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SECTION 1: LEAD

1.1 INTRODUCTION

Lead is a bluish-gray metal found in the earth's crust and does not occur naturally in humans. The metal is dense, malleable, resistant to corrosion, and has a low melting point. The most common forms of lead occur as lead oxides, lead salts, and organic salts. Due to its use in industrial activities, lead has been distributed widely, and is ubiquitous in the environment today. Humans have lead in their bodies as a result of exposure to the manmade sources. Lead bioaccumulates and persists in living organisms. It has no known physiological function and has been identified as a toxin in humans. The toxic effects of lead in the human body are known to cause developmental, neurological, reproductive, and cellular damage (Yule, 1992).

Lead is classified as a priority pollutant on the Superfund hazardous waste sites (Federal Register 1998). Increased health concerns regarding lead exposure have significantly decreased the use of lead in gasoline, paints, ceramic products, caulking, and pipe solder (Hunter 1977). Despite substantial reductions of lead exposures over the past 25 years, lead poisoning continues to be a serious health risk, especially for children. Chronic exposures to low levels of lead are an environmental reality in the United States today (NIEHS/USEPA 1999). Investigating factors that confer individual susceptibility to lead toxicity is imperative to setting environmental and occupational standards that are protective of public health.

Lead abatement programs have been studied for their effectiveness in reducing blood lead levels. Several studies have found that improper lead abatement practices can actually increase lead levels in children. Results indicate that any type of abatement method—soil, dust, paint, and educational intervention— must be thorough and continual in order to be beneficial. Abated areas often become recontaminated or actually expose people to higher levels of lead than pre-abatement conditions. Favorable results are most often seen when a combination of proper abatement techniques are utilized (ISSI, 1999).

Measuring the amount of lead in the blood is considered to be the most useful screening and diagnostic test for lead exposure. This measurement, referred to as the blood lead level, reflects lead's dynamic equilibrium between absorption, excretion, and deposition in soft- and hard-tissue compartments. Blood lead levels often underrepresent the total body burden, but they are still a widely accepted measurement of exposure to lead. This is due to the fact that blood lead levels respond relatively rapidly to changes in lead intake and, within a limited range, have a linear relationship to intake levels (ATSDR 1992).

1.2 Factors that Confer Susceptibility to Lead Poisoning

There is a marked variation in susceptibility to lead-induced toxic effects between human population groups and individuals. Blood lead levels may vary substantially from exposure to lead. Across populations, variation in health effects may be due to higher lead exposures or associated with higher adverse responses to the same dose. Factors which may confer susceptibility to lead include:

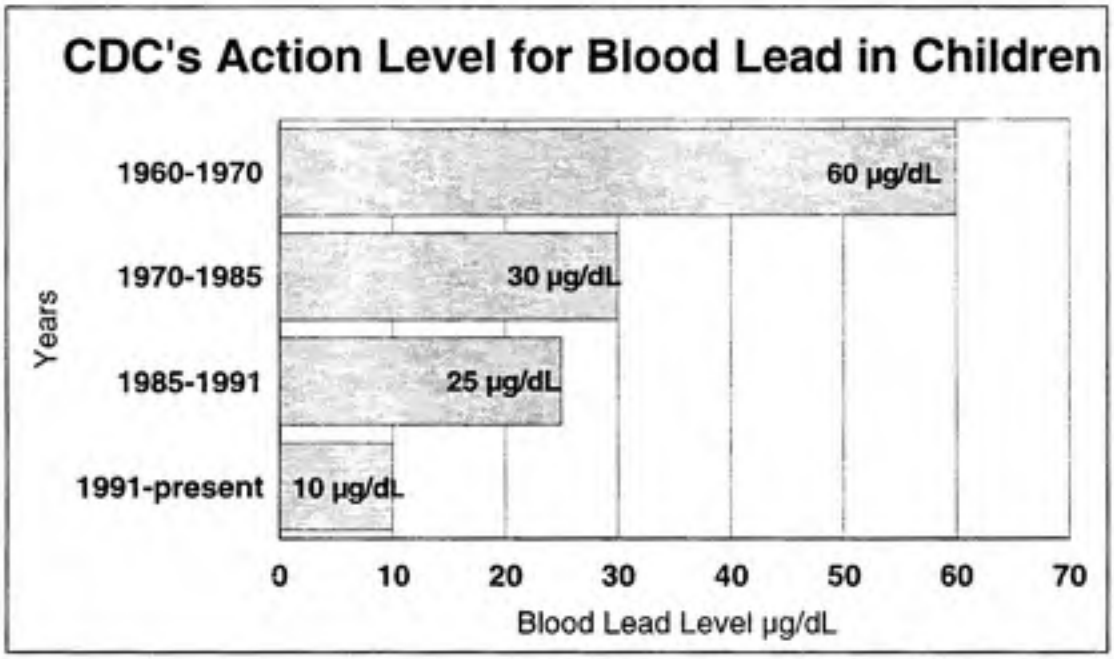
- Age;
- Occupation;
- Nutrition;
- Seasonality;
- Sociodemographic status; and
- Genetics.

Young children are the most susceptible age group to the effects of lead poisoning, for both biological and behavioral reasons. Certain occupations may also increase the risk of exposure to lead. Nutrient—lead interactions, particularly with calcium and iron, have also been shown to increase the bioavailability of lead. Seasonal fluctuations in blood lead levels have been observed during the warmer months, suggesting that exposure and absorption of lead may vary seasonally. Demographically, people living in poor urban communities with older housing have been found to have higher rates of lead poisoning. And perhaps most recently, researchers are discovering that genetic polymorphisms may be responsible for conferring susceptibility to lead poisoning in humans.

1.3 LEVELS OF CONCERN

The action level for blood lead in children has steadily been lowered over the past 50 years. The CDC lowered the threshold for blood lead in children from 60 μg/dL to 30 μg/dL in 1970, then again to 25 μg/dL in 1985, and to the current level of 10 μg/dL in October 1991 (Figure 1.1).

FIGURE 1.1 CDC'S ACTION LEVEL FOR BLOOD LEAD IN CHILDREN



Adapted from Figure 2, Case Studies, ATSDR

Studies have shown that little or no margin of safety was associated with the older values. Between 1986 and 1988, several studies (Bellinger et al. 1987; Schwartz and Otto, 1987) demonstrated neurobehavioral impairment in children with blood lead levels as low as 10 to 14 µg/dL, causing the level of concern to be lowered to 10 µg/dL. At the current level (10 µg/dL), over 10 million children in the U.S. are considered to be at risk for lead poisoning (Sargent 1995). The action levels for elevated blood lead, undue lead absorption, lead toxicity, and lead poisoning were revised to serve as guidelines for lead poisoning prevention programs throughout the U.S. (CDC MMWR 2/8/85).

The EPA has not yet established a reference dose (RfD) or a reference concentration (RfC) for lead. In comparison to most other environmental toxicants, the

degree of uncertainty about the health effects of lead is quite low. It appears that some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral impairment, may occur at blood lead levels so low as to be essentially without a threshold. For this reason, the Agency's RfD Work Group considered it inappropriate to develop an RfD for inorganic lead. EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, considers lead to be a "high concern" pollutant based on severe chronic toxicity. Lead is currently regulated by several government agencies (Table 1.1), while some others have only issued advisory levels (Table 1.2) (USEPA, 1986).

TABLE 1.1 REGULATIONS FOR LEAD

Agency*	Level	Focus	Comments
OSHA	50 $\mu g/m^3$	Air	Permissible Exposure Limit (PEL): No employees exposed to lead at concentrations ≥ 50 $\mu g/m^3$ of air averaged over an 8-hour period
EPA	1.5 $\mu g/m^3$	Air	3-month average
OSHA	50 $\mu g/dL$	Blood	Medical removal from exposure required
CPSC	600 ppm (0.06%)	Paint	By dry weight

Adapted from Summary of standards and regulations for lead (ATSDR, 1992)

TABLE 1.2 ADVISORIES AND RECOMMENDED LEVELS FOR LEAD

Agency*	Level	Focus	Comments
CDC	10 $\mu g/dL$	Blood	Level of concern for children
ACGIH	150 $\mu g/m^3$	Air	Time weighted average concentration for a normal workday (8 hr and 40 hr week) to which workers may be exposed w/out adverse effects (under revision)
CDC (NIOSH)	100 $\mu g/m^3$	Air	Recommended Exposure Limit (REL): Air concentration maintained so that worker blood <0.06 mg/100g of whole blood
EPA	15 $\mu g/L$	Water	
FDA	100 μg/day	Food	

Adapted from Summary of standards and regulations for lead (ATSDR, 1992)

*ACGIH=American Conference of Governmental Industrial Hygienists; CDC=Centers For Disease Control and Prevention; CPSC=Consumer Product Safety Commission; EPA=Environmental Protection Agency; FDA=Food and Drug Administration; NIOSH=National Institute for Occupational Safety and Health; OSHA=Occupational Safety and Health Administration

