ARCHIVED: THIS DOCUMENT IS ARCHIVED FOR HISTORICAL PURPOSES AND IS NO LONGER BEING MAINTAINED OR UPDATED.

CDC now uses a blood lead reference value of 5 micrograms per deciliter to identify children with blood lead levels that are much higher than most children's levels. This new level is based on the U.S. population of children ages 1-5 years who are in the highest 2.5% of children when tested for lead in their blood.

This reference value is based on the 97.5th percentile of the National Health and Nutrition Examination Survey (NHANES)'s blood lead distribution in children.

This document was archived for historical purposes on July 30, 2020.

CDC

CENTERS FOR DISEASE CONTROL

Preventing Lead Poisoning in Young Children

A STATEMENT BY THE CENTERS FOR DISEASE CONTROL – JANUARY 1985

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES/PUBLIC HEALTH SERVICE/CENTERS FOR DISEASE CONTROL

CENTERS FOR DISEASE CONTROL
CHILDHOOD LEAD POISONING PREVENTION AD HOC ADVISORY COMMITTEE

May 17, 1984 - September 28, 1984

CHAIRPERSON
Rosen, John F., M.D.
Head, Division of Pediatric Metabolism
Albert Einstein College of Medicine
Montefiore Medical Center
Bronx, New York 10467

EXECUTIVE SECRETARY
Houk, Vernon N., M.D.
Director
Center for Environmental Health
Centers for Disease Control
Atlanta, Georgia 30333

Braud, Sara M., M.D.
Health Deputy Assistant Secretary
Office of Health Services and
Environmental Quality
Louisiana Department of Health and
Human Resources
P.O. Box 60630
New Orleans, Louisiana 70160

Beljan, John R., M.D.
Provost and Vice President for
Academic Affairs
Dean, School of Medicine
Hahnemann University
Broad and Vine Streets
Philadelphia, Pennsylvania 19102

Cole, Jerome F., Sc.D.
President
International Lead Zinc Research
Organization
292 Madison Avenue
New York, New York 10017

Davidson, Cliff I., Ph.D.
Associate Professor of Civil
Engineering
Department of Civil Engineering
Carnegie-Mellon University
Pittsburgh, Pennsylvania 15213

Davis, Devera Lee, Ph.D.
Executive Director
Board of Toxicology and
Environmental Health Hazards
National Academy of Sciences
2101 Constitution Avenue, N.W.
Washington, D.C. 20418

Field, Patricia H., Ph.D.
Director, Toxicology Laboratory
State Laboratory of Hygiene
465 Henry Hall
Madison, Wisconsin 53706

Gebbie, Kristine M., R.N.
Administrator, Health Division
Department of Human Resources
1400 S.W. 5th Avenue
Portland, Oregon 97201

Jackson, Rudolph Ellsworth, M.D.
Acting Chairman
Department of Pediatrics
Morehouse School of Medicine
720 Westview Drive, S.W.
Atlanta, Georgia 30310

MacLean, Robert A., M.D.
Deputy Commissioner
Professional Health Services
Texas State Department of Health
1100 West 49th Street
Austin, Texas 78756

Piomelli, Sergio, M.D.
Director of Pediatric Hematology-
Oncology
College of Physicians and Surgeons
of Columbia University
3959 Broadway
New York, New York 10012

Reigart, J. Routt, M.D.
Associate Professor
Department of Pediatrics
Medical University of South
Carolina
171 Ashley Street
Charleston, South Carolina 29425

99-2230

Preventing Lead Poisoning in Young Children

A STATEMENT BY THE
CENTERS FOR DISEASE CONTROL
JANUARY 1985
Reprinted July 1985

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
CENTER FOR ENVIRONMENTAL HEALTH
CHRONIC DISEASES DIVISION
ATLANTA, GEORGIA 30333

Use of trade names is for identification only and does not constitute endorsement by the Public Health Service or by the U.S. Department of Health and Human Services.

Preface

This second revision of the Centers for Disease Control's (CDC's) statement, Preventing Lead Poisoning in Young Children, is more comprehensive than the two previous versions. With help from members of CDC's Ad Hoc Advisory Committee on Childhood Lead Poisoning Prevention and other expert consultants, we have considered new research findings on lead toxicity, redefined lead poisoning at a lower blood lead level, and updated our recommendations on lead-based paint abatement. In addition, a recent article on a new treatment scheme for lead poisoning (symptomatic and asymptomatic) is included.

The precise threshold for the harmful effects of lead on the central nervous system is not known. In the meantime, we have used our best judgment as to what levels of lead are toxic and what practical interventions will lower blood lead levels. As public health officials, our duty is to protect children as best we can—given the limitations of science and the need to make decisions without perfect data. This is the Department of Health and Human Services' major policy statement on the issue.

The progressive removal of lead from leaded gasoline is lowering average blood lead levels in the United States, but the problem of the major source of high blood lead levels in our country—millions of old housing units painted with lead-based paint—is largely unsolved. Until better approaches and more resources are available for removing lead paint hazards in older dwellings where children live, lead poisoning will continue to be a public health problem.

The Committee considered a number of controversial issues, and members vigorously debated until a majority indicated that they could support the point under consideration. Readers should carefully weigh the recommendations in this document, and they should pay particular attention to references to work done since the 1978 CDC statement on lead. This 1985 statement represents agreement of 11 of the 12 Advisory Committee members. One member, Dr. Jerome F. Cole of the International Lead Zinc Research Organization, did not support the recommendations. Minutes of the Advisory Committee meeting on May 17-18, 1984, and Dr. Cole's statement of dissent are available upon request.

ACKNOWLEDGMENTS

The time, effort, and meticulous care the Committee devoted to this statement are gratefully acknowledged. This group of dedicated health professionals, along with notable expert consultants, labored through the results of several years of research in order to gain consensus on extremely complex issues. The various drafts of this document had the benefit of thoughtful suggestions from Committee members and consultants alike. Their work will help protect the children of this nation from this preventable disease for many years to come.

Vernon N. Houk, M.D.
Director
Center for Environmental Health

Contents

I. INTRODUCTION 1
Definitions 1

II. BACKGROUND 3

III. SOURCES OF LEAD EXPOSURE 5
Lead-Based Paint 5
Airborne Lead 5
Soil & Dust 7
Occupational Sources 7
Food & Drinking Water 7
Lead-Glazed Pottery 7
Other Sources 7

IV. SCREENING 8
Goal of Childhood Lead Poisoning 8
Target Population 8
Screening Schedule 8
Screening Methods 9
Intervention Levels 9
Measurements of Erythrocyte Protoporphyrin 10
Measurement of Blood Lead 12
Screening Schemes 12
Interpretation of Screening 12

V. DIAGNOSTIC EVALUATION 14
Tests 14

VI. CLINICAL MANAGEMENT 16
Urgent Risk 16
High Risk 17
Moderate Risk 17
Low Risk 17

VII. ENVIRONMENTAL EVALUATION AND LEAD HAZARD ABATEMENT 18
Lead-Based Paint 18
Airborne Lead 20
Soil & Dust 20
Food & Water 20
Occupational 20
Lead-Glazed Pottery 21

VIII. HEALTH EDUCATION 22

IX. REPORTING LEAD TOXICITY AND ELEVATED BLOOD LEAD LEVELS 22

X. REFERENCES 23

APPENDIX — Management of Childhood Lead Poisoning: Special Article 26

Contents - continued

Figure 1. Sources of Lead in a Child's Environment 6

Table 1. Suggested Priority Groups for Lead Screening 8

Table 2.A Zinc Protoporphyrin (ZnPP) by Hematofluorometer: Risk Classification of Asymptomatic Children for Priority Medical Evaluation 11

Table 2.B Erythrocyte Protoporphyrin (EP) by Extraction: Risk Classification of Asymptomatic Children for Priority Medical Evaluation 11

I. Introduction

Lead is ubiquitous in the human environment as a result of industrialization. It has no known physiologic value. Excessive absorption of lead is one of the most prevalent and preventable childhood health problems in the United States today. Children are particularly susceptible to its toxic effect.

Since 1970, the detection and management of children exposed to lead has changed substantially. Before the mid-1960's, a level below 60 micrograms of lead per deciliter (μg/dl) of whole blood was not considered dangerous enough to require intervention (Chisolm, 1967). By 1975, the intervention level had declined 50%—to 30 μg/dl (CDC, 1975). In that year, the Center (now Centers) for Disease Control (CDC) published *Increased Lead Absorption and Lead Poisoning in Young Children: A Statement by the Center for Disease Control.* Since then, new epidemiologic, clinical, and experimental evidence has indicated that lead is toxic at levels previously thought to be nontoxic. Furthermore, it is now generally recognized that lead toxicity is a widespread problem—one that is neither unique to inner city children nor limited to one area of the country.

Progress has been made. The Second National Health and Nutrition Examination Survey (NHANES II) has established average blood lead levels for the U.S. population; lead-contaminated soil and dust have emerged as important contributors to blood lead levels, as has leaded gasoline, through its contribution to soil and dust lead levels. An increasing body of data supports the view that lead, even at levels previously thought to be "safe," is toxic to the developing central nervous system; and screening programs have shown the extent of lead poisoning in target populations.

A major advance in primary prevention is the phased reduction of lead in gasoline. It is probably responsible for the findings of reduced average blood lead levels in children nationwide (Annest et al., 1983) and in two major cities (Rabinowitz and Needleman, 1982; Billick et al., 1980; Kaul et al., 1983). Lead is no longer allowed in paint to be applied to residential dwellings, furniture, and toys.

The sources of lead are many. They include air, water, and food. Despite the 1977 ruling by the Consumer Product Safety Commission (CPSC) that limits the lead content of newly applied residential paints, millions of housing units still contain previously applied leaded paints. Older houses that are dilapidated or that are being renovated are a particular danger to children. In many urban areas, lead is found in soil (Mielke et al., 1983) and house dust (Charney et al., 1983). Consequently, screening programs—a form of secondary prevention—are still needed to minimize the chance of lead poisoning developing among susceptible young children.

Lead poisoning challenges clinicians, public health authorities, and regulatory agencies to put into action the findings from laboratory and field studies that define the risk for this preventable disease. Although screening programs have been limited, they have reduced the number of children with severe lead-related encephalopathy and other forms of lead poisoning.

The revised recommendations in this 1985 Statement reflect current knowledge concerning screening, diagnosis, treatment, followup, and environmental intervention for children with elevated blood lead levels. Clearly, the goal is to remove lead from the environment of children before it enters their bodies. Until this goal is reached, screening, diagnosis, treatment, followup, and secondary environmental management will continue to be essential public health activities.

DEFINITIONS

The two terms defined below—elevated blood lead level and lead toxicity—are for use in classifying children (whose blood has been tested in screening programs) for followup and treatment. The terms should not be interpreted as implying that a safe level of blood lead has been established. Furthermore, they are to be used as guidelines. They may not be precisely applicable in every case. Each child needs to be evaluated on an individual basis.

The CDC is lowering its definition of an elevated blood lead level from 30 to 25 μg/dl. The definitions below are simplified versions of those in *Preventing Lead Poisoning in Young Children: A Statement by the Center for Disease Control: April 1978* (CDC, 1978).

- **elevated blood lead level**, which reflects excessive absorption of lead, is a confirmed concentration of lead in whole blood of 25 μg/dl or greater;

- **lead toxicity** is an elevated blood lead level with an erythrocyte protoporphyrin (EP)* level in whole blood of 35 μg/dl or greater.

As defined by blood lead and EP levels, the terms lead *toxicity* and lead *poisoning* are used synonymously in this document. "Poisoning" is generally used to describe episodes of acute, obviously symptomatic illness. The term "toxicity" is used more commonly in this document, since screening programs usually involve asymptomatic children.

According to this Statement, the severity of lead toxicity is graded by two distinct scales—one for use in screening, the other for use in clinical management. In the scale used in screening, children with lead toxicity are divided into classes I, II, III, and IV (section IV). These classes indicate the urgency of further diagnostic evaluation (section V). After the diagnostic evaluation, they are placed in one of four risk groups: urgent, high, moderate, and low (section VI).

*EP results are expressed in equivalents of free erythrocyte protoporphyrin (FEP) extracted by the ethyl acetate-acetic acid-HCl method and reported in micrograms per deciliter of whole blood. In this Statement, zinc protoporphyrin (ZnPP) and FEP are referred to as EP.

II. Background

A nationwide survey, conducted from 1976-1980, showed that children from all geographic areas and socioeconomic groups are at risk of lead poisoning (Mahaffey, Annest et al., 1982). Data from that survey indicate that 3.9% of all U.S. children under the age of 5 years had blood lead levels of 30 ug/dl or more. Extrapolating this to the entire population of children in the United States indicates that an estimated 675,000 children 6 months to 5 years of age had blood lead levels of 30 μg/dl or more. There was, in addition, a marked racial difference in those data. Two percent of white children had elevated blood lead levels, but 12.2% of black children had elevated levels. Further, among black children living in the cores of large cities and in families with annual incomes of less than $6,000, the prevalence of levels of 30 μg/dl or more was 18.6%. Among white children in lower income families, the prevalence of elevated lead levels was eight times that of families with higher incomes.

In the past decade, our knowledge of lead toxicity has greatly increased. Previously, medical attention focused on the effects of severe exposure and resultant high body burdens associated with clinically recognizable signs and symptoms of toxicity (Perlstein and Attala, 1966; Chisolm, 1968; Byers and Lord, 1943). It is now apparent that lower levels of exposure may cause serious behavioral and biochemical changes (De la Burde and Choate, 1972, 1975; NAS, 1976; WHO, 1977). Recent studies have documented lead-associated reductions in the biosynthesis of heme (Piomelli et al., 1982), in concentrations of 1,25-dihydroxy vitamin D (Rosen et al., 1980; Mahaffey, Rosen et al., 1982), and in the metabolism of erythrocyte pyrimidine (Angle and McIntire, 1978; Paglia et al., 1977). Results of a growing number of studies indicate that chronic exposure to low levels of lead is associated with altered neurophysiological performance and that the young child is particularly vulnerable to this effect (Needleman et al., 1979; Winneke, 1982; Yule et al., 1981). Investigations have also shown alterations in electroencephalograms (EEG's) (Burchfiel et al., 1980; Benignus et al., 1981; Otto et al., 1982) and decreased velocity in nerve conduction (Seppalainen and Hernberg, 1982; Feldman et al., 1977).

Many factors can affect the absorption, distribution, and toxicity of lead. Children are more exposed to lead than older groups because their normal hand-to-mouth activities introduce many nonfood items into their bodies (Lin-Fu, 1973). Once absorbed, lead is distributed throughout soft tissue and bone. Blood levels reflect the dynamic equilibration between absorption, excretion, and deposition in soft- and hard-tissue compartments (Rabinowitz et al., 1976). Young children absorb and retain more lead on a unit-mass basis than adults. Their bodies also handle lead differently. Higher mineral turnover in bone means that more lead is available to sensitive systems. The child's nutritional status is also significant in determining risks. Deficiencies in iron, calcium, and phosphorus are directly correlated with increased blood lead levels in humans and experimental animals (Mahaffey, 1981; Mahaffey and Michaelson, 1980). Increased dietary fat and decreased dietary intake of calcium (Barltrop and Khoo, 1975; Rosen et al., 1980), iron (Mahaffey-Six and Goyer, 1972), and possibly other nutrients enhance the absorption of lead from the intestine (NAS, 1976; Barltrop and Khoo, 1975).

Since lead accumulates in the body and is only slowly removed, repeated exposures to small amounts over many months may produce elevated blood lead levels.

Lead toxicity is mainly evident in the red blood cells and their precursors, the central and peripheral nervous systems, and the kidneys. Lead also has adverse effects on reproduction in both males and females (Lane, 1949). New data (Needleman et al., 1984) suggest that prenatal exposure to low levels of lead may be related to minor congenital abnormalities. In animals, lead has caused tumors of the kidney. The margin of safety for lead is very small compared with other chemical agents (Royal Commission on Environmental Pollution, 1983).

The heme biosynthetic pathway is one of the biochemical systems most sensitive to lead. An elevated EP level is one of the earliest and most reliable signs of impaired function due to lead. A problem in determining lead levels in blood specimens is that the specimen may be contaminated with lead, and thus the levels obtained may be falsely high. Therefore, in the initial screening of asymptomatic children, the EP level (instead of the lead level) is determined.

The effects of lead toxicity are nonspecific and not readily identifiable. Parents, teachers, and clinicians may identify the altered behaviors as attention disorders, learning disabilities, or emotional disturbances. Because

of the large number of children susceptible to lead poisoning, these adverse effects are a major cause for concern.

Symptoms and signs of lead toxicity are fatigue, pallor, malaise, loss of appetite, irritability, sleep disturbance, sudden behavioral change, and developmental regression. More serious symptoms are clumsiness, muscular irregularities (ataxia), weakness, abdominal pain, persistent vomiting, constipation, and changes in consciousness due to early encephalopathy. Children who display these symptoms urgently need thorough diagnostic evaluations and, should the disease be confirmed, prompt treatment.

In this Statement, screening is distinct from diagnosis. "Screening" means applying detection techniques to large numbers of presumably asymptomatic children to determine if they have been exposed to lead and, if so, what the risks of continued exposure are. Diagnosis, on the other hand, means the categorization of a child appearing to have excess exposure to lead according to the severity of burden and toxicity so that appropriate management can be started. No child with symptoms suggesting lead toxicity should be put through the screening process. He or she should be brought directly to medical attention.

