

Lead Poisoning in Children

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Keywords

• Blood lead level • Primary prevention • Chelation • Neuro-developmental

Key points

- Lead is ubiquitous. It comes from a variety of sources and can be ingested or inhaled.
- There is no safe lead level. The presence of any amount of lead in the blood can lead to neuro-developmental deficits, and in larger amounts lead can cause multiorgan damage and even death.
- "Treatment" of lead poisoning should be geared toward primary prevention, targeting environmental hazards, particularly that of lead-based paint used in pre-1978 housing.

BACKGROUND

Lead poisoning in children is a persistent worldwide problem. According to the World Health Organization, it accounts for about 0.6% of the global burden of disease [1]. Although recent data have shown a decline in the prevalence of elevated blood lead levels (BLLs) in children in the developed world, lead remains a well-known environmental health threat.

WHAT IS LEAD?

Lead is a naturally occurring, bluish-grey metal that exists in both organic and inorganic forms. It is soft, pliable, and resistant to corrosion. It does not conduct electricity and is effective in shielding against radiation. It has been used by humans for thousands of years in a variety of ways and is still widely used today [2].

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HISTORY

The earliest record of lead mining dates back to as far 6500 BC in Turkey; decorative lead beads were found in a tomb in the ancient city of Anatolia [3]. The effects of lead *toxicity* have been documented as early as 2000 BC. Even back then, lead was readily available, inexpensive, and durable. Because of its low melting point, it is easily malleable and therefore its widespread use in civilized societies led to chronic low-level exposure that has been described by various philosophers and historians over the years. Hippocrates (460–370 BC) wrote about a man mining lead that had loss of appetite, colic, weight loss, pallor, fatigue, and irritability [4], all consistent with symptoms of lead poisoning that we see today.

During the Roman period, lead was used extensively in the building of the aqueducts. It also was used as a pigment in paint, face powders (ie, “rouge”), and mascaras. Lead sugar, or lead (II) acetate, was used to sweeten wine and preserve fruit. Because of its diverse uses and widespread availability, the Romans minimized the hazards of lead use and this was theorized to be the cause of the fall of the Roman Empire [5]. Although this belief has since been refuted, the mental instability described in many Roman rulers, the sterility of many aristocratic men, and the infertility in many aristocratic women were thought to be caused by their daily low-level exposure to the metal [4].

In the Renaissance period, alchemists used lead in their attempts to turn metals into gold, and painters used lead-based colors for their work. It also was used as a slow-acting poison by Lucrezia Borgia and Catherine De Medici in the 1400s [6]. In 1621, lead found its way to the New World, when the earliest colonists settling in Virginia began lead mining and smelting.

The Industrial Revolution saw an increase in the number of workers who exhibited symptoms of metal intoxication and prompted scientists and physicians to study these symptoms and identify a cause [7]. In the late 1800s, the first form of legislation was passed in the United Kingdom to minimize workers' exposure to harmful metals in the workplace (Factories' Prevention of Lead Poisoning Act of 1883).

In the United States, it was not until the early twentieth century that the occupational and environmental toxicity of lead was acknowledged. In 1914, a Baltimore boy died of lead poisoning from ingesting white lead paint from his crib [8]. In the 1920s, the discovery of tetraethyl lead as an antiknock, fuel-efficient gasoline additive boosted the American automotive industry. This compound was later linked to the development of mental illness and, eventually, the death of 15 factory workers in New Jersey and Ohio. In May 1925, the production and sale of leaded gasoline was suspended temporarily while the Surgeon General appointed a panel of experts to investigate the cause of these deaths. This panel was largely composed of industry representatives and in 1926, their report said that there was not enough time or sufficient evidence to prove a link between exposure to triethyl lead and the symptoms of chronic disease [6].

Throughout the world war II and postwar era, there continued to be no regulations on leaded gasoline or on lead-based paint, which were the major sources of lead exposure at the time. Deaths from acute lead poisoning continued to

be common. In the 1940s, BLLs of 40 $\mu\text{g}/\text{dL}$ (1.9 $\mu\text{mol}/\text{L}$) were considered within “expected” limits, and the absence of symptoms was reassuring [8]. In 1965, geochemist Clair Patterson published that the high environmental lead levels in developed countries were from industrial sources. But industry scientist Robert Kehoe challenged his findings and denied the link between environmental lead and public health issues [9].

Over the next few decades, many more studies revealed that severe behavioral and learning deficits resulted from chronic exposure to lead. In 1972, 4 workers developed tetraethyl-lead poisoning after cleaning a tank of lead petrol. Their BLLs were between 64.2 and 92.5 $\mu\text{g}/\text{dL}$ [10]. In 1974, Herbert Needleman, in an article in *Nature*, established the use of deciduous teeth to establish lead levels. Then in 1979, he published the seminal findings detailing an inverse relationship between dentine lead and intelligent quotient. He noted the frequency of nonadaptive classroom behavior increased in a dose-related fashion to dentine lead level. Further, he noted that lead exposure, at doses below those producing symptoms leading to a diagnosis, were associated with neuropsychological deficits that might interfere with classroom performance [11,12].

But it was not until 1975 that the US Environmental Protection Agency (EPA) was given the authority to regulate leaded gasoline. In 1977, the US Consumer Product Safety Commission banned the use of lead-based paint in residential housing. By 1985, the primary phase-out of leaded gas in the United States was complete. Blood lead levels declined by almost 80% from 1978 to 1991 during the phase-out [9].

In 1994, the United Nations Commission on Sustainable Development called on all governments to eliminate lead from gasoline, and on January 1, 2000, the European Union banned leaded gasoline as a public health hazard [13].

