Chapter 12

Metals: Arsenic, Lead, Mercury, and Metal Fume Fever

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Overview

Arsenic

Arsenic is a well-known poison that has been used throughout history. Arsenic exposure may occur through intentional poisoning or contaminated drinking water (a worldwide problem). Arsenic is tasteless and odorless and is well absorbed by the respiratory or gastrointestinal tract (Box 12-1).

Lead

Lead poisoning or plumbism is a particular concern in children. The Centers for Disease Control and Prevention recommends universal screening of children for lead poisoning and community intervention if the child's blood lead level (BLL) is equal to or >10 μg/dL. BLLs declined 78% overall in the United States between 1976 and 1991 due to better environmental controls, banning of lead-based residential paint, and regulated removal of leaded gasoline[2] (Box 12-2).

Mercury

Mercury was used in the felt industry, and patients with mercury poisoning were labeled "Mad Hatters." Mercury-contaminated

Box 12-1 ▪ Potential Sources of Arsenic Exposure[1]

- Intentional poisoning
- Rock and volcanic eruptions
- Organic arsenic from eating fish or seafood
- Arsenic containing wood preservatives
- Smelting of metals
- Arsenical pesticides
- Contaminated drinking water
- Gallium arsenide used in computer and semiconductor
- Arsine gas
- Opium

Box 12-2 ▪ Sources of Lead Poisoning[3,4]

- Leaded paint in older homes or commercial sites
- Industrial waste
- Automobile exhaust
- Remodeling of structures with lead-based paints
- Lead solder
- Lead refiners
- Lead-based pigments and stabilizers
- Leaded ammunition
- Ethnic fold remedies such as azarcon, greta
- Drinking water
- Soil and dust
- Lead battery manufacturers or recyclers
- Lead smelters
- Tetraethyl lead
- Lead-glazed ceramics

fish is a concern throughout the world. Organic mercury or methylmercury bioaccumulates in the food chain and thus large predatory fish such as **shark, swordfish, king mackerel,** and **tilefish** have higher mercury levels than do small fish[5] (Box 12-3).

Metal Fume Fever

Metal fume fever is a self-limiting, acute illness that occurs after exposure to metal oxide fumes. It results in flulike symptoms (Box 12-4).

Substances

- Arsenic, lead, mercury, zinc, chromium, iron, magnesium, brass
- 70% of the world's production of arsenic is used as copper chrome arsenate (CCA) as a wood preservative.
- 22% of the world's arsenic production is used as pesticides in agricultural chemicals.
- The remainder is used in metallurgy, glass, and pharmaceuticals.

Box 12-3 ▪ Sources of Mercury Exposure[6,7]

- Food or grain treated with fungicides containing mercury
- Dental amalgams*
- Thimerosal (preservative that contains ethylmercury)
- Disc batteries
- Fish from contaminated bodies of water
- Amalgam makers
- Mercury thermometers
- Dyes

**Most experts do not believe that this can cause significant symptoms; however, there is not universal agreement on this topic.*

Box 12-4 ▪ Sources of Exposure[8,9]

- Welding of mercury, zinc, chromium, or galvanized iron
- Zinc smelting
- Magnesium fumes
- Molten metal fabricators
- Steel alloy manufacturers
- Bronzing, galvanizing, casting, brazing
- Brass foundry workers
- Brass solderers
- Metal grinders

Toxicity

Arsenic

- Multiple forms: elemental, inorganic, organic, arsine gas, trivalent (As^{+3}), pentavalent (As^{+5})
- Range of toxicity: arsine > trivalent > pentavalent > elemental[1]
- Organic arsenic may be present in seafood, is nontoxic, and is cleared within days from the body.
- Arsenic is well absorbed via GI or respiratory routes and distributed to all body tissues.
- Arsenic impairs cellular respiration, inhibits sulfhydryl-containing enzymes, and may substitute for phosphates in high-energy compounds.[10,11]
- Cancers associated with arsenic
  - Lung, bladder, skin leukemia, lymphoma

Lead

- Major route of exposure is ingestion or inhalation.
- Most of lead in bloodstream is bound to red blood cells, but lead is also stored in soft tissue and bone.

- Binds to sulfhydtyl groups and othet ptoteins, causes abnormal hemoglobin synthesis, and interferes with numerous metabolic processes
- Lead is structurally similar to calcium and interferes with calcium-mediated processes.
- Children absorb 40% to 50% of ingested lead; adults absorb 10% to 15%.[2]

Mercury

- Multiple forms: elemental, inorganic, organic
- Elemental mercury is a mobile, liquid metal, and exposure is typically through inhalation. Elemental Hg is poorly absorbed in the GI tract.
- Inorganic mercury is primarily absorbed via the GI tract and is corrosive.
- Mercury is a general protoplasmic poison and binds to sulfhydryl groups.
- Organic mercury or methylmercury is found in seafood and shellfish and primarily absorbed via the GI tract.

