EDUCATIONAL COMMENTARY – LEAD TESTING

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Learning Objectives

On completion of this exercise, the participant should be able to

- characterize the biochemical effects of lead on human health;
- compare and contrast the methods used to detect the presence of lead in various samples;
- characterize the challenges involved in obtaining accurate lead screening data;
- outline the current regulations from the Centers for Disease Control and Prevention, the Environmental Protection Agency, and the Department of Housing and Urban Development on action levels for lead in blood, paint, dust, plumbing, and air; and
- discuss the best practices for preventing a recurrence of the Flint, Michigan, disaster.

Introduction

Lead is naturally found in soil at 50 to 400 parts per million (ppm) and is introduced into air and water by natural and human activities that churn up the soil (e.g., mining, earthquakes, road construction), and through the use of lead in gasoline, paint, ceramics, pipes, solders, batteries, toys, ammunition, and cosmetics.\(^1,2\) Its malleability as a metal and its lower cost than iron has made it particularly appealing for transporting water, a use that has been documented since the plumbing of ancient Roman times. In fact, the chemical symbol for lead is Pb, from the Latin plumbum.\(^3\) All of the benefits associated with those uses, however, come at the price of toxicity. A particularly disastrous example involving the city of Flint, Michigan, made national news in 2015.

Flint, Michigan, as a Case Study on Misunderstandings and Mishandling of Lead Safety Realities

The Flint episode began on April 25, 2014, when city officials, in a cost-saving move, decided to use a different distributor to obtain water from Lake Huron. The officials anticipated that the project would require a 2-year temporary use of Flint River water while the new pipelines to Lake Huron were put into place. Mandatory corrosion control treatments that would have prevented lead from leaching from the entire Flint water pipe delivery system were not done. For months, city officials continued to claim that the water met safe drinking water standards, despite turning “a rainbow of industrial colors—‘light yellow to nasty, dark-looking cooking grease.’”\(^4\) Tests finally done by the city in February 2015 showed lead levels of 104 parts per billion (ppb), seven times the Environmental Protection Agency (EPA) limit of 15 ppb. By August 2015, the Michigan Department of Environmental Quality admitted to dropping two samples from its July 2015 report on lead levels in the city’s water, an action that had placed the results
below the action level. The omission was considered justified because the two samples did not meet federal sampling criteria, as one involved a water filter and the second came from a business rather than from a home.\textsuperscript{5} Independent tests by investigators from Virginia Tech University in September 2015 revealed water lead levels as high as 13,200 ppb, where 5000 ppb is considered hazardous waste.\textsuperscript{5} The investigators also reported that the Flint River water, itself, did not contain an increased amount of lead.

A method required by the 2011 Reduction of Lead in Drinking Water Act\textsuperscript{6} had previously been used with the Lake Huron water to decrease the chance of lead leaching from the water pipes into the water. A water treatment chemical was added that would react with the lead to form scales, a deposit on the inner lining of the pipe, coating the inside surface of the pipe. Many times, this added chemical would be orthophosphate, resulting in a coating of crystalline Pb(II) orthophosphate compounds such as hydroxypyromorphite, Pb_9(PO_4)_6, or Pb_3(PO_4)_2.\textsuperscript{7} The city’s decision not to add orthophosphate treatment to the Flint River water for corrosion control,\textsuperscript{8} combined with the increased corrosivity of the Flint River water compared with the Lake Huron water, resulted in deterioration of that protective scale, allowing the lead from the pipes to leach into the water.

In September 2015, a local pediatrician, Dr. Mona Hanna-Attisha, released data from 1473 Flint children younger than 5 years\textsuperscript{9} showing a significant increase in the proportion of children with elevated blood lead levels in the period after the water system was changed (4.9\% in January 1, 2015, to September 15, 2015) compared with the period before the change (2.4\% in January 1, 2013, to September 15, 2013). Dr. Hanna-Attisha and colleagues published these findings in February 2016 in the American Journal of Public Health.\textsuperscript{10} The Centers for Disease Control and Prevention (CDC) reported in July 2016 that their records of 9422 tests from April 2013 to March 2016 showed the adjusted probability of children younger than 6 years having a blood lead level greater than 5 μg/dL (50 ppb) was 46\% higher after the switch from Detroit-supplied Lake Huron water to Flint River water.\textsuperscript{11} In addition, Flint residents were experiencing symptoms of rashes, hair loss, and abdominal pain.\textsuperscript{4} This data finally led Michigan governor Rick Snyder, President Obama, and the EPA to declare a state of emergency in January 2016. Unfortunately, consensus in the medical community was that, because there is no “safe” degree of lead exposure,\textsuperscript{12} the damage had already been done, especially to children exposed to the lead.\textsuperscript{10} There was also agreement that any of the studies done during the crisis most likely underestimated the true level of lead exposure in the affected Flint population.\textsuperscript{5,10,11}