In 2011, an independent study from California State University estimated that the global phase-out of lead from gasoline resulted in considerable health, social, and economic benefits. More than 1 million deaths per year (of which 125,000 were children) were prevented and an estimated \$2.4 trillion (4% of global GDP) costs were saved per year. Previous research had shown that children with elevated lead levels were more likely to be aggressive, violent, and delinquent. Since the global phase-out of leaded gas, there have been higher intelligence quotients (IQs) and lower crime rates (58 million fewer crime cases reported) [14,15].

EPIDEMIOLOGY

- There has been a precipitous decline in BLLs in the pediatric population since the 1970s. A compilation of the National Health and Nutrition Examination Survey (NHANES) results from the periods of 1976 to 1980, 1991 to 1994, 1999 to 2002, and 2007 to 2010 are shown in Table 1. The mean BLLs during these periods are shown in Table 2 [16].
- In 1991, the Centers for Disease Control and Prevention (CDC) identified a BLL of 10 $\mu\text{g}/\text{dL}$ or higher as the “level of concern” for children aged 1 to 5 years.

Table 1Decrease in the prevalence of BLL greater than 10 $\mu\text{g}/\text{dL}$ in children aged 1 to 5 years

NHANES survey	Children aged 1–5 y with BLL >10 $\mu\text{g}/\text{dL}$, %
1976–1980	88.0
1991–1994	4.4
1999–2002	1.6
2007–2010	0.8

Abbreviations: BLL, blood lead level; NHANES, National Health and Nutrition Examination Survey.

- In 2012, the CDC replaced the term “level of concern” with an upper reference interval value defined as the 97.5th percentile of BLLs in US children aged 1 to 5 years from 2 consecutive cycles of NHANES (2007–2008 and 2009–2010). This reference value was calculated as 5 $\mu\text{g}/\text{dL}$ (0.24 $\mu\text{mol}/\text{L}$) [16].
- Based on the 2007 to 2010 NHANES data, the percentage of children aged 1 to 5 with BLLs greater than 5 $\mu\text{g}/\text{dL}$ was 2.6%, indicating an estimate of 535,000 children [16].
- Mean BLLs are higher in younger children, those that belong to low-income families, and/or those who are enrolled in Medicaid. Those who live in homes built before 1970 also have higher BLLs. Race and ethnicity also are predictive of high lead levels, with the greatest risk being in the non-Hispanic black population [16].
- Although the disparity in risk for BLLs greater than or equal to 10 $\mu\text{g}/\text{dL}$ by income and race are no longer statistically significant, disparities by race/ethnicity and income still persist at lower BLLs [17].
- Children who live in certain areas identified to have the highest prevalence of lead levels also are at risk. National and state-specific surveillance data from 1997 to 2012 that identify these zip codes is available at <http://www.cdc.gov/nceh/lead/data/national.htm>.

EXPOSURE AND SOURCES

Lead is ubiquitous, especially in industrialized societies, and exposure to lead can happen in a variety of ways. Ingestion or inhalation are the primary modes by which toxicity occurs; however, prenatal and dermal exposure have also been reported. Lead is absorbed through the respiratory and digestive tracts,

Table 2

Decline in estimated GM BLLs of children aged 1 to 5 years

NHANES survey	GM BLL, $\mu\text{g}/\text{dL}$	95% CI
1976–1980	15.0	14.2–15.8
1988–1991	3.6	3.3–4.0
1999–2002	1.9	1.8–2.1
2007–2010	1.3	1.3–1.4

Abbreviations: BLL, blood lead level; CI, confidence interval; GM, geometric mean; NHANES, National Health and Nutrition Examination Survey.

enters the bloodstream, and is distributed to all tissues throughout the body. The toxic effects of lead are related to its concentration in the blood. Children are at risk of lead poisoning by ingestion because of their propensity for chewing on things and placing objects in their mouths. Also, lead makes things taste sweet, further attracting ingestion by children. Adults are more likely to be exposed occupationally to lead through inhalation of lead dust and vapor.

Ingestion

Lead-based paint

Before the 1950s, white house paint was 50% lead, which is why old houses are high risk for lead exposure. In 1971, federal law reduced the maximum allowable lead content in paint to 1%, and by 1977 it was down to 0.06%. Although most homes have since been repainted with nonleaded paint, lead may still be released into the home during renovations or if paint is peeled, chipped, or cracked. Once believed to be due to ingested paint chips, lead toxicity has now been linked more so to household dust containing lead, which may be inhaled or ingested during a child's hand-to-mouth and toy-to-mouth activity [8,18].

Water

Drinking water can be contaminated by the lead solder that is used to hold copper pipes together. Municipal water supplies are usually regulated to prevent contamination at the source, but when older fixtures are corroded, lead can leach into the water supply that is delivered to homes. In 1991, the EPA published the Lead and Copper Rule to control the amount of lead and copper in drinking water. The EPA "action level" of lead in water is 15 parts per billion. This is unlikely to cause clinically significant elevation of BLL in adults; however, children may be more susceptible to lead poisoning because of their relatively smaller body size and specifics of their metabolism and storage of lead. In January 2011, Congress enacted the Reduction of Lead in Drinking Water Act to amend Section 1417 of the Safe Drinking Water Act regarding the use and introduction into commerce of lead pipes, plumbing fittings or fixtures, solder, and flux [19,20].

Soil

Lead released from combustion of leaded gasoline, deterioration of lead-based paint, factory and smelter emissions, and other industrial sources can become airborne and eventually settle onto the surrounding soil. The accepted safety standard for soil in residential areas is 400 parts per million (ppm) in play areas and 1200 ppm for nonplay areas [21,22].

