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is benign, and treatment is symptomatic. More severe exposures may cause lung damage and fatality. Cd oxide fume is a severe pulmonary irritant. Cd dust is a less potent irritant than Cd fume because of its larger particle size, which appears to be a more important determinant of toxicity.

Inhalation of fumes with a high Cd concentration has been responsible for fatalities, while nonfatal cases are seen at lower concentrations. Pulmonary symptoms and clinical signs reflect lesions ranging from nasopharyngeal and bronchial irritation to pulmonary edema and death. Other possible symptoms include, headache, chills, muscle aches, nausea, vomiting, and diarrhea. Respiratory symptoms linger for several weeks, and impairment of pulmonary function persists for months.

24.6.5 Signs and Symptoms of Chronic Toxicity

Chronic exposure to Cd affects the kidney, lungs, and bone. In kidney, chronic exposure is implicated in the development of cancer. In lungs, long-term inhalation results in decreased lung friction and emphysema. Even if absorption by ingestion is low, chronic exposure to high levels of Cd in food has caused bone disorders, including osteoporosis and osteomalacia.* Other consequences of Cd exposure are anemia, yellow discoloration of the teeth, rhinitis, occasional ulceration of the nasal septum, damage to the olfactory nerve, and loss of the sense of smell (anosmia).

24.7 COPPER (Cu)

24.7.1 Occurrence and Uses

In ancient times, copper (Cu) was useful for its curative powers, largely due to its antibacterial and antifungal properties, in the treatment of wounds and skin diseases, and pulmonary diseases. Today, it is widely recognized for its effectiveness in the treatment of a number of internal diseases including anemia, cancer, rheumatoid arthritis, stroke, and heart disease. For instance, Cu complexes, such as Cu aspirinate and Cu tryptophanate, markedly increase the healing rate of ulcers and wounds. While studies have shown that nonsteroidal anti-inflammatory drugs, such as ibuprofen, suppress wound healing, Cu complexes of these drugs promote normal wound healing in addition to retaining anti-inflammatory activity.

24.7.2 Physiological Role

Cu is both a toxic and essential element for living systems. Cu occurs as part of the prosthetic group of proteins. As a cofactor for the enzyme Cu/Zn superoxide dismutase, Cu protects against free radical damage that may affect proteins, membrane lipids, and nucleic acids. It is necessary for enzymes involved in aerobic metabolism, such as cytochrome c oxidase in mitochondria, lysyl oxidase

* In a Japanese population, long-term ingestion of water and food contaminated with Cd was associated with a crippling condition, "*itai-itai*" (*ouch-ouch*) disease. The syndrome is characterized by pain in the back and joints, osteomalacia (adult rickets), bone fractures, and occasional renal failure. Women are more commonly affected.

in connective tissue, dopamine β-hydroxylase in the CNS, and ceruloplasmin, a Cu transport protein. Cu deficiencies have been linked to mental retardation, anemia, hypothermia, bone fragility, and impaired cardiac, neuronal, and immune functions.

24.7.3 Mechanism of Toxicity

Although poorly understood, the mechanism of Cu toxicity is related to the dose and length of exposure (acute or chronic toxicity). Acute toxicity via oral ingestion of high doses of Cu results in nausea and vomiting. Acute Cu toxicity appears to be related to direct irritation of the stomach by Cu ions.

Similarly, the mechanism of chronic toxicity is not clearly defined. It has been postulated to participate in Fenton-type reactions and lysosomal lipid peroxidation leading to cell death.

24.7.4 Toxicokinetics

Ingested Cu is absorbed in the stomach, where low stomach pH frees bound Cu ions from partially digested food particles. Cu complexes and solubilizes with amino acids and organic acids in the intestinal tract. The largest portion of ingested Cu is absorbed by the duodenum and ileum through simple diffusion. Cu-transporting ATPases discharge Cu into the serosal capillaries where they bind to albumin and amino acids for transport to the liver. Circulating Cu may also combine with ceruloplasmin (a sialoglycoprotein) in the circulation and returned to the liver as ceruloplasmin-bound Cu.