III. Sources of Lead Exposure

Children may be exposed to lead from a wide variety of man-made sources. All U.S. children are exposed to lead in the air, in dust, and in the normal diet (Figure 1). Airborne lead comes from both mobile and stationary sources. Lead in water can come from piping and distribution systems. Lead in food can come from airborne lead deposited on crops, from contact with "leaded" dust during processing and packaging, and from lead leaching from the seams of lead-soldered cans. In addition to exposure from these sources, some children, as a result of their typical, normal behavior, can receive high doses of lead through accidental or deliberate mouthing or swallowing of nonfood items. Examples include paint chips, contaminated soil and dust, and, less commonly, solder, curtain weights, bullets, and other items.

LEAD-BASED PAINT

Lead-based paint continues to be the major source of high-dose lead exposure and symptomatic lead poisoning for children in the United States (Chisolm, 1971). Since 1977, household paint must, by regulation, contain no more than 0.06% (600 parts per million (ppm)) lead by dry weight. In the past, some interior paints contained more than 50% (500,000 ppm) lead. The interior surfaces of about 27 million households in this country are contaminated by lead paint produced before the amount of lead in residential paint was controlled. Painted exterior surfaces are also a source of lead. Unfortunately, lead-based paint that is still available for industrial, military, and marine usage occasionally ends up being used in homes.

Usually, overt lead poisoning occurs in children under 6 years of age who live in deteriorated housing built before World War II. Pica, the repeated ingestion of nonfood substances, has frequently been implicated in the etiology of lead toxicity in young children. In many cases, however, lead-paint ingestion is simply the result of the normal mouthing behavior of small children who live in lead-contaminated homes. Cases of children poisoned by lead paint have been reported from all regions of the United States and from both urban and rural settings. Increasingly, this poisoning has been reported when families move into a city as "urban homesteaders," and the children are inadvertently exposed to chips, fumes, or dust from lead-based paint as houses are rehabilitated. Clusters of lead-based paint poisonings have also resulted from demographic shifts within cities, when families with young children have moved into neighborhoods with deteriorating older housing. Increased lead absorption has been reported in children exposed to chips or dust from lead-based paint produced during the deleading of exterior painted steel structures, such as bridges and expressways (Landrigan et al., 1982).

AIRBORNE LEAD

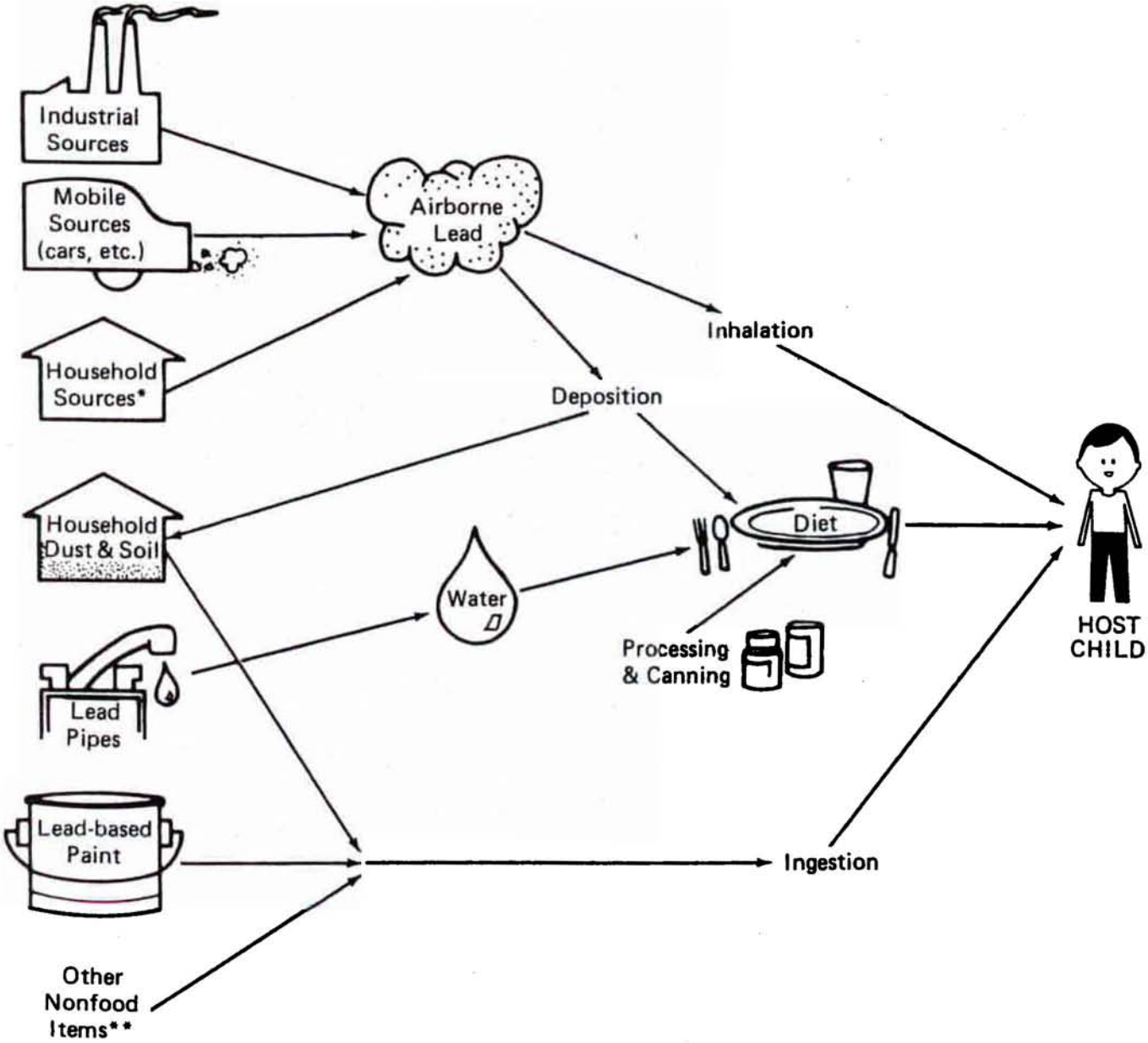
Generally, inhalation of airborne lead is a minor exposure pathway for individual children, but lead-containing particles—airborne and then deposited—can be responsible for high concentrations of lead in dust that children ingest. Studies in New Jersey (Caprio et al., 1974) and California (Johnson et al., 1975) have shown that children living within 100 feet of major roadways have higher blood lead levels than those living farther away. These levels also correlate positively with the average daily traffic volume on roads near homes (Caprio et al., 1974).

Previous estimates of the quantitative relationship between ambient air lead levels and blood lead levels may need to be revised because of new experimental and survey data. Preliminary results from an isotopic lead experiment (Facchetti and Geiss, 1982) suggest that lead from leaded gasoline is a much more important contaminant than it was previously thought to be. The preliminary estimates from that study indicate that at least 25% of the blood lead of residents of Turin, Italy, is derived from lead in gasoline. In Turin, the average blood lead level in adult males is 25 μg/dl; this corresponds to about 6 μg/dl attributable to gasoline.

Data from NHANES II also indicate that leaded gasoline is a more significant source of lead than previously thought. Annest et al. (1983) correlated major reductions in the amounts of lead added to gasoline sold in the United States with significant reductions in children's blood lead levels. They found that between 1976 and 1980, the overall mean blood lead levels in the U.S. population dropped from 14.6 μg/dl to 9.2 μg/dl. A similar relationship between leaded gasoline sales and umbilical cord blood lead levels has been shown by Rabinowitz and Needleman (1983).

Stationary sources can produce concentrated zones of exposure, especially where climatic conditions such as

Figure 1
SOURCES OF LEAD IN A CHILD'S ENVIRONMENT



*Production of bullets or fishing sinkers
Soldering and stained-glass work
Gasoline sniffing
Pottery glazing
Burning of batteries, colored newsprint, lead-painted objects, and waste oil

**Toys and figures containing lead
Folk remedies
Cosmetics (especially Oriental cosmetics, e.g., Surma, a black eyeliner)
Jewelry (painted with lead to simulate pearl)
Lead-containing dust transmitted on clothing from workplace

aridity, low wind velocity, and frequent thermal inversions minimize dispersal of airborne lead. The worst situations of this kind in the United States have existed in the vicinity of primary lead smelters (Baker, Hayes et al., 1977).

SOIL AND DUST

Soil and dust that contain lead are often an important source of lead exposure for children. The particles of airborne lead deposited in soil and dust usually come from automotive, industrial, and similar sources. Flaking lead paint adds to this contamination, particularly in and around houses. In soil, lead tends to remain in the top centimeter, but most soils are contaminated to a much greater depth when the topsoil is disturbed and turned under.

Children appear to obtain lead from dust and soil as a result of their normal exploratory behavior (Barltrop, 1966; Sayre et al., 1974; Roels et al., 1976), coupled in some instances with pica. Because of those mouthing tendencies, young children who live near major sources of airborne lead pollution must be considered at risk of exposure both by inhalation of airborne lead and by ingestion of deposited lead from soil and dust.

In general, lead in soil and dust appears to be responsible for blood lead levels in children increasing above background levels when the concentration in the soil or dust exceeds 500-1,000 ppm.

OCCUPATIONAL SOURCES

Lead dust can cling to the skin, hair, shoes, clothing, and vehicles of workers, and lead can be carried from workplace to home in this way. In a study in Memphis, Tennessee, when a parent worked with lead, the amount of lead in the children's blood correlated with the concentration of lead in dust in their homes (Baker, Folland et al., 1977). Of 91 children tested, 38 (41.8%) had blood lead levels of 30 μg/dl or more, and 10 either had blood lead levels of 80 μg/dl or more or EP levels above 190 μg/dl.

Strict compliance with Occupational Safety and Health Administration (OSHA) standards is quite effective in decreasing this type of exposure. However, many occupational exposures to lead are not covered by the OSHA standards. Companies with fewer than 10 employees (cottage industries, "hobby" production of pottery and stained glasswork, and home manufacturing of bullets and fishing sinkers) are excluded from OSHA standards.

The OSHA standard for lead workers is a blood lead level of 40 μg/dl. In a pregnant woman, lead crosses the placenta, and lead concentrations in umbilical cord blood are nearly equal to those in maternal blood (Barltrop, 1966). Since the growing brain of the fetus is likely to be at least as sensitive to the neurologic effects of lead as the brain of a young child, umbilical cord blood levels should be at least below 25 μg/dl. Therefore, the OSHA standard is probably not sufficiently strict to protect the fetus. Further study is needed to define acceptable lead levels among women of childbearing age.

FOOD AND DRINKING WATER

Lead in food, although rarely responsible for lead poisoning in the United States, is a ubiquitous source of background low-dose exposure for children (Beloian, 1982). Agricultural crops grown near heavily traveled roads or near stationary sources of lead can have significant concentrations because of airborne lead deposited on them. Lead may also be inadvertently added to foods during processing and handling. Canned foods may have particularly high lead contents, because acidic foods can leach lead from the solder in the seams of the cans (Lamm et al., 1973).

Generally, lead in drinking water has been leached from pipes and soldered joints by soft water having an acidic pH. Severe lead exposure has been reported among children in Glasgow, Scotland, where pure, acidic water was allowed to stand overnight in attic cisterns lined with lead (Beattie et al., 1972). The problem was alleviated by changing the pH of the water in the water treatment plant. In the United States, lead water pipes are most commonly found in older sections of northeastern cities and, occasionally, in rural areas of the northeast (Morse et al., 1979).

LEAD-GLAZED POTTERY

Although not a widespread source of lead, lead-glazed pottery can release large amounts of lead into food and drink. It has been responsible for outbreaks of serious poisoning (Klein et al., 1970). In several episodes reported to CDC, the pottery had been imported. Homemade or craft pottery and porcelain-glazed vessels have been found to release large quantities of lead, particularly if the glaze is chipped, cracked, or improperly applied (Osterud et al., 1973). If the vessels are repeatedly washed, the glaze may deteriorate and pottery previously tested as safe can become unsafe (D. M. Wallace, personal communication).

OTHER SOURCES

Lead is found in a variety of items, some of which endanger specific populations or ethnic groups. A variety of folk remedies contain lead, including azarcon and greta used by Mexican groups and pay-loo-ah used by Hmong refugees from Laos. Serious poisoning can also result from gasoline sniffing; the burning of waste oil, colored newsprint, battery casings, or lead-painted wood; and target practice in poorly ventilated, indoor firing ranges.

IV. Screening

GOAL OF A CHILDHOOD LEAD POISONING PREVENTION PROGRAM

The goal of a childhood lead poisoning screening program is to identify children with significant exposure to lead early enough to prevent serious toxicity. Elevated blood lead levels must be detected in asymptomatic children, and appropriate medical and environmental interventions must follow. The goal can be reached only through —

1. A screening program that enrolls the maximum number of children in high-risk populations.
2. A referral system that ensures a comprehensive diagnostic evaluation of every child with a positive screening test.
3. A program that assures identification and elimination of the source(s) of the child's lead exposure.
4. A system that monitors the adequacy of the treatment and the followup of each child with a diagnosis of lead toxicity.

Screening is of no value without prompt, thorough, and continuing medical and environmental followup for those children found to have lead toxicity—that is, as stated earlier, an elevated blood lead level (a confirmed concentration in whole blood of 25 μg/dl or greater) and an EP level in whole blood of 35 μg/dl or greater. Also as stated earlier, screening must be distinguished from diagnosis:

Screening refers to the testing of large numbers of children considered to be ASYMPTOMATIC in order to identify those who need further evaluation.

Diagnosis, on the other hand, refers to categorizing a child's condition according to severity of lead burden and toxicity. Then, on the basis of the category, management is selected.

Children whose elevated blood lead levels are detected by screening should be brought directly to medical attention, and the diagnostic process should be started without delay. Children with symptoms suggestive of lead poisoning require urgent and thorough diagnostic evaluation and, if the diagnosis is confirmed, immediate treatment. The symptoms of lead poisoning are nonspecific: they are described in section V.

TARGET POPULATION

Lead is most harmful to children between the ages of 9 months and 6 years. Ideally, all children in this age group should be screened. As more children are screened for iron deficiency with EP testing, simultaneous lead screening of these same groups becomes feasible. The list of priority groups in Table 1 highlights groups for which screening is strongly indicated. Testing children in low-risk groups for lead toxicity may not be practical unless it is done simultaneously with EP tests for iron deficiency.

Children in the 12- to 36-month-old age group who live in or are frequent visitors in deteriorating older buildings (including day-care centers) make up the highest priority group.

Siblings, housemates, and playmates of children with identified lead toxicity probably have similar exposures to lead, and they should be promptly screened. Suggested rankings for these and other priority groups are in Table 2.

Table 1
Suggested Priority Groups for Lead Screening

Priority	
1.	HIGHEST—Children, age 12 to 36 months, who live in or are frequent visitors in older, dilapidated housing
2.	Children, age 9 months to 6 years, who are siblings, housemates, visitors, and playmates of children with known lead toxicity
3.	Children, age 9 months to 6 years, living in older, dilapidated housing
4.	Children, age 9 months to 6 years, who live near lead smelters and processing plants or whose parents or other household members participate in a lead-related occupation or hobby
5.	Children, age 9 months to 6 years, who live near highways with heavy traffic or near hazardous waste sites where lead is a major pollutant
6.	All children 12 to 36 months of age
7.	All children 9 months to 6 years of age

SCREENING SCHEDULE

Screening for lead poisoning should be incorporated into a general pediatric health care program, and children in the target population should be screened at least once a year. The first screening should be done when the child is between 9 and 12 months old. Children generally have higher blood lead levels between May and October (NAS, 1976), so screening efforts should be concentrated in those months. Since negative screening tests in children living in a hazardous environment do not rule out subsequent exposure, children 12 to 36 months old who are at high risk of exposure should be screened every 2 to 3 months, especially during the summer. Children who move into a high-risk area after age 3 years may also need to be screened more than once a year.

SCREENING METHODS

Currently, the most useful screening tests are those for erythrocyte protoporphyrin (EP) and blood lead. Venous or capillary blood can be used for both tests, but capillary specimens are easier to collect and are, therefore, more widely used. Capillary blood may be transported in a capillary tube with an anticoagulant or dried on filter paper. Sampling methods used in the field must be compatible with laboratory capabilities.

EP and blood lead tests measure different aspects of lead toxicity. As stated earlier, EP tests measure the level of EP in whole blood, and a level of 35 μg/dl or more indicates impaired heme synthesis, which may be due to the toxic effects of lead; blood lead tests measure lead absorption, and a confirmed concentration of 25 μg/dl or more, referred to as an elevated blood lead level, reflects an excessive absorption of lead. Usually, there is a close correlation between results of the two tests for specimens from the same child, but, occasionally, the result of one test may be elevated and the result of the other, not elevated. The EP test has three advantages over the blood lead test: (1) when blood lead levels are moderately elevated, the EP test better identifies children with rising blood lead levels (Reigart and Whitlock, 1976); (2) if the specimen is contaminated with lead, the contamination does not affect the EP test; and (3) the EP test is an accepted screening test for iron deficiency.

INTERVENTION LEVELS

Children screened for lead poisoning can be grouped into two categories: those who require further evaluation and those who do not. Choosing the intervention level that divides these two groups is based on a compromise among the following:

(1) the desire to identify all children with any degree of lead toxicity
(2) a judgment about the urgency of preventing various detectable effects
(3) the sensitivity and specificity of a practical screening test
(4) society's ability to remove the sources of lead exposure

A. Pathophysiological Considerations

In recent years, levels of exposure previously considered "safe" have been shown to produce adverse effects. In addition, contemporary people (including children) living in remote areas with negligible exposure to lead have blood lead levels much lower than people living in the United States (Piomelli, 1980). Thus, the blood lead levels of U.S. children reflect a high degree of environmental contamination by lead. Today, the average blood lead level in the U.S. population is about 10 μg/dl—approximately three times the average level found in some remote populations. These observations suggest that the average level in the U.S.A. should be reduced. At present, however, because of practical considerations, the goal of reducing U.S. levels to those of remote populations is unattainable. Therefore, the blood lead level at which intervening action should be taken should be based on (1) criteria that indicate significant risk to the individual child and (2) the best combination of tests: a test for the blood lead level as an indicator of absorption and a test for EP as an indicator of biochemical derangement.

