Toxic Metals

By

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Aluminum

- **Introduction**
- Aluminum (Al) is a crystalline silver-white ductile metal.
- Aluminum is the most abundant metal in the earth's crust (~8%). It is always found combined with other elements such as oxygen, silicon, and fluorine.
- Aluminum as the metal is obtained from aluminum-containing minerals.
- Due to its good conductivity of heat and electricity, ease of welding, tensile strength, light weight, and corrosion- resistant oxide coat, aluminum is applicable to a wide variety of industrial and household uses.

Absorption, Transport, and Excretion

- The average adult in the United States ingests about 7 to 9 mg aluminum per day in their food. The human organism can absorb aluminum and its compounds orally, by inhaling, and parenterally.
- There is no indication of dermal absorption. Approximately 1.5% to 2% of inhaled and 0.01% to 5% of ingested aluminum is absorbed.
- The absorption efficiency is dependent on chemical form, particle size (inhalation), and concurrent dietary exposure to chelators such as citric acid or lactic acid.
- After a relatively quick uptake of aluminum into the intestinal walls, its passage into the blood is much slower. In plasma, aluminum is bound to carrier proteins such as transferrin.
- Urine accounts for 95% of aluminum excretion with 2% eliminated in the bile.

Health Effects and Toxicity

- The mechanism by which aluminum applies its toxicity is not well understood, though aluminum has been shown to interfere with a variety of enzymatic processes, and administration of aluminum to experimental animals is known to produce encephalopathy similar to that seen in Alzheimer disease in man.
- Workers who breathe large amounts of aluminum dusts can have lung problems, such as coughing or changes that show up in chest X-rays.

Signs and symptoms of aluminum toxicity include

- encephalopathy (stuttering, gait disturbance, myoclonic jerks, seizures, coma, and abnormal EEG); osteomalacia or aplastic bone disease (painful spontaneous fractures, hypercalcemia, and tumorous calcinosis); proximal myopathy; increased risk of infection; microcytic anemia; and increased left ventricular mass and decreased myocardial function.
- Aluminum toxicity occurs in people with renal insufficiencies who are treated by dialysis with aluminum contaminated solutions or oral agents that contain aluminum. The clinical manifestations of aluminum toxicity include anemia, bone disease, and progressive dementia with increased concentrations of aluminum in the brain.

Laboratory Evaluation

- Accurate measurements are often complicated by the increased risk of environmental contamination of specimens. Urine and serum levels are useful in determining toxic exposures, monitoring exposure over time, and monitoring chelation therapy.

Arsenic

- **Introduction**
- Arsenic (As) is a ubiquitous element displaying both metallic and non-metallic properties. Its content in the earth's crust is estimated at 1.5 to 2.0 mg/kg.
- For most people, food is the largest source of arsenic exposure (about 25 to 50 µg/d), with lower amounts coming from drinking water and air.
- The main current use of arsenic is as a wood preservative. Other current and past uses of arsenic include pesticides, pigments, poison gases, semiconductor processing, and medicines.

Health Effects and Toxicity

- The relation of clinical signs and symptoms to arsenic exposure depends on the duration and extent of the exposure to inorganic and methylated species of arsenic, as well as the underlying clinical status of the patient.
- For acute arsenic exposure, the symptoms may include gastrointestinal (nausea, emesis, abdominal pain, and rice water diarrhea), bone marrow (pancytopenia, anemia, and basophilic stippling), cardiovascular (ECG changes), central nervous system (encephalopathy and polyneuropathy), renal (renal insufficiency and renal failure), and hepatic (hepatitis) systems.
- For chronic arsenic exposure, signs and symptoms may include dermatologic (hyperkeratosis, hyperpigmentation, and alopecia), hepatic (cirrhosis and hepatomegaly), cardiovascular (hypertension and peripheral vascular disease [PVD]), central nervous system ("socks and glove" neuropathy and tremor), and malignancies (squamous cell, hepatocellular, skin, bladder, lung, and renal carcinomas).

Absorption, Transport, and Excretion of Arsenic

- The main routes of exposure are ingestion of arsenic containing foods, water, and beverages or inhalation of contaminated air; however, arsenic toxicity is a complex topic.
- Organic forms of arsenic such as arseno choline and arseno betaine are commonly found in fish and seafood, are considered relatively non-toxic, and are cleared rapidly (1 to 2 d).
- Inorganic species of arsenic are highly toxic and occur naturally in rocks, soil, and groundwater.
- Laboratory Evaluation
- Arsenic is best detected by urine due to the short half-life of arsenic in blood.