By July 2016, two state regulators had resigned and nine state and city employees faced felony charges ranging from misconduct in office to conspiracy, willful neglect of duty, and tampering with evidence. Two corporations hired as consultants were sued for “failing miserably in their job.”\textsuperscript{5}
EDUCATIONAL COMMENTARY – LEAD TESTING (cont.)

The Flint details highlight sampling errors, multiple reporting units for lead, toxic effects in children and adults, detection method differences, and inadequacies of state and federal reporting guidelines.

Sampling Error

There were numerous reasons why the water sampling techniques used during the Flint crisis were inadequate to provide accurate data. In December 2015, Flint reintroduced orthophosphates to the water to rebuild the protective scales within the pipes. The EPA guidelines at that time required residents to preflush the night before, beginning a 6 to 8 hour “stagnant” period of no water flow before sampling. Residents were still being charged for the water wasted in the preflush, however, and thus would not do that step, thereby preventing the corrosion control from reaching the very pipes it was intended to rescale. One reporter stated that “people in Flint don’t want to pay for contaminated water that they can’t use.” In addition to this, those who did follow the instructions had been provided with sample collection bottles with small openings, requiring a low-flow rate during collection. This led to reduced levels of lead in the samples. There was evidence that only 71 of the 100 samples required by the 1991 Lead and Copper Rules were collected by city officials for analysis.

The EPA protocols were updated in light of the Flint experience on February 29, 2016. Changes include eliminating the practice of flushing the tap before the mandatory 6- to 8-hour stagnation period, use of kitchen or bathroom cold-water faucets for testing, avoiding faucets with water softeners if possible, ensuring that faucet aerators are not removed before tap sampling, and encouraging the use of wide-mouth bottles for collection of tap samples to avoid the loss of any of the first-draw sample.

Multiple Lead Reporting Units

Reporting units used for lead concentrations differ depending on the sample being tested. As a conversion reference, for water, blood, or paint, 1 μg/dL = 0.01 ppm = 10 ppb = 10,000 μg/m³; 1 ppm = 100 μg/dL = 1 mg/L; 1 ppb = 1 μg/L.

The Reduction of Lead in Drinking Water Act of 2011 applies to an estimated 68,000 public water systems in the United States. It specifies that the maximum allowable lead content in plumbing products is 0.25%. In 1986, those guidelines specified a lead content of 8.0%. The regulation affects kitchen, bar, and lavatory faucets, water dispensers, drinking fountains, water coolers, glass fillers, residential refrigerator ice makers, supply stops, and end point control valves. Exempt from the 0.25% maximum are pipes, fittings, and fixtures for nonpotable water, and “fill valves, flushometer valves, tub fillers, shower valves, service saddles, or water distribution main gate valves that are 2 inches in diameter or larger.” A 2013 update also exempted fire hydrants.
Regarding regulations for lead in drinking water, the 1991 Lead and Copper Rules (LCR) specified a goal of zero for acceptable concentration of lead in drinking water. The previously allowable level was 50 ppb, measured at the entry point to the distribution system. The 2007 revision of the LCR established an action level of 0.015 mg/L (15 ppb) for lead in drinking water, measured at the customer tap.

Discussions and recommendations from multiple stakeholders led to the publication of the *Lead and Copper Rule Revisions White Paper* by the EPA in 2016. Among proposals currently being considered are a “household action level” approach recommended by the National Drinking Water Advisory Council, enhanced public education requirements, and rules related to schools and other priority locations.

Lead-based paints were legally banned in 1978; therefore, houses built before that year have the highest likelihood of having lead on walls, baseboards, and windowsills (Figure 1). The paint itself is not a problem, but its deterioration into paint chips and dust increases the exposure of vulnerable populations to the lead. The EPA estimates that 24 million homes have such paint deterioration, with 4 million of these homes being the residences of young children.

