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1

INTERNATIONAL SYMPOSIUM

Environmental health aspects of lead

Die gesundheitlichen Aspekte der Umweltverschmutzung durch Blei

Les problèmes sanitaires posés par le plomb présent dans l'environnement

AIRBORNE LEAD IN PERSPECTIVE

DINMAN B.

Institute of Environmental and Industrial Health
The University of Michigan
ANN ARBOR, MICHIGAN, USA

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ABSTRACT

AIRBORNE LEAD IN PERSPECTIVE - A REPORT OF THE NATIONAL ACADEMY OF SCIENCE-NATIONAL RESEARCH COUNCIL OF THE USA

No definitive health hazards can presently be ascribed to ambient atmospheric lead burdens. Thus, potential hazards are considered within the perspective of known clinical and subclinical responses.

The major source of atmospheric lead derives from lead alkyls in gasoline; such urban air contains approximately 20-fold more lead than rural regions. Despite rapidly increasing consumption, present dispersal patterns apparently have prevented recent increments in urban atmospheric lead. While other sources contribute even more lead to this marked localized total increase such probably do not contribute greatly to airborne lead. The data limitations underlying these observations and research needs are noted.

Potential hazards of atmospheric lead devolve upon children and certain few occupations. Airborne lead fallout in street dirt, plus lead paint pica can impose considerable risk on children. Although work in high vehicular densities may increase blood lead, such increments is believed insufficient to precipitate lead poisoning. The extreme sensitivity of ALAD to lead intake presents a poorly defined risk to heme metabolism requiring more research. Potential brain damage at high levels engenders questions regarding possible subtle effects on neurologic and other organ function with low level protracted dosing.

Total body lead appears to increase with age. Although largely in bone, potential metabolic hazards to soft tissue (as well as bone) metabolism require investigation.

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Introduction

This report is the result of nine months of collaborative efforts of the Panel on Lead of the Committee on Biological Effects of Atmospheric Pollutants. It was produced under the aegis of the Division of Medical Sciences of the National Research Council and National Academy of the United States. The chairman of the panel to whom considerable credit must be apportioned was Dr. Paul B. Hammond of the University of Minnesota.

The main purpose of the report was evaluation of the likelihood that man, animals, or plants might be subjected to harmful ranges of ambient lead exposure now or in the near future. Accordingly, the panel addressed itself to considerations of the present magnitude and distribution of lead in the environment. In addition, estimates of future trends regarding lead exposure were attempted, based on the premise of a continuation of current technology.

The intent of the report was to place in perspective the role of airborne lead as it exists in the biosphere. Thus there is consideration available scientific data relating to effects of lead on human health and welfare, as well the parameters which alter such effects. However, because presently harmful effects of lead can only be attributed to concentrations higher than those found under ambient conditions, the panel necessarily was impelled to consider biological effects of lead at higher levels than can be associated with present atmospheric loadings. Hence, by considering conditions in which lead is clearly deleterious, a perspective might be obtained regarding the potential harmful contributions of general airborne concentrations.

In presenting a necessarily abbreviated summary of this report, I do not speak for the Panel, its parent committee, or the National Academy of Science-National Research Council. A careful reading of the report in its entirety will speak for itself, and is strongly recommended to all concerned.

Extent of Environmental Pollution With Airborne Lead

The data assembled in the report clearly indicate that man has contaminated to a considerable degree his environment, particularly in certain locales. A review of the document also confirms that a major portion of such contamination is attributable to lead alkyl compounds stemming from combustion and dispersion of vehicular fuel additives. Because such lead alkyl compounds occur as readily, dispersed aerosols, their contribution to atmospheric loadings exceed those increments generated by all other lead users. However, because of the highly efficient dispersion patterns associated with combusted and vented gasoline additives, the effect of a rapidly increased usage of loaded gasoline has not led to a significant rise

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in the average atmospheric lead content of the air of major US cities during the last 15 years. Nevertheless, because of evidence that: 1) lead concentrations over the air of American cities is 20 times greater than found over rural areas, and 2000 times greater than over the mid-Pacific Ocean, and 2) that such concentration profiles probably stem from gasoline lead-additives, the major contribution of alkyl lead to such loadings must be recognized.

