Environmental Health Perspectives
Vol. 89, pp. 49-54, 1990

Implications of New Data on Lead Toxicity for Managing and Preventing Exposure

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Recent advances in research on low-level lead poisoning point to the need to increase efforts to prevent exposure. Current biomedical consensus accepts that blood lead levels as low as 5 to 15 mcg/dL are risky to fetuses, young children, and adults. Lead at low dose is associated with increased blood pressure in adults, and chronic exposure has been associated in cohort studies with kidney disease and cancer. Data on lead toxicokinetics also points to the hazards of low-level, chronic exposure, since the lead that is accumulated over time in bone can be released at a relatively rapid rate during pregnancy and menopause. Sources that contribute to current lead exposure of the general population include unabated lead-based paint and contaminated soils, as well as lower level but pervasive sources in drinking water, food, and consumer products.

Recent information on the nature and extent of lead toxicity has presented a challenge for preventing disease that continues to exceed our ability to formulate effective public health and environmental policy. It can be claimed that of the major environmental factors in human disease, more has been done worldwide to reduce sources of lead exposure than for any other single toxicant. Although overall the net usage of lead has not substantially declined in the world economy, some of the more dispersive and more directly available sources of lead in the general environment have been controlled in several countries to an extent, through such major actions as reducing the allowable concentrations of lead in paint, automotive fuels, and certain canning and printing materials. These control measures have been associated with subsequent reductions in median blood lead levels, as demonstrated in surveys conducted in the U.S., U.K., and other countries (*1–3*).

However, at the same time, in general, the overall prevalence of lead toxicity has not been reduced. There are two reasons for this continuing failure in management and prevention: first, the lack of effective action to remediate known sources of lead in the environment; and second, the impact of new biomedical data on the definition of lead toxicity. With respect to the first issue, in most cases, the high-impact sources of lead, such as lead in old paint found in housing stock in the U.S. and to a lesser extent in other countries, and lead contamination of soils in the vicinity of primary and secondary smelters around the world have yet to be effectively cleaned up. The magnitude of these two sources, in terms of estimated population impact, is shown in Tables 1 and 2 (*4*).

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Table 1. Estimates on numbers of children under 7 years exposed to lead-based paint (LBP).[a]

Age of housing	Number of houses with LBP	Unsound housing units	Number of children in LBP houses	Number in unsound housing
Pre-1940	20,505,000	964,000	5,885,000	277,000
1940–1959	16,141,000	758,000	4,632,000	218,000
1960–1974[b]	5,318,000	250,000	1,526,000	72,000
Total	41,964,000	1,972,000	12,043,000	567,000

[a]Data from ATSDR (*4*).
[b]Lead-based paint was banned from residential use in 1973. Nevertheless, some houses constructed or painted after that time may have LBP.

Table 2. Estimates of numbers of children under 7 years exposed to lead from primary and secondary lead smelters in the U.S.[a]

Source	Number	Numbers of children exposed
Primary smelter	5	21,000
Secondary smelter	23	187,000
Total		208,000

[a]Data from ATSDR (*4*). These data refer only to operating smelters. Additional populations live near closed facilities with high levels of environmental contamination.

Methods for the safe and effective abatement of lead-based paint in houses have yet to be developed and validated (*5,6*). A pilot-scale project in the U.S. is addressing the methods necessary to evaluate and abate sites with high concentrations of lead in surface dusts and soils (*7*), which were identified as a hazard over a decade ago (*8,9*). In some instances, levels of lead in surface soils in residential areas are extraordinarily high: in a small survey of backyards on Staten Island downwind from a secondary lead smelter in Cartaret, New Jersey, concentrations of lead between 1000 and 4000 ppm were found (*10*). An unpublished survey conducted for

the New York City Department of Planning reported that levels of lead in street dust were frequently above 2000 ppm, with an arithmetic mean of 5777 ppm (*11*). The unsolved problems of managing both industrial and municipal wastes present continuing inputs of lead; for example, the shift toward incineration of processing municipal solid waste has the potential to generate tons of lead in ash residues (*12*).

