Recommendations for the Prevention of Lead Poisoning in Children (1976)

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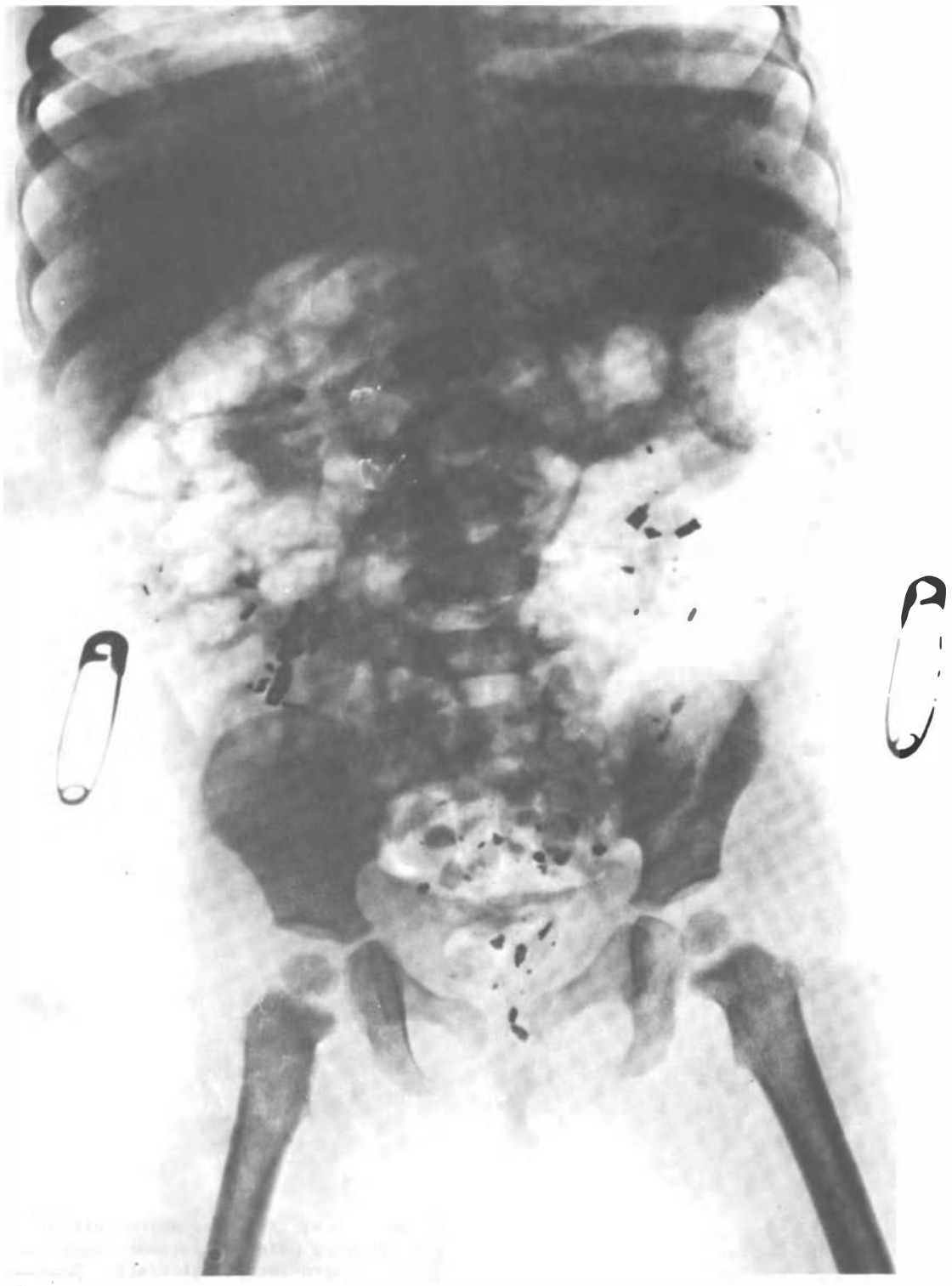
Frontispiece. X-ray of a 16-month-old girl showing paint chips containing lead in the gastro-intestinal tract. Reproduced with the permission of Henrietta K. Sachs, M.D.



Recommendations for the Prevention of Lead Poisoning in Children

Committee on Toxicology

Assembly of Life Sciences
National Research Council

Prepared for the

Consumer Product Safety Commission

National Academy of Sciences
Washington, D.C.

July 1976

NOTICE

The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the Committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of sciences, the National Academy of Engineering, and the Institute of Medicine.

ACKNOWLEDGMENTS

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The Subcommittee wishes to acknowledge with thanks the assistance of Maureen B. Barrett and Thomas O. Wilson who served as consultants in the preparation of this report.

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Preface

This document was prepared by the ad hoc Committee on Lead in Paint of the National Research Council, National Academy of Sciences under contract CPSC-C-75-0018, from the Consumer Product Safety Commission. The CPSC requested that the Academy recommend a "safe level" of lead in paints and other coatings based on an evaluation of four studies submitted to the Academy by the CPSC. The Commission also requested additional advice and recommentations related to the safety of lead in paints and coatings.

The ad hoc Committee on Lead in Paint met December 13 and 14, 1974 to review the four studies in which lead coupounds used in paints were fed to rats and baboons. The studies reviewed were:

1. Purdy, Robert H.
   Southwest Foundation for Research (SWFRE).
   A Toxicological Investigation of Chronic Lead Paint Ingestion in the Juvenile Baboon (Nov. 1974). Contract No. CPSC-C-74-159.

2. Kneip, T.J., V.P. Rulon, E.A. Pfitzer, N. Cohen and D.H. Goldstein,
   New York University Institute of Environmental Medicine (NYU).
   Lead Toxicity Studies in Infant Baboons - A Toxicological Model for Childhood Lead Poisoning (Nov. 1974). Contract No. CPSC-C-74-153.

3. Castles, T.B.
   Midwest Research Institute (MRI)
   Lead Paint Ingestion Study (Feb. 1974). Contract No. 62-W-62GC and NPC.

4. Barltrop, D.
   St. Mary's Hospital Medical School (St. MHM's)
   Assessment of the Health Hazard of Various Lead Compounds Interim Report (Sept. 1974). Contract No. HSM-99-73-28.

The first two studies were contracted by the CPSC, the third by the National Paint and Coating Association and the fourth by the Environmental Health Service Division of the Center for Disease Control, U.S. Department of Health, Education, and Welfare.

Since the studies supplied insufficient data for recommending a "safe level" of lead in paint, the Committee sent a preliminary report to the CPSC on December 20, 1974 in which it stated ".... this Committee believes it is desirable to retain the present recommended level (0.5 percent) and to defer final action until data, adequate to support a change, have been obtained."

A second meeting of the Committee was held on February 6 and 7, 1975 to determine a plan tor arriving at a recommended "safe level" of lead in paints and coatings. The Committee discussions centered on the etiology of childhood lead poisoning with particular reference to the role of lead paint ingestion. The Committee decided to institute a literature

Introduction

The primary question that this report was designed to answer may be stated as follows: "Given the fact that some children eat paint, what is a safe level of lead in paint?" An answer to this question presupposes answers to three preliminary questions; namely: 1) What are the adverse effects of lead? 2) What dose of lead is sufficient to produce adverse effects? and, 3) What is the estimated daily intake of lead in a child with pica for paint?

These questions are discussed succinctly in the above sequence in the body of this report. Following this is a discussion of the lead content of paints available on the current retail market and a discussion of future research needs. The Committee recommendations appear at the end of the report. Detailed discussions and supporting data for statements made in the body of the report are given in the appendices. Detailed Appendices have been prepared which are designed to stand along in support of the report. Although the total amount of lead assimilated may be derived from a variety of environmental sources, this report is concerned mainly with the absorption of lead due to the ingestion of lead-containing paints by young children.

WHAT ARE THE ADVERSE EFFECTS OF LEAD?

In man, lead exerts its effects in the renal, hematopoietic and nervous systems. The severity of effects is related to both the degree of illness and the frequency of recurring illness as well as the dosage and duration of exposure. There are basically three stages in childhood lead poisoning: 1) asymptomatic lead poisoning, in which no clinical symptoms are apparent, but in which measurable metabolic changes occur, 2) symptomatic lead poisoning, in which clinical symptoms such as anorexia, vomiting, apathy, ataxia, drowsiness or irritability occur, and 3) lead encephalopathy with cerebral edema, in which coma or convulsions occur (see Appendix D).

The sequelae of lead encephalopathy include seizure disorders, severe mental retardation and death. The sequelae of symptomatic but less severe lead poisoning includes seizure disorders as well as various behavioral and functional disorders, usually grouped under the heading of minimal brain dysfunction. Clinical studies suggest that the latter syndrome may include hyperactivity, impulsive behavior, prolonged reaction time, perceptual disorders and slowed learning ability. Recent evidence suggests that minimal brain dysfunction might also follow asymptomatic lead poisoning. The sequelae associated with each diagnostic category of lead poisoning do not necessarily occur in every child with a particular diagnosis. Each individual is unique in his response.

The effects of lead in the hematopoietic system are reversible and therefore do not constitute sequelae. Lead interferes with the formation of hemoglobin at several stages. In addition, lead reduces the life span of the red blood cells and this results in lead induced anemia. In cases of encephalopathy, acute renal injury (Fanconi syndrome) may also occur, and in children this is reversible.

The "critical effect" concept, provides a framework for examining the effects of lead. The term "critical effect" is used to mean first effect, rather than most serious effect. Since effects in the kidney do not appear in the early stages of lead poisoning, the kidney cannot be considered the site of the critical or first effect. It is not presently known whether the first effects occur in the neurologic or hematopoietic systems. Subtle neurologic effects are difficult to measure. There are currently no simple neurochemical tests for measuring early metabolic changes in the nervous system. However, several laboratory tests are currently available for measuring early effects in the hematopoietic systems. At the present time, the hematopoietic system is considered the site where the "critical effect" occurs (see Appendix A). If this is correct, then environmental limits, set to prevent reversible effects in the hematopoietic system, should serve to prevent potentially irreversible effects in the nervous system.

WHAT DOSE OF LEAD IS REQUIRED TO PRODUCE ADVERSE EFFECTS?

In relation to lead, the general term "dose" may be variously interpreted to mean: 1) the quantity of lead administered, 2) the

quantity of lead absorbed, or 3) the quantity of lead present in the affected organs or tissues. In this report, we will use the terms "external dose" and "internal dose" where necessary, to provide clarity. The external dose may be defined as the amount of lead entering the body through the gastrointestinal tract, lung, etc., some of which will be excreted before reaching the organs or tissues potentially affected by lead. The internal dose, or tissue concentration, may be defined as the amount of lead present in the organs or tissues. In experimental animals, the internal dose can be measured after sacrificing the animal. In humans, the analysis of tissue lead levels through biopsy or autopsy is rarely done; therefore, it is necessary to use some other indicator of "internal dose." We will use blood lead concentrations as an indicator of internal dose (see Appendix A).

Individual Variability. We have found that individual variability influences the estimate of a dose necessary to produce an adverse effect. In a heterogeneous population, numerous factors modify the relationship between dose and effect in the individual so that some members of the population will appear to be affected by comparatively low doses of lead, while others will appear to be highly resistant, showing little or no effect at higher doses. In general, however, the percentage of individuals in a population who exhibit a specific effect will increase in relation to an increase in dose. Not all factors which influence susceptibility are known. Therefore, this Committee feels that any estimate of a safe dose level should allow a margin of safety for highly susceptible individuals (see Appendix A) who are affected by relatively low doses.

Known Conditions Affecting Susceptibility. Evidence in both animals and humans indicates that age and diet are primary factors influencing the absorption and effects of lead. Detailed discussions of these factors are given in Appendices B and D.

Due to the very rapid rate of brain growth, the young animal or child is at greater risk for lead-induced neurologic damage than the adult. In humans, the "growth spurt" begins during the sixth month of pregnancy and continues into the third or fourth year postpartum. Glial replication and differentiation and cerebellar growth is most rapid during the first 18 months of life. Myelination continues into the third or fourth year of life. Permanent neurologic deficits can result from an insult to the brain during the growth spurt. Studies of children malnourished during the first two years of life have shown permanent adverse effects on learning ability and general adjustment. Studies in rats and lambs administered lead during the growth spurt have shown slowed learning abilities which persist in the adult animal, even after blood lead levels have returned to normal. Behavioral changes, including hyperactivity, aggressiveness, tremors and repetitive grooming behavior, have been produced in rats poisoned during the "growth spurt." The brain of suckling rats has been shown to have a significantly higher rate of lead uptake than the brain of adult rats. This may, in part, account for the greater central nervous system (CNS) vulnerability observed in young animals.

Age also appears to modify the intestinal absorption rate for lead. Alexander's balance study in eight healthy children showed that approximately 50 percent of dietary lead was absorbed. Kehoe's balance studies in adults showed that only 10 percent of dietary lead was absorbed. Studies in rats confirm these observations in humans (see Appendix B). Using the average dietary lead intake for normal "non-exposed" adults and the different absorption ratios and caloric requirements for children and adults, a 3-year-old child would absorb 12 times more dietary lead than an adult receiving the same diet (see Appendix F).

Both dietary components and dietary deficiencies have been shown to alter the intestinal absorption rate of lead. In experimental animals, the intestinal absorption of lead is significantly increased if lead is administered in oils, fats or milk rather than in a diet of dry feed. Similar studies are not available, nor would they be possible, in young children. Dietary deficiencies, including deficiencies of calcium, copper, and iron have been shown to increase the absorption of lead in rats. Dietary deficiencies of calcium and particularly iron have been reported to be prevalent among preschool age children, especially those in the lower socioeconomic groups. Because of the rapid growth rate during early childhood, iron stores are marginal even in apparently healthy children. Pica, as an additional risk factor, occurs among preschool age children. Pica, the repetitive ingestion of non-food substances, occurs in at least 50 percent of children between 12 and 36 months of age.

In summary, a variety of factors combine to make the young child less resistant to lower levels of lead than the adult. The habit of pica may lead to ingestion of lead-containing paint chips; the young age makes the child vulnerable to lead-induced neurologic damage; and both age and diet contribute to produce a relatively high intestinal absorption rate for lead.

Relationship Between Dose and Effect. The effects of lead occur in the hematopoietic, neurologic and renal systems. Whether the critical (first) effect of lead occurs in the hematopoietic or neurologic system is unknown. Presently, the hematopoietic system is considered the critical site for lead's effect. Using blood lead (Pb-B) as a measure of the "internal dose" of lead, different effects can be seen as blood lead levels increase.

Lead-induced anemia has been reported in both children and adults. Lead's interference in the formation of hemoglobin results in the accumulation of free erythrocyte protoporphyrin (FEP) in blood and δ-aminolevulinic acid (ALA-U) in urine. In several small groups of women and children FEP begins to increase as levels rise above a range of 25-30 μg Pb/dl (micrograms of lead per deciliter). The urinary excretion of ALA begins to increase in children and adults when blood lead levels reach a range of 40-50 μg Pb/dl. Decreasing hematocrit levels have been reported in children when blood lead levels exceed 40 μg Pb/dl while decreasing hemoglobin levels in both adults and children have been reported at levels equal to or greater than 50-60 μg Pb/dl. In summary, the first metabolic evidence of lead's effect in the hematopoietic system appears at approximately 25-30 μg Pb/dl, while anemia usually does not

appear until blood lead levels reach 50-60 μg Pb/dl (see Appendix D).

