212	VERY UNHEALTHY	
Narayanganj[c]	170	UNHEALTHY	
Sylhet[c]	182	UNHEALTHY	
Khulna[c]	180	UNHEALTHY	
Rajshahi[c]	286	VERY UNHEALTHY	
Barisal[c]	106	CAUTION	
SavarC	DNA	DNA	
Mymensingh[C]	211	VERY UNHEALTHY	
Rangpur[c]	228	VERY UNHEALTHY	
Cumilla[c]	158	UNHEALTHY	
Narsingdi[c]	132	CAUTION	

Approved AQI for BD

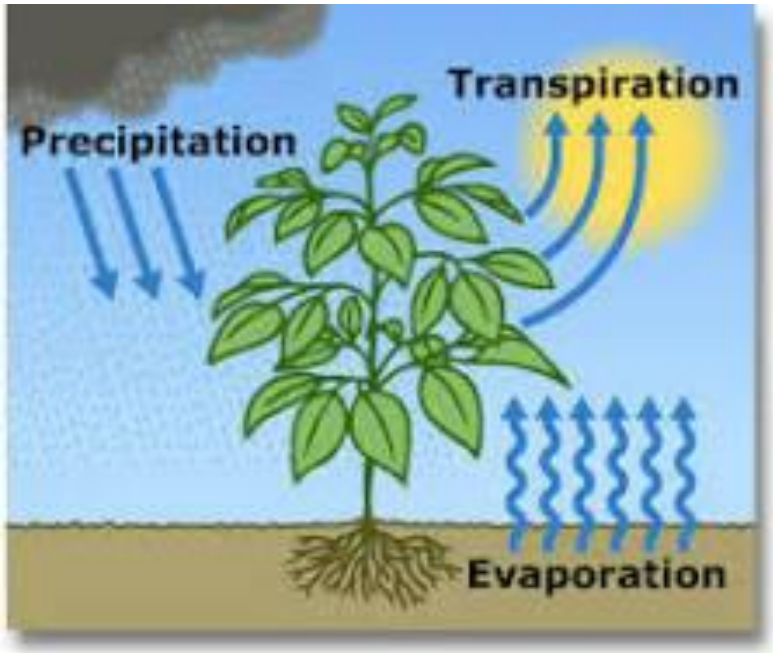
0-50	Good
51-100	Moderate
101-150	Caution
151-200	Unhealthy
201-300	Very Unhealthy
301-500	Extremely Unhealthy

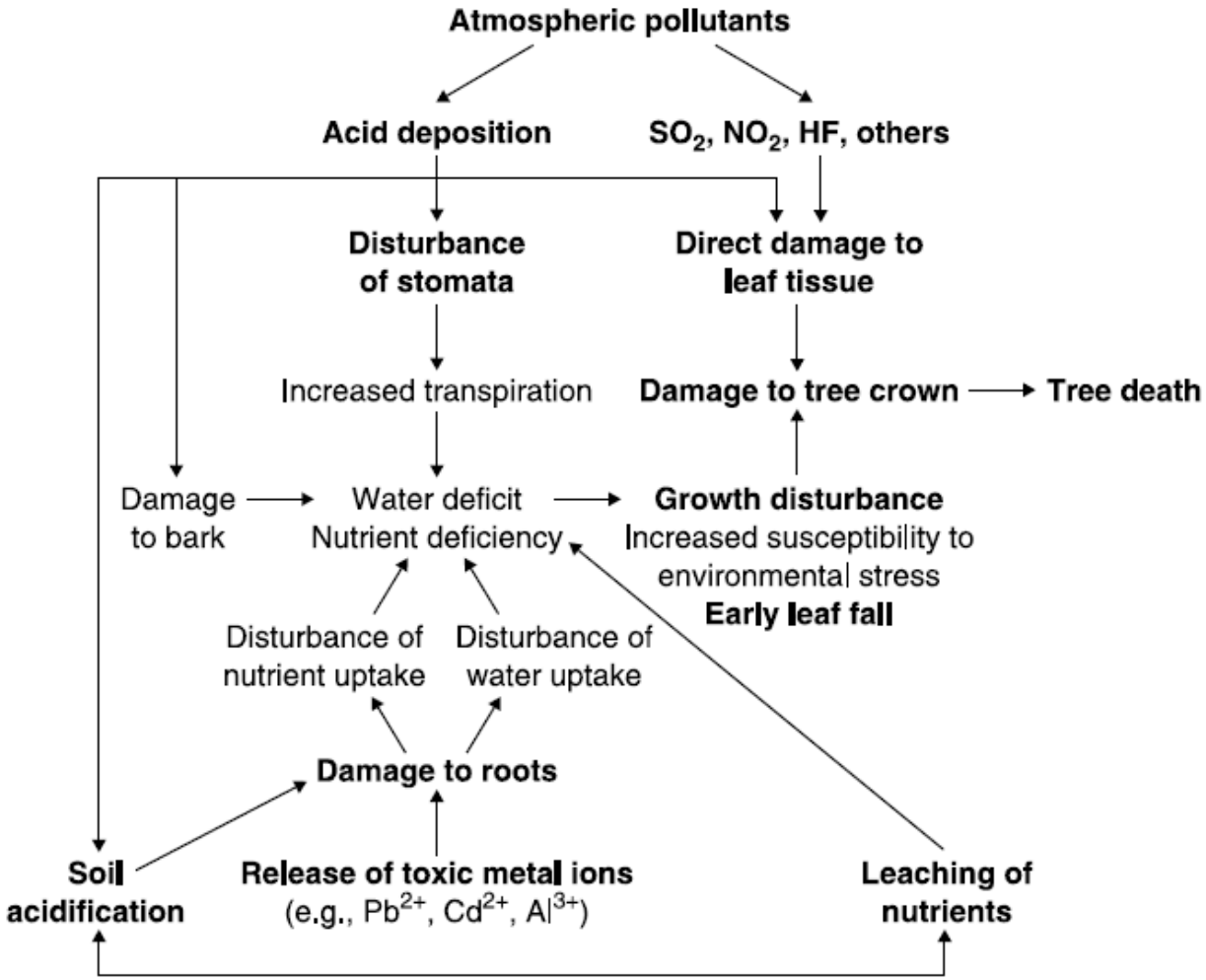
NOTE : (a),(b) and (c) Refer to the AQI Average in one city based on three, two and one CAMS respectively. In Bangladesh the AQI is based on 5 criteria pollutants; Particulate Matter (PM10 and PM2.5), NO_2, CO, SO_2 and Ozone (O_3)