Of particular relevance to evaluating the advances in lead research that have taken place since 1979, there has been a substantial revision in consensus opinion as to the levels of lead exposure that are associated with damage to human health. As pointed out by Needleman (*13*), over the past 50 years in medicine, this evaluation of exposure and risk has changed radically, from an opinion held through the 1950s that blood lead levels as high as 80 mcg/dL were not risky to health to the current opinion that blood lead levels as low as 10 mcg/dL may be hazardous to children and the fetus (*14*). As shown in Figure 1, this revision in defining lead toxicity is alone responsible for increasing by a factor of 10 the estimated prevalence of medically unacceptable levels of exposure to lead in the U.S. population. [See "The Nature and Extent of Lead Poisoning in Children in the U.S." (*4*) for a complete discussion on the prevalence of lead exposure in the U.S.].

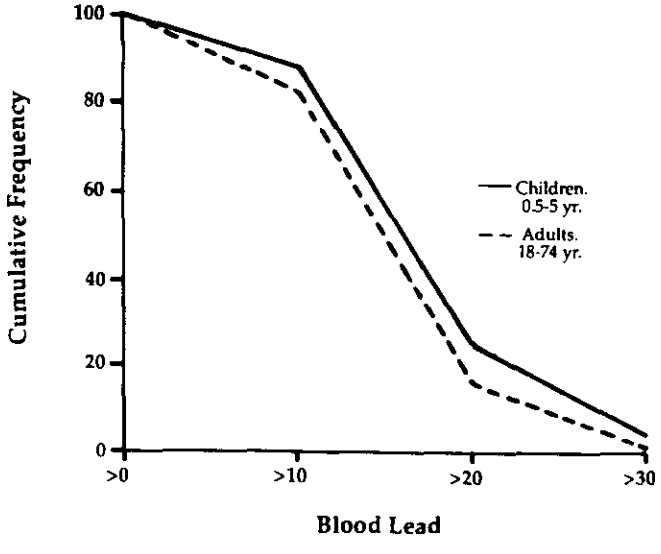

FIGURE 1. Distribution of blood lead levels in the U.S. population, based upon data in Annest et al. (*1*). These data were collected from 1976 to 1980; blood lead levels in the U.S. population in 1988 are estimated to be somewhat lower (*4*), but a similar distribution probably holds.

In addition, newer information on the adverse health effects of lead has broadened the scope of concern beyond the child to include other members of the population. Since the pioneering work of Blackfan and McKhann in the early years of the century, environmental lead toxicity has been generally considered a pediatric disease (*15–17*). However, lead is known to affect adults, and occupational lead toxicity remains a major problem in industry throughout the world (*18–20*). Some recent studies have reported associations between relatively low levels of chronic lead exposure and increased blood pressure (*21*). Increases in blood pressure have been found in populations whose blood lead levels were as low as 12 mcg/dL; an analysis of the NHANES II data set could not define a threshold for this effect in men. In an Australian population exposed to environmental lead in soils, dusts, drinking water, and air, an increased risk of spontaneous abortion was found in women whose blood lead levels were only slightly increased above control levels (*22*). Spontaneous abortion is likely to reflect actions of lead on both fetus and mother (*23*). In a group of men with kidney failure, higher levels of lead in bone were found than in age-matched controls, suggesting a correlation with earlier chronic, low-level lead exposure (*24*). Cohort studies conducted on occupationally exposed persons in the U.S. and Sweden have reported increased incidence of cancer in lead workers (*25–28*); while these exposures were likely to have been heavy during employment, as compared to general environmental exposures of the present time, particularly in older cohorts whose work experience took place before regulation of working conditions in the lead trades, the mechanisms and dose response for lead-induced cancer is unknown.