Neurologic changes, including slowed learning ability, paraplegia, clumsiness and hyperactivity have been produced by administering lead to young experimental animals. The slowed learning ability appears to be an irreversible effect (see Appendix B).

Studies in children have been difficult to perform. None by itself has provided all of the requisite data. Only one truly prospective study has been reported. Taken together, the several reports strongly suggest that both decreased cognitive functioning and an increased frequency of behavioral abnormalities become evident in groups of school-aged children who have been unduly exposed to lead during the preschool years (see Appendix D). The behavioral aberrations which include hyperkinesis, short attention span and impulsive and aggressive conduct, appear to be more important than minimal intellectual deficits in impeding progress in school. A similar observation was made by Byers and Lord over 30 years ago. In addition, a higher frequency of seizure disorders and school failures are reported in children with lead poisoning. An increased frequency of neurologic effects has been demonstrated only in those children with blood lead elevations greater than 50-60 μg Pb/dl.

Severe mental retardation, blindness and death have been reported in children with lead encephalopathy. In children, lead encephalopathy is usually associated with blood lead levels greater than 120 μg Pb/dl.

Relationship Between External Dose and Internal Dose. An estimate of the external dose (lead intake) necessary to produce a specific internal dose (blood lead) concentration must abcount for the chemical and physical form of lead ingested (see Appendix A). In children, up to 50 percent of dietary lead may be absorbed and 50 percent excreted in the feces. Although balance data in children are limited they are in agreement with data from suckling animals which show a high rate of lead absorption (see Appendix B). Animal studies have also shown that lead in paint films is less well absorbed than dietary lead. Lead chromate, one of the least well absorbed compounds found in paint, is absorbed approximately one-third as well as the free salts of lead when added to the diet. Other lead compounds found in paint, such as lead naphthenate, have higher rates of absorption but are still absorbed to a lesser extent when incorporated into a paint matrix. Thus, 17 percent (1/3 x 50%) would be a conservative estimate for the amount of lead absorbed from paint by a young child (see Appendix E).

Barltrop found a mean daily fecal excretion of 67.8 μg Pb/day in a group of two- to three-year-old children with a mean blood lead level of 20 μg Pb/dl. These data would be consistent with a dietary intake of 135 μg Pb/day if 50% is absorbed. On the basis of body weight for an average three-year-old child weighing 15 kg., Barltrop's group of children with a mean blood level of 20 μg Pb/dl would have a daily intake of 9.0 μg Pb/kg/day with an absorption of 4.5 μg Pb/kg/day. This agrees well with Alexander's estimates of dietary intake in young children (see Appendix D).

There are no published data relating external dose to internal dose in children with blood lead levels in the range of 40-60 μg Pb/dl. Kehoe added lead to the diet of adult volunteers. His studies have shown that the absorption of 1.43 μg Pb/kg/day due to the added lead was associated over a period of approximately nine months with an increase in blood lead level of 17 μg Pb/dl (see Appendix E). One can calculate that if the absorption of 4.5 μg Pb/kg/day will produce an average blood lead level of 20 μg Pb/dl in a two- to three-year-old child, then an absorption of an additional 1.43 μg Pb/kg/day or a total of 5.9 μg/kg/day could produce a blood lead level of 37 μg Pb/dl. Similarly one could calculate that the total absorption of 7.4 μg Pb/kg/day could produce a blood lead level of 54 μg Pb/dl. The external dose (amount of ingested lead) necessary to produce these blood lead levels will depend in part on the chemical and physical form of lead ingested.

Because of the dearth of information relating external dose to internal dose (blood level or other tissue concentration) in children, the calculations given above are only estimates based on the best available data.

WHAT IS THE ESTIMATED LEAD INTAKE IN A CHILD WITH PICA FOR PAINT?

Pica, the repetitive ingestion of non-food substances, occurs in approximately 50 percent of children between one and three years of age. This habit is considered normal behavior until about three years of age. Psychosocial factors or organic brain damage may cause the persistence of pica beyond three years of age. Pica for paint generally begins at the time of ambulation or at about 10 to 12 months of age and is believed to be episodic, occurring perhaps two to three times per week (see Appendix D).

Abdominal x-ray films showed radiopaque materials in the intestinal tract in 35 percent of children attending the Chicago Lead Clinic. The best available clinical evidence indicates that children with pica may ingest one to three grams of paint per week (see Appendices D, E). If the paint contained the present legal limit of 0.5 percent lead (5,000 μg/g paint), then the daily ingestion of lead from paint would be 714 μg Pb/day, 1,429 μg Pb/day or 2,143 μg Pb/day, respectively, for one, two or three grams of paint ingested per week. Calculated on the basis of body weight for a two-year-old child weighing 12.5 kg, and using an absorption factor of 17 percent for lead from paint, the amount of lead absorbed would be 9.7 μg Pb/kg/day, 19.4 μg Pb/kg/day and 29.1 μg Pb/kg/day, respectively, for one, two and three grams of paint ingested per week (see Appendix E). The daily absorption of 4.5 μg Pb/kg/day has been found in children with essentially normal blood lead levels of approximatly 20 μg Pb/dl. The estimated daily absorption of lead from paint must be superimposed on the estimated absorption of lead from diet, in order to obtain a total daily absorption. Thus, the daily absorption of lead in a child with pica for paint (containing 0.5 percent Pb) may be three to seven times that found in a child receiving a normal diet. For a child with pica for paint, a level of 0.5 percent lead in paint clearly represents a hazard.

WHAT IS THE LEAD CONTENT OF CURRENTLY AVAILABLE HOUSEHOLD PAINTS?

The limit of 0.06 percent lead in paint was proposed to allow for trace amounts of lead present in the raw materials, for possible contamination during processing and for limits of precision in the analytical methods of determining the lead content of paint. An industry formulary indicates that alternative, less toxic substances such as zinc and calcium salts may be used in place of lead as auxiliary driers.

A market place survey conducted by the CPSC found that 70.8 percent of oil-based paints and 96.1 percent of water-based paints contained less than the proposed limit of 0.06 percent lead in paint (see Appendix G). The four colored oil-based paints which consistently exceeded this limit were black, green, yellow, and white. Among these paint colors, 50% of the black, 76% of the green, 62% of the yellow and 81.5% of the white contained <0.06% lead. These figures strongly suggest that at least some paint manufacturers have found it technologically and economically possible to meet the proposed limit of 0.06 percent lead in most paints.

None of the members of the ad hoc Committee on Lead in Paint are paint technologists. Therefore, we could reach no conclusions relative to any possible change in paint quality if lead levels are reduced to trace amounts. In addition, the Committee members did not have the expertise necessary to predict the economic impact of meeting the proposed limit of 0.06 percent lead in paint.

Based on the evidence in children and experimental animals, this Committee concludes that 0.5 percent lead in paint represents a hazard to young children with pica for paint.

WHAT FUTURE RESEARCH IS NECESSARY OR DESIRABLE?

Numerous studies of lead's effects have been carried out in experimental animals and humans; nevertheless, no single study has provided a comprehensive model for establishing a "safe level" of lead intake in children. This Committee could arrive at estimates of safety only by collating the results of various studies. We feel that a comprehensive study, designed to determine the interrelationships between lead intake, absorption and effects would provide a more precise method for estimating a safe level of lead intake. Properly designed animal studies simulating conditions in human infants are needed to identify the relationships between external dose (dose of lead administered), absorption rate of various forms at various ages, internal dose, vulnerability of the brain (at various ages), influence of nutritional factors, time between exposure and appearance of effects, and permanence or reversibility of effects.

In addition, we feel that studies in preschool-age children are necessary to define more accurately the relationships between lead intake, absorption and effects and to provide more precise data regarding the amount of paint which a child with pica may ingest. Information

relative to the absorption and effects of minimal lead exposure in the human fetus and infant less than 12 months of age is virtually non-existent. Since studies in experimental animals indicate that the suckling animal is extremely vulnerable to the effects of lead, we feel that primary consideration should be given to examining the effects of lead in human infants less than one year of age, particularly in regard to effects in the neurologic system.

CONCLUSIONS AND RECOMMENDATIONS

The conclusions given below are based on what is known from studies in experimental animals and humans. Unfortunately, some factors which may influence a child's susceptibility to lead are poorly understood. Studies in both experimental animals and children have shown that the brain is particularly vulnerable to permanent damage if injury to the developing brain occurs during infancy. In addition, young animals and children have been shown to absorb a higher proportion of ingested lead than adults. Animal experiments have shown a higher retention of ingested lead in animals receiving lipids or milk in the diet than in those receiving dry feed. In addition, dietary deficiencies of calcium, copper, and iron increased the absorption of lead in experimental animals. No data relative to these points are available in children. However, the average child's diet contains both lipids and milk. Dietary deficiencies, particularly iron deficiency, have been shown to exist in a significant number of American children. No firm data are available to elucidate genetic factors which may possibly influence susceptibility to lead. Although the best available evidence suggests that some children may ingest 1 to 3 grams of paint per week, there is no basis for assuming that 3 grams of paint is the maximum amount ingested. In summary, the conclusions and recommendations, where possible, are based on known available information in children; where information is lacking, they are based on the extrapolation of data from studies in either adults or in experimental animals which most closely approximate the conditions found in preschool-age children.

Conclusions

1. Since the CPSC-supplied studies did not adequately simulate the conditions found in young children, particularly in relation to age and diet, we were unable, on the basis of these studies, to determine that 0.5 percent lead in paint is safe.

2. Since the first metabolic effects in children become evident when the blood lead concentration exceeds 30 μg/dl, and since the most desirable means of controlling disease is prevention, we recommend that the total daily lead exposure, including exposure from food, ambient air and paint, for a one- to five-year-old child not exceed levels sufficient to raise the blood lead concentration above 30 μg Pb/dl. In order to allow for variations among individuals, the mean blood lead concentration for groups should not exceed 20 μg Pb/dl. Among two to three year old children an absorption of 4.5 μg/kg/day is apparently associated with a mean blood lead concentration of 20 μg/Pb/dl.

3. Since control of the lead paint hazard is difficult to accomplish once multiple layers have been applied in homes over two to three decades, and since control is more easily regulated at the time of manufacture, we recommend that a limit for the lead content of paints be set and enforced at the time of manufacture.

4. Since 0.5 percent lead in paint represents a hazard to a child with pica for paint, and since most currently available household paints contain <0.06 percent lead in paint, thus demonstrating that lead is not an essential ingredient for all paints, and since a reasonable allowance must be made for variations due to contamination of raw materials and detection limits and precision of analytical methods for analyzing the lead content of paints, we recommend that the deliberate addition of lead to paint for residential buildings or other surfaces accessible to young children be immediately discontinued and that a level not to exceed 0.06 percent lead in the final dried product be set for regulatory purposes. Since paints without lead additives may contain up to 0.03 percent lead, a level of 0.06 percent lead provides reasonable latitude for regulatory purposes.

5. Since a time allowance is necessary to implement these recommendations, and since extensions may be sought to delay compliance, we recommend that variances be allowed only on the basis of demonstrated economic hardship and that none be allowed to extend beyond five years. A time limit of five years will prevent accumulation of lead to dangerous levels from repeated applications.

6. Since most cases of serious childhood lead poisoning found today are clearly related to the ingestion of old lead paints, and since this hazard may be expected to exist in older homes for some time, we strongly recommend that research be conducted to determine methods for the removal of old lead paints, which will provide adequate safety for both the residents and the workmen performing the renovation procedures.

7. Since the infant is most vulnerable to the effects of lead and since little is known about the relationship between lead dose and effect in the child from birth to one year of age, we recommend that the lead content of paints or coatings on infant toys and furniture should not exceed 0.06 percent lead and that food commonly fed to infants should contain the lowest practical level of lead as determined by FDA.

8. Since few studies in experimental animals have provided adequate designs to simulate the conditions found in a young child and since no research has been conducted on the relationship between lead dose and effect in the human infant less than 12 months of age, and since few studies in preschool-age children have provided adequate information on the dose-response relationship for lead in the one- to five-year-age group, we recommend that future research focus on these areas.

9. Lead continues to have diverse uses, the regulation of which falls under numerous different governmental agencies depending on

its use. We recommend that these various agencies coordinate their research efforts in relation to the dangers of lead and that they coordinate their policies regarding the limits for human exposure from industrial sources, consumer products, air, food and water so that an individual's total exposure from various sources falls within a range which allows a margin of safety for those individuals in the population who are affected by relatively low doses.

Appendix A

Dose-Effect, Dose-Response Concepts of Toxicology

The dose-effect, dose-response concepts of toxicology provide a framework for examining the biologic effects of toxic metals. These concepts and their application to human exposures to heavy metals are discussed fully in "Effects and Dose-Response Relationships of Toxic Metals."[71] Here we will initially summarize these concepts through a series of definitions and then discuss their specific application to lead.

Critical Effect - The critical effect is not the most serious, but rather the most sensitive and specific biologic change, beyond acceptable physiologic variation, which is caused by the presence of a toxic substance. Although many different effects may occur, the critical effect is defined as the first measurable adverse effect. "Sub-critical effects" are measurable biologic changes which do not impair cellular function, but which are directly related to the concentration of a toxic substance.

Critical Site - The critical site is the location in the body where the critical effect occurs. It may be a system, organ, cell type or cell component.

Dose - In experimental animals, an administered dose is readily quantified but this is not true of humans. For humans we can estimate the amount taken in and for this we use the term "external dose." Since this is an indefinite amount for humans we must relate response to a tissue level such as blood concentration and we use the term "internal dose" for this tissue level. The "external dose" is the quantity of a toxic agent which enters the organism through the lungs, gastrointestinal tract, skin, etc., a portion of which may be excreted before reaching the "critical site." The "internal dose" is the quantity of a toxic agent which is absorbed and reaches the critical site. Since the concentration of a toxic agent at the critical site can rarely, if ever, be measured in human studies, the concentration is measured in a body fluid such as blood or urine. The concentration of a toxic agent in blood or urine is then used as an indicator of the internal dose.

Dose-Effect Relationship - The dose-effect relationship is a relationship in which a quantitative change in a metabolite (effect) is directly related to the concentration (dose) of a toxic substance. A typical dose-effect relationship is graphically illustrated by an "s" shaped curve when dose is plotted on the abscissa and degree of effect on the ordinate.

Dose-Response Relationship - The dose-response relationship is a relationship in which the percentage (response) of a population exhibiting an effect is related to the concentration (dose) of a toxic substance. Those exhibiting an effect are termed "reactors," and those not exhibiting an effect, "non-reactors." A typical dose-response relationship is illustrated by an "s" shaped curve when dose is plotted on the abscissa and percent positive reactors is plotted on the ordinate.