Since the CDC's 1978 statement on lead poisoning, several investigators have demonstrated effects of low-level lead exposures in these areas:

1. children's behavior and intelligence (Needleman et al., 1979; Winneke, 1982; Yule et al., 1981)
2. the central and peripheral nervous systems of adult workers (Mantere et al., 1982; Seppalainen and Hernberg, 1982)
3. heme biosynthesis in children (Piomelli et al., 1982)
4. nucleotide metabolism (Angle and McIntire, 1978)
5. vitamin D metabolism in children (Rosen et al., 1980; Mahaffey, Rosen et al., 1982).

The precise level at which lead exposure begins to cause developmental or neurobehavioral problems in children may be impossible to define in the near future. In the meantime, decisions on public health measures have to be made on the basis of (1) other, more objectively measurable effects and (2) an adequate margin of safety.

The elevation of EP, a toxic effect of lead in humans, has been well studied and it can be measured objectively. Among the biologic markers of lead toxicity, EP measurements have been the most useful in screening programs for lead poisoning. Recent studies have shed new light on the effects of lead and of iron deficiency on EP levels.

Several years ago, Roels et al. (1976), basing their argument on EP measurements, stated that a blood lead level of 25 μg/dl should be the maximum permissible concentration. Cavalleri et al. (1981), who made a study around a lead smelter, indicated that even this level may be too high. This group found an EP response at blood lead levels ranging between 10 and 20 μg/dl, suggesting that the EP no-response level is lower than 10 μg/dl. In a more recent and comprehensive examination of the issue, Piomelli et al. (1982) studied data from over 2,000 children. Blood lead and EP tests were done on venous specimens collected from children throughout New York City. Piomelli and his colleagues were trying to find the blood lead level at which the EP level began to increase. A variety of statistical techniques were used, and the findings were consistent; when blood lead levels increased linearly above the area of 15-18 μg/dl, the EP level increased exponentially.

Recent studies of EDTA (calcium disodium ethylene diamine tetraacetic acid) mobilization testing indicate that the amount of lead excreted by children with blood lead levels of 30-40 μg/dl may often be comparable to that excreted by children with levels of 50-70 μg/dl (Markowitz and Rosen, 1984). This finding suggests that the

blood lead level may underestimate the body burden of lead.

In summary, the EP data, with data from the other studies referred to, indicate that the 1978 blood lead guideline of 30 μg/dl has little or no margin of safety and should be lowered.

B. Practical Considerations

Although the biologic threshold for lead toxicity, as manifested by increasing EP levels, is less than 20 μg/dl, the criteria for a screening program have to take into account additional factors: (1) acceptability, sensitivity, and specificity of the screening procedure; (2) cost-effectiveness; and (3) the feasibility of effective intervention and followup.

The identification of children with blood leads below 25 μg/dl would require screening with a blood lead assay rather than an EP test, since the latter screening test has a very poor sensitivity and specificity below a blood lead level of 25 μg/dl. Such a recommendation would require most programs to use venous blood samples or to adopt impractically rigorous training and quality control procedures. Capillary blood samples are prone to environmental contamination with lead. In most programs, particularly those in high-risk areas, the use of "routine" capillary blood-drawing techniques results in an unacceptably high frequency of falsely elevated blood lead levels. On the other hand, taking blood samples from the veins of small children is less acceptable to parents and technically much more difficult. In addition, the cost of the screening program would increase severalfold. For all these reasons, an intervention level set at blood lead values below 25 μg/dl might ultimately substantially decrease the number of children being screened.

If local screening programs evaluate the distribution of moderately and highly elevated blood lead levels within a community, the findings may identify sources of lead that might go unnoticed if the program focused solely on children with high lead levels.

Even when slightly elevated blood lead levels are found, some interventions are possible and effective. House dust is an insidious but apparently effective carrier of lead to children in contaminated environments. In urban areas dust frequently contains large amounts of lead, thought to come primarily from airborne sources or leaded paint. Charney et al. (1983) have documented the effectiveness of controlling house dust; thus, in some situations, low and moderately elevated blood lead levels can be reduced simply by controlling house dust.

Considering these factors, CDC recommends as the intervention level a blood lead level of 25 μg/dl associated with an EP level of 35 μg/dl. When the blood lead level is 25 μg/dl or greater associated with an EP value of 35 μg/dl or greater, *lead toxicity is present; identification of such children is the focus of CDC's new recommendations.* Children may have mildly elevated blood lead levels without concurrent increases in EP concentrations, and it is desirable to identify these children, but, at present, this is impractical and beyond the criteria set for screening programs. Nonetheless, when resources and capabilities permit both blood lead and EP to be measured in the primary screening program, additional children with elevated blood lead levels will be identified. A more practical method for identifying such children needs to be developed.

The CDC recommends the following cutoff levels for determining a high risk for lead toxicity: for EP screening, a level of 35 μg/dl (whole blood should be tested); for followup testing, all children with a blood lead of 25 μg/dl or more should be considered at risk for the toxic effects of lead. Since the EP level is also elevated in iron deficiency, an elevated EP test alone should not be considered to be diagnostic of lead toxicity.

MEASUREMENT OF ERYTHROCYTE PROTOPORPHYRIN

Erythrocyte protoporphyrin (EP) may be measured by fluorometry after it has been extracted from the red blood cells or by direct fluorescence in intact cells (Lamola et al., 1975; Blumberg et al., 1977). In lead toxicity and iron deficiency, this metabolite is present in the red cells mainly as zinc protoporphyrin (ZnPP), but the ethyl acetate-acetic acid extraction procedure converts zinc protoporphyrin to erythrocyte protoporphyrin. Measuring ZnPP by hematofluorometer and EP after it has been extracted from the cells reflects essentially the same compound. In erythropoietic protoporphyria, an extremely rare disease, EP is markedly elevated—usually above 300 μg/dl. This is the free EP base, but it is detected by the EP extraction method and, to a lesser extent, by the hematofluorometer.

EP is also elevated in sickle cell anemia and other hemolytic anemias (Langer et al., 1972). Hyperbilirubinemia (jaundice) will cause falsely elevated EP readings with the hematofluorometer, but not with the extraction method (Buhrmann et al., 1978). Recent colds, ear infections, and other minor illnesses may also cause slight elevations of EP (Reeves et al., 1984). Nevertheless, lead toxicity should always be ruled out as the cause of elevated EP levels.

A. Use of Hematofluorometers

Hematofluorometers measure ZnPP and report values in EP equivalents. They are calibrated against the extraction method and theoretically should yield corresponding values. In practice, the values obtained with these instruments are usually not 100% of the EP present and may be considerably less. At least two studies (Kaul et al., 1983; Hammond et al., 1984) indicate that, at high levels, values obtained with hematofluorometers are lower than those obtained with the extraction method, but that up to 35 μg/dl the results are similar. Because hematofluorometers give immediate results and are economical, they are eminently suitable for field screening.

For both the hematofluorometer and the extraction method, the distinction between a positive and negative screening test should be based on a cutoff level of 35 μg/dl. However, for risk classification, the cutoff points for ZnPP measured by hematofluorometer (Table 2.A) differ from those for EP measured by the extraction method (Table 2.B). If possible, centralized laboratories should use extraction methods, and, if the followup laboratory has extraction capability, all confirmatory tests for EP should be done by extraction, not hematofluorometer. Hematofluorometers are most likely to give accurate results when used to analyze freshly collected blood specimens. The differences between methods need further study.

B. Erythrocyte Protoporphyrin and Iron Deficiency

A benefit of EP screening is that when an elevated EP level proves not to be due to lead, it usually reflects iron deficiency (Piomelli, 1977). The first signs of iron deficiency are biochemical abnormalities (low serum ferritin, low transferrin saturation, and high EP) followed by cellular abnormalities (microcytosis and hypochromia). Iron deficiency anemia follows these changes as the hemoglobin and hematocrit values fall.

The EP test proved to be practical in screening for iron deficiency in a population of 4,160 children (Yip et al., 1983). The upper limit of normal for EP in this study was 35 μg/dl. The predictive value appeared to be satisfactory.

Iron deficiency is common in many of the groups at risk for lead poisoning—especially among inner-city children of low socioeconomic status living in old, dilapidated housing. Iron deficiency is common among infants ages 9 to 24 months; the highest frequency of lead poisoning extends through 36 months. Iron deficiency and lead toxicity may occur in the same child. Furthermore, experimental evidence indicates that iron deficiency increases the proportion of lead absorbed from the intestine and aggravates the toxic effects of lead.

Analysis of the NHANES II data has clarified the relationship between elevated EP values, blood lead levels, and iron deficiency in a representative sample of the U.S. population. Among children in the NHANES II survey with elevated EP values, 31% have elevated blood lead levels, 18% have iron deficiency (as evidenced by a transferrin saturation of less than or equal to 12%), and 11% have evidence of both conditions (R. Yip, personal communication). On the other hand, among children with elevated blood lead levels, only about 26% have lead toxicity—that is, an elevated EP level (NCHS, 1984). In high priority populations (Table 1), in which iron deficiency is more common and lead levels are higher, a greater proportion of children with elevated blood lead levels would have elevated EP levels. Analyses by both Yip and NCHS confirm that a synergistic effect exists between lead toxicity and iron deficiency in children, as experimental studies in animals have suggested.

Table 2.A
Zinc Protoporphyrin (ZnPP) by Hematofluorometer
Risk Classification of Asymptomatic Children for Priority Medical Evaluation

Blood Lead #	Erythrocyte Protoporphyrin (EP) #			
	<35	35-74	75-174	>175
Not done	I	•	•	•
<24	I	Ia	Ia	EPP+
25-49	Ib	II	III	III
50-69	**	III	III	IV
> 70	**	**	IV	IV

= Units are in μg/dl of whole blood.
• = Blood lead test needed to estimate risk.
EPP+ = Erythropoietic protoporphyria. Iron deficiency may cause elevated EP levels up to 300 μg/dl, but this is rare.
** = In practice, this combination of results is not generally observed; if it is observed, immediately retest with whole blood.

NOTE: Diagnostic evaluation is more urgent than the classification indicates for—

1. Children with any symptoms compatible with lead toxicity.
2. Children under 36 months of age.
3. Children whose blood lead and EP levels place them in the upper part of a particular class.
4. Children whose siblings are in a higher class.

These guidelines refer to the interpretation of screening results, but the final diagnosis and disposition rest on a more complete medical and laboratory examination of the child.

Table 2.B
Erythrocyte Protoporphyrin (EP) by Extraction
Risk Classification of Asymptomatic Children for Priority Medical Evaluation

Blood Lead #	Erythrocyte Protoporphyrin (EP) #			
	<35	35-109	110-249	>250
Not done	I	•	•	•
<24	I	Ia	Ia	EPP+
25-49	Ib	II	III	III
50-69	**	III	III	IV
>70	**	**	IV	IV

= Units are in μg/dl of whole blood.
• = Blood lead test needed to estimate risk.
EPP+ = Erythropoietic protoporphyria. Iron deficiency may cause elevated EP levels up to 300 μg/dl, but this is rare.
** = In practice, this combination of results is not generally observed; if it is observed, immediately retest with venous blood.

NOTE: Diagnostic evaluation is more urgent than the classification indicates for—

1. Children with any symptoms compatible with lead toxicity.
2. Children under 36 months of age.
3. Children whose blood lead and EP levels place them in the upper part of a particular class.
4. Children whose siblings are in a higher class.

These guidelines refer to the interpretation of screening results, but the final diagnosis and disposition rest on a more complete medical and laboratory examination of the child.

MEASUREMENT OF BLOOD LEAD

Unlike elevated EP levels (which may be caused by iron deficiency or other illnesses), elevated blood lead levels are specific for lead absorption. Fluctuations in blood lead values over a short period can be due to physiologic variations or sporadic acute lead exposure.

Capillary samples are highly sensitive to contamination with environmental lead. If such samples are to be taken for blood lead assays, the personnel must be rigorously trained before any screening program is begun, and duplicate capillary blood specimens should be drawn. A single tube of capillary blood should never be used for the diagnosis of elevated blood lead, because an elevated value may be caused by contamination. If results of tests for blood lead from two tubes differ substantially, the higher value can be considered spurious. Even when the results are equally elevated, contamination cannot be excluded. Therefore, only venous blood samples should be used to confirm a diagnosis or to determine or assess treatment. There is less likelihood of contamination in a venipuncture, but venous blood may be difficult to collect from very young children. Neither the blood lead nor the extraction EP test should be considered a routine procedure in the clinical laboratory. To help insure credible test results, laboratories performing these tests should participate in the CDC proficiency testing program or the equivalent.

SCREENING SCHEMES

Three feasible screening strategies are—

1. Screening with EP tests, followed by blood lead measurements if indicated. This is the most common procedure.
2. Screening with both EP and blood lead tests.
3. Screening with blood lead tests, followed by EP measurements if indicated.

The CDC recommends EP tests, followed by blood lead measurements for all children with an elevated EP level. The EP test has these advantages:

1. Ease of measurement by hematofluorometer or the extraction method.
2. Results that are not affected if specimens are contaminated with environmental lead.
3. More cost effective than screening with the blood lead test.
4. Ability to detect a child's metabolic response to the toxicity of lead.
5. Possibility of differentiating between children with stable blood lead levels and those with declining levels.
6. Possibility of identifying children who have iron deficiency.

In some areas, where the environment is grossly contaminated with lead, a strategy of simultaneous testing for EP and blood lead levels is recommended. In these cases, venous samples should be used for measuring lead.

When EP is the primary screening tool, two approaches are possible:

1. **EP measured on site.** A capillary blood specimen is collected, and while the child waits at the screening site, EP is determined by hematofluorometer. Children found to have EP values of 34 μg/dl or less are discharged until the next routine screening. For those with EP values of 35 μg/dl or more, additional blood samples are taken (preferably by venipuncture) for laboratory analysis of blood lead and of EP—by extraction, if the method is available.
2. **EP measured off site.** A venous blood sample or duplicate capillary samples are collected at the screening site and sent to the laboratory for measurement of EP, preferably by the extraction method. The amount of blood collected should be sufficient for confirmatory tests. Unused specimens of blood from children whose EP levels are 34 μg/dl or less may be discarded. For those children with EP levels of 35 μg/dl or more, the blood lead levels and hematocrits or hemoglobin concentrations should be determined.

On site, EP is nearly always measured by hematofluorometer; off site—preferably—it is measured by the extraction method. If the blood specimen is protected from temperature extremes and light, it may be stored for a week to 10 days before being analyzed by the extraction method. Blood collected on filter paper may be stored for several weeks before it is analyzed.

INTERPRETATION OF SCREENING RESULTS

A single screening test, either for EP or blood lead, cannot be used to categorize children for priority in followup. Both EP and blood lead levels must be used to determine the potential risk of lead toxicity in the children screened.

Children can be arbitrarily divided into four classes on the basis of EP and blood lead screening results. In view of the observed discrepancy between results from the hematofluorometer and extraction methods, two tables are given: Tables 2.A and 2.B (derived from Kaul et al., 1983). This classification merely suggests the relative risk and the priority for medical evaluation and environmental intervention, and the tables should be used only as general guidelines. Children 12 to 36 months old should be given priority over older ones, and children whose EP and blood lead levels fall into the upper range of a class should be given priority over those whose levels fall into the lower range. For example, the urgency for followup is greater for a 1-year-old whose EP level by extraction is 109 μg/dl and whose blood lead level is 49 μg/dl than for a 5 1/2-year-old whose EP level, by the extraction method, is 36 μg/dl and whose blood lead level is 26 μg/dl. Yet both children fall into class II.

Children in class IV—at urgent risk of lead toxicity—should be medically evaluated within 24 hours,

and in no case later than within 48 hours. Children in class III are at high risk. Those in class II are at moderate risk, and those in class I, at low risk.

Class I can be subdivided into two additional categories. Class Ia (blood lead, 25 μg/dl or less, and EP, 35 μg/dl or more) includes children with iron deficiency. These children should be retested, with additional assessment of iron status. Class Ib (blood lead, 25-40 μg/dl, and EP, less than 35 μg/dl) covers children who appear to have transient, stable, declining, or increasing blood lead levels. Results should be confirmed by retesting, and the children should be carefully followed. In some cases, the blood lead and EP results will differ. When the EP value is significantly higher than the value suggested by the blood lead level, the child probably has both iron deficiency and excessive lead absorption.

Screening should focus on asymptomatic children. Children with symptoms should be referred for immediate evaluation, regardless of their risk classification.

V. Diagnostic Evaluation

Screening tests are not diagnostic. Therefore, every child with a positive screening test should be referred to a physician for evaluation, with the degree of urgency indicated by the risk classification. At the first diagnostic evaluation, if the screening test was done on capillary blood, a *venous blood lead level* should be determined in a laboratory that participates in CDC's blood lead proficiency testing program. Even when tests are done by experienced personnel, blood lead levels may vary 10% to 15%, depending on the level being tested. Tests for the same child may vary as much as ±5 μg/dl in a 24-hour period. Thus, differences of 1 to 5 μg/dl between screening and diagnostic levels in either direction should not necessarily be interpreted as indicative of actual changes in the child's lead absorption or excretion.