Food

Lead makes its way into food products during its production, handling, packaging, preparation, and/or storage. As mentioned previously, lead from the air settles onto soil and results in the contamination of any produce that is grown on it. If lead solder is used during the canning process, this too makes its way into food once the can is opened and oxidation occurs. Imported spices from other countries that are not tested for lead content also can contaminate food during its preparation. Food stored, prepared, or served in lead crystal,

lead-glazed pottery, or porcelain can be contaminated as well. Lead also has been found in some candies imported from Mexico, particularly some candy ingredients, such as chili powder and tamarind [23].

Leaded objects, including children's toys, cosmetics, and other recreational items

Children's toys, jewelry, and or furniture may contain lead-based paint. Many lipsticks are manufactured using lead. Topical exposure or contact with these objects presents a low risk of contamination; however, ingestion of these products (chewing and/or swallowing) may cause lead poisoning. Since 2008, the federal government has banned lead greater than 100 ppm in weight in most children's products [23,24].

Alternative medicine or "folk remedies"

Hispanic traditional remedies called *Greta* and *Azarcon* are used to treat an upset stomach, diarrhea, and vomiting. These are fine orange powders that may have as much as 90% lead content. *Ba-baw-san* is a Chinese herbal remedy used to treat colic pain or to pacify young children, and *Ghasard* is a brown powder used as a tonic in India. These have both been found to contain lead. *Daw Tway* is a folk remedy from Thailand and Myanmar (Burma) used to aid digestion that has been found to contain extremely high levels of lead and arsenic [25].

Inhalation

Leaded gasoline

Before the 1970s, leaded gasoline was responsible for most lead exposure through inhalation. More recently, lead-based paint in older housing has become the most important source of lead toxicity in vulnerable populations, particularly children. The use of lead in gasoline was gradually phased out from the United States from 1975 to 1986, and from Europe in the 1990s.

Occupational hazards

Lead dust is created through occupational means and can be extremely hazardous to the exposed workers and those who live with them. It settles on skin, hair, and clothes and can be brought home where family members are exposed [26]. Increased risk of occupational exposure occurs in the following:

- Battery manufacturing and recycling plants
- Demolition, remodeling, and renovation projects
- Rubber and plastic industries
- Ammunition manufacturing
- Automotive/radiator repair
- Lead soldering (ie, electronic manufacturing) and welding
- Painting
- Plumbing

Artificial turf

Artificial turf used as playing fields are made of nylon or nylon/polyethylene blend fibers that may contain lead. With frequent use, wear, and tear, lead dust is released into the air where it may be inhaled or even ingested. The

amount of exposure, BLLs, and/or extent of lead poisoning from this source has not yet been determined [27].

Prenatal exposure and breastfeeding

In utero lead poisoning occurs when lead enters the maternal bloodstream during environmental exposure or from mobilization of bone lead stores accumulated from past exposure. This prenatal exposure to lead has been linked to neurodevelopmental delays after birth, although a threshold level for toxicity has yet to be identified. Lead crosses the placenta readily, hence the presence of any lead in maternal blood should be a cause for concern [28]. Additionally, studies have estimated a direct relationship between maternal blood levels at 1 month postpartum and the BLLs of their breastfed infants [29].

Dermal exposure

Skin absorption is not considered a significant mode of exposure among the general population. Organic lead is more likely to be absorbed through the skin than inorganic lead, and mostly occurs among people who work closely with it [2].

Additional sources of lead can be found on the following Web site: www.cdc.gov/nceh/lead/CaseManagement/caseManage_appendixes.htm.

PATHOGENESIS

Lead exerts its effects by binding to the sulfhydryl group of proteins, making it particularly toxic to multiple enzyme systems. Much of its toxicity also results from its binding to calcium-activated proteins with much higher affinity than calcium, interfering with various calcium-dependent cellular functions. It interferes with heme production by inhibiting the enzyme delta-aminolevulinic acid dehydratase and by preventing the incorporation of iron into the protoporphyrin molecule via the enzyme ferrochelatase; the result is a hypochromic, microcytic anemia.

The half-life of lead is approximately 30 to 40 days in the blood of adult men, but in children and pregnant women this may be longer. It then diffuses into the soft tissues (including the kidneys, brain, liver, and bone marrow), where it may stay for several months. In the liver, lead interferes with the cytochrome P450 enzymes. In the kidneys, vitamin D synthesis also is impaired. Lead then enters bone and is stored there for as long as several years. Lead in the bones, teeth, hair, and nails is bound tightly and not available to other tissues, and is generally thought not to be harmful [30]. Compared with 94% in adults, only 70% of absorbed lead is deposited in the bones in children, which may partially explain why children are more susceptible to the clinical effects of lead toxicity [31]. This also means that the BLL is not an accurate reflection of the total body lead burden.

CLINICAL PRESENTATION

Today, most lead-exposed children are asymptomatic at the time of screening. When present, the early symptoms of lead poisoning may be vague and nonspecific (eg, anorexia, abdominal pain, irritability). With continued

exposure, these symptoms may worsen and develop into a spectrum of multi-organ dysfunction, as described in the following sections.

Nervous system

The neurologic effects of lead poisoning range from subtle developmental delays to frank encephalopathy. At high levels (BLL >100–150 µg/dL [4.8–7.2 µmol/L]), lead can cause acute symptoms, such as ataxia, stupor, coma, convulsions, hyperirritability, and death. Lower levels (BLL >10 µg/dL [0.48 µmol/L]) have been linked to the development of behavioral changes and neurocognitive decline [32,33].

