

# Nutrition and Lead: Strategies for Public Health

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Over the past two decades, blood lead levels among U.S. children have been reduced by approximately 80%. This decline reflects both primary interventions (removal of lead solder from food beverage cans and virtual elimination of lead additives from gasoline) and secondary prevention strategies (public health programs and nutritional intervention). Nonetheless, pediatric lead poisoning (i.e., blood lead concentrations  $\geq 10$   $\mu\text{g}/\text{dl}$ ) continues to occur in 8.9% of 1- to 5-year-old children. Currently, blood lead concentrations exceed the U.S. Centers for Disease Control's targeted value (10  $\mu\text{g}/\text{dl}$ ), most often among minority and low-income populations. These same subpopulations are at greatest risk of marginal nutrition status (especially for iron and calcium), which increases their susceptibility to lead toxicity. Adverse child feeding practices (e.g., irregular temporal patterns of food intake) are also of concern among the subpopulations at highest risk to excessive lead exposure. This paper describes nutrition interventions and public health strategies aimed at minimizing the transfer of lead from external or environmental dose to internal dose as reflected by blood lead concentration.

Public health strategies have evolved over the past half-century to assess the risks and benefits of trace quantities of chemicals. Trace quantities typically describe substances present in sources at parts per million concentrations (ppm) or less. Virtually all of these chemicals can produce adverse effects on human health if the con-

centration of these chemicals that reaches target organs is high enough (1). A small subset of this broad group of chemicals is required for human life (2) and is designated as nutrients. A few chemicals, such as fluorine, are not required to sustain life, but over a narrow range of concentrations produce beneficial effects, e.g., reduction in the prevalence of dental caries. For many trace elements, the ratio between quantities required nutritionally and quantities that produce toxicity is narrow. Often this ratio is as low as 1:10 and may be as narrow as 1:3.

During the past 15 years, lead exposures in the United States have fallen; this is reflected by a decrease of approximately 80% in blood lead concentrations of the general population (3–5). This decline resulted from both primary and secondary efforts at prevention of lead toxicity. Major sources of lead exposure have been dramatically reduced—elimination of lead solder from U.S.-produced food and beverage cans and a virtual phase-out of lead additives to gasoline. Despite these successes, lead sources remain, predominantly in lead-based paint in deteriorating housing. More than ever, lead has become an environmental justice issue.

Lead poisoning prevention programs organized by federal, state, and local governments have been a major secondary prevention strategy; nutrition components are part of these public health programs (6). Most states have nutrition strategies as part of their secondary lead poisoning prevention programs; these are part of the complex history of food, nutritional status, and public health with respect to toxic chemicals. A toxic substance can either enter or be made in the food chain from natural or anthropogenic contaminants. The toxicant may also be concentrated in the food chain (e.g., methylmercury in the aqueous food chain or dioxin in the terrestrial food chain). Depending on selection of foods, some portions of the general population can be

disproportionately exposed; for example, the elevated methylmercury exposure to subsistence fishers. With regard to nutritional status, particular subpopulations may be more frequently at risk of poor nutrition such as marginal iron nutrition and low dietary calcium intakes among low-income families. The combined risks of marginal nutritional status, as well as elevated exposure to toxic chemicals, result in a subpopulation at elevated risk. Although multiple examples of this situation have been identified, lead is a particularly useful example because the subpopulation that is more highly exposed to lead is also more likely to be inadequately nourished.

## Public Decisions and Nutritional Status

Strategies to assess or manage adverse health risks must reflect fundamental differences between chemicals, primarily those considered nutrients and those viewed as toxicants. The role of nutrition in prevention of the adverse effects of environmental chemicals is quite broad.