Approximately one half of the Cu consumed is absorbed by the GI tract, two thirds of which is secreted into the bile and excreted in the feces. Small amounts of Cu are also excreted in the urine, hair, and sweat. Cu bioavailability is influenced by age and amount ingested.

Cu has a great affinity for metallothionein, a small cysteine-rich protein thought to be involved in its storage and transport. High Cu levels stimulate metallothionein synthesis. Glutathione, amino acids, ATP, and recently identified Cu metallochaperones have been shown to help in intracellular transport. Cu-binding ligands protect against toxicity by regulating its movement. The ligands transport Cu within the cell, making it available for intracellular enzymes.

24.7.5 Signs and Symptoms of Acute Toxicity

Most human cases of acute poisonings with high doses of Cu result from attempted suicides and accidental ingestion of contaminated food and beverages. Acute Cu toxicity is associated with bleeding and ulceration of the GI mucosa, acute hemolysis, and hemoglobinuria. Hepatic necrosis accompanied with jaundice, hypotension, tachycardia, tachypnea, nephropathy, and CNS manifestations, including dizziness, headache and convulsions, can result from acute exposure. The principal targets are the GI tract, liver, kidney, blood, CNS, and cardiovascular system. There are little known effects on the muscular, integumentary, or ocular systems.

24.7.6 Signs and Symptoms of Chronic Toxicity

The liver is the major target of chronic Cu toxicity. Liver disease due to chronic Cu exposure is well characterized in individuals with Wilson's disease, a genetic disorder that results in systemic accumulation of Cu. Chronic exposures have been reported, with high-dose Cu supplements and in drinking water, whose pathology resembles that seen in Wilson's disease. Chronic exposure has also resulted in CNS effects and hemolytic anemia. The anemia is secondary to hepatic necrosis that releases Cu into the circulation, resulting in red blood cell destruction.

24.7.7 Treatment of Acute Poisoning

Removal from Cu exposure is recommended and is often sufficient to resolve most symptoms associated with Cu toxicity. Drinking 4 to 8 ounces of milk or water prior to gastric lavage is recommended for acute poisonings. To prevent further absorption, activated charcoal is suggested. If symptoms persist, Ca disodium-EDTA or intramuscular dimercaprol is given, followed by penicillamine. Vigorous irrigation with water is used for ocular exposure. Application of topical corticosteroids is applied for cases of Cu dermatitis.

24.8 IRON (Fe)

24.8.1 Chemical Characteristics

Iron (Fe) forms ferrous (2^+) and ferric (3^+) compounds. Ferrous compounds are easily oxidized to ferric compounds. Ferrous sulfate (green vitriol or Cuas), the most important of the ferrous compounds, usually occurs as pale-green crystals. The ferrous and ferric ions combine with cyanides to form complex cyanide compounds.

24.8.2 Occurrence and Uses

Ferric ferrocyanide, a dark-blue, amorphous solid formed by the reaction of potassium ferrocyanide with a ferric salt (*Prussian blue*), is used as a pigment in paint and in laundry bluing. Potassium ferricyanide (*red prussiate of potash*) is obtained from ferrous ferricyanide (*Turnbull's blue*) and is used in processing blueprint paper. Fe compounds are also employed in the treatment of hypochromic or Fe-deficiency anemia.

24.8.3 Physiological Role

Fe is an essential metal for almost all living systems, due to its involvement in a number of Fe-containing enzymes and proteins. It is estimated that one third of the world's population suffers from anemia due to Fe deficiency. It is an important component of hemoglobin, myoglobin, and cytochrome enzymes.