![Figure 1. Percentage of homes that are likely to contain lead. Reprinted from *The Lead-Safe Certified Guide to Renovate Right*. Environmental Protection Agency, 2011.](image)

Analysis of paint flakes for lead should be reported in mg/cm² if the surface area can be accurately measured and if all paint within that area is collected. Methods must be able to detect at least 1 mg/cm² (0.5% lead in total weight). Lead in dust is hazardous if greater than 40 µg/ft² on floors, 250 µg/ft² on interior windowsills, 400 ppm in bare soil in children’s play areas, or 1200 ppm in bare soil in the rest of the yard. For air quality, the EPA in 2016 recommended that action levels for lead be greater than 0.15 µg/m³ in total suspended particles as a 3-month average.

Establishment of action levels for blood lead in children has varied widely over the years. Before 2012, the US Department of Housing and Urban Development (HUD) held that the level should be 20 µg/dL (0.2 ppm) and the CDC posed an action level of 10 µg/dL (0.1 ppm). In 2012, to identify more children at risk for lead exposure more quickly, the CDC reduced the level to 5 µg/dL (0.05 ppm), and HUD has adopted this lower level. When a HUD housing provider is notified of a child’s elevated blood lead level, they must test the child’s surroundings within 15 days, and control for any lead hazards within 30 days.
Toxic Effects in Children and Adults

The EPA has published, both on its website and in print, the summary of medical research defining the risks of lead exposure.\textsuperscript{1} Children are vulnerable because they have a tendency to place objects possibly contaminated with lead into their mouths, their food and drink may be in containers containing lead (lead-glazed ceramics or lead-soldered containers), they may inhale lead dust from paint or soil, and toys may be coated with lead-based paint. Compared with adults in the final absorption of the same amount of ingested lead, children will absorb more.\textsuperscript{24} In addition, their nervous systems and brains are more sensitive to lead toxicity before the age of 2 years when the blood-brain barrier has not completely developed, and in utero exposure can affect the development of the central nervous system.

Flora et al\textsuperscript{25} attribute the major effect of lead to be oxidative stress produced by inactivating glutathione, δ-amino levulinic acid dehydratase, glutathione reductase, glutathione peroxidase, and glutathione-S-transferase.\textsuperscript{26} The fetal brain capillaries have a lower resistance to lead, allowing it to enter the brain.\textsuperscript{27} Lead easily damages the immature astroglial cells and obstructs the formation of a myelin sheath, both factors in the development of the blood brain barrier.\textsuperscript{25} Within the cells, lead can compete with calcium as a second messenger,\textsuperscript{27} and block the N-methyl-D-aspartate subtype of the glutamate receptor, which is involved in the maturation of brain plasticity.\textsuperscript{28} Markowitz\textsuperscript{29} reported that approximately one-fourth to one-half of an IQ point is permanently lost per 0.04826 μmol/L increase in blood lead level during the preschool years. Toscano\textsuperscript{30} estimated an IQ deficit of 0 to 5 points for every 10 μg/dL (0.1 ppm) increase in blood lead levels. Khan’s findings\textsuperscript{31} suggest that the effects may be reversible if the lead exposure happens after the child is 2 years old.

Although it is acknowledged that the best action for managing lead poisoning is to reduce lead exposure, chelation therapies (succimer, dimercaprol [BAL] and/or CaNa$_2$EDTA) are available and can be provided based on whether the child is symptomatic and the blood lead level.\textsuperscript{32} Children with blood lead levels ≥70 μg/dL (with or without symptoms) have an acute medical emergency and both BAL and CaNa$_2$EDTA are given. Chelation treatment for asymptomatic children with blood lead levels between 45 and 69 μg/dL should be limited to CaNa$_2$EDTA only. Less evidence is available for effectiveness of chelation therapy in children with blood lead levels of 20 to 44 μg/dL.\textsuperscript{32}

Encephalopathy can be directly attributed to lead exposure, with symptoms including dullness, irritability, poor attention span, headache, muscular tremor, loss of memory, and hallucinations. More severe manifestations occur at very high exposure and include delirium, lack of coordination, convulsions, ataxia, paralysis, and coma.\textsuperscript{33}
A CDC infographic document targeted to families mentions only the neural effects of lead poisoning. However, there are other effects, including nephropathy (Figure 2), hypertension, gout, future kidney failure, decreased sperm count and increased abnormal sperm forms, myocardial morphologic abnormalities, irregular systolic and diastolic numbers, electrocardiographic disturbances, hearing loss, abdominal pain, vomiting, constipation, weight loss, and seizures. Physical examination could include gingival lead lines (Figure 3) wrist drop (Figure 4), and bone growth arrest lines (Figure 5). In 2007, Stewart and Schwartz suggested “a significant proportion of what is considered to be ‘normal’ age-related cognitive decline may, in fact, be due to past exposure to neurotoxicants such as lead.”