### Nutrition

**Primary Prevention.** Nutrition as a primary cause of disease forms the basis for many public health programs. The food or water supply has been supplemented with trace minerals or vitamins. Examples include (a) the addition of iodine to salt to prevent goiter or, in some remote areas, addition of iodine to water to prevent cretinism (7); (b) the controlling of concentrations of fluoride in public water systems to reduce the prevalence of dental caries; (c) the addition of vitamin D to milk to prevent rickets; and (d) the supplementation of refined flours and cereals with B-complex vitamins and iron to prevent deficiency diseases such as pellagra, beriberi, and anemia.

Over the decades, the success of nutritional intervention has been substantial. To most health professionals in the United

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States, clinical presentations of deficiency diseases are considered remote possibilities in most daily lives, e.g., pellagra, iodine-deficiency goiter. Occasional case reports appear to remind health professionals that such conditions still are possible. By contrast, other nutritional problems are routinely identified in clinical practice, especially among patient populations living in rural areas or in poverty. Pediatric dentists continue to see rampant dental caries among some children who obtain water from wells rather than from fluoride-controlled municipal water supplies.

**Secondary Prevention.** Beyond these primary prevention programs to correct nutritional deficiencies, there are nutritional programs aimed at dietary changes to alter the course of disease. These are illustrated by interventions to control types of fatty acids (8,9) and quantities of dietary fat to prevent or modify the course of atherosclerotic disease or smoking-related chronic obstructive pulmonary disease (10). Supplementation of diets with nutrients having antioxidant activities gained popularity during the 1980s as a means of reducing the risk of various types of cancer. Rates of colorectal cancer are lowest in populations with diets typically rich in vegetables and fruits (11). However, scientific evaluation of the efficacy of interventions with specific nutrients raises serious questions about the efficacy of nutritional supplementation in isolation from changes in food patterns. For example, supplementation of patients' diets with beta carotene and vitamins C and E did not prevent the occurrence of new colorectal adenomas, a precursor of invasive cancer.

### Toxicology

Recognition that the dose makes the poison is central to understanding how chemicals may adversely affect human health. The risk assessment process (12,13) used in the United States relies on a series of steps: hazard identification, exposure assessment, dose response, and risk characterization. An important component of the risk assessment process is understanding human dose response through development of quantitative data that associate quantity of the chemical with occurrence of adverse health effects. More broadly based risk assessment strategies such as holistic risk assessment (14) add elements that include eco-risk and indirect exposures (e.g., accumulation of the agent in the food web).

Assessment of exposures to environmental chemicals typically considers multimedia sources such as air, water, food, soil, and dust. Risk management strategies are focused on how to reduce exposures from many media. Some media are centrally controllable (e.g., phase-down and phase-out of lead additives for gasoline or restrictions of use of lead solders in food cans), while other exposure media are much more difficult to change through regulation (e.g., residential lead-based paints present in millions of homes in the United States). Those hazards that are not centrally controlled raise particularly vexing problems to public health decision makers. To clinicians, local public health officers, nurses, etc., finding effective secondary intervention techniques to reduce the effects of such exposures remains a challenge while primary prevention strategies are implemented.

### Nutrition as a Component of Intervention in Lead Toxicity

The role of nutritional status in altering susceptibility to lead toxicity has been recognized through most of this century. A variety of methods (e.g., experimental studies, clinical assessments, epidemiology investigations) have been used to establish the association between nutritional status and susceptibility to lead toxicity. Typically, data derived from feeding animals rigidly controlled, nutritionally inadequate diets for most of their growth period have shown the greatest influence of nutritional status on susceptibility to lead toxicity. Research based on these animal experiments has yielded a great deal of useful information on how nutrients modify lead toxicity and, in more recent years, how lead modifies metabolism of nutrients. Typically, human dietary patterns are far more complex. Patterns of food intake and selection rarely yield a diet containing inadequate or excessive amounts of only one nutrient. Typically individuals' dietary selections do not produce overt dietary deficiency. Consequently, human studies have confirmed the association between marginal nutritional status and susceptibility to lead toxicity but rarely show the magnitude of the effects identified with experimental animals.