Despite at least 25 years of concern regarding air pollution, considerable more understanding of the factors that bear upon dispersion of atmospheric pollutants os needed. Considerably more effort should be exerted in the field of meteorology--especially using tracer techniques--to gain more adequate understanding of the dispersion process. In addition, most meteorological data are collected near the fringes of cities, e.g., at airports, so that visualization of urban conditions (where are located the major man-made emission sources) is not readily attained. Similarly data describing urban-rural gradient are not adequately represented. The report recommends establishment of aerometric networks in cities which will provide pollutant and meteorologic data representative of each individual area as well as the city as a whole. In order to analyze natural air movements between cities or regions, such networks should be extended and interconnected to form a pollutant-oriented national meteorological system. The Storage and Retrieval of Aerometric Data (SAROAD) system of the Environmental Protection Agency presently in operation should be further developed.

The report points out that air sampling for pollutants should be more clearly related to those at risk. Thus, rather than placing samplers on rooftops, since the target at risk is man, more samples should be taken closer to or at street level. Similarly, if the population at risk are children, samplers should be placed near street levels. Inter alia, the same principle applies to the sampling of natural water, subject to industrial pollution. Analysis of waters should be at sites removed from water treatment plants and should be so placed so as to reflect lead concentration alterations induced by lead using or producing industries.

To summarize the situation in re: atmospheric lead, it appears that the qualitative and quantitative effects of airborne lead upon biological systems will change little for some years to come. In essence, it would appear that the scene is not rapidly shifting. However, recent geochemical findings appear to cast some doubt upon this position and could somewhat alter biological systems.

As regards the total environment, industries utilizing lead have added more than the single ambient source, i.e., burned lead containing fuel. Lead pigments and metallic (inorganic and alkyl) products have been added in two- to three-fold greater quantities. The amount of such lead recycled to the ecosystem is unclear;

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however, some of such lead undoubtedly finds its way back to the environment as a result of weathering, leading, dumping and burning. Such lead is probably chiefly returned to the soil; nevertheless, the environmental flows of such lead are not well defined. Accordingly, any proposal seeking removal of lead from automotive fuels should take into consideration such gaps in our knowledge.

In view of such information deficits, the report recommends expanded study of the behavior and characteristics of lead in nature. Although the physics of particulates and aerosols is relatively well-known, the chemical assumed by environmental lead needs more complete elucidation before such flows and distribution can be known. Atmospheric chemists are necessary to undertake such studies; alternately reorientation of trained chemists can fulfill such manpower needs. With such competence study of lead in emitted particulate matter, in soil and in water will aid in filling such deficiencies in our present comprehension.

Directly related to soil concentrations is transfer from vehicular traffic. The density of such loadings is directly proportional to the density of such traffic, occurring in street dust in large cities, surface soils of parks and in relatively narrow bands adjacent to major roadways. It likewise appears that the gradient of soil concentration falls off steepest in the first 75 feet (25 meters) from such nearby traffic roadways; conversely crops from rural areas show little such lead alkyl contamination. Furthermore, the lead concentrations found in streams and waters in 1940 appear similar to levels found today, despite the considerable increase in lead alkyls since that time.

Consistent with the observed trends of lead in air in water are observations that dietary lead has not <u>appeared</u> to change from 1940 intakes. In keeping with this observation are findings that despite atmospheric deposition in plants, the amount of lead incorporated in edible portions of flora is relatively small. Finally, the lead content of animal foods seems to have barely changed--if at all—in the past 30 years.

Nevertheless, it is recommended that monitoring of lead in common food forms be instituted now so as to provide adequate benchmarks for future comparisons. Despite the foregoing, the evidence of a lack of increasing lead content in food is based upon questionable data. Past samplings have been deficient in size and have been inadequately defined, casting considerable doubt on use of such levels as bench-marks or comparisons. Accordingly, the protocols for compilation of data should be standardized and detailed as to sampling methods, analytical techniques, water content, and geographical and environmental characterizations. In evaluation of dietary intake possible contamination incurred in preparation and storage of foods

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must be recognized. Finally, periodic publication of such data in a useful, readily available form would make this information of considerable utility to public health officials and nutritionists.

The over-all picture of environmental lead that emerges indicates a steep gradient as one approaches cities; such gradation is proportionate to urban size. A large effect upon human lead uptake--except possibly from inhalation--has not been apparent; this is consistent with the absence of any perceptible upward trends for lead in rural soils, waters or in food products. In view of the fact that vehicular alkyl lead utilization has increased, and because air monitoring has not continued over a sufficiently long period to allow definite statements regarding this apparent situation, firm conclusions on these points cannot be reached.