SECTION 2: MECHANISMS OF LEAD ABSORPTION AND ITS PHYSIOLOGICAL EFFECTS

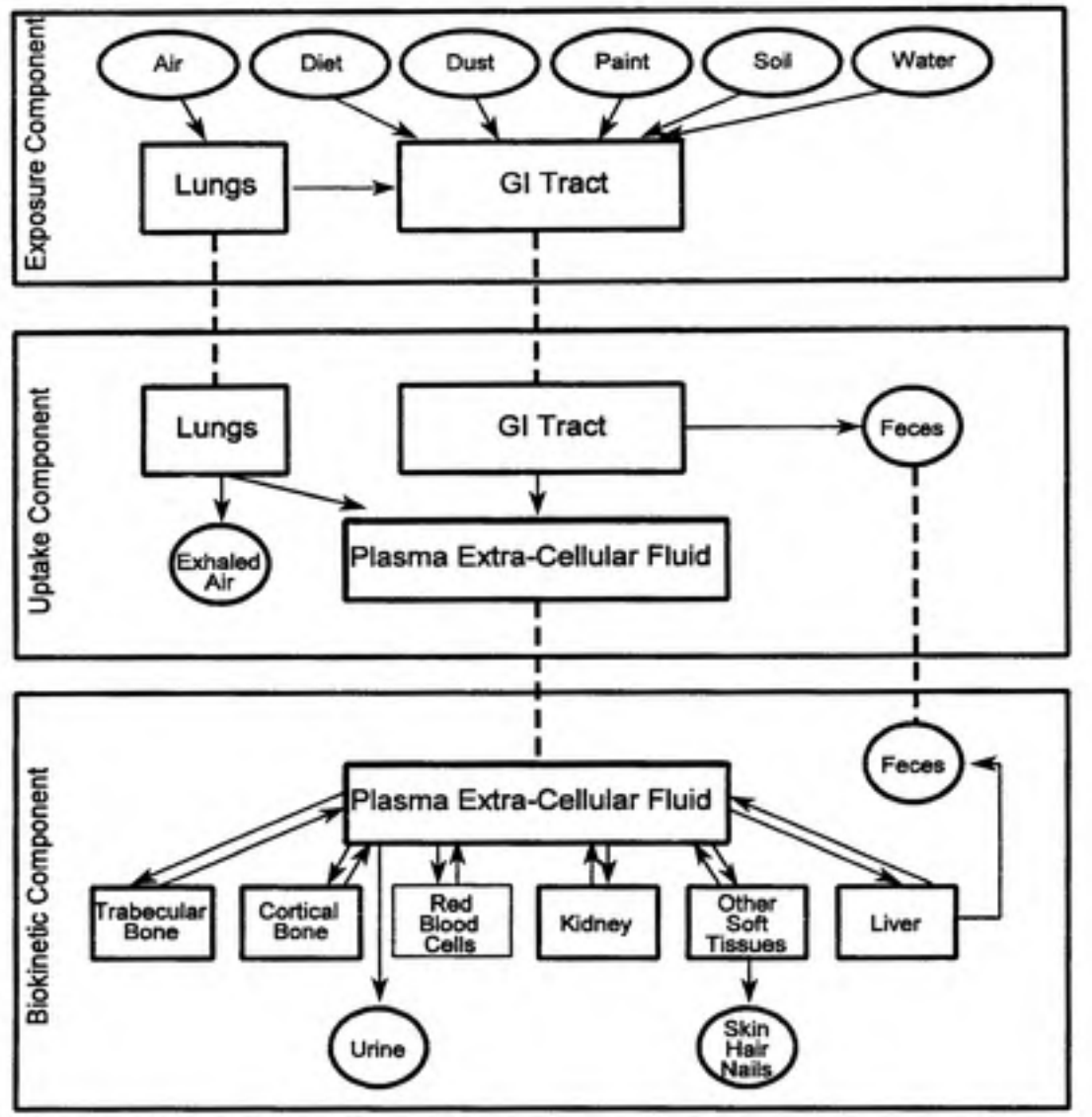
2.1 LEAD ABSORPTION AND BIOAVAILABILITY

Lead absorption, or the uptake of lead into the circulation, is referred to as the biological availability (bioavailability) of lead. There is a potential human risk associated with a substance when it is delivered to sites of toxic action in a bioactive form. The bioavailability of lead depends on (Mushak 1991):

- Site of uptake
- Physiology of uptake/transport to blood
- Stage of development
- Interactions with nutrients
- Size of particles
- Amount entering the body

The biological and physiological characteristics of absorption, the subcellular mechanisms of absorption, and the factors which influence absorption all must be examined to understand the bioavailability of lead. The movement of lead into and through the body is illustrated conceptually in Figure 2.1.

FIGURE 2.1 CONCEPTUAL DIAGRAM OF THE MOVEMENT OF LEAD INTO AND THROUGH THE HUMAN BODY



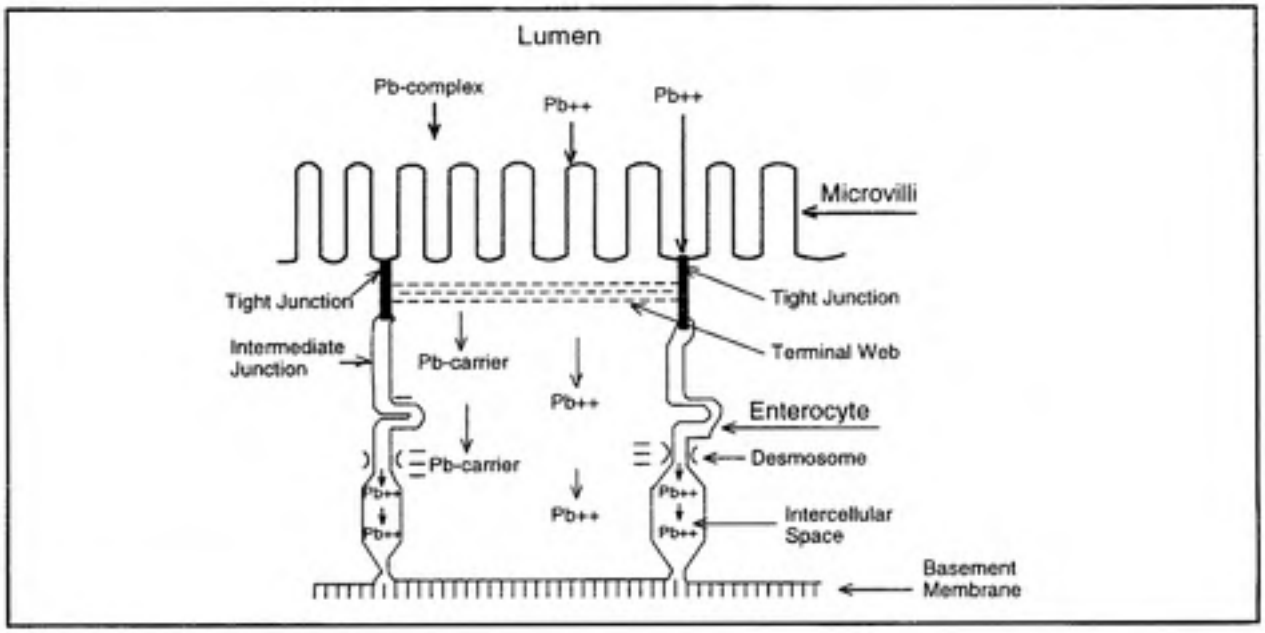
Source: Figure 1–1. Guidance Manual for the Integrated Exposure Uptake Biokinetic Model for Lead in Children, 1994

The intake (and uptake) of lead in the general population occurs most often through the gastrointestinal (GI) tract. This is usually 10 to15 percent of the total ingested quantity in normal adults, but it is higher in pregnant women and children. The inorganic divalent form of lead (Pb^{2+}) is the most environmentally significant chemical form of the metal. Inorganic lead does not undergo biologic transformation, while the organic forms of lead (*e.g.*, tetraethyl lead) are metabolized in the liver. Organic lead was previously found in gasoline, though it is no longer an environmental concern as a result of the phase-out of leaded gasoline (ATSDR, 1992). The uptake of lead can include the divalent cation or various soluble complexes. Simultaneously, a sizeable fraction of the divalent lead ion will form relatively insoluble, excretable lead complexes (*e.g.*, hydroxide, bicarbonate). Two important biological factors which influence the uptake of lead in the GI tract are the maturity of the GI tract and nutrient interactions (TRW, 1994).

2.1.1 Cellular Mechanisms

Several mechanisms by which lead is thought to be absorbed from the gut are depicted in Figure 2.2. These mechanisms involve enterocytes, the cells which line the intestinal wall. Absorption entails interactions with the uptake of essential nutrients such as calcium, iron, and phosphate (Mushak, 1991).

FIGURE 2.2 DIAGRAM OF VARIOUS ROUTES OF UPTAKE FROM THE INTESTINAL LUMEN



Source: Morton et al. 1985

2.1.1.1 Diffusion

One mechanism by which lead may be absorbed into the gut is diffusion. This mechanism is driven by a concentration gradient from the luminal surface lining to the basolateral surface (the vascular side). Diffusion likely depends on the solubility characteristics of the lead species of interest, *e.g.,* the concentration of the ionic or unbound lead ion (Pb^{2+}). It involves either intracellular or paracellular movement of lead across the cell wall. Paracellular transport is the movement of lead ions across the area between cells called "tight junctions" (TRW, 1994).

2.1.1.2 Pinocytosis

Another mechanism by which lead may enter the gut tissue is pinocytosis (or other vesicular mechanisms). In this mechanism, the lead-bearing media in a liquid micro region of the gut is engulfed by the enterocyte, or cell membrane. The encapsulation of lead may be a soluble or suspended form of the element, which is then carried to the blood or site of toxic action. This process is similar to the handling of solid particles in phagocytosis (TRW, 1994).

2.1.1.3 Active Transport

The third, and possibly most important, transport mechanism in environmental exposures is energy-driven, active transport. This mechanism is responsible for the transport of calcium and iron (*e.g.*, calcium binding protein [CaBP] or calbindin D) and is under the control of an enzyme—calcium-, magnesium- dependent ATPase. Some transport systems have a higher affinity for lead than for nutrients. These components are responsible for the absorption and regulation of blood calcium levels and take place in the basolateral membrane of mucosal epithelial cells (TRW, 1994).