For some nutrients the basis for their alteration in susceptibility to lead toxicity is well delineated, e.g., the physiological and biochemical basis for susceptibility altered by calcium or iron status. By contrast, it is not well understood how total food intake and percent dietary fat modify lead retention.

### Total Food Intake

Among adults, ingestion of lead during a period of fasting results in greater absorption of lead than if lead were ingested with food. For example, Rabinowitz et al. (15) reported that among adult male subjects, lead ingested without food was 35% absorbed, whereas tracer amounts of lead ingested with food were 8.2% absorbed. Blake et al. (16) and Flannagan et al. (17) have also identified greater fractional absorption of lead when lead was ingested by either adult male or adult female subjects while in a fasting state. The period evaluated by Flannagan et al. (17) was an overnight fast. There are no data available for children on whether fasting increases lead absorption. It is very likely that this result in adults can be extrapolated to children. It may be that children have increased lead absorption following even shorter fasting times than adults because they have more rapid gastric emptying times than adults. Since children have more rapid gastric emptying times than adults, the fasting/nonfasting retention of lead is likely to be even more important.

### Total Fat Intake

Although the influence of dietary fat level as a determinant of the fraction of lead absorbed has provoked a number of inquiries, data on this topic are limited to a few studies with experimental animals. Barltrop and Khoo (18) observed that lead absorption depends on both the quantity and type of dietary fat. Increasing the corn oil content of the rat's diet from 5 to 40% resulted in 7- to 14-fold increases in lead content of several tissues. Quarterman et al. (19) observed that the degree of lead absorption varied with the type of dietary fat and showed that lecithin, when mixed with bile salts, and to a smaller extent, choline, increased lead uptake. However, the importance of small amounts of phospholipid remains in doubt. In 10-week studies, Ku et al. (20) found that, for both young and mature rats, ingesting either lead acetate or a complex of lead and phospholipids resulted in similar concentrations of lead in femur, kidney, liver, and brain. By comparison with the degree of documentation of the effects of other nutrients (e.g., calcium or iron), the role of dietary fat remains poorly established.

### Calcium Intake

Extensive data indicate that dietary calcium intake and nutritional status of calcium influence susceptibility to lead toxicity.

These have been reviewed in detail by Mahaffey (21–23). As understanding of calcium-mediated cell functions has expanded, the hypothesis that a fundamental calcium-agonist role might be central to lead toxicity has been postulated (24,25). In particular, lead-induced changes in skeletal development and regulation of skeletal mass assume particular significance because of the role of bone as the major internal source of lead and calcium (25).

In 1926, Aub (26) stated that the lead stream follows the calcium stream. Early studies with experimental animals indicated that there were some aspects of physiological responses to calcium that altered biological responses to lead. However, nutritional investigation of trace elements was not well developed during this period. Many of the early studies used diets that were deficient or imbalanced in more than one nutrient, making clear identification of the role of calcium uncertain.

In the early 1970s, Mahaffey and colleagues (27,28) identified a clear role of nutritional status for calcium on susceptibility to lead toxicity. These investigators observed that rats ingesting a low-calcium diet had blood-lead concentrations about four times higher than rats on a normal calcium diet, although the quantities of lead ingested were equal. Bone-lead concentrations also increased on the low-calcium diet. However, at the lowest level of dietary calcium intake, renal and blood-lead concentrations also increased sharply. Lead-induced impairment of hematopoiesis and changes in renal histology were much greater on the low-calcium diets. Although approximately two decades have passed since these studies, it is still not clear to what extent the rise in nonosseous tissue lead concentrations reflects greater absorption of lead from the gastrointestinal tract, reduced bone formation or mobilization of lead as skeletal mineral is resorbed.

