Series Editor: Lewis S. Nelson, MD

Adventures in Gold Mining
Extracting a Diagnosis

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A thorough history of a 36-year-old man includes a recent trip to Mexico, where he participated in gold mining. What potential hazard does this unusual vacation activity present, and what is at the root of his toxicity?

A 36-year-old man presents to the emergency department with a 1-week history of nausea and vomiting. Over the past several days, he has also developed diarrhea, fatigue, and mild intermittent tremors of his hands. His physical examination is significant for sunken eyes and dry mucous membranes. He has a petechial rash on his face, thought to be due to his vomiting. His bowel sounds are hyperactive, and he displays a mild, intermittent tremor most notable in his hands. The remainder of his examination is unremarkable, including vital signs. His electrolytes, renal function, electrocardiogram, and chest radiograph are normal.

The patient takes no medications or over-the-counter supplements, and his family history is unremarkable. He works as a handyman for a nearby apartment building. His hobbies include playing the drums, swimming, and geology. He denies any travel other than a recent trip to Mexico, where he participated in extracting gold from ore. He notes that he did have a cough while in Mexico 1 week ago.

Why is gold extraction potentially poisonous?

Mining for precious metals is a profitable and important industry, and in many developing countries this occupation is of paramount importance to the economic survival of certain sectors of the population. Artisan gold mining, or "small-scale mining," is common in these areas, where miners use hand tools, manual labor, and other readily available techniques to mine and extract gold.[1] Aside from workplace trauma, working in these mines can also pose other significant health risks, particularly exposure to various metals.

Elemental mercury is used to amalgamate the precious metals gold and silver as a means of extracting them from their ores.[1] In this process, the ore is submerged in elemental mercury, which is a liquid under standard conditions, and the mercury attracts gold particles to form a gold-mercury amalgam. The gold-mercury amalgam is heated during the purification stage to volatilize the mercury, posing a significant risk for inhalation by workers.[1] Perhaps more commonly in the United States, attempts to "unplate" gold and silver from jewelry and other similar products using elemental mercury have led to significant mercury exposure and poisoning.

What are the three forms of mercury and what are their toxicities?

The routes of exposure, toxicity, treatment strategies, and medical sequelae vary with the form of mercury.

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However, regardless of the form of mercury to which one is exposed, the clinical toxicity arises from mercury's ability to bind to sulfhydryl groups within the human body and disrupt the proper functioning of sulfhydryl-containing enzymes.[2] The variability in the affected organ systems is related to the chemical properties of the metal, such as water solubility and chemical reactivity.

Inorganic mercury exists as a salt and has been used in disinfectants, paints, and dyes. Oral ingestion of certain forms, such as mercuric (Hg^{2+}) chloride, causes caustic damage to the gastrointestinal tract. Although only 10% to 40% of inorganic mercury is absorbed from the gut when ingested, this is a sufficient amount to result in systemic toxicity.[3] Dermal absorption of inorganic mercury, such as mercurous (Hg^{1+}) chloride, found in certain skin-lightening creams, is associated with human toxicity.[4] The systemic toxic effects of inorganic mercury are diverse, but peripheral neuropathy and renal injury are typical.

Elemental mercury has been used in precision instruments, including barometers and thermometers.[2] Ingestion of elemental mercury, such as occurs in certain cultural practices, rarely leads to toxicity, since gastrointestinal absorption of this form from an intact gastrointestinal tract is minimal. Elemental mercury evaporates slowly at standard temperatures, but this process is accelerated by heating (explaining the complication of artisan metal extraction described above).[3] Large exposures can produce direct pulmonary toxicity, such as cough, chills, and shortness of breath; more severe complications such as pneumonitis, pulmonary edema, and restrictive lung disease can also occur. Smaller exposures, such as after evaporation from spilled elemental mercury in a home or workplace, while not directly causing pulmonary toxicity, may produce systemic toxicity.[3] Due to the high lipophilicity of elemental mercury, alveoli can absorb up to 80% of inhaled mercury vapor. Once it enters the systemic circulation, elemental mercury is oxidized in various tissues to mercurous and mercuric cations. The lipophilic elemental mercury readily enters the central nervous system (CNS), where it is oxidized to the less lipophilic mercurous and mercuric species, which subsequently accumulate in the brain.[3]

Exposure to elemental mercury can also lead to renal toxicity, tremor, gingivitis, and erethism, a syndrome characterized by shyness, personality changes, and memory loss.[2] Elemental and inorganic mercury exposure can lead to acrodynia, a condition marked by a wide range of clinical manifestations, including a painful, pruritic dusky pink discoloration of the hands and feet,[2] a reddish maculopapular skin rash, excessive sweating, hypertension, and tachycardia.[3] This condition is also known as *pink disease*. A similar constellation of symptoms has been described in children who had calomel (mercurous chloride, Hg_2Cl_2) teething powders applied; mercury exposure due to calomel use was most common in the first half of the 20th century but still occurs.[5]

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Organic mercurials include aryl, short-chain alkyl, and long-chain alkyl forms. Traditionally found in fungicides (banned in the United States since 1990), organic mercury is typically most concerning following chronic exposure. The discharge of industrial waste contaminated with mercury has introduced mercury into the aquatic food chain. Inorganic mercury is organified by microbes, and the organic mercury bioaccumulates, leading to human exposure through consumption of contaminated fish. Emission from burning coal is the largest source of mercury entering waterways in the United States today.