Finally, new data on the mobilization of lead stored in bone may alter estimations of the long-term risks of very low-level chronic exposure. Over 95% of the lead that is absorbed and retained is stored in bone (*29,30*). Because the turnover of this pool is very slow, on the order of decades (*29,31*), over time bone accumulates considerable concentrations of lead even in the absence of unusual or peak exposures. This compartment is not static, however, and factors that influence bone cell function and status appear to affect lead retention. As shown in Table 3, we have found a significant release of lead stored in bone during menopause

Table 3. Effect of menopause and prior pregnancy on blood and plasma lead levels in women.[a]

	All women		White		Black	
	mcg/dL	% Change	mcg/dL	% Change	mcg/dL	% Change
Change in blood lead						
Pre/postmenopause	1.47	12.6	1.67	14.7	0.62	4.6
Pre/postmenopause						
Never pregnant	2.56	22.0	2.67	23.4	1.31	9.8
Ever pregnant	1.37	11.8	1.45	12.7	0.50	3.7
Change in plasma lead						
Pre/postmenopause	0.136	16.2	0.150	18.3	0.030	3.0
Pre/postmenopause						
Never pregnant	0.347	41.3	0.386	47.2	0.104	10.3
Ever pregnant	0.113	13.4	0.125	15.3	0.015	1.5

[a]From Silbergeld et al. (*32*).

and pregnancy (*32*). Mobilization of bone lead during pregnancy (and also probably lactation, as reported in experimental studies) may combine with ongoing maternal exposures to increase the total dose presented to the fetus and neonate (*33*).

Mobilization of bone lead during bone demineralization states raises questions as to the potential toxic effects of lead in aging populations and other groups at risk for demineralizing diseases, such as kidney dialysis patients and other conditions of osteopenia or osteomalacia induced by dietary deficiency or disease. With the shift in demographics in the U.S. and western Europe toward an increase in numbers of persons over 70, the health of this aging population becomes of greater concern (*34*). It is important to begin investigations of the potential effects of lead on this group.

New concern over low-level lead toxicity will guide decisions as to methods for reducing overall exposures to lead in order to prevent disease. In the absence of effective treatment for lead toxicity, prevention of exposure remains the appropriate method for preventing disease (*13,35*). In addition to developing and implementing effective abatement of existing lead sources, particularly those that present high risks to specific populations, reconsideration of continuing uses of lead must be undertaken in light of their contribution to overall exposure.

Three examples may illustrate this. In the U.S. since 1983, a major reduction in the use of lead in gasoline has been achieved through regulation by the EPA. However, in the third quarter of 1988, 430 million g of lead were used in gasoline in the U.S. (Around the world, the use of lead in gasoline is still increasing, due to lack of regulation on lead additives in many of the countries where the number and use of automobile vehicles is increasing the fastest.) Some of that leaded gasoline is used in farm vehicles, which continue to enjoy an exemption from regulations imposed on other vehicles. Lead emissions from farm vehicles, while a small fraction of the total vehicle miles in the U.S., may contribute to general lead exposures through contamination of the food supply. We have examined data from the U.S. Food and Drug Administration (FDA) and found that in foods which grow naturally exposed to ambient air (such as apples, tomatoes, and beans), concentrations of lead are approximately four times those in naturally covered foods (such as corn and peas) (*36*). These concentrations are relatively low, but in the context of a revised evaluation of the hazards of lead toxicity, it is useful to identify all potentially controllable sources of lead exposure.

Another source of lead exposure that has escaped much notice and control until recently has been the release of lead from plumbing into drinking water. Possibly because of increasing acidity of surface waters due to atmospheric pollution sources and because of the overall aging of the water distribution infrastructure, lead concentrations in drinking water in the U.S. are relatively high. EPA has estimated that 42 million Americans are currently exposed to drinking water in excess of 20 ppb. Patterns of water use tend to weight the importance of this source, since water lead concentrations increase as a function of time of contact of aggressive water (low pH and low mineral content) with lead-containing plumbing. Thus, first-draw use or intermittent use, which often occurs in the morning and at schools, tends to have relatively higher concentrations of lead, sometimes as much as 10 times the concentration of fully flushed water (Table 4). Based on some of the data in Table 4, if a child consumed only 500 mL of such water per day, this exposure alone would exceed recommended dietary intake for lead.

