

CHAPTER 8

ENVIRONMENTAL TOXINS

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Abstract

Environmental toxins represent a diverse category of hazardous substances encountered outside controlled pharmaceutical contexts, often producing distinctive toxicity patterns requiring specialized recognition and management. Heavy metal exposures include lead poisoning, with its neurodevelopmental effects in children and multisystem impacts in adults, requiring chelation therapy in severe cases. Arsenic toxicity presents with gastrointestinal, dermatological, and neurological manifestations alongside characteristic findings like Mees lines and garlic breath. Mercury exists in elemental, inorganic, and organic forms, each with unique toxicokinetics and target organ effects, particularly neurological and renal systems. Pesticide exposures vary by chemical class, with organophosphates and carbamates inhibiting acetylcholinesterase to produce cholinergic crisis requiring atropine and pralidoxime therapy. Pyrethroid insecticides primarily cause dermal and respiratory irritation, while organochlorine compounds produce CNS excitation and seizures. Industrial chemicals like cyanide rapidly inhibit cellular respiration, necessitating immediate hydroxocobalamin or sodium thiosulfate administration, while corrosives cause direct tissue damage requiring careful supportive care without neutralization attempts. Air pollutants include carbon monoxide, with its deceptive presentation and high mortality without prompt oxygen therapy, and irritant gases that produce progressive respiratory compromise potentially leading to delayed pulmonary edema. Management principles emphasize rapid identification, decontamination, specific antidotes where available, and supportive care addressing the unique pathophysiology of each environmental toxin.

Keywords: Heavy Metals, Organophosphates, Carbon Monoxide, Chelation Therapy, Industrial Chemicals, Environmental Exposure

Learning Objectives

After completion of the chapter, the learners should be able to:

- Identify clinical manifestations of common heavy metal poisonings including lead, arsenic, and mercury, and implement appropriate chelation therapies when indicated.
- Differentiate between various pesticide classes based on clinical presentation and cholinesterase activity, with emphasis on managing cholinergic crisis from organophosphate and carbamate exposures.
- Recognize and treat industrial chemical exposures including cyanide, hydrofluoric acid, and corrosives, with attention to specific antidotes and decontamination procedures.
- Evaluate carbon monoxide poisoning using appropriate diagnostic tests and determine indications for hyperbaric oxygen therapy versus normobaric oxygen treatment.
- Implement proper management of inhaled irritant gas exposures with attention to the risk of delayed-onset pulmonary edema and appropriate respiratory support.
- Develop surveillance and prevention strategies for environmental toxin exposures in occupational and community settings, including proper use of personal protective equipment.

HEAVY METALS

Hheavy metals represent persistent environmental contaminants with significant human health effects through occupational, environmental, and occasionally deliberate exposures.

Lead

Lead toxicity remains a global public health challenge despite regulatory restrictions, with exposure sources including deteriorating lead-based paint in older housing, contaminated soil near industrial sites or roadways, lead-containing plumbing, certain occupations, contaminated folk remedies, and retained bullets or shrapnel. Toxicokinetics include gastrointestinal absorption significantly enhanced in children compared to adults (40-50% versus 10-15%), initial distribution in blood with approximately 95% bound to erythrocytes, subsequent redistribution to soft tissues and eventually to bone which serves as a long-term repository containing over 90% of total body

burden in chronic exposure. This bone reservoir creates prolonged internal exposure through continuous mobilization, particularly during physiological states involving increased bone turnover including pregnancy, lactation, menopause, and immobilization. Elimination occurs predominantly through renal excretion, with biological half-life ranging from 30 days for blood lead to years or decades for bone lead stores.

Remember

Lead toxicity affects multiple organ systems with particular concern for neurodevelopmental effects in children, requiring environmental intervention alongside medical management including chelation therapy at elevated blood levels.

Pathophysiological mechanisms involve lead's strong affinity for sulfhydryl groups, resulting in inhibition of numerous enzymes, displacement of essential metals in metalloenzymes, disruption of calcium-dependent processes, and generation of

oxidative stress. Specific enzyme targets include delta-aminolevulinic acid dehydratase and ferrochelatase in the heme synthesis pathway, contributing to anemia; sodium-potassium ATPase affecting cellular energy utilization; and various mitochondrial enzymes disrupting energy metabolism. Neurodevelopmental toxicity involves additional mechanisms including interference with neurotransmitter release, disruption of synaptic pruning, and impairment of cellular migration during critical developmental periods.