2.1.2 Blood, Dentine, and Bone Lead

Once lead enters the bloodstream it is primarily distributed among three compartments: blood, soft tissue, and mineralizing tissue. The bones and teeth of adults contain more than 95 percent of the total lead in the body. The lead which is in the mineralizing tissue may accumulate in subcompartments which differ in the rate at which lead is resorbed. In bone, there is a labile component, which readily exchanges lead with the blood, and an inert pool of lead, which may become mobilized in times of stress. In

single exposure studies, lead has a half-life (in adults) of 25 days in blood, 40 days in soft tissue, and over 25 years in the nonlabile portion of the bone (ATSDR, 1992; Rabinowitz et al. 1976).

Lead exposure can be evaluated by measuring erythrocyte protoporphyrin (EP), a component of red blood cells which contains 99 percent of lead in blood (the remaining one percent is found in the plasma). This method is commonly used to screen children for iron deficiency and lead poisoning . Methods to measure lead in teeth or bones by X-ray fluorescence techniques are currently being developed (TTNWeb, UATW).

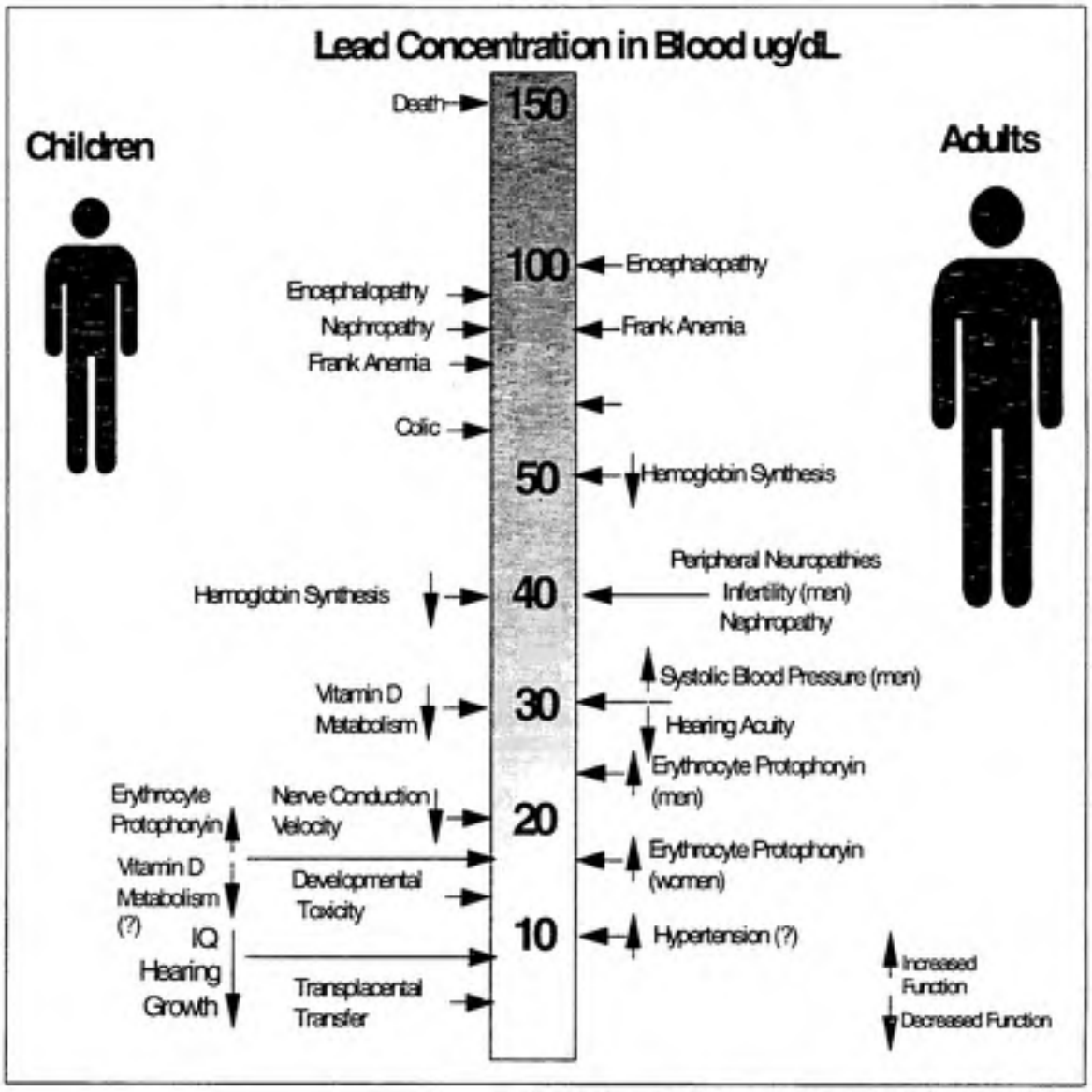
2.2 Dose Response

Some of the cellular and physiologic effects of chronic lead exposure at the lowest observable blood lead levels in children and adults are presented in Figure 2.3.

2.2.1 Acute Effects

Acute exposures to lead at blood lead levels greater than 125 μg/dL may cause death in children. Brain and kidney damage have been reported in blood lead levels at approximately 100 μg/dL in adults and 80 μg/dL in children. Gastrointestinal effects have been associated with acute exposures around 60 μg/dL in adults and children (TTNWeb, UATW).

FIGURE 2.3 EFFECTS OF INORGANIC LEAD IN CHILDREN AND ADULTS—LOWEST OBSERVABLE ADVERSE EFFECTS LEVEL



Adapted from ATSDR, Toxicological Profile for Lead (1989)

2.2.2 CHRONIC NON CANCER EFFECTS

Long term exposure to lead in humans has been associated with blood effects, such as anemia, at blood lead levels of 50 to 80 μg/dL in adults, and at levels of 40 to 70

μg/dL in children. Nervous system effects have been noted in workers with blood lead levels of 40 to 60 μg/dL. Slowed nerve conduction in peripheral nerves occurs at blood lead levels of 30 to 40 μg/dL in adults, while neurotoxic effects in children are thought to occur at blood lead levels of 10 to 30 μg/dL or lower. Children with blood lead levels of 10 to 50 μg/dL have been shown to have decreased IQ scores. Yule (1992) suggested that the detrimental effects of lead on neurotransmitters may be a cause of attention disorders and hyperactivity in children. Chronic exposure to lead in humans can also result in problems in blood pressure, kidney function, and vitamin D metabolism (TTNWeb, UATW).

2.2.3 Reproductive/ Developmental Effects

In male workers, acute and chronic exposures to lead have resulted in a significant decrease in sperm count and depressed function of the prostate and/or seminal vesicles at blood lead levels of 40 to 50 μg/dL. In women, spontaneous abortion is thought to be associated with acute and chronic occupational exposure to high levels of lead (though the lowest level at which this occurs has not yet been established) (Xintaras 1992).

Developmental effects from lead exposure include the increased risk of preterm delivery, low birth weight, and impaired mental development. These effects have been noted at maternal blood lead levels of 10 to 15 μg/dL, and may be possibly lower than this (Yule 1992). Though human studies have thus far been inconclusive, animal studies have shown a relationship between high lead exposure and birth defects (Xintaras 1992).

2.2.4 CARCINOGENICITY

The Department of Health and Human Services (DHHS) has determined that lead acetate and lead phosphate may reasonably be considered to be carcinogens based on animal studies. Kidney cancer in rats and mice from exposure to lead via the oral route has been reported (Calabrese and Kenyon 1991).

Four major studies have been done on workers exposed to lead and the associated risk of developing cancer. Two of these studies did not find an association between lead and development of cancer (Dingwall-Fordyce and Lane, 1963; Nelson et al. 1982); one study found an increased incidence of respiratory tract and kidney cancers (Selevan et al. 1985); and the fourth study found excesses for lung and stomach cancers (Cooper and Gaffey 1975; Gaffey [update] 1985). The results of these studies were limited by the fact that route and levels of exposures to the workers were not reported. Additionally, the workers in these studies were likely exposed to substances other than lead. Therefore, there is currently inadequate evidence to determine lead's carcinogenicity in humans. EPA has classified lead as a Group B2 carcinogen, indicating that it is a probable human carcinogen and sufficient animal evidence of carcinogenicity exists. Ten rat assays and one mouse assay have shown statistically significant increases in renal tumors with dietary and subcutaneous exposures to several soluble lead salts (IRIS, 1999).

2.3 ROUTE OF EXPOSURE

Human exposure to lead occurs primarily through a combination of inhalation and oral routes. Lead exposure usually occurs through the inhalation route in older children and adults and through the oral route for young children (six months to two years)

(Lanphear et al. 1998). For occupationally exposed groups, the inhalation route contributes a greater proportion of the dose, while the oral route is the primary route of exposure to lead in the general population. The effects of lead are qualitatively the same regardless of whether the route of exposure is inhalation, oral, or both (TTNWeb, UATW).

SECTION 3: SOURCES OF LEAD

3.1 LEAD IN PAINT

The Consumer Product Safety Commission banned the addition of lead to interior and exterior residential paint in 1978 (Staes et al. 1994). Paint, by regulation, must contain no more than 0.06 percent (600 parts per million [ppm]) lead by dry weight. Some paint manufactured for indoor use in the 1940's contained more than 50 percent (500,000 ppm) lead.

