Lead toxicity from Ayurvedic medicines

Julian Gitelman MD MPH, Howard An MD MSc, Vincent Spilchuk MD MScCH, JinHee Kim MD MPH

Cite as: *CMAJ* 2023 August 8;195:E1010-2. doi: 10.1503/cmaj.230592

A 39-year-old woman presented to the emergency department 3 times over 6 weeks with abdominal pain, constipation, nausea and vomiting. She had a medical history of hypothyroidism and infertility, and was taking levothyroxine, follitropin alfa injections and folic acid. She lived in a condominium and worked in an office. She did not drink alcohol and was a nonsmoker. She did not have a notable family history.

On her third visit to the emergency department, the patient reported abdominal pain, fatigue, nausea and vomiting. Her vital signs were normal. Her hemoglobin level was 67 (normal 115–155) g/L with a mean corpuscular volume of 88.5 (normal 80.0–98.0) fL. She was admitted to hospital to investigate the anemia and possible gastrointestinal bleeding. Her blood film showed basophilic stippling, slight microcytosis and hypochromasia with no hemolysis. Levels of electrolytes, calcium, magnesium, phosphate, vitamin B_{12}, thyroid-stimulating hormone and liver enzymes were normal. Cultures of blood and urine samples were negative. Results of esophagogastroduodenoscopy, colonoscopy and computed tomography and ultrasonography of her abdomen and pelvis were normal. A bone marrow biopsy to investigate the anemia showed a moderate to marked increase in iron storage. Diagnostic laparoscopy for possible endometriosis showed no visible endometriosis. Biopsies of simple ovarian cysts were sent for pathologic examination. The patient's abdominal pain improved and her hemoglobin remained higher than 70 g/L after transfusions. Her discharge diagnosis was anemia of unknown cause and possible mild endometriosis. She was prescribed analgesics, laxatives and her usual medications, and was scheduled for follow-up with the internal medicine and hematology services.

At the outpatient follow-up with the internal medicine service 2 weeks after discharge, the patient reported improved abdominal pain but ongoing fatigue, shortness of breath, headaches and tinnitus. A urine sample was sent out for porphyria screening. At the second follow-up 4 weeks after discharge, at which point one of the authors became involved (H.A.), her porphyria screen showed elevated levels of coproporphyrin III and δ-aminolevulinic acid. Her biopsies did not show endometriosis. On further inquiry, the patient reported having taken Ayurvedic medications daily to treat infertility for more than a year. Her regimen varied, ranging from a few to a dozen pills daily. She had stopped taking them before her admission to hospital because of the abdominal pain, but had resumed them after discharge. Her blood lead level was 55 (normal < 2) µg/dL. A history of the patient's occupational and environmental exposure did not reveal other potential sources of lead exposure.

Key points

- Use of Ayurvedic medications is relatively common; these medications may be contaminated with lead and other heavy metals.
- Clinicians should consider lead toxicity in patients with microcytic anemia of unknown cause, particularly if basophilic stippling is present, or in patients with abdominal pain, headache, fatigue, new or worsening cognitive impairment and a suspicious exposure history.
- An elevated lead level in blood samples confirms the diagnosis of lead toxicity.
- Clinicians should contact public health organizations to identify and remove Ayurvedic medications that are contaminated with lead from the market.

The patient stopped her Ayurvedic medications and underwent chelation with 400 mg of succimer (dimercaptosuccinic acid) taken orally 3 times per day for 5 days, then twice per day for 14 days. She was advised to avoid pregnancy until her lead levels had decreased. Lead levels were 19.5 µg/dL shortly after chelation and 12.1 µg/dL 1 year later. The patient reported improving energy and no nausea, vomiting or abdominal pain. Six months after chelation, her hemoglobin level was 119 g/L, with a mean corpuscular volume of 93.1 fL.

When the diagnosis of lead toxicity was made, the clinicians contacted Public Health Ontario, a provincial public health agency that provides scientific and technical support to the Ontario government and health care system. Public Health Ontario facilitated testing of 17 visually distinct pills and 2 incense samples provided by the patient. Of these, 11 pills contained lead levels greater than the detection limit and 1 pill contained 129 000 µg/g of lead (about 13% lead by weight), strongly suggesting that the pills were the source of the lead toxicity. Four additional pills contained 7900—33 000 µg/g of mercury. Public Health Ontario involved the local public health unit (Toronto Public Health) and Health Canada, which regulates the importation and sale of natural health products. A joint investigation of the Ayurvedic clinic confirmed the practitioner's noncompliance with the *Natural Health Products Regulations* and resulted in the seizure of hundreds of pills.[1]

