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LEAD IN THE ENVIRONMENT AND ITS EFFECTS ON HUMANS

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LEAD IN THE ENVIRONMENT AND ITS EFFECTS ON HUMANS

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LEAD IN THE ENVIRONMENT AND ITS EFFECTS ON HUMANS

I. BACKGROUND OF THE PROBLEM

Lead is widely distributed in man's environment. It is found in his food, water, and in the air he breathes. Most of the lead in the atmosphere derives from the uses of lead by man for many purposes, and particularly, from the combustion of gasoline containing lead antiknock additives. The possible effect of lead contamination on man's environment has been and is now of concern to the California State Department of Public Health. This concern extends to all segments of the population, workers in lead industries, children, and the general public. For a number of population groups, the quantity of lead in the air to which they are exposed, and concentrations in the blood and urine have been established to the satisfaction of most scientists, but there is not agreement on the degree of safety or hazard presented by the existing lead body burdens.

There are certain aspects of the lead problem which are indisputable; others are hotly disputed. In the former category is the fact that the people in the urban areas of California, particularly Los Angeles, are and have been in the last two decades exposed to atmospheric lead levels which are generally higher than those of most other metropolitan areas. The lead is predominantly inorganic and derived from leaded motor fuel additives. A second indisputable fact is that no detectable cases characteristic of lead poisoning due to community exposures have been reported. A third indisputable fact is that the bulk of human experiences with reactions to lead are based on exposures in industry; therefore, the situation posed by high community lead levels represents a new type of problem. The fourth indisputable fact is that evidence based on occupational exposure is not directly translatable into criteria of hazard from general community exposure. This is because of the possibility of increased susceptibility of certain sectors of the population and because of the differing periods of time during which the exposure occurs. There are also different patterns of responsibility for prevention or control of the exposures. Another indisputable fact is that there is a need for criteria for community hazard associated with lead exposures.

Dispute exists concerning the extent to which the exposures to lead as a community air pollutant have increased or are capable of increasing the storage of lead in the body. Dispute exists concerning the question of whether long-term health damage occurs under conditions

which are unlikely to give rise to signs or symptoms of acute toxicity. Dispute occurs concerning the relative contributions of air, water, tobacco smoking, occupation and dietary practices to the data available for urban-rural differences. Dispute or uncertainty exists concerning the validity and reliability of sensitive indices of the earliest deleterious effects of lead.

It is pertinent to consider the reasons why some of these disputes exist. The first reason is that the evaluation of community exposures has been based on experience with occupational exposure. This experience has been considered inappropriate with respect to community air quality criteria guides and standards by those who have seriously considered them, including the American Conference of Governmental Industrial Hygienists. The second reason for these disputes lies in the fact that, since the question of the possible community hazards associated with the use of fuel additives containing tetraethyl lead was raised in 1923, there has not been an adequate effort by public health authorities to collect independently the data which might be relevant to this problem, or to establish uniform bases for interpreting the available data. Another cause for dispute lies in the difficulty of translating technical information collected into policies aimed at protecting the public health.

The California State Department of Public Health has been the most active of all state health departments in investigating the problem of atmospheric contamination from antiknock compounds and in expressing a need for information on the effects of atmospheric lead contamination. In its Technical Report of California Standards for Ambient Air Quality and Motor Vehicle Exhaust (1959) (See Reference 41), the Department reviewed the current knowledge on the public health hazards from lead in motor vehicle exhaust, and listed six research problems which it felt would need to be tackled before an adequate basis would be laid for scientifically valid ambient air quality standards. Substantial progress has been made in these problems.

The Lead Industries Association, Inc., is currently spending about six million dollars annually on fourteen research projects. Most of these are concerned with lead body burden, exposure to inhaled or ingested lead, the toxicity and effects of lead, or a continuation of the Survey of Lead in the Atmosphere of Three Urban Communities (Three-City Study, see Reference 5). In addition there are many projects being sponsored and conducted by members of the lead industry.

The American Petroleum Institute is sponsoring or planning ten research projects. Among these are investigations on the elimination of the use of lead in gasoline, the effects of lead on man, the effects of automotive exhaust on lead body burden, lead fallout on soils near highways, lead in heavy traffic, and a continuation of the Three-City Study.

The U.S. Public Health Service and other Federal agencies are conducting or sponsoring 41 research projects. These include studies in biochemistry, pathology and toxicology, and effects on widelife of lead.

In 1966. the Governor of the State of California directed the Department to report on lead contamination of the environment and its effect on the people in California. This report represents information on the sources, occurrence and distribution of lead in the environment; on studies conducted by the Department; on body burdens of lead in the population; on the state of knowledge of effects of lead on humans; and on the need for additional information to answer questions that now exist on the effects of lead on humans.

