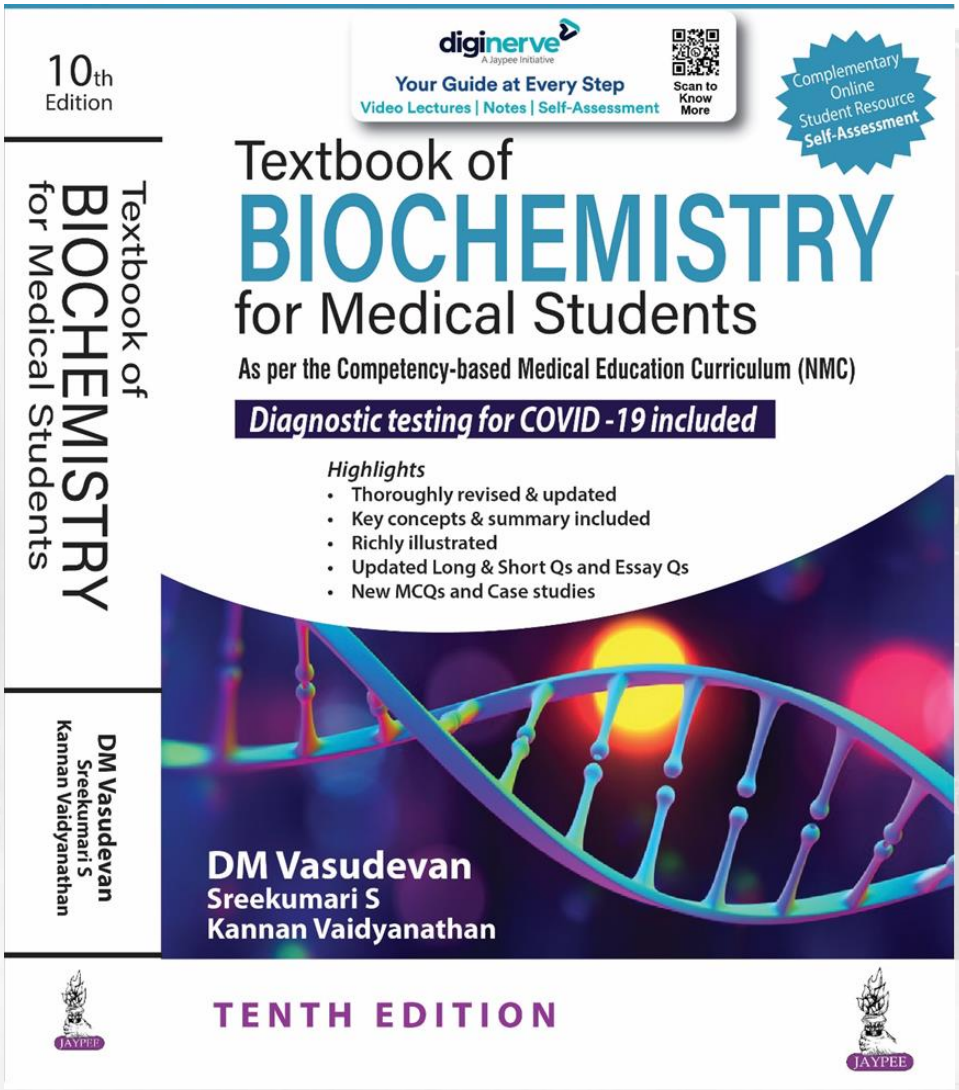


Chapter 32:

Heavy Metal Poisons and Environmental Pollution

Textbook of
BIOCHEMISTRY
for Medical Students

By DM Vasudevan, *et al.*

TENTH EDITION

Common Environmental Poisons

Effect on human body	Common environmental toxins and poisons
Carcinogen	Asbestos, formaldehyde, vinyl chloride, polycyclic aromatic hydrocarbons
Teratogen	Alcohol, cigarette smoke
Mutagen	Radioactivity, x-rays, ultraviolet radiations, ionizing radiations
Neurotoxins	Heavy metals like lead and mercury
Endocrine disruptors	Polychlorinated biphenyls (PCBs), pesticides, plasticizers like bisphenol (BPA), arsenic, dioxin