Table 4. Lead levels in drinking water in Philadelphia (1987): first draw and fully-flushed samples.[a]

Test results	Standing/flush, ppb
Residence	464/045
Residence	353/021
Residence	174/009
Residence	056/005
Sheraton Society Hill	032/078
Residence	041/048
Residence	050/050
Schmidt's Brewery	028/005
Bright Star Child Care	047/005
Residence	079/014
The Piers at Penn's Landing	1294/066
Police SOD building	119/106
The Chocolate Factory	1186/399
Philadelphia Protestant House and Romper Room Family Concept	077/005
The Chart House	216/129
Residence	012/005
YWHA	5067/087
Residence	043/005
Delran Builders	226/045
Residence	075/005
Residence	733/614
Curtis building	043/012
EPA Regional Offices	162/165

[a]Testing done by Water Test Corporation, NH.

Similarly, it is important to re-evaluate current uses of lead in solders, glass, plastics, and pigments. These lead sources occur in many consumer products. Although during consumer use it is unusual for lead to become bioavailable (with rare exceptions, such as the unfortunate use of lead-based paints on decorative drinking glasses distributed as promotional items recently in the U.S.), it is during disposal that these lead-bearing items can release lead into the environment. A recent EPA report calculated that almost 50,000 short tons of lead are discarded in municipal waste each year (excluding lead-acid storage batteries). Many of these uses are potentially substitutable. Since lead does not biodegrade, disposal of lead-containing items will inevitably result in releases of lead from the product matrix: plastic, paper, or other materials. Some types of waste processing can accelerate this process. High temperature incineration, which is increasingly employed in waste management around the world, mimics secondary smelting in causing the selective enrichment of residues in lead and other metals, which are indestructible by incineration. Moreover, modern incinerators tend to yield residues composed of small diameter ash particles, which are more easily transported throughout the environment by wind and water and more readily incorporated into biota, including humans, by ingestion and inhalation, than the lead in its original form in products. Concentrations of lead in ash and in distilled water leachate from

Table 5. Concentrations of lead in municipal solid waste incineration ash (*12*).

Fly ash	Total, ppm	Short-term leachable[a]	Long-term leachable[a]
Bottom ash[b]	1950	12 ppm	Not done
Fly ash			
Fabric filter	7055	75%	95%
Dry scrubber	3792	56%	80%
Wet-dry scrubber	1919	25%	63%

[a]Concentration or percent extracted into distilled water by standard tests designed to predict short or long-term interactions of percolate through landfills.
[b]Average of samples collected by Silbergeld at Heimdal, Norway, and Jersey (Channel Islands).

ash are very high, as reported in measurements made on the residues from operating incinerators, as shown in Table 5 (*12*).

In addition to health effects information, efforts at identifying and preventing lead toxicity must be based on new information on lead toxicokinetics. The distribution and retention of lead reflect the fact that almost all environmental exposures are chronic rather than acute. Initial distribution may reflect the rate of delivery of blood to various organs, but the major factors governing long-term distribution of lead are specific lead binding and transport proteins (*37*), cellular sites with high affinity for lead, such as ATP (*38*), and hormonal and other regulatory factors related to essential mineral metabolism (*32*). Under conditions of relatively continuous exposure over long periods of the life span, a near steady state may be achieved with predictable distribution of lead among body compartments (*31*). However, this distribution can be altered either by large fluctuations in external lead exposure or by physiological changes that influence the stability of lead storage sites, such as bone. There is substantial redistribution of lead even within bone over the lifespan, reflecting changes in bone physiology coincident with growth and senescence (*39*). We know that lead metabolism differs greatly between children and adults, with young children estimated to retain about 30 times the ingested dose of lead as adults (*3*), but we know little about metabolic variations among different subsets of adults and children: for instance, pregnant women, calcium-deficient children, the aged, or those with demineralizing diseases.