DOSE-EFFECT RELATIONSHIPS FOR LEAD

The effects of lead are seen in the neurologic, hematopoietic and renal system. Acute adverse functional effects in the kidney are generally seen in association with symptoms and high levels of lead exposure in adults. Similarly, late lead nephropathy is also associated with prolonged high levels of lead exposure. Therefore, the kidney is not currently considered the first organ affected by lead.[29,71]

Derangement of hemoglobin synthesis in the erythroid cells of the bone marrow is currently considered the critical effect for lead.[20,36,70,71,105] Increases in urinary δ-aminolevulinic acid (ALA-U), urinary coproporphyrin (CP-U) and erythrocyte protoporphyrin (EP) are indicators of lead's effect in the hematopoietic system. In lead poisoning (and iron deficiency), it is the metalloporphyrin, zinc protoporphyrin, rather than free protoporphyrin IX which is present in excess in the circulating erythrocytes.[55] Increased ALA-U and EP reflect *in vivo* inhibition of the enzymes ALA-D and ferro chelatase by lead.[70,71] The mechanisms responsible for the coproporphyrinuria of plumbism are not well understood. Inhibition of ALA-D by lead has been extensively studied.[70,71,105] In a number of epidemiological studies in which ALA-D activity is measured *in vitro* in hemolysates of peripheral blood, a significant negative log-normal relationship has been found between ALA-D activity and whole blood lead concentration. This relationship is found over a wide range in blood lead concentration, including the normal range (5 to approximately 40 μg Pb/dl whole blood). More recently, Granic *et al* [37] have developed an assay for ALA-D in which the ratio of activated to non-activated ALA-D activity can be measured. With this particular assay, a positive linear relationship between the ratio of activated to non-activated ALA-D activity and blood lead concentration is found over a range of 20-90 μg Pb/dl whole blood. On the basis of this and kinetic studies, they[37] propose that inhibition of ALA-D by lead is non-competitive and that there is probably no interaction with lead at concentrations of <15 μg Pb/dl whole blood. Under physiologic conditions in man, however, accumulation and increased excretion of ALA-U, the substrate of ALA-D, does not begin to occur until Pb-B exceeds approximately 40 μg Pb/dl whole blood, a level at which most *in vitro* assays for ALA-D indicate substantial inhibition. This has been interpreted as evidence that there is a substantial reserve of ALA-D adequate to meet physiologic needs at lower concentrations of lead in whole blood. For this reason, reduction in AlA-D activity, as measured

in vitro in peripheral blood, is considered a sub-critical effect within the context of the above definitions; while increases in ALA-U, CP-U and EP are considered indicators of lead's critical effect on hematopoiesis. [70,71,105]

Significant dose-effect relationships are found between these metabolic precursors of heme and the concentration of lead in body fluids. As an example, a dose-effect curve, using blood lead concentration (Pb-B) as an indicator of internal dose and quantitative 24-hour output of ALA-U as an indicator of effect, is given in Figure 1. One can begin to see the typical s-shaped curve usually associated with this relationship. Differences in individual susceptibility can also be seen at each dose (Pb-B) level. Zielhuis[105] and others[78,81,86] have found similar relationships for lead's effect on the hematopoietic system. These effects begin to occur when Pb-B levels reach the 40-60 µg Pb-B range, although preliminary data suggest that EP begins to increase as Pb-B rises above 30 µg Pb/dl whole blood.[105] Adverse effects in the hematopoietic system are reversible.

At the present time, there is no well-defined set of sensitive biochemical indicators of lead's effect on the nervous system. However, preliminary studies in rats[91] use neurochemical tests which may become useful as measures of neurologic changes in humans. Published reports to date have used functional tests to measure lead's effect on the human nervous system. A relationship has been tentatively suggested between decreased intelligence,[3,23,24,73] hyperactivity,[22] behavioral and psychological changes,[24] and loss of fine motor function,[78] in young children with blood lead concentrations in the 50-70 µg Pb-B range. In some instances, the effects of lead on the nervous system are clearly irreversible. Sequelae are related to the severity and duration of signs and symptoms. The risk of permanent neurological complications increases with repeated acute clinical episodes of lead poisoning.[19] Whether the effects reported in subclinical lead poisoning are reversible is unknown; however, de la Burdé's most recent study suggests that they are not.[24]

Currently, no data exist to show whether neurochemical or neurophysiological changes precede changes in the hematopoietic system. The hematopoietic system is currently considered the "critical" or first system to be affected. If this is true, then medical intervention based on evidence of reversible effects in the hematopoietic system should prevent possible irreversible effects in the nervous system.

DOSE-RESPONSE RELATIONSHIPS FOR LEAD

The results of population surveys which measure both dose and effect in each individual may be expressed as dose-response curves. Figure 2[18] illustrates this relationship for lead when Pb-B is used as an indicator of internal dose and erythrocyte protoporphyrin as an indicator of effect. Positive reactors are those individuals who exhibit an effect greater than the expected mean plus two standard deviations.

The percentage of positive reactors for each blood lead group is plotted. Highly susceptible individuals show a positive response at relatively low blood lead levels, while highly resistant individuals show a normal response at relatively high blood lead levels. Similar dose-response curves can be plotted for each measure of lead's effect, so that a series of dose-response relationships may be shown.[105,106]

For the groups charged with recommending "safe levels" of toxic substances, this approach to analysis of the data is helpful. However, appropriate interpretation of the data requires that the population under study be well-defined for factors such as age, sex, concurrent illnesses, etc., which may influence test results. Background response must also be considered. Background response refers to the percentage of the population exhibiting an effect caused by factors other than the specific agent under consideration. When using erythrocyte protoporphyrin as a measure of lead's effect, some "background response" may be expected due to the presence of iron deficiency in the population. Separate dose-response curves may be drawn to correct for background response. Based on inspection of Figure 2, an epidemiologist seeking to prevent early hematologic effects in 90 percent of the preschool-age population, would recommend that environmental lead sources not exceed a limit known to raise Pb-B levels to the neighborhood of 30 μg.

Dose-response relationships for lead are generally not available because of inadequately designed population surveys which consist solely of the collection and analysis of biologic samples. The population characteristics, including those which influence background response, must be known. No published data are available for children less than one year of age.

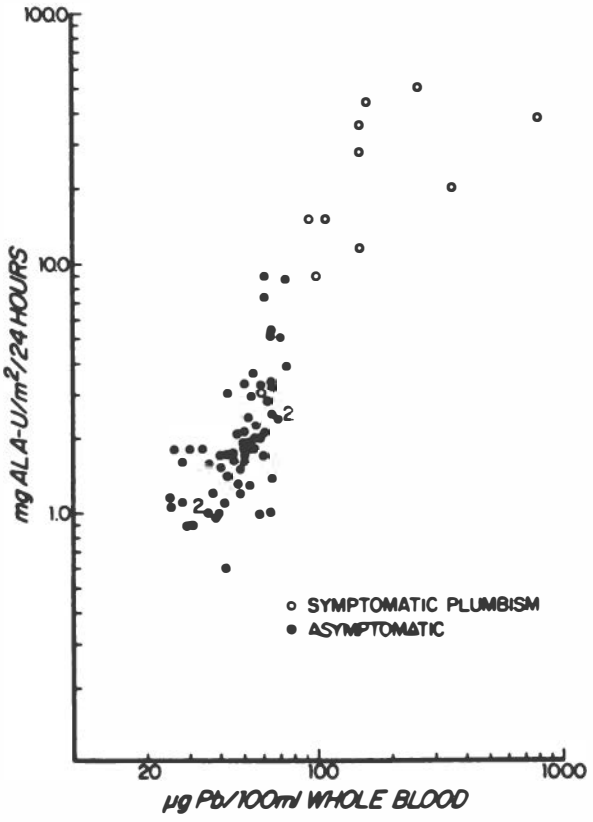

FIGURE 1. Dose-effect relationship between an indicator of internal dose (Pb-B) and an indicator of effect (urinary excretion of ALA, ALA-D).

(From Chisolm, J. Julian Jr., Barrett, Maureen B., and Mellits, E. David:[20] Dose-effect and dose-response relationships for lead in children. J. Pediatr. 87:1152-1160, 1975. Reprinted with permission.)

Note: 2 indicates 2 superimposed data points.

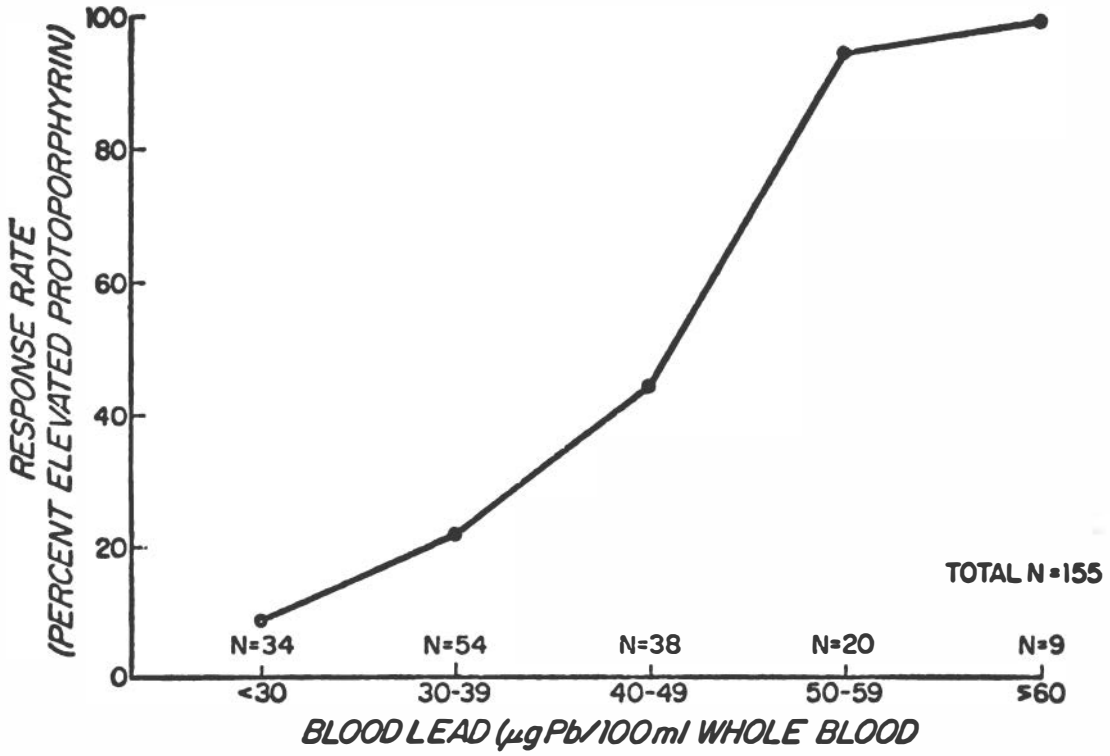

FIGURE 2. Dose-response relationship for the effects of internal doses of lead as Pb-B on erythrocyte protoporphrin.

(From Chisolm, J.J., Jr.[18] Arh. Hig. Rada Toksikol. (Archives of Industrial Hygiene & Toxicology), Suppl. to vol. 26, 1976 [in press]. Reprinted by permission.)

Appendix B

Toxicology of Lead in Experimental Animals

SELECTION OF A PROPER MODEL

Ethical considerations dictate that potentially dangerous experiments involving toxic metals be carried out in animals, not man. Unfortunately, no one species of animal is a perfect model for man. Therefore, it is crucial to insure that the organs or systems known to be affected by the toxic metal in man are closely approximated in the experimental animal species. Many recent animal studies involving lead have sought to study lead's effect on the nervous system. If the results of these studies are to be used to predict comparable effects in young children, then the stage and rate of brain growth in the animals studies are of crucial importance.

Neural Development in Humans - Dobbing and Sands have described the quantitative growth and development of the human brain for the period from 10 weeks gestational age to seven postnatal years.[27] The "growth spurt," the time of most rapid growth, begins in humans during mid-pregnancy. Three major components of the brain were examined to delineate the period of growth spurt. Glial replication and differentiation extends to at least the end of the first postnatal year and quite possibly beyond 18 months (see Fig. 3). Myelination continues into the third and fourth years (Fig. 4). Cerebellar growth is most rapid during the first 18 months of postnatal life (Fig. 5 and Fig. 6). Approximately 83 percent of the human brain growth spurt is postnatal.[25]

Sutdies of malnutrition in human infants have shown that the brain is particularly vulnerable during the growth spurt. Klein and associates studied the relationship between starvation, caused by pyloric stenosis, and intelligence.[48] Pyloric stenosis occurs between birth and three months of age, is surgically correctable and is not associated with any particular socioeconomic or cultural group. Klein found that the brief period of starvation in infancy, prior to surgery, had permanent effects on learning abilities and general adjustment, as measured 5-14 years later. Hertzig et al[39] found reduced I.Q. levels in school-age boys who had been malnourished during the first two years of life. In humans, the initial exposure to lead in paint usually coincides with ambulation and so begins at 10-12 months postpartum, while exposure to lead from some canned nutrients may begin at or shortly after birth.

Neural Development in Experimental Animals - Dobbing and associates have demonstrated the vulnerability of the developing brain to moderate hyponutrition in experimental animals.[2] Hyponutrition occuring during the growth spurt produced a permanent reduction in both body and brain weight as well as behavioral changes. Hyponutrition before this critical period had less severe effects on CNS development.

The growth spurt in rats occurs during the first 25 days *postpartum*.[25] Glial cell multiplication occupies the first half of this period. The second half extending to about the 25th postnatal day, is a period of rapid myelination. Dendritic authorization and synaptic connections are also occurring during this period, along with dramatic metabolic and neurochemical development and rapid cerebral growth. Demonstrable and permanent clumsiness is associated with cerebellar deficits caused by hyponutrition during the growth spurt.[25]

Figure 7 shows the velocity of human brain growth compared to the rat, pig and guinea pig. Striking differences are apparent in relation to the stage of brain development at time of birth. There is a dearth of information regarding the rate of brain growth in primates other than man. Nothing could be found concerning the rate of brain growth in the baboon which would have permitted a direct comparison of the CPSC studies with man. However, Portman and associates,[76,77] in studying the rhesus monkey, found that 70 percent of the adult brain weight was obtained by 165 days gestational age (mean age of birth). Allen and associates[5] produced obvious behavioral abnormalities in infant rhesus monkeys exposed to lead. No obvious behavioral abnormalities occurred in adolescent or adult mankeys exposed to a similar dose. These findings are consistent with the concept that the baboons in the CPSC studies were beyond the comparable period of growth spurt in young children.

Absorption Factor in Relation to Age - Studies in both humans and animals[13,31,43] indicate that the rate of absorption of lead from the gastrointestinal tract is greater in the young than in the adult. Studies in rats (See Tables B1 and B1.a) illustrate the rapid decrease in absorption of lead as age increases from birth. The balance data of Alexander *et al* in children are too limited to permit any statement concerning possible differences in the rate of absorption during early childhood; however, the average absorption of dietary lead found in these children (53%) is substantially greater than the 5 to 10% absorption found in adults.

Scientists seeking to evaluate the CNS effects of lead in human infants should select animals experiencing rates of brain growth and rates of intestinal absorption comparable to the human infant.