Additional blood samples may be needed for tests such as complete blood counts, serum iron, total iron binding capacity, and serum ferritin. The amounts necessary for these tests, which usually exceed the amount obtainable by capillary sample, can be obtained with a single venipuncture.

Symptoms, if present, constitute an urgent risk, warranting prompt hospitalization (section VI). Symptoms must be *looked for*, and they can be missed (Piomelli et al., 1984):

Acute lead encephalopathy is characterized clinically by some or all of these symptoms: coma, seizures, bizarre behavior, ataxia, apathy, incoordination, vomiting, alteration in the state of consciousness, and subtle loss of recently acquired skills. Any one or a mixture of these symptoms, associated with an elevated blood lead level, constitutes an acute medical emergency. Lead encephalopathy is almost always associated with a blood lead level exceeding 100 μg/dl, although, occasionally, it has been reported at blood lead levels as low as 70 μg/dl.

Symptomatic lead poisoning without encephalopathy is characterized by one or several symptoms: decrease in play activity, lethargy, anorexia, sporadic vomiting, intermittent abdominal pain, and constipation. It is usually associated with a blood lead level above 70 μg/dl, although, occasionally, cases are associated with a level as low as 50 μg/dl. *If the blood lead level is below 50 μg/dl, other causes should be vigorously sought.* Since any symptomatic child may develop acute lead encephalopathy, treatment and supportive measures must be started immediately on an emergency basis.

Whether or not symptomatic lead poisoning is present, the child should have a complete pediatric evaluation.

Special attention should be given to—

1. A detailed history, including the presence or absence of clinical symptoms, child's mouthing activities, existence of pica, nutritional status, family history of lead poisoning, possible source of exposure, and previous blood lead or EP determinations.
2. The physical examination, especially the neurologic examination.
3. Nutritional status and hematologic evaluation for iron deficiency. Iron deficiency contributes to an elevated EP and can enhance lead absorption and toxicity.
4. Confirmatory diagnostic tests.
5. Trends in EP and blood lead levels.

Since trends are important in diagnosis and management, serial measurements of blood lead and EP (and other measurements as indicated) are far more valuable than data obtained at one time. To be comparable and interpretable, serial EP levels should be analyzed by the same method.

Probably the most reliable method for determining the source of exposure is obtaining a careful, complete environmental history (section III), inspecting the home for lead hazards, and learning about the child's hand-to-mouth behavior through careful questioning. Pica, the Latin word for "magpie," describes the habitual ingestion of nonfood substances. This should not be regarded as synonymous with the normal oral behaviors of small children, such as finger and thumb sucking and nail biting.

An initial plan for management requires that all interacting factors be taken into account. The plan should be modified as indicated by long-term trends in lead absorption, exposure, and clinical status.

TESTS

In addition to confirmatory and serial EP and blood lead determinations, the following tests can be useful (if available) in assessing the patient's lead absorption status.

1. Tests for Iron Deficiency

Because the EP can reflect iron deficiency as well as lead exposure, the presence of iron deficiency must be established or ruled out if EP levels are to be properly interpreted.

A common misconception is that a child with a "normal" hematocrit (33% or more) or hemoglobin concentration (11 g/dl or more) could *not* be iron deficient. This is not true, particularly with respect to iron deficiency sufficient to affect EP and, worse, to enhance lead absorption and retention. Thus, although a complete blood count (CBC) and a reticulocyte count are indicated in the evaluation of lead toxicity, they are not sensitive enough to rule out iron deficiency.

Of the red blood cell (RBC) indices, a decreased mean corpuscular volume (MCV) is a useful indicator of iron deficiency. Normal values depend on age (Dallman, 1982).

Serum iron and **iron binding capacity** are more sensitive than the MCV. In general, an elevated iron binding capacity of more than 350 μg/dl is more likely to accurately indicate iron deficiency than a normal or low serum iron, since the serum iron is quite sensitive to both dietary iron and diurnal variation. Thus, if a child has eaten an iron-rich food within 2-4 hours before the blood for the test is drawn, the result may be closer to the normal level than is actually the case. Under standardized conditions, an abnormally low ratio of serum iron to iron binding capacity (transferrin saturation) is consistent with iron deficiency. In addition to the level of EP itself, the *serum ferritin* level is an accurate indication of overall iron status.

2. Flat Plate of the Abdomen

Radiologic examination (flat plate) of the abdomen may reveal radiopaque foreign material, but only if the material has been ingested during the preceding 24 to 36 hours. Since lead ingestion is sporadic, this examination is significant only if the results are positive; negative results do *not* rule out lead poisoning. Positive results indicate recent ingestion of large amounts of lead.

3. X-ray of Long Bones

X-rays of the long bones, usually the knees, may help estimate the duration of exposure. Lines of increased density in the metaphyseal plate of the distal femur and proximal tibia and fibula are "growth arrest lines." They are caused by lead, which disrupts the metabolism of the bone matrix. As a result, areas of increased mineralization or calcification may be present at the metaphyses of the long bones. Though sometimes called "lead lines," they are not an x-ray shadow of deposited lead.

Although definitive data are not available, these lines are thought to become visible after at least 4 to 8 weeks from the time exposure began; the length of time depends on the age of the child and the degree of lead exposure. The width and intensity of the lines reflect prolonged previous lead absorption but do not indicate current ingestion. They are seldom seen in children under 24 months of age. Negative x-rays do not rule out lead poisoning.

4. Calcium Disodium EDTA Mobilization (or Provocative Test)

This test is used to identify children who will respond to chelation therapy with a brisk lead diuresis. Children whose blood lead level exceeds 55 μg/dl should not receive a provocative chelation test. Instead, appropriate chelation therapy should be started. The mobilization test is particularly useful when the screening test indicates that the child has lead toxicity and there is some question as to whether chelation therapy is indicated. This test provides an index of the mobile or potentially toxic fraction of the total body lead burden (Saenger et al., 1982).

Since CDC's 1978 statement, an 8-hour mobilization test has been shown to be as reliable as a 24-hour mobilization test (Markowitz and Rosen, 1984). Although an 8-hour test may be done on an outpatient basis, the patient should not leave the clinic. The careful use of "lead-free" apparatus is mandatory.*

5. Lumbar Puncture

CAUTION:

If a lumbar puncture is needed to rule out meningitis or other serious disease, it should be performed cautiously and only after a careful search for signs and symptoms of increased intracranial pressure. The fluid should be obtained drop by drop, and no more than 1 milliliter (ml) should be removed.

The following tests are not useful in diagnosing lead toxicity.

1. Microscopic Examination of Red Cells for Basophilic Stippling

Since basophilic stippling is not universally found in chronic clinical lead poisoning and is relatively insensitive to lesser degrees of lead toxicity, it is *not* considered useful in diagnosis.

2. Tests of Hair and Fingernails for Lead Levels

The levels of lead in hair or fingernails are not well correlated with blood lead levels; therefore, tests for these levels are *not* considered useful in diagnosis.

*Special lead-free collection apparatus must be used if valid test results are to be obtained. The laboratory performing the analysis may supply the proper collection apparatus. Preferably, urine should be voided directly into polyethylene or polypropylene bottles that have been cleaned by the usual procedures, then washed in 1% nitric acid, and thoroughly rinsed with deionized, distilled water. For children who are not toilet trained, plastic pediatric urine collectors, with double compartments, may be used. Urine collected in this manner should be transferred directly to the urine collection bottles. Preserving the collected urine with hydrochloric acid will stabilize not only lead but also δ-aminolevulinic acid (ALA).

VI. Clinical Management

The system described in section IV is for an initial classification, to be modified by results of the diagnostic evaluation. Thus, after all information is available to the clinician, the child's true risk classification is established. Clinical management includes eliminating the source of the child's lead exposure; providing general pediatric care, family education, and, when appropriate, chelation therapy; and correcting any nutritional deficiencies. In addition, followup examinations must be performed until the risk of further damage is minimal. *The single most important factor in pediatric management is to reduce the amount of lead ingested.* The family must be fully informed of the child's condition and of the clinical and environmental actions to follow.

One recommended approach to the treatment of children with symptomatic and asymptomatic lead poisoning is described in detail in the Appendix. The major new feature of this approach is an increased reliance on calcium disodium EDTA mobilization testing among children with moderate blood lead levels. The test results are used to decide whether chelation is indicated. A full course of chelation therapy should not be given without either a confirmed blood lead level equal to or greater than 56 μg/dl or a positive mobilization test in children with blood lead levels of 25-55 μg/dl. This approach is recommended by four major medical centers in which the staffs have had extensive experience in the diagnosis and treatment of children with lead poisoning.

The cornerstones of clinical management are careful clinical and laboratory surveillance of the child and a reduction in lead exposure to prevent further accumulation of lead. This approach allows previously absorbed lead to be slowly excreted. Most children with lead toxicity do not require chelation therapy, but those who do may need more than one course of treatment.

The followup program for asymptomatic children depends upon the degree of risk determined during the diagnostic evaluation.

For the purposes of clinical management and followup, the risk categories are ranked from urgent to low.

Urgent — Blood lead levels of 70 μg/dl or more with or without symptoms.

High — Children whose repeat EP and confirmatory venous blood lead levels fall in the class II and III ranges of the screening test, but who also have a positive calcium disodium EDTA mobilization test or other confirmatory diagnostic tests or risk factors. Children in class III who have not had confirmatory diagnostic tests should be considered high risk until evidence places them in another risk category.

Moderate — Children whose repeat EP and venous blood lead levels fall into the class II range of the screening test but whose other confirmatory diagnostic tests are negative.

Low — Children whose repeat EP and venous blood lead levels fall into the class I range of the screening tests. These children are usually not given other diagnostic tests.

This categorization is arbitrary and can be adapted to a particular child. For example, a 20-month old with persistent pica whose environmental lead hazard cannot be controlled satisfactorily may be considered high risk, even if his or her repeat EP and venous blood lead levels fall in the range of class II and other diagnostic tests are negative.

URGENT RISK

Children with blood lead levels of 70 μg/dl or more, regardless of the presence or absence of clinical symptoms, should be treated with the same intensity as children with frank neurologic manifestations. The higher the confirmed venous blood lead, the greater the need for chelation therapy. Severe and permanent brain damage may occur in as many as 80% of children who have acute encephalopathy (Perlstein and Attala, 1966). Treatment before onset of encephalopathy will improve this grim prognosis.

Lead toxicity is a chronic medical problem. Children who require chelation therapy will need long-term medical surveillance and care. The EP levels can fluctuate during and immediately after chelation therapy. After an apparently successful course of therapy with calcium disodium EDTA (incorporating BAL, British Anti-Lewisite, as necessary), the "rebound" phenomenon may be observed.

First, the blood lead level drops during treatment. This is not a reason to interrupt therapy. Then, after treatment is stopped, the blood lead level almost invariably rises again. This phenomenon reflects a reequilibration of

stored lead. The decision to repeat chelation therapy is based on the blood lead level after the "rebound."

Reduction of lead intake is urgent for all children in this category, both as part of immediate therapy and as part of the followup preventive procedure. Children receiving chelation therapy should not be released from the hospital until lead hazards in their homes and environment are controlled. Otherwise, suitable alternative housing must be arranged. Thus, the appropriate public agency in the community must be notified immediately so that environmental investigation and intervention can begin.

After their hospitalization and after lead has been removed from their environments, these children are still at high risk. Close followup, with blood lead and EP measurements, is required. At first, these tests should be done every 1 to 2 weeks. If the blood lead level rebounds to its pretreatment level, a repeat of the chelation therapy should be considered. If the blood lead level remains stable or shows a continual decline after the first few weeks, the interval between testing may be incrementally increased from 1 to 6 months until the blood lead and EP levels return to normal or the child reaches 6 years of age.

HIGH RISK

Many children in the high-risk category will have been given a calcium disodium EDTA mobilization test to determine whether chelation therapy is needed. If it is needed, inpatient chelation should be performed. Under some conditions, however, children without urgent risk factors may be treated as outpatients. Outpatient treatment should be reserved, however, for those centers capable of providing closely monitored outpatient care and followup supervision, and in those centers it should be provided only if the child's source of lead exposure has been eliminated (Piomelli et al., 1984). In addition, the parents should be cooperative and should demonstrate that they can follow instructions.

Followup of high-risk children should consist of blood lead or EP tests, or both, at least monthly (especially in the summer), until the sources of lead in their environments have been removed. If their blood lead or EP levels have declined or stabilized, the interval between testing may be incrementally increased, except in summer, from 1 to 6 months, until the blood lead and EP levels return to normal or the child reaches 6 years of age. Careful neurological and psychological assessment is advised so that any behavioral or neurological deviation can be detected early and proper therapy and school placement begun.

MODERATE RISK

Generally, children in this category do not require chelation therapy. Reducing lead intake from all sources and careful monitoring of the child usually suffices.

Until the lead hazards are eliminated from their environment, these children should be tested monthly in the summer and every 2 months in other seasons. If the blood lead and EP levels remain stable or show a continual decline after the first few months, the interval between testing may be incrementally increased from 2 to 6 months until the blood lead and EP levels return to normal or the child reaches 6 years of age.

NOTE: All children in the urgent-, high-, and moderate-risk categories may have concomitant nutritional deficiencies. These deficiencies may increase the child's risk from lead by increasing absorption, retention, and toxicity. All children in these categories should receive a careful nutritional evaluation, including appropriate laboratory tests. In addition to the care given for lead toxicity, nutritional therapy should be provided. When increased lead absorption is found, it may be particularly important to correct iron deficiency and maintain an adequate calcium intake.

LOW RISK

When tested, children in this category do not have significant evidence of lead toxicity. However, they require periodic screening until they reach their sixth birthday. Children whose elevated EP levels are not caused by lead absorption should receive medical attention and care for the medical condition responsible for the elevation. Children with elevated blood lead levels but no evidence of toxicity should be evaluated monthly until lead toxicity can be ruled out. This can usually be done within 3 months.

In conclusion, the clinical management of children with lead poisoning must include appropriate treatment, adequate followup, environmental intervention, and family education. Chelation therapy is indicated for some children with lead toxicity. Using it indiscriminantly is unwise, but so is withholding or delaying it when it is indicated. The physician providing clinical management must know the current status of the child's environment. The optimal frequency of followup depends on many factors, including the child's age and environment and the trend in results of the child's tests.

VII. Environmental Evaluation and Lead Hazard Abatement

Environmental investigation and intervention should begin as soon as lead toxicity is confirmed. Lead hazards must be identified and removed from the environments of these children. Priorities for action should be determined by the child's risk classification. The higher the blood lead level and the lower the child's age, the higher the priority for removing the lead hazards. Children who require hospitalization and chelation therapy are at the highest risk of permanent neurologic damage from continued high-level exposure and another episode of lead toxicity. Therefore, children in the urgent- and high-risk categories should receive first priority for environmental investigation and intervention. It is strongly recommended that abatement of lead hazards in a hospitalized child's home be completed during the first few days of the child's hospitalization.

Children in the moderate-risk category are next in priority. For them, identifying lead hazards and reducing lead intake are as much a medical necessity as clinical management. The effectiveness of environmental intervention is judged by the child's response and not by the services performed. Environmental management is not successful or complete until the child's EP and blood lead levels have declined and stabilized for at least 12 months. The identification and removal of one source of lead exposure does not necessarily mean that the child's exposure to lead has ended.

Because lead is a ubiquitous and powerful toxin, with no known beneficial function in the human body, the goal of prevention is to reduce children's exposure to lead to the maximum extent. Lead-based paint is the most common, remediable source of lead that causes symptomatic lead poisoning. Detailed procedures for removing lead paint from the home environment are described, but only general guidelines are given for controlling other sources of lead discussed in section III. Ideal prevention goals are given first; when these goals cannot be reached immediately, short-term, substitute goals are offered.

LEAD-BASED PAINT

The ultimate goal is to remove all leaded paint from housing in the United States. Reaching that goal will be expensive. Short-term goals of partial removal help, but they tend to postpone efforts for complete removal.

All painted interior and exterior surfaces should be tested for lead. Portable x-ray fluorescence (XRF) analyzers are most convenient for identifying lead-based paint hazards. These instruments can measure lead content in paint surfaces within ± 0.2 mg/cm^2 of exposed surface. Readings of 0.7 mg/cm^2 are considered positive. The XRF analyzer is a probability sampling device, and reliability depends on repeated readings. If an XRF analyzer is not available, wet chemical methods of analysis must be used.

A lead-based paint hazard exists when (a) the XRF reading is positive and (b) the surfaces being tested are chewable or contain damaged (cracked, chipped, loosened, chewed) paint. Lead-based paint on *intact* walls, ceilings, or other surfaces that are not chewable does not constitute an immediate hazard. Inspectors should obtain measurements on any interior or exterior surface that may constitute a lead hazard. This includes walls, doors, window frames, baseboards, guardrails, fences, and sidings. Outside inspection should encompass garages and other adjacent structures as well as the main building.

Next, the inspector should classify each interior and exterior part of the building where lead is found according to the degree of hazard. If nonchewable surfaces with lead paint are smooth and intact and the supporting structure is sound, they do not present an immediate hazard and may be left alone. Property owners and residents, however, should be warned that smooth surfaces containing lead can become hazardous if they are not properly maintained and are allowed to fall into disrepair. All lead-painted surfaces that are identified as positive by XRF (or wet chemical analysis) and that are in unsound condition are classified as immediate hazards requiring prompt abatement. This includes all wood trim—both interior and exterior—with blistering, scaling, peeling, or powdering paint and walls with unsound paint, painted plaster, or painted, peeling wallpaper. Floors and ceilings, if painted with lead-based paint and if in an unsound condition, are also included.

New information has revealed the importance of lead-bearing dust as another major hazard for young children.