Lead-based paint continues to be a source of lead exposure and asymptomatic lead poisoning today. It is the most common source of high-dose lead poisoning among children in the U.S. In urban areas, the main source of lead poisoning in children is the ingestion of lead-based paint which is peeling, flaking, and chipping (Freudenburg, 1987). It is estimated that 74 percent of all pre-1980 housing units, approximately 57 million units, contain lead-based paint in the U.S.. It is also estimated that children are exposed to non-intact paint or high dust lead levels in 3.8 million homes (Staes et al. 1994).

Amitai et al. (1991) found that removing lead-based paint by various methods was effective in reducing blood lead levels in children who had at least one blood lead measurement >25 µg/dL, and levels remained lower in the 8-month follow-up to the retrospective paint abatement study. Results from the Baltimore Traditional and Modified Lead-Based Paint Abatement Study (Farfel et al. 1990) were not as favorable. In the Baltimore study, blood lead levels, which had dropped significantly one month

after intervention, were not significantly lower than pre-abatement levels six months later. Additionally, lead dust levels in treated homes tended to increase.

Lead-based paint removal can be an effective method to lower lead levels in older homes. Charney et al. (1983) noted that if the abatement method is not thorough and continual, the dust levels may worsen as the housing conditions worsen—actually increasing exposure levels.

3.2 LEAD IN AIR

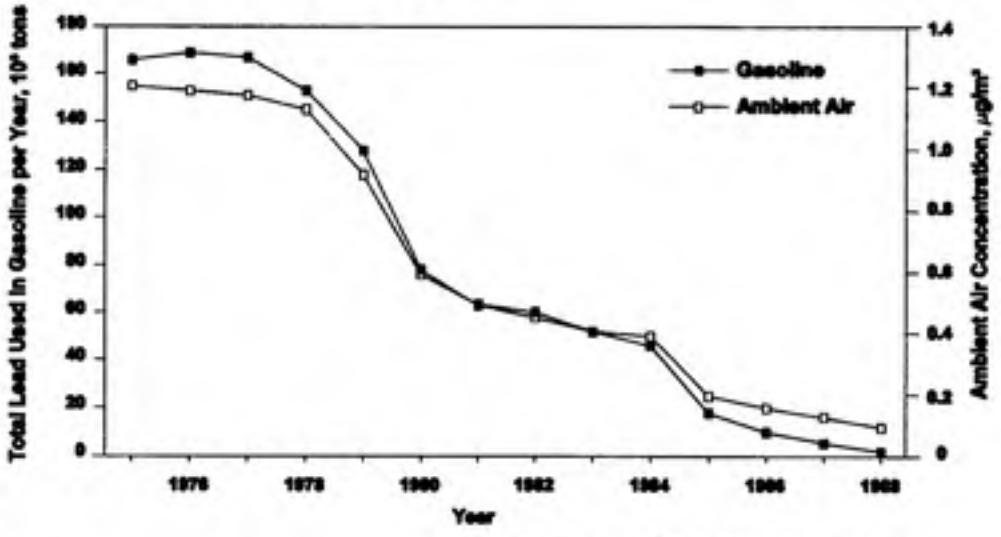
In communities where there are point sources, such as smelters and associated works (*i.e.*, slag dumps), the lead concentration in soil and air decreases exponentially with distance from the source. Exterior dust lead from these sources may accumulate on outside walls, roofs, and vegetation (Calder et al. 1994). Most of the lead in soil comes from the deposition of particles from the air (ATSDR ToxFAQs). Sources of interior dust include cracks and open spaces which allow dust lead to enter homes, while humans and animals may transport lead contaminated soil indoors. Interior dust accumulates on carpets, soft furnishings, and dusty areas of the home (Calder et al. 1994). Tobacco smoke is also a source of lead in the air (Rabinowitz et al. 1976).

Particles which are greater than 2.5 microns are deposited in the ciliated regions of the respiratory tract where they are passed to the GI tract by the mucociliary lift mechanism. Smaller particles may be absorbed into the systemic circulation from the alveolar region of the lungs (TRW, 1994). Rabinowitz et al. (1976) found that about 90 percent of the deposited lead (in respiratory tract) was absorbed daily.

The EPA requires lead in air not to exceed 1.5 $\mu g/m^3$ averaged over 3 months. The outdoor air lead concentration provides a large part of the total air lead exposure; considering that the indoor air lead concentration is typically about 30 percent of the outdoor concentration for the general population (USEPA 1986).

Gasoline combustion has historically been the major source of airborne lead in the environment. The U.S. government phased out the use of leaded gasoline in 1976 in order to reduce potentially hazardous concentrations of lead in ambient air (Pirkle et al. 1994). In 1990, Congress prohibited the use of lead or lead additives in gasoline after December 1995 as part of the Clean Air Act Amendments (USEPA, 1998). The result of this legislation was a significant reduction in ambient air concentrations between the years 1970-1990 (Figure 3.1). Although lead from gasoline is no longer considered to be a public health problem, lead from past automobile emissions continues to persist in soil (ATSDR, 1992).

FIGURE 3.1 HISTORICAL RELATIONSHIP BETWEEN LEAD IN GASOLINE AND LEAD IN AIR IN THE UNITED STATES



Source: USEPA (1986) [updated]

3.2.2 DUST/SOIL

The amount of lead in dust and soil is considered to be the sum of lead from leaded paint, gasoline combustion and stationary sources in the surrounding area (CDC MMWR 8/19/88). Dust and soil abatement have proven to be difficult and often useless, if not detrimental, to decreasing lead exposure. In a study by Hilts et al. (1995), High Efficiency Particulate Air (HEPA) vacuuming of floors inside homes in the smelter community every six weeks was not found to significantly lower blood lead levels in children. In fact, recontamination was thought to have occurred between vacuumings. In the same study, a correlation with lower blood lead levels were found in children whose families removed shoes at the door, and increased blood lead levels were found in children with pets. The investigators associated these findings with the transport of lead-contaminated soil indoors. Interventions in lower risk areas, further from lead point sources (*e.g.*, smelters), tend to be more effective, since recontamination near the source is more significant in re-elevating blood lead levels (Calder et al. 1994).

3.3 LEAD IN FOOD AND WATER

Historically lead exposure has come from many sources, including the direct atmospheric deposition of lead to soil and food, and from cans with lead-soldered seams. Lead contamination in homegrown fruits and vegetables may also be the result of atmospheric deposition of lead to the soil in which they are grown. The Food and Drug Administration has made significant progress in reducing lead in food processing in the last decade, including removal of lead from soldered cans (Bolger et al. 1996). Another potential source of lead exposure from food is the use of imported lead-glazed pottery. In

some cases even "safe" ceramicware may become harmful if the glaze chips or flakes off, exposing lead-containing pigments (ATSDR, 1992).

Lead in water may originate from lead pipes or lead soldered fittings used in the plumbing of some older homes. Direct consumption of, and/or cooking in, lead-contaminated water may also lead to increased lead exposure. The EPA currently limits lead in drinking water to 15 µg/L. The Consumer Product Safety Commission (CPSC), the EPA, and selected State agencies control the levels of lead in drinking water coolers. Older water coolers that are found to release lead are either recalled or repaired. New coolers are required to be lead-free. Furthermore, drinking water in schools is required to be tested regularly for lead (ATSDR ToxFAQs). These efforts have significantly decreased the public's daily lead intake, but EPA estimated that 241,000 children less than six years of age have blood lead greater than 15 µg/dL due to elevated concentrations of lead in drinking water (CDC MMWR 8/19/88).

The amount of dietary lead absorption is not known. There is evidence from studies that the absorption of lead from food consumption by infants is 40 to 50 percent of the amount of lead in the food. The EPA (1989) estimates this range to be about 42 to 53 percent. The bioavailability of lead salts in drinking water is high when consumed between meals. The maximum retention of lead in children is estimated to be about 60 percent on an empty stomach, and absorption is considered to be somewhat smaller than retention (TRW, 1994).

SECTION 4: VARIATION IN SUSCEPTIBILITY TO LEAD POISONING

4.1 POPULATIONS AT RISK

4.1.1 CHILDREN

Certain populations are more susceptible to lead poisoning than others. In comparison with the normal adult population, children under the age of seven are at much higher risk of lead poisoning. A combination of intrinsic behavioral exposure and biological factors make children more vulnerable to lead exposure.