Clinical manifestations vary significantly with exposure intensity, duration, and patient age. Acute high-dose exposure, now rare in developed countries, produces lead encephalopathy with headache, confusion, seizures, coma, and potentially death through cerebral edema. More commonly encountered chronic toxicity presents with insidious multisystem effects: neurological manifestations include subtle neurocognitive deficits, peripheral neuropathy predominantly affecting motor function, and behavioral changes; hematological effects encompass microcytic anemia through both hemolysis and impaired hemoglobin synthesis; gastrointestinal symptoms include abdominal pain, constipation, and the classic but now rarely observed "lead line" (gingival hyperpigmentation); renal toxicity manifests as proximal tubular dysfunction and progressive nephropathy with chronic exposure. Children demonstrate enhanced susceptibility with neurodevelopmental effects occurring at substantially lower exposure levels than those causing symptomatic toxicity in adults, resulting in reduced intellectual function, attention deficits, behavioral problems, and diminished academic achievement without other obvious clinical signs.

Table 8.1: Heavy Metal Toxicity Profiles

Metal	Major Sources	Clinical Manifestations	Diagnostic Tests
Lead	Paint in older homes, contaminated water, industrial exposure	Abdominal pain, encephalopathy, peripheral neuropathy, anemia	Blood lead level, ZPP, CBC with peripheral smear
Mercury	Seafood, dental amalgams, industrial processes	Neurotoxicity, tremor, ataxia, sensory disturbances	Urine or blood mercury levels
Arsenic	Contaminated water, wood preservatives, pesticides	Garlic odor, GI symptoms, "rice milk" urine, peripheral neuropathy	24-hour urine arsenic, hair/nail analysis
Cadmium	Battery manufacturing, metal plating, cigarette smoke	Renal tubular damage, pulmonary irritation, bone effects	Urine cadmium, β_2 -microglobulin
Chromium	Metal plating, leather tanning, welding	Skin/mucous membrane irritation, nasal septum perforation	Urine chromium, nasal examination

Diagnostic evaluation centers on blood lead level (BLL) measurement, which primarily reflects recent exposure rather than total body burden. Interpretation has evolved dramatically over decades, with current recognition that no safe threshold exists, particularly for neurodevelopmental effects. The CDC reference value for children, set at 3.5 $\mu\text{g}/\text{dL}$ based on the 97.5th percentile of the population distribution, identifies children with exposures above most of the population, warranting investigation and intervention. Clinical toxicity becomes increasingly likely at higher levels: subtle neurocognitive effects begin below 5 $\mu\text{g}/\text{dL}$; hematological effects typically emerge above 20-25 $\mu\text{g}/\text{dL}$; frank symptomatic poisoning usually requires levels exceeding 60-70 $\mu\text{g}/\text{dL}$; and encephalopathy risk increases substantially above 100

µg/dL. Additional laboratory findings include basophilic stippling of erythrocytes, elevated zinc protoporphyrin reflecting impaired heme synthesis, hypochromic microcytic anemia, and elevated urinary delta-aminolevulinic acid. Radiographic findings in children may include metaphyseal lead lines representing increased metaphyseal density at long bone growth plates.

Management strategies encompass exposure identification and elimination, supportive care, chelation therapy when indicated, and long-term monitoring. Source identification requires detailed environmental and occupational history, home evaluation for lead hazards, and consideration of cultural practices or hobbies potentially involving lead exposure. Nutritional optimization, particularly ensuring adequate iron, calcium, and zinc intake, may reduce lead absorption and toxicity. Chelation therapy indications vary by blood lead level and clinical presentation: levels above 45 µg/dL generally warrant chelation in children, with lower thresholds for symptomatic patients; adult chelation typically begins at higher thresholds, often 70-100 µg/dL for asymptomatic cases. Specific chelating agents include succimer (2,3-dimercaptosuccinic acid, DMSA) for oral outpatient treatment at lower levels, calcium disodium ethylenediaminetetraacetic acid (CaNa₂EDTA) for parenteral therapy in more significant poisoning, and dimercaprol (British Anti-Lewisite, BAL) for severe toxicity, encephalopathy, or combined therapy with EDTA. Chelation endpoint typically targets blood lead reduction below chelation threshold levels, recognizing that bone lead stores will continue replenishing blood levels necessitating extended monitoring and potential repeated treatment courses.