In the past, blistering, scaling, peeling, or powdering paint was frequently removed only to a level of 4 or 5 feet above the floor, because, usually, a small child can reach no higher. However, dust or paint chips from unsound lead paint above this level could fall into the child's play area. CDC now recommends that *all* unsound leaded paint be removed from the interiors of dwellings, including areas beyond the reach of children. Likewise, exterior leaded paint (on porches, woodwork, and walls) that either is in or can fall into the child's play area should be removed immediately. Places in and about the home where young children spend much of their time—namely, near windows, doors, and porches—are particularly hazardous.

In summary, paint in unsound condition or on chewable surfaces is classified as an immediate hazard requiring prompt abatement: other lead paint in sound condition may not require immediate attention, but it must be identified as a potential hazard.

Next, some common methods for reducing lead-based paint hazards are outlined.

Phase I — Emergency Intervention

As soon as an elevated blood lead level is confirmed, residents should be advised to remove all scaling paint from places such as window sills, door frames, doors, and porch railings that are within easy reach of the child. A stiff brush should be used for this. Residents should also be advised to avoid inhaling the dust or contaminating other areas. The debris should be vacuumed and bagged for safe disposal. Then the area should be thoroughly scrubbed, preferably with high-phosphate detergents such as Spic and Span (Milar and Mushak, 1982). If a crib is next to a surface with scaling paint, the crib should be moved away. Similarly, a piece of furniture should be moved to prevent the child from reaching areas of scaling paint. In the past, it was advised that window sills and other wood trim with peeling paint be covered with masking tape or some other adhesive-backed paper. This is no longer recommended. Inquisitive young children often remove this tape, thereby rendering the technique ineffective. Families should be instructed on ways to keep these areas free from loose or flaking paint until more definitive steps can be taken to reduce the hazard. Housekeeping techniques such as frequent wet mopping and damp dusting are essential in maintaining a reduced level of hazard.

Phase II — Long-Term Hazard Reduction

Only when an old dwelling with lead-based paint is gutted and completely restored can the lead hazards be considered "permanently abated." Less extensive, commonly used procedures may be called "long term"; however, how long the hazard will remain under control depends on such factors as the thoroughness of the procedure, the soundness of the underlying structure, and the condition of the plumbing. Increased moisture from leaky pipes behind walls can quickly cause paint that was smooth and intact to blister and scale.

Abatement entails four steps:

1. Removing lead paint from wood trim or walls.
2. Thorough vacuuming to clean up the debris.
3. Wet scrubbing for maximum elimination of fine lead-bearing particles.
4. Repainting the area with lead-free paint (that is, paint containing less than 0.06% of lead in the final dried solid).

The property owner's responsibility is not met until all four steps have been completed.

Just prior to and during abatement, certain precautions are essential. Carpets, rugs, upholstered furniture, bedding, clothing, and eating and cooking utensils must be sealed as tightly as possible in plastic to protect them from the enormous increase in lead-bearing dust created by the removal procedures. Once items such as rugs are impregnated with fine, lead-bearing particles, it is almost impossible to remove the lead (Milar and Mushak, 1982). When feasible, this work should be carried out in one room at a time, with the room closed off and all furnishings removed. Until steps 1, 2, and 3 of the cleanup process are completed, all young children and pregnant women should live elsewhere both day and night. If this is not possible, they, as well as the child with the index case, should have serial blood lead tests before, during, and after the abatement work. Those doing the work should comply with OSHA standards; they should use respirators and wear coveralls, which must not be taken to the workers' homes for laundering.

Walls

Removing lead paint from walls, particularly lead paint applied to plaster, is usually difficult. In most cases, a barrier, such as wallboard, hardboard, fiberglass, plywood paneling or a similar durable, fire-resistant material, can be placed over the lead paint on the walls. These materials must be firmly nailed, cemented, or glued in place to prevent the child from removing them. The barriers should be verminproof and, in certain areas of the dwelling (that is, next to furnaces and stoves and in common hallways), fire retardant. Wallpaper painted with lead paint should be stripped off to the maximum extent possible.

Woodwork

Lead-based paint in unsound condition on both interior and exterior *wood trim* (for example, *window units, door units, stair risers, bannisters, and railings*) presents considerable danger for children. Paint can be removed from wood surfaces by heat (from gas torches and heat guns), sanding, scraping, and with liquid paint removers. All of these methods are hazardous. Most solvents in liquid paint removers evaporate rapidly and are flammable and toxic. These removers must be used with the utmost caution and only in well-ventilated areas with proper protective clothing and equipment. When the underlying wood has rotted, no attempt should be made to remove the paint. Instead, the wood should be replaced, including, when necessary, entire window units and doors or door frames. Exterior rotted wood should also

be replaced. When torches, heat guns, and sanding devices are used to remove paint, air lead levels increase enormously in the work area. Of these, sanding is by far the worst offender. It also produces the greatest deposition of lead in dust, with rates as high as 10 mg of lead/sq ft/hour (Inskip and Attenbury, 1983). Therefore, fine sanding down to the bare wood surface is not recommended. Scraping the surface after a heat gun has been used will probably produce fewer fine particles than sanding.

The above information emphasizes the urgency of proper cleanup after lead-based paint has been removed. After the dust has settled, the entire area, including walls, floors, and ceiling, should be vacuumed, preferably with an industrial vacuum cleaner. All surfaces should be wet-scrubbed with phosphate-containing detergents. Immediately thereafter, all surfaces from which paint has been removed should be repainted with lead-free paint. For safe disposal the debris should be placed in a toxic waste dump approved by the Environmental Protection Agency, not in an ordinary landfill or storm or sanitary sewer system. For best results, the wet cleaning procedures should be repeated (Milar and Mushak, 1982). Workers who remove the paint should be responsible for the cleanup, inasmuch as many of the affected families have neither the equipment nor the resources to carry out an adequate cleanup.

Supplemental Addresses

Children often spend substantial amounts of time with relatives or babysitters who live at a different address. If lead-based paint in unsound condition is found at these addresses, it should be removed in the manner described. Similarly, day-care centers and other facilities may be located in old buildings with lead-based paint. These, too, should be checked and handled accordingly.

Followup

The effectiveness of the initial abatement can be determined only through coordinated medical and environmental followup. When the initial abatement has been inadequate, a high recurrence rate of blood lead levels above 50 μg/dl has been found (Chisolm, 1983). Ideally, a communitywide code-enforcement program should be developed to remove all lead-based paint in housing. But, until then, the appropriate governmental unit in which the child lives is responsible for identifying and abating lead hazards for children with lead toxicity. Removing lead hazards in housing is *the* major factor in the success of a lead poisoning prevention program.

AIRBORNE LEAD

Blood lead levels are decreasing as the use of leaded gasoline decreases (Annest et al., 1983). In terms of reducing background blood lead levels, removing lead from gasoline as rapidly as feasible is probably *the* most important public health measure.

Emissions from industrial sources should be reduced sufficiently to achieve the current ambient air lead standard. New factories, as part of their licensing specifications, should be required to have minimal lead emissions.

The public should be informed about the hazards associated with burning old battery casings, colored newsprint, waste oil, and lead-painted wood.

SOIL AND DUST

The optimal goal is to prevent lead from being transferred from any source to soil and dust. For the goal to be reached, air lead levels must be reduced to near zero. For those areas where concentrations of lead in soil and dust are high, large-scale excavation of soil or relocation of populations is the ideal means of reducing the exposure of children to lead.

When the lead content of household dust is high, wet-mopping and other cleanup measures help reduce children's blood lead levels (Charney et al., 1983). These measures provide a reasonable, short-term and mid-term solution to the problem of contaminated house dust.

In severely contaminated residential areas, unless an effective barrier can be established between the children and the soil, surface soil must be removed and replaced with soil having a low lead content.

FOOD AND WATER

The lead content of air and soil, important contributors to the contamination of food and water, should be reduced. Food cans should be made so that lead does not leach from soldered seams. Lead is also added inadvertently to foods during processing and handling (Wolnik et al., 1983). Although the percentage of canned foods packaged in cans with lead-soldered side seams has declined substantially, some are still packaged this way. These foods should not be stored in the opened cans because, after the cans have been opened, even more lead migrates from the side seam into the food.

When feasible, lead plumbing and lead water mains should be replaced. Water from taps in the home should be assessed for lead content. If a hazard is found, consumers should be educated to run water for several minutes before drinking it and not to drink water from the "hot" side of the tap. Acidic water supplies should be alkalinized to help prevent leaching.

OCCUPATIONAL

Ideally, engineering features should prevent workers from being exposed to lead dust and vapors. When workers are exposed, compliance with Occupational Safety and Health Administration (OSHA) regulations appears to be effective in protecting them and in preventing them from transporting lead home to children. Under the OSHA lead standard, factories that use lead must provide workers with facilities for showering and changing

clothes and shoes before going home from work. This standard now applies only to industries covered by OSHA regulations. For the protection of children, it should be extended to all industries that use lead. The prevention of lead exposure to the fetus needs special emphasis. Women of childbearing age should be excluded from working at jobs where significant lead exposure occurs.

LEAD-GLAZED POTTERY

All glazed pottery used for foodstuff should be free of leachable lead. Hobbyists and consumers should be educated to the risks associated with pottery glazes. Consumers should not use pottery for cooking or for storing food or beverages unless the pottery has recently been determined to be free of leachable lead.

VIII. Health Education

The community and especially parents of preschool children who live in older, deteriorating neighborhoods should be informed at every available opportunity of the need to have children screened periodically for lead poisoning. Basic preventive measures should be emphasized. These include frequent wet mopping and vacuuming of accessible paint flakes and dust to reduce potential lead hazards in the child's environment. The danger of ingesting paint chips, dust, and soil should be stressed. Older siblings of children at high risk should also be informed about the sources and risks of lead poisoning because they often take care of younger children.

If a child is screened and the lead level is not elevated, the risk remains, and until the sixth birthday, rescreening is required, particularly during the summer. Until hazard-free housing is available for all and other high-risk sources of lead are removed, periodic screening will reduce the risk of lead poisoning.

Education should start when the child is screened, and physicians, nurses, environmentalists, and aides should reinforce it at every opportunity. When a child is found to have lead toxicity, education of the family is essential for successful followup of the child. The family must be fully informed about the condition and the clinical and environmental actions to follow. Health professionals must emphasize the importance of the family's understanding the child's condition, its cause, and the possible result of lead toxicity. In addition, they should stress the importance of the child's having a balanced diet that includes enough calcium and iron.

IX. Reporting Lead Toxicity and Elevated Blood Lead Levels

Primary care physicians and persons in charge of screening programs should report both presumptive and confirmed cases of lead toxicity to the appropriate health agency, and laboratories performing blood lead or EP tests should report any abnormal results to the appropriate health agency.

X. References

Angle CR, McIntire MS. Low level and inhibition of erythrocyte pyrimidine nucleotidase. Environ Res 1978;17:296-302.

Annest JL, Pirkle JL, Makuc D, Neese JW, Bayse DD, Kovar MG. Chronological trend in blood lead levels between 1976 and 1980. N Engl J Med 1983; 308:1373-7.

Baker EL Jr, Folland DS, Taylor TA, et al. Lead poisoning in children of lead workers: home contamination with industrial dust. N Engl J Med 1977;296:260-1.

Baker EL Jr, Hayes CG, Landrigan PJ, et al. A nationwide survey of heavy metal absorption in children living near primary copper, lead, and zinc smelters. Am J Epidemiol 1977;106:4.

Barltrop D. The prevalence of pica. Am J Dis Child 1966;112:116-23.

Barltrop D, Khoo HE. The influence of nutritional factors on lead absorption. Postgrad Med J 1975;51:795-800.

Beattie AD, Moore MR, Devenay WT, et al. Environmental lead pollution in an urban soft water area. Br Med J 1972;2:491.

Beloian A. Use of a food consumption model to estimate human contaminant intake. Proceedings of the International Workshop on Exposure Monitoring. Las Vegas, Nev., USA, Oct. 19-22, 1981. Environ Monit Assess 1982;2(1-2):115-28.

Benignus BA, Otto DA, Muller KE, Seiple KJ. Effects of age and body lead burden on CNS function in young children: II. EEG spectra. Electroencephalogr Clin Neurophysiol 1981;52:240-8.

Billick IH, Shier DR, Curran AS. Relation of pediatric blood lead levels to lead in gasoline. Environ Health Perspect 1980;34:213-7.

Blumberg WE, Eisinger J, Lamola AA, Zuckerman DM. The hematofluorometer. Clin Chem 1977;23(2): 270-4.

Buhrmann E, Mentzer WC, Lubin BH. The influence of plasma bilirubin on zinc protoporphyrin measurement by a hematofluorometer. J Lab Clin Med 1978;91(4): 710-6.

Burchfiel JL, Duffy FH, Bartels PH, Needleman HL. The combined discriminating power of quantitative electroencephalography and neuropsychologic measures in evaluating central nervous system effects of lead at low levels. In: Needleman HL, ed. Low level lead exposure: the clinical implications of current research. New York: Raven Press: 1980:75-89.

Byers RK, Lord EE. Late effects of lead poisoning on mental development. Am J Dis Child 1943;66:471.

Caprio RJ, Margulis HL, Joselow MM. Lead absorption in children and its relation to urban traffic densities. Arch Environ Health 1974;28:195-7.

Cavalleri A, Baruffini A, Minoia C, Bianco L. Biological response of children to low levels of inorganic lead. Environ Res 1981;25:415-23.

Center for Disease Control (CDC). Increased lead absorption and lead poisoning in young children: a statement by the Center for Disease Control. Atlanta: US Department of Health, Education, and Welfare, 1975.

Center for Disease Control (CDC). Preventing lead poisoning in young children: a statement by the Center for Disease Control: April 1978. Atlanta: US Department of Health, Education, and Welfare, 1978.

Charney E, Kessler B, Farfel M, Jackson D. Childhood lead poisoning: a controlled trial of the effect of dust-control measures on blood lead levels. N Engl J Med 1983;309(18):1089-93.

Chisolm JJ Jr. Treatment of lead poisoning. Modern Treatment 1967;4(4):710-28.

Chisolm JJ Jr. The use of chelating agents in the treatment of acute and chronic lead intoxication in childhood. J Pediatr 1968;73(1):1-38.

Chisolm JJ Jr. Lead poisoning. Sci Am 1971;224:15-23.

Chisolm JJ Jr. Relationship between level of lead absorption in children and type, age, and condition of housing in Baltimore, Maryland, USA. In: Proceedings of the International Conference on Heavy Metals in the Environment: Heidelberg, West Germany. Edinburgh: CEP Consultants, 1983:vol 1, 282-5.

Dallman PR. Blood and blood forming tissues; red blood cells. In: Rudolph JM, Hoffman JIE, eds. Pediatrics. Norwalk, Connecticut: Appleton Century Crofts, 1982:1035-87.

De la Burde B, Choate MS Jr. Does asymptomatic lead exposure in children have latent sequelae? J Pediatr 1972;81:1088-91.

De la Burde B, Choate MS. Early asymptomatic lead exposure and development at school age. J Pediatr 1975;87:638-42.

Facchetti S, Geiss F. Isotopic lead experiment: status report. Brussels-Luxembourg: Office for Official Publications of the European Communities, 1982.

Feldman RG, Hayes MK, Younes R, Aldrich FD. Lead neuropathy in adults and children. Arch Neurol 1977:34:481-8.

Hammond PB, Bornschein RL, Succop P. Dose-effect and dose-response relationships of blood lead to erythrocytic protoporphyrin in young children. Environ Res (in press), 1984.

Inskip M, Attenbury N. The legacy of lead-based paint: potential hazards to "do-it-yourself" enthusiasts and children. In: Proceedings of the International Conference on Heavy Metals in the Environment: Heidelberg, West Germany. Edinburgh: CEP Consultants, 1983:vol 1, 286-9.

Johnson DE, Tillery JB, Prevost RJ. Levels of platinum, palladium, and lead in populations of southern California. Environ Health Perspect 1975;12:27-33.

Kaul B, Davidow B, Eng YM, Gewirtz MH. Lead, erythrocyte protoporphyrin, and ferritin levels in cord blood. Arch Environ Health 1983;38:296-300.

Kaul B, Slavin G, Davidow B. Free erythrocyte protoporphyrin and zinc protoporphyrin measurements compared as primary screening methods for detection of lead poisoning. Clin Chem 1983;29(3):1467-70.

Klein M, Namer R, Harpur E. Earthenware containers as a source of fatal lead poisoning: case study and public health considerations. N Engl J Med 1970;283:669-72.

Lamm SH, Cole BL, Glynn KL, Ullmann WW. Lead content of milks fed to infants, 1971-1972. N Engl J Med 1973;289:574-6.

Lamola AA, Joselow M, Yamane T. Zinc protoporphyrin (ZPP): a simple, sensitive, fluorometric screening test for lead poisioning. Clin Chem 1975;21(1):93-7.

Landrigan PF, Baker EL, Himmelstein JS, Stein GF, Weddig JP, Straub WE. Exposure to lead from the Mystic River bridge: the dilemma of deleading. N Engl J Med 1982;306:673-6.

Lane RE. The care of the lead worker. Br J Ind Med 1949;6:125-43.

Langer EE, Haining RG, Labbe RF, Jacobs P, Crosby EF, Finch CA. Erythrocyte protoporphyrin. Blood 1972;40(1):112-28.

Lin-Fu JS. Preventing lead poisoning in children. Children today. Rockville, Maryland: Maternal and Child Health Service, 1973; DHEW publication no. (HSM) 73-5113.

Mahaffey KR. Nutritional factors in lead poisoning. Nutr Rev 1981;39(10):353-62.