Metal Fume Fever

- Caused by exposure to metal oxide fumes, which are small particles formed by vaporization of metals with subsequent condensation.[8]
- Its pathogenesis is poorly understood, but metal oxide fumes may have direct toxic effects on the respiratory tract or may cause a delayed hypersensitivity reaction.[15]

Clinical Presentations

Arsenic

- Diagnosis is based on appropriate symptoms and elevated urine arsenic levels.
- Acute arsenic ingestion may cause acute nausea, vomiting, abdominal pain, or diarrhea within minutes to hours of exposure.[1,12]
- Arsenic toxicity may cause cardiovascular instability, hypotension, intravascular volume depletion, myocardial dysfunction, a **prolonged QT interval,** and dysrrthymia.[10,12]
- Severe poisoning may result in coma, acute encephalopathy, fevers, pulmonary edema, respiratory failure, toxic hepatitis, rhabdomyolysis, acute renal failure, GI ulcerative lesions, hemorrhage, seizures, and death.[1,2]

- Subacute ot long-term symptoms may include anemia, leukopenia, aplastic anemia, or sensory motor neuropathy (more sensory symptoms than motor).
- *Subcute or chronic skin findings include:* hyperkeratosis of palms and soles, alopecia, keratosis, desquamation, pigmentation changes, and eczematous changes.[2,10]
- Arsenic exposure has been linked to lung cancer, skin cancer, and bladder cancer.
- Arsine gas is a colorless, nonirritating gas and causes triad of abdominal pain, hematuria, and jaundice due to massive hemolysis.

Lead

- May cause multisystem signs and symptoms including:
  - With acute lead poisoning, GI symptoms such as anorexia, abdominal pain (lead colic), constipation, and vomiting
  - Normochromic or microcytic anemia (with basophilic stippling)
  - Neurologic symptoms such as headache, fatigue, irritability, tremor, encephalopathy, and coma
- Overt encephalopathy is more common in children with a BLL over 100 µg/dL but may occur with BBLs as low as 70 µg/dL.[2]
- Adults with overt encephalopathy typically have BLLs >100 µg/dL.[3]
- Lead poisoning may also cause a peripheral neuropathy (**more motor than sensory**), vague aches and pains, and renal disease.
- Reproductive effects include infertility, stillbirth, cognitive dysfunction in children, spontaneous abortions, and decreased sperm counts.[2,3]
- Children have more symptoms than adults at comparable BLLs.

Mercury

- Diagnosis of mercury toxicity is based on appropriate symptoms following an exposure.
- Elemental mercury
  - Elemental mercury may cause cough, chills, fever, metal fume fever, interstitial pneumonitis, and fibrosis.[6,10]
  - See Boxes12-5 and 12-6.
  - Erethism symptoms include shyness, anxiety, emotional lability, irritability (think Mad Hatter), delirium, and Parkinson disease-like features.[7]

- Ingestion of elemental mercury (liquid at room temperature) is relatively harmless unless the mercury becomes trapped in the gut.[10]
- Inorganic mercury salts such as in mercury disc battery[7] (Box 12-7)
- **Ingestion of organic or alkyl mercury** (Box 12-8)

Box 12-5 ▪ Possible Results of Chronic Exposure to Mercury

Tremors	Gingivitis
Cheilitis	Rash
Erethism	Fatigue
Headaches	Stomatitis

Box 12-6 ▪ Clinical Effects of Elemental Mercury Inhalation

Cough, chills, shortness of breath, fever
Metallic taste, nausea, vomiting, diarrhea, headache
Interstitial pneumonitis

Box 12-7 ▪ Clinical Effects of Inorganic Mercury Salts

Irritant or caustic gastrointestinal irritation	Bloody diarrhea
Acute renal failure	Circulatory collapse
Tremor	Erethism

Box 12-8 ▪ Organic Mercury

CNS symptoms

Paresthesias
Tremor
Ataxia
Dysarthria
Dementia
Tunnel vision

Maternal exposure

Cerebral palsy-type abnormalities
Mental retardation
Seizures
Cataracts
Hearing loss
CNS abnormalities (in the fetus)

- Mercury may also cause allergic contact dermaritis or urticaria.

Metal Fume Fever

- Metal fume fever results in flulike symptoms.
- Complete recovery usually occurs within 24–48 hr, with no permanent lung damage.
- Patients typically present within 3–12 hr of exposure (median 5 hr).[8]
- See Box 12-9.
- Most of rhe patients have a fever on presentation (90% are febrile).
- Chest radiographs are usually normal but may show a diffuse increase in bronchovascular markings.