II. SUMMARY

Much is known about the toxicity of airborne lead at high concentrations. There is disagreement, however, concerning the biochemical effects at the lower concentrations found in the atmosphere over urban areas and on sensitive groups in the population. While some problems of interpretation will remain, resolution of these questions requires first of all the collection of additional data on reactions of human populations to lead.

Industrial consumption of lead in California was approximately 109,000 tons in 1964, and about 20 percent of this amount was used in gasoline antiknock additives. Almost all of the lead in the atmosphere of California communities comes from motor vehicle exhausts. Because of the large number of motor vehicles in the state and the nature of their use, atmospheric lead is widely distributed throughout the state. Most of the lead from vehicles, however, is discharged into the atmosphere over the metropolitan areas where the largest number of automobiles are to be found.

In 1965, motor vehicles emitted about 6,000 tons of lead in Los Angeles County and about 16,000 tons in the state. With a continuation of current rates of increase of gasoline usage in California, and with no change in the concentration of lead in gasoline, these figures will be doubled in 1977.

There are no regulations which limit the amount of lead antiknock compounds in motor fuel. At present, the amount of lead in gasoline is voluntarily limited by industry to 4.0 cubic centimeters of tetraethyl lead per gallon.

Studies by the Department, by the U.S. Public Health Service, and others have shown that:

1. The deposition of lead in the body is related to the intake by inhalation of airborne lead and the ingestion of lead in foods, beverages, and water. Cigarette smoking appears to contribute a small increment to blood lead levels and to total body lead. While there is not a consensus on the health consequences of the lead deposited in the body, it is widely believed that an increase is undesirable.

2. The exposure to lead from food and water is several times higher than the exposure to inhaled lead. However, the percentage of inhaled lead absorbed by the body is higher than the percentage for ingested lead.

3. In general, the higher the atmospheric exposure to lead, the higher the blood level of lead. Blood lead levels are generally higher in urban than in rural areas, and are higher in the central urban area than in suburban areas.

4. In California urban areas almost all of the atmospheric lead comes from motor vehicle exhaust, and about 50 to 80 percent of the lead is contained in particles that are small enough to remain airborne for long periods of time. Over 90 percent of the lead in the atmosphere is contained in particles of sizes which can be retained in the lung.

5. Of the cities where lead has been measured, Los Angeles consistently had the highest atmospheric lead concentrations in California, and among the highest concentrations in the United States cities. The average concentration at eight stationary sampling sites in Los Angeles during 1961-62 was 2.5 micrograms per cubic meter and the highest single sample concentration at a station was 11.4 micrograms per cubic meter, also in Los Angeles.

6. Concentrations of lead over freeways in Los Angeles during daylight hours averaged approximately 25 micrograms per cubic meter, and in downtown traffic the average was about 15 micrograms per cubic meter.

7. The concentration of blood lead in the population is 1/4 to 1/2 of that recognized as hazardous to workers in industries using lead. Mean ambient air concentrations of inorganic lead are 1/80 to 1/8 of the Threshold Limit Value used as a guide in industrial exposure.

8. There have been no cases of characteristic lead toxicity ascribable to lead as a community air pollutant.

III. RECOMMENDATIONS

A. The California State Department of Public Health should continue its research on the health consequences of lead stored in the body and proceed to set air quality criteria, guides, and standards for lead. Emphasis should be placed on studies to elucidate the biological effects of lead exposures on man. The U.S. Public Health Service should be encouraged to support such research in this State and elsewhere and to join with the Department to work on criteria and standards for lead.

1. Research on the effects of defined exposures of selected California populations should have first priority. This should include both adults and children, with determinations of blood and urine lead levels, levels of delta-aminolevulinic acid, other indices of altered porphyrin metabolism, red blood cell survival time, and other reactions.

2. Data are also needed on the extent to which atmospheric lead may be deposited on and absorbed from food in homes and restaurants, from field crops, and from the soil.

3. The State Department of Public Health should measure the concentration of atmospheric lead at the State network stations and conduct special studies of lead concentrations in areas of heavy traffic and in the proximity of lead-emitting industries.

B. In the interim, while the above is being accomplished, it is recommended that:

1. No further increase in the quantity of lead in gasoline should be allowed.

2. The U.S. Public Health Service or other Federal agencies should join with industry to study the feasibility of reducing and/or eliminating lead additives from gasoline.

3. Because expected increases in motor fuel use at present concentrations of additives will result in an overall increase in exposure, the State should study the feasibility and implications of a policy of preventing any increase in overall exposures to lead from motor vehicle emissions in California.

4. Each producer or blender of motor fuel sold in the State should provide the Department with data on concentrations and amounts of lead and other additives which have or may have health effects, such as nickel, manganese, alkyl halides, and phosphates.