Cadmium

- **Introduction**
- Cadmium (Cd) is a soft, bluish-white metal, which is easily cut with a knife. Principal industrial uses of cadmium include manufacture of pigments and batteries, as well as in the metal-plating and plastics industries.

Absorption, Transport, and Excretion

- Based on renal function (development of proteinuria), the reference dose for cadmium in drinking water is 0.0005 mg/kg/d and the dose for dietary exposure to cadmium is 0.001 mg/kg/d.
- Absorption of cadmium is higher in females than in males due to differences in iron stores. The absorption of inhaled cadmium in air is 10% to 50% with gastrointestinal absorption of cadmium estimated to be 5%. The absorption of cadmium in cigarette smoke is 10% to 50% and smokers of tobacco products have about twice the cadmium abundance in their bodies as nonsmokers.
- For nonsmokers, the primary exposure to cadmium is through ingested food. About 90% of ingested cadmium is excreted in the feces due to the low absorbance of cadmium from the gut.

Health Effects and Toxicity

- Cadmium has no known role in normal human physiology. Toxicity is believed to be a result of protein-Cd adducts causing denaturation of the associated proteins, resulting in a loss of function . Ingestion of high amounts of cadmium may lead to a rapid onset with severe nausea, vomiting, and abdominal pain.
- Acute effects of inhalation of fumes containing cadmium include respiratory distress due to chemical pneumonitis and edema and can cause death.
- Breathing of cadmium vapors can also result in nasal epithelial damage and lung damage similar to emphysema.
- Cadmium exposure can affect the liver, bone, immune, blood, and nervous systems.

Laboratory Evaluation

- In blood, cadmium is found mostly (70%) in the RBCs. Cadmium in blood reflects the average uptake during the past few months and can be used for monitoring purposes but does not accurately reflect a recent exposure. Urinary excretion is about 0.001% and 0.01% of the body burden per 24 hours.
- At low exposure, urine cadmium reflects the total accumulation.

Chromium

- **Introduction**
- Chromium (Cr), from the Greek word chroma (“color”), makes rubies red and emeralds green.
- Chromium is the 21st most abundant element in the earth’s crust and is used in the manufacturing of stainless steel.
- Occupational exposure to chromium occurs in wood treatment, stainless steel welding, chrome plating, the leather tanning industry, and the use of lead chromate or strontium chromate paints.

Absorption, Transport, and Excretion

- Cr(6+) is better absorbed and much more toxic than Cr(3+). Both transferrin and albumin are involved in chromium absorption and transport.
- Transferrin binds the newly absorbed chromium at site B, while albumin acts as an acceptor and transporter of chromium if the transferrin sites are saturated. Other plasma proteins, including ß- and γ-globulins and lipoproteins, bind chromium.

Health Effects, Deficiency, and Toxicity

- Cr(3+) is an essential dietary element and plays a role in maintaining normal metabolism of glucose, fat, and cholesterol.
- Dietary chromium deficiency is relatively uncommon and most cases occur in persons with specific clinical situations such as total parenteral nutrition, diabetes, and malnutrition.
- Chromium deficiency is characterized by glucose intolerance, glycosuria, hypercholesterolemia, decreased longevity, decreased sperm counts, and impaired fertility.
- When inhaled, Cr(6+) is a respiratory tract irritant, resulting in airway irritation, airway obstruction, and possibly lung cancer. The target organ of inhaled chromium is the lung; the kidneys, liver, skin, and immune system may also be affected.

Laboratory Evaluation

- Plasma, serum, and urine do not indicate the total body status of the individual, whereas urine levels may be useful for metabolic studies.

Copper

- Introduction
- Copper (Cu) is a relatively soft yet tough metal with excellent electrical and heat conducting properties.
- Copper is widely distributed in nature both in its elemental form and in compounds. Copper forms alloys with zinc (brass), tin (bronze), and nickel (cupronickel, widely used in coins).
- Copper is an essential trace element found in four oxidation states, Cu(0), Cu(1+), Cu(2+), and Cu(3+), with Cu(2+) the most stable of all oxidation states.