Toronto Public Health, consistent with their legislated authority to investigate and manage health hazards, attempted to contact all known customers of the practitioner (about 200 customers) and

advised that the products should not be consumed. Health Canada independently tested 15 types of pills seized at the practitioner's clinic and found high levels of arsenic, mercury or lead in 14 of the samples. Three pills also contained prescription medications including diclofenac, dexamethasone, progesterone, norgestrel and cetirizine. Both Health Canada and Toronto Public Health issued public advisories to warn consumers that the products sold at this business posed a health hazard.[1]

Discussion

Given that lead toxicity is uncommon and its presentation nonspecific, patients are often seen by many health care providers before the diagnosis is made. A careful exposure history is essential to suggest the diagnosis. Lead toxicity should be considered in patients with abdominal pain and microcytic anemia, particularly if basophilic stippling is present. It should also be considered in patients with abdominal pain, headache, fatigue, new or worsening cognitive impairment and a suspicious exposure history. Making the diagnosis with a blood lead level can avoid extensive investigations for abdominal pain and anemia. Hair lead and urine lead levels, including from chelation-provoked urine analysis, are not clinically meaningful.[2]

Ayurveda is a traditional Indian system of medicine that can include the use of herbal medications.[3] A nationally representative survey in the United States found that 1 in 1000 people had used Ayurvedic medicines in the previous year.[4] A random sample of Ayurvedic pills bought on the Internet from manufacturers based in the United States and India showed that 21% contained lead, mercury or arsenic.[5] Heavy metals are sometimes intentionally added for their perceived healing properties.[3] A recent systematic review of case reports on lead poisoning found traditional or herbal medications to be a common cause.[6] People can obtain Ayurvedic medicines by importing them privately; this circumvents regulated pathways that may flag products with toxic substances.

Lead exposure has decreased over the past 40 years given increasingly strict regulations on leaded gasoline and consumer products. Exposures to lead include contaminated food, drinking water, household dust, consumer products, air and soil, but these would not typically be expected to cause toxicity.[7] Lead toxicity in Canada is uncommon.[8] In 2018–2019, the geometric mean blood lead level in people in Canada aged 3–79 years was 0.81 μg/dL; the 95th percentile was 2.3 μg/dL.[7] Clinical symptoms become apparent at lead levels around 40–79 μg/dL.[2] In the toxic range, exposure is often from occupational or recreational sources (Table 1).

Clinical symptoms of lead toxicity occur in a dose-dependent manner, with interindividual variability.[2] The most common initial symptoms are abdominal pain (lead colic) and other gastrointestinal symptoms (e.g., nausea, vomiting, constipation, diarrhea). Other affected systems include the central nervous (e.g., fatigue, malaise, impaired cognition, tinnitus, headaches, mood changes), peripheral nervous (e.g., peripheral neuropathy), hematologic (e.g., anemia with basophilic stippling), musculoskeletal (e.g., arthralgias, myalgias, saturnine gout), renal (e.g., impaired estimated glomerular filtration rate) and reproductive (e.g., decreased sperm count, decreased libido) systems.[2] Lead toxicity causes enzyme inhibition in the heme synthesis pathway, which can result in elevation of protoporphyrin levels.[11] Elevated lead levels are associated with adverse pregnancy outcomes including preterm birth, small-for-gestational-age infants and pre-eclampsia.[12] Prenatal lead exposure is associated with impaired cognitive development in children.[13]

Table 1: Sources of lead that may lead to elevations in blood lead levels

Category	Source
Occupational	• Lead and nonferrous smelting and manufacturing[6,9,10] • Battery manufacturing, repair and recycling[6,9,10] • Welding[9] • Automotive manufacturing and repair[6,9,10] • Copper, nickel, lead, zinc and coal mining[6,10] • Some types of construction (e.g., bridge construction)[9,10] • Plumbing, heating and air-conditioning contracting[10] • Making crystal glass[9] • Polyvinyl chloride plastic manufacturing[9]
Hobbies	• Shooting guns with leaded munitions[6,9] • Ceramic crafting[6,9] • Furniture refinishing[9] • Home refinishing[9] • Painting (fine artist's pigments)[6,9] • Repair of automobiles or boats[6,9] • Making stained glass[6,9]
Other	• Retained bullets or pellets[6] • Contaminated substances of abuse[6,9] • Paint chips[6] • Folk, traditional or herbal remedies[6]