Mahaffey KR, Annest JL, Roberts J, Murphy RS. National estimates of blood lead levels: United States 1976-1980: association with selected demographic and socioeconomic factors. N Engl J Med 1982;307:573-9.

Mahaffey KR, Michaelson IA. The interaction between lead and nutrition. In: Needleman HL, ed. Low level lead exposure: the clinical implications of current research. New York: Raven Press, 1980:159-200.

Mahaffey KR, Rosen JF, Chesney RW, Peeler JT, Smith CM, Deluca HF. Association between age, blood lead concentration, and serum 1,25-dihydroxycholecalciferol levels in children. Am J Clin Nutr 1982;35: 1327-31.

Mahaffey-Six KR, Goyer RA. The influence of iron deficiency on tissue content and toxicity of ingested lead in the rat. J Lab Clin Med 1972;79:128-36.

Mantere P, Hanninen H, Hernberg S. Subclinical neurotoxic lead effects: two-year follow-up studies with psychological test methods. Neurobehav Toxicol Teratol 1982;4:725-7.

Markowitz ME, Rosen JF. Assessment of lead stores in children: validation of an 8-hour $CaNa_2EDTA$ provocative test. J Pediatr 1984;104:337-41.

Mielke HW, Anderson JC, Berry KJ, Mielke PW, Chaney RL, Leech M. Lead concentrations in inner-city soils as a factor in the child lead problem. Am J Public Health 1983;73(12):1366-9.

Milar CR, Mushak P. Lead contaminated housedust: hazard, measurement and decontamination. In: Chisolm JJ Jr, O'Hara DM, eds. Lead absorption in children: management, clinical, and environmental aspects. Baltimore-Munich: Urban & Schwarzenberg, 1982:143-52.

Morse DL, Watson WN, Housworth J, Witherell LE, Landrigan PJ. Exposure of children to lead in drinking water. Am J Public Health 1979;69:711-2.

National Academy of Sciences (NAS), Committee on Toxicology. Recommendations for the prevention of lead poisoning in children. Washington, D.C.: National Research Council, July 1976.

National Center for Health Statistics (NCHS). Blood lead levels for persons ages 6 months-74 years: United States, 1976-80. Hyattsville, Maryland: US Department of Health and Human Services, 1984.

Needleman HL, Gunnoe C, Leviton A, et al. Deficits in psychologic and classroom performance of children with elevated dentine lead levels. N Engl J Med 1979;300:689-95.

Needleman HL, Rabinowitz M, Leviton A, Linn S, Schoenbaum S. The relationship between prenatal exposure to lead and congenital anomalies. JAMA 1984;251:22.

Osterud HT, Tufts E, Holmes MA. Plumbism at the Green Parrot Goat Farm. Clin Toxicol 1973;6:1-7.

Otto D, Benignus V, Muller K, et al. Effects of low to moderate lead exposure on slow cortical potentials in young children: two-year follow-up study. Neurobehav Toxicol Teratol 1982;4:733-7.

Paglia DE, Valentine WN, Fink K. Further observations on erythrocyte pyrimidinenucleotidase deficiency and intracellular accumulation of pyrimidine nucleotides. J Clin Invest 1977;60:1362-6.

Perlstein MA, Attala R. Neurologic sequelae of plumbism in children. Clin Pediatr 1966;5:292.

Piomelli S. Free erythrocyte porphyrins in the detection of undue absorption of Pb and of Fe deficiency. Clin Chem 1977;23(2 Pt 1):264-9.

Piomelli S. Blood lead concentrations in a remote Himalayan population. Science 1980;210:1135-7.

Piomelli S, Rosen JF, Chisolm JJ, Graef JW. Management of childhood lead poisoning. J Pediatr 1984;105(4):523-32.

Piomelli S, Seaman C, Zullow D, Curran A, Davidow B. Threshold for lead damage to heme synthesis in urban children. Proc Natl Acad Sci USA 1982;79:3335-9.

Rabinowitz MB, Needleman HL. Temporal trends in the lead concentrations of umbilical cord blood. Science 1982;216:25.

Rabinowitz MB, Needleman HL. Petrol lead sales and umbilical cord blood lead levels in Boston, Massachusetts. Lancet 1983;63(1):8314-5.

Rabinowitz MB, Wetherill GW, Kopple JD. Kinetic analysis of lead metabolism in healthy humans. J Clin Invest 1976;58:260-70.

Reeves JD, Yip R, Kiley VA, Dallman PR. Iron deficiency in infants: the influence of mild antecedent infection. J Pediatr (in press), 1984.

Reigart JR, Whitlock NH. Longitudinal observations of the relationship between free erythrocyte porphyrins and whole blood lead. Pediatrics 1976;57:54.

Roels H, Buchet JP, Lauwerys R, et al. Impact of air pollution by lead on the heme biosynthetic pathway in school-age children. Arch Environ Health 1976;31(6):310-5.

Rosen JF, Chesney RW, Hamstra A, DeLuca HF, Mahaffey KR. Reduction in 1,25-dihydroxyvitamin D in children with increased lead absorption. N Engl J Med 1980;302:1128-31.

Royal Commission on Environmental Pollution. Ninth report: lead in the environment. Presented to Parliament by command of Her Majesty. London: Her Majesty's Stationery Office, April 1983.

Saenger P, Rosen JF, Markowitz M. Diagnostic significance of edetate disodium calcium testing in children with increased lead absorption. Am J Dis Child 1982;136:312-5.

Sayre JW, Charney E, Vostal J, Pless IB. House and hand dust as a potential source of childhood lead exposure. Am J Dis Child 1974;127:167.

Seppalainen AM, Hernberg S. A follow-up study of nerve conduction velocities in lead exposed workers. Neurobehav Toxicol Teratol 1982;4:721-3.

Winneke G. Neurobehavioural and neuropsychological effects of lead. Letter. Lancet. Sept 4, 1982:550.

Wolnik KA, Fricke KL, Caspar SG, et al. Elements in major raw agricultural crops in the United States. I. Cadmium and lead in lettuce, peanuts, potatoes, soybeans, sweet corn and wheat. J Agric Food Chem 1983;31:1240-4.

World Health Organization (WHO), Task Group on Environmental Health Criteria for Lead. Environmental health criteria 3: lead. Geneva: WHO, 1977.

Yip R, Schwartz S, Deinard AS. Screening for iron deficiency with the erythrocyte protoporphyrin test. Pediatrics 1983;72:214-9.

Yule W, Lansdown R, Millar IB, Urbanowicz MA. The relationship between blood lead concentrations, intelligence and attainment in a school population: a pilot study. Dev Med Child Neurol 1981;23:567-76.

Appendix

Reprinted with permission by the
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
from the Journal of Pediatrics, Volume 105, October 1984, Number 4, pp. 523–532

SPECIAL ARTICLE

Management of childhood lead poisoning

Sergio Piomelli, M.D., John F. Rosen, M.D., J. Julian Chisolm, Jr., M.D., and John W. Graef, M.D. *New York, New York, Baltimore, Maryland, and Boston, Massachusetts*

CHELATION TREATMENT for childhood lead poisoning may be life-saving and decreases the body burden of lead far more rapidly than normal excretory processes can.[1] Furthermore, chelating agents markedly enhance removal of that fraction of body lead that is readily mobile and considered to be the most toxic.[1-4] However, lead poisoning is a wholly preventable disorder caused by the wide dissemination of lead into the environment.[7,8] Medical treatment with chelating agents must not be considered a substitute for dedicated preventive efforts to eradicate controllable sources of lead (e.g., substandard housing that contains lead-bearing paints, combustion of leaded gasoline). Although repeated courses of chelation therapy may be necessary for medical reasons, the source(s) of environmental lead must be identified and removed for preventive reasons.

This review is based on our experience in four different lead poisoning treatment clinics and reflects our consensus on current management criteria.

PHARMACOLOGIC CONSIDERATIONS

Lead poisoning is treated with drugs capable of binding (chelating) lead and of enhancing its excretion. These drugs deplete the soft tissues of lead and may thus reduce its acute toxicity. They are also used, in asymptomatic children, to reduce a potentially dangerous body burden of lead. All drugs are used to enhance the slow process of natural lead excretion. All drugs have potential side effects and should be used carefully. A brief description of the essential pharmacologic aspects of the various drugs follows. Detailed guidelines for specific situations are given in the next section.

From the Division of Pediatric Hematology/Oncology, Department of Pediatrics, Columbia University, College of Physicians and Surgeons; the Department of Pediatrics and Clinical Research Center, Albert Einstein College of Medicine, Montefiore Medical Center; the Department of Pediatrics, John Hopkins University School of Medicine and the John F. Kennedy Institute, and the Baltimore City Hospitals; and the Division of Clinical Pharmacology and Toxicology, Department of Pediatrics, Children's Hospital Medical Center.

Supported by Grant ES02343 from the National Institutes of Health, and by a grant from the Francis Florio Fund of the New York Community Trust (S.P.); by Projects 917 and MCJ-240458, Maternal and Child Health, Department of Health and Human Services (J.J.C.); and by Grants ES01060-09 and RR-53 from the National Institutes of Health, and by Project MCJ-360488-01, Maternal and Child Health, DHHS (J.F.R.).

Reprint requests: Sergio Piomelli, M.D., Columbia University, College of Physicians and Surgeons, Division of Pediatric Hematology/Oncology, 630 West 168th St., New York, NY 10032.

BAL

Mechanism of action. Two molecules of BAL combine with one atom of heavy metal to form a stable complex. BAL enhances fecal as well as urinary excretion of lead and diffuses well into erythrocytes. It can be administered in the presence of renal impairment because it is predominantly excreted in bile.[1]

BAL	(British anti-lewisite) Dimercaptopropanol
$CaNa_2$-EDTA	Disodium calcium-edetate
EP	Erythrocyte protoporphyrin
G-6-PD	Glucose-6-phosphate dehydrogenase

Route of administration and dosage. BAL is available only in oil for intramuscular administration. It must be given every 4 hours. Dosages are discussed below.

Toxicity. Mild febrile reactions may occur, and transient elevation of hepatic transaminase activities may be observed. Other minor adverse effects include, in order of frequency, nausea and occasional vomiting, headache, mild conjunctivitis, lacrimation, rhinorrhea, and salivation. Most side effects are transient and rapidly subside as the drug is metabolized and excreted.

Precautions. In patients with G-6-PD deficiency, BAL should be used only in life-threatening situations, because it may induce hemolysis. Medicinal iron should never be administered during BAL therapy, because the combination is very toxic. If iron deficiency coexists, its management should be postponed until BAL therapy is concluded. In cases of extreme anemia blood transfusions are preferable.

$CaNa_2$-EDTA[9-14]

Only $CaNa_2$-EDTA (calcium disodium versenate) should be used for treatment of lead poisoning. Na_2-EDTA (endrate disodium) should never be used for treatment of lead poisoning, because it may induce fatal hypocalcemia and tetany.

Mechanism of action. $CaNa_2$-EDTA increases urinary lead excretion 20- to 50-fold. $CaNa_2$-EDTA does not enter the cells; thus it removes lead from the extracellular compartment. Indirectly, lead is reduced in the soft tissue, central nervous system, and red blood cells.[1]

Route of administration and dosage. $CaNa_2$-EDTA may be given intravenously or intramuscularly. The preferred and most effective route is a continuous intravenous infusion; a given dose is most effective if infused over 6 hours.[10] $CaNa_2$-EDTA should be diluted to a concentration <0.5% in dextrose and water or 0.9% saline solution. When administered intravenously as a single dose, it should be similarly diluted and administered by slow infusion over 15 to 20 minutes. Intramuscular administration of $CaNa_2$-EDTA is extremely painful and should be given with procaine (0.5%) by deep injection.

$CaNa_2$-EDTA should not be given orally, because it may enhance absorption of lead from the gastrointestinal tract.

Dosages vary in different situations and are discussed below. In all cases, courses should be limited to 5 days, followed by at least 2- to 5-day intervals to allow recovery from zinc depletion.

Toxicity. The kidney is the principal site of toxicity. Renal toxicity is dose related, reversible, and rarely occurs at doses <1500 mg/m^2. The renal toxicity may be reduced by assuring adequate diuresis. $CaNa_2$-EDTA should never be given in the absence of an adequate urine flow. Before administering it intramuscularly in children in good clinical condition, adequate oral intake of fluids must be assured.

Precautions. During chelation with $CaNa_2$-EDTA, urine and its sediment, BUN, serum creatinine, and liver function tests must be carefully monitored. The appearance of protein and formed elements in urinary sediment, and rising BUN and serum creatinine values signify impending renal failure, the serious toxicity associated with excessive or prolonged administration of EDTA. Inasmuch as $CaNa_2$-EDTA may deplete zinc stores and cellular injury may be associated with zinc depletion, $CaNa_2$-EDTA should be used with great caution.

$CaNa_2$-EDTA, used alone without concomitant BAL therapy, may aggravate symptoms in patients with very high blood lead levels. Thus it should be used exclusively in conjunction with BAL when the blood lead level is >70 μg/dl or clinical symptoms consistent with lead poisoning are present. In such cases the first dose of BAL should always precede the first dose of $CaNa_2$-EDTA by at least 4 hours.

D-Penicillamine. D-Penicillamine is not licensed by the Food and Drug Administration for the treatment of lead poisoning. Its use for this indication is thus to be considered experimental. It is the only commercially available oral chelating agent. It can be given over a long period (days). Toxic side effects may occur in as many as 20% of patients given the drug.[17]

Mechanism of action. D-Penicillamine enhances urinary excretion of lead, although not as effectively as $CaNa_2$-EDTA. Its specific mechanism of action is not well understood.

Route of administration and dosage. D-Penicillamine is administered orally. It is currently available in capsules (125 and 250 mg). These capsules may be opened and suspended in liquid, if necessary. The usual dose is 30 mg/kg. Side effects can be minimized by initiating therapy with small doses, for example, 25% of the desired final dose, increased after 1 week to 50% and again after 1 week to the full dose, while monitoring for possible toxicity.

Toxicity. The main side effects of D-penicillamine are reactions resembling those of penicillin sensitivity, including fevers, rashes, leukopenia, thrombocytopenia, and eosinophilia. Rarely, more severe and even life-threatening reactions (autoimmune hemolytic anemia, Stevens-Johnson syndrome) have been observed. Anorexia, nausea, and vomiting are infrequent. Of most concern, however, are isolated reports of nephrotoxicity, possibly from hypersensitivity reactions. For these reasons, patients should be carefully and frequently monitored for clinically obvious side effects, and frequent blood counts, urinalysis, and renal function tests should be performed. In particular, blood counts and urinalysis should be done twice weekly, at least in the first 3 weeks of treatment. If the absolute neutrophil count falls to <1500/μl it should be immediately rechecked, and treatment should be stopped if it falls to <1200/μl. D-Penicillamine should therefore not be given on an outpatient basis if there is any question about compliance with appointments.

D-Penicillamine should not be administered in patients with known penicillin allergy.

New agents. Dimercaptosuccinic acid and 2-3-dimercapto-propane-1-sulphonate are both water-soluble derivatives of BAL. Although both appear promising and safe and have been used successfully in treatment of other heavy-metal poisoning, these drugs are presently in the investigative stage for the treatment of lead poisoning.[18,19]

ACUTE LEAD ENCEPHALOPATHY

Acute lead encephalopathy is characterized clinically by some or all of the following symptoms: coma, seizures, bizarre behavior, ataxia, apathy, incoordination, vomiting, alteration in the state of consciousness, and subtle loss of recently acquired skills. Any one or a matrix of these symptoms associated with an elevated blood lead concentration constitutes an acute medical emergency. Lead encephalopathy is almost always associated with a blood lead concentration >100 μg/dl, although it has been reported at blood lead levels as low as 70 μg/dl.[1,4]

General supportive management. All oral intake is prohibited initially until the child's condition has significantly improved. Parenteral fluid therapy is begun immediately; volume is restricted to basal requirements plus a careful assessment of continuing losses. Excessive intravenous fluid administration must be avoided. Once urine flow is established by administering dextrose in water (10 to 20 ml/kg body weight), chelation treatment, already begun with BAL alone for one dose, is continued with simultaneous administration of $CaNa_2$-EDTA. An adequate flow of urine must be established before intravenous chelation therapy. Parenteral fluid therapy minimizes vomiting that may accompany administration of BAL and ensures prompt excretion of $CaNa_2$-EDTA, a drug excreted exclusively by the kidney. For initial control of seizures, diazepam or paraldehyde is the preferred drug. Barbiturate and phenytoin are reserved for the long-term management of recurring seizures, only after the acute episode is managed and consciousness has been fully recovered. Although it is desirable to evacuate any residual lead from the bowel, this should not delay the start of chelation therapy. Surgical decompression and hypertonic solutions to relieve intracranial pressure and cerebral edema are contraindicated.

The diagnosis of acute lead encephalopathy can usually be made without lumbar puncture, which is extremely risky because of the presence of increased intracranial pressure. In fulminant lead encephalopathy, increased intracranial pressure may be present in the absence of any of the usual preliminary signs (changes in blood pressure, pulse or respiration, retinal hemorrhage or edema). If examination of the CSF is absolutely essential for the differential diagnosis, the very least amount of fluid, not exceeding a few drops, should be carefully obtained.