The percentage of children between the ages of one and five with blood lead levels ≥ 10 μg/dL has decreased dramatically over the past 20 years with more public awareness and regulation regarding the dangers of lead exposure. According to data from the National Health and Nutrition Examination Survey (NHANES)[1] II and III, the estimates dropped from 88.2 percent in 1976-1980 to 4.4 percent in 1991-1994 (Figure 4.1). Phase two of NHANES III (1991-1994) data identified 2.2 percent of the population over the age of 1 with blood lead levels ≥ 10 μg/dL and a mean of 2.3 μg/dL. The data also identified 4.4 percent of U.S. children between the ages of one and five years with blood lead levels ≥ 10 μg/dL and a mean of 2.7 μg/dL. This percentage denotes that 890,000 children in the U.S. had elevated blood lead levels (Pirkle 1998). There was also

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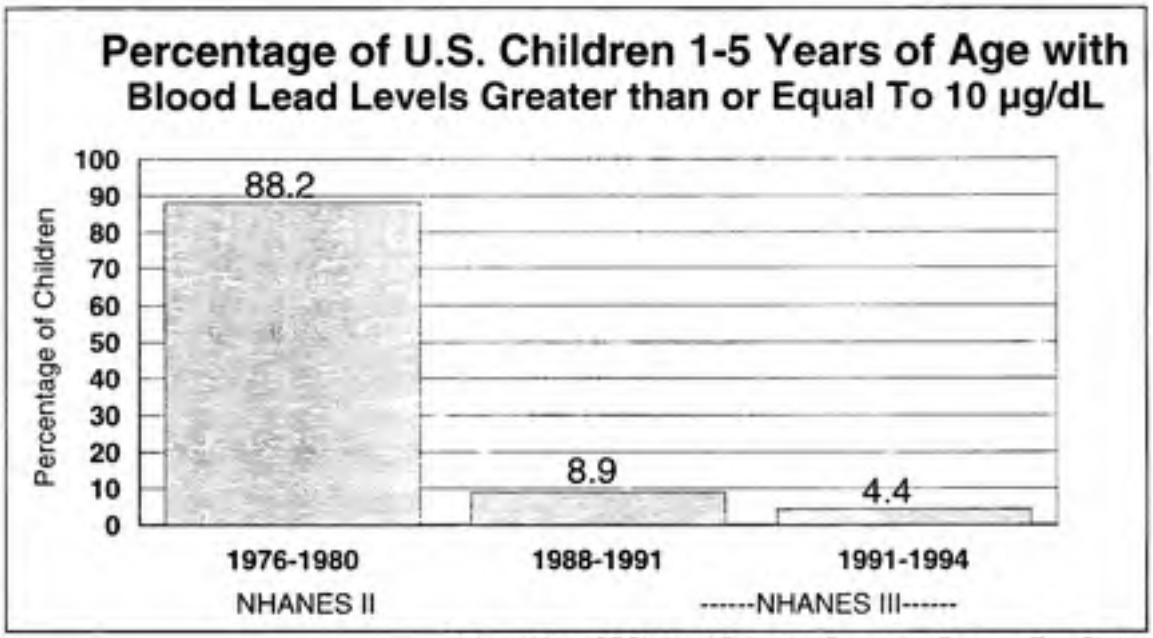
[1] NHANES is conducted by the National Center for Health Statistics, Centers for Disease Control (NCHS/CDC); it is a series of studies designed to assess the health and nutritional status of adults and children in the United States through interviews and direct physical examinations. NHANES is considered to be a representative survey of the U.S. population.

FIGURE 4.1 PERCENTAGE OF U.S. CHILDREN 1-5 YEARS OF AGE WITH BLOOD LEAD LEVELS GREATER THAN OR EQUAL TO 10 μG/DL



Adapted from CDC's Lead Poisoning Prevention Program Fact Sheet

variability in blood lead levels among children between one to five years old. Children aged one to two years had a geometric mean blood lead of 3.1 μg/dL, with 5.9 percent suffering from elevated blood lead levels. Children aged 3 to 5 years had a geometric mean blood lead of 2.5 μg/dL, with 3.5 percent suffering elevated blood lead levels.

4.1.1.1 Behavioral Factors

Today the major factor that leads to excess absorption of lead in children in certain areas is the amount of residential lead found in soil and dust. Children living in smelter communities often have a higher risk of lead poisoning. In long-term studies of these communities, lead abatement programs that aim to control either outdoor lead contamination, indoor lead contamination, or both, have proven to be only moderately successful in lowering children's blood lead levels. Behavioral factors increase a child's

susceptibility to lead poisoning because of increased exposures to lead. This behavior includes:

- playing in contaminated areas (*i.e.*, soil);
- mouthing items contaminated with lead from paint, dust, and soil; and
- pica, the tendency to eat nonfood items, such as dirt (Hunter, 1977).

4.1.1.2 Biological Factors

The mechanism of active transport displays a strong age dependence, being more important at younger ages for lead (TRW, 1994). Biological factors are associated with a greater sensitivity to the effects of lead at the same dose levels as adults. The risk factors which confer a biological susceptibility in children include:

- the developing nervous system;
- the efficiency of lead absorption in the GI tract; and
- nutritional deficiencies.

Children absorb about half of ingested lead—a rate that is about five times higher than the adult rate. Young children often show a greater prevalence of nutritional deficiency, a condition which is known to increase GI absorption of lead. The GI system of a child responds to increased nutritional needs by increasing absorption of the particular nutrient. This is responsible for the enhanced absorption in children (Bearer 1995). They absorb and retain more lead in proportion to their weight than adults do (ATSDR, 1992). Experimental animal studies have been found to support this data; pre-

weanling animals were found to absorb 40 to 50 times more of a given dose adult animals (Kostial et al. 1971, Kostial et al. 1978; Forbes and Reina, 1972).

The incomplete development of the blood-brain barrier in children (up to 36 months of age) increases the risk of lead entering into the developing nervous system, which may result in prolonged neurobehavioral disorders (ATSDR 1992) .

4.1.1.3 Fetal Susceptibility

Maternal exposure to lead also produces toxic effects in the fetus. The "inert" pool of lead which is found in the bones can be mobilized when the body is under physiologic stress during pregnancy or lactation (ATSDR 1992). Lead crosses the placenta by active transport (*i.e.*, via the mechanism involved in calcium transport), exposing the developing fetus to levels proportional to maternal lead stores. Fetal blood lead concentrations have been found to be equivalent to maternal blood lead concentrations (Bearer 1995). Studies have shown that increasing blood lead results in higher breast milk lead levels, exposing nursing infants to lead, particularly if the mother has chronic lead exposure (Gulson et. al. 1999). Fetal exposure is thought to potentially cause adverse neurological effects *in utero* and during post-natal development (ATSDR, 1992). In 1984, the Public Health Service estimated that over 400,000 fetuses were exposed to lead through maternal blood lead concentrations which resulted in early developmental effects (ATSDR, 1992).

TABLE 4.1 ACUTE EFFECTS OF LEAD EXPOSURE IN CHILDREN

Blood Lead Level (μg/dL)*	Effect
≥125	Death
80-100	Brain and Kidney Damage
~60	Gastrointestinal symptoms *e.g.*, colic

TABLE 4.2 CHRONIC EFFECTS OF LEAD EXPOSURE IN CHILDREN

Blood Lead Level (μg/dL)*	Effect
40-70	Anemia
20	Decreased IQ
10-15 (maternal exposure)	Spontaneous abortion, Preterm birth, Reduced birth weight, Impaired mental development
10-30 (or lower)	Detrimental to hearing threshold, growth

Adapted from TTNWeb, UATW Website http:/www.epa.gov/ttn/uatw/hlthef/lead.html

*The blood lead levels are toxicological numbers from animal testing or risk assessment values developed by the EPA.

4.1.2 OLDER ADULTS

Information on lead poisoning in older adults is limited. In humans, there seems to be falloff of lead body burden, either as a result of metabolic or dietary changes after the age of 60 (Mushak 1991). There is evidence that menopause and osteoporosis may increase the risk of lead toxicity in aging women. Studies indicate that there can be a marked mobilization of calcium from the bone matrix during the first few years of menopause. Analysis of data from NHANES II demonstrated a highly significant increase in the whole blood lead concentration after menopause (Mahaffey, 1990).

Mineral changes and enhanced bone lead resorption are thought to be associated with elevated blood lead levels in older women (Mushak 1991).

4.1.3 Occupational Risk

Certain occupational environments increase the probability of lead ingestion. It is estimated that more than one million workers in over 100 different occupations may be exposed to lead. In certain industrial work environments, workers may not only inhale lead dust and lead oxide fumes, but they may eat, drink, and smoke in or near lead-contaminated areas. These factors increase the probability of lead ingestion and, moreover, workers can bring lead dust home on their skin, shoes, and clothing—inadvertently exposing other members of their household (ATSDR, 1992). A study in Port Pirie, Australia, found higher blood lead levels in children whose parents worked in the lead industry. It was concluded that lead contaminated work clothes and shoes brought into the home were the major source of lead exposure (before protective regulations were implemented in the workplace in 1985) (Baghurst et al. 1992).

4.2 Nutritional Status

Lead uptake is known to decrease with the consumption of meals compared with fasting conditions in humans. The interaction between lead and nutrients in humans has been studied in terms of synergistic, antagonistic, or additive effects that may occur.

Two nutrients that figure prominently are calcium and iron (Barton and Huster 1987). Intracellular lead uptake may occur via the binding of lead ion to receptors in the enterocyte that serve for active transport of iron and calcium (Mushak, 1991). Other

nutrients, such as phosphates and vitamin D metabolites, are associated with lead uptake, although they have not been fully characterized epidemiologically. Some studies indicate that increases in lead absorption in the gastrointestinal tract are due to increased synthesis of vitamin D in the body stimulated by solar radiation. Lead interactions with zinc, protein, fats, saccharides, and natural chelators are known from animal studies (ATSDR, 1992). In a study by Lucas et al. 1996, dietary fat was found to have a significant positive independent association with blood lead ($p = 0.05$) at blood lead levels ≥ 15 µg/dL in humans. Dietary fat was considered to increase the level of blood lead because of the stimulation of bile flow during fat digestion, which increases lead absorption.

4.2.1 Iron Deficiency

The NHANES II database has been examined in terms of interactions between iron levels and blood lead. The data show that iron status is inversely related to blood lead, especially in children who often have more iron deficiency than adults. Animal models have been used to show that iron deficiency produces increased lead uptake and retention. Iron deficiency stimulates iron absorption; this stimulation enhances the uptake of lead through binding at intestinal receptors for the nutrient (Mushak 1991). Iron-deficient diets decrease the competition of iron with lead for shared intestinal metal binding sites necessary for absorption. The iron binding transferrin is thought to shuttle iron across the absorptive cell and regulate iron absorption. Lead is thought to bind to transferrin and other mucosal iron-binding proteins (Barton and Huster 1987). Mahaffey et al. 1990 found that iron deficient diets lead to increased lead absorption and retention of lead in humans.