Absorbed organic mercury primarily affects the CNS, causing paresthesias, ataxia, and vision abnormalities. The most severely affected patients are children exposed to high levels of organic mercury in utero during critical CNS development; at birth these children are mute, with rigid posture punctuated only by spontaneous crying and primitive reflexive movements

or feeding efforts.[6] This severe form of organic mercury poisoning occurred on a wide scale in the 1950s in Minamata Bay, Japan. Pollution of the bay with industrial runoff led to in utero methylmercury poisoning, producing devastating neurologic disease. Exposed infants exhibited decreased birth weight and muscle tone, profound developmental delay, seizure disorders, deafness, blindness, and severe spasticity.[6] The bay has since been cleaned and its fish have been deemed acceptable for consumption.

How is mercury measured or detected?

The diagnosis of mercurialism can be challenging. Due to early nonspecific symptoms and a lack of commonly seen abnormalities on early routine laboratory tests, detection is difficult. If mercury toxicity is suspected, a complete history should be taken, and this should include questions regarding occupational exposures, ritualistic practices, herbal and traditional medications, hobbies, and access to mercury-containing products. There are several options available when testing for mercury. Whole blood concentrations can be used after acute exposure to all forms of mercury. This method is able to detect mercury within the red blood cell, which is where mercury is likely to accumulate.[3] Whole blood values will become less useful as time passes following exposure, since distribution of mercury from blood into other tissues will occur.[3]

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Urine mercury concentrations can be useful to confirm inorganic and elemental mercury exposure; urine testing is not useful for suspected organic mercury exposure. There may be a rough correlation between urine level and exposure history, but the relationship to total body burden is poor.[6] Hair analysis has been used as a tool for measuring mercury burden, since mercury accumulates in the hair. However, because hair binds ambient mercury avidly, the reliability of hair analysis is questionable due to the risk for environmental contamination; this method is not recommended for diagnosing acute poisoning.[6]

How is mercury poisoning treated?

The most important intervention in the treatment of mercury poisoning is removal from the environment and from exposure. Once the patient with mercury poisoning becomes symptomatic, treatment centers on the use of chelation agents to remove the element from body storage sites. Chelation describes the administration of an agent (chelator, from the Greek *chele* meaning "claw") that can reduce the heavy metal burden of the body by forming metal-chelator complexes. Chelating agents contain thiol groups which compete with endogenous sulfhydryl groups for binding mercury.[3]

The compound 2,3-dimercapto-1-propanol (British anti-lewisite, or BAL) was developed during World War II as an antidote for lewisite, an arsenic-containing chemical warfare agent. BAL, available only in intramuscular form mixed in peanut oil, contains two sulfhydryl groups that bind to various metals, including inorganic mercury. BAL is not indicated for patients with elemental mercury toxicity because animal models have shown elevated brain elemental mercury levels secondary to redistribution. Toxic effects include hypertension, tachycardia, gastrointestinal symptoms, and allergic reactions in those with peanut allergies.[3]

2,3-Dimercaptosuccinic acid (succimer) is an orally administered chelator that has been used to treat poisoning from all three forms of mercury.[7] It improves survival, decreases renal damage, and enhances elimination of mercury in animals following exposure to inorganic mercury and methylmercury.[7] Adverse effects are mild and include gastrointestinal symptoms such as nausea, vomiting, flatus, and diarrhea. Mild elevations in hepatocellular enzymes may occur, and these levels typically return to baseline after therapy is discontinued.[3]

2,3-Dimercapto-1-propanesulfonate (DMPS) is a

water-soluble dimercaprol derivative that is used in Europe. N-acetyl-D,L-penicillamine (NAP) is an investigational chelator. Animal studies investigating NAP have shown an increase in urinary excretion rates of organic compared with inorganic mercury.[3] Other treatments also are under investigation. Antioxidants, including vitamin E and N,N'-diphenyl-p-phenylenediamine sulfate (DPPD), have shown some protective benefit in rats.[3] Corticosteroids have also been used in the case of mercury-induced nephritis and inhaled mercury vapor toxicity; their effectiveness is unknown.[3]

Case Conclusion

The patient was admitted to the hospital, where mercury poisoning was suspected. He received symptomatic care and was found to have an initial urine mercury level of 170.5 µg/g creatinine (reference <35 µg/g creatinine). Unfortunately, measurement of his blood mercury level was recommended but was not obtained. The patient received a 19-day course of succimer, and over the course of treatment had resolution of his tremors. Measurement of urine mercury after completion of succimer therapy revealed a level of 50.3 µg/g creatinine. **EM**

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