IV. LEAD AND ITS USES

Lead is widely used. Large amounts are consumed in the manufacture of metal products, pipe, solder, pigments, chemicals, ammunition, cable covering, typemetal, glass and glazes, storage batteries, pesticides, and plumbing (caulking of pipes). Of the lead used in chemicals, almost all (99.8 percent) is in the production of gasoline antiknock additives (tetraethyl and tetramethyl lead).[1] This accounts for nearly 20 percent of all lead consumed annually in the United States. Fumes and dusts from industries using lead and from the combustion of gasoline or other fuels containing lead are sources of atmospheric lead. Because motor vehicles are in such common use, the combustion of gasoline permits lead compounds to be widely distributed in the atmosphere.

A. Use of Lead in California

About 1,500 tons per year, equal to about 1/2 of 1 percent of the lead mined in the United States annually, are mined in California.[1] The one primary smelter in California, located in Selby, refines 60,000 tons per year mainly from imported ores and wastes from the lead industries.

All of the petroleum refineries in California add lead antiknock compounds to gasoline which is distributed in California and to other states or countries. The gasoline consumed in the State in 1965 contained about 21,000 tons of lead.

Lead pesticides are manufactured in California and used in small quantities for control of codling moth in Northern California walnut and fruit crops.[2] In 1965, about 500 tons of lead arsenate pesticide were manufactured and about 150 tons were sold in California.[3] This pesticide is designed to adhere to plant surfaces, to settle, and not to remain airborne. The main concern with the use of such sprays is the introduction of lead into the food supply rather than with atmospheric contamination. In recent years the development of other types of pesticides has resulted in a decrease in the use of lead compounds for controlling agricultural pests.

In most of the major cities of California, there are a number of battery manufacturers, printing firms, lead salvage operations, and other industries using lead. Tetraethyl lead is manufactured at Antioch, California. The annual consumption of lead has remained fairly stable since 1941, although the uses have changed.[4] A decline of lead pesticides and pigments, for example, has been offset by an increased use in storage batteries and antiknock additives. Table 1 shows the consumption of lead in the United States and in California during 1964. In addition to this a considerable amount of lead is remelted and reused. Newspaper publishers, for example, remelt their entire stock of typemetal at frequent intervals for recasting, and about 80 percent of the lead in batteries is salvaged and reused.

B. Sources of Atmospheric Lead in California

Lead is emitted to the atmosphere from industrial operations, combustion of gasoline, open burning of wastes and salvage operations, and from soils or settled dusts which may contain lead.

1. Soils and Dusts

Table 2 shows the percent by weight of lead in soil, dusts, and in airborne particulate matter.[4,5] Soils and settled dusts have a much lower percentage of lead than airborne particulate matter and thus are not a major source of atmospheric lead.

2. Open Burning and Burning of Fuels other than Gasoline

Open burning and salvage operations, such as the burning of junk cars, are sources of atmospheric lead. In most of the metropolitan areas of California, these operations are prohibited or closely controlled.

Coal contains some lead, but coal is not extensively used in California. Fuel oils and natural gas contain practically no lead.

3. Industrial Emissions of Lead

In Los Angeles County, lead is processed in a large number of industrial operations. The emissions from most large lead furnaces are controlled by filtering through fabric (baghouses). Small, low temperature melting pots, such as those in small plumbing shops, or as used in the occasional pouring of mechanical bearings, are generally not controlled. Low temperature mechanical operations involving lead, as for example, battery grid-plate stamping, contribute to the lead content of the air within the plant. These operations create potential hazards to employees in the immediate vicinity but are considered insignificant in their contributions to overall urban atmospheric lead levels in California. Total lead emissions to the atmosphere from all industrial sources in Los Angeles County are estimated to be less than 100 tons per year.[6] Table 3 shows the type and number of furnaces and the control methods in Los Angeles County.

In the San Francisco Bay Area, there are a smaller number of all types of lead furnaces than in Los Angeles County, and the emissions usually are controlled.[7] Emissions from California's one primary lead smelter, which is in the Bay Area, are controlled with an electrostatic precipitator.[7] Total Bay Area atmospheric lead emissions from industrial sources are estimated to be lower than those in Los Angeles County.

4. Fuel Additives

Almost all of the gasoline sold in California contains organic lead antiknock compounds. The concentration of lead in gasoline varies from time to time and with different grades and brands of gasoline. For example, of 13 premium fuels sold in Los Angeles during January, 1965, the lead content ranged from 1.79 to 3.87 grams per gallon.[9] The simple average was 2.93 while in the preceding month it was [illegible]. In January, 1964, it was 2.97 grams per gallon. These simple arithmetic averages of the fuels sampled do not take into account the amounts of each type or brand of fuel sold. Thus, variations of such averages may not necessarily reflect changes in the actual emissions by motor vehicles.