Chelation therapy. Treatment is begun with a priming dose of 75 mg/m² BAL only, given by deep intramuscular injection; BAL is administered at a dose of 450 mg/m²/24 hours, in divided doses of 75 mg/m² every 4 hours. Once the priming dose is given and an adequate urine flow is established, administration of $CaNa_2$-EDTA is begun at a dose of 1500 mg/m²/24 hours. $CaNa_2$-EDTA is given by continuous intravenous drip in dextrose and water or 0.9% saline solution. The concentration of $CaNa_2$-EDTA should not exceed 0.5% in the parenteral fluid. (In the treatment of acute encephalopathy, restriction of parenteral fluids takes precedence, so that $CaNa_2$-EDTA may have to be given intramuscularly if fluid overload is to be avoided.) Combined BAL–$CaNa_2$-EDTA therapy is given for a total of 5 days. During treatment, renal and hepatic function and serum electrolyte levels should be monitored daily.

A second course of chelation therapy with $CaNa_2$-EDTA alone or with BAL, depending on the blood lead concentration, may be required after a 2-day interval. A third course is required only if the blood lead concentration rebounds to a value ≥50 μg/dl within 48 hours after treatment. Unless there are compelling clinical reasons, it is desirable to wait at least 5 to 7 days before beginning a third course of $CaNa_2$-EDTA.

SYMPTOMATIC LEAD POISONING WITHOUT ENCEPHALOPATHY

Symptomatic lead poisoning without encephalopathy is characterized by one or several of the following symptoms: decrease in play activity, lethargy, anorexia, sporadic vomiting, intermittent abdominal pain, and constipation. Symptomatic lead poisoning is usually associated with a blood lead concentration >70 μg/dl, although occasionally may be associated with a blood lead concentration as low as 50 μg/dl. *If the blood lead concentration is <50 μg/dl, other diagnostic possibilities should be vigorously sought.* Because all symptomatic children potentially have acute lead encephalopathy, treatment and supportive measures must be instituted immediately on an emergency basis.[1,4]

General supportive management. All oral intake is prohibited and the guidelines of parenteral fluid therapy are followed as noted above for the treatment of lead encephalopathy. Intravenous fluids are given at a rate consistent with basal requirements plus ongoing losses. Excessive fluid administration must be avoided.

Chelation therapy. Treatment is begun with a priming dose of 50 mg/m² BAL by deep intramuscular injection; BAL is administered at a dose of 300 mg/m²/24 hours in divided doses of 50 mg/m² every 4 hours. Once the priming dose is given and an adequate urine flow is established, administration of $CaNa_2$-EDTA is begun at a dose of 1000 mg/m²/24 hours. $CaNa_2$-EDTA is given by continuous intravenous drip in dextrose and water or 0.9% saline solution. Although continuous infusion of $CaNa_2$-EDTA is preferable, it may be replaced by doses of 175 mg/m² every

4 hours, given either intravenously over 15 to 20 minutes through a heparin lock or by deep intramuscular injection mixed with procaine. The concentration of $CaNa_2$-EDTA should not exceed 0.5% in the parenteral fluid. Combined BAL–$CaNa_2$-EDTA therapy is given for a total of 5 days.

During treatment, renal and hepatic function and serum electrolyte levels should be monitored daily. It is advisable to measure the blood lead concentration daily. (It will be necessary to interrupt the $CaNa_2$-EDTA infusion for 1 hour before this sample is obtained, to avoid a spuriously high value). If the blood lead concentration reaches ≤ 50 μg/dl, as it may within 3 days of combined BAL–$CaNa_2$-EDTA therapy, BAL may be safely discontinued and $CaNa_2$-EDTA continued for a full 5-day course of treatment. If measurements of blood lead cannot be obtained in time, it is safe to continue BAL for the full 5-day course. Except under highly unusual circumstances, $CaNa_2$-EDTA should not be administered for more than 5 consecutive days.

A second course of chelation therapy may be required after a 2- to 4-day interval, to be started with $CaNa_2$-EDTA alone or with concomitant BAL, depending on the blood lead concentration. A third course may be required if the blood lead concentration rebounds to a value ≥ 50 μg/dl within 7 to 10 days after treatment. Unless there are compelling clinical reasons, it is highly desirable to allow 5 to 7 days before beginning a third course of $CaNa_2$-EDTA.

ASYMPTOMATIC CHILDREN WITH INCREASED BODY BURDEN OF LEAD

Although children with increased body burden of lead are clinically asymptomatic, it is likely that they have pervasive metabolic effects involving heme synthesis,[20-23] red cell nucleotide metabolism,[24] vitamin D and cortisol metabolism[25-27] and renal function,[1-4] and subclinical neurobehavioral effects.[28-31] Some of these profound metabolic and cellular effects of lead have been observed at blood lead concentrations <25 μg/dl.[20, 24, 26, 30, 31]

Diagnostic assessment. In asymptomatic children it is essential to have a firm diagnosis based on an elevated blood lead level before treatment is initiated. Measurements of blood lead concentration in capillary samples are subject to contamination and should never be the only basis for treatment. Treatment should be initiated only after a confirmatory measurement of the venous blood lead concentration. Even when there is strong additional evidence of lead poisoning, such as paint flakes in the abdomen or lead lines in the bones on x-ray examination, it is preferable to wait for a confirmatory measurement of venous blood lead. Although measurements of erythrocyte protoporphyrin may be helpful in evaluating overall toxicity, blood lead measurement is the criterion on which to base a decision as to whether chelation therapy should be considered. (The EP may increase initially during chelation therapy.) Therapeutic decisions should also be based on the results of the $CaNa_2$-EDTA provocative test.

Chelation therapy

Blood lead concentration ≥ 70 μg/dl. If the blood lead level is ≥ 70 μg/dl, BAL and $CaNa_2$-EDTA should be given, in the same doses and with the same guidelines as for treatment of symptomatic lead poisoning without encephalopathy.

A second course of chelation therapy with $CaNa_2$-EDTA alone may be required if the blood lead concentration rebounds to a value ≥ 50 μg/dl within 5 to 7 days after treatment. Unless there are compelling clinical reasons, it is highly desirable to allow at least 5 to 7 days before beginning a second course of $CaNa_2$-EDTA.

Blood lead concentration 56 to 69 μg/dl. If the blood lead value is between 56 and 69 μg/dl, treatment should be limited to $CaNa_2$-EDTA only.

$CaNa_2$-EDTA is given for 5 days at a dose of 1000 mg/m^2/day, preferably by continuous infusion (or in divided doses intravenously as above). Alternatively, however, if environmental control of the lead hazards has been achieved, this treatment may be given on an outpatient basis, at a dose of 1000 mg/m^2/day, preferably by intravenous infusion over 1 hour, with adequate hydration (250 ml/m^2). As a least preferable option, $CaNa_2$-EDTA may be administered intramuscularly mixed with procaine, at the same single daily dose of 1000 mg/m^2 for 5 consecutive days. This route of administration may represent a painful but practical alternative, when circumstances dictate it.

During treatment, renal and hepatic function and serum electrolyte levels should be monitored. A blood lead concentration should be obtained at 72 hours of treatment (it will be necessary to interrupt the $CaNa_2$-EDTA infusion for 1 hour before this sample is obtained, to avoid a spuriously high value) to monitor the effectiveness of treatment.

$CaNa_2$-EDTA treatment should be continued for 5 days. Except under highly unusual circumstances, it should not be administered for more than 5 consecutive days.

A second course of chelation therapy, with $CaNa_2$-EDTA alone, may be required if the blood lead concentration rebounds to a value ≥ 50 μg/dl within 5 to 7 days after treatment. Unless there are compelling clinical reasons, it is highly desirable to allow a period of 5 to 7 days before beginning a second course of $CaNa_2$-EDTA.

Blood lead concentration 25 to 55 μg/dl. When the blood lead value is persistently between 25 and 55 μg/dl and accompanied by EP persistently >35 μg/dl, the decision to proceed with chelation therapy should be based

Table. Choice of chelation therapy based on symptoms and blood lead concentration

Clinical presentation	*Treatment*		*Comments*
Symptomatic children			
Acute encephalopathy			
	BAL	450 mg/m²/day	Start with BAL 75 mg/m² IM every 4 hours.
	$CaNa_2$-EDTA	1500 mg/m²/day	After 4 hours start continuous infusion of $CaNa_2$-EDTA 1500 mg/m²/day.
			Therapy with BAL and $CaNa_2$-EDTA should be continued for 5 days.
			Interrupt therapy for 2 days.
			Treat for 5 additional days, including BAL if blood Pb remains high.
			Other cycles may be needed depending on blood Pb rebound.
Other symptoms			
	BAL	300 mg/m²/day	Start with BAL 50 mg/m² IM every 4 hours.
	$CaNa_2$-EDTA	1000 mg/m²/day	After 4 hours start $CaNa_2$-EDTA 1000 mg/m²/day, preferably by continuous infusion, or in divided doses IV (through a heparin lock).
			Therapy with $CaNa_2$-EDTA should be continued for 5 days.
			BAL may be discontinued after 3 days if blood Pb <50 μg/dl.
			Interrupt therapy for 2 days.
			Treat for 5 additional days, including BAL if blood Pb remains high.
			Other cycles may be needed depending on blood Pb rebound.
Asymptomatic children			
Before treatment, measure venous blood lead.			
Blood Pb >70 μg/dl			
	BAL	300 mg/m²/day	Start with BAL 50 mg/m² IM every 4 hours.
	$CaNa_2$-EDTA	1000 mg/m²/day	After 4 hours start $CaNa_2$-EDTA 1000 mg/m²/day, preferably by continuous infusion, or in divided doses IV (through a heparin lock).
			Treatment with $CaNa_2$-EDTA should be continued for 5 days.
			BAL may be discontinued after 3 days if blood Pb <50 μg/dl.
			Other cycles may be needed depending on blood Pb rebound.
Blood Pb 56 to 69 μg/dl			
	$CaNa_2$-EDTA	1000 mg/m²/day	$CaNa_2$-EDTA for 5 days, preferably by continuous infusion, or in divided doses (through a heparin lock).
			Alternatively, if lead exposure is controlled, $CaNa_2$-EDTA may be given as a single daily outpatient dose IM or IV.
			Other cycles may be needed depending on blood Pb rebound.
Blood Pb 25 to 55 μg/dl			
Perform $CaNa_2$-EDTA provocation test to assess lead excretion ratio (see text).			
If ratio >0.70	$CaNa_2$-EDTA	1000 mg/m²/day	Treat for 5 days IV or IM, as above.
If ratio 0.60 to 0.69			
Age <3 years of age	$CaNa_2$-EDTA	1000 mg/m²/day	Treat for 3 days IV or IM, as above.
Age >3 years of age	No treatment		Repeat blood Pb and $CaNa_2$-EDTA provocation test periodically.
If ratio <0.60	No treatment		Repeat blood Pb and $CaNa_2$-EDTA provocation test periodically.

on positive findings of a carefully performed $CaNa_2$-EDTA provocation test. (It must again be emphasized that chelation therapy should complement, not replace, abatement of controllable lead sources.)

$CaNa_2$-EDTA PROVOCATION TEST. First, a repeated baseline blood lead level is obtained and the patient is asked to empty the bladder. Then $CaNa_2$-EDTA is administered at a dose of 500 mg/m² intravenously in 250 ml/m² of 5% dextrose, infused over 1 hour. (A painful but practical alternative is to administer the same dose intramuscularly mixed with procaine and to encourage the child to drink as much as possible in the first 2 hours). All urine must be collected with lead-free equipment over 8 hours. The urine volume should be carefully measured, and aliquots should be sent to the laboratory for measurement of the concentration of lead. Extreme care should be exercised to use only lead-free equipment. If this is not available in the clinic, it may be best that the entire urine volume be sent to

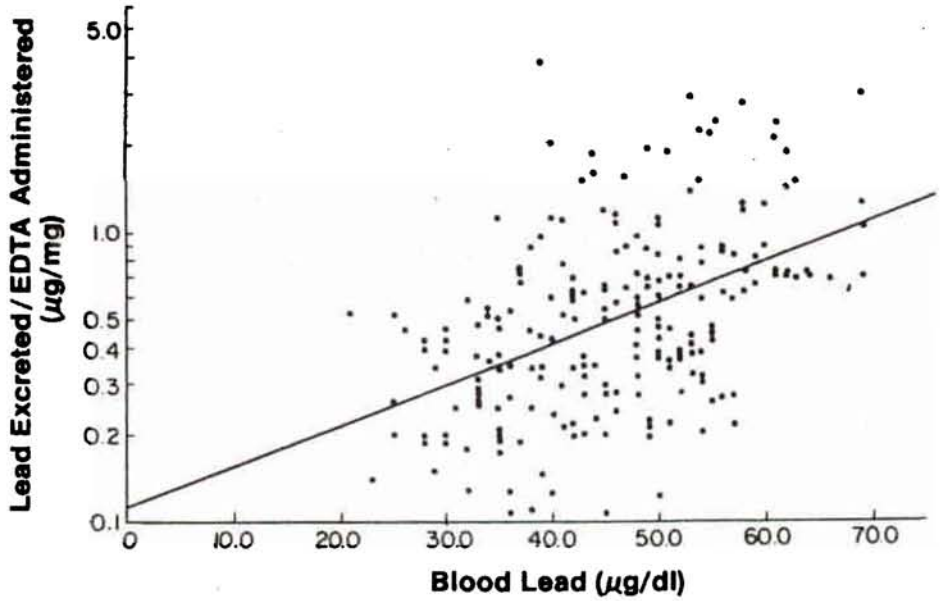


Figure. Lead excretion ratio as a function of blood lead. Data expressed as decimal logarithm of $CaNa_2$-EDTA excretion ratio (μg lead excreted/mg EDTA administered) versus blood lead. There is a significant correlation ($r = 0.466$, $P < 0.001$), with a slope of 0.014 and an intercept of −0.95.

Data shown were obtained by different techniques. At Columbia University, 77 children in an outpatient setting received $CaNa_2$-EDTA as a 20-minute intravenous infusion at a dose of 50 mg/kg, followed by 250 ml/m² 5% dextrose over 1 hour; urine was collected for 7 to 8 hours. At Albert Einstein College of Medicine (Montefiore Hospital), 37 hospitalized children received $CaNa_2$-EDTA intramuscularly with procaine at a dose of 500 mg/m²; urine was collected for 8 hours. At John Hopkins University School of Medicine, 50 hospitalized children received $CaNa_2$-EDTA intramuscularly at a dose of 25 mg/kg at 0 and 12 hours; urine was collected for 24 hours. At Children's Hospital Medical Center, 46 children in the outpatient clinic received $CaNa_2$-EDTA intramuscularly with procaine at a dose of 50 mg/kg; urine was collected for 6 to 7 hours. Despite these differences, slopes and intercept of regression lines were remarkably similar: excretion ratio makes the $CaNa_2$-EDTA provocation test independent of both the dose administered and the child's age and body weight. Therefore, data could be pooled together in a single regression line. Combined data represent, to the best of our knowledge, the largest series of $CaNa_2$-EDTA provocation tests in children.

a laboratory where the volume can be measured with lead-free equipment and aliquots for lead and creatinine measurements can be taken without contaminating the sample.

INTERPRETATION OF $CaNa_2$-EDTA PROVOCATION TEST. The concentration of lead in the urine (in micrograms per milliliter) is multiplied by the volume (in milliliters), to obtain the total excretion (in micrograms). The total urinary excretion of lead (micrograms) is divided by the amount of $CaNa_2$-EDTA given (milligrams) to obtain the "lead excretion ratio":

$$\frac{\text{Lead excreted } (\mu g)}{CaNa_2\text{-EDTA given (mg)}}$$

The $CaNa_2$-EDTA provocation test is considered positive if the lead excretion ratio exceeds 0.60.

The recommendations of the authors are based on their experience with 210 provocation tests[1-3, 6, 32, 33] (Figure). Inspection of the Figure shows that a ratio >0.60 is never obtained in 12 children with blood lead level <30 μg/dl, and is always obtained in 19 children with blood lead level >60 μg/dl. At blood lead level 30 to 39 μg/dl, the ratio is >0.60 in six (11.5%) of 52 children; at blood lead level 40 to 49 μg/dl the ratio is >0.60 in 25 (37.9%) of 66 children; and at blood level 50 to 59 μg/dl the ratio is >0.60 in 30 (49.2%) of 61 children.

It appears, therefore, that a ratio <0.60 represents an appropriate cutoff point to distinguish children with "markedly increased" excretion. (It is not possible to define a normal excretion range because no data are available and it would be unethical to obtain them in children with blood lead values <25 μg/dl. In addition, even the lower blood lead levels observed in children from industrialized countries are significantly higher than those in children from remote areas uncontaminated by lead, which most likely represent the truly normal blood lead level.[34] However, extrapolation from these data predicts, at

blood lead level 1 μg/dl, an excretion ratio of 0.1, six times lower than the proposed cutoff of 0.60).

GUIDELINES FOR TREATMENT BASED ON $CaNa_2$-EDTA PROVOCATION TEST. If the lead excretion ratio is >0.70, a 5-day course of $CaNa_2$-EDTA 1000 mg/m² intramuscularly or intravenously should be given, as above.

If the lead excretion ratio is between 0.60 and 0.69, (1) children younger than 3 years should receive treatment for 3 consecutive days with 1000 mg/m² $CaNa_2$-EDTA, as discussed above; and (2) in children older than 3 years the test should be repeated every 2 to 3 months and treatment started if the lead excretion ratio increases to >0.70 (in which case treatment shall consist of 3 days with 1000 mg/m² $CaNa_2$-EDTA, as above).

In children who have received chelation therapy, repeated cycles are indicated if the blood lead concentration rebounds to within 5 μg/dl of the original value, 7 to 10 days after treatment.

In all children, regardless of age, with elevated blood lead and EP values but with an excretion ratio <0.60, blood lead and EP should be monitored frequently. If the elevation of blood lead values persists, the $CaNa_2$-EDTA provocation test should be repeated periodically (every 2 to 3 months).