Absorption, Transport, and Excretion

- The copper content in the normal human adult is 50 to 120 mg.
- Copper is distributed through the body with the highest concentrations found in liver, brain, heart, and kidneys.
- Hepatic copper accounts for about 10% of the total copper in the body. Copper is also found in the cornea, spleen, intestine, and lung. The amount of copper absorbed from the intestine is 50% to 80% of ingested copper.
- The average daily intake is approximately 10 mg or more of copper.
- Copper is transported to the liver and bounds to albumin, transcuprein, and low-molecular-weight components in the portal system. In the liver, copper is incorporated into ceruloplasmin for distribution throughout the body.

Health Effects, Deficiency, and Toxicity

- Copper is a component of several metalloenzymes, including ceruloplasmin, cytochrome C oxidase, superoxide dismutase, tyrosinase, metallothionein, dopamine hydroxylase, lysyl oxidase, clotting factor V, and an unknown enzyme that cross-links keratin in hair.
- Copper deficiency is observed in premature infants and copper absorption is impaired in severe diffuse diseases of small bowel, lympho sarcoma, and scleroderma.
- Copper deficiency is related to malnutrition, malabsorption, chronic diarrhea, and prolonged feeding with low copper, total-milk diets.
- Signs of copper deficiency include (1) neutropenia and hypochromic anemia in the early stages, (2) osteoporosis and various bone and joint abnormalities that reflect deficient copper-dependent cross-linking of bone collagen and connective tissue, (3) decreased pigmentation of the skin and general pallor, and (4), in the later stages, possible neurologic abnormalities (hypotonia, apnea, and psychomotor retardation).

Laboratory Evaluation

- Serum copper and urine copper are used to monitor for nutritional adequacy and subacute management of copper toxicity. Direct measurement of free copper and ceruloplasmin in serum is used to screen for Wilson's disease.
- Common trends in laboratory testing seen in various diseases states are summarized in Table 18-2.

TABLE 18-2 INTERPRETATION OF COPPER TESTING RESULTS[7]

	SERUM COPPER	URINE COPPER
Nutritional deficiency	↓	↓
Menkes syndrome	↓	↑
Acute copper toxicity	↑ or ↑↑	↑
Chronic copper toxicity	↑	↑
Wilson's disease	N or ↓	↑ or ↑↑
Smoking, inflammatory conditions	↑ or ↑↑	N
Estrogen, pregnancy	↑ or ↑↑	N

N, normal; ↓, decreased; ↑, increased; ↑↑, Significantly increased.

Mercury

- Introduction
- Mercury (Hg), also called quicksilver, is a heavy, silvery metal. Along with bromine, mercury is one of only two elements that are liquid at room temperature and pressure.
- There are three naturally occurring oxidation states of mercury: Hg(0), Hg(1+), and Hg(2+). Organic mercury refers to various forms of mercury bound to a carbon atom, with mercury usually in the +2 oxidation state.
- Mercury is used in dental amalgams, electronic switches, germicides, fungicides, and fluorescent light bulbs.
- The use of mercury in medicine has greatly declined in all respects; however, mercury compounds are found in some over-the-counter drugs, including topical antiseptics, stimulant laxatives, diaper-rash ointment, eye drops, and nasal sprays. Mercury is widely used in the production of eye cosmetics, especially mascara.

Absorption, Transport, and Excretion

- Routes of exposure include (1) inhalation, primarily as elemental mercury vapor but occasionally as dimethyl mercury; (2) ingestion of $HgCl_2$ and mercury-containing foods such as predatory fish species; (3) cutaneous absorption of methyl mercury (MeHg) through the skin and even through latex gloves; (4) injection of relatively inert liquid mercury and mercury-containing tattoo pigments; and (5) dental amalgams.
- Inhaled mercury vapor is retained in the lungs to about 80%, whereas liquid metallic mercury passes through the gastrointestinal tract largely unabsorbed.

Health Effects and Toxicity

- Mercury has no known function in normal human physiology. Toxicities have been observed following inhalation, ingestion, and dermal absorption of mercury compounds.
- Mercurial salts were historically used as diuretics, topical disinfectants, and laxatives before mercury toxicity was well understood.
- Although it was widely speculated that this mercury-based preservative can cause or trigger autism in children, scientific studies showed no evidence supporting any such link.
- Laboratory Evaluation
- Mercury is usually determined as total mercury levels in blood and urine without regard to chemical form.