The initial observations with rodents were confirmed in several species including humans (16,29,30). Lower dietary calcium intake among children with higher blood-lead concentrations occurred among high-risk (31–33) and general population groups [e.g., Second National Health and Nutrition Examination Survey (NHANES) II data reported by Mahaffey et al. (34)]. A major difficulty in these surveys of calcium status is the assessment techniques. Dietary recall or dietary history provide only a very approximate indicator of nutritional status for calcium.

The interaction between lead and calcium has been described at the cellular level. Many of the physiological processes that exercise metabolic control over calcium are affected by the presence of lead. Lead is known to mimic  $\text{Ca}^{2+}$  in various biological systems or to alter  $\text{Ca}^{2+}$ -mediated cellular processes (35). Lead will compete with calcium in enzyme systems, alter regulation of calcium metabolism [e.g., synthesis of 1- $\alpha$ -25-hydroxyl-cholecalciferol (36) or inhibit 1,25-dihydroxyvitamin D-3 regulation of calcium metabolism (37)]; modify the calcium second messenger system [e.g., Long et al. (38)]; impair normal modulation of intracellular calcium homeostasis (39); modify induction of calcium regulating proteins [e.g., lead inhibition of renal increases in the vitamin D-dependent, calcium-binding protein calbindin (40)]; and interfere with energy metabolism [e.g., reduced rate of glucose metabolism in brain capillaries of calves (41)].

Broadly speaking the research and public health experiences provide a substantial basis to identify an increased susceptibility to lead toxicity resulting from inadequate-to-marginal dietary calcium intakes; and a fundamental, lead-induced alteration in calcium-mediated cellular processes and in physiological mechanisms that are  $\text{Ca}^{2+}$  dependent or control  $\text{Ca}^{2+}$  homeostasis.

### Iron Intake

As with dietary calcium, susceptibility to lead toxicity is modified by nutritional status for iron. In 1972, Mahaffey-Six and Goyer first reported that rodents fed an iron-deficient diet experienced increased susceptibility to lead toxicity (42). Unlike calcium deficiency, iron deficiency in rats appeared not to result in a redistribution of lead to nonosseous tissues. These original observations were confirmed by others including Ragan (43) and Hamilton (44). Iron-deficient rodents increased lead absorption (17,44,45) but not excretion (45). A newly identified iron-binding protein recently isolated from rat duodenum and named mobilferrin [which competitively binds lead, as well as iron (46)] has been isolated from human duodenal mucosa (46). Low-iron status of adult human subjects has been reported to increase (47) or not significantly change (17) gastrointestinal absorption of lead.

Modification of the hematological and neurological effects of lead by iron status has been investigated. Impairment of cognitive function among iron-deficient

children has been recognized (48–51). Likewise, deficits in intellectual development associated with increasing blood-lead concentration over the range of 10 to 30  $\mu\text{g}/\text{dl}$  are recognized among children, independent of social and economic background (52–54). Comparatively few studies have carefully assessed both nutritional status for iron and body stores of lead as indexed by blood-lead concentration. One of the few reported studies to date is the prospective assessment of lead exposure, iron status and infant development among groups of young children living in a low-lead exposed town and a high-lead exposed (smelter-based exposure) town in Yugoslavia (55). Independent associations between blood-lead and hemoglobin concentrations were found for this population. A rise in blood-lead concentrations at 2 years of age from 10 to 30  $\mu\text{g}/\text{dl}$  was associated with an estimated 2.5 point decrement in the Mental Development Index at 6, 12, and 18 months of age. A decrease in hemoglobin concentration at 18 months of age from 12 to 10  $\text{gm}/\text{dl}$  was associated with an estimated 3.4 point decrement in Mental Development Index. The finding of the iron effect in both towns suggests that the iron-related decrement occurred independent of the effects of lead. The importance of the severity of iron deficiency or lead exposure as well as the timing of these conditions can be expected to greatly influence the extent of the cognitive deficit.