Momčilović and Kostial[68] found that the uptake of lead in the brain of suckling rats was six to eight times greater than that found in the brain of the adult rat. Krigman *et al*, by adding $PbCO_3$ to the diet of the mother, induced a four-fold increase of lead in the brain of sucklings over the amount found in the mother.[53,54] Total brain growth was inhibited and myelin production was reduced in the brain and in the sheath about the axons. Reduced amounts of galactolipids, cholesterol, plasmalogens and total phospholipids were observed in these animals. No data were reported for the lead content of milk or blood.

SELECTION OF PROPER EXPERIMENTAL CONDITIONS

Once the proper model has been selected to simulate a comparable rate of brain growth and comparable rate of intestinal absorption in

man, the experimental conditions, particularly those relating to diet and method of lead administration, should be selected to simulate those conditions seen in man.

Diet - Most experimental animals are fed optimal diets. Studies in rats[47,64,92] reveal that dietary deficiencies of calcium, copper and iron increase the absorption of lead from the intestinal tract. Dietary deficiencies have been shown to exist in a significant number of American Children.[1,98] In addition, fats and milk have been found to increase the absorption of lead in experimental animals.[43,51,52,68] In two groups of rats of the same age, lead absorption decreased to a greater extent in the group switched from a milk diet to a dry dood diet, while those who continued to receive a milk diet showed only an age-related decrease in absorption [51] (see Table I, p. 28). Experimental animals receiving dry feed diets containing all nutrient requirements do not simulate a child's diet, which may contain both fats and milk and which may be inadequate in other respects.

Method of Lead Administration - Administration of lead by injection in animals is the easiest method of determining the exact quantity administered, but does not simulate the method of exposure in man. It is difficult to determine the amount of lead ingested from loose feed, some of which the animal scatters about his cage. Studies designed to determine the rate of gastrointestinal absorption in relation to dose administered must contain a provision for accurately measuring the quantity of lead actually ingested by the animal. In order to make valid comparisons, the chemical form of lead administered to the animal should be the same as that ingested by a young child.

Measures of Internal Dose - Many animal studies do not provide a measure of internal dose such as blood lead or tissue lead levels. Because of this, it is difficult to compare the results to human studies in which levels of lead in the blood are known.

Measures of Subtle Metabolic or Functional Effects - Experiments designed to produce dramatic effects, such as death, are only the first step in demonstrating the toxic effects of lead. We do not believe that the absence of dramatic clinical symptoms at a particular dose level demonstrates the safety of that dose. Testing of animals for subclinical metabolic or functional effects, particularly those effects seen in the hematopoietic and neurologic systems, would be far more helpful in attempting to extrapolate the results of such studies to humans.

RESULTS OF LEAD EXPOSURE IN YOUNG EXPERIMENTAL ANIMALS

The work of Brown[13] appears to be an appropriate experimental model in terms of dose administered, age and neurodevelopmental stage. In addition, blood lead levels (Pb-B) were determined. Brown used suckling rats to investigate the vulnerability of the brain in relation to its developmental stage. Lead acetate was administered to the dam by gavage (35 mg/kg/day). The pups were dosed through the maternal

milk either during days 1-10 or days 11-21. No further exposure to lead occurred throughout the study and the dose was controlled to prevent impaired physical growth.

Suckling rats fed maternal milk dosed with lead during postnatal days 1-10 showed significantly slower learning compared to those fed maternal milk with equal doses of Pb during days 11-21. Learning ability in the 11-21 day group was not significantly different from controls. Blood lead levels were significantly higher in the 1-10 day group (45.8 µg Pb/dl) than in the 11-21 day group (20.4 µg Pb/dl), which did not differ significantly from controls (21.75 µg Pb/dl). The higher blood lead levels found in the younger rats suggest a higher absorption rate for Pb during the 1-10 day period than during the 11-21 day period. It is significant that learning deficits persisted at the 8-10 week level, even though Pb-B levels had returned to normal. The persistence of effect was also seen in lambs after Pb-B levels had returned to normal.[15]

In an attempt to produce slowed learning in the 11-21 day group, Brown administered higher lead doses to the dams (35, 70 and 140 mg Pb/kg/day). Only when the dose was increased four-fold, did the 11-21 day group show slowed learning comparable to that found in the 1-10 day group. This indicates that the brain is still vulnerable at the latter stage of development, but that a much higher dose is required to produce the same effect as seen in the younger animal.

Additional animal experiments show impaired CNS function due to lead. However, none contain the combination of appropriate dose, age, neuro-developmental status and blood or tissue levels seen in Brown's study. The most common information lacking is the blood lead concentration. Pentschew and Garro introduced an experimental model for studying the development of lead encephalopathy.[72] At parturition, maternal rats were fed a diet containing 4 percent lead. The sucklings received maternal milk containing 45.9 ppm Pb. Paraplegia was observed in 90 percent of the young animals near the end of the suckling period (23-29 days) and 85-90% of the paraplegic animals died. There were no data on blood lead levels in the pups. Rosenblum and Johnson[83] used this model, but used mice fed smaller doses of lead than did Pentschew and Garro. These mice had a high mortality rate, retardation of growth, delayed eye opening, broad-based gate, poorly developed righting reflex and changes in vascular and glial cells. There were no data on the lead concentrations in maternal milk or suckling's blood.

More recently, Michaelson and Sauerhoff, using a modification of the lead-in-maternal milk feeding model, were able to produce hyperactivity, aggressiveness, tremors, and repetitive grooming behavior without extensive histopathology.[65,66] The maternal milk contained approximately 25 ppm lead. No blood lead concentrations were reported. Both Golter and Michaelson,[35] and Silbergeld and Goldberg,[90] have experimentally produced hyperactivity using this same model. Golter and Michaelson found a slight increase in norepinephrine. Silbergeld and Goldberg's work linked hyperactivity to altered catecholamine metabolism.[91] In addition, they applied current drug therapy, used in the diagnosis and treatment

of hyperactive children, to their control and experimental animals. CNS stimulants (d- and l-amphetamine and methylphenidate) suppressed hyperactivity, whereas phenobarbital increased the activity in the animals exposed to lead. The same drugs given to control animals produced the opposite effects. Chloral hydrate suppressed the activity in both groups. The suppressed activity from d-amphetamine is similar to the response observed in some hyperactive children.[90,91] There were no data on the lead concentration of the maternal milk or of the suckling's blood.

Sobotka and Cook were able to demonstrate long-term behavioral deficits in neonatal rats administered oral doses of lead.[95] Initially, the dose level did not produce obvious CNS disturbances. Feeding started at 3 days and continued through day 21 at dose levels of 9, 27 and 81 mg lead/kg body weight. Blood lead concentrations performed after 35 days showed 9 µg Pb/dl for control animals and 24 µg Pb/dl for those receiving the highest dose. Activity in the high-dose lead group was decreased by administration of 3 mg amphetamine/kg body weight.

We believe that properly designed animal studies, simulating conditions in human infants, are needed to identify the relationships between external dose (dose of lead administered), absorption rate (at various ages), internal dose (blood or tissue lead levels), vulnerability of the brain (at various ages), time between exposure and appearance of effect, and permanence or reversibility of effect.

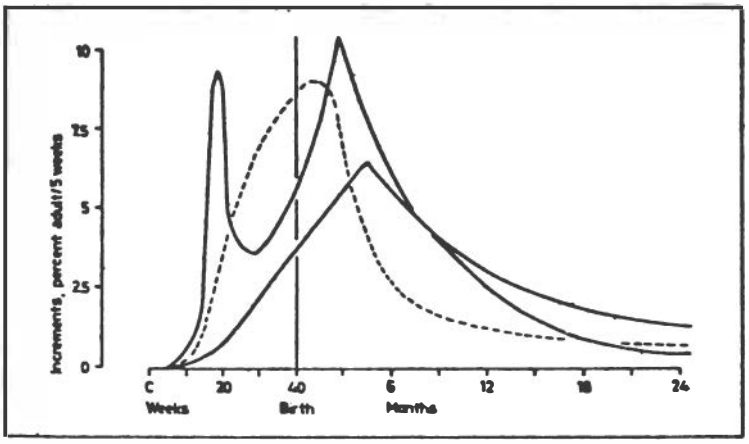

FIGURE 3. Velocity curves showing incremental rates of DNA (2 peaks, ____), cholesterol (single peak, ____) and fresh weight (----) in whole human brain. Note the bimodel curve for DNA, representing neuroblast followed by glial multiplication.

(From Dobbing.[26] Bibl. "Nutr. Diet." 17:36-45, 1972. Publisher, S. Karger AG, Basel. Reprinted with permission.)

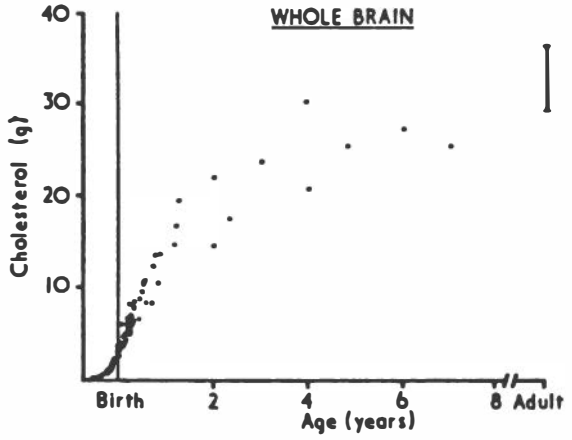

FIGURE 4. Total cholesterol in whole brain

(From Dobbing and Sands.[27] Arch. Dis. Child. 48:757-767, 1973. Ed.: Douglas Gairdner and Roger Robinson. Reprinted with permission.)

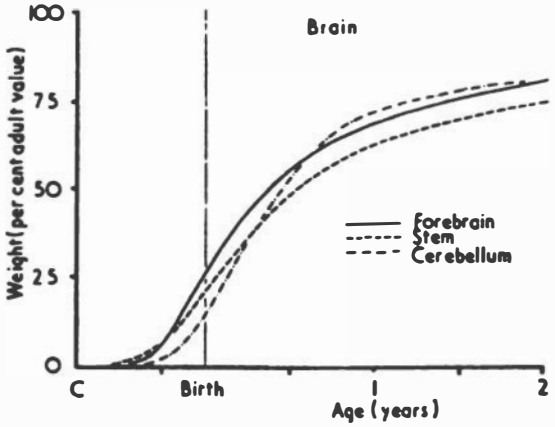

FIGURE 5. Comparative fresh weights of 3 brain regions during growth. Weights for forebrain, cerebellum, and stem have been calculated as a percentage of adult value, and smooth lines drawn by eye through the points.

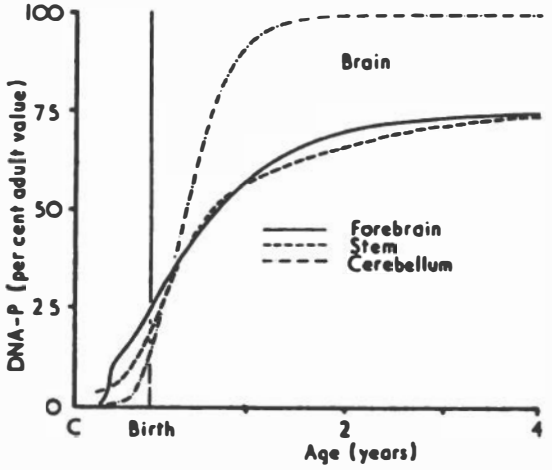

FIGURE 6. Comparative values for total DNA-P, equivalent to total numbers of cells (see text), in 3 brain regions. Values shown for forebrain, cerebellum, and stem have been calculated as a percentage of adult value, and smooth lines drawn through the points.

(From Dobbing and Sands.[27] Arch. Dis. Child. 48:757-767, 1973. Ed: Douglas Gairdner and Roger Robinson. Reprinted with permission.)

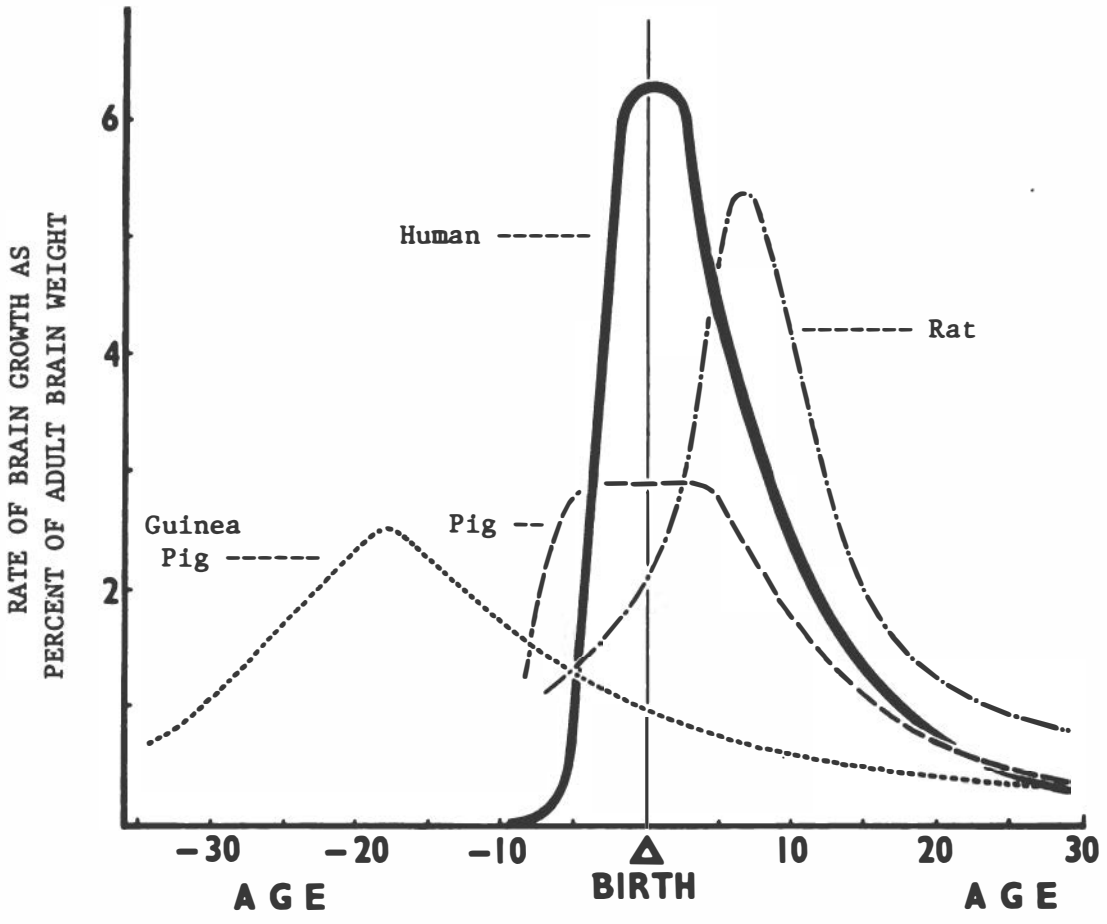

FIGURE 7. Velocity of human brain growth (wet weight) compared with that in other species. Prenatal and postnatal age expressed as follows: human ———— in months; guinea pig -------- in days; pig - - - - - - in weeks; rat -·-·-·-·-·- in days.