Lead affects brain development and results in loss of milestones, reduced IQ, shortened attention span, increased antisocial behavior, and reduced educational attainment. Effects on learning behavior have been found to be associated with the degree of exposure to lead between the ages of 12 and 36 months [34].

Hematologic system

Anemia associated with lead poisoning may be due to either disruption of heme synthesis or hemolysis. At BLLs of 40 µg/dL (1.9 µmol/L), lead interferes with heme biosynthesis and results in decreased hemoglobin production [35]. A hypochromic microcytic anemia results and symptoms of weakness and fatigue develop. At higher levels (BLL >70 µg/dL [3.4 µmol/L]) acute hemolysis occurs and the anemia may be normocytic [2].

Renal system

Even at a blood level lower than 10 µg/dL, lead poisoning can result in impairment of proximal tubular function, manifested by aminoaciduria, glycosuria, and hyperphosphaturia [36]. Chronic exposure results in lead nephropathy, seen histologically as an interstitial nephritis that is often irreversible. In addition, lead in the kidney interferes with activation of vitamin D 1,2-dihydroxy cholecalciferol, which has an important role in calcium metabolism.

Other effects

Gastrointestinal effects of lead poisoning include anorexia, vomiting, constipation, and abdominal pain. Lead poisoning has been linked to the development of hypertension and its sequelae. Reproductive studies in men have revealed that chronic lead exposure may diminish sperm concentrations, total sperm counts, and total sperm motility. Effects on actual fertility are unclear. Developmental studies suggest that low-level exposure may lead to premature births and low birth weights. There is no evidence to suggest the development of major congenital anomalies, although learning disabilities have been reported in children whose parents were previously exposed to lead [2].

PREVENTION

The Lead Contamination Control Act of 1988 led to the creation of the CDC Childhood Lead Poisoning Prevention Program for the purpose of eliminating childhood lead poisoning in the United States. The CDC has helped state and local governments to develop and implement lead poisoning prevention

programs, which include public health education, policy development, screening protocols, and case management guidelines. The CDC has provided funding and research support to enhance lead poisoning prevention at the federal, state, and local levels. This included the creation of a Childhood Blood Lead Surveillance System that allows states to report data to the CDC. In 2010, the Advisory Committee on Childhood Lead Poisoning Prevention convened a Work Group to reconsider the approach, terminology, and strategy for elevated BLLs in children [37].

Primary prevention

Health management: the role of the clinician

The task of educating families about lead exposure prevention should fall on the primary care physician. Anticipatory guidance should include information regarding in-home exposures to lead, unsafe renovation practices, and potential exposure from parental occupations and hobbies. Effective prevention requires the identification of populations that are at high risk because of their physical and social environment. Non-Hispanic black individuals have the highest prevalence of elevated BLLs. Furthermore, the clinician should recognize a higher risk of exposure in specific immigrant populations, refugees, and children from foreign countries [37]. The CDC provides fact sheets for prospective parents who wish to adopt children from other countries, as well as toolkits for newly arrived refugee children that give guidance on lead exposure screening and prevention.

Personal lead risk assessment questionnaires. Lead risk questionnaires are useful in identifying children who should be screened for elevated BLLs. This assessment should be performed annually for all children aged 6 months to 6 years. The tool varies in every state and for each health department, but should include questions based on current public health guidelines. Box 1 lists some common questions included in a risk assessment questionnaire.

Nutritional assessment. Lead absorption is enhanced by high fat intake and/or calcium and iron deficiency. A careful assessment of the patient's nutritional status should be done and parents should be advised to serve foods that are rich in calcium, iron, and vitamin C. Supplementation should be started if necessary.

Occupationally exposed adults. When evaluating lead exposure in children, their parents also should be questioned for lead exposure at work. The Occupational Safety and Health Administration is responsible for issuing standards and regulations for workplace exposure to lead.

Pregnant and breastfeeding women. Since 2010, the CDC has recommended follow-up activities and interventions beginning at BLLs of 5 $\mu\text{g}/\text{dL}$ in pregnant women. Their Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women includes advice on preventing lead exposure, assessment and lead level testing during pregnancy, and strategies to reduce fetal exposure to lead. It also includes guidance for breastfeeding, as well as follow-up of infants and children exposed to lead in utero [28].

Box 1: Lead risk assessment questions

1. Does your child live in or regularly visit an older home/building with peeling or chipping paint, or with recent or ongoing renovation or remodeling?
2. Has your child spent any time outside the United States in the past year?
3. Does your child have a brother/sister, housemate/playmate being followed or treated for lead poisoning?
4. Does your child eat nonfood items (pica)? Does your child often put things in his/her mouth, such as toys, jewelry, or keys?
5. Does your child often come in contact with an adult whose job or hobby involves exposure to lead?
6. Does your family use traditional medicine, health remedies, cosmetics, powders, spices, or food from other countries?
7. Does your family cook, store, or serve food in leaded crystal, pewter, or pottery from Asia or Latin America?

Adapted from New York State Department of Health. Available at: www.health.ny.gov/publications/2501/#questions. Accessed January 27, 2014.

Removal of lead from the environment

The environment should be assessed thoroughly and repeatedly to identify and mitigate lead hazards before children demonstrate BLLs at or higher than the reference value. Each state and local health department should develop prevention strategies to reduce environmental lead exposures in soil, dust, paint, and water before children are exposed [38]. Fig. 1 illustrates how correct public policy and aggressive implementation over the past several decades have resulted in a drastic decline in BLLs from the 1970s.