Plants: Uptake

- Vegetation growing near industrial facilities, such as smelters, aluminum refineries, coal-burning power plants, and brick kilns may absorb airborne pollutants through the leaves and become injured
- Important to understand the uptake of the pollutants by the plants
- Conductance through the stomata, which regulate the passage of ambient air into the cell is important
- The extent of uptake depends on the chemical and physical properties of the pollutant along the gas-to-liquid diffusion pathway

Mechanisms of tree damage by toxicants

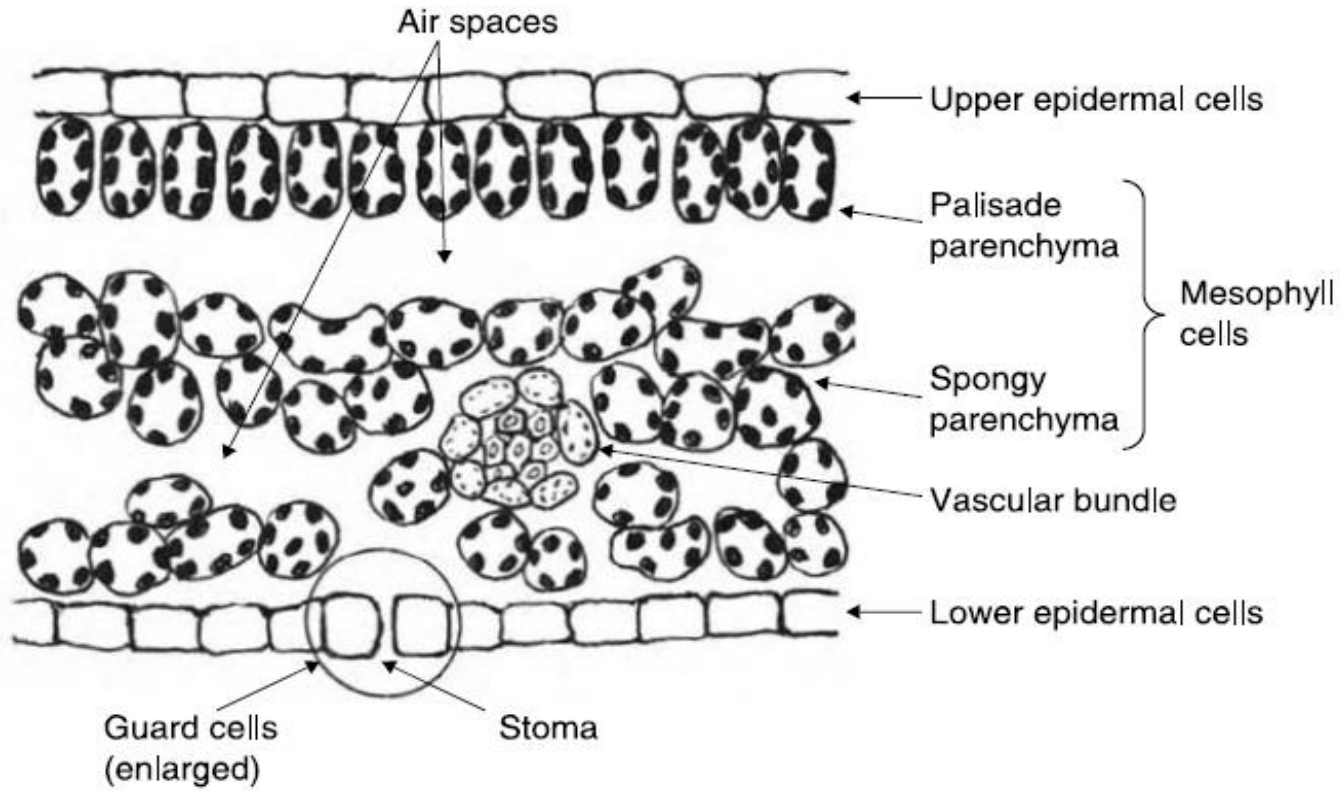


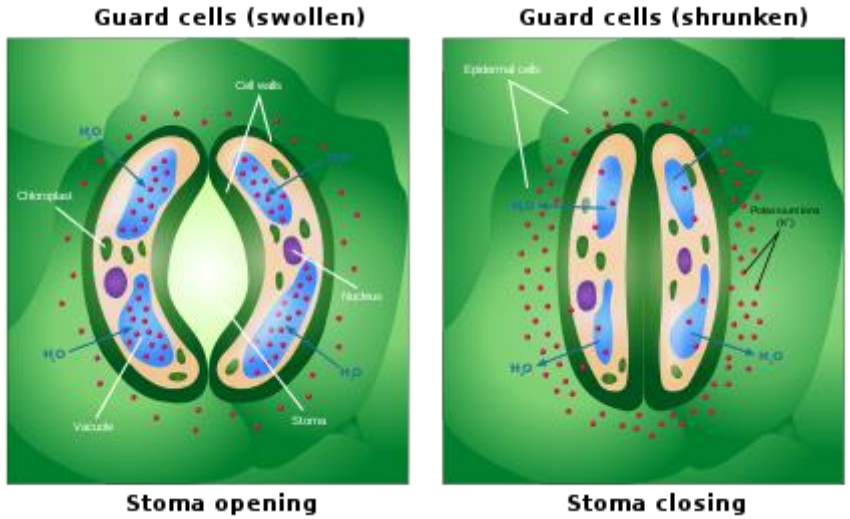


Plants: Factors

- The flow of pollutant may be restricted by leaf's physical structure, or by scavenging chemical reactions within the leaf.
- Leaf orientation and morphology, including epidermal characteristics, and air movement across the leaf.
- Stomatal resistance (determined by: stomatal size and number, size of the stomatal aperture, and other anatomical characteristics).

Guard Cells


Air spaces
Upper epidermal cells
Palisade parenchyma
Mesophyll cells
Spongy parenchyma
Vascular bundle
Lower epidermal cells
Guard cells (enlarged)
Stoma


Guard cells (swollen)
Guard cells (shrunken)
Stoma opening
Stoma closing

Plants: Factors

- **Stomatal opening**: regulated by: light, humidity, temperature, internal carbon dioxide content, water and nutrient status, particularly potassium (K^+) ions transported into the guard cells.
- For most plants, the stomata are **open** during the daylight hours, and most damage from sulfur dioxide occurs then.
- Stomatal opening is induced by low CO_2 concentrations, high light intensity and high humidity. By contrast **closing** is promoted by high CO_2 concentrations, darkness, drought and the plant hormone ABA
- Stomatal opening is extremely important: little or no uptake may occur when the stomata is closed.
- Exposure of roots to toxicants in contaminated soils: waste sites: high levels of heavy metals such as Pb and Cd , often occur
- Metallic ions are more readily released, and thus more readily absorbed, when the soil is acidified by acid deposition.