Prevention strategies have evolved from treatment-focused approaches to primary prevention emphasizing exposure prevention before elevated levels occur. Public health interventions include elimination of lead from gasoline, residential paint, plumbing materials, and consumer products; remediation of contaminated housing through lead hazard control programs; enhanced surveillance systems identifying affected communities; and targeted screening programs for high-risk populations. Occupational protections include engineering controls minimizing workplace exposure, personal protective equipment, biological monitoring programs, and worker education regarding take-home exposure prevention. Clinical preventive services encompass anticipatory guidance regarding lead hazards, nutrition optimization, and selective screening based on risk assessment. Despite significant progress, ongoing challenges include legacy contamination from historical lead use, inadequate resources for housing remediation, and emerging exposure sources requiring continued vigilance and policy development.

Mercury

Mercury toxicity manifests in distinctive patterns determined by the specific chemical form, exposure route, and duration. Elemental mercury (Hg^0), found in thermometers, dental amalgams, certain religious practices, and artisanal gold mining, creates toxicity primarily through inhalation of mercury vapor. Inhaled elemental mercury readily crosses the blood-brain barrier and placenta due to its lipophilicity, subsequently oxidizing to inorganic forms that become trapped within tissues. Inorganic mercury compounds (Hg^+ , Hg^{2+}), including mercurous and mercuric salts used in some batteries, explosives, and historically in medications, demonstrate limited gastrointestinal absorption (approximately 10-15%) and poor central nervous system penetration due to their charged nature. Organic mercury compounds, particularly methylmercury formed through microbial methylation in aquatic environments, show extensive gastrointestinal absorption (>90%), pronounced lipophilicity facilitating blood-brain barrier and placental transfer, and undergo extensive enterohepatic circulation creating prolonged half-life (approximately 50 days).

Pathophysiological mechanisms center on mercury's strong affinity for sulfhydryl groups, resulting in enzyme inhibition, protein structural alteration, and disruption of cellular transport mechanisms. Specific cellular targets include mitochondrial enzymes creating energy production impairment, glutathione depletion reducing antioxidant capacity, microtubule disruption affecting neuronal function and cellular division, and metalloprotein displacement altering essential enzyme functions. These effects manifest predominantly in tissues with limited regenerative capacity, particularly the central nervous system where both direct toxicity and inflammatory responses contribute to progressive damage, and the kidneys where proximal tubular concentration of mercury creates focal injury patterns.

Clinical manifestations differ substantially between mercury forms. Acute elemental mercury vapor inhalation produces respiratory irritation progressing to pneumonitis, with systemic absorption leading to tremor, neurobehavioral changes, and potentially renal failure with higher exposures. Chronic elemental mercury exposure classically causes the triad of tremor, neuropsychiatric disturbances (historically termed "erethism" and including irritability, shyness, memory loss, and depression), and gingivostomatitis. These features contributed to the phrases "mad as a hatter" and "hatter's shakes" reflecting occupational toxicity in felt hat manufacturing which utilized mercury compounds. Inorganic mercury ingestion produces predominant gastrointestinal and renal effects, with corrosive gastroenteritis, hemorrhagic colitis, and acute tubular necrosis potentially progressing to oliguric renal failure. Classic manifestations include metallic taste, gingival inflammation with

distinctive blue-black "mercurial line," and chelosis (inflammation at mouth corners).