In contrast to our admittedly limited understanding of the interaction of lead and iron in cognitive deficits, the effects of lead and iron on the heme biosynthetic pathways have been well characterized biochemically. Lead inhibits three major enzymes,  $\delta$ -aminolevulinic acid synthetase, porphyrinogen synthetase, and ferro synthetase (56), as well as interferes with mitochondrial energy metabolism. Ferro synthetase activity is modified by lead and iron. Kapoor et al. (57) reported that when low iron levels are present, ferro synthetase is more sensitive to lead effects.

As with calcium, broadly speaking, research and public health experience indicate that: inadequate dietary intake of iron as well as long-term modifications to marginal nutritional status for iron increases absorption and tissue concentrations of lead; iron-mediated biochemical and physiological processes are modified by lead toxicity; adverse effects of lead on the hematologic system appear to be more severe among iron-deficient subjects;

whether iron status modifies the influence of lead on intellectual or cognitive development remains to be determined.

### What is the Role of Nutrition in Public Health Management of Lead-exposed Children?

At least four nutritional conditions increase the adverse consequences of environmental lead exposures: irregular food intake (i.e., periods of fasting), high fat intake, marginal calcium ingestion, and subtle iron deficiency. Although marginal nutritional status is more common among subpopulations at greater risk of lead toxicity, any risk assessment or risk management decision on the role of nutrition must rest on the fundamental understanding that lead toxicity is caused by exposure to lead and not by nutritional deficiency. However, the fractional transfer of lead from the environment (referred to as external dose) to target tissues (described as internal dose) can be modified by nutritional status. Likewise, many biochemical and physiological processes that are  $\text{Ca}^{2+}$  or  $\text{Fe}^{2+}/\text{Fe}^{3+}$  dependent are adversely affected by lead.

Adverse effects of lead occur at exposures previously considered acceptable; for example, contrast the Centers for Disease Control (6) recommendations for prevention of childhood lead toxicity in 1985 (blood-lead  $< 25 \mu\text{g}/\text{dl}$  combined with erythrocyte protoporphyrin in an acceptable range) and 1991 (blood-lead  $< 10 \mu\text{g}/\text{dl}$ ) (58). Fortunately interventions to lower lead exposure in the United States produced a marked decrease in blood-lead concentrations over the past 15 years. For example, mean blood-lead concentrations for children in the United States 1 to 5 years of age was  $12.8 \mu\text{g}/\text{dl}$  in the period 1976 to 1980 (3). By 1989 to 1991, mean blood-lead levels for 1- to 5-year-old children declined to  $2.8 \mu\text{g}/\text{dl}$ , approximately an 80% decrease (5). These changes were produced by virtual elimination of the lead-soldered side seam cans for foods and beverages and a near total phase-out of lead in gasoline. In addition, public health programs aimed at identification and management of lead-poisoned children contributed to the decline in blood-lead levels.

Public health programs for management of elevated blood-lead levels in children included nutrition as part of the intervention (58). The nutritional component is a secondary prevention strategy focused on reducing both the body burden of lead and the toxic effects resulting from the absorbed dose of lead. Nutritional

intervention as a secondary prevention strategy occurs at several levels: (a) individual choices of diet to reduce risk of lead toxicity; (b) intervention programs by state and local health departments that provide food supplements and nutrients to infants, young children, and pregnant women at increased risk of lead exposure; (c) selection of dose-response assessments in the risk assessments that recognize nutritional deficient persons as a particularly vulnerable subpopulation (these risk assessments are conducted by the federal government and international organizations; e.g., Pan American Health Organization); (d) potential use of nutrients in a pharmaceutical approach to patient treatment.

Nutritional intervention has become part of the practice in management of lead-exposed clients. This author is not aware of published data on how nutrients are used in food choices made by individuals. By contrast, a large number of state and local health departments have developed nutrition education materials providing guidelines on food choices for patients or clients at elevated risk of lead toxicity. In the 1991 guidelines "Prevention of Childhood Lead Poisoning," the U.S. Centers for Disease Control included nutrition modification in their recommendations. In many states blood-lead levels may be an entry criteria for admitting children to food supplement programs such as the Women, Infants, and Children's Program. The nutrition components of lead-poisoning prevention programs may be managed through maternal-child health programs, environmental programs, and by individual clinics treating lead-poisoned patients as well. A major issue in clinics is applying the general nutrition guidance in developing diets that reflect the food habits of the social, economic, and ethnic group of the patients.