No single discipline or profession is responsible for the elimination of lead hazards, which involves housing, public health, and environmental dimensions. The Healthy People Initiative is a collaborative health promotion and disease prevention effort dedicated to improving the health of the nation over the course of a decade. “Healthy People 2020” was launched in December 2010, and one of their goals included the elimination of childhood lead poisoning as a public health problem. The CDC, EPA, Department of Housing and Urban Development, and other agencies have developed a federal interagency strategy to achieve this goal by 2020. More information can be found on www.healthypeople.gov.

Removal of lead in the home

Title X of the 1992 Housing and Community Development Act, also known as the Residential Lead-Based Paint Hazard Reduction Act (Public Law 102-550), mandated the creation of an infrastructure that would correct lead paint hazards in housing. Depending on the level of suspicion, a lead hazard screen, risk assessment, or inspection can be done, preferably by a certified risk lead inspector or risk assessor, to determine the presence of lead risk hazards and how they should be addressed. The risk assessor may then recommend either *interim controls* (ie, short-term or temporary actions and recommendations) or long-term or permanent

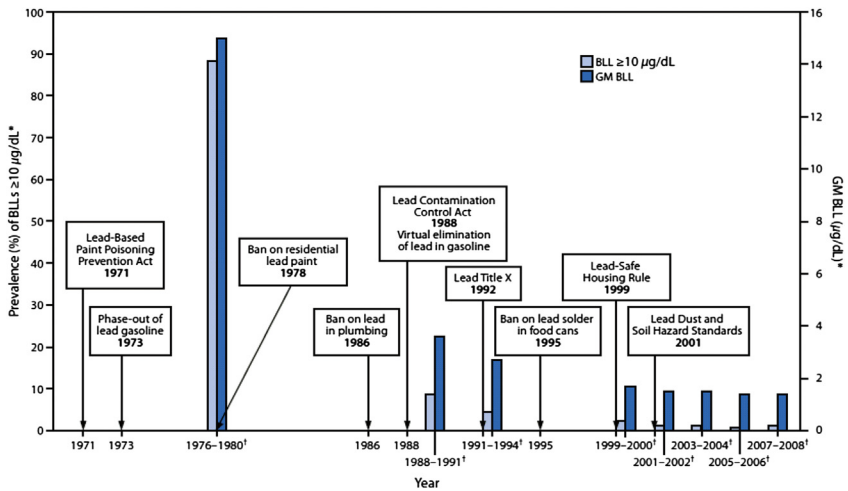


Fig. 1. Timeline of lead poisoning prevention policies and BLLs in children aged 1 to 5 years, by year: National Health and Nutrition Examination Survey, United States, 1971–2008. * National estimates for GM BLLs and prevalence of BLLs ≥ 10 $\mu\text{g}/\text{dL}$, by NHANES survey period and sample size of children aged 1–5 years: 1976–1980: N = 2,372; 1988–1991: N = 2,232; 1991–1994: N = 2,392; 1999–2000: N = 723; 2001–2002: N = 898; 2003–2004: N = 911; 2005–2006: N = 968; 2007–2008: N = 817. † NHANES survey period. (From Brown MJ, Margolis S. Lead in drinking water and human blood lead levels in the United States. *MMWR Surveill Summ* 2012;61(Suppl):3.)

interventions to remove lead or *abatement*. The EPA recommends hiring a certified lead-based paint professional to perform the abatement if a child residing in the house has a blood-lead level of 20 $\mu\text{g}/\text{dL}$ or higher for a single venous test (or 15–19 $\mu\text{g}/\text{dL}$ in 2 consecutive tests taken 3–4 months apart) (Table 3) [39].

Table 3

Evaluation of lead in the home

Lead hazard screen	A <i>lead hazard screen</i> is a limited version of a risk assessment for houses with a low chance of lead risks. The outcome is either a conclusion that lead-based paint hazards are probably not present or a recommendation that a full risk assessment be conducted to determine if such hazards are present.
Risk assessment	A <i>risk assessment</i> is an on-site investigation to determine the presence, type, severity, and location of lead-based paint hazards. The presence of deteriorated lead-based paint or high levels of lead in dust or soil pose potential hazards to children who may ingest lead inside or while playing outside.
Lead-based paint inspection	A lead-based paint <i>inspection</i> is a surface-by-surface investigation to determine whether there is lead-based paint in the home and where it is located. An inspection may be particularly useful before renovation, repainting, or paint removal.

Adapted from EPA. Testing your home for lead in paint, dust, and soil. 2002. Available at: www.epa.gov.

Secondary prevention: lead screening

The presence of any amount of lead in blood is no longer acceptable, because even lower levels have been associated with subtle neurobehavioral deficits. Because most children with lead poisoning are asymptomatic, screening criteria should be based on risk of exposure, rather than the presence of signs and symptoms. In 1991, the CDC called for *universal screening* of all children ages 1 and 2 years. In 1997, because of the declining lead levels in the United States, the CDC and the American Academy of Pediatrics (AAP) recommend *targeted screening* of all children deemed to be at risk based on their age, ethnicity, housing age, high-risk zip code, and/or enrollment in Medicaid.

Screening should be done in children who live in areas where at least 27% of houses were built before 1950 and in places where the prevalence of elevated blood levels in children ages 1 to 2 years is greater than 12%. BLL testing is required at ages 1 and 2 years for all Medicaid-enrolled children, and if they have not been screened by the age of 6 years, they should be tested at presentation. If a personal risk questionnaire elicits a positive response to at least 1 or more of the items, then they should be screened as well. All foreign-born children (ie, refugees, immigrants, and international adoptees) should be screened immediately on arrival to the United States and again 3 to 6 months later if they are 6 months to 6 years of age. Each state or local health department should develop their own guidelines for lead screening based on local BLL prevalence and data on housing age, but in the absence of such information, universal screening should still be done (Table 4) [40,41].