Lead Poisoning

Sources of Lead Poison

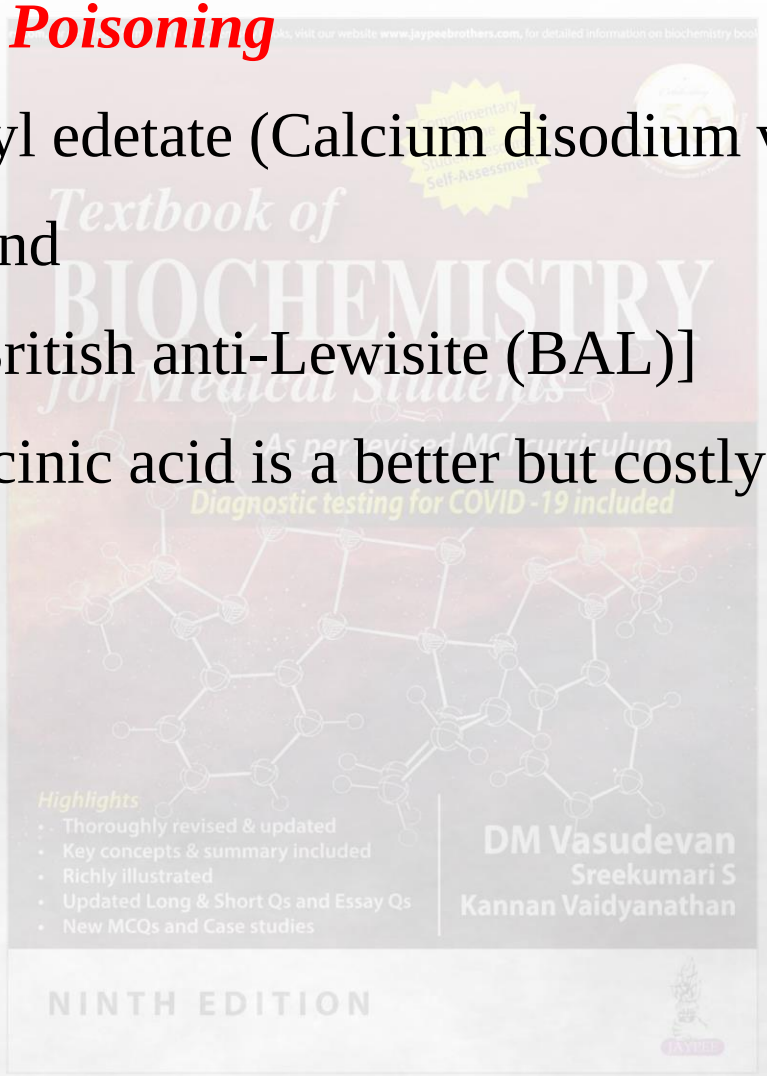
- Lead is the most common environmental poison in India.
- **Paint** is the major source for exposure, especially in children, as they bite painted toys. Paint is peeled off as small flakes from walls of living rooms.
- **Lead pipes** are important sources for contamination.
- One pack of **cigarette** contains 15 μg of lead.
- Lead chromate is commonly used as adulterant in curcumin.
- **Battery** repair, radiator repair, soldering, painting and printing are occupations prone to get lead poisoning.

Signs and Symptoms of Lead Poisoning

- Lead is a **cumulative poison** and is accumulated in tissues over the years. It is not biodegradable. 90% of lead is seen in bones, 9% in blood and 1% in brain and kidneys.
- More than 10 mg/dL in children and more than 25 mg/dL in adults leads to toxic manifestations.
- **Miscarriage**, still birth and premature birth are reported in lead poisoning of mothers.
- In children, **mental retardation**, learning disabilities, behavioral problems, hyperexcitability and seizures are seen.
- Lead particularly inhibits delta aminolevulinic acid (ALA) synthase and ALAdehydratase, leading to **anemia.**
- If the blood level is more than 70 mg/dL, **acute toxicity** as encephalopathy, convulsions, mania, neuropathy, abdominal colic, severe anemia

Treatment of Lead Poisoning

- Calcium dodecyl edetate (Calcium disodium versenate)
- Penicillamine and
- Dimercaprol [British anti-Lewisite (BAL)]
- Dimercaptosuccinic acid is a better but costly antidote.



Mercury Poisoning

It is the most common industrial poison. The source for poisoning may be elemental, inorganic or organic mercury.

Elemental Mercury

- Poisoning can occur by inhalation of mercury vapor from broken thermometers, sphygmomanometers or from dental amalgam.
- In acute poisoning, pulmonary edema and encephalopathy may result.
- A classical triad of (a) oral lesions (gingivitis, salivation and stomatitis), (b) tremor and (c) psychological changes (insomnia, shyness, emotional instability, memory loss) are the hallmark of chronic elemental mercury poisoning. This is called **erethysm** (Mad Hatter's disease).