The average adult human stores about 3.9 to 4.5 g of Fe. Of this, 65% is bound to hemoglobin, 20 to 30% is bound to the Fe storage proteins ferritin and hemosiderin, and the remaining 10% is a constituent of myoglobin, cytochromes, and

Fe-containing enzymes. Hemoglobin is required for oxygen and carbon dioxide transport. As a component of cytochromes and nonheme Fe proteins, Fe is required for oxidative phosphorylation. Myeloperoxidase, a lysosomal enzyme, requires Fe for proper phagocytosis and killing of bacteria by neutrophils. Fe deficiency results in anemia and decreased immune competence.

24.8.4 Mechanism of Toxicity

Although Fe deficiency is a widespread concern, Fe toxicity, or Fe overload, still presents a significant problem. Organ and cell damage arising from chronic Fe overload affects the liver, heart, and pancreatic beta cells. Hemosiderosis is a rare condition caused by excess Fe intake or improper Fe metabolism. Cirrhosis and hepatoma account for a large number of premature deaths in individuals with the hereditary form of this disease, hematochromatosis.

Since Fe metabolism is important for the maintenance of homeostasis, Fe overload will likely have a negative effect on its regulation. Accumulation results in cell and organ damage. The precise mechanism of toxicity of overload remains unknown, but a number of possibilities have been explored. Metals such as Fe tend to amplify oxidant damage via the Fenton reaction. Subsequently, Fe overloads have been observed to target systems with very active mitochondria. The use of antioxidants effectively combats Fe-mediated oxidative damage. In addition, Fe accumulation within the cellular lysosomal compartment sensitizes lysosomes to damage and rupture. Release of lysosomal enzymes into the cytoplasm of the cell induces autophagocytosis, apoptosis or necrosis.

24.8.5 Toxicokinetics

Fe metabolism is unique in that it operates primarily as a closed system, with Fe stores being efficiently reused by the body. Fe losses are minimal (< 1 mg/day), but absorption is usually poor. The metal generally is present in foods in the ferric form, bound to proteins and organic acids. Release of Fe from these carriers is a prerequisite for Fe to be absorbed. While only 10% of Fe ingested in the diet is absorbed, severe deficiency increases absorption to about 30%.

Low pH in the stomach reduces the ferric form to the ferrous form, which is then absorbed by the intestinal mucosal cells. Under the influence of apoferritin, ferrous Fe is converted back to the ferric form and eventually enters the plasma. Transferrin transports Fe to the liver, where it is bound to ferritin and hemosiderin. Fe is transported via transferrin from the liver to the bone marrow for the production of hemoglobin and myoglobin, and to other tissues for the incorporation into cytochromes and nonheme Fe.

24.8.6 Signs and Symptoms of Acute Toxicity

Acute Fe poisoning has been well documented and is divided into 5 clinical stages: (1) GI toxicity, (2) relative stability, (3) shock and acidosis, (4) hepatotoxicity, and (5) GI scarring.

GI toxicity occurs within a few hours of ingestion. Symptoms include nausea, emesis, and diarrhea. These symptoms are often mistakenly interpreted as caustic damage to the gut but are instead a result of free radical generation. Approximately 6 to 12 h after ingestion there is a period of **relative stability** in severely poisoned patients. This stage must be differentiated from mild poisoning, and careful clinical assessment usually will identify some degree of hypovolemia and acidosis. **Shock and acidosis** may occur a few hours to 24 to 48 h after ingestion. Hypovolemic shock occurs in response to fluid and blood losses from the gut. Cardiogenic shock usually occurs 24 to 48 h after ingestion and represents a depressant effect of Fe upon myocardial cells. **Hepatotoxicity** occurs within 2 days of ingestion and is the second most common cause of death in Fe poisoning. The liver is at risk because its portal circulation exposes it to the highest concentrations of Fe. Liver cells have a high metabolic activity that favors production of free radicals. Finally, **GI scarring** occurs 2 to 4 weeks after ingestion. Patients present with partial or complete bowel obstruction as the initial injury to the gut lumen heals by scarring and stenosis.