4.2.2 Calcium Deficiency

Many of the cellular processes involving calcium are affected by the presence of lead. Lead is known to mimic calcium in biological systems and alter calcium mediated processes. Data from NHANES II showed that there was a statistically significant inverse association between dietary calcium intake and blood lead. Calcium is known to block the absorption of lead from the gastrointestinal tract. A number of animal studies have been done to describe the mechanistic and quantitative interactions between lead and calcium. Mahaffey et. al. 1973 found that rats ingesting a low calcium diet had blood lead levels approximately four times higher than rats fed a normal calcium diet, with the same quantities of ingested lead. Mechanisms in the gut include a ternary interaction of lead, calcium, and phosphate. There is also a competitive uptake of lead on the calcium carrier protein, which would be an active saturable transport process for lead (Mushak, 1991).

According to data from NHANES II, African American children have significantly lower calcium intakes than their Caucasian counterparts. Kimborough et al. 1994 suggested that African American children may be more susceptible to lead poisoning because of the high rate of lactose intolerance among the African American population leads to lower consumption of calcium-rich dairy products.

4.3 Seasonality

Lead poisoning is considered to be a summer disease. Seasonal fluctuations observed in blood lead concentrations in the U.S. prior to the regulation of lead in gasoline are considered to be heavily influenced by automobile emissions. More recent

studies indicate less dramatic seasonality in blood lead levels. In fact, data from NHANES III did not indicate that the season of the year was a statistically significant predictor of blood lead levels in children (Pirkle 1998).

Some researchers have found the months of peak blood lead vary from June through October. The trends have been observed in studies done both before and after the prohibition of leaded gasoline (USEPA, 1986). Blood lead concentrations are considered to show seasonal fluctuations due to factors such as (TRW, 1994):

- the relatively short half-life of lead in blood (about 25 days for adults);
- reduced outdoor exposures in the wintertime; and
- possible physiological or hormonal changes.

Annual peaks in blood lead levels are reached in the warmest months of the year. Cold weather, time spent in school, and snow cover tend to reduce the amount of time spent outdoors and limit the child's direct contact with soil.

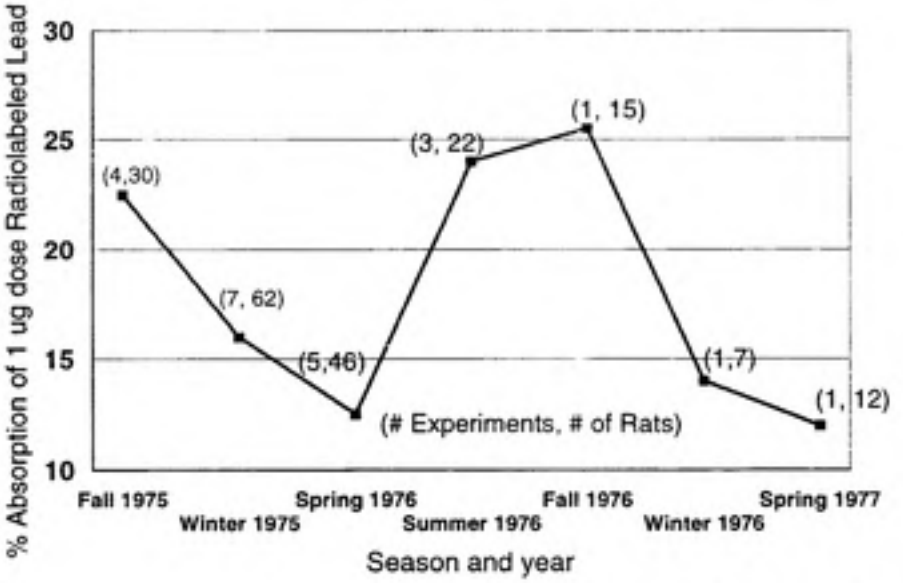
4.3.1 Physiological Mechanisms

Researchers have proposed several possible physiological mechanisms for the seasonality of lead poisoning. Solar radiation increases the biosynthesis of vitamin D (calciferol). The increased availability of calciferol improves calcium absorption; this in turn may result in increased lead absorption through nutrient uptake mechanisms (Section 4.2.2). Some researchers have indicated that the increased absorption of lead from the gastrointestinal tract is due to increased synthesis of vitamin D in the skin associated with

increased solar radiation in the summer. Others argue that the seasonality of the disease is due to increased absorption and recirculation of lead stored in body tissues, including long bones, because of elevated vitamin D levels in the summer. Weather conditions may also effect aerosol levels, increasing the amount of lead in the atmosphere, resulting in increased levels of deposited lead (Hunter 1977). Skin pigmentation is thought to reduce vitamin D synthesis, therefore one would expect to see decreased lead uptake among African American children. Studies to support this hypothesis regarding racial differences in the circulation of vitamin D and its metabolites have been inconclusive (TRW, 1997).

Studies on the potential impact of vitamin D and its metabolites on lead absorption from the intestinal tract of animals have been conducted. Results indicated increases in intestinal Pb absorption when vitamin D was administered to deficient animals (Mahaffey et al. 1982). Barton and Huster (1987) studied the seasonality of lead toxicity in rats. The investigators found increased radiolead absorption in the summer and fall and significantly different seasonal means ($p < 0.0001$). The increases in lead absorption occurred with minimal environmental variations, therefore the investigators noted that either internal factors or the minimal exposure to daylight could have modulated lead absorption. The investigators associate vitamin D metabolites with increased lead absorption, but postulated that iron-lead interactions may be responsible for lead absorption in the summer months for rats. The results of the study are depicted in Figure 4.2.

FIGURE 4.2 MEAN QUARTERLY VALUES OF RADIOLEAD ABSORPTION IN RATS



Source: Barton and Huster, 1987

4.4 SOCIODEMOGRAPHIC STATUS

Lead exposure affects many groups of people, regardless of race or class, but demographically, lead poisoning disproportionately affects minorities who tend to reside in low income, urban communities where many concomitant risk factors may be present. The sociodemographic variables that affect blood lead levels include factors such as:

- poor housing conditions, particularly problems with lead-based paint, lead dust, and lead plumbing;
- inadequate health resources such as public awareness funding and health education initiatives; and

- inadequate blood lead screenings and lack of health insurance for the treatment of lead poisoning.

In a large scale study of lead poisoning in Massachusetts communities, a significant, independent relationship was found for certain variables in community case identification for the rate of lead poisoning. These variables were median *per capita* income, housing built before 1950, and iron deficiency. The study involved 238,275 children from birth to 4 years of age who were screened between 1991 and 1992. The communities surveyed were urban, suburban, and rural. The rate of lead poisoning was found to be 10 times higher in single-parent homes, communities with high rates of poverty, housing built before 1950, and low rates of home ownership (Sargent et al. 1995).

4.4.1.1 Race/Ethnicity

A significantly higher percentage of African Americans compared to Caucasians have unacceptably high blood lead levels. The number of African Americans affected by lead has been found to be disproportionate to their number in the U.S. population. In 1984, African American children were 46 percent of all the children at risk. Other minorities are similarly affected; 15-20 percent of Mexican Americans and Puerto Rican Americans have been found to have blood lead levels greater then 15 µg/dL (ATSDR, 1992). Analysis of NHANES III data correlated highest blood lead levels, with a few exceptions, in non-Hispanic blacks, followed by Mexican-Americans, with non-Hispanic whites having the lowest levels (Table 4.3) (Pirkle, 1998). As mentioned previously, African Americans also have higher rates of lactose intolerance, therefore they have less calcium intake, which is considered to increase lead

absorption. Alternatively, the genotype thought to be associated with higher lead levels (ALAD 2) was not detected among an African population by researchers and vitamin D increases due to solar radiation have been proposed to account for higher lead levels in the warmer months, though skin pigmentation is considered to reduce vitamin D synthesis.

TABLE 4.3 GEOMETRIC MEANS OF BLOOD LEAD LEVELS BY RACE/ETHNICITY

Table 5. Geometric means and 95% confidence intervals (CI) of blood lead levels (µg/dl) for persons 1 year of age and older by age category, sex, and race/ethnicity: United States, 1991–1994

		Non-Hispanic white			Non-Hispanic black			Mexican American		
	Age (years)	Sample size	Geometric mean	CI	Sample size	Geometric mean	CI	Sample size	Geometric mean	CI
Males	1–2	183	2.8	2.5–3.2	148	5.4	4.8–6.3	172	3.6	3.1–4.1
	3–5	153	2.1	1.7–2.4	246	4.3	3.6–5.0	248	3.1	2.6–3.5
	6–11	162	1.7	1.5–1.9	291	3.2	2.7–3.5	201	2.2	1.8–2.7
	12–19	149	1.7	1.4–1.9	315	2.5	2.1–2.8	246	2.4	2.2–2.5
	20–49	526	2.7	2.4–2.9	663	3.3	3.0–3.6	732	3.3	3.1–3.5
	50–69	399	3.4	3.1–3.6	245	5.9	5.2–6.7	249	4.3	3.9–4.8
	≥70	423	4.4	4.2–4.6	112	6.6	5.5–7.8	105	4.0	3.3–4.7
Females	1–2	139	2.6	2.0–3.2	145	4.2	3.4–5.0	158	3.0	2.4–3.5
	3–5	176	2.1	1.9–2.3	244	3.9	3.2–4.6	249	2.9	2.4–3.3
	6–11	148	1.7	1.4–2.0	294	2.8	2.4–3.1	178	2.2	1.9–2.5
	12–19	192	1.2	1.0–1.3	360	1.5	1.3–1.7	260	1.4	1.2–1.5
	20–49	801	1.5	1.4–1.6	1,001	1.8	1.7–2.0	770	1.7	1.6–1.8
	50–69	483	2.5	2.3–2.7	278	3.3	2.7–3.8	255	2.4	2.1–2.7
	≥70	639	2.9	2.7–3.1	116	3.3	2.8–3.8	100	2.7	2.4–3.0

Source: Pirkle (1998)

4.4.1.2 Income

Low income is generally indicative of other sociodemographic which may be associated with elevated blood lead levels. Low income often correlates to housing conditions and location (inner-city, industrialized areas) and accessability to health resources. Data from NHANES III indicated that blood lead levels were found to be elevated among 4.5 percent of persons living in lower income households, with a geometric mean of 2.6 μg/dL. Persons from high income households had mean blood lead levels of 2.1 μg/dL (0.7 percent of the population) (Table 4.4).