Inorganic Mercury

Poisoning may arise from calomel (cathartic), topical medicines and in plastic industry. Acute effects include gingivitis, gastritis, vomiting and pulmonary edema. In chronic cases, erethism is seen.

Organic Mercury poisoning

- Poisoning may occur from paints, fungicides and cosmetics.
- From mercury salt wastes, the bacteria synthesize **methyl mercury** (CH3–Hg+). This then enters into the fish. Eating of such fish is the most common cause for organic mercury poisoning. Organic mercury poisoning is called **Minamata disease**.
- The classical triad of methyl mercury exposure is dysarthria, ataxia and visual field constriction.
- Normal level of mercury in blood is less than 1 mg/dL. When it is increased to 2–5 mg/dL, symptoms of toxicity appear. A level of 15 mg/dL is fatal.
- Dimercaprol derivatives, D-penicillamine and N-acetylcysteine can increase the excretion of mercury and are useful in treatment.

Aluminum Toxicity

- Exposure is from packing and building materials, paint pigments, insulating materials, cosmetics, antacids and aluminum cooking vessels.
- Tolerable upper limit of absorption is 1 mg/day. Only up to 100 μg/day can be eliminated through urine.
- Aluminum stimulates production of free radicals.
- It prevents absorption of calcium, phosphorus and iron.
- It interferes with heme synthesis.
- Aluminum precipitates Alzheimer precursor proteins and may lead to **Alzheimer's disease**.
- It is also involved in **Parkinson's disease**.
- Osteomalacia and microcytic hypochromic anemia are other manifestations of toxicity.

Arsenic Toxicity

The oxides of arsenic are commonly used as fruit sprays, pesticides, rat poisons, etc. It acts on sulfhydryl enzymes and interferes with cell metabolism. It may also cause intravascular hemolysis, which leads to hemoglobinuria. The trivalent or pentavalent organic arsenic compounds are less toxic than inorganic compounds. The symptoms are anaphylactic reactions or later development of agranulocytosis, hepatitis, jaundice and encephalitis.

Cyanide Poisoning

- Cyanide causes tissue anoxia by chelating the ferric ions of cytochrome oxidase. Poisoning may be due to suicidal attempts.
- Industrial exposure may occur in the persons working with hydrocyanic (prussic) acid or with potassium cyanide.
- Ingestion of amygdalin, present in kernels of certain fruits (apricots, almonds, peaches) is also a common cause.
- Dicobalt edetate (kelocyanor) is the antidote, which chelates the cyanide. Another method is to give sodium nitrite and sodium thiosulfate intravenously. The nitrite converts hemoglobin to methemoglobin. Ferric ion of Met-Hb takes up cyanide as cyanmethemoglobin, so that cytochrome oxidase is now free of cyanide.
- But in practice, death is instantaneous and time may not be available for the treatment.

Carbon Monoxide Poisoning

Carbon monoxide (CO) poisoning occurs from vehicle engines, furnaces and fires. It can bind to hemoglobin (Hb) and produce carboxy-hemoglobin (COHb), which competes with oxygen for Hb binding. Hence CO is very toxic. CO reduces oxygen delivery to tissues. Above 10%, COHb produces respiratory symptoms, and it is immediately fatal above 80%.

It has a cherry red appearance, and this is used as a spot (screening) test. In an alkaline medium, the color intensifies. Differential spectrophotometry and gas chromatography (GC) are used as quantitative tests for COHb measurement. Spectrophotometric methods work on the basis of spectral lines produced by COHb, and are commonly used for its assay.

Pesticides and Insecticides

Dichlorodiphenyltrichloroethane (DDT)

It is fat-soluble and deposited in the adipose tissue. It is not excreted. Thus, concentration inside the body goes on increasing. Many antifungal agents are having long-term effects of depressed spermatogenesis and fertility.

Organophosphorus Compounds

- Organophosphorus (ORP) and organocarbamates (ORC) are the common pesticides and organosulfur compounds (dithiocarbamates) are fungicides. Organophosphorus compounds, Parathion and Malathion are powerful
- Neurotoxic agents. They inhibit **acetylcholine esterase,** through phosphorylation of the active center of the enzyme. Thus, the transfer of nerve impulse across synapses is prevented.
- Diagnosis depends on the estimation of cholinesterase in serum and RBC.
- The antidote is atropine sulfate and cholinesterase re-activators (diacetyl monoxime or pralidoxime).