The yearly arithmetic average concentrations of lead in about a dozen gasolines sampled monthly in three California areas are shown in Table 4.[8] Of the fuel sold in the three areas, about 65 percent was premium and 35 percent was regular gasoline.[9]

In 1964, 6,920 million gallons of gasoline were sold in California.[10] Assuming that the average lead content of premium fuels was 3.0 grams per gallon, the lead consumed in premium fuels was 14,900 tons in 1964. The lead consumed in regular gasolines, assuming an average lead content of 2.1 grams per gallon, was 5,600 tons, and the total from both grades of fuel was 20,500 tons. In 1965, 7,193 million gallons of gasoline were sold in California,[10] and the total lead consumed in the combustion of gasoline was 21,300 tons.

Since 1950, there has been an increase of about six percent per year in motor vehicle gasoline sold in the State.[11] If the same rate of increase continues, and there is no change in the amount of lead in gasoline, by 1977 the lead consumed in the combustion of gasoline will be double that in 1965. It will be more than double if the lead content of gasoline is increased from present values to the maximum of 4.0 cubic centimeters of tetraethyl lead per gallon permitted under the voluntary agreement (see Section V).

The organic lead additives decompose almost completely in the engine combustion process into inorganic compounds of lead chloride-bromide, complex ammonium or phosphate chloride-bromide and lead oxides. Some of the lead compounds deposit in the engine, the exhaust system, and in the oil; but from 70 to 80 percent is eventually exhausted out of the tailpipe as particulates, more during high speed driving than during stop-and-go or idling conditions.[12,4,5]

The amount of lead consumed and emitted in several California counties is estimated in Table 5. The number of motor vehicles in each county is reported by the California Department of Motor Vehicles.[13] It was assumed that, of the total lead consumed in the State, the fraction consumed in a county was equal to the fraction of the motor vehicles registered there, and the lead emitted was equal to 75 percent of the lead consumed.

High correlations between lead or carbon monoxide (CO) and traffic density suggest that motor vehicles are the principal source of both of these atmospheric contaminants.[14,5] This indicates the need to measure lead in those California cities where carbon monoxide readings have been relatively high, but where no data have been obtained on atmospheric lead concentrations.

V. CURRENT STATUS OF ADMINISTRATIVE AND LEGAL CONTROL

There are no Federal or State laws or regulations limiting the content of lead antiknock compounds or other additives in motor fuels. At present the amounts of lead antiknock compounds in fuels are limited by industry under a voluntary agreement.

In 1925, about two years after tetraethyl lead (TEL) began to be used commercially in motor fuels, a series of fatalities had already established that the manufacture and handling of TEL or ethyl fluid, and the production of leaded gasoline involved serious health considerations for the workmen. Little or nothing was known of the public health effects of using leaded gasoline. At that time, the U.S. Surgeon General appointed an advisory committee to investigate the health aspects involved in the retail distribution and general use of leaded gasoline.[15]

In 1926, on the basis of the recommendations of this Advisory Committee, the Surgeon General formulated proposed regulations to protect the health of workers who were industrially or occupationally exposed to TEL, ethyl fluid, or ethyl gasoline. The Conference of State and Territorial Health Officers approved the proposed regulations, a part of which was to limit TEL in motor fuels to a maximum of 1 part in 1260 by volume (3.0 cubic centimeters per gallon) for commercial grade TEL, and 1 part in 1300 for the chemically pure grade.[16] This part of the recommendations was based on commercial practice rather than on hygienic considerations. While the proposed regulations were never adopted into law, the Ethyl Corporation in 1926, and the E. I. Dupont de Nemours Company, when it began marketing TEL in 1946, voluntarily agreed to abide by the proposed limit of 3.0 cubic centimeters per gallon.

The Surgeon General's Committee had concluded that while garage, repair shop, and service station workers may have shown evidence of lead absorption and storage, there were no good grounds for prohibiting the use of ethyl (leaded) gasoline of the composition specified above, providing that its distribution and use were controlled by proper regulations. The Committee stated that its studies had involved a relatively small number of individuals for a relatively brief time period, when considering the possibilities in connection with lead poisoning. The Committee also stated that widespread use of leaded gasolines might bring about conditions very different from those studied including a menace to the health of the general public, and that longer experience might reveal lead poisoning or less obvious chronic degenerative diseases from even slight storage of lead in susceptible individuals.[16]

In view of such possibilities, the Committee felt that investigations begun by it must not be allowed to lapse. It was suggested that lead dust as well as carbon monoxide from automobiles might be additional sources of danger to health. Finally, the Committee strongly urged that, due to the vast increase in the number of automobiles throughout the country and because the health of the general public

was involved, the U.S. Public Health Service should request appropriations to continue these investigations and to study related problems connected with the use of motor fuels.[16]

Minor revisions to the recommendations have been necessary since 1926, including the increase of the TEL content in aviation gasoline to 4.5 cubic centimeters per gallon in 1934, and the establishment of a color system for various grades of aviation gasoline.