(From Dobbing.[25] Pediatrics 53:2-6, Jan. 1974. Reprinted by permission.)

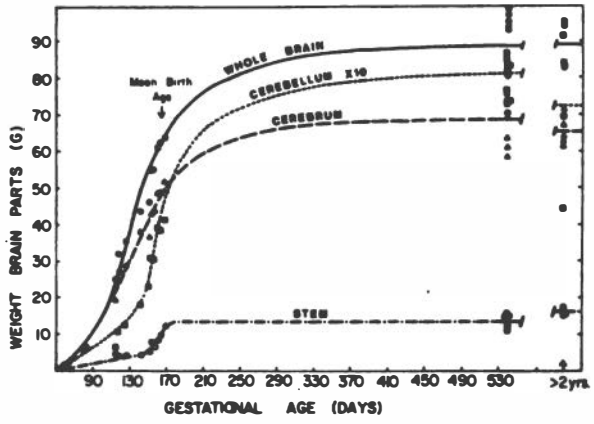

FIGURE 8. The relationship of weight of parts of the brain to gestational age of rhesus monkeys.

(From Portman et al.[76] Brain Res. 43:197-213, 1972. Reprinted by permission.)

Table I

The Effect of Milk on the Absorption of Lead

Age of Rats (days)	Rats Receiving Milk Diet (Percent ^{203}Pb absorbed)	Control Rats* (Percent ^{203}Pb absorbed)
9	65.01 (16)	71.50 (12)
15	70.46 (15)	65.28 (16)
25	57.47 (14)	6.75 (15)
37	52.72 (17)	2.50 (15)

* Control rats received only milk until day 15, when they began eating their mother's food. Numbers in parentheses show the number of animals in each group.

Adapted from Kostial, K., Kello, D., Jugo, S. and Gruden, N.: The effect of milk diet on toxic trace element absorption in rats. Presented before the XVIII International Congress on Occupational Health, Brighton, England, Sept. 14-19, 1975.[51]

Table I-a

Gastrointestinal absorption as a function of age (avg ± SD)

Age	^{59}Fe	^{85}Sr	^{212}Pb
days	%	%	%
13	100.2 ± 9.9 (4)[1]		
14	90.0 ± 11.2 (8)		
15	97.0 ± 9.4 (12)	84.8 ± 6.4 (7)	
16	90.1 ± 8.0 (9)		83.3 ± 3.3 (6)
17	86.5 ± 9.7 (7)	79.4 ± 6.2 (8)	
18			84.9 ± 3.6 (6)
19	71.1 ± 13.7 (16)		
20	78.4 ± 15.1 (5)	73.1 ± 8.5 (5)	89.7 ± 6.7 (6)
21	72.5 ± 31.5 (6)		
22	32.1 ± 9.9 (18)	54.4 ± 10.6 (7)	74.0 ± 13.3 (6)
23	25.6 ± 12.1 (14)		
24		35.6 ± 15.0 (7)	42.4 ± 11.9 (6)
25	26.6 ± 4.8 (4)		
27	19.1 ± 4.4 (8)		36.9 ± 10.2 (6)
29	23.1 ± 13.5 (7)		
32			15.2 ± 12.3 (6)
33	9.7 ± 2.5 (8)		
37	15.6 ± 4.6 (8)		
39		15.3 ± 11.8 (6)	
89+	4.7 ± 3.7 (14)	8.2 ± 8.1 (5)	16.0 ± 3.4 (3)

[1] Number of animals in parentheses.

(Adapted from Forbes and Reina.[31] J. Nutr. 102:647-652, 1972. Reprinted by permission.)

Appendix C

CPSC-Supplied Animal Studies

Of the four studies submitted to the National Research Council for evaluation, three were initially intended to answer the question "What is a safe level of lead in paint?" The fourth study carried out by Barltrop under a contract from the Center for Disease Control was intended to study the relative absorption of various lead compounds.* In evaluating these studies, this Committee sought to determine whether or not the animals studied represented a proper model for comparison to a young child. The two crucial points considered were age and diet. A summary of the study designs and results are given in Tables I and II. Supporting data for statements made in this appendix relative to diet and age are given in Appendix B.

AGE

Age is an important factor in both the susceptibility of the brain to the effects of lead and the intestinal absorption rate of lead. Young animals, particularly suckling animals, are more susceptible to nervous system injury than juvenile or adult animals.[5,13,25,26] In addition, the intestinal absorption rate of lead is significantly higher in suckling animals (see Appendix B).

The starting age of the rats used in the Midwest study[16] ranged from 30-34 days, and in the St. Mary's study[6] from 30-32 days. In rats, the "growth spurt" of the brain occurs during the first 24 days postpartum. In humans, the "growth spurt" continues well into the third or fourth year postpartum. In rats, the intestinal absorption rate of lead drops significantly at the time of weaning (approximately 22 days) and reaches adult values at about 30 days. Thus, the rats in both studies were too old for comparison to human infants and young children.

This committee could find no data relative to the rate of brain growth in the baboon. In rhesus monkeys, 70 percent of the adult brain weight is reached at the time of birth. The baboons used in the Southwest study[79] ranged in age from 18.2-31.0 months, and in the NYU study, from 3-23 months. The fact that all animals were weaned suggests that they were essentially beyond the vulnerable period. Extrapolation of the data on brain growth in rhesus monkeys also suggests this.

Diet - The intestinal absorption of lead is influenced both by dietary composition and dietary deficiencies. In particular, a diet containing lipids or milk increases the absorption of lead. Several dietary deficiencies, including deficiencies of iron, calcium and copper,

* The fact that Barltrop's study (St. Mary's study) did not meet the criteria established by this committee should not be interpreted as a criticism of study design, since this study was not intended to determine a "safe level" of lead in paint.

also increase the absorption of lead. The average child's diet contains both fats and milk. In addition, a significant percentage of children in the U.S.A. have been found to have dietary deficiencies of both calcium and iron.[1,98]

None of the animals in the CPSC-supplied studies received milk in their diets. With two exceptions, the diets did not contain added fats or oils. Two baboons from the New York study were fed lead octoate (100 µg/kg/day and 500 µg/kg/day) in olive oil. After approximately 100 days, blood lead concentration ranged from 60 to 80 µg/dl in these animals. The St. Mary's study showed that lead compounds dissolved in vegetable oils were absorbed better than the same compounds not mixed with oil.

All animals received diets formulated to provide optimum nutrition for the particular species of animal used. In addition, the baboons from the New York study had dietary supplements of fruit and multivitamins twice a day and Imferon® (iron) injections to prevent anemia.

We are forced to conclude that the nutritional status and dietary components of the study animals did not simulate the conditions found in the young child at risk for lead poisoning.

Method of Lead Administration - Neither of the baboon studies used old paint. The paint was pulverized to simulate the weathering found in old paints. Nevertheless, there is no assurance that this method closely approximates the weathered old paint films available to a child. The Midwest rat study may be condidered a replication of earlier studies by Gage and Litchfield.[32,33] The results confirm the earlier work and further document the higher availability of lead in older paint formulations.

Both the St. Mary's study and the New York study had adequate controls for measuring the dose of lead administered. Barltrop (St. Mary's study) combined the lead dose with feed and baked it into a hard stick form to prevent scattering. The diet was weighed before and after feeding to determine the amount actually consumed. The New York group fed the lead dose in a gelatin capsule so that the consumption of the entire dose was easy to determine. In the Midwest study lead was mixed in the loose diet and in the Southwest study lead was administered in a Fig Newton.

Measures of Internal Dose and Effect - All studies provided blood lead values for the control period and at various intervals during the study period. The control blood lead levels (mean approximately 10 µg Pb/dl) for all animals were significantly lower than those found in the average child living in an urban area (range of means 17-32 µg/dl).[40,59] Tissue lead concentrations were provided as follows: Brain (SW and MW), bone (SW, NYU, MW), kidney (all studies), liver (SW, NYU and MW). The Southwest study provided the greatest number of measures for metabolic change. These included ALA-D, FEP, erythrocyte porphyrinogen synthetase, plasma acetylcholinesterase, blood choline concentration, corticosteroid acetyltransferase and choline acetyltransferase. Both New York and Midwest provided measures of ALA-D, FEP and hematocrit. Most results

showed values indicating no significant change after lead administration. Unfortunately, since the animals did not adequately simulate the physiologic state or dietary conditions of young children, we feel that these results cannot be used to determine that similar doses of lead are safe for young preschool children, especially children less than three years of age.

Significant Findings - We feel that several significant findings resulted from these studies. They are as follows:

1. The presence of lipids in the diet increases the absorption of lead (New York and St. Mary's - see Table III).

2. Lead octoate is absorbed more readily than lead chromate (St. Mary's).

3. A dose of 100 μg Pb/kg/day (as 0.28 percent Pb paint) is sufficient to increase blood lead levels by approximately 12 μg Pb/dl (from 10 μg Pb/dl to 22.3 μg Pb/dl) in juvenile baboons (New York).

4. ALA-D activity is immediately depressed in all baboons when blood lead levels reach 50 μg Pb/dl (New York).

5. Plasma acetylcholinesterase is significantly decreased in baboons fed lead napthenate or lead octoate at 200 μg/kg/day (Southwest).

6. Younger baboons show a greater uptake of lead in bone than older baboons (New York).

7. The chemical form and particle size influence the absorption of lead (Midwest, St. Mary's and New York).

8. Comparable doses of lead compounds incorporated into a paint matrix are less well absorbed than the simple salts (New York).

9. Absorption and retention are related to the dose fed (St. Mary's).

10. Considerable variation in effects occurs in animals fed the same dose, thus indicating that even inbred laboratory animals have varying degrees of susceptibility for lead (all studies).

Additional Studies - The studies of Gage and Litchfield[32,33] are often quoted as evidence that negligible risk is associated with the ingestion of lead in modern paint formulations. Their studies did show that lead in paint is about 1/3 - 1/4 as well absorbed as inorganic lead salts. Thus, the New York study on lead octoate is corroborated and the two studies form the basis for estimating that the paint matrix reduces absorption by a factor of 3-4. The studies of Gage and Litchfield were carried out on rats weighing between 105 - 120 g which indicates that the animals were more than 30 days old. Thus, the neurologic development and intestinal absorption rates were not comparable to those of a young child. Based on the studies of Chisolm and Harrison[19] in which a mean fecal lead output of 44 mg/day was found in children

with severe lead poisoning, Gage and Litchfield concluded that an intake of approximately 50 mg/day would represent a dangerous level.[32] What the authors failed to realize was that this mean fecal Pb output was found in symptomatic children, most of whom had encephalopathy, and that although the mean fecal lead output was 44 mg Pb/day, the median output was 27 mg/day (range 5.04-104.0 mg Pb/day). In addition, the asymptomatic group of children described by Chisolm and Harrison[19] all had $\geq$ 60 µg Pb/dl in whole blood with positive roentgenographic evidence of lead storage in the bones and a median fecal lead output of 1.11 mg Pb/day. Thus, Gage and Litchfield's estimate of a dangerous level of lead intake was based on a fecal lead output 40 times greater than that found in children with positive evidence of long-term lead exposure and blood lead levels in a range associated with the appearance of neurologic damage.

In summary, this Committee was unable to recommend a "safe level" of lead in paint on the basis of the four studies provided by the CPSC. None of the studies were carried out on animals whose age and dietary components simulated the conditions of a young child. These studies do show that lead salts used as driers in paint are less well absorbed than the same salts not incorporated in a paint film.

Table I Experimental Design of CPSC Supplied Data

ORGANIZATION AND PRINCIPAL INVESTIGATOR			
Southwest Foundation for Research and Education (SWFRE) Robert H. Purdy[79]	New York University (NYU) Theo. J. Kneip[49]	Midwest Research Institute (MRI) Thos. R. Castles[16]	St. Mary's Hospital Medical School, London (St. MHMS) Donald Barltrop[6]
STUDY ANIMAL AGE AND WEIGHT RANGE			
Baboon 18.2 - 31.0 mo 3.3 - 7.7 kg	Baboon - Papio sp 3 - 23 mo 1.2 - 5.2 kg	Rat - Charles River 40 - 60 g (30 - 34 days) (80 - 90 g)	Rat - Wistar 30 - 32 days 90 - 110 g Pilot Study 20 - 40 days
DIET AND DIET LEAD CONTENT			
Ralston Baboon Chow 0.72 µg lead/g H_2O: 0.5 µg/liter	Purina Monkey Chow 0.36 µg lead/g H_2O: not reported Fruit 2 times/day Multivitamins/daily	Purina Rat Chow 4 µg lead/g H_2O: not reported	Oxoid (powder) 41B 2.0 µg lead/g H_2O: 10 µg/liter
PREVENTIVE THERAPY			
	IMMERON Intramuscular Injection 2 mg iron/ml blood drawn		
MODE OF LEAD ADMINISTRATION			
Fig Newton	Gelatin Capsule	Mixed in Loose Diet	Mixed and Baked in Stick Form

Table I
Experimental Design (Cont'd)

DOSE, LEAD COMPOUND &/OR MATERIAL FED, NUMBER OF ANIMALS/GROUP DURATION (T)

SMITH

µg/kg/day	% Lead	No.	T (mo)
0	-	4	6
	PAINT CHIPS [a]		
	Naphthenate		
11.5	0.44	4	6
50.0	"	4	6
100.0	"	4	6
200.0	"	4	6
500.0	"	4	4
	Octoate		
11.5	0.5	4	6
50.0	"	4	6
100.0	"	4	6
200.0	"	4	6
500.0	"	4	4
	Lead Acetate		
100	[b]	4	4

NYU

µg/kg/day	% Lead	No.	T (mo)
	PAINT CHIPS [c]		
	Octoate		
12	0.5 lead	1	10
"	"	1	12
100	"	1	8
"	"	2	10
"	"	1	12
"	"	2	5
200	"	2	11
500	"	2	6
100	0.06	2	-
100	0.28	2	-
100	0.5 [d]	2	6
100	2.0	2	6
	Lead Acetate		
100		2	4
100		2	6
200		2	4
500		2	5
10,000		2	4
20	intravenous	2	6
	Lead Octoate in Corn Oil		
100	40.7 lead	2	5
500	40.7	2	5

MRI

µg/g	Diet	% Lead	No.	T (wks)
0		Film [e]	40 [f]	13 (max)
		PAINT CHIPS		
		Octoate		
1.1		0.08	20	13
7.9		0.53	20	13
23.1		2.05	20	13
		Chromate		
6.9		0.42	20	13
19.4		1.95	20	13
136.1		12.43	20	13
		Carbonate Old Paint		
511.9		66.5% NBS [g]	20	13
119.9		11.92%	20	13

St. HIMS

PAINT CHIPS [h]
Dose 0.02% Lead
Fed 1 wk

Octoate
500 - 1,000 µ Chip Size
< 50 µ " "

Chromate
500 - 1000 µ Chip Size
< 50 µ " "

All doses contained 0.075% Lead
Diet Fed for 48 hrs
6 animals/test group
2 pretest control

Lead Octoate
Mixed in Corn Oil
Acetate
Alsynate
Napthenate
Octoate
Tallate
Not Mixed with Oil
Acetate
Oxide
Sulfide
Metal < 180 µ
Metal 180 - 250 µ

Basic carbonate

FOOTNOTES:

[a] Paint Chip Size < 500 µ

[b] This group received 1000 µg/kg/day for 2 weeks instead of 100 µg/kg/day. Data not considered.