Bisphenol Toxicity

Bisophenol A (BPA) is a component of polycarbonated beverages and metal can coatings. It is banned by FDA in 2012. It has been used in plastics, PVCs, food packaging, dental sealants, and thermal receipts. The biologically active of BPA is the 'unconjugated' form and it has a half-life of approximately 6 hrs. It is excreted through urine and bile. Exposure to humans can be by ingestion, inhalation and skin contact. It was found to have adverse health effects, on the brain and prostate glands, in fetuses, infants and children. It can also affect behavior, and aggravate Type 2 diabetes mellitus, hypertension and cardiovascular diseases. Possible adverse effects have also been related to neurological diseases, including Alzheimer's disease. It may also be carcinogenic and cause infertility. The effects may be permanent, even after short exposure.

Methanol Toxicity

It is the organic solvent widely used in paints and anti-freezes. It may be consumed in place of ethanol as a substitute.

Alcohol dehydrogenase converts methanol to **formaldehyde** which is more toxic than methanol.

Optic neuritis with consequent blindness is the characteristic toxicity.

The treatment is to give large doses of ethanol, which is preferentially oxidized in the body so that formaldehyde formation is reduced.

Air Pollutants

- The permissible level of total suspended particles (TSPs) in air is 230 mg/cu m.
- A chemical other than those conventionally accepted in the composition of clean air is called a **contaminant**.
- A contaminant that occurs in the atmosphere in sufficiently high concentrations to cause an adverse effect is called a **pollutant.**
- The main *natural sources* of pollution are due to forest fires, dust storms and air-borne particles.
- S*uspended particulate matter* like dust and soot, also adds to the contamination of air.
- The major *artificial sources* of pollution arise due to emissions from automobiles, industry and power plants. These are carbon dioxide, **carbon monoxide**, hydrocarbons, oxides of nitrogen, oxides of sulfur and lead.

Air Pollutants, Continued

- The poisonous mixture of smoke, fog, air and other chemicals is called smog. The *chemically reducing smog* is derived from the combustion of coal and oil, and contains **sulfur dioxide** (SO2), sulfur trioxide (SO3), mixed with soot.
- Exacerbations of bronchitis were associated with high concentrations of smoke and sulfur oxide. Children living in polluted areas show diminished ventilatory function.
- **Heart diseases** are also related to pollutants such as ozone, sulfur dioxide, sulfates and cadmium in the air.
- High level of carbon monoxide decreases ability to concentrate and decreases visual threshold.
- Inhalation of air-borne lead can cause neurological disturbances.

Passive Cigarette Smoking

The particulate load in a household is directly proportional to the number of cigarette smokers living at home.

Increased prevalence of respiratory illnesses and reduced levels of pulmonary function measurements have been found in children of smoking parents.

Studies have also concluded that lung cancer risk is higher in non-smokers who live under the same roof with smokers.

Common Industrial Pollutants

Agents	Causative Industry	Acute manifestation	Chronic manifestation
Acid fumes (H_2SO_4, HNO_3)	Fertilisers, chlorinated organic com pounds, dyes, explosives, plastics	Mucous membrane irritation followed by chemical pneumonitis	Chronic bronchitis
Cyanides	Electroplating, extraction of gold or silver, manufacture of fumigants	Increased respiratory rate; respiratory arrest; lactic acidosis	No data
Formalde-hyde	Resins, rubber; laboratory works; urethane foam	Same as for acid fumes	Cancers in animals; no data in humans

Common Industrial Pollutants, Continued

Agents	Causative Industry	Acute manifestation	Chronic manifestation
Halides (Cl, Br, F)	Bleaching in pulp, paper textile industry; synthetic rubber, plastics	Mucous membrane irritation, pulmonary edema	**Bronchitis, epistaxis, dental fluorosis**
Isocyanates	Polyurethane foams, plastics, adhesives, surface coatings	Mucous membrane irritation, dyspnea, pulmonary edema	**Upper respiratory tract irritation, asthma**
Nitrogen dioxide	Metal etching, explosives, welding	Cough, dyspnea, pulmonary edema, bronchiolitis	**Emphysema, chronic bronchitis**
Sulphur dioxide	**Coating of nonferrous metals, food processing, burning of fossil fuels**	**Mucous membrane irritant, epistaxis**	**Asthma, chronic bronchitis**

Toxic Substances in Foodstuffs

Toxins Normally Present in Plants

Protease inhibitors: Many legumes (soy bean, field bean, peanut), cereals (corn) and tubers (potato, sweet potato) contain trypsin inhibitors. They are destroyed by cooking. But partially cooked food may have this activity, inhibiting digestion and absorption of amino acids.