24.8.7 Signs and Symptoms of Chronic Toxicity

Chronic Fe toxicity can be caused by hereditary hematochromatosis due to abnormal absorption of Fe from the intestinal tract, from excess dietary Fe, and from repeated blood transfusions for certain forms of anemia (transfusional siderosis). The symptoms of all three types are very similar and result in disturbances of liver function, diabetes mellitus, endocrine disturbances, and cardiovascular effects.

24.8.8 Treatment of Acute Poisoning

Treatment of acute poisoning is aimed toward removal of Fe from the GI tract by the induction of vomiting and gastric lavage. Deferoxamine is an Fe chelator and is the treatment of choice for acute Fe overload. Repeated phlebotomy has also been suggested, as it is effective in removing as much as 20 mg of Fe per treatment.

24.8.9 Clinical Monitoring

Calculation of percent transferrin saturation indirectly measures Fe stores (serum Fe and Fe binding capacity). The serum ferritin correlates well with Fe stores, but it can also be elevated with liver disease, inflammatory conditions, and malignant neoplasms. A complete blood count (CBC) is also an indirect measure of Fe stores, because the mean corpuscular volume (MCV) of the RBC is increased with Fe overload. The amount of storage Fe for erythropoiesis is quantified by performing an Fe stain on a bone marrow biopsy. Excessive Fe stores are determined by bone marrow and liver biopsies.

24.9 LEAD (Pb)

24.9.1 Occurrence and Uses

One of the oldest known metals, lead (Pb) was used by the ancient Babylonians, Egyptians, and the Romans to make water pipes and solder. Pb ranks 36th in

24.1). As Pb redistributes to bone, the use of radiographic techniques occasionally proves useful for the detection of "lead lines."

24.10 MERCURY (Hg)

24.10.1 Chemical Characteristics

There are three toxic forms of Hg: elemental, inorganic, and organic. Hg compounds are considered to be major pollutants of the biosphere, with organic mercurials as the most toxic forms.

24.10.2 Occurrence and Uses

Two major sources of Hg deposition in the biosphere are the natural degassing of the earth's crust and the leaching of sediment. This natural source of contamination is estimated at 25,000 to 150,000 tons of Hg per year, which binds to organic or inorganic particles and to sediment that has a high sulfur content. Although discharges of Hg have been strictly regulated, some industrial activities still release substantial quantities of the metal. For example, fossil fuel contains as much as 1.0 ppm. Since 1973, approximately 5,000 to 10,000 tons of Hg per year has been discharged from burning coal, natural gas, and the refining of petroleum products, with one third of the atmospheric Hg due to industrial releases. Hg is used in a number of products including thermometers, barometers, electrical apparatus, paints, and pharmaceuticals.

Regardless of the source, both organic and inorganic Hg undergoes environmental transformation. Conversion of inorganic Hg to methyl Hg results in its release from sediment at a relatively fast rate and leads to its wider distribution. Inorganic Hg may be methylated and demethylated by microorganisms. Elemental Hg at ambient air temperatures volatilizes and is extremely dangerous.

24.10.3 Occupational and Environmental Exposure

Methyl Hg released in the aqueous environment bioaccumulates in plankton, algae, and fish. In fish the absorption rate of methyl Hg is faster than that of inorganic Hg, and its clearance rate is slower, resulting in high methyl Hg concentrations. This is of interest since fish enter the food chain.

The pollution of the environment with Hg compounds has resulted in an increased level of neurotoxicity, referred to as Minamata disease, named after a historic outbreak of Hg poisoning in Japan. Two poisonings, one in Minamata Bay (1956–1975) and in Niigata (1964), occurred as a consequence of industrial releases of Hg compounds into Minamata Bay and the Agano River. An additional outbreak occurred in Iraq (1971–1972), resulting from eating bread made from seed grain coated with a methyl Hg fungicide.

Most human exposure to Hg is by inhalation, because it readily diffuses across the alveolar membrane due to its lipid solubility. Because of this property it has a high affinity for RBCs and the CNS.