Plants: Transport

- Following uptake, a toxicant may undergo mixing with the surrounding medium of the plant, and then be transported to various organs and tissues.
- Mixing involves microscopic movement of molecules and is accompanied by compensation of concentration differences

➢ Mode of transport:

- Generally, transport of chemicals in plants occurs passively by diffusion and flux.
- Diffusion refers to movement across phase boundaries, from a high-concentration compartment to a low-concentration compartment. Flux, on the other hand, is due to the horizontal movement of the medium

Plant Injury

- To cause leaf injury, an air pollutant needs to pass through the stomata of the epidermal tissue, as the epidermis is the first target for the pollutant
- In passing into the intercellular spaces, the pollutant may dissolve in the surface water of the leaf cells, affecting cellular pH
- The pollutant may then react with specific cellular constituents, such as, cytoplasmic membrane of the organells, enzymes, thus affecting cell metabolism, causing plant injury
- Pollutant may then adversely affect cellular metabolism, resulting in plant injury
- Pollution injury is commonly divided into acute (destruction of tissues, collapsed leaf margin or other areas changes of leaves colour) and chronic (chlorophyll and carotenoids are destroyed) injury.

Plant Injury: Example

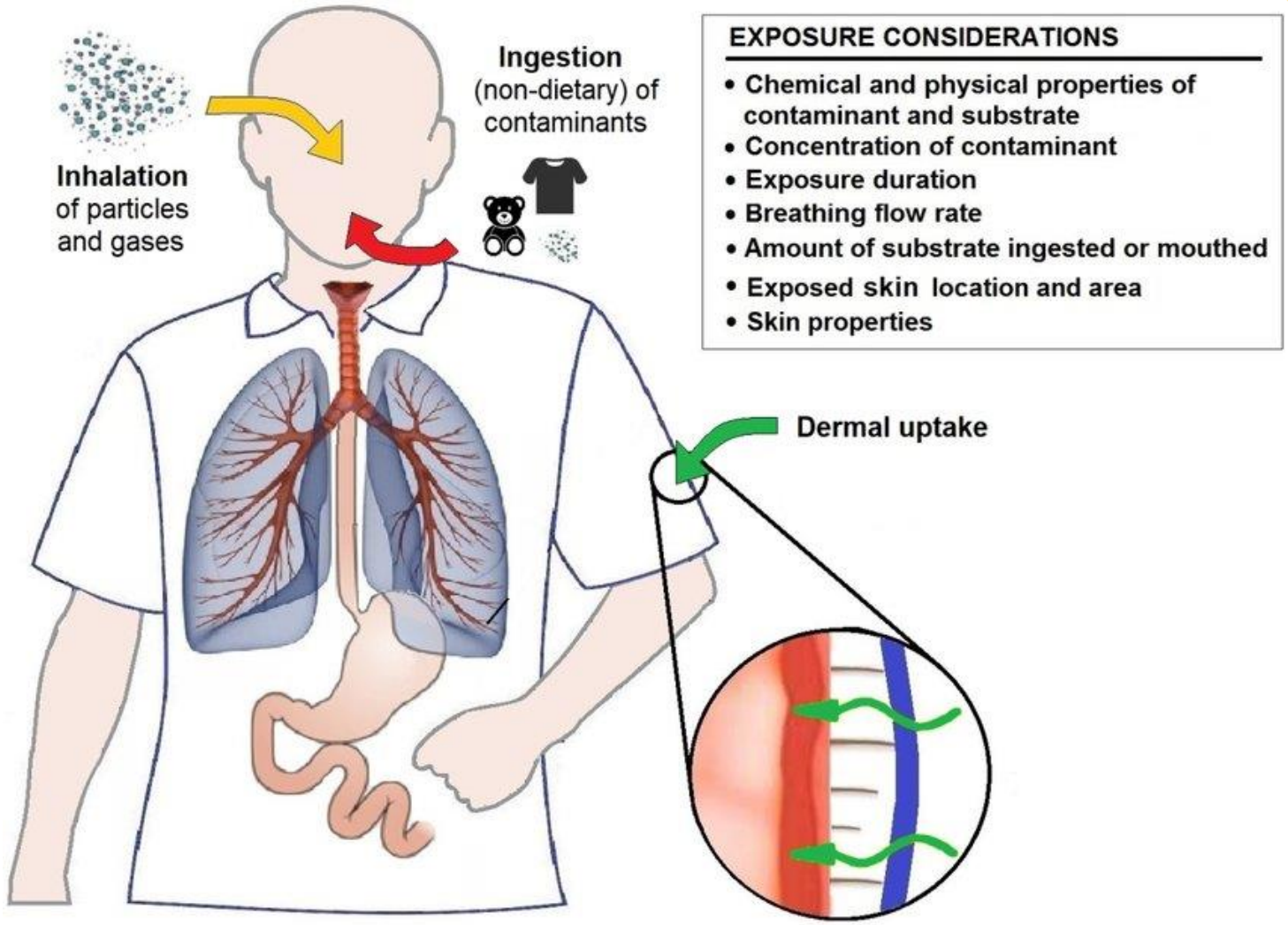
- SO_2 : once absorbed into the leaf, SO_2 can induce injuries to the ultrastructure of chloroplasts and mitochondria, which in turn disrupt photosynthesis or cellular energy metabolism
- Alternately, SO_2 may oxidize and break apart the sulfur bonds in critical enzymes of the membrane, disrupting cellular function
- O_3: may react with membrane material and induce peroxidation of the lipid components. This is followed by the formation of various forms of toxic substances, such as aldehydes, ketones, and free radicals
- Cellular enzyme inhibition is often observed when leaves are exposed to atmospheric pollutants