Effects of Lead on Man

The toxicity of lead for man revolves about the central nervous, gastrointestional, and hematopoietic system and kidneys. Other organ systems, e.g., endocrines, reproductive and cardiovascular, may be involved, although relatively less information is available concerning such possible lead hazard. It thus appears that the most severe form of acute poisoning occurs in children affecting the central nervous system and holding potentials for permanent sequellae. Damage to the kidney appears to be a well-established entity, although dose-effect relationships regarding permanent affects leaves several questions open. The life span of erythrocytes is shortened although anemia may not be clinically manifest. The acute, severe form is most commonly seen in the United States today in infants and those consuming illicit, lead contaminated spirits.

The least severe forms of clinical lead intoxication occur where close medical surveillance permits early detection of minimal signs and symptoms, e.g., in lead using industries. Nonspecific malaise, muscle aches and headache plus mild anemia and shortened erythrocyte life spans occur. If permitted to progress, the more characteristic effects of chronic lead intoxication are seen, i.e., diffuse abdominal pain and constipation. Removal from exposure is usually sifficient to reverse these changes.

Because of its readily accessibility, concentrations of blood lead have been widely used as indicators of whole body burdens. Except for the finding of anemia, apparent signs of clinical lead poisoning usually do not occur until blood lead levels reach 80µg/100gm of whole blood. However where anemia does occur, symptoms may be associated with lower blood lead levels. This paradox stems from the fact that 90% of blood lead is associated with the erythrocyte; accordingly, the analysis of lead per unit volume is based upon an abnormally low number of red blood cells.

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The report calls for standardization of diagnostic tests, particularly suggesting a need for standardization of the Ca-EDTA mobilization test in asymptomatic individuals. Fixing uniform doses based on body size (preferably determined by body surface area); studies of Ca-EDTA given parenterally over defined periods are needed. Similarly urine collection periods and intervals should be standardized. The modification of such tests in the presence of coexistent renal insufficiency requires more exploration.

At blood lead levels of 40-80µg/100gm of whole blood inhibition of ALAD activity results in increased excretion of ALA in urine. This results from the blocked enzyme's failure to convert the heme precursor, ALA, to porphobilinogen. Such effect in adults does not appear too capable of affecting hematoporesis; such complusation can be accomplished without leading to anemia. However, implications regarding the impact of such enzymatic inhibition upon the metabolism of other heme pigments requires further investigation. In effect, such resultant cannot be viewed as other than deleterious, since it represents an interference with the availability of an essential metabolite necessary for normal body activity.

For these reasons, the report urges that further efforts be made to elucidate the biological significance of this observation, ALAD inhibition. This assay in blood may represent a model of lead induced hence synthesis impairment in other tissues. In particular the implications of the dose-response relationship between lead and hence synthesis in the central nervous system--as well as other organs--should be explored. Study is needed of the relationships between ALA, ALAD and the chelatable fraction of total body lead; this is particularly pertinent in ranges of 5-80µg/100gm of whole blood lead in order to elucidate the "threshold" for such effect. Research should consider a broad spectrum of age groups, since compensatory responses to lead loadings and these effects may be age dependent. Well conceived epidemiologic design, timed, quantitative urine collections, standardized mobilization procedure and more specific ALA measuring techniques all are needed since careful dosage control may be difficult in man, correlative studies of dose-response relationships in intact animals should be developed. Clarification of other, less well understood deleterious metabolic and functional effects attributed to lead loading may be achieved by a clear elucidation of the dose-response relationships associated with body lead burdens.

It is in these areas of low lead body burdens, i.e., less than 40µg/100gm whole blood, that the significance of red blood cell ALAD inhibition <u>in vitro</u> requires clarification. (Fig. 1). While this relationship appears to vary as a function of erythrocytic lead

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in vitro, its biological importance is open to question, since detectable effects in the function of intact man is demonstrable at this time. In this connection, the effects of lead burdens on those populations with genetic defects in hematopoiesis should be investigated.

Aside from classical lead poisoning, subtle effects of long duration, low concentration absorption on human health performance have long been under discussion. Although a number of health studies of populations not suffering classical poisoning the subject to abnormally high concentrations of lead have been reported, it is difficult to perceive any connection between such situation diseases other than lead intoxication. Likewise, evidence of enhanced susceptibility to other disease processes could not be demonstrated in such groups.