24.10.4 Mechanism of Toxicity

The mechanism of Hg toxicity is believed to be related to high-affinity binding of divalent mercuric ions to thiol or SH groups of proteins. Inactivation of various enzymes and structural proteins, and alterations of cell membrane permeability, are believed to contribute to the severe toxicologic effects. Increased oxidative stress, disruption of microtubule formation, interference with protein synthesis, DNA replication, and Ca homeostasis are purported pathways.

24.10.5 Toxicokinetics

Inhaled Hg vapor is efficiently absorbed (70 to 80%); absorption of liquid metallic Hg is considered insignificant. The absorption rate for inorganic mercuric salts varies greatly and is dependent largely on the chemical form. Oral absorption of organic Hg is nearly 100%.

For all forms of Hg, the highest accumulation is in kidney. Because of the high lipophilicity of metallic Hg, transfer through the placenta and the blood-brain barrier is complete. Inorganic Hg compounds have a lower lipophilicity and, although there is distribution to most organs, penetration is not as effective.

Metallic Hg is oxidized to the divalent form by the catalase pathway, and the divalent form is reduced to the metallic form. Elimination occurs via urine, feces, and expired air for metallic Hg. Inorganic Hg is eliminated in urine and feces, while organic Hg is eliminated primarily in the feces. Renal excretion of inorganic Hg increases with time. Both inorganic and organic forms are excreted in breast milk. A small fraction of Hg may be exhaled after exposure to Hg vapor. About 90% of methyl Hg is excreted in feces after acute or chronic exposure. Methyl Hg excretion however does not increase with time.

24.10.6 Signs and Symptoms of Acute Toxicity (Inhalation and Ingestion)

Accidental acute exposure to high concentrations of metallic Hg vapor has resulted in human fatalities. The most commonly reported symptoms of acute inhalation exposure are cough, dyspnea, tightness, and burning pain in the chest. GI effects include acute inflammation of the oral cavity, abdominal pain, nausea, and vomiting. Increased heart rate and blood pressure are evidence of cardiovascular effects. Renal effects resulting in proteinuria, hematuria, and oliguria have been demonstrated, and severe neurotoxic effects resulting in behavioral, motor, and sensory disruptions are common.

Ingestion of inorganic mercurial salts causes severe GI irritation including pain, vomiting, diarrhea, and renal failure. Contact dermatitis, hyperkeratosis, acrodynia (*pink disease*), shock, and cardiovascular collapse are observed in patients with acute exposure to inorganic mercurial salts.

24.10.7 Subacute or Chronic Poisoning

The major clinical symptoms of methyl Hg toxicity are neurologic and include, in order, paresthesia, ataxia, dysarthria, and deafness. There may be a latency period

of weeks or months from the time of exposure until the development of symptoms. Some pathological features include degeneration and necrosis of neurons in focal areas of the occipital cortex and in the granular layer of the cerebellum. This particular distribution of lesions in the CNS is thought to reflect a propensity of Hg damage to small neurons in cerebellum and visual cortex.

24.10.8 Clinical Management of Hg Poisoning

Treatments of Hg poisonings are considered to be experimental. Even prompt action and monitoring may result in fatality. For dermal or ocular exposure, washing of exposed areas is suggested. Reducing absorption from the GI tract refers mostly to inorganic forms. Oral administration of a protein solution has been suggested to reduce absorption, based on Hg's affinity for binding to SH groups. Administration of activated charcoal has been used in the case of acute high-dose situations. Gastric lavage and induction of emesis are also recommended, although emesis is contraindicated following ingestion of mercuric oxide, due to its caustic nature.

To reduce body burden, chelation therapy is the treatment of choice. The chelator used will depend on the form of Hg, route of exposure, and possible side effects that might be experienced. BAL is one of the more effective chelators for inorganic Hg salts, while D-penicillamine is marginally effective as a chelator for elemental and inorganic Hg.