The effect of lead on red blood cells, leading to anemia, is infrequently mentioned in the literature. In 1899, Behrend first reported the nonspecific finding of erythrocyte stippling (Figure 6) associated with lead.
Lead downregulates δ-aminolevulinic acid dehydratase, aminolevulinic acid synthetase, and ferrochelatase. This results in the plasma/urine increase of aminolevulinic acid (ALA) and higher levels of zinc protoporphyrin (ZPP) in red blood cells. The increased ALA originally inside the red blood cells can lead to hemolysis. Although measurement of blood lead levels is the usual way to assess lead exposure, assessing these porphyrin compounds in plasma, urine, and red blood cells can be helpful for monitoring levels in adults who regularly work with or have hobbies using lead. An advantage of red blood cell ZPP measurements is that there is no interference if lead is present as a skin contaminant at the time of sample collection.

Detection Method Differences

Table 1 summarizes methods for analyzing lead levels in various samples. Included in the chemical tests in Table 1 are point-of-care blood tests. The only tests approved by the U.S. Food and Drug Administration (FDA) are manufactured by Magellan Diagnostics; products include LeadCare, LeadCare II, LeadCare Plus, and LeadCare Ultra. LeadCare II is listed on the company’s website as a CLIA-waived test. On May 17, 2017, the FDA issued a warning regarding all of these instruments: “The FDA’s warning is based on currently available data that indicate Magellan lead tests, when performed on blood drawn from a vein, may provide results that are lower than the actual level of lead in the blood. Currently, the FDA believes the issue may date back to 2014. The warning includes all four of Magellan Diagnostics’ lead testing systems: LeadCare; LeadCare II; LeadCare Plus; and LeadCare Ultra.” When testing is performed with capillary samples, no error occurs. Magellan Diagnostics’ own investigation uncovered a possible cause: a curing agent in the caps of blood-collection tubes leached into the venous samples. This explanation has not been confirmed by the FDA.
Table 1. Methods for Analyzing Lead in Various Samples.

<table>
<thead>
<tr>
<th>Method</th>
<th>Sample Type</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flame atomic absorption spectrometry</td>
<td>Blood</td>
<td>Requires only basic lab expertise, Rapid analysis, Small sample size with Delves cup, Low cost, Few interferences, Most accurate for paint</td>
<td>Detection limit, approx. 10 µg/dL, Time needed to process sample, Large sample size if no Delves cup, Should not run unattended, Paint surface must be disturbed, Results not immediately available</td>
</tr>
<tr>
<td></td>
<td>Paint</td>
<td></td>
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<tr>
<td>Graphite furnace atomic absorption spectrometry</td>
<td>Blood</td>
<td>Detects &lt; 1-2 µg/dL, Small sample size, Moderate cost, Few interferences</td>
<td>Longer analysis time, Needs more lab experience than FAAS, Greater potential spectral interference than FAAS</td>
</tr>
<tr>
<td></td>
<td>Water</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Paint</td>
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<tr>
<td>Anodic stripping voltammetry</td>
<td>Blood</td>
<td>Detection limit 2-3 µg/dL, Low cost, Rapid, Small sample size, Portable ASV detection limit 3.3 µg/dL</td>
<td>Needs more lab experience than FAAS, Sample pretreatment needed, Copper may affect measurement, Becoming less available, Portable ASV levels above 8 µg/dL should be confirmed by another method</td>
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<td></td>
<td>Water</td>
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<td>Paint</td>
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<tr>
<td>Inductively coupled plasma mass spectrometry</td>
<td>Blood</td>
<td>Detects approx. 0.1 µg/dL, Rapid, Small sample size, Few interferences, Multi-element capability, Economic if large number of samples</td>
<td>High cost, High skill needed</td>
</tr>
<tr>
<td></td>
<td>Water</td>
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<tr>
<td></td>
<td>Paint</td>
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<tr>
<td>Portable x-ray fluorescence spectrometry</td>
<td>Paint</td>
<td>Good accuracy, Immediate results, Low use costs, No damage to paint surface, Rapid</td>
<td>Potentially large margin of error compared with laboratory analysis, Requires certification, High purchase cost, Cannot measure lead in small objects, curved surfaces, including toys</td>
</tr>
<tr>
<td></td>
<td>Water</td>
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<tr>
<td></td>
<td>Paint</td>
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</tr>
<tr>
<td>Chemical tests</td>
<td>Blood</td>
<td>Immediate results, Inexpensive, Simple to use</td>
<td>Limited accuracy, Qualitative or semiquantitative, Tests mainly top layers of paint, May need to damage paint surface, Difficult to observe color change for dark paints</td>
</tr>
<tr>
<td></td>
<td>Water</td>
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<td></td>
<td>Paint</td>
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Abbreviations: ASV, anodic stripping voltammetry; FAAS, flame atomic absorption spectrometry