TABLE 4.4 GEOMETRIC MEANS OF BLOOD LEAD LEVELS BY INCOME LEVEL

Population Group	Sample Size	Geometric Mean Blood Lead Level (μg/dL)	Confidence Interval	% Persons with Blood Lead Levels $\geq$ 10 μg/dL	Confidence Interval
Low Income	4,390	2.6	2.5-2.8	4.5	3.7-5.4
Middle Income	4,460	2.2	2.1-2.3	1.8	1.3-2.6
High Income	2,188	2.1	2.0-2.2	0.7	0.4-1.2

Modified from: Pirkle (1998)

4.4.1.3 Housing

Poorly maintained housing built before 1940, when paint containing high lead concentrations was used, is a major public health problem in terms of lead poisoning (Committee on Environmental Health, 1993). Lanphear et al. (1998) concluded that the differences in housing conditions and exposures to lead-contaminated house dust were the major contributors to the racial disparity in urban children's blood lead levels. They found that the homes of African American children had higher levels of lead dust and their interior surfaces were in poorer condition. NHANES III data indicate that higher blood lead levels are correlated with persons living in older homes except for the oldest age group ($\geq$70 years) (Table 4.5) (Pirkle 1998).

TABLE 4.5 GEOMETRIC MEANS OF BLOOD LEAD LEVELS BY AGE OF HOUSING

Table 8. Geometric means and 95% confidence intervals (CI) of blood lead levels (µg/dl) for persons 1 year of age and older by age category, sex, and year housing built: United States, 1991–1994

		House built before 1946			House built 1946–1973			House built after 1973		
	Age (years)	Sample size	Geometric mean	CI	Sample size	Geometric mean	CI	Sample size	Geometric mean	CI
Males	1–2	93	4.1	3.3–4.8	184	3.6	3.0–4.3	389	2.6	2.2–3.1
	3–5	113	3.8	2.9–4.8	260	2.5	2.1–2.8	197	1.7	1.5–1.9
	6–11	112	2.6	2.2–3.0	262	2.0	1.7–2.2	207	1.4	1.3–1.6
	12–19	126	2.1	1.6–2.5	293	1.9	1.5–2.3	221	1.6	1.4–1.8
	20–49	327	3.2	2.8–3.5	749	2.8	2.4–3.1	645	2.5	2.2–2.7
	50–69	188	4.1	3.6–4.6	478	3.7	3.3–4.1	190	3.3	3.0–3.6
	≥70	213	4.7	4.3–5.0	319	4.3	3.9–4.7	82	4.9	4.4–5.5
Females	1–2	60	5.2	4.2–6.1	177	2.9	2.5–3.4	152	2.2	1.9–2.4
	3–5	102	2.9	2.3–3.5	268	2.6	2.3–2.9	232	2.0	1.7–2.2
	6–11	112	2.6	2.1–3.2	232	1.9	1.5–2.2	196	1.4	1.2–1.7
	12–19	147	1.5	1.1–1.9	336	1.3	1.1–1.4	261	1.1	0.9–1.2
	20–49	430	1.7	1.5–1.8	1,026	1.6	1.5–1.7	853	1.5	1.3–1.6
	50–69	242	2.9	2.5–3.3	557	2.5	2.4–2.7	197	2.5	1.9–3.0
	≥70	286	2.9	2.6–3.2	389	2.8	2.6–3.0	139	2.9	2.5–3.2

Source: Pirkle 1998

Air pollution is primarily an urban phenomenon—where industrial emissions tend to be highest. Therefore, location of housing, *i.e.,* living near a pollutant source, is thought to be a factor which may increase an individual's, or group's susceptibility to elevated blood lead (USEPA, 1992).

4.5 GENETICS

The binding of lead by specific proteins in different tissues is thought to have a major influence on the toxicokinetics and toxicity of lead. Polymorphisms in the genes which code for several of these proteins may account for significant variations in intravascular and soft tissue binding, and in the long term deposition of lead (Schwartz et al. 1997). Variation in response to lead exposure has been studied in terms of genetic polymorphism in the population. Genetic polymorphism is the occurrence of two or more forms (alleles) of the same gene in a population.

Scientists have found that genetic polymorphism in the second enzyme of the heme synthesis pathway, delta-aminolevulinic acid dehydratase (ALAD), has been associated with differential responses of individuals to lead. ALAD has two common alleles in humans which are referred to as ALAD 1 and ALAD 2. The two forms differ from each other by only one base pair, though they function similarly to condense two molecules of the aminolevulinic acid to produce a precursor of the heme molecule. However, their slight structural difference is thought to greatly modify the disposition of lead in the body. ALAD 2 has been associated with elevated blood lead levels in children and adults though researchers are not clear whether ALAD 2 actually enhances or reduces the ultimate toxicity of lead (Alexander et. al. 1998). Wetmur et. al. 1991 found that the ALAD 2 allele is found among 10 to 20% of the Caucasian population, while Benkmann et. al. 1983 did not detect the allele in an African population.

Researchers from the Harvard University Superfund Basic Research Program, Johns Hopkins University, and Soonchunhyang (Republic of Korea) collaborated in an effort to further define the relationship between ALAD polymorphism and susceptibility to lead toxicity. The study involved a group of 57 lead-exposed battery workers in Korea. The scientists identified which of the three ALAD genotypes (ALAD 1-1, ALAD 1-2, and ALAD 2-2) each subject had using a protocol based on the Polymerase Chain Reaction (PCR) technique. The researchers confirmed that the variant genotype (ALAD 1-2) was associated with higher blood lead levels in the exposed workers. These variant gene carriers were also found to have lower serum concentrations of aminolevulinic acid (ALA) which is thought to be responsible for some of the neurotoxic effects associated with lead. ALA is known to accumulate in the bloodstream upon lead exposure because

of lead's inhibition of ALAD activity. The results of these study were heavily influenced by three of the study subjects who had high plasma concentrations of ALA. However, the association was still present after the removal of these three individuals, though it did not reach significance (Schwartz et al. 1997). These results indicate that workers who have the ALAD 1-2 genotype may be protected from some of the neurotoxic effects of lead exposure which result from elevated levels of ALA in the bloodstream (NIEHS/USEPA 1999).

The researchers also studied the association between the ALAD genotype and the levels of bioavailable lead in the study population. They measured the amount of lead that was excreted in the urine after the administration of the chelating agent dimercaptosuccinic acid (DMSA) to matched subjects with ALAD 1-1 and ALAD 1-2. DMSA removes lead from soft tissue storage sites such as the kidney and liver. The results of this part of the study indicated that the DMSA chelatable levels of lead varied by ALAD genotype. The subjects with ALAD 1-2 had, on average, 25 µg less lead excreted in the urine than subjects with ALAD 1-1 ($p=0.05$). This data indicates that the ALAD genotype may modify the retention and deposition of lead in the body (Schwartz et al. 1997).

The findings of the study indicate that the enzyme's polymorphism may modify not only the uptake and distribution of lead in humans, but also the neurotoxic effects of lead that are mediated by aminolevulinic acid (NIEHS/USEPA 1999).

SECTION 5: CONCLUSIONS

5.1 DISCUSSION

Lead poisoning is one of the most common environmental diseases among children in the United States (CDC MMWR 8/19/88). Lead levels that once were considered to be safe are now considered to be hazardous. The level of concern for blood lead in children has declined from 60 μg/dL to 10 μg/dL in the past 50 years as new findings concerning the dangers of lead exposure were made. As more data become available, the definition of unacceptable lead levels will likely continue to be lowered.

Elucidating the factors that confer individual susceptibility to lead poisoning is imperative to setting environmental and occupational standards that are protective of public health. The information presented in this paper indicate that certain factors increase the susceptibility to lead toxicity among humans. Considering the factors examined and data from NHANES III, age and sociodemographic factors (race/ethnicity, income level, and age of housing) are the two most important risk factors which increase susceptibility to lead. Currently there is a need for research to fill data gaps in terms of determining the roles of nutrition, genetics, and seasonality in increasing susceptibility to lead toxicity. Based on current knowledge, nutrition and genetics seem to be less significant than age and sociodemographic status. Seasonality was found to be the least important in terms of conferring susceptibility to lead.

5.1.1 AGE

Age is one of the most important determining factors in terms of susceptibility to lead exposure. Both biological and behavioral factors increase the susceptibility and sensitivity of children to lead toxicity in comparison to adults. The elevated blood lead levels among older adults may be explained by metabolic or dietary changes, however, there is a need for further study on the effects of lead exposure on the older population.