Goitrogens: They prevent iodine uptake or utilization by thyroid gland. Thio-oxazolidone is present in cabbage, radish, turnip and Brussels sprouts. Thiocyanates and isothiocyanates are seen in mustard and other oilseeds.

Antivitamins: Orange peel, used in making orange marmalade, contains citral, which inhibits vitamin A activity. Linseed oil, which contains linetin, interferes with pyridoxine utilization. Black berries and red cabbage contain thiaminase, which destroys vitamin B1. Raw eggs, containing avidin, can lead to biotin deficiency..

Toxic Substances in Foodstuffs

Toxins Normally Present in Plants, continued

Cyanogenic glycosides: Cereals (sorghum), legumes (lima beans) and tubers (tapioca or cassava) contain cyanogenic compounds, which on hydrolysis produce hydrocyanic acid. Hence, they are highly toxic when taken raw. The toxins can be removed by cooking and decanting the supernatant water.

Favism: Ingestion of uncooked broad bean (*Vicia faba*) may cause **hemolytic anemia** in susceptible persons with glucose-6-phosphate dehydrogenase (GPD) deficiency.

Alkaloids: Some mushrooms contain poisonous alkaloids. In small quantities, they produce nausea, vomiting, diarrhea, etc. In large quantities, it may produce acute necrosis of liver and death may result.

Pressor amines: They increase the blood pressure. Histamine, tyramine, tryptamine, serotonin and epinephrine are present in significant quantities in plantains, banana and cheese. Tyramine is present in cheese, wine and beer.

Contamination Occurring during Cultivation

This is due to pesticides and insecticides. These toxins could be removed by repeated washing and by peeling of outer layers of vegetables and fruits.

Storage Contamination

Fungal infections: During postharvest storage, contamination with fungus is very common. *Aspergillus flavus* produces **aflatoxins,** which are hepatotoxic and carcinogenic. The fungus grows in moist conditions in groundnut, coconut, rice, maize, wheat, etc.

Ergot (*Claviceps purpurea*): It is the fungus that usually grows in moist food grains (rye, millet, wheat, barley, bajra). Ergotamine, ergotoxin and ergometrine are present in this fungus. The toxins may produce peripheral vascular contraction, causing gangrene in extremities. The disease is called **ergotism**.

Toxic Substances in Foodstuffs

Contamination during Food Processing

Mineral oils: Petroleum products are used to extract oil from seeds. These solvent residues may remain in the extracted oil. Mineral oils have hepatotoxic and carcinogenic properties

Adulterants

Lathyrism: It is characterized by paralysis of lower limbs. It is seen in persons consuming large quantities of *Lathyrus sativus* (**Khesari dal**). **Neurotoxins** present in *Lathyrus* cause damage of upper motor neurons. The toxic principle Is **beta oxalyl amino alanine** (BOAA). It inhibits lysyl oxidase, resulting in reduced cross-linking in collagen.

Argemone oil: Mustard oil may be adulterated with argemone oil. This is from a wild plant, *Argemone mexicana*. Argemone oil contains the alkaloid, sanguinarine which causes vomiting, diarrhea, congestive cardiac failure and edema. It is then called **epidemic dropsy.**

Toxic Substances in Foodstuffs

Toxins Entering during Food Preparation

Monosodium glutamate (Ajinomoto):

- It is a common food additive.
- Packets of mono sodium glutamate carry the statutory warning that it is unsuitable for children below the age of 5.
- It produces transient symptoms like numbness and palpitation.
- It may deteriorate mental alertness in children.

Common Household Pollutants

Item	Pollutant	Effect
Furniture, Carpets, Vinyl floor tiles ,wall paper	Volatile organic compounds (VOCs)	Irritant / mutagenic / carcinogenic
Air freshners and deodorants	Formaldehyde	Irritant and carcinogen
Bleach	Hypochlorite	Corrosive, irritant
Disinfectants	Hypochlorite, phenol	Irritant, toxic to respiratory system, skin and eyes
Drain cleaner	Sodium and potassium hydroxide	Corrosive

Cosmetics

- Many hair dyes contain phenylenediamine, which is an irritant and may damage DNA leading to cancer.
- Formaldehyde and paraformaldehyde are known carcinogens
- Quaternium 15 releases formaldehyde.
- Mercury can damage the kidneys and nervous system.
- Dibutyl and diethylhexyl phthalates, as well as isobutyl and isopropyl parabens can disrupt hormones and can cause early puberty in boys and other changes in the reproductive system.
- The nail polishes may contain chemicals like dibutylphthalates, toluene and formaldehyde
- Phthalates are present in perfumes and hairsprays, shampoos and moisturizers