24.11 SELENIUM (Se)

24.11.1 Occurrence and Uses

Selenium (Se) closely resembles sulfur and is chemically related to tellurium. Like sulfur, it exists in several different forms. The burning of fossil fuels and coal accounts for much of the Se released into the environment. Se is used in photoelectric devices (Gray Se) and is used to impart a scarlet red color to glass and enamels (Red Se, sodium selenide) and as a decolorizer of glass. Sodium selenate is used as an insecticide, while Se sulfide is used clinically in the treatment of skin disorders such as dandruff, acne, eczema, and seborrheic dermatitis.

The amount of Se in food sources, whether consumed directly as plants or as meat from animals that have eaten the vegetation, varies according to soil levels. Most Se in foods is lost during processing, such as in the making of white rice or white flour. Many natural foods contain a much less toxic organic form of Se. Se is sometimes added to drinking water when deficient.

24.11.2 Physiological Role

Se, once classified solely as a toxic mineral, was recognized in the 1970s as an essential **trace** element. It is a component of the enzyme glutathione peroxidase, which accounts for its antioxidant function. It is also found in deiodinases, and thioredoxin reductase. Selenocysteine is the biologically active form of Se found in each of the above. The metal has a variety of properties ranging from anticancer and antioxidant to effects on the immune, reproductive, and nervous systems.

Two endemic diseases have been associated with Se deficiency. Keshan's disease is a form of heart disease characterized by cardiomegaly, congestive heart failure, abnormal ECG, and multifocal necrosis of the myocardium. The disease is prevalent in children and women of childbearing age and has been successfully treated with Se supplementation. Kashin-Beck disease is an osteoarthropathic disease characterized by atrophic necrosis and degeneration of the cartilage. Se has proven to be a successful treatment in this disease as well.

There is less than 1 mg of Se present in the average adult, most of it concentrated in liver, kidneys, pancreas, testes, and seminal vesicles. Men have a greater need for Se, which may function in sperm production and motility. Some Se is lost through the sperm as well as through the urine and feces. It is absorbed fairly well from the intestines, with an absorption rate of nearly 60%.

24.11.3 Mechanism of Toxicity

Long-term effects of excess Se on the hair, nails, skin, liver, and nervous system have been well documented; however the biochemical mechanisms by which Se exerts toxicity remain largely unknown.

Acute Se toxicity may be the result of inactivation of sulfhydryl enzymes that are necessary for cellular respiration. High Se concentrations have the ability to replace sulfur in biomolecules, especially under conditions of low sulfur, possibly resulting in toxicity. Replacement of selenomethionine for selenocysteine in protein synthesis is another purported mechanism of toxicity.

24.11.4 Toxicokinetics

Se compounds are absorbed by the GI route, ranging from 44 to 95% of ingested dose. Absorption depends on the physical state of the ingested form, the chemical form, and the dose, with soluble Se having greater absorption rates than solid. Se is also absorbed via inhalation. The metal distributes to all tissues, with the highest concentrations found in kidney, liver, spleen, and pancreas. Se also tends to concentrate in RBCs and is amenable to placental transfer.

Excessive amounts of Se are excreted primarily via the urinary system, leaving trace amounts of Se in the body. Excretion of Se occurs in feces, expired air, and sweat.

24.11.5 Signs and Symptoms of Acute Toxicity

Clinical signs of acute toxicity following ingestion of high doses of Se include excessive salivation, garlic odor to the breath, shallow breathing, and diarrhea. Pulmonary edema and lung lesions were observed in acute lethal doses. Tachycardia, abdominal pain, nausea, vomiting, and abnormal liver functions were seen in human acute *selenosis*. Inhalation of Se or its compounds results in irritation of the mucous membranes of the respiratory tract, dyspnea, bronchial spasms, bronchitis, and chemical pneumonias.