Screening may be done with a capillary or venous blood sample, but if a capillary lead level is elevated (greater than the reference level of 5 $\mu\text{g}/\text{dL}$), it should be confirmed with a venous lead level. Guidelines for confirmatory testing (if the initial lead test is performed using a capillary blood sample) and recommendations on a follow-up schedule may vary among states (Table 5).

Table 4
Standard surveillance definitions and classifications

Screening test	A blood lead test for a child age <72 mo who previously did not have a confirmed elevated BLL. (NOTE: A child may be screened in multiple years or even multiple times within a given year, but would be counted only once for each year.)
Elevated BLL	A single blood lead test (capillary or venous) at or above the reference range value of 5 $\mu\text{g}/\text{dL}$ established in 2012.
Confirmed elevated BLL $\geq 5 \mu\text{g}/\text{dL}$	A child with 1 venous blood specimen $\geq 5 \mu\text{g}/\text{dL}$, or 2 capillary blood specimens $\geq 5 \mu\text{g}/\text{dL}$ drawn within 12 wk of each other.
Unconfirmed elevated BLL $\geq 5 \mu\text{g}/\text{dL}$	A single capillary blood lead test $\geq 5 \mu\text{g}/\text{dL}$, or 2 capillary tests $\geq 5 \mu\text{g}/\text{dL}$ drawn more than 12 wk apart.

Abbreviation: BLL, blood lead level.

Adapted from the Centers for Disease Control and Prevention. Available at: www.cdc.gov/nceh/lead/data/definitions.htm.

Table 5

Recommended schedule for obtaining a confirmatory venous sample

Blood, $\mu\text{g}/\text{dL}$	Time to confirmation testing
≥ 5 –9	1–3 mo
10–44	1 wk–1 mo*
45–59	48 h
60–69	24 h
≥ 70	Urgently as emergency test

*The higher the BLL on the screening test, the more urgent the need for confirmatory testing.

Adapted from the Advisory Committee on Childhood Lead Poisoning Prevention of the Centers for Disease Control and Prevention. Low level lead exposure harms children: a renewed call for primary prevention. Atlanta: CDC; 2012.

The CDC used the term “blood level of concern” to indicate the reference value by which children are identified as having been exposed to lead and thereby require intervention. Since 1960, the BLL of concern has been lowered incrementally from greater than 60 $\mu\text{g}/\text{dL}$ (2.9 $\mu\text{mol}/\text{L}$) to 10 $\mu\text{g}/\text{dL}$ by 1991. In 2012, the CDC replaced the term “level of concern” with a reference value of greater than 5 $\mu\text{g}/\text{dL}$ (0.24 $\mu\text{mol}/\text{L}$) [37]. This change allows earlier detection of children who have been exposed to lead and thus results in earlier action to prevent further exposure, rather than simply treating those who have already been exposed.

For example, in New York City, all BLLs higher than the reference value of 5 $\mu\text{g}/\text{dL}$ are reported to the Department of Health and Mental Hygiene (DOHMH). If a child is found to have a BLL of 5 to 14 $\mu\text{g}/\text{dL}$, the DOHMH contacts their families and medical providers to ensure timely follow-up and suggest strategies for lead exposure reduction. Educational materials are sent, including a brochure on tenant rights. The threshold for environmental intervention and care coordination is a BLL of 15 $\mu\text{g}/\text{dL}$. If a child younger than 18 is found to have a BLL of 15 $\mu\text{g}/\text{dL}$ or greater, an inspection of the home is performed. More recently, home inspection has been recommended for children younger than 3 with even lower BLLs (5–9 $\mu\text{g}/\text{dL}$) [42,43].

For adults, the reference BLL is 10 $\mu\text{g}/\text{dL}$, according to the National Institute for Occupational Safety and Health [44]. The US national BLL geometric mean among adults was 1.2 $\mu\text{g}/\text{dL}$ in 2009–2010 [45]. The current biologic exposure index (a level that should not be exceeded) for lead-exposed workers in the United States is 30 $\mu\text{g}/\text{dL}$ in a random blood specimen.

EVALUATION OF THE PATIENT WITH SUSPECTED LEAD EXPOSURE AND POISONING

History and physical examination

A careful history should be obtained from the families of all children suspected of lead toxicity. The onset and duration of each symptom should be characterized, and dietary history should be obtained as well. History of pica, ingestion of nonfood substances after the age of 18 months, any recent travel to endemic

areas, and a history of lead exposure in any family member are also relevant. Preventive screening questionnaires should be used to identify potential environmental sources [37].

This should be followed by a complete physical examination, paying particular attention to the systems most likely to be affected by lead toxicity. The neurologic examination should include an assessment of language and behavior. Developmental milestones should be evaluated and documented. Blood pressure should be checked for hypertension. A purplish line on the gums (lead line) is rarely seen in children nowadays, but if present indicates prolonged exposure to lead [2,37].

Diagnostic tests

BLL

A venous BLL is the most useful screening and diagnostic test for lead exposure. Initial screening may be performed using a fingerstick capillary sample. However, a poorly collected capillary sample may be contaminated with environmental lead and could be falsely positive. Levels greater than 10 $\mu\text{g}/\text{dL}$ must be confirmed with a venous sample [40]. BLLs reflect recent or current lead exposure, but not necessarily the total body lead burden, as lead may be stored in bones.