In 1958, the Ethyl Corporation asked the advice and guidance of the U.S. Public Health Service on increasing the maximum TEL concentration in motor vehicle fuels from 3.0 to 4.0 cubic centimeters (4.23 grams of lead) per gallon. At the request of the U.S. Surgeon General, an Ad Hoc Committee on Tetraethyl Lead was appointed to consider the public health aspects of this proposed increase. This Committee included as one of the seven members, the Connecticut Commissioner of Health as the representative of the State and Territorial Health Officers. This Committee published its findings on August 21, 1959.[17] They concluded that there would be no increased hazard in manufacturing and distributing leaded gasoline, and that available data did not indicate a significant increase in "the hazard to public health from air pollution." It was pointed out that a conclusive answer to the question on health effects was not possible at that time due to lack of data.[17]

The Ad Hoc Committee expressed concern about the inadequacy of medical data on the public health aspects of atmospheric lead contamination. This Committee expressed regret that the health investigations recommended by the Surgeon General's Committee in 1926 were not carried out by the U.S. Public Health Service, thereby establishing a baseline for lead body burdens and human exposure. In view of this, the Committee recommended that the TEL concentration be increased cautiously over a period of years, that the industry supply annually to the U.S. Public Health Service the domestic consumption figures of TEL, and that the U.S. Public Health Service and others study the levels and trends of atmospheric lead contamination and of human body burden of lead to assess further the public health aspects. It was stated that these recommended studies "should be undertaken without further delay to assure the validity of the decision and to guide future committees, particularly since some authorities believe that the tolerable limit of lead absorption is being approached."[17]

"The Committee recognized that the permissive amount of lead in drinking water may be lowered in the near future," and welcomed similar efforts to reduce the amounts of lead in the atmosphere.[17]

The U.S. Public Health Service has no legal authority to control the concentration of lead in gasoline, and the findings of the 1959 Ad Hoc Committee cannot be interpreted as a regulation. Industry has voluntarily stated to the U.S. Public Health Service that it will abide by the various Committee findings and recommendations. California and other states had no direct part in the making of any of these decisions.

The Committee findings have resulted in no direct action by any state. By all indications, the industry has adhered to the 1926 and the 1959 recommendations to limit the amounts of lead antiknock compounds in motor fuels.

VI. STUDIES ON ATMOSPHERIC LEAD

The California State Department of Public Health has conducted a number of studies to determine the atmospheric concentrations of lead, the size distribution of particles emitted from motor vehicles and in air, and the lead content of a food crop near and away from traffic. In addition to these studies, the Department has participated with the U.S. Public Health Service and other agencies in conducting lead sampling programs, including the National Air Sampling Network[18] and the Survey of Lead in the Atmosphere of Three Urban Communities (the Three-City Study).[5]

A. Surveillance of Lead in Air

During 1957, the Department measured lead concentrations in the air at several places in the State, and eight years later measurements were again made.[19,20] The results are shown in Table 6.

Concentrations of lead at Mt. Hamilton were much less than in the cities, and the highest concentrations were found in Los Angeles. The sampling sites were changed between the two sampling periods in Berkeley and Los Angeles; the two sampling periods are therefore not comparable. In addition, only one 24-hour sample was taken every two weeks, and differences in meteorology during times of sampling could account for the differences in lead concentration shown.

B. Lead Content and Size of Particles

Particles of more than 5 microns equivalent diameter settle rapidly and do not constitute a large part of airborne particulates in urban atmospheres. Those of more than 2 microns equivalent diameter are to a large extent trapped out in the nasal and throat passages. Particles of sizes less than 2 microns equivalent diameter are of the most concern because they can reach the lower respiratory passages.[4,5]

In 1962, the Department determined the size of particles in exhaust emissions under cruise conditions from three popular makes of cars.[21] It was found that from 62 to 80 percent by weight of the particles were smaller than 2 microns equivalent diameter. Of these fine particles, more than 68 percent were smaller than 0.3 microns. The fine particles contained about 40 percent of lead by weight.

In 1960, a study in Berkeley, California showed the total atmospheric content of inorganic lead to be distributed among particles by size as shown in Table 7.[22] It was found that 50 to 80 percent of the atmospheric lead was contained in particles of less than 1 micron equivalent diameter. A study in downtown Los Angeles found 90 percent of the atmospheric lead to be in particles smaller than 1.6 microns equivalent diameter.[23]

The typical mass median equivalent diameter of airborne lead particles in urban atmospheres is about 0.3 microns, with 25 percent smaller than 0.1 micron and with 25 percent greater than 0.5 microns.[23,5] These data on size distribution and lead content of particles in the atmosphere and emitted from motor vehicles again indicated the importance of motor vehicles as a source of atmospheric lead and that the lead is in particles of sizes which are respirable, much of which will be retained in the lung.