24.11.6 Signs and Symptoms of Chronic Toxicity

Clinical signs of chronic *selenosis* include loss of hair and fingernails, skin lesions, and clubbing of the fingers. Nervous system effects such as numbness, convulsions, paralysis, and motor disturbances have been described.

24.11.7 Clinical Management of Poisoning

There are no specific methods that are recommended for the treatment of acute high-dose exposure to Se via inhalation, and only supportive treatment has been recommended for oral overdose. Gastric lavage and induction of vomiting with emetics may reduce absorption, but because selenious acid is caustic, both procedures would be contraindicated. Chelators such as EDTA and BAL have not been successful treatments and, in fact, may increase its toxic effects.

24.12 ZINC (Zn)

24.12.1 Occurrence and Uses

Zinc (Zn) is used extensively as a protective coating or galvanizer for iron and steel. Its brass alloy is used as plates for dry cells and die casting. Clinically, Zn oxide has antiseptic and astringent properties. Zn salts have also been used in electroplating, for soldering, as rodenticides, herbicides, pigments, wood preservatives, and as solubilizing agents (zinc insulin suspensions).

24.12.2 Physiological Role

Zn is an essential metal required for proper functioning of a large number of metalloenzymes, including alcohol dehydrogenase, alkaline phosphatase, carbonic anhydrase, Zn-Cu superoxide dismutase, leucine peptidase, and DNA and RNA polymerase. Zn deficiency results in dermatitis, growth retardation, impaired immune function and congenital malformations. The metal has a role in the maintenance of nucleic acid structure of genes through the formation of "Zn finger" proteins.

Zn interacts with other physiologically important metals. Zn and Cu have a reciprocal relationship — i.e., large intake of Zn may result in Cu deficiency. The metal also interacts with Ca and is necessary for proper bone calcification. Cd competes with Zn in binding to sulfhydryl groups present on macromolecules. It also induces the metal-binding protein, metallothionein, which is involved in the absorption, metabolism, and storage of both essential and nonessential metals.

24.12.3 Mechanism of Toxicity

The mechanism of Zn toxicity has not been fully elucidated, although it enters cells via channels that are shared by Fe and Ca. This pathway may be a prerequisite for cell injury.

24.12.4 Toxicokinetics

Under normal physiologic conditions 20 to 30% of an ingested dose of Zn is absorbed via the GI route. Zn absorption is influenced by P, Ca, and dietary fiber, but once absorbed, it is widely distributed. The highest content is found in muscle, bone, GI tract, brain, skin, lung, heart, and pancreas. In blood, about two thirds of Zn is bound to albumin. The principal route of excretion is in the feces and, to a lesser extent, through the urinary system.

24.12.5 Signs and Symptoms of Acute Toxicity

Acute toxicity varies depending on the form ingested or inhaled. Metal fume fever, which is a result of inhalation of Zn oxides, causes chest pains, cough, and dyspnea. Zn chloride is more damaging and corrosive to the mucous membranes. Bilateral diffuse infiltrates, pneumothorax, and acute pneumonitis have been described. Oral ingestion of large doses of Zn sulfate has been associated with GI distress and alterations of GI tissue, including vomiting, burning in the throat, abdominal cramps, and diarrhea.

24.12.6 Signs and Symptoms of Chronic Toxicity

Hematological changes have been reported in patients with chronic exposure to Zn. Long-term administration of Zn supplements has been implicated in cases of anemia.

24.12.7 Clinical Management of Poisoning

General recommendations for management of excess Zn exposure include removal of the victim from the immediate area of exposure in the case of inhalation and irrigation with water for ocular and dermal exposure. For acute oral toxicity, administration of ipecac to induce vomiting is not recommended in the presence of caustic Zn compounds. Ingestion of large amounts of milk and cheese may reduce Zn absorption in the GI tract due to the high levels of phosphorus and Ca present in these products.

To reduce body burdens of Zn, administration of $CaNa_2$-EDTA is the treatment of choice, while dimercaprol has also been recommended.

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