Contaminated soils: Toxicant uptake

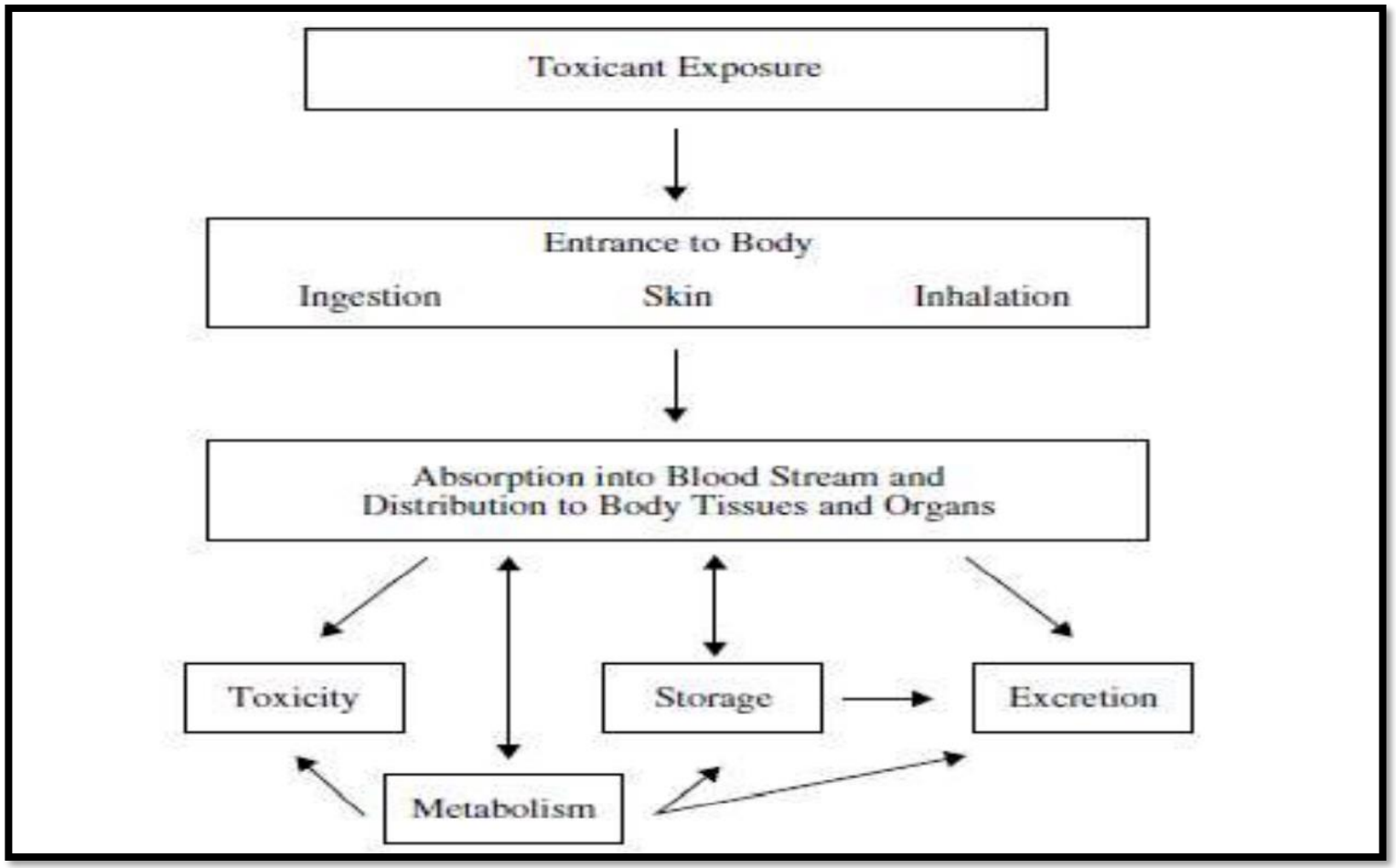
- Exposure of roots to toxicants in contaminated soils is another important process whereby toxicant uptake by plants occurs. Can absorb toxicants through the roots.
- In the contaminated sites, high levels of heavy metals, such as lead (Pb) and cadmium (Cd), chromium (Cr), and aluminum (Al) often occur
- Metallic ions are more readily released, and thus more readily absorbed, when soil is in lower pH condition
- These metal ions may directly damage roots by disrupting water and nutrient uptake, resulting in water deficit or nutrient deficiency
- Following uptake, a toxicant may undergo mixing with the surrounding medium of the plant, and then be transported to various organs and tissues.