[c] Paint chip size < 500 µ

[d] Two animals died of un-related causes.

[e] Film and Paint in form of chips 500-1000 µ. Material added to diets 0.1% (weight/weight)

[f] 50% females

[g] National Bureau of Standards

[h] The same materials used by Midwest Research Institute.

Blood Sampling Sequence

Dose of Lead	Week 1	2	Other
0	2x	2x	7
11.5 µg	Alt.Da	1x	1x
50 µg	Alt.Da	1	1
100 µg	Alt.Da	1	1
200 µg	Alt.Da	1	1
500 µg	Daily Alt. da.		1

NECROPSY

Dose	Week 1	2	3-4	Other
< 500 µg lead	2x	1x	½ wk	½ wk
≥ 500 µg lead	3x	2x	1x	1x

NECROPSY

At 4, 8 and 13 weeks, several male and female animals isolated 24-hrs in metabolism cages for urine collection.

NECROPSY

Animals weighed before and after 4-hr exposure.

Diet weighed before and after.

NECROPSY

Table II Results from CPSC Supplied Data

Southwest	NYU	Midwest	St. Mary's
ABSORPTION COEFFICIENTS			
Significant increase as dose level of lead is increased	Attempted; indeterminant results	Not determined	Not determined
BLOOD PARAMETERS			
Blood lead			
Control 10.8 ± 0.039 µg % 50 µg/kg/day napthenate caused significant increase to 11.9 ± 0.046 µg %. Greatest level 15.1 ± 0.045 µg % was caused by 500 µg/kg/day	Controls varied around 10 µg %. Experimental data too limited to make adequate evaluation. Reported "steady state" data for appropriate age (4-8 months) animals fed paint chips 9 months at dose levels 12 µg/kg/day and 100 µg/kg/day caused blood levels < 20 µg %. Animals fed 100 µg/kg/day in the series 0.06%, 0.28%, 0.50% and 2.0% lead in paint. The "steady state" data was normal for the least lead in paint. The greatest concentration caused an average blood elevation of 19.1 µg %. However, 0.28% lead caused a blood lead elevation of 21.8 µg %.	All data lost for sample weeks 4 and 8. Four determinations in all groups except the NBS Group were dropped for week 13 data. Authors state blood values for lead concentration in paint less than 2.05% was no different from control. All others were significantly higher.	Control values vary around 9 µg %. Lead Octoate absorbed more than lead chromate. Smaller particle size allowed greater uptake. Octoate 500-1000µ 19.3µg % < 50 µ 27.2 Chromate 500-1000µ 14.5 Lead Acetate 38.3
δ-aminolevulinic acid dehydratase (ALAD)			
No significant difference between average values in all groups studied.	"Steady state" values reported. Insufficient data to evaluate trends and rates of development. Authors report immediate depression in all animals where blood-lead levels reached a steady state concentration of 50 µg % or more. /Proposed the measurement as predictive determinant to lead exposure/	Enzyme activity not significantly different from controls for all lead concentrations in the paints containing octoate and chromate. Significantly depressed by old paints containing carbonate. Earliest response in 8th week for paint containing 66% lead.	Not determined
Free erythrocyte porphyrin (FEP)			
No significant difference between average values in all groups studied.	Data selected to show only measurable response for "induction period." No dose-response relationships established. Did compare 3 different materials of varying lead availability. Did not compare by plotting data from studies in 1973 and 1974. /Propose FEP as the critical biological effect/	No significant difference	Not determined
Erythrocyte porphyrinogen synthetase (EPS)			
Random change.	Not determined	Not determined	Not determined
Plasma acetylcholinesterase			
Significantly decreased in animals fed napthenate and octoate at 200 µg/kg/day	Not determined	Not determined	Not determined
Blood choline concentration			
No significant difference between arterial and venous levels.	Not determined	Not determined	Not determined
Hematocrit			
Not determined	Measured; data not correlated to response to paint lead content.	No significant difference between controls and experimental animals, except for animals fed carbonate (NBS) paint. Difference occurred at week 13.	Not determined
Hemoglobin			
Not determined	Measured; data not correlated to response to paint lead content.	Not determined	Not determined
Other hematologic measurements			
Not determined	Not determined	Erythrocyte count, reticulocyte count, leukocyte count, differential leukocyte count, RBC Osmotic fragility, and serum proteins. No differences observed.	None determined

Table II
Results (Cont'd)

Southwest	NYU	Midwest	St. Mary's
		OTHER TISSUE DETERMINATIONS	
Brain			
Lead Content Slight elevation. Does not show dose-response relationship.	Not determined	Not detected in all groups at 4, 8 and 13 weeks; exception week 13 for animal fed NBS carbonate paint (0.2 µg/g tissue).	Not determined
Corticosteroid Acetyltransferase No significant difference.	Not determined	Not determined	Not determined
Choline Acetyltransferase Some alterations not significantly correlated to dose.	Not determined	Not determined	Not determined
Bone			
Lead Content Not determined	Younger animals have greater uptake. Preponderance of evidence indicates doses from 100 to 500 µg lead/kg/day as lead in paint at a concentration of 0.5% lead does not cause significant increase in tissue burden.	Elevated at 4 weeks in animal fed old carbonate paint. Lead level significantly elevated at 8 and 13 weeks.	No paint data
Kidney			
Lead Content No significant difference between controls and experimental animals.	No significant increase in tissue burden.	Not detected in all groups at 4 and 8 weeks. Exception at 8 weeks on NBS-carbonate paint (1.4 µg/g tissue). At 13 weeks detected lead in all groups not in a consistent dose response relationship.	Control mean total lead .51 µg Octoate 500-1000µ 2.38 µg < 50 µ 4.30 µg Chromate 500-1000 µ 2.18 µg < 50 µ 3.35 µg
Liver			
Lead Content No marked difference between controls and experimental animals.	No significant increase in tissue burden.	Not detected in all groups at 4, 8 and 13 weeks; except at 13 weeks animals fed both carbonate paints had detectable lead concentration.	No point data.

Table III Comparison of Lead Accumulation in Tissues of Weanling Rats.[a]

	Dietary Concentration	Kidney Total lead µg	Blood µg lead/100 ml	Bone Total lead µg
Lead acetate	0.02%	11.28 11.52	56.31 51.81	5.87 6.08
Lead acetate in oil	0.02%	20.25 22.75	97.5 93.3	9.03 11.53

a Data from Barltrop.[6]

Appendix D

Etiology and Consequences of Childhood Lead Poisoning

The National Bureau of Standards estimates that 600,000 children in the United States have unacceptably high blood lead levels ($\geq$40 µg Pb/dl).[34] This estimate was based on data from large to medium sized standard metropolitan statistical areas (SMSA) in the East and Midwest only. The incidence of lead poisoning is highest among one- to five-year-old inner city children who live in substandard housing containing multiple layers of old lead paint.[12,60,70] A relatively small number of cases result from exposure to improperly glazed pottery or exposure to industrial point sources such as smelters and battery factories.[56]

RISK FACTORS

Multiple factors serve to increase the risk of lead poisoning in the 1-5 year old child. Among these are age, pica, diet and multiple sources of exposure.

Age - The process of growth itself produces stress, making the child more susceptible to a host of disease agents which affect adults to a lesser degree. Both increased vulnerability of the brain and increased intestinal absorption of Pb have been identified as two significant risk factors related to age. Studies in both humans[39,48] and animals[13,72,83,90] have shown the brain to be most vulnerable during the "growth spurt" which, in humans, begins during the sixth month of pregnancy and continues into the third or fourth year postpartum[25] (see Appendix B for a detailed discussion).

Balance studies in adults have shown an intestinal absorption rate of 10 percent.[42] Alexander and co-workers carried out lead balance studies over a three-day period in healthy children ranging from 3 months to 8-1/2 years of age. They found that healthy children absorb an average 53 percent of ingested lead and retain 18 percent.[4] Animal studies also show a higher rate of intestinal absorption[13,31,43] prior to weaning than after weaning.

Pica - The young child first learns to explore the world orally. From the time he is able to grasp and lift objects, he places everything in his mouth. This is a normal activity, which persists in 50 percent of the children until age three.[61,94] Beyond this age, pica is generally considered an aberrant behavior. Pica may be defined as the compulsive ingestion of non-food substances. The older child with pica may be highly selective in his choice of substances. Psychosocial factors are important components of repetitive and selective pica.[94] Pica for paint is believed to be essentially episodic, occurring perhaps two to three times per week. Variations in fecal lead output tend to confirm this observation.[19] Pica for paint generally begins after the child learns to crawl or walk; however, later onset of pica for paint has been observed.[21] Abdominal x-ray plates showed radiopaque material

in the intestinal tract in 35 percent of children seen in the Chicago Lead Clinic.[84]

Diet - Both dietary components and nutritional deficiencies have been found to increase the absorption of lead from the intestinal tract. Studies in rats[6] and baboons[49] have shown that the presence of lipids in the diet increases absorption. Kostial's studies of rats show greater absorption of lead if administered in milk than if administered in dry feed.[51,52] Animal studies involving dietary deficiencies of calcium, copper and iron have shown that these deficiencies increase the absorption of lead.[6,47,64,92] In long-term experiments in growing rats, restriction of dietary iron and calcium to 20 percent of the Recommended Daily Allowance for growing young rats increased the absorption and retention of lead by a factor of two or more.[64,92] This degree of reduction in dietary intake of calcium and iron has been reported in two- to three-year-old children from low-income families.[63,98] A population survey of American children showed less than optimal calcium intake ranging between 12-14 percent for white children and 23-25 percent for black children.[1] Iron deficiency, defined as hemoglobin levels <10 grams, was seen in approximately 4 percent of white children from families above the poverty line, 10.8 percent of white children in families below the proverty line, 17.6 percent of Negro children in families above the poverty line and 15 percent of Negro children from families below the poverty line.[1] Others[93,98] have also reported dietary deficiencies of calcium and iron in young children. Iron deficiency is most prevalent among children 12-24 months of age.[1,93]

Sources of Exposure - The preschool-age child is exposed to multiple sources of lead. These include dust, canned foods and liquids, and paint. The last is usually considered a "high dose" source of lead while the others in which the concentration of lead is much lower, are considered "low dose" sources. It is the cumulative intake and absorption from these various sources that is important. Direct inhalation of average urban air (1-3 μg Pb/m^3) is considered insignificant in comparison with the sources given above.

Recognizing that city children showed a higher prevalence of elevated blood lead levels than did rural children and that not all children with elevations had a history of pica for paint, Lepow[59] decided to examine the possibility of exposure from dust and dirt. She found a mean level of 11,000 μg Pb/g house dust. Samples of dust from the hands of children residing in these houses contained a mean level of 2,400 μg Pb/g dust with a mean weight of 11,000 μg dust per hand sample. The authors suggested that lead emissions from automobiles contributed significantly to the high dirt and dust lead levels found in the city. Sayre and Vostal[88,102] found that house dust levels in inner city homes contained median concentrations of lead five times greater than that found in suburban homes and that the concentration of lead on the hands of a child was related to the concentration of lead in house dust from his home. Their first study[88] did not differentiate between old and new inner city housing; the second study did.[102] It was found that old inner city housing contained 33-486 μg Pb/sq. foot floor surface, new inner city housing contained 2-24 μg Pb/sq. foot and suburban housing contained 0-60 μg Pb/sq. foot. Since the dust lead levels in the newer inner city houses were significantly lower than in the older inner city houses, the authors concluded that the source of lead originated from within the homes, presumably from the powdering of old lead paints.

Ter Haar[99] examined dirt samples around 18 painted frame farm houses remote from traffic. The concentrations of lead in dirt were similar in both rural and city yards and decreased in relation to distance from the house. In addition, Ter Haar studied the relative contribution of lead from fallout dust by measuring the fecal output of both stable lead and ^{210}Pb in two groups of children. A naturally occurring tracer, ^{210}Pb is almost absent from paint, but occurs in significantly higher concentrations in air-suspended particulates or dust fall. The first group of children was suspected of having elevated body lead burdens; the second group lived in good housing in which lead poisoning was not a problem. The first group had fecal lead outputs ranging from 4-1640 µg Pb/g; the second had outputs of 2-7 µg Pb/g. Despite the wide difference in total lead output, both groups had essentially identical outputs of ^{210}Pb.[99] The conclusions reached were that lead paint from the houses was the principle cause of elevated soil lead levels and that lead from air-suspended particulates was not a significant source of lead intake in the children studies.

Canned foods, particularly acidic foods such as fruits and fruit juices, have been found to contain higher concentrations of lead than similar food packaged in glass or plastic containers. Mitchell and Aldous[67] found a mean lead concentration of 202 µg Pb/liter in canned foods and 35 µg Pb/liter in bottled products. Many of the canned baby foods analyzed in this study were fruit juices, some of which contained >500 µg Pb/liter. Canned evaporated milk had from 10 µg Pb/liter to 820 µg Pb/liter (mean 202 µg Pb/liter). The National Canners Association sponsored a study of lead intake in 333 infants aged 1-12 months (unpublished but cited by Kolbye, et al[50]). Their estimate of dietary intake was 93 ± 36 µg Pb/day, or approximately 50 percent of the adult dietary intake. To one observing Mitchell's data, it seems obvious that wide variations in Pb intake could occur as a result of the parents' choice of food for their child.

Paint provides the most concentrated source of lead potentially available to a young child. House paints containing the present legal limit of 0.5 percent lead would provide 5,000 µg Pb/g paint. Sachs[85] has indirectly estimated the quantity of paint ingested by a child with pica for paint. Model x-ray films were made, using known quantities of paint. These were then compared to abdominal x-ray films taken of children known to have pica for paint. Seven out of 10 randomly selected films showed radiopacities equivalant to an estimated 1 gram of paint.[46] At least one film was estimated to show 20 grams of paint.[85]

Generally speaking, lead intake in adults is from "low dose" sources such as food, water and ambient air. The child has additional sources of lead exposure from dirt, house dust and paint. Based on the data presented above, the most hazardous "high dose" source available to the average child is paint.