C. Lead in Some Foods

Whether lead emissions could contaminate food or forage crops grown near freeways or roads was investigated by the Department during April and May of 1965.[24] Samples of head lettuce, and of the soils in the immediate vicinity of each lettuce sample, were collected in Monterey County at distances from roads or freeways ranging from 15 feet to two miles. One-half of the lettuce samples were washed, much as a housewife would wash lettuce, before analysis for lead.

The concentrations of lead in washed and unwashed lettuce are shown in Table 8. The data are grouped according to whether the samples were collected at a distance from traffic of less than 100 yards or 100 yards and more.

The highest lead concentrations were in the lettuce grown near the roads; washing removed a substantial portion of the lead, showing that much of the lead was deposited upon the surface of the lettuce. The lead concentration in vegetation can be influenced by the amount and solubility of lead in soils. In this study no clear cut relationship was found between lead concentrations in the lettuce and in the corresponding soil samples. This might have been because the effect of lead in soil was obscured by the more pronounced effect of the lead from traffic.[24]

Almost no data are available on the lead in food or beverages consumed in California. The diet is composed of a variety of individual food items, no one (or group) of which is either a large or constant source of lead ingestion. Foods from different locations differ in lead content. Lead content may also vary over time; one of the reports presented at the recent U.S. Public Health Service Symposium on Environmental Lead Contamination[4,5,25] suggested that the lead levels in milk may be higher than 20 or 30 years ago.[4] The lead contents of some food and beverages are shown in Table 9.

Since World War II, the increased use of stainless steel, aluminum, and teflon have reduced the lead in foods acquired from contact with lead-bearing metals. Solder in tin cans remains as a point of lead contact, but the lead uptake is small and is less for lacquered cans than for unlacquered cans. The increase in lead of canned vegetables over uncanned vegetables has been reported as 0.02 milligram per kilogram for string beans, 0.06 for tomatoes, and 0.09 for peas.[4]

Lead in Water

U.S. Public Health Service Drinking Water Standards limit lead to a maximum of 0.05 milligram per liter.[26,27] The Department of Water Resources has determined lead in samples from ground water in Los Angeles County since 1955. Approximately 40 different wells have been sampled yearly. The lead concentration has generally been low. For 1965 and 1966, the concentration of lead averaged about 0.003 milligram per liter and the maximum was 0.017 milligram per liter.[28]

Samples of drinking water from reservoirs and treatment plants in Southern California and in the San Francisco Bay Area were recently analyzed for lead. Eleven locations were sampled in the San Francisco Bay Area and 16 in the Los Angeles Area. Only two had as much as 0.01 milligram of lead per liter; both were at the Silver Lake Reservoir (inlet - 0.016, outlet - 0.010) of the Los Angeles Department of Water and Power.[29]

Sources of lead contamination of water include contact with soils containing lead, the discharge of industrial wastes into streams and rivers, the settling of airborne particles on water surfaces and lead in water supply piping. It has been estimated that for each gallon of gasoline burned in an outboard motor, 0.53 grams of lead gets into the water, and that in 1963, 450 tons of lead in water supplies were from this source.[4] In a study made at Seattle, Washington, it was calculated from dustfall data that the lead content in a reservoir was increased by 0.038 milligram per thousand liters from dustfall in one month.[27] A study in Cincinnati involved the collection of rain water at two elevations adjacent to a very busy main traffic artery; the highest lead concentration noted was 0.49 milligram per liter, with five out of twelve observations showing lead in excess of 0.10 milligram per liter.[4]

E. The Three-City Study

Over a 12-month period in 1961 and 1962, a group of investigators representing governmental agencies, private industry, and universities conducted a study of the levels of atmospheric lead and of the blood and urine lead levels of people in Cincinnati, Los Angeles, and Philadelphia. The details of the program and the results obtained were presented in a report, Survey of Lead in the Atmosphere of Three Urban Communities, by the U.S. Public Health Service in January, 1965.[5] The biological findings of this study are included in Section VII, the environmental findings are summarized below.

1. Distribution of Atmospheric Lead

During the 12-month period of June 1961 through May 1962, samples were collected continuously over periods of 24, 48, or 72 hours at eight sites in Los Angeles. The average lead concentrations and the location of the eight sites are shown in Table 10.

These data show that atmospheric lead is widely distributed throughout the Los Angeles metropolitan area, and that the average lead concentrations are similar at many sites. The two-fold variation in the annual mean (1.5 vs. 3.0 micrograms per cubic meter) at two different stations may be due to differences in traffic density, average vehicle speeds in the proximity of the stations, and/or meteorological conditions. Westwood, which had the lowest average, is the site nearest the ocean and benefits from prevailing sea breezes.

Los Angeles had the highest average lead concentrations of the three cities as shown in Table 11.

All atmospheric lead concentrations in this report are for the inorganic lead in particulate matter. Organic (alkyl) lead vapors are highly toxic and rapidly absorbed by the body. The Three-City Study and a study of lead emissions from compact cars indicated that less than ten percent of the lead in the atmosphere may be organic.[30] However, very little is known of the levels of organic lead compounds in the atmosphere or emitted from motor vehicles; much of the data from these studies was inconsistent, pointing to the need for improved sampling and analytic methods.