Methylmercury toxicity, most commonly resulting from contaminated seafood consumption, demonstrates pronounced neurological tropism with a latency period between exposure and symptom development sometimes extending weeks to months. Classic manifestations of significant exposure include paresthesias beginning peripherally and progressing in a centripetal pattern, concentrically constricted visual fields, ataxia, dysarthria, hearing impairment, and eventually neuromuscular weakness potentially progressing to paralysis. Prenatal methylmercury exposure from maternal seafood consumption creates particular concern due to the developing brain's enhanced vulnerability, with large-scale poisoning incidents demonstrating severe neurodevelopmental consequences including cerebral palsy, microcephaly, intellectual disability, and sensory impairments. Milder exposures may produce subtle neurodevelopmental effects detectable only through specialized neuropsychological testing.

Diagnostic confirmation requires appropriate specimen selection based on exposure pattern. Blood mercury measurement primarily reflects recent exposure to elemental or inorganic mercury but may remain elevated for extended periods with organic mercury due to its longer half-life. Urinary mercury provides the best assessment of inorganic and elemental mercury body burden and current exposure, with 24-hour collections preferred over spot samples due to significant excretion variability. Hair analysis effectively documents methylmercury exposure through longitudinal analysis allowing retrospective exposure timing assessment, though external contamination remains a potential confounder requiring careful interpretation. Neuroimaging typically demonstrates nonspecific findings in mercury toxicity, though magnetic resonance imaging may reveal characteristic patterns in severe methylmercury poisoning, particularly bilateral damage to the visual cortex and cerebellum.

Management strategies depend on mercury form, exposure timing, and symptom severity. For elemental mercury vapor exposure, immediate removal from the contamination source and respiratory support represent initial priorities, with chelation consideration for symptomatic patients or those with significantly elevated mercury levels. Acute inorganic mercury ingestion may benefit from gastric lavage if performed within one hour of exposure, followed by activated charcoal administration. Methylmercury poisoning management emphasizes supportive care with limited evidence for chelation efficacy due to the strong tissue binding and established cellular damage often present before diagnosis. Chelation agents include succimer (DMSA) for

oral outpatient treatment of less severe cases, dimercaprol (BAL) for more significant poisoning requiring parenteral therapy, and occasionally penicillamine though with higher adverse effect profile. Specific chelation thresholds vary by mercury form: urinary mercury exceeding 50 $\mu\text{g/g}$ creatinine or blood mercury above 50 $\mu\text{g/L}$ for elemental/inorganic exposure; blood mercury above 100 $\mu\text{g/L}$ for organic mercury exposure. Hemodialysis may provide adjunctive therapy for acute inorganic mercury poisoning with renal failure, both supporting renal function and enhancing mercury elimination.

Public health approaches emphasize exposure prevention through regulatory standards limiting industrial emissions, occupational exposure limits with biological monitoring programs, consumer product restrictions, and fish consumption advisories for vulnerable populations including pregnant women and young children. The Minamata Convention on Mercury, a global treaty effective since 2017, commits signatory nations to reducing mercury use and emissions through multiple strategies including phasing out certain mercury-containing products, implementing emission control technologies, regulating artisanal gold mining practices, and ensuring proper waste management for mercury-containing materials. Despite these measures, ongoing challenges include legacy contamination, atmospheric transport creating global distribution patterns, and socioeconomic factors limiting implementation of safer alternatives in certain industries and regions.

Arsenic

Arsenic toxicity presents complex clinical and diagnostic challenges due to its diverse chemical forms, exposure sources, and manifestation patterns. Environmental sources include naturally contaminated groundwater affecting millions globally, particularly in Bangladesh and parts of India, China, Taiwan, Argentina, Chile, and the United States; industrial contamination from mining, smelting, and wood preservation; agricultural sources including pesticides and animal feed additives; and certain foods naturally concentrating arsenic, particularly rice and some seafoods. Occupational exposures occur in metal refining, semiconductor manufacturing, wood treatment, and glass production. Intentional poisoning cases, though rare, continue occurring due to arsenic's availability, delayed symptom onset, and nonspecific initial presentation.

Toxicokinetics vary significantly between inorganic and organic arsenic compounds. Inorganic arsenic, the predominant form in contaminated water and most toxic species, demonstrates high gastrointestinal absorption (80-90%), undergoes hepatic methylation to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA), and eliminates primarily through urinary excretion with a typical half-life of

END OF PREVIEW

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