*Data from Environmental Protection Agency and World Health Organization.*
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Jennifer Lowry, a pediatrician at Children’s Mercy Hospital in Kansas City, Missouri, noted that physicians may not be using the point-of-care devices properly. “A child’s finger needs to be cleaned well before sample collection because a tiny speck of lead on the skin can cause a high reading.”47

A new testing sample type may be helpful in the future. Gardner et al48 tested the correlation between lead assays using blood versus oral fluid and found a 100% negative predictive value using the oral sample, eliminating the need for blood for lead screening in more than half of the 407 children tested.

Inadequacies of State and Federal Reporting Guidelines

The CDC recommends blood lead screening for high-risk populations and for children insured by Medicaid at age 1 and 2 years.49 This recommendation does not include fetuses in utero (as prenatal testing is currently not done) or infants younger than 12 months.10 Hanna-Attisha reported that her own studies on the Flint children had that as a limitation, as well as the reality of housing instability, in which the lead level of a child may reflect exposure from a previous residence.10

Although there is quite an exhaustive set of references, laws, and regulations mandating testing, plus helpful aids for all citizens describing the dangers of lead, a review of the literature strongly suggests that reporting guidelines are not universal, not followed, and results are manipulated and/or underreported. A comprehensive summary of state requirements was compiled in 2015 by Genevieve Sykes at the University of Alaska.50 Among the important findings is that only Iowa, Massachusetts, Delaware, and Maryland require proof of lead testing for school-aged children.

A 2017 report in Pediatrics, describing the Public Health Institute’s research on lead screening from 1999 to 2010, revealed “1.2 million cases of elevated blood lead levels among children under 6 … only half of those were reported to the Centers for Disease Control and Prevention. In some states, as many as 80 percent of lead-burdened children were not diagnosed at all.”51 Figure 7 shows the geographic distribution of the Pediatrics data.50,52

![Figure 7. Percent of lead-poisoned children missed, by region. From Cabrera 2017.52](image-url)
Of the roughly 600,000 children not reported in the Pediatrics study, Roberts et al\textsuperscript{51} noted that “\textasciitilde 45\% (278,299) occurred in years during which the child’s state was not reporting to the CDC, and 55\% (337,405) were not reported because of incomplete case ascertainment in states engaged in reporting efforts.”\textsuperscript{51} A listing of CDC data provided by states can be found at https://www.cdc.gov/nceh/lead/data/state.htm. The following states do not submit lead surveillance data to the CDC: Alaska, Arkansas, Hawaii, Idaho, Montana, North Dakota, Nebraska, Nevada, South Carolina, South Dakota, Utah, and Wyoming.

Policies that defer to state and local health agencies to mandate blood lead testing for children in their jurisdictions make the following assumptions: (1) good communication with stakeholders and (2) mechanisms and resources for enforcement. Roberts and colleagues conclude that “both of these assumptions have proven to be false, with the effect that large numbers of children with [elevated blood lead levels] (indeed, the majority of these children in many parts of the country) have been missed by clinicians.”\textsuperscript{51} Added to this, the National Center for Healthy Housing reported that “the budget for the CDC Childhood Lead Poisoning and Healthy Homes program was itself reduced from $29 million to $2 million in 2012, leading to a loss of 57\% of state positions responsible for primary prevention, environmental assessments, enforcements of lead-safe building laws, and outreach and education to lay and professional audiences, as well as for surveillance itself.”\textsuperscript{53} This would suggest that a more proactive physician initiative, to learn about lead exposure risks and rely less on state and even national data, will provide better service to their local patients in identifying those at risk and decreasing the effects of lead exposure.

\textit{References}


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9. Roy S. Pediatric lead exposure presentation from Hurley Medical Center doctors concerning Flint MI Flint Water Study website. 


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