Laboratory Evaluation

Arsenic

- Normal whole blood arsenic is <5 µg/L, and normal 24-hr urine arsenic is <50 µg/L, with an action level for urine >100 µg/L.[1]
- Urine arsenic levels are more useful and reliable than blood levels.
- Organic arsenic from seafood or shellfish ingestion
  - May cause an elevated urine arsenic level for several days, up to 2000 µg/L[10]
  - Is relatively nontoxic and is rapidly cleared from the body. Therefore it is important to speciate the total arsenic level (determine whether it is organic or inorganic, trivalent, or pentavalent).[13,14]
- Hair and nail arsenic may be reliable for long-term exposure.[12]
- *Consider ordering the following tests in the ED:*
  - CBC, electrolytes, BUN/Cr

Box 12-9 ▪ Metal Fume Fever Presentation

Fever	Chills
Headache	Myalgia, cough
Shortness of breath*	Metallic taste in mouth*
Nausea and vomiting*	Rales on exam

*Complaints in some patients.

- ECG
- Arsenic level (preferably 24-hr urine, although spot urine may be used in emergency) with speciations (it may be a few days before you receive results in most EDs)
- Consider abdominal and chest radiographs (looking for radiopaque material) if acute ingestion.

Lead

- Whole blood lead is the best screening tool for lead toxicity. A normal BLL is <10 μg/dL.[2]
- Always confirm an elevated capillary or fingerstick BLL with a venous or whole BLL.
- BLL may be an unreliable indicator of whole body lead burden or bone lead levels in those with chronic or remote poisoning.
- Erythrocyte protoporphyrin is not sufficiently sensitive for screening but may reflect chronic toxicity.[15]
- In lead-poisoned children, lead lines may be seen on radiographs of long bones.
- X-ray fluorescence is available in some parts of the country and can be used to document lead body burden.
- *Order the following tests in the ED:*
  - CBC with differential, BUN, Cr
  - BLL
  - Abdominal radiograph
  - Rule out other etiology for patient's symptoms because BLL results will probably **not** be received quickly.

Mercury

- Normal whole blood mercury level is <10 μg/dL, but the acrion level is greater than 35 μg/dL. Normal 24-hr urine mercury level is <20 μg/dL, and the action level is >150 μg/dL.[16]
- Urine mercury may correlate with inorganic mercury toxicity but is not as useful for methylmercury or organic mercury toxicity (for methylmercury or organic mercury, use blood mercury instead).
- Elevated urine or blood mercury levels may occur after seafood or fish consumption.
- *Order the following tests in the ED:*
  - Electrolytes, BUN, Cr
  - Urinalysis
  - 24-hour urine mercury, blood mercury
  - Consider abdominal x-ray if recent ingestion.[10]

Metal Fume Fever

- There is no pathognomic laboratory test for metal fume fever.
- A history of classic symptoms after exposure to metal fumes in the workplace, particularly in operations involving heating of metals shown to cause metal fume fever, is the key to diagnosis.[9]
- A chest x-ray should be ordered to evaluate for pneumonitis.

Treatment

Arsenic

- Requires good supportive care.
- If radiopaque material is present in the GI tract, then lavage or activated charcoal followed by whole bowel irrigation is appropriate.
- Avoid medication that will prolong the QT interval.
- A severely ill patient in whom arsenic poisoning is suspected may be started on chelation prior to your receipt of urine arsenic results.
- Severe arsenic toxicity with significant GI and CNS symptoms plus elevated blood or urine arsenic levels is usually treated by British anti-lewisite (BAL): 3–5 mg/kg IM every 4–6 hr until the 24-hr urine is <50 μg/L or 2,3-dimercaptosuccinic acid (DMSA).[2] DMSA appears more effective than BAL (BAL may increase brain arsenic levels) but has not been approved by the FDA for arsenic toxicity.[10]
- DMSA is well tolerated and may be the chelator of choice for subacute or chronic toxicity.
  - **Dose:** DMSA 10 mg/kg tid for 5 days, then 10 mg/kg for 14 days[10,11]

Lead

- It is important to evaluate the source of the lead exposure in every patient with an elevated BLL to determine whether significant exposure has occurred.
- Treatment is based on BLL, age of the patient, and severity of symptoms.
- If radiopaque material is present in the GI tract, then lavage followed by whole bowel irrigation is appropriate.