Most inquiries about the first two uses of nutritional intervention come from physicians actively engaged in patient care or from local public health professionals (e.g., public health physicians, nurses, or dietitians) seeking to offer a means of reducing risk to individuals while waiting for primary prevention that involves removal of the hazard. From a public decision perspective, the role of nutritional status becomes evident in decisions requiring identification of the most vulnerable or highest risk subpopulation. One step in the risk assessment process involves identification of the highest risk population subgroup. If lead exposures are comparable, a

nutritionally marginal person has greater risk of lead toxicity.

Regarding the use of pharmacological levels of nutrients, the potential for development of secondary nutritional imbalances must be seriously considered. For example, high intakes of dietary calcium can induce secondary zinc deficiency (2), or elevated iron intakes can make a marginal zinc or copper intake inadequate (2). These effects depend, of course, on the chemical species of the element and the quantity of the element in the diet.

Fortunately, most food patterns that reduce susceptibility to lead toxicity (e.g., regular meals, low- to modest-fat diets, adequate dietary intake of calcium and iron) are consistent with most other recommendations for an optimal diet. The public health dilemma is not should these diets be chosen, but how to foster these food and nutrition patterns.

The success of the past 15 years in lowering blood-lead concentrations of the general population by about 80% demonstrates that public health measures can succeed. This success reflects primary interventions that reduced lead exposure from food and water, in addition to dust—virtual elimination of lead from the soldered food and beverage cans and near total phase-out of lead-based gasoline additives. Secondary interventions by public health programs and individual physicians included nutritional components. Both components are part of the success for the general population. Despite these achievements, lead exposures remain a health problem for a portion of children in the United States. Children of low-income families continue to have blood-lead values substantially above those of the general population. Most of these exposures are from lead-based, residential paint. The NHANES III data (5) show that 4.5% of all 1- to 2-year-old children had blood-lead levels  $\geq 10 \mu\text{g}/\text{dl}$ ; however, 21.6% of 1- to 2-year-old non-Hispanic black children had blood-lead levels  $\geq 10 \mu\text{g}/\text{dl}$ . Among non-Hispanic black children 3 to 5 years of age, the prevalence of blood lead levels  $10 \mu\text{g}/\text{dl}$  or greater was 20.0% compared with 3.7% among non-Hispanic children (5). Cleanup of residential lead sources remains a particularly recalcitrant problem. The need for nutritional intervention as a component of secondary interventions strategies remains. For example, low-iron status and elevated lead exposure both are more common in minority and poor populations. To illustrate, iron-deficiency anemia was

identified among 29% of children of low-income families in contrast to less than 5% among higher income families' children (59). Anemia among pregnant women (due to iron deficiency or other causes) occurs throughout pregnancy among low-income women: first trimester (hemoglobin < 11.0 g/dl or hematocrit < 33.0), 9.8%; second trimester (hemoglobin < 10.5 g/dl and

hematocrit < 31.5), 13.8%; and third trimester (hemoglobin < 11.0 g/dl or hematocrit < 33.0), 33% (60). The prevalence of anemia was highest among women of African-American ancestry (60).

Knowledge about the physiological basis of nutritional intervention and about lead exposure and adverse health effects must be combined with understanding of families'

food habits and eating patterns. Successful nutrition intervention strategies draw on expertise of nutrition educators, dietitians, social workers, and nurses involved with families at a local level. Both the inequity of patterns of lead exposure and marginal nutritional status reflect environmental justice issues; the poor and minorities are disproportionately adversely affected.

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