Free erythrocyte protoporphyrin level

Lead interferes with heme synthesis by inhibiting the enzyme ferrochelatase in mitochondria. This results in the accumulation of free erythrocyte protoporphyrin (FEP). FEP levels have a high threshold for detection; its sensitivity decreases below BLLs less than 35 $\mu\text{g}/\text{dL}$. In light of the lower criterion for BLL used to prompt action, FEP alone is no longer used as a screening tool for lead poisoning. When used in conjunction with BLL, FEP levels are useful to discriminate between acute and chronic lead exposure. If FEP is normal in the setting of high BLLs, the exposure is more likely acute; if both are elevated, the exposure is more likely chronic.

Complete blood count

A complete blood count can reveal *hypochromic microcytic anemia*. Basophilic stippling, although pathognomonic for lead poisoning, is uncommon in children.

Hair samples

Analysis of hair samples has been used to measure environmental exposure to some heavy metals; however, this is not as sensitive as BLLs. This has been used for screening in other countries, but is not currently used in lead surveillance in the United States.

Imaging

Abdominal radiographs may show radiopaque foreign bodies in the gastrointestinal tract and is helpful in cases of acute ingestion (Fig. 2). Long-bone radiographs may demonstrate radiodensities found at the distal end of long bones called "lead lines" (Fig. 3) and indicate chronic lead exposure.



Fig. 2. Plain abdominal radiograph in a 3-year-old patient showing multiple metallic particles due to ingested flakes of lead paint. (Image reprinted with permission from Medscape Reference (<http://emedicine.medscape.com/>), 2014. Available at: <http://emedicine.medscape.com/article/410113-overview>.)

MANAGEMENT OF THE PATIENT WITH LEAD POISONING

The management of patients with lead exposure involves not only the pharmacologic management of toxicity, but also strategies for intervention and prevention of further exposure. Once an elevated lead level is found, the local health department should be notified and a home risk assessment should be

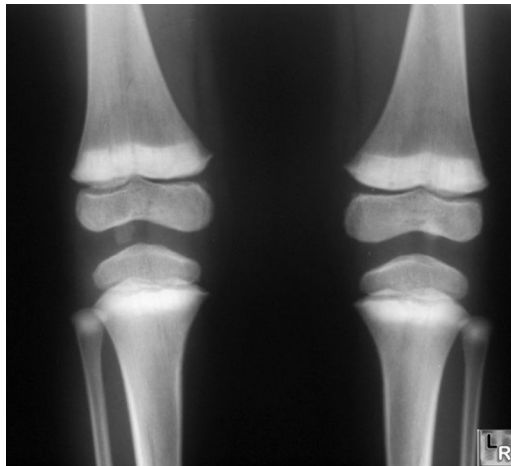


Fig. 3. Long-bone radiograph of both knees of a child with lead poisoning showing dense metaphyseal bands involving the distal femurs, proximal tibias and proximal fibulas. (From LearningRadiology.com; and Courtesy of William Herring, MD, FACR; with permission. Available at: <http://www.learningradiology.com/notes/bonenotes/leadpoisonpage.htm>. Accessed February 14, 2014.)

performed to determine the need for abatement strategies. With the gradual lowering of the “BLL of concern” by the CDC, the threshold for action has decreased as well. The Pediatric Environmental Health Specialty Unit Network has made recommendations on further evaluation and/or intervention based on the BLL, as outlined in Table 6 [46].

Decontamination

There is no benefit to using activated charcoal for lead ingestion, as it binds lead poorly. Gastric lavage may be performed; however, the American Academy of Clinical Toxicology stated that there is no evidence to show that its use improves clinical outcomes. Whole bowel irrigation has a theoretical benefit for decontamination of heavy metal ingestions; however, there are insufficient data to support or exclude its use.

Chelating agents

Chelation is recommended for BLLs of 45 $\mu\text{g}/\text{dL}$ or higher. Before starting therapy, the level must be repeated immediately for confirmation. The patient must be admitted to a hospital that has proficiency with chelation therapy or an expert in the field should be consulted. The decision on which agent should be used will depend on the blood lead concentration, the patient’s symptoms, and the environmental lead burden. The chelating agents available for use are as follows:

2,3 dimercaptosuccinic acid (DMSA, succimer)

Succimer is the water-soluble analog of dimercaprol. It has a wider therapeutic index than dimercaprol and edetate calcium disodium (CaNa_2EDTA); hence, it is recommended by the AAP for initial management of children with blood levels greater than 45 $\mu\text{g}/\text{dL}$ and less than 70 $\mu\text{g}/\text{dL}$. It can rapidly decrease lead levels and repletes sulfhydryl-dependent enzymes. The most common adverse effects are abdominal distress, transient rash, elevated hepatocellular enzyme levels, and neutropenia [41]. Studies have shown that despite being able to lower blood lead concentrations, succimer does not reverse or diminish the cognitive impairment or other behavioral or neuropsychologic effects of lead in children with lower lead levels; hence, it is not recommended for levels less than 45 $\mu\text{g}/\text{dL}$ [47,48].

Dimercaprol, or British anti-Lewisite

British anti-Lewisite forms a nonpolar compound with lead that is excreted in bile and urine. Its ability to rapidly cross the blood-brain barrier makes it the drug of choice in patients with acute lead encephalopathy. However, it has a narrow therapeutic range and is recommended for use (in combination with CaNa_2EDTA) only in children whose BLLs are greater than 70 $\mu\text{g}/\text{dL}$ or in children with lead encephalopathy [41].