Despite these apparent observations, the report recommends that further study should be devoted to possible subtle effect of prolonged low-level lead exposure. Current information does not provide an adequate basis for evaluation of such question. As regards long-term effects of respiratory uptake of lead and behavior, the only studies in this area are in the Russian literature. Although patient encephalopathic changes resulting from severe childhood absorption are clearly defined, the evidence regarding late sequellae of such less apparent childhood poisoning is nuclear. Subtle behavioral effects with long-direction, low-level lead exposure may be manifest by dulling of mentation and chronic hyperkinesis. No information relating possible cause and effect relationships is available. Thus, information in this area is of prime importance in order to resolve this serious potential for behaviorial abbreviation at relatively low, prolonged dose levels. Accordingly, populations studied need be relatively stable so that long-term effects may be evaluated; whole family groups should be studied. Such investigations should include multiple health parameters, physical and mental.

In addition, animal studies to expand this area of concern are in order. Such efforts should be directed toward determining "thresholds" for effects in fundamental processes, e.g., oxidative phosphorylation, electron transport, effects on dithiol dependent enzymes. Animals on extremely low lead diets should be compared with those in normal diets to compare the kinetics of uptake, distribution, biological half-times for storage and turnover in various tissues and effects on several sites of heme synthesis. Similar comparisons should be made with animals on diets with moderate lead burdens, e.g., 100µg/gm dry weight.

On the basis of such studies prospective correlations should be sought in man. More insight might be gained into such unanswered

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questions of dose-response relationships at low level exposure and; 1) threshold for behavioral and performance decrement; 2) possible relationships between aging--as it affects renal and vascular function--soft tissue lead kinetics; and 3) relative sensitivity to lead among children and adults.

More lead balance studies such as pioneered by Kehoe are needed; however, such data should include atmospheric intake in addition to food and beverage sources of body loadings. Comparable studies are needed regarding lead metabolism in the human fetus, infants and children. Because of ethical considerations, nonhuman primates may provide appropriate experimental models for approaching these problems, particularly as related to nervous system function.

Sources of Lead Poisoning in Man

Although gross over-exposures and intoxication among workers in large industries have become rare, occupational poisoning among those in small plants presents a problem of unknown dimensions. Another major source of severe lead intoxication is lead paint of poorly-maintained, pre-1945 housing. Although such paints are no longer used in interior paints in the United States, this severe and socially crippling form of intoxication in children remains a special hazard to populations living in such deteriorated quarters. Illicitly distilled spirits, inadequately glazed earthware, toys containing lead pigments and an assortment of fabricated items represent a potential source of lead uptake.

Aside from gross occupational lead exposures, only in urban settings are atmospheric lead loadings a potential source of hazard. Unusually high concentrations may be encountered in nonlead using trades (e.g., garage workers, traffic policemen) which may result in blood lead levels exceeding 40µg/100gm of whole blood. However, within this small population only relatively few reach this level. To attain blood concentrations productive of frank clinical intoxication necessitates in such groups a long-term five-fold increase of lead assimilation.

Another large segment of the urban population, infants and young children may also be at special risk because of atmospheric blood. Large scale surveys covering 210,000 children in two large United States cities revealed that between 5 and 13% of children had blood leads greater than 50µg/100gm whole blood. It would not appear that such high levels could come from inhaled lead alone. Some of such intake probably comes from lead paint ingestion (pica). However, some of this burden probably also comes from ingestion of street dirt; this detritus has been shown in the United States often to contain lead in excess of 2000µg/gm. If the present assumptions regarding the relationship between daily ingested lead intake and blood concentrations are valid, daily ingestion of 0.41gm of such

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street dirt (i.e., 2000μ/gm) by a 10 kg child would result in blood lead levels compatible with clinical poisoning. It should be pointed out that such calculated loading does not include additional respiratory or dietary uptakes or concomitant lead panel ingestion. Similarly, daily ingestion of 44mg of street dust would be sufficient to double blood lead levels of 20μg/100gm whold blood. However, these estimates of intake sufficient to raise lead body burdens to dangerous levels may be unduly conservative; such calculations are based upon uniform prolonged intake.

Because the actual amounts of street dust swallowed by children is not known, research is recommended in the subject of patterns of pica and street dirt lead content. Likewise, considering both special urban risk grous, i.e., workers and children, prospective epidemiologic study to evaluate their potential hazard, as well as the effectiveness of control measures, are required. In such program total exposure patterns from all environmental sciences are needed.