2. Seasonal Variation

The concentration of lead in the atmosphere depends on meteorological conditions as well as on the amounts of pollutants emitted. During the 12-month period from June, 1961, through May, 1962, the average lead concentration measured by the State Department of Public Health at the eight stations in Los Angeles ranged from a low of 1.7 micrograms per cubic meter for the month of June to a high of 3.9 for the month of December.[5] The higher lead concentrations are associated with meteorological conditions that greatly restrict the dispersal of pollutants. These conditions frequently occur during winter months when the highest concentrations of carbon monoxide are also found.

3. Lead Concentrations Near Freeways

The highest concentrations of lead would be expected on freeways when both traffic density and average vehicle speeds are high. During the Three-City Study, samples were obtained in Cincinnati and in Los Angeles by means of mobile samplers to determine atmospheric levels in or near heavy traffic streams. On the average, the mean concentrations in Los Angeles traffic were about twice as high as in Cincinnati traffic.

Concentrations of lead on the shoulder or along freeways in Los Angeles for samples taken during the daylight hours and during rush periods averaged about 25 micrograms per cubic meter. The highest concentration found for a single sample in heavy traffic was 71.3 micrograms per cubic meter. The average concentration along the freeways

were ten times the average measured at the eight sites shown in Table 10, but the latter were for 24-hour periods or longer, which included times of low traffic density.

In Los Angeles downtown traffic, the average concentration was 15, and the maximum value was 29.9 micrograms per cubic meter. In downtown Pasadena traffic the average concentration was about 12 and the maximum value was 14.6 micrograms per cubic meter.

4. Daily Variation of Lead at Sampling Sites

Since motor vehicles are the principal source of atmospheric lead, the highest lead concentrations would be expected during or shortly after peak traffic conditions. Samples collected over four-hour periods show that the peak lead concentrations occurred in the morning from 7:00 to 11:00 a.m. and in the evening from 7:00 to 11:00 p.m. The mean morning peaks were 20 percent greater than the average, while the afternoon peaks were ten percent greater. The bimodal pattern reflects the variations of both motor vehicle traffic and meteorological conditions. Concentrations of other pollutants from motor vehicles such as carbon monoxide and the oxides of nitrogen also have a bimodal pattern in which a peak is reached during the morning hours and again during the late afternoon or evening hours.

VII. HEALTH EFFECTS OF ATMOSPHERIC LEAD IN CALIFORNIA

A. Introduction

Inorganic lead is thoroughly implicated as a causative agent in decreased hemoglobin synthesis, liver and kidney damage, mental retardation in children and in abnormalities of fertility and pregnancy.[31,32,4] In adults the data supporting the implications are mostly from occupational exposure. Alkyl lead, on the other hand, mainly affects the nervous system although various organs are also injured. Clinical observations are often used in denoting the effects of undue lead exposure and it is against the onset of clinical pathology in occupational exposure situations that blood and urine levels of inorganic lead have been established in setting presumed "normal" values.

There is evidence that exposure to moderately low lead levels may produce abnormalities in the synthesis of porphyrins (substances necessary for the production of hemoglobin and other compounds in the human body). With moderately high occupational exposures, a considerable increase in delta-aminolevulinic acid (a substance from which porphyrins are formed by the body) in blood and urine can be detected prior to other clinical or biochemical symptoms.[33] With a loss in capacity of reticulocytes (young red blood cells) to synthesize porphyrins, hemoglobin concentration is altered (thus, perhaps, the transport of oxygen and carbon dioxide). Survival time of red blood cells is also lessened.[34,35] Some decrease in other porphyrin structures, cytochromes, myoglobin, peroxidase and catalase may be expected. The most specific, but not the only, site of damage by lead in porphyrin biosynthesis is the inhibition of aminolevulinic acid dehydrase (an enzyme essential to the body's production of aminolevulinic acid). Increases in blood and urine levels of aminolevulinic acid immediately reflect this inhibition while blood and urine lead levels may remain unchanged even as accumulation in organs and bones take place. Indeed, in rats treated with alkyl lead, organ lesions have been shown to occur when other indications of intoxication were not present.[36]

Lead is absorbed rapidly by bone and apparently is released at a slow rate over extended periods of time. Lead workers removed several years from exposure still have shown high levels of porphyrins in their blood.[37] Presumably, sufficient lead was released slowly from accumulated reserves to interfere with porphyrin metalbolism.

Bacterial endotoxins proved fatal to 100 percent of infected rats which had previously been treated with lead.[38] Normally, the rats are not very susceptible to these bacterial strains. Rats also exhibit shortened life spans after lead intoxication.