According to NHANES III data, the distribution of blood lead levels among the age groups tended to be a "U-shape", with the geometric mean blood lead levels being highest for persons ≥70 years (3.4 μg/dL) and children aged one to two years (3.1 μg/dL). The lowest levels were observed in younger adults between the ages of 12 and 19 years (1.5 μg/dL). Therefore, the mean blood lead level for children between the ages of one and two was on average twice as high compared to younger adults. The NHANES III data also indicate that the percentage of children between the ages of one and two with blood lead levels ≥10 μg/dL (5.9 percent) was 7.4 times higher than the percentage of young adults with elevated blood lead between the ages of 12 and 19 years (0.8 percent). The mean blood lead levels of children aged one to five years were higher for all three race/ethnicity groups surveyed (Table 4.3).

5.1.2 NUTRITION

Animal and human studies have demonstrated various nutrient—lead interactions. The association between nutritional status and lead susceptibility appears to be a strong one. Nutritional status greatly increases the susceptibility of young children, who have previously been described as the most susceptible population to the detrimental effects of

lead toxicity. In relation to other risk factors, poor nutrition has a significant, additive effect for lead toxicity in children.

Nutritional status is a factor which increases susceptibility to lead toxicity, however there is a need for more research. Iron and calcium deficiency are not uncommon in children and poor nutrition is also identified with sociodemographic factors such as race and low income. In this paper nutrition was not considered to be a sociodemographic factor, but perhaps should be associated with an individual's sociodemographic status. To illustrate, iron-deficiency anemia was identified among 29% of children of low-income families in contrast to less than 5% among higher income children (Yip et al. 1992). Data from NHANES II show that iron status is inversely related to blood lead, especially in children who often have more iron deficiency than adults. NHANES II data also showed that there was a statistically significant inverse association between dietary calcium intake and blood lead.

Improving the nutritional status of children who already have elevated blood lead may increase the effectiveness of abatement. Findings on nutrient-lead interactions will help identify the need for dietary interventions.

5.1.3 SEASONALITY

The phase-out of leaded gasoline has decreased the importance of seasonality as a risk factor in lead poisoning. NHANES III data did not associate seasonality with elevated blood lead, while other studies have. Traditionally, the months of peak blood

lead have been found to vary from June through October. The seasonality of lead has not been definitively characterized, though many behavioral factors and biological mechanisms for elevated blood lead levels during the summer months have been proposed. In comparison with other risk factors such as age, nutrition, and sociodemographic status, seasonality seems to be a minimal risk factor in determining lead toxicity. Further research is needed to explain the increased number of cases of lead poisoning during the summer months.

5.1.4 Sociodemographic Status

Sociodemographic status is one of the most important risk factors for susceptibility to lead. Lead poisoning disproportionately affects non-Hispanic blacks who tend to reside in urban, low income communities. Factors which increase susceptibility to lead poisoning in these communities include poor housing conditions, inadequate health resources, and lack of public awareness. Increasing family income is associated with lower blood lead concentrations for both blacks and whites. Table 5.1 addresses urban populations, however the figures for the country as a whole are similar (USEPA 1992).

Table 5.1 Estimated Percentage of Children (Living in Cities with Populations Over One Million) 0.5-5 Years Old with Blood Lead Levels Greater Than 15 μg/dL by Race and Income

	Less than $6,000	$6,000-$15,000	More than $15,000
Black	68%	54%	38%
White	36%	23%	12%

Source: ATSDR (1988)

NHANES III data indicated low income as the most significant sociodemographic factor for reflecting elevated blood lead. The geometric mean blood lead of people living in low income households (2.6 μg/dL) was 23.8% higher than for those living in high income household (2.1 μg/dL). The percentage of people living in low income households (4.5 percent) with blood lead ≥10 μg/dL was 6.4 times higher than those who live in high income households (0.7 percent) with blood lead levels ≥10 μg/dL (Table 4.4).

Data from NHANES III indicate that the mean blood lead levels of non-Hispanic blacks (2.8 μg/dL) was 27.3 percent higher than the mean blood lead levels of non-Hispanic whites (2.2 μg/dL). The percentage of non-Hispanic blacks with blood lead levels ≥10 μg/dL (5.2 percent) was 3.5 times higher than non-Hispanic whites (1.5 percent) with blood lead levels ≥10 μg/dL (Table 4.3).

The geometric mean blood lead of people living in housing built before 1946 (2.6 μg/dL) was 36.8 percent higher than for those living in housing built after 1973 (1.9 μg/dL). NHANES III data also indicate that the percentage of people living in housing built before 1946 (3.3 percent) with blood lead ≥10 μg/dL was 2.75 times higher than those who live in housing built after 1973 (1.2 percent) with blood lead levels ≥10 μg/dL (Table 4.5).

5.1.5 GENETICS

The variation among individuals in response to lead exposure due to genetic polymorphism is not clearly defined. The binding of lead by specific proteins in different

tissues has an effect on the toxicokinetics and toxicity of lead. Polymorphisms in the genes which code for several of these proteins may account for variations in the binding and long term deposition of lead and the neurotoxic effects of lead that are mediated by aminolevulinic acid (Schwartz et al.1997). Genetic susceptibility is thought to be associated with the ALAD 2 allele. Although further research needs to be done in terms of the distribution of the ALAD 2 allele among certain ethnic groups, this allele was found to be prevalent in studies among whites, but not among blacks. However, NHANES III data showed that the geometric mean blood lead levels of non-Hispanic blacks to be much higher among every age group compared to non-Hispanic whites. This data implies that genetic susceptibility does not significantly confer susceptibility in comparison with factors such as age, nutrition, and sociodemographic status.

Currently, there are no conclusive studies on the role of genetic polymorphism and susceptibility to lead. Continued research of genetic susceptibility is needed to study the health effects and identify individuals who are biologically more susceptible to lead than others at the same dose levels. Genetic susceptibility is especially important when there are low levels of lead exposure which may not be easily identifiable.

5.2 Recommendations Regarding Lead and Public Health

Ideally, lead poisoning is a totally preventable disease—remove the sources of lead exposure and the disease will disappear. In practice, eliminating lead poisoning will be a substantial and concerted effort by government, industry, and individuals.

Early screening and detection of exposure and toxicity have reduced the rate of lead poisoning. The success of these programs has been limited by (MMWR 8/19/88):

- Difficulty locating children with lead toxicity
- Inability to identify remedial sources of lead for lead-poisoned children
- Incomplete removal of lead from the child's environment

The following recommendations address the future needs for protecting public health from lead poisoning in the United States.

- **More Research to Identify Susceptible Groups to Lead Poisoning**

As blood lead levels in the general population decline because of increased regulation (such as restrictions on leaded gasoline), race and income are thought to become better indicators of the likelihood of exposure to leaded paint, and consequently the blood lead levels (ATSDR, 1992).

There is a need for more experimental and epidemiological studies to identify factors that confer susceptibility to lead poisoning in individuals. As high-risk groups are identified through research, comprehensive approaches to control lead exposure may be taken.

- **Develop Efficient, Reliable and Sensitive Screening Tools for Lead**

Screening tools which are affordable and reliable also need to be developed for environmental investigation to detect lead hazards in older homes and buildings.

Until recently the EP was the the test of choice for screening for lead poisoning. It is still considered to be a good screening test for iron deficiency anemia, however it

may not be ideal for screening blood lead. An elevated level of protoporphyrin in the blood is a result of accumulation secondary to enzyme dysfunction in the erythrocytes. A steady state is reached in the blood only when the entire population of circulating erythrocytes has turned over; about 120 days. This estimate lags behind blood lead levels and is an indirect measure of long term exposure to lead (ATSDR, 1992).

Findings from NHANES II indicate that 58 percent of 118 children with blood lead levels above 30 μg/dL had EP levels within normal limits. This finding indicates that a significant number of children would be missed based on the reliance of the EP test alone as a screening tool (ATSDR, 1992).

Screening programs must be both acceptable and cost-effective in order to be successful. In addition, medical follow-up and preventing future exposure to lead are also necessary (CDC MMWR 2/8/85). As high-risk groups of people are identified, steps should be taken to educate family members on preventable hazards of lead (ATSDR, 1992). As the role of genetic susceptibility to lead becomes more clear, molecular screening tools may be become useful in the future to identify sensitive populations.

- **Implement Effective Lead Abatement/Intervention**

Lead intervention and abatement treatments need to involve environmental, social, and medical components in order to be successful. Studies have shown that improper lead abatement practices can actually increase blood lead in children.

Environmental, social, and medical abatement treatments need to be applied to prevent lead poisoning. Favorable responses are most often observed in children with blood lead levels >25 μg/dL. The most significant changes occur when abatement is frequent and consistent over the long term to prevent recontamination. A combination of more than one type of abatement seems to be most effective in lowering blood lead levels. The most notable results in reducing blood lead levels have been observed when a thorough lead abatement program was implemented in the home by professionals, followed by continual lead abatement housekeeping practices (Charney et al. 1983). For high exposure environments, environmental lead abatement should be implemented, especially if children are involved. The benefits of abatement will likely outweigh the costs if one examines the lifelong effects associated with lead poisoning.

For low level lead exposures, educational intervention may have a more lasting effect on blood lead levels. Providing information on avoiding preventable lead hazards has been found to reduce blood lead levels in children. Information that may decrease lead toxicity in the home includes:

- Identification (and removal) of lead sources and "hot spots" around the home
- Thorough housekeeping and hygiene practices
- Proper nutrition
- Yearly blood lead screenings for young children

SECTION 6: REFERENCES

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