Concerning the general urban population, lead is undoubtedly assimilated from air, food and beverages to a greater extent than found in other populations. Atmospheric lead contributes to body burdens in a variable fashion as a function of the place of residence, place of work and the specific urban complex. There are suggestions, derived from a survey of men in three large United States cities, of a strong association between time spent in high automobile traffic density areas and blood lead concentrations. Although inferential at present, these findings are consistent with limited experimental data indicating that inhaled lead constitutes about 50% of the amount that comes from diet. However, under special circumstances, such inhaled lead may represent 200% of the dietary lead. Such uptake data is, of course, dependent on the microclimes encountered as a result of daily activities. In general however, there is no epidemiologic data available to indicate that blood lead levels are increased as a consequence of mean ambient concentrations below 2 to 3μg/m^3. In perspective, only circumscribed population groups have been found to be exposed to higher mean ambient concentrations.

Despite these observations, more precise studies are needed of the relationship between atmospheric lead exposure in urban areas and blood lead concentrations. Personal monitoring devices present a unique technologic device for such studies. Such investigations will require careful balance studies precisely to determine the contribution of atmospheric lead to body burdens.

Total body lead appears to increase with age. Although such burden largely represents bone loadings, other tissues are likely involved. By contrast, accumulation in blood does not appear to increase with age; this has suggested that the exchangeable stored lead pool in the body reaches a steady state early in life. The

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increase of body burden with age probably thus represents biologically relatively inert, slowly exchangeable pool; the toxicologic significance of such pool is not known at present.

It must be recognized that there is a relative paucity of data regarding lead body burdens, distribution, and its biological significance as a age dependent process. The suggestions that "mobile: fractions of total body burdens remain constant throughout life requires confirmatory evidence. Study of the biological effects of increasing soft tissue lead concentrations with age should be attempted, e.g., ALAD in blood and excretion of ALA in urine. The long established concept that the tightly bound lead in bone is biologically inert should be more closely scrutinized. Further study is required of the relationship between lead metabolism and clearance as these are affected by inter-relationship between parathyroid hormone, thyrocalcitonin, bone and kidney. Such studies could clarify questions regarding the health significance of "non-diffusible" body lead.

Significance of Environmental Lead to Other Life-Forms

Most wildlife and livestock do not live in close approximation to areas with relatively high atmospheric lead concentrations. The apparent exceptions are those animals grazing sufficiently close to traffic arterials (greater than 50,000 vehicles per day) where surface deposition of lead on foliage might occur. However, it is clear that the fall off in such deposition would confine the hazardous area to a band of about 125 feet (v45 meters) on either side of the road; such a grazing pattern is extremely unlikely. As concerns domestic pets, it would appear that clinical lead poisoning cannot be attributed to atmospheric lead intakes. Causality here is similar to that seen in young children and infants, i.e., young animals tend to chew on and eat foreign objects, which may contain lead. As in the case of children, whether they eat lead-contaminated street soil or dust is unknown. In contrast to the foregoing, hazards of lead intoxication via atmospheric exposure near smelters have been inadequately controlled.

Newer methods used in humans for assessment of body lead burdens and its physiological implications have not been extensively applied to study of animals. Accordingly, it is recommended that more precise estimates of the tolerance limits for lead intake be undertaken, with special emphasis being placed upon study of major domestic animals that could be at risk.

In contrast to mercury, lead does not appear biologically available to aquatic animals, since little of such lead appears to exist in solution. Lead has been shown to pose an important health problem for water fowl in the United States; the source of such lead appears to be spent shot.

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Regarding plants, similarly there appears to be relatively little biological availability of atmospheric and soil lead.

Despite the foregoing, we cannot regard our knowledge in this area as totally sufficient to justify complacency. The uptake, and tolerance or susceptibility for lead should be studied in a variety of indigenous plant species; special emphasis should be placed upon those flora consumed by man and animals. Recalling the unexpected biological availability of mercury in a form previously not considered accessible to animal systems, it would be wise to determine whether some plants may also have an unusual capacity for uptake from the biosphere. It is also recommended that studies of lead effects at low concentrations should be studied in plants. The end in mind is by detection of possible "thresholds" for mutagenesis in plants.

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Reference

1. Airborne Lead in Perspective. A Report of the Committee on Biological Effects of Atmospheric Pollutants, National Academy of Science-National Research Council, Washington, D.C., 1972, pp. 330.