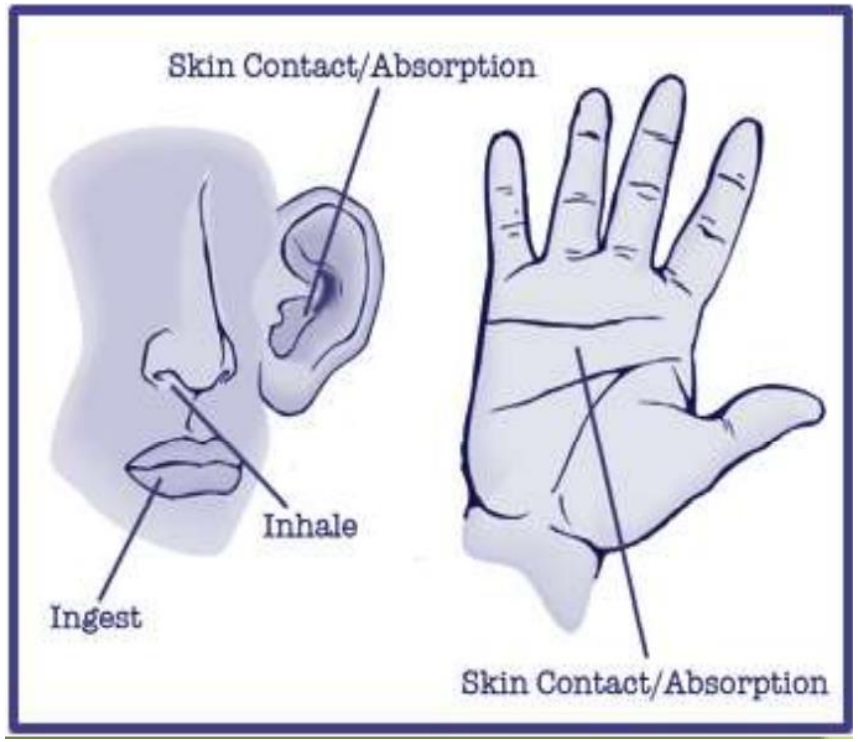
Mammalian Organisms: Exposure

- An environmental pollutant may enter an animal or human through a variety of pathways:
- Inhalation;
- Dermal contact;
- Eye contact; or
- Ingestion