IMMEDIATE TREATMENT FOLLOW-UP

The goal of chelation therapy is to permanently reduce the blood lead level to <25 μg/dl and that of EP to <35 μg/dl. To achieve this goal it may be necessary to give several courses of treatment. It cannot be overemphasized, however, that repeated courses of therapy are counterproductive unless the source of lead has been identified and eradicated. Children receiving chelation therapy should not be released from the hospital until all lead hazards in their homes and elsewhere have been controlled and eliminated and, if necessary, suitable alternative housing has been arranged. With vigorous public health measures complete and safe abatement should be achieved during the treatment period.[8] If a child with elevated blood lead concentration cannot be moved to new housing, multiple repeated courses of $CaNa_2$-EDTA in a clinically asymptomatic child with stable blood lead values may be counterproductive; parents may despair at the ineffectiveness of therapy and fail to return to the clinic. It is more important in these unfortunate situations to maintain follow-up so that a rise in blood lead concentrations is detected promptly.

At the end of each treatment cycle the blood lead concentration usually declines to values <25 μg/dl. However, within a few days reequilibration takes place and results in a rebound; thus the blood lead level must be rechecked 7 to 10 days after the end of treatment.

If the blood lead level rebounds to within 5 μg/dl of the value before the last cycle, additional treatment cycles are indicated (unless the concentration after rebound is <25 μg/dl). A blood lead concentration that rebounds to above the pretreatment value is evidence of renewed and excessive intake.

If the blood lead level remains low, its measurement must be repeated, initially biweekly, then at monthly intervals, to assure that the decreased level is permanent.

Iron deficiency states, which may accompany lead poisoning, require therapeutic doses of iron in addition to the correction of other possible nutritional deficiencies.

LONG-TERM CLINICAL FOLLOW-UP AND MANAGEMENT

The vast majority of children with lead poisoning now referred to pediatricians from screening clinics are asymptomatic. Acute lead encephalopathy is rare. Lead poisoning (with or without clinical symptoms) should be reported to the local health authorities, who usually have prime responsibility for environmental investigation and abatement of lead hazards in the home or elsewhere.

Because lead has been widely disseminated into the environment, thereby providing multiple opportunities for repeated overexposure, lead poisoning should be managed as a chronic disorder. A team approach involving public health personnel, pediatrician, pediatric nurse practitioner, and social worker is likely to be the most effective. Commonly this can be accomplished best if children with lead poisoning are referred for long-term follow-up to a special clinic where all phases of clinical management can be coordinated and continuity of care is maintained.

At the outset, a long-term plan of management is developed. Age, the intensity of hand-to-mouth activity, pica, diet modification; environmental exposure, and serial laboratory data are taken into account. The objectives are to reduce the body burden of lead and to prevent recurrences. All preschool-aged housemates of index cases should be examined. All cases should be reported to social service for assistance in obtaining safe housing. Extended follow-up to at least 6 years of age is usually necessary.

Identification of lead source(s). In all cases, first priority is given to identification of important sources of excess lead in the child's environment and prompt separation of the child therefrom.[8] A thorough history can facilitate the identification and abatement of the most important sources of lead. Although this crucial part of therapy (abatement) is usually performed by health department personnel, not uncommonly information obtained in the clinic provides clues to unsuspected sources. The environmental history obtained in the clinic should include a list of all dwellings currently or recently visited by the child

(primary residence, homes of relatives and baby sitters, schools, daycare centers) and evaluation of each building's age and state of repair. In the United States a high proportion of buildings constructed prior to 1960 have lead-bearing paints and putty on both exterior and interior areas accessible to the child. Structures in poor repair often have lead-containing chips or pulverized fragments in the household dust. Play areas, especially urban playgrounds near vehicular traffic, dirt playgrounds and dirt yards, painted metal fences and walls, and vacant lots formerly containing lead-painted structures should be identified as potential lead sources. Occupational histories for all adults in various dwellings should be ascertained to learn if any are working in lead-related industries. Lead trades include, but are not limited to, secondary lead smelting (recovery of lead from old storage batteries), lead scrap smelting, storage battery manufacturing and repair, metal founding, ship breaking, automobile assembly and body and radiator repair, demolition of painted metal structures (such as bridges), and demolition and renovation of old houses and other structures. Adults who work in lead industries must shower before coming home and must leave all work clothes, including shoes, at the work place; these clothes must not be cleaned or washed at home. Thus lead-bearing dust from the place of employment will not contaminate the house. Additional sources may include old lead-painted cribs and beds and the burning of lead-painted wood in wood-burning stoves. Proximity to lead smelters, ingestion of lead-containing dust, and inhalation of lead from the combustion of gasoline contribute to the overall body burden of lead in children, but the high concentration of lead that ultimately results in clinical lead poisoning is most frequently associated with ingestion of lead-bearing paint. Uncommon causes of poisoning include ingestion and retention in the stomach of metallic lead (fishing weights, curtain weights, shot, jewelry painted with lead to simulate pearl), contamination of acidic foods and beverages from improperly lead-glazed ceramic pitchers, pots, and cups and from opened lead-soldered food cans, and the home burning of battery casings. Inhalation of fumes (sniffing) from small leaded-gasoline containers has occurred in older children. Poisoning has also been traced to oriental cosmetics (surma, a black eyeliner containing up to 85% lead) and to Mexican and Oriental folk remedies (azarcon, greta, paylooah).

Medical management during abatement of lead paint hazards. If the source of lead is limited to such items as retention of a metallic lead object in the stomach or an improperly lead-glazed food or beverage container, the child can be promptly separated from the source. Such is not the case when lead paint in the home is the principal source. Several methods are used to remove old lead-based paint from walls and woodwork. Some methods, particularly removal by burning and sanding, greatly increase the amount of air and dustborne lead in the home. Very fine lead-bearing particulates settle out slowly over many hours after burning and sanding is completed. *It is of the utmost importance to remove all young children and pregnant women from a dwelling until the abatement process is completed. They should live elsewhere day and night,* and should not return until removal of all lead-bearing paint has been completed and the dwelling has been thoroughly vacuumed and scrubbed with high-phosphate-detergent solutions. The sources that have been denuded during the abatement process should be repainted to seal any residual lead behind the surface. Children should be removed from the home during abatement whether or not they have increased lead absorption. When this procedure is not followed, it is not uncommon to observe 30 to 50 μg/dl increments in whole blood lead concentration within a matter of a few days or weeks.

Long-range dust control. *It must be understood that dust control is not a substitute for abatement.* In areas heavily contaminated with lead, such as deteriorating old housing and dwellings adjacent to lead-emitting industrial plants or heavy vehicular traffic, it may be helpful to institute a regular program in and about the home to control lead-bearing dust, which constantly reaccumulates. Because hand-to-mouth activity is common in young children, parents must institute a specific type of cleaning program; vacuuming and wet cleaning are recommended. Sweeping with a broom, although it may remove large fragments, serves only to stir up smaller particulates. It is recommended that all floors and woodwork be scrubbed weekly with high-phosphate detergents such as Tide or Spic and Span. For all surfaces that the child can touch, the weekly scrubbing should be supplemented with daily damp dusting with a cloth rinsed in a solution of high-phosphate detergent. Although such cleaning programs may be helpful, the definitive way to prevent recurrences is for affected children and their families to move into housing free of lead paint hazards.

Dietary factors. Although reduction in exposure to environmental lead must receive first priority, steps should be taken to identify and correct deficient dietary intake, particularly of calcium[25, 15] and iron as well as excessive dietary fat, each of which may increase the absorption and retention of lead. A diet adequate in minerals and limited in fat should be assured. For those intolerant of cow milk, lactose-free milk products such as yogurt or some alternative source are necessary to ensure adequate calcium intake. The use of low-fat milk and the avoidance of fried foods should limit excessive dietary fat. Acidic foods such as fruits, fruit juices, tomatoes, sodas, and cola drinks may

leach lead from cans with leaded-soldered seams. Dietary lead intake may be reduced if the above items are purchased fresh, frozen, or packaged in aluminum, glass, cardboard, or plastic containers.

Neurobehavioral considerations. A major problem is presented by the high level of hand-to-mouth activity of many preschool-aged children. If hand-to-mouth activity or pica (ingestion of nonfood items) is particularly severe, a behavioral psychologist can be helpful in developing a program to reduce the activity.

For children given any combination of chelating agents, neurologic and psychologic assessment should be obtained at the time of initial diagnosis and during the following years. This will facilitate appropriate school placement for children with learning handicaps, if they are identified through thorough psychometric evaluation prior to the child's entry into the school system. For the child who has had acute lead encephalopathy, long-term anticonvulsant therapy with phenytoin (or phenobarbital) is indicated if there were seizures or coma during the encephalopathic episode. Additional clinical and laboratory evaluation may be indicated to detect other sequelae of chronic lead poisoning, such as renal impairment. Metabolic disorders associated with acute lead poisoning are reversible after chelation therapy and substantial reduction of lead exposure.

Frequency of follow-up. When the results of initial venous blood lead and EP values and CaNa2-EDTA testing indicate the need for chelation therapy, long-term follow-up is indicated. For those children who have not received chelation therapy, follow-up at 3-month intervals, together with abatement and dust control in the home and correction of dietary deficiencies, should be continued until the child has maintained normal blood lead and EP values for 1 year.

Those children who initially received a course of chelation therapy require more intensive follow-up. Abatement of environmental lead hazards in the home is rarely accomplished within a matter of a few days, so that as a general rule the first course of chelation therapy is given in the hospital. Outpatient chelation therapy while a child is still overexposed to lead is counterproductive and likely to be associated with enhanced absorption and retention of lead. In children who have received a course of chelation therapy, blood lead and EP determinations should be repeated 5 to 7 days after therapy and then after another 1 to 4 weeks, depending on the progress. If some improvement is observed, follow-up may be scheduled at 2- to 4-week intervals for 6 months. Thereafter, blood lead and EP tests should be repeated at 3-month intervals until the child is 6 years of age. At each visit the environmental and housing situations are updated and reevaluated and dust control and diet are reviewed. If serial blood lead and EP data show continued improvement, it may be assumed that new assimilation of new lead is not occurring; rising blood lead concentrations, which may be followed by a rising EP level, indicate increased ingestion of lead. Often, reinvestigation reveals new sources of environmental lead not previously detected. When a child with earlier elevated blood lead concentrations approaches school age, psychometric evaluation may be indicated, even though the blood lead concentration at the time is <25 μg/dl.

Summary. Increased body lead burden must be managed as a chronic disorder. The final evaluation and disposition of each case must take into account the entire prior record. It is prudent to observe mentally or developmentally handicapped children with persistent pica during school years, because recurrences after the age of 6 years are most likely to occur in these children. The need to remove infants, young children, and pregnant women from a home during abatement of lead paint hazards is crucial to prevent acute episodes of sharply increased lead toxicity.

We thank Ms. Barbara Cirella, P.N.P., for performing the CaNa-EDTA provocation studies, and Ms. Carol Seaman for statistical analysis of the data; Dr. Morri E. Markowitz, and the CRC staff at Albert Einstein College of Medicine; Ms. Barbara Mahan, and the nursing staff in the Pediatric Lead Clinic at Children's Hospital; and Ms. Victoria Sadoff for careful and painstaking assistance with preparation of the manuscript.

REFERENCES

1. Chisolm JJ Jr: The use of chelating agents in the treatment of acute and chronic lead intoxication in childhood. J PEDIATR 73:1, 1968.
2. Markowitz ME, Rosen JF: Assessment of lead stores in children: Validation of an 8-hour $CaNa_2$-EDTA provocation test. J PEDIATR 104:337, 1984.
3. Chisolm JJ Jr, Mellits ED, Barrett MB: Interrelationship among blood lead concentration, quantitative daily ALA-U and urinary lead output following calcium EDTA. *In* Nordberg GF, editor: Effects and dose-response relationship of toxic metals. Amsterdam, 1976, Elsevier Scientific.
4. Chisolm JJ Jr, Barltrop D: Recognition and management of children with increased lead absorption. Arch Dis Child 54:249, 1979.
5. Graef JW, Kopito L, Shwachman H: Lead intoxication in children. Postgrad Med 50:133, 1971.
6. Saenger P, Rosen JF, Markowitz ME: Diagnostic significance of edetate disodium calcium testing in children with increased lead absorption. Am J Dis Child 136:312, 1983.
7. Mahaffey KR, Annest JL, Roberts J, Murphy RS: National estimates of blood lead levels, United States 1976-1980: Association with selected demographic and socioeconomic factors. N Engl J Med 307:573, 1982.
8. Preventing lead poisoning in young children: A statement by the Centers for Disease Control. J PEDIATR 93:709, 1978.
9. Emmerson BT: Chronic lead nephropathy: The diagnostic use of calcium EDTA and the association with gout. Aust Ann Med 12:310, 1963.

10. Hammond PB: The effects of chelating agents on the tissue distribution and excretion of lead. Toxicol Appl Pharmacol 18:296, 1971.
11. Leckie WJH, Tompsett SL: The diagnostic and therapeutic use of edathamil calcium disodium (EDTA, versene) in excessive inorganic lead absorption. Q J Med 27:65, 1958.
12. Whittaker JA, Austin W, Nelson JD: Edathamil calcium disodium (versenate) diagnostic test for lead poisoning. Pediatrics 29:384, 1962.
13. Teisinger J, Srbova J: The value of mobilization of lead by calcium ethelene diaminetetraacetate in the diagnosis of lead poisoning. Br J Ind Med 16:148, 1959.
14. Hansen JPB, Dossing M, Paulev PE: Chelating lead body burden (by calcium-disodium EDTA) and blood lead concentration in man. J Occup Med 23:39, 1981.
15. Lahaye D, Roosels D, Verwilghen R: Diagnostic sodium calcium edetate mobilization test in ambulant patients. Br J Ind Med 25:148, 1968.
16. Chiesura P: Remarks on the use of shortened procedures in evaluating EDTA-induced urinary lead excretion. Lavoro Umano 28:97, 1976.
17. Vitale LF, Rosalinas-Bailon A, Folland D, Brennan JF, McCormick B: Oral penicillamine therapy for chronic lead posioning in children. J PEDIATR 83:1041, 1973.
18. Graziano JH, Leong JK, Freidheim E: 2,3-Dimercaptosuccinic acid: A new agent for the treatment of lead poisoning. J Pharmacol Exp Ther 206:696, 1978.
19. Aposhian VH: DMSA and DMPS water-soluble antidotes for heavy-metal poisoning. Ann Rev Pharmacol Toxicol 23:193, 1983.
20. Piomelli S, Seaman C, Zullow D, Curran A, Davidow B: Threshold for lead damage to heme synthesis in urban children. Proc Natl Acad Sci 79:3335, 1982.
21. Piomelli S: A micromethod for free erythrocyte porphyrins: The FEP test. J Lab Clin Med 81:932, 1973.
22. Chisolm JJ Jr: Heme metabolites in blood and urine in relation to lead toxicity and their determination. Adv Clin Chem 20:225, 1978.
23. Alessio L, Bertazzi PA, Toffoletto F, Foa V: Free erythrocyte protoporphyrin as an indicator of the biological effect of lead in adult males. Int Arch Occup Environ Health 37:73, 1976.
24. Angle CR, McIntire MS, Swanson MS, Stohs SJ: Erythrocyte nucleotides in children: Increased blood lead and cytidine triphosphate. Pediatr Res 16:331, 1980.
25. Rosen JF, Chesney RW, Hamstra A, DeLuca HF, Mahaffey KR: Reduction in 1,25-dihydroxyvitamin D in children with increased absorption. N Engl J Med 302:1128, 1980.
26. Mahaffey KR, Rosen JF, Chesney RW, Peeler JT, Smith CM, DeLuca HF: Association between age, blood lead concentration and serum 1,25-dihydroxycholecalciferol levels in children. Am J Clin Nutr 35:1327, 1982.
27. Saenger P, Markowitz ME, Rosen JF: Depressed excretion of 6β-hydroxycortisol in lead-toxic children. J Clin Endocrinol Metab 58:363, 1984.
28. Needleman H, Gunnoe C, Leviton A, Reed R, Peresic H, Maher C, Barrett P: Deficits in psychologic and classroom performance of children with elevated dentine lead levels. N Engl J Med 300:689, 1979.
29. Winneke G, Kramer U, Brochkaus E, Ewers U, Kajanek G, Lechner H, Janke W: Neuropsychological studies in children with elevated tooth-lead concentrations: Extended study. Int Arch Occup Environ Health 51:232, 1983.
30. Otto DA, Benignus V, Muller K, Barton CN: Effects of age and blood lead burden on CNS function in young children. I. Slow cortical potentials. Electroencephalogr Clin Neurophysiol 52:229, 1981.
31. Otto DA, Benignus V, Muller K, Barton CN, Seiple K, Prah J, Schroeder S: Effects of low to moderate lead exposure on slow cortical potentials in young children: Two-year follow-up study. Neurobehav Toxicol Teratol 4:733, 1982.
32. Graef JW: Outpatient use of a six-hour lead mobilization test in chelation therapy [abstract]. Pediatr Res 10:330, 1976.
33. Chisolm JJ Jr, Barrett MB, Harrison HV: Indicators of internal dose of lead in relation to derangement in heme synthesis. Johns Hopkins Med J 137:6, 1975.
34. Piomelli S, Corash L, Corash MB, Seaman C, Mushak P, Glover B, Padgett R: Blood lead concentrations in a remote Himalayan population. Science 210:1135, 1980.
35. Sorell M, Rosen JF, Roginsky M: Interations of lead, calcium, vitamin D and nutrition in lead-burdened children. Arch Environ Health 32:160, 1977.

☆U.S. GOVERNMENT PRINTING OFFICE: 1990/734-913

Notes

Notes