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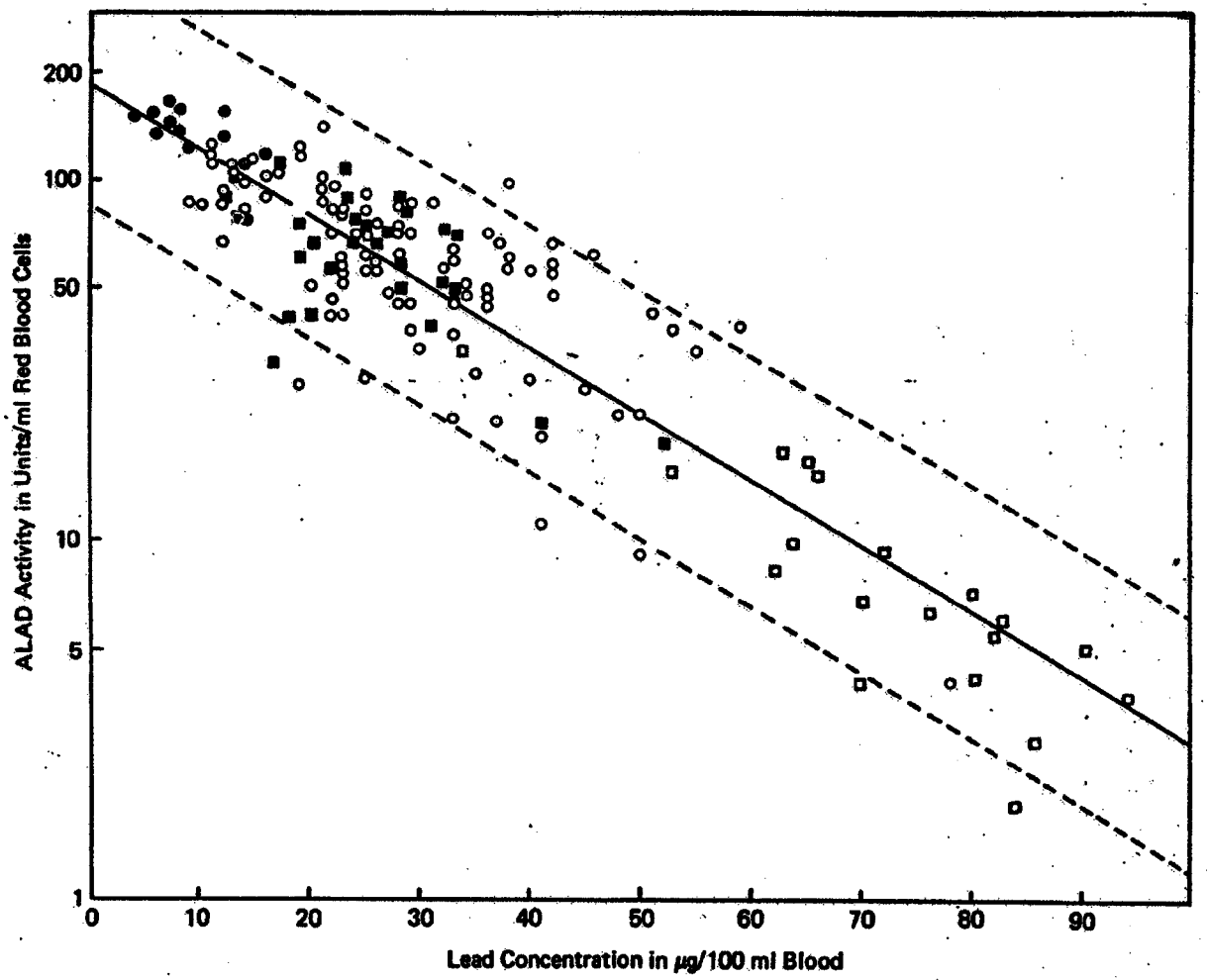
Figure 1



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$\frac{1 lbm}{1{,}000{,}000 lbm} = 1 ppm$

$\frac{1 lbm}{1{,}000 Kg} = 1 ppm.$

$\frac{1000 mg}{1000 Kg} = 1 ppm$

$\frac{1 mg}{Kg} = 1 ppm$

$\frac{1000 ug}{Kg} = 1 ppm$

1 Kg food = 10 mg Pb

1000 gm = 10 mg Pb

1,000,000 mg = 10 mg Pb

100,000 mg Food = 1 mg Pb

1 mg Food = .000001 mg Pb

.25 mg Food = .00000025 mg Pb.

10 ppm = $\frac{10{,}000 ug}{Kg}$ of food or 10 mg Pb/Kg food.

.25 mg of food / Kg wt = .00025 ug Pb/Kg wt.

$\frac{350 ug}{70} = 5 ug/Kg.$

5 ug/Kg human consumption

350 ug/Kg = .35 mg/Kg