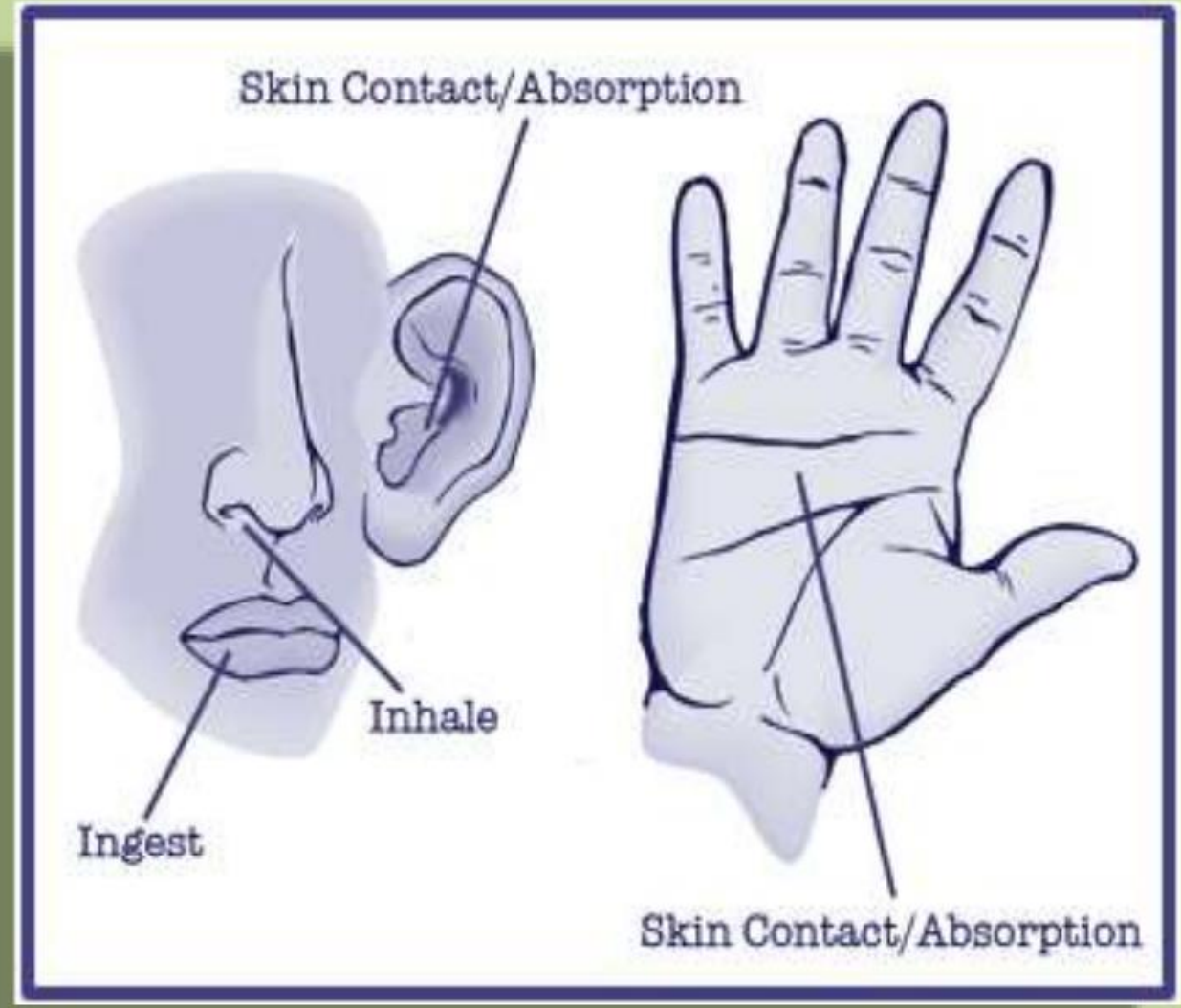


Process of poisoning in animals and humans






DANGER
CORROSIVE CHEMICALS
AVOID CONTACT WITH EYES & SKIN

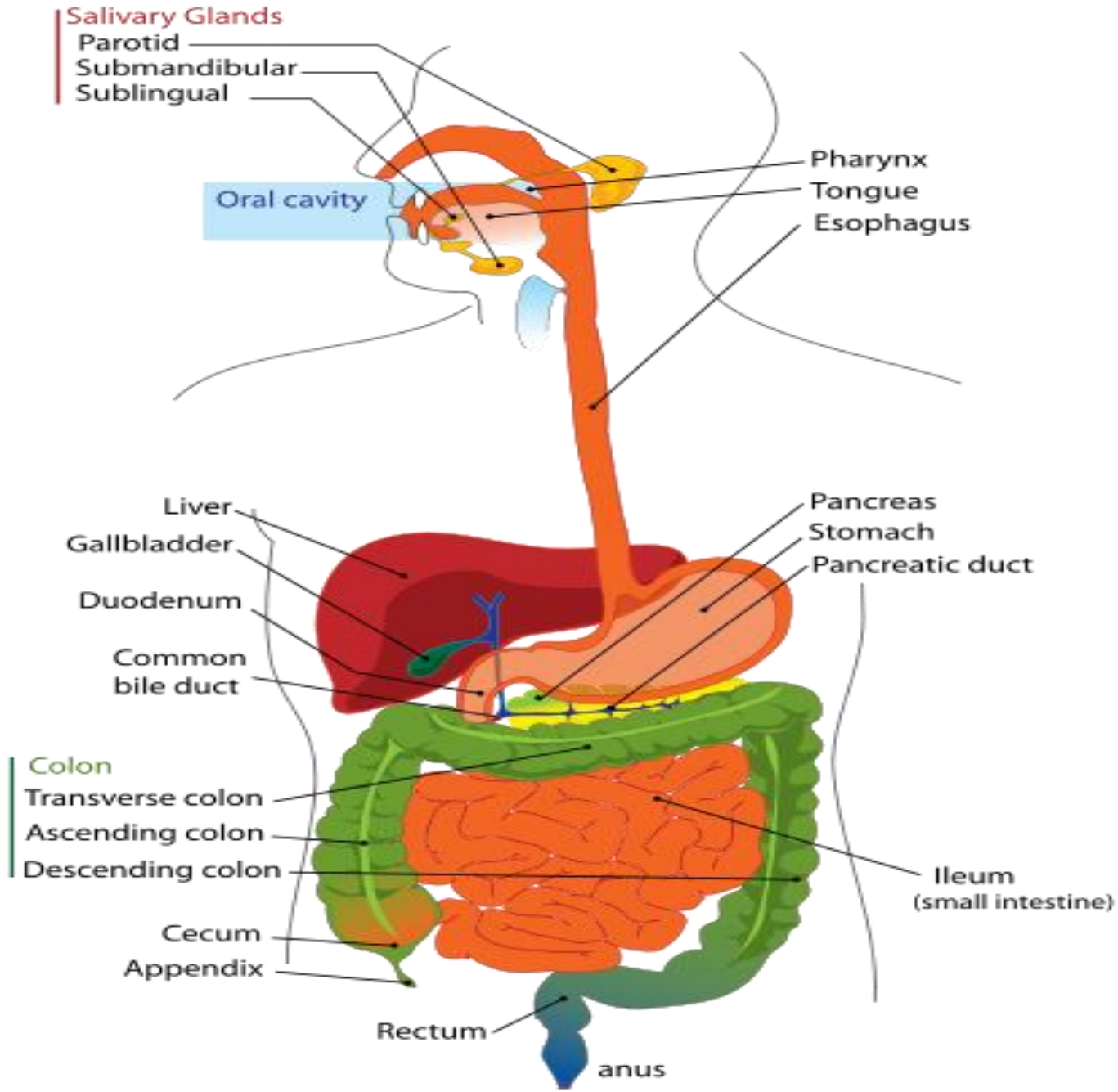

Skin Contact/Absorption
Inhale
Ingest
Skin Contact/Absorption

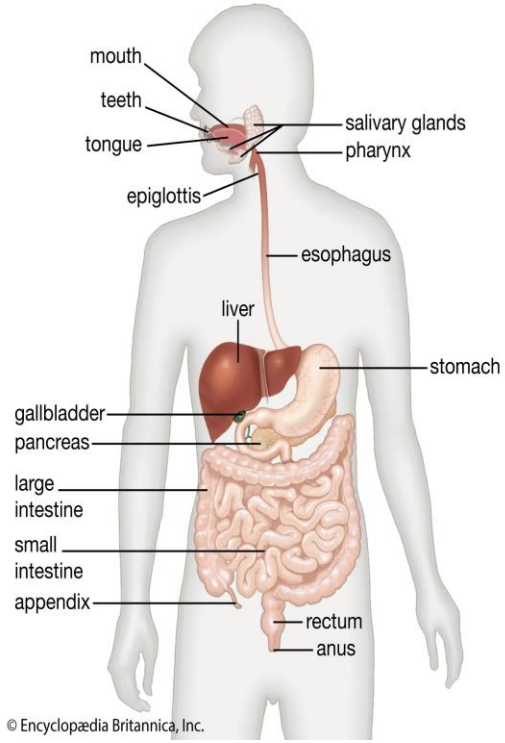
Mammalian Organisms: Uptake

- The immediate and long-term effects of a pollutant are directly related to its mode of entry
- The portals of entry for an atmospheric pollutant are skin, eyes, lungs, and gastrointestinal tract
- And the hair follicles, sweat glands, and open wounds are the possible entry sites where uptake from the skin may occur
- Uptake of toxicants by gastrointestinal tract may occur when consumed foods or beverages are contaminated by air pollutants, such as Pb, Cd, or sprayed pesticides

Mammalian organisms: Uptake

- For a pollutant to be taken up into the body and finally carried to a cell, it must pass through several layers of biological membranes.
- These include not only the peripheral tissue membranes, but also the capillary and cell membranes.
- Therefore, the nature of the membranes and the chemical and physical properties of the toxicant in question are important factors affecting uptake.


Salivary Glands
Parotid
Submandibular
Sublingual
Oral cavity
Pharynx
Tongue
Esophagus
Liver
Gallbladder
Duodenum
Common bile duct
Pancreas
Stomach
Pancreatic duct
Colon
Transverse colon
Ascending colon
Descending colon
Cecum
Appendix
Rectum
anus
Ileum (small intestine)


mouth
teeth
tongue
salivary glands
pharynx
epiglottis
esophagus
liver
stomach
gallbladder
pancreas
large intestine
small intestine
appendix
rectum
anus
© Encyclopædia Britannica, Inc.