CaNa_2EDTA

CaNa_2EDTA is an intravenous medication used in combination with dimercaprol in children whose BLLs are greater than 70 $\mu\text{g}/\text{dL}$ or in children with lead encephalopathy. It may also be used as an alternative initial treatment for

Table 6
Management of childhood lead exposure and poisoning

Blood lead concentration	Recommendation
<5 µg/dL	<ol style="list-style-type: none"> 1. Review laboratory results with family. For reference, the geometric mean BLL for children 1–5 y is <2 µg/dL. 2. Repeat the BLL in 6–12 mo if the child is at high risk or risk changes during the time frame. Ensure levels are done at 1 and 2 y of age. 3. For children screened at age <12 mo, consider retesting in 3–6 mo, as lead exposure may increase as mobility increases. 4. Perform ROUTINE HEALTH MAINTENANCE, including assessment of nutrition, physical and mental development, and iron deficiency risk factors. 5. Provide ANTICIPATORY GUIDANCE on common sources of environmental lead exposure: paint in homes built before 1978, soil near roadways or other sources of lead, take-home exposures related to adult occupations, imported spices, cosmetics, folk remedies, and cookware.
5–14 µg/dL	<ol style="list-style-type: none"> 1. Perform steps as described previously for levels <5 µg/dL. 2. Retest venous BLL within 1–3 mo to ensure the lead level is not rising. If it is stable or decreasing, retest the BLL in 3 mo. Refer patient to local health authorities if such resources are available. Most states require that elevated BLLs are reported to the state health department. Contact the CDC at 800-CDC-INFO (800-232-4636) or the National Lead Information Center at 800-424-LEAD (5323) for resources regarding lead poisoning prevention and local childhood lead poisoning prevention programs. 3. EDUCATION: Take a careful environmental history to identify potential sources of exposures (see recommendation 5 described previously for levels <5 µg/dL) and provide preliminary advice about REDUCING/ELIMINATING exposures. Take care to consider other children who may be exposed. 4. Provide NUTRITIONAL COUNSELING related to calcium and iron. In addition, recommend having a fruit at every meal, as iron absorption quadruples when taken with foods that contain vitamin C. Encourage the consumption of iron-enriched foods (eg, cereals, meats). 5. IRON STATUS: Ensure iron sufficiency with adequate laboratory testing (CBC, Ferritin, CRP) and treatment per AAP guidelines. Consider starting a multivitamin with iron. 6. NEURODEVELOPMENTAL MONITORING: Perform structured developmental screening evaluations at child health maintenance visits, as lead's effect on development may manifest over years.
15–44 µg/dL	<ol style="list-style-type: none"> 1. Perform steps as described previously for levels of 5–14 µg/dL. 2. Confirm the blood lead level with repeat venous sample within 1–4 wk. 3. IMAGING: Specific evaluation of the child, such as abdominal radiograph should be considered based on the environmental investigation and history (eg, pica for paint chips, mouthing behaviors). Gut decontamination may be considered if leaded foreign bodies are visualized on radiographs. 4. TREATMENT: Any treatment for BLLs in this range should be done in consultation with an expert. Contact local PEHSU or PCC for guidance.

(continued on next page)

Table 6
continued

Blood lead concentration	Recommendation
>44 µg/dL	<ol style="list-style-type: none"> 1. Follow guidance for BLL 15–44 µg/dL as listed previously. 2. Confirm the BLL with repeat venous lead level within 48 h. 3. Consider HOSPITALIZATION and/or CHELATION therapy (managed with the assistance of an experienced provider). Safety of the home with respect to lead hazards, isolation of the lead source, family social situation, and chronicity of the exposure are factors that may influence management. Contact your regional PEHSU or PCC for assistance.

Abbreviations: AAP, American Academy of Pediatrics; BLL, blood lead level; CBC, complete blood count; CDC, Centers for Disease Control and Prevention; CRP, C-reactive protein; PCC, Poison Control Center; PEHSU, Pediatric Environmental Health Specialty Unit.

Adapted from Newman N, Binns HJ, Karwowski M, et al. Recommendations on Medical Management of Childhood Lead Exposure and Poisoning. Pediatric Environmental Health Specialty Unit (PEHSU) Network. June 2013 update; with permission. Available at: <http://aoec.org/pehsu/facts.html>.

BLL greater than 45 µg/dL if the child is allergic to succimer. It decreases blood lead concentration, reverses the hematologic effects of lead, and forms nonionizing soluble complexes with lead, thereby enhancing its excretion in the urine. However, if used alone, it may aggravate symptoms in patients with very high BLLs. It is contraindicated for use in pregnancy or during breastfeeding.

D-penicillamine

D-penicillamine has been used since 1957 for the treatment of lead poisoning and was the only oral chelator for lead until the availability of DMSA. Its sulfhydryl group combines with lead to form ring compounds to facilitate elimination. However, it is not approved by the Food and Drug Administration for use in the United States.

Supportive therapy

Airway protection may be necessary in the event of acute encephalopathy. Benzodiazepines and/or barbiturates may be useful for seizures. For prolonged seizures, intracranial hypertension is likely and must be addressed accordingly (eg, hyperosmolar therapy).

Discharge criteria

Medical management of lead poisoning always should be accompanied by aggressive environmental interventions, and the patient should not be returned to the same home and/or workplace until it is deemed lead free.

SUMMARY

There is no safe lead level in children. Primary prevention is the most effective way to bring about the complete removal of lead from the environment and

eliminate lead poisoning as a public health concern. The National Lead Information Center can be reached via the Internet at www.epa.gov/lead and www.hud.gov/lead, or via phone at 1-800-424-LEAD (5323).

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