Removing the exposure to lead is the most important part of management. Ongoing lead exposure is generally a contraindication to chelation.[12] The threshold for chelation of symptomatic patients is a blood lead level greater than 70–100 μg/dL, with lower thresholds for children and pregnant people.[12] The quality of the evidence for the effectiveness of chelation is not strong; thus, the decision should be made on an individualized basis in consultation with an expert.[2] With prolonged lead exposure, most lead is distributed to bone, with a smaller proportion to soft tissues, causing end-organ damage. The biological half-life of lead can be decades long in cortical bone.[12] Chelation reduces blood lead levels, but little evidence indicates that it can access lead in bone. A rebound of blood lead levels can occur after chelation but usually not to the pre-chelation level.[9]

Conclusion

This case highlights the risks and clinical manifestations of lead toxicity from Ayurvedic medicines and the importance of collaboration between clinicians and public health authorities to control the health risk from lead in consumer products. When consumer products may be contaminated with lead, or when lead exposure is linked to sources in the community, involving public health can facilitate broader actions to reduce and prevent exposures to other people at risk.

References

1. Health Canada warns that products sold by Kerela Ayurvedic & Natural Herbal Consultation in Toronto, ON, may pose serious health risks [public advisory]. Ottawa: Government of Canada, Health Canada, Communications and Public Affairs Branch; updated 2022 Feb. 1. Available: https://recalls-rappels.canada.ca/en/alert-recall/health-canada-warns-products-sold-kerela-ayurvedic-natural-herbal-consultation-toronto (accessed 2022 Oct. 9).
2. Kosnett MJ, Wedeen RP, Rothenberg SJ, et al. Recommendations for medical management of adult lead exposure. *Environ Health Perspect* 2007;115:463-71.
3. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: concept of ayurveda. *Pharmacogn Rev* 2014;8:73-80.
4. Clarke TC, Black LI, Stussman BJ, et al. Trends in the use of complementary health approaches among adults: United States, 2002–2012. *Natl Health Stat Report* 2015;(79):1-16.
5. Saper RB, Phillips RS, Sehgal A, et al. Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. *JAMA* 2008;300:915-23.
6. Samarghandian S, Shirazi FM, Saeedi F, et al. A systematic review of clinical and laboratory findings of lead poisoning: lessons from case reports. *Toxicol Appl Pharmacol* 2021;429:115681.
7. *Sixth report on human biomonitoring of environmental chemicals in Canada*. Ottawa: Health Canada; modified 2021 Dec. 14. Available: https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/sixth-report-human-biomonitoring.html (accessed 2022 Sept. 1).
8. Reduce your exposure to lead. Ottawa: Health Canada; modified 2016 May 2. Available: https://www.canada.ca/en/health-canada/services/home-garden-safety/reduce-your-exposure-lead.html (accessed 2023 Apr. 14).
9. Nelson LS, Howland M, Lewin NA, et al., editors. *Goldfrank's toxicologic emergencies*. 11th ed. New York: McGraw Hill; 2019.
10. *Toxicological profile for lead*. U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry; 2020:1-583.
11. Martin CJ, Werntz CL III, Ducatman AM. The interpretation of zinc protoporphyrin changes in lead intoxication: a case report and review of the literature. *Occup Med (Lond)* 2004;54:587-91.
12. *Guideline for clinical management of exposure to lead*. Geneva: World Health Organization; 2021. Available: https://www.who.int/publications-detail-redirect/9789240037045 (accessed 2023 May 23).
13. Bellinger D, Leviton A, Waternaux C, et al. Longitudinal analyses of prenatal and postnatal lead exposure and early cognitive development. *N Engl J Med* 1987;316:1037-43.

Competing interests: None declared.

This article has been peer reviewed.

The authors have obtained patient consent.

Affiliations: University of Toronto Dalla Lana School of Public Health (Gitelman, Kim); Division of Internal Medicine (An), St. Joseph's Health Centre, Unity Health Toronto; Ontario Poison Centre (An), The Hospital for Sick Children; Division of Occupational Medicine (Spilchuk), Temerty Faculty of Medicine, University of Toronto; Environmental and Occupational Health (Spilchuk, Kim), Public Health Ontario, Toronto, Ont.

Contributors: All of the authors contributed to the conception and design of the work. Julian Gitelman drafted the manuscript. All of the authors revised it critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Correspondence to: Julian Gitelman, julian.gitelman@gmail.com

The section Cases presents brief case reports that convey clear, practical lessons. Preference is given to common presentations of important rare conditions, and important unusual presentations of common problems. Articles start with a case presentation (500 words maximum), and a discussion of the underlying condition follows (1000 words maximum). Visual elements (e.g., tables of the differential diagnosis, clinical features or diagnostic approach) are encouraged. Consent from patients for publication of their story is a necessity. See information for authors at www.cmaj.ca.