Mammalian organisms: Uptake

- The mechanisms by which chemical agents pass through the membrane include:
- Filtration through spaces or pores in membranes
- Passive diffusion through the spaces or pores, or by dissolving in the lipid material of the membrane
- Facilitated transport, where a specialized protein molecule, called a carrier, carries a water-soluble substance across the membrane
- Active transport, which requires both a carrier and energy

Mammalian organisms: Transport

- After absorption, a toxicant may be bound to a blood protein, forming a complex, or it may exist in a free form
- Transport of a toxicant may occur through the bloodstream or lymphatic system
- The toxicant may then be distributed to various body tissues, including those of storage depots and sites of metabolism

Mammalian organisms: Storage

- A toxicant may be stored in the liver, lungs, kidneys, bones, or adipose tissue
- These storage depots may or may not be the sites of toxic action.
- A toxicant may be stored in a depot temporarily and then released and translocated again.
- Similarly, a toxicant or its metabolite may be transported to a storage site and remain there for along period of time, even permanently

Metabolism

- The set of chemical reactions that occur in living organisms in order to maintain life. These processes allow organisms to grow and reproduce, maintain their structures, and respond to their environments.
- Metabolism is usually divided into two categories: **Catabolism** breaks down organic matter, for example to harvest energy in cellular respiration, **Anabolism**, on the other hand, uses energy to construct components of cells such as proteins and nucleic acids.