Average Daily Intake of Lead in Normal Children - Alexander's studies in eight healthy children receiving a normal diet, showed a mean daily intake of 10.61 µg Pb/kg body weight.[4] Of this amount, 5.47 µg Pb/kg/day were absorbed and 5.13 µg Pb/kg/day were excreted in the feces. Thus, the children absorbed approximately 50 percent of the lead

available from dietary sources. In contrast, Kehoe's studies in adults showed an absorption rate of approximately 10 percent for lead from dietary sources.[42] These findings are in agreement with studies in experimental animals which show a higher intestinal absorption rate in the young than in the adult. Barltrop, et al studied the relationship between fecal lead output and blood lead levels in two- to three-year-old children.[8] A mean fecal lead output of 67.8 μg Pb/day was observed in a group of 35 children with a mean blood lead level of 20 μg Pb/dl. Recalculated on a body weight basis for an average three-year-old child weighing 15 kg, the daily fecal lead output would be 4.5 μg Pb/kg/day. Assuming a 50 percent absorption rate, the daily intake necessary to produce this excretion would be 9.0 μg Pb/kg/day. This is not far different from Alexander's figure of 10.6 μg/kg/day. In addition, the mean blood lead level of 20 μg Pb/dl is comparable to that observed by others in normal "unexposed" children.[40,59,70]

CONSEQUENCES OF CHILDHOOD LEAD POISONING

Permanent effects of lead poisoning include blindness, mental retardation, behavior disorders and death. Clinically obvious effects of this magnitude are associated with the later stage of lead poisoning in which encephalopathy occurs.[14,74] Therapeutic intervention at this stage is only partially successful in preventing severe permanent deficits.[17] Lead encephalopathy in children generally does not occur until blood lead levels exceed 120 μg Pb/dl.[70] The current focus of research interest involves studying whether or not more subtle but permanent effects result from less severe cases in which no symptoms, or only mild symptoms, are apparent.

Lead exerts its toxic effects in the renal, hematopoietic and nervous systems. Kidney damage is a reversible effect seen in severe cases and no published data are available to suggest that damage occurs in asymptomatic cases. Adverse, but reversible, effects are seen in the hematopoietic system in asymptomatic cases. A current controversy centers around conflicting reports of neurologic damage occurring in asymptomatic or mildly symptomatic cases.

Hematopoietic Effects - Lead-induced anemia has been reported in both adults and children. Lead causes multiple interferences in the formation of hemoglobin,[70] including inhibition of the enzymes, δ-aminolevulinic acid dehydratase (ALA-D) and ferro chelatase.[28] The inhibition of these enzymes results in an accumulation of δ-aminolevulinic acid in urine (ALA-U) and "free" erythrocyte protoporphyrin (FEP) in blood.

European studies have shown that increases in free erythrocyte protoporphyrin begin to occur in women and children when blood lead levels reach a range of 25-30 μg Pb/dl, and in men at 35-45 μg Pb/dl.[81,97,104,105] It is now known that it is zinc protoporphyrin rather than the free protoporphyrin IX which is present in excess in the circulating erythrocytes in lead poisoning and iron deficiency.[55] Population studies of children in the United States have rarely included a sufficient number of children

with < 20 μg Pb/dl to determine this lower threshold level. A second threshold is seen in children when blood lead levels reach the range of 35-40 μg Pb/dl.[20,41,75,87] The excretion of ALA-U begins to rise in both adults[89,100] and children[20] when blood lead levels reach the range of 40-50 μg Pb/dl. In children, quantitative collections of urine are required for ALA-U. The determination of ALA-U in random urine specimens from children is of little value.[71,96]

Hernberg has demonstrated that lead shortens the life span of the red blood cell and that this is a mechanism by which lead produces anemia.[38] Tola has demonstrated a significant decrease in hemoglobin levels in new workers occupationally exposed to lead.[100] Decreased hemoglobin levels became evident within two to three months, as Pb-B approached 50 μg/dl. Pueschel found a significant negative relationship between hemoglobin levels and blood lead levels in children.[78] Blood lead levels ≥60 μg Pb/dl were almost always associated with hemoglobin levels <10 g/dl. Betts[11] found hemoglobin levels <11 g/dl in 36 percent of children with 37-60 μg Pb/dl, 71 percent with 60-100 μg Pb/dl and 89 percent with ≥100 μg Pb/dl. Rosen et al[82] found a negative relationship between hematocrit and blood lead concentrations at levels exceeding 40 μg Pb/dl.

Neurologic Effects - Subtle deficits in neurologic functioning are difficult to measure and even more difficult to attribute to a single cause such as lead poisoning. There is currently no set of neurochemical tests for measuring changes in the nervous system that is comparable to the set of tests (ALA-D, ALA-U, UCP and FEP) available for measuring changes in the hematopoietic system. Current measurements of neurologic changes are accomplished through the use of functional tests such as I.Q. tests. Confounding factors such as parential I.Q., parental education level, socio-economic status, birth trauma, etc., also influence the results of these tests. Studies purporting to show a relationship between I.Q. and exposure to lead should include control subjects carefully matched with study subjects for age, birth rank, parental I.Q. socio-economic status, nutrition, pica, etc. In addition, they should be prospective studies in which the presence or absence of exposure to lead in the early years is well documented. Most of the current controversy results because studies were undertaken without a proper design and lack either a proper control group or firm documentation of the degree of lead exposure during the early years of life.

The studies of de la Burdé[23,24] meet most of the criteria of a prospective study. Both study and control children were drawn from an on-going Child Development Study at the Medical College of Virginia in Richmond. Mothers were followed during pregnancy and delivery and children followed for eight postnatal years. The study group consisted of 67 asymptomatic children who had a positive history of pica for paint or plaster, lived in deteriorated old housing, had positive urinary coproporphyrin tests and either a blood lead level ≥40 μg Pb/dl or blood lead ≥30 μg Pb/dl and positive radiographic findings for lead lines in the long bones. Because of the analytical problems inherent in blood lead methodology, as performed in the 1960's,[44] we feel that this combination of criteria for selecting the study group was more reliable

than a selection based on blood lead levels alone. Even so, the absence of serial blood lead levels, which were not feasible at the time, is the major weakness of this study. This weakness is largely overcome by dependence on x-rays and repeatedly positive urinary coproporphyrin tests. Positive bone x-rays[11] and positive urine coproporphyrin tests[10] are generally associated with blood lead concentrations equal to or greater than 60 μg Pb/dl. Lead levels in shed deciduous teeth were performed several years later on teeth from 29 of the lead-exposed children and 32 of the control children. The mean tooth lead level for the study group was significantly higher than the mean tooth lead level of the control group. The control group consisted of 70 children who had a negative history of pica for paint or plaster, lived in modern housing, did not visit older housing for day care and had negative tests for coproporphyrin in urine. In addition, all children were excluded from both groups who showed neurologic abnormalities or developmental lag either during the newborn period or at four months, if abnormalities were noted on the Bayley scale at eight months, or if confirmed or suspected disease of the central nervous system was noted anytime before seven years of age. In addition, the groups were comparable in age, sex, race, mother's non-verbal I.Q., socio-economic status, family composition and possible sources of family upheaval such as death in the family, foster home placement or working mother.

Neurological and psychological tests were administered to both groups at four years of age and again at seven years of age. Fifty-eight children from each group also had tests repeated at eight years of age. At four years of age, the most significant differences between the groups were in the areas of fine motor coordination and behavior. Failure on fine motor tests occurred almost twice as frequently in the lead-exposed group as in the control group. Deviation in overall behavior ratings occurred almost three times as frequently in the lead-exposed group. Mean I.Q. scores, as measured by the Stanford-Binet test, were 89 ± 13.1 for the lead-exposed group and 94 ± 10.5 for the control group. At seven years of age, neurologic examination revealed deficits in more than twice as many children from the study group as from the control group. Full-scale I.Q., as measured on the Wechsler Intelligence Scale for Children revealed that the majority of children from both groups had average intelligence, although the mean I.Q.'s were statistically significantly ($p < 0.01$) lower in the lead-exposed group. The frequency of results in the borderline or mentally defective range was higher in the lead-exposed group. Short attention span and minimal goal orientation occurred in 32 percent of lead-exposed children and 14 percent of control children. Poor academic progress was noted in 27.8 percent of lead-exposed children and 4.1 percent of control children. The number of children repeating at least one grade was higher in the lead-exposed group (25.9 percent) than in the control group (6.1 percent). Eleven lead-exposed children and four control children were receiving speech therapy for speech impediments.

The authors felt that the most significant difference between the groups was in the area of behavior and that this was the primary cause for poor school performance. Among the lead-exposed group, five had been seen by psychiatrists, one had been institutionalized and three

were subject to seizures. None of these findings occurred in any of the control children. A review of school records revealed that hyperactivity, explosive behavior and frequent temper tantrums occurred in 19 lead-exposed children and 5 control children. The behavior problems which had been apparent at four years of age, but which were adequately handled in the home environment, persisted at seven years and prevented appropriate functioning in the school environment. It is of interest to note that these findings in asymptomatic children are similar to the findings of Byers and Lord in symptomatic children.[14] Although Byers and Lord found little difference between lead-poisoned and control children, in relation to overall I.Q., the lead-poisoned children were found to have significantly poorer school performance.

The results of several additional studies have suggested a relationship between increased lead absorption and neurologic deficits in young children. Albert et al[3] obtained data on 371 children with varying degrees of lead exposure. A record of blood lead levels was obtained from the New York City Health Department blood lead registry. The mean age at time of blood test was 2.5 years. Relocation and evaluation of the patients took place 3-11 years after blood lead testing. The children were divided into five groups according to degree of exposure. Group I contained six children with lead encephalopathy, Group II contained 154 children treated for lead poisoning who did not have encephalopathy. Group III contained 65 children with blood lead levels $\geq$60 µg Pb/dl who were not treated, Group IV contained 57 children with <60 µg Pb/dl, but elevated tooth lead levels, and Group V contained 89 children with both low blood lead and tooth lead levels. Neurologic disorders, including mental retardation, organic brain syndrome, seizure disorders and behavior disorders, were found in 66.7 percent from Group I, 11.0 percent from Group II, 18.5 percent from Group III, 3.5 percent from Group IV and 4.5 percent from Group V. Psychometric tests were performed on 159 of the 371 children. A composite rating based on Intelligence Quotient, Bender-Gestalt quotient, Figure Drawing quotient and Purdue Pegboard error score was made by a clinical psychologist. Groups I and III had significantly lower ratings than Group V. Groups II and IV did not differ significantly from Group V. It is not surprising that the encephalopathy group showed neurologic deficits. The fact that the untreated children with $\geq$60 µg Pb/dl (Group III) showed a higher frequency of neurologic deficits than the diagnosed and treated cases of lead poisoning (Group II), led the suthors to conclude that this group contained children who should have received chelation therapy. Clinical records revealed that 37 of the 65 children in Group III had symptoms compatible with lead poisoning.

Perino and Ernhart[73] reported a significant negative relationship between blood lead levels and cognitive, verbal and perceptual abilities in 80 asymptomatic children, ages 3 years to 5 years, 11 months, who had blood lead levels ranging from 10-70 µg Pb/dl. They also found a significant negative relationship between parental education level and blood lead levels in the children. Their "low lead" group (10-30 µg Pb/dl) did not differ significantly from the "moderate lead" group (40-70 µg Pb/dl) in socio-economic status, sex, age, parental intelligence, number of siblings, birth order or birth weight.

Landrigan[57] and McNeil[62] each studied different groups of asymptomatic children exposed to lead emissions from an ore smelter in El Paso, Texas. Both studies contained an exposed and a control group. Landrigan found impaired non-verbal cognitive and perceptual skills, as well as slowed finger-wrist tapping in his exposed group. McNeil found no significant intellectual or behavioral differences between carefully matched exposed and control groups. Several factors make it difficult to evaluate the results of these studies. The children studied had multiple exposures to metals, including lead, arsenic, copper, zinc and cadmium.[56] Landrigan's criteria for selection of children for the study group were based on a blood lead level $\geq$40 µg/dl, while McNeil's criteria were based on residence in proximity to the smelter. In addition, normal hemoglobin and hematocrit levels found in these children[62] indicate that nutrition was probably adequate. This may have served as a protective factor in these children.

Lansdown's[58] study of British children exposed to lead emission from an ore smelter showed no significant correlation between blood lead levels and either intelligence quotients or behavior ratings. However, of the 215 school age children studied, only 12 had $\geq$50 µg Pb/dl and 31 had 40-49 µg Pb/dl. Thus, the correlation coefficients were heavily influenced by the 172 children with <40 µg Pb/dl. In addition, there was no attempt to match the study group with a control group of the same age, parental intelligence, socio-economic status, birth rank, family size, etc.

Retrospective studies carried out by Beattie *et al*[9] and David *et al*[22] have suggested a relationship between lead exposure and I.Q. and lead exposure and hyperactivity, respectively. Neither study, however, provided adequate documentation of the degree of early lead exposure in the children studied.

This committee realizes the difficulties inherent in designing and executing longitudinal studies in children to detect subtle neurologic differences between groups. Although no single study cited represents a perfect model, we feel that the general trends seen in these studies indicate a relationship between asymptomatic lead poisoning and neurologic and behavioral handicaps.

In conclusion, we feel that the question of individual susceptibility must be taken into account when setting "safe levels" of toxic substances. Studies of both hematologic effects and neurologic effects show varying degrees of response among individuals with equivalent exposure to lead. Hematologic effects begin to occur in some 1-5 year old children when blood lead levels reach the range of 35-40 µg Pb/dl, while an increased frequency of neurologic effects have been demonstrated only in those children with elevations in the range of 50-60 µg Pb/dl or above.

Appendix E

Evaluation of the Hazard of 0.5 Percent Lead Paint

No single study of children with pica for paint has combined the numerous measurements necessary to estimate a "safe level" of lead in paint. Therefore, a decision regarding the safety of 0.5 percent lead paint must be made by relating measurements found in various studies. Ultimately, the estimated intake of paint chips in a child with pica must be related to the appearance of adverse effects in that child.

The potential hazard of ingesting lead-containing paints is related to the average amount absorbed on a daily or weekly basis over a period of months. The percentage of ingested lead that is actually absorbed from the gastrointestinal tract into the body varies according to the chemical and physical form of the ingested lead (i.e., paints, dust, etc.), age and other factors. Differences in the rates of absorption of lead from each source can be largely compensated, if the available data are recalculated as µg Pb absorbed/kg body weight/day. In this way, a reasonable estimate of the amount of paint containing 0.5 percent lead necessary to raise Pb-B to a hazardous level can be made. We will use two methods for estimating the hazard of paint containing 0.5 percent lead:

Method A - The first method of estimating the safety of 0.5 percent lead paint will be made by relating estimated paint intake to fecal lead outputs found in children with blood lead levels (Pb-B) $\geq$60 µg Pb/dl. Pica for paint has been observed to be episodic, occurring up to two to three times per week. The analysis of lead in consecutive fecal samples seems to confirm this observation.[19] Through the use of abdominal x-rays, Sachs has demonstrated that some children with pica for paint are capable of consuming more than 1 gram of paint in the 24-36 hour period preceding the time of x-ray.[46] One child was estimated to have consumed 20 grams of paint during this time.[85]

An estimated range of lead intake can be calculated, using a figure of 0.5 percent lead in paint (5000 µg Pb/g paint), a figure of 1 gram paint per ingestion and a figure varying from one to three for frequency of ingestions per week. The estimated weekly intake is then divided by seven to obtain an average daily intake. Using these figures, the average daily intakes would be 714 µg Pb, 1,429 µg Pb and 2,143 µg Pb, respectively, for one, two and three ingestions per week.