Lead is excreted into breastmilk during lactation (*40,41*). The kinetics of lead excretion are not understood, and nothing is known of nutritional or other factors that might modulate the rate or amount of transfer of lead from mother to nursing infant. One study found that women over 30 years of age have higher levels of lead in breastmilk than to younger women (*42*), which may reflect the greater concentrations of lead in mineralized tissue as a function of age, since bone serves as a reservoir for calcium during lactation.

The need to estimate lead exposure over longer time periods than 1 or 2 months and increased concern over the potential release of long-term stores of lead both focus attention on developing new methods to determine body burdens of lead. Because mineralized tissues represent the compartment with the longest temporal integration term, this is the ideal compartment for exposure assessment. At present, methods for determining bone stores of lead are under development. In occupational cohorts, with long-term, relatively high exposures, *in vivo* measurement of lead in bone by X-ray induced fluorescence techniques has been shown to be useful (*43*). For pediatric populations, or persons with relatively lower chronic exposures, it is not yet clear that current methods have sufficient sensitivity under conditions that meet criteria of radiological safety.

Biological markers that reflect longer term exposure than erythrocyte protoporphyrin (EP) or levels of lead in compartments other than blood may provide indicators of exposure that predict risk more accurately than only measuring lead in blood. Blood is the compartment in which both lead and porphyrin markers are most commonly measured as markers of exposure; however, these markers only indicate relatively recent exposures. Since the target organs of concern for lead include the brain, heart, and kidney, it is rational to consider biological signals of organ function that are derived from these tissues. Unfortunately, the brain is relatively inaccessible, and it is difficult to discern from peripherally available markers the status of the central nervous system. No work has been done on biological markers of cardiovascular function that might indicate lead-induced effects. For the kidney, it may be that recently identified lead-binding proteins of renal origin may reflect exposures of that organ and signal increased uptake and potential damage (*36,44*).

A critical need in this area is to develop methods to assess lead exposure and predict outcome for fetuses exposed to lead. For reasons noted above, monitoring maternal blood lead may not completely predict fetal exposures or risk of lead-associated effects on growth and development. Monitoring pregnant women is constrained by particular concerns to protect health; thus, X-ray analysis of bone during pregnancy may be even more difficult to do than at other times or in other populations. Work is needed to identify markers of embryofetal status during intrauterine development that signal increased exposure to lead. Monitoring bone status during pregnancy may be useful as an indicator of potential mobilization of maternal lead stores.

Research on markers is also needed because of the relative insensitivity of EP to increases in lead exposure at the low end of the range. Detectable increases in EP are found when blood lead levels exceed 25 mcg/dL (*45*); however, recent health data establish a range of concern as low as 5 to 10 mcg/dL. Measuring these concentrations of lead in blood is also difficult; external contamination becomes a great problem, and the recommended method for sample collection is by venipuncture. Demands of quality control and quality assurance also increase.

Thus, in conclusion, the newer data on the health effects of lead enlarge the scope of public health concern for lead toxicity in three ways: first, the levels of lead exposure that are associated with demonstrably adverse effects are significantly lower than the current pediatric guidance level of 25 mcg/dL and the OSHA biomonitoring standard of 40 mcg/dL for adults; second, the populations potentially at risk for low-level lead toxicity has been expanded beyond the young child to include the fetus, adults, and the aging; and

third, the toxicokinetics of lead points to the significant role of lead stored in mineralized tissue as a contributing source of internal lead dose under certain physiological conditions that may coincide with periods of target vulnerability. These findings serve to refocus concern over the need to remediate existing high-level sources of lead in the environment, such as dilapidated housing and contaminated soils, and to control ongoing sources that have been considered of relatively minor importance, such as the continued use of lead additives in fuels and the widespread uses of lead in consumer products. Although the past decade has seen substantial success in controlling certain lead sources, the advances in our knowledge of lead toxicity have outstripped our ability to identify and control lead exposure overall. The only way out of the treadmill is to develop an integrated public health and environmental policy based upon a goal of reducing lead in all persons below 10 mcg/dL by substantially reducing all controllable sources of lead.

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