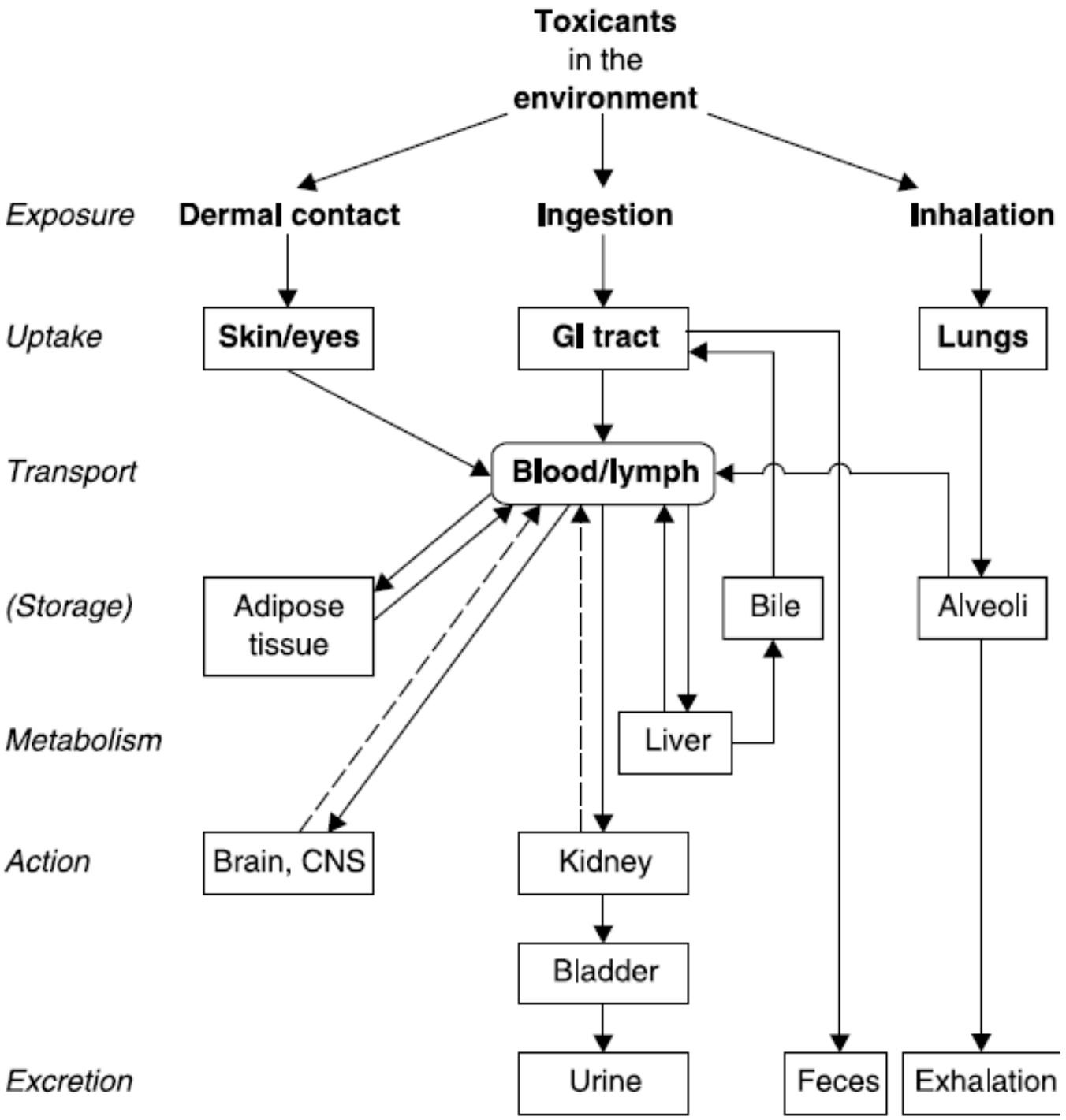
Metabolism of Toxicants

- Metabolism of toxicants may occur at the portals of entry, or in such organs as the skin, lungs, liver, kidney, and gastrointestinal tract
- Liver plays a central role in metabolism of environmental toxicants (xenobiotics)
- Liver contains a rich supply of nonspecific enzymes, enabling it to metabolize a broad spectrum of organic compounds

Mammalian organisms: Excretion

- The final step in the pathway of a toxicant is its excretion from the body.
- Excretion may occur through the lungs, kidneys, or gastrointestinal (GI) tract.
- A toxicant may be excreted in its original form or as its metabolites, depending on its chemical property.
- Excretion is the most permanent means whereby toxic substances are removed from the body.

Processes of poisoning in animals and humans



Mechanism of Action

- Toxic action of pollutants involves: either compounds with intrinsic toxicity or activated metabolites
- The duration of toxic action depends on the characteristics of the toxicant and the physiological or biochemical functioning of the host organism
- The ways xenobiotics can induce adverse effects in living organisms include:
  - Disruption or destruction of cellular structure
  - Direct chemical combination with a cell constituent
  - Inhibition of enzymes
  - Initiation of a secondary action
  - Disruption of reproductive function

Disruption or destruction of cellular structure

- A toxicant may induce an injurious effect on plant or animal tissues by disrupting or destroying the cellular structure
- Atmospheric pollutants, such as SO_2, NO_2, and O_3, are phytotoxic – they can cause plant injuries.
- Studies show that low concentrations of SO_2 can injure epidermal and guard cells, leading to enhanced stomatal conductance and greater entry of the pollutant into leaves
- In animals and humans Inhalation of sufficient quantities of NO_2 and sulfuric acid mists can damage surface layers of the respiratory system
- High levels of O_3 can cause problems with the lipid portion of the membrane, resulting in disruption of membrane structure.

Chemical combination with a cell constituent

- A pollutant may combine with a cell constituent, forming a complex and disrupting cellular metabolism
- CO has the ability to bind to hemoglobin (Hb); after inhalation and diffusion into the blood, CO readily react with Hb to form carboxyhemoglobin (COHb).

$$CO+Hb=COHb$$

- Presence of a large amount of COHb in the blood disrupts the vital system for exchange of CO_2 and O_2 between the blood and lungs and other body tissues. Interference with the functioning of hemoglobin by COHb accumulation is detrimental to health and can lead to death.

Effect of Enzymes

- Reactions in living cell: Participation of enzymes as biological catalysts
- Almost all enzymes are proteins with a globular structure; few requires non protein components (cofactors) e.g., metal ions (K^+, Na^+, Cu^{2+}, Fe^{2+}, Fe^{3+}, Mg^{2+}, organic molecules (coenzymes)
- However, the optimum activity of many enzymes depend on the presence of non protein substances called cofactors
- The molecular partnership of protein-cofactor is holoenzyme and exhibits maximum catalytic activity
- The protein component without its cofactor is termed an apoenzyme and exhibits very low activity or none at all

Protein + Cofactor ⟷ Protein-Cofactor (a complex)

(apoenzyme: inactive or less active)

(Inorganic ion or organic substance: inactive as catalyst)

(Holoenzyme: optimally active catalyst)

Effect of Enzymes

- Ways in which environmental pollutants may inactivate an enzyme systems
- A pollutant may bind to the active site of an enzyme thus inactivating it
- For example, a heavy metal such as Pb, Cd or Hg, after absorption into the body may attach itself to the thiol or sulfhydryl (-SH) group on a protein enzyme, forming a covalent bond with the sulfur atom. This will lead to the inactivation of the enzyme, with active site being blocked, the activity of the enzyme will be depressed or lost.

$$2\text{Enz-SH} + Pb^{2+} \longrightarrow \text{Enz-S-Pb-S-Enz} + 2H^{+}$$