Adults who have less than 0.08 milligram of lead per 100 grams of blood, and urine lead less than 0.15 milligram per liter, are considered to be within "normal" limits.[25] They ordinarily do not show clinical lead intoxication (even though blood and urine aminolevulinic acid levels may be high). There is considerable individual variation, however.

Children are much more susceptible to lead intoxication than adults. Encephalopathy and mental deterioration in lead-poisoned children have been well documented. One study disclosed that 200 normal children had blood lead levels of 0.014 to 0.030 milligram per 100 grams while 100 mentally defective children showed 0.04 to 0.08 per 100 grams of blood.[39] Aminolevulinic acid levels in the blood of these latter children were also high. It has been stated that an upper limit for blood lead in children should be 0.04 milligram per 100 grams. This figure already borders on the lower value found in affected children, though general population studies of children have not been done.

The available data indicate that blood or urine lead levels alone are not adequate criteria upon which to base judgments of health effects in adults, and certainly not for children. However, blood lead level generally parallels the total "body burden" and may be regarded as an indicator of total storage. Most studies of comparative environmental exposure have used blood lead level as an index of total exposure or relative hazard.

B. Absorption, Transport, Storage and Excretion of Lead

1. Body Burdens of Lead

By body burden of a pollutant is meant the amount in the organs, hard tissues, and in blood, plasma and other fluids of the body of a substance which either produces or is capable of producing damage or significant interference with functions of the body or of the respective organ or tissue.[40] Air pollution is not the only source of the body burden of a pollutant. Some of the pollutants occur naturally - that is, they are contained in uncontaminated food, water or air.

The body burden concept was used by the Department to establish the air quality standard for carbon monoxide. In this case, the exposure to community air pollution was allotted an approximate 50 percent of the defined tolerable level of 10 percent carboxyhemoglobin. Thus, the air quality standard was based on such a level of carbon monoxide as would produce a body burden of five percent carboxyhemoglobin.[41] A similar approach has been suggested for lead in a footnote to the Department's ambient air quality standards.

Work has been under way to set air quality standards for lead based on its body burden. The time scale for uptake and excretion is much longer than that for carbon monoxide, but the fundamental concepts are very similar.

The basic principle for evaluation of lead exposures is that public health policies should be directed toward preventing increases in the body burden of lead since the health hazard increases with increased stored lead. As Kehoe states,

> "It is evident that the only certain provision for human safety, with respect to continuous exposure to lead, lies in the avoidance of a persistent level of alimentary and respiratory dosage that will result in a measureable accumulation of lead in the bodies of exposed persons in the course of a life time."[42]

The balance studies at the Kettering Laboratory, using both orally administered and airborne lead, have been interpreted as indicating that storage did not continually increase when exposures and rates resembling those of the industrial threshold limits were continuous. Nevertheless, the evidence suggests that when there is increased respiratory exposure over sufficiently long periods there is increased lead storage. Since the amount of lead stored is estimated from data on lead concentrations in various tissues, it is not a practical index. Blood lead levels are often used for an approximate guide to the amount of lead stored.

Other criteria of possibly important exposure are the condition of red blood cells and factors relating to hemoglobin and porphyrin metalbolism. Alterations in these could reflect nutritional or other factors and it may be difficult to attribute differences in time or area solely to variations in atmospheric lead levels.

2. Routes of Absorption for Lead

Organic forms of lead, such as tetraethyl lead and tetramethyl lead, may be absorbed through the skin.[4,25] Such routes of absorption are infrequent in occurrence and probably of no relevance to community air pollution problems. The largest amounts of lead are absorbed through the respiratory tract and the gastro-intestinal tract. In the case of the gastro-intestinal tract, lead which is swallowed is largely excreted in the feces and only between five and ten percent of the swallowed lead is likely to be absorbed and interact with the body's metabolism. The proportion absorbed depends on the form of lead and on other substances present, as well as on the solubility of the particular compound.[4,25]

Inhalation of sufficiently small lead particles leads to their deposition in the deeper spaces of the lung from which they may be gradually absorbed. Larger particles, if they are insoluble, are likely to be trapped in the mucus layer of the respiratory tract and ultimately swallowed; hence, their fractional absorption is as though they had been ingested by mouth. Most lead compounds of importance in air pollution are relatively insoluble. When particles small enough to be deposited deep in the lung are inhaled, a fraction of them are expired and, hence, are not absorbed. Of those which are retained in the lung (between 25 and 50 percent of the total inhaled) most are absorbed sooner or later.[4] Hence, particles of small size are likely to be absorbed into the body at a rate that is five to ten times greater than larger particles that are inhaled or than lead which is ingested with food. Thus, in comparing the multiple sources of lead, particle size is important.

It is generally felt that the average diet in the United States contains about 300 micrograms per day of lead (that is, 0.3 milligram).[4] If one-tenth of this were absorbed, this would lead to a dietary ingestion into the metabolic pool of approximately 30 