It is estimated that 50 percent of lead from foods is absorbed by a young child.[4] However, studies in rats have shown that lead chromate in paint films is not as well absorbed as the simple inorganic salts of lead. Gage and Litchfield[32] estimate that lead chromate pigment in paint is absorbed one-fourth to one-third as well as the simple inorganic salts, when incorporated into standard laboratory rat feed, and that lead napthenate is absorbed about one-half as well. Similarly, lead octoate in dried ground paint, when fed to monkeys, yields Pb-B's one-third to

one-half as high as when lead octoate is fed directly. These data indicate that lead compounds, incorporated into a paint matrix, are absorbed only one-fourth to one-half as well as the free lead salts. We will use an average of one-third for estimating a child's absorption of lead from paint. This average is used because a variety of lead compounds are used in paint. Thus, if children absorb 50 percent of dietary lead, experimental data indicate that they will absorb only one-third of this amount or an average of 17% of the lead from paint. Table I gives the estimated amounts of lead absorbed and excreted, based on an absorption factor of 17% and estimates of weekly intakes of 1, 2 or 3 grams of 0.5 percent paint. Average daily intakes are also calculated on a per kilogram basis for an average two-year-old child weighing 12.5 kg.

Table I

Calculated Lead Intake and Absorbed Dose from Paint Pica

Amount of Paint Ingested/Week (grams paint)	Intake if Paint Contains 0.5 per cent Pb (5,000 µg Pb/g paint) (µg Pb/day)	(µg Pb/kg/day)*	Amount Pb Absorbed (17 percent) (µg Pb/day)	(µg Pb/kg/day)*	Amount Pb Excreted in Feces (83 percent) (µg Pb)
1	714	57.1	121	9.7	593
2	1,429	114.3	243	19.4	1,186
3	2,143	171.4	364	29.1	1,779

*For average two year old child weighing 12.5/kg.

Chisolm and Harrison found a median fecal lead output of 1,110 µg Pb/day in asymptomatic children with blood lead levels ≥60 µg Pb/dl and positive roentgenographic evidence of lead storage in bones. Some also had elevations in urinary coproporphyrin levels.[19] Barltrop found fecal lead outputs ranging from 570 - 1,900 µg Pb/stool sample in three two-year-old symptomatic children with blood lead levels ranging from 68-92 µg Pb/dl, positive roentgenographic evidence of lead storage and hemoglobin levels <10 g/dl.[7] From the estimates given in Table I and the studies of Chisolm and Harrison and Barltrop and Killala, it appears that the ingestion of between 1 and 2 grams of paint (containing 0.5 percent Pb) per week could produce fecal lead outputs equal to those found in children with ≥60 µg Pb-B. Clinical studies in children have indicated that blood lead levels ≥60 µg Pb/dl are associated with increased risk of later CNS effects.[3,23,24,57,73]

In contrast, Alexander's balance studies in eleven healthy children receiving a normal diet showed a mean lead intake of 10.61 µg Pb/kg body weight/day and a mean fecal lead output of 5.13 µg/kg/day.[4] Using the

figures from Table I, a 12.5 kg child consuming 1 gram of 0.5 percent PB paint per week would have a daily lead intake of 57.1 µg Pb/kg body weight, a five-fold increase above that found in a normal diet. Two grams of paint would produce an eleven-fold increase and 3 grams, a sixteen-fold increase.

Since the best available clinical evidence indicates that children with pica can and do ingest 1-3 grams of paint per week and, since the ingestion of between 1 and 2 grams of 0.5 percent lead paint per week would be sufficient to produce daily fecal lead outputs equivalent to those found in children with ≥60 µg Pb-B, a level of 0.5 percent lead in paint cannot be considered a "safe level."

Method B - An alternate method for determining the safety of 0.5 percent lead paint is based on the absorption studies carried out by Kehoe on adult volunteers.[42] Kehoe found that blood lead levels increased 17 µg/dl over a period of nine months for each additional mg of lead administered per day. Lead acetate or lead chloride were administered with the diet at dosages of 0.3, 1.0, 2.0 and 3.0 mg Pb/day. Increases in blood lead levels were proportional to dosage. For the sake of simplicity, we will discuss the subject receiving 1.0 mg Pb/day. An observed intestinal absorption rate of 10 percent resulted in an absorption of 100 µg Pb/day. Calculated on a body weight basis for a standard 70 kg man, this represented 1.43 µg Pb absorbed/kg/day. Thus, the absorption of 1.43 µg Pb/kg/day would be sufficient to produce a rise in blood lead of 17 µg/dl and an absorption of 2.86 µg Pb/kg/day could produce a rise of 34 µg/dl. Similar increments in blood lead concentration have recently been reported by Stuik[97] who has administered lead acetate at 20 µg Pb/kg/day to 5 adult male and 5 adult female volunteers over a period of 12 weeks. If one assumes an absorption of 10% of the dose, the rate recently found by Rabinowitz et al,[80] then these healthy volunteers would have absorbed 2.0 µg Pb/kg/day. In Stuik's subjects blood lead concentrations increased by 17.7 µg Pb/dl in the females and 20.3 µg Pb/dl in the males after 2-1/2 weeks. These short-term studies essentially confirm and extend the earlier long-term study of Kehoe in adult volunteers.

The average blood lead level in normal unexposed children is approximately 20 µg Pb/dl.[59] Early metabolic changes in the hematologic system begin to occur in children when blood lead levels reach the range of 30-40 µg Pb/dl. From the standpoint of preventive medicine, it would seem appropriate to insure that mean blood lead levels for groups do not exceed 20 µg Pb/dl. An additional daily absorption of 1.43 µg Pb/kg/day could increase blood lead levels from 20 µg Pb/dl to 37 µg Pb/dl, while an additional absorption of 2.86 µg Pb/kg/day could increase levels to 54 µg Pb/dl.

Based on an absorption factor of 17 percent for lead in paint, Table II shows the amount of lead intake necessary to produce absorption of either 1.43 µg/kg/day or 2.86 µg/kg/day. Total daily intakes are also calculated for an average one-year-old 10 kg child and a two-year-old 12.5 kg child.

Table II

Calculated Daily External Dose and Associated Internal Dose

Increase in Blood Lead (Pb-B) (µg/dl)	Lead Absorbed Each Day (µg Pb/kg/day)	Necessary Intake to Produce Corresponding Absorption* (µg Pb/kg/day)	Total Intake Necessary for 10 kg child (µg Pb/day)	Total Intake Necessary for 12.5 kg child (µg Pb/day)
17	1.43	8.41	84.1	105.1
34	2.86	16.82	168.2	210.3

*Based on absorption factor of 17 percent for lead in paint.

Absorption of lead from foods is approximately 50 percent.[4]

The safety of 0.5 percent lead paint can be determined from Table II. The ingestion of 16.82 mg paint/day or 33.64 mg paint per day containing 0.5% lead would result in raising blood lead levels by 17 µg/dl or 34 µg/dl, respectively, in a 10 kg child. Similarly, a 12.5 kg child would need to ingest either 21.02 mg paint/day or 42.06 mg paint per day. King and Schaplowsky have summarized the work of Sachs wherein she demonstrated that some children can consume more than 1 g (1,000 mg) paint per week or 143 mg paint per day.[46] For a child with pica for paint, a level of 0.5 percent lead in paint clearly represents a hazard.

Because multiple factors serve to modify lead intake, absorption rates and individual susceptibility, the foregoing mathematical calculations used for determining the hazard of 0.5 percent lead paint, cannot be considered suitable for application to every child. Age, frequency of pica, dietary constituents, and nutritional status all contribute toward increasing or decreasing the amount of lead absorbed by any one individual (see Appendix D).

The first method used for determining the hazard of 0.5 percent lead paint is based on relating lead intake to the appearance of early clinical illness and significant risk of later CNS effects. The second method relates lead intake to blood lead levels known to be associated with the appearance of early metabolic effects in children. In either case, a level of 0.5 percent lead in paint cannot be considered a "safe level."

Appendix F

Daily Permissible Intake, Reconsidered

In 1971, an ad hoc committee convened by the Bureau of Community Environmental Management, Public Health Service, DHEW, proposed the concept of a daily permissible intake (DPI) to be used as a reference point for establishing policies to prevent childhood lead poisoning.[45] Based on the knowledge available at that time, the committee decided that blood lead levels should not exceed 40 µg Pb/dl and that the DPI for children should not exceed 300 µg Pb/day. Kehoe's balance studies,[42] carried out on adult volunteers, were used as a reference for establishing a daily lead intake which would result in levels <40 µg Pb/dl. In adults, Kehoe found an intestinal absorption rate of 10 percent for lead ingested in the diet. The one volunteer whose blood lead level did not consistently exceed 40 µg Pb/dl had a daily intake of approximately 600 µg Pb/day. Unfortunately, the studies on this volunteer were discontinued after 15 months. Therefore, the effect of chronic exposure to 600 µg Pb/day was not established.

More recent evidence indicates that the absorption of dietary lead is approximately 50 percent in young children. Alexander[4] found that an intake of 10 µg/kg/day resulted in a daily fecal excretion of 5 µg/kg/day. Barltrop found that children with a fecal excretion of approximately 5 µg/kg/day had a geometric mean blood lead level of 20 µg Pb/dl with a range of 11-38 µg Pb/dl.[8] Studies in suckling animals suggest that the intestinal absorption rate of lead from milk may be as high as 70-90 percent.[31,51] These studies suggest that the absorption rate of lead in children less than one year of age may be higher than 50 percent. In addition, the brain of infant rats accumulates lead to a greater extent than the brain of adult rats.[68]

Based on this new information, the daily absorption of lead from diet can be recalculated. The caloric requirement of a three year old child weighing 15 kg is one-half of the caloric requirement of an adult weighing 70 kg. Tepper, cited in King,[45] reported that the average adult diet contained 220 µg Pb/24 hrs. If a three year old child consumed the same diet, reduced to one-half to meet his caloric requirements, his dietary lead intake would be 110 µg Pb/24 hrs. Based on a dietary absorption factor of 10 percent, the adult would absorb 22 µg Pb/24 hrs or 0.31 µg Pb/kg body weight/day ((220 x 10 percent) ÷ 70 kg). Based on the dietary absorption factor of 50 percent, the child would absorb 55 µg Pb/24 hrs or 3.67 µg Pb/kg body weight (110 x 50 percent ÷ by 15 kg). Thus, when dietary lead absorption is expressed in terms of body weight, it can be calculated that the child would absorb 12 times as much lead as an adult receiving the same diet.

The safety of blood lead levels in the range of 25-40 µg Pb/dl has recently been questioned. Early hematologic changes can be seen in women and children when blood lead levels reach 25-30 µg Pb/dl.[78,97] Neurologic changes have not been documented at this low level. No data are available relating blood lead levels to possible adverse effects in children less than one year of age.

Because of new evidence available in both human and animal studies, this Committee believes that the DPI should be recalculated. Specifically, consideration should be given to:

1. Lowering the currently acceptable blood lead level of 40 µg Pb/dl for children.

2. Accounting for a higher intestinal absorption rate in young children.

3. Allowing a "safety factor" for children less than one year of age, since no data regarding effects or absorption rates is known for this group.

4. Expressing the DPI on either a body weight (µg Pb/kg/day) or caloric (µg Pb/Kcal) basis.

The World Health Organization, FAO, has recently recommended that lead intake in adults should not exceed 3.0 mg of lead per week (429 µg of lead per day).[103] For a standard 70 kg man, this would be equivalent to 6.12 µg of lead per kg/day.

Appendix G

Lead Contents of Current Household Paints

In 1974, CPSC conducted a market place survey to evaluate the formulations of paint on the retail market.[101] Five hundred selected household paint samples were collected by ten state agencies under contract to the CPSC. The paints selected for the survey were representative of the types and colors in current usage. Table I gives the annual percentage of sales for each type of paint.

Table I

Household Paint Marketing Data

		Percent	Percent
1.	Interior Finishes (wall, ceiling, trim, etc.)		60
	Water Emulsion (latex), acrylic, vinyl acetate, etc.	25	
	Oil or alkyd based (including enamels)	20	
	Metal enamels, etc.	5	
	Primers and/or sealers	5	
	Stains and/or varnishes	5	
2.	Exterior Finishes (house, etc.)		40
	Water Emulsion (latex), acrylic, vinyl acetate, etc.	15	
	Oil or alkyd based (including enamels)	15	
	Metal enamels, stains, varnishes, primers, sealers, etc.	10	
	TOTAL		100 percent

Four hundred and eighty-nine samples were analyzed for lead content. The results of paint analyses are given in Table II (See next page).

Ninety-two percent of oil based paints and 99 percent of water based paints contained less than the current statutory limit of 0.5 percent lead. In addition, 70.8 percent of oil based paints and 96.1 percent of water based paints contained less than the proposed limit of 0.06 percent lead. Four colored oil based paints (black, green, yellow and white), consistently exceeded the 0.5 percent lead limit. Table III shows the results of lead analyses for these colors.

Table II

Lead Content of Household Paints

		Oil Based		Latex		Total		
	Percent Lead*	Number	Percent	Number	Percent	Number	Percent	
Do not conform to 1974 Statutory Limit	>1.50	6	2.1	0	0	6	1.2	
	1-1.49	3	1.1	0	0	3	0.6	
	0.50-0.99	14	4.9	2	1.0	16	3.3	
			8 percent		1 percent			5 percent
Conform to 1974 Statutory Limit	0.25-0.49	21	7.4	1	0.5	22	4.5	
	0.10-0.24	34	12.0	3	1.5	37	7.6	
	0.06-0.09	5	1.8	2	1.0	7	1.4	
	<.06	201	70.8	197	96.1	398	81.4	
			92 percent		99 percent			95 percent
	TOTALS	284	100	205	100	489	100	

*Percent by weight based on final dried solids.

Table III

Lead Content of Oil Based Household Paints

Percent Lead*	Black**		Green		Yellow		White	
	#	Per Cent	#	Per Cent	#	Per Cent	#	Per Cent
>1.0	3	12.5	2	8.0	3	19.0	1	1.2
0.50-0.99	3	12.5	0	0.0	1	6.0	1	1.2
0.06-0.49	6	25.0	4	16.0	2	13.0	13	16.0
>0.06	12	50.0	19	76.0	10	62.0	66	81.5
Total	24	100.0	25	100.0	16	100.0	81	99.9

*Percent by weight based on final dried solids.

**Including charcoal

The proposed limit of 0.06 percent lead in paint was originally intended to allow for variations due to impurities in raw materials, contamination during processing and detection limits for the analytical methods used in determining the lead content of paints. The proposed limit does not allow a margin for lead additives, including dryers. An industry formulary[30] indicates that trace amounts of cobalt and manganese are used as essential driers and that lead is used as an auxiliary dryer. Zinc and calcium are listed as alternative auxiliary dryers.

This Committee has no expertise in either paint technology or economics; therefore, no conclusions could be reached relative to either a change in the quality of paint or the economic impact which might result from reducing the level of lead in paint to trace amounts. Nevertheless, the data from Tables II and III clearly demonstrate that the production of paint with <0.06 percent lead is possible. More importantly, a large proportion of paints sold in the current retail market already meet the proposed limit of 0.06 percent lead.

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