- DMSA is the chelator of choice in the United States unless the patient presents with protracted vomiting, severe toxicity, or encephalopathy (usually a child).[15]
- Patients with overt encephalopathy are treated with:
  - BAL (75 mg/m^2 IM every 4 hr for 5 days) plus
  - $CaNa_2$ EDTA started 4 hr after the BAL at a dose of 1500 mg/m^2 per day as a continuous infusion or in 2–4 divided IV doses for 3–5 days[2]
- Symptomatic adults with BLL >100 µg/dL or symptomatic children or any child with BLL >70 µg/dL are treated with:
  - BAL (50–75 mg/m^2 IM q 4 hr for 5 days) plus
  - $CaNa_2$ EDTA started 4 hr after the BAL at a dose of 1000–1500 mg/m^2 per day as a continuous infusion or in 2–4 divided IV doses for 3–5 days[2]
- Symptomatic adults or symptomatic children or asymptomatic children with BLL >45 µg/dL may be treated with:
  - Oral DMSA or succimer given as 10 mg/kg or 350 mg/m^2 tid for 5 days, then bid for 14 days[2]
- Chelation may not be indicated in asymptomatic adults with BLL <70 µg/dL, but they should be removed from lead exposure[2] and followed with serial BLLs. Draw repeat BLL several days after each course of chelation, and if it is still elevated, a repeat course of treatment may be recommended.

Mercury

- General supportive care is appropriate treatment.
- Elemental inhalation: Monitor respiratory status.
- If an inorganic salt was ingested and corrosive lesions or ulcers are concerns, then GI upper endoscopy should be considered before lavage and whole bowel irrigation are performed.
- If metallic mercury is seen in the GI tract on the abdominal radiograph, then activated charcoal followed by whole bowel irritation is appropriate.
- Oral DMSA is the preferred chelator if the patient has normal renal function.[7]
- BAL may be contraindicated with methylmercury.[10]
- DMSA is given as 10 mg/kg tid for 5 days, then bid for 14 days.[12]
- Chelation with BAL is appropriate if there is renal dysfunction or severe toxicity.[7]

Metal Fume Fever

- General supportive care such as use of oxygen, IV fluids, and antipyretics is appropriate.
- Antacids may alleviate GI symptoms such as nausea and vomiting.
- Glucocorticoids have been used in patients with severe symptoms or interstitial infiltrates, but their efficacy has not been well proven.
- Preventing or minimizing subsequent exposure is essential.
- Recommending good worksite ventilation is important; respiratory protection may also be needed.
- Cadmium inhalation may cause more severe pneumonitis.[15]

Special Considerations

Arsenic

Arsenic-contaminated drinking water is present in numerous areas around the world, but in many areas results in low-level exposure.

Lead

- Children are more sensitive to adverse effects of lead.
- Children absorb 40%–50% of ingested lead; adults absorb only 10%–15%.
- Children tend to be more symptomatic than adults at a given BLL and are more susceptible to CNS toxicity than adults.
- In pregnancy:
  - Lead crosses the placental barrier and is found in breast milk.
  - Elevated lead levels may cause infertility, low birth weight, cognitive dysfunction in child, and spontaneous abortions.
  - Remove pregnant woman with elevated BLL from exposure and consider chelating the pregnant woman with severe lead toxicity. However, there is a theoretical risk of teratogenesis or fetal effect in early pregnancy.[2]

Mercury

- FDA recommendations for women who might become pregnant, pregnant woman, nursing mothers, and young children:

- Do not eat shark, swordfish, king mackerel, or tilefish.
- Eat up to 12 oz (2 average meals) per week of a variety of fish and shellfish that are lower in mercury (e.g., shrimp, canned light tuna, salmon, pollock, catfish).
- Check local advisories about the safety of fish caught by family or friends.[5]

Admission Criteria

Arsenic

- Severe toxicity, cardiac toxicity
- Psychiatric evaluation if suicidal

Lead

Encephalopathy, severe CNS toxicity, severe vomiting

Mercury

Life-threatening toxicity, renal failure, acute pneumonitis with respiratory distress[7]

Metal Fume Fever

Moderate or severe respiratory distress and pneumonitis; observe for 24 to 48 hr.

Pearls and Pitfalls

- If a patient has arsenic, mercury, or lead toxicity, then it is important to evaluate the source of the exposure and remove or minimize future exposures.
- Check renal function and urine output before giving BAL or DMSA because both increase urinary excretion of metals.
- Lead, arsenic, and mercury all cause GI, renal, and neurologic symptoms.
- Urine arsenic is more reliable than blood arsenic.
- Blood lead is more reliable than urine lead.
- Venous blood is more specific for lead poisoning and more reliable than capillary blood.[15]
- Blood mercury is more reliable for organic or methylmercury exposure.

- The CDC recommends clinical intervention if a child's BLL is >10 μg/dL.
- Children are more likely than adults to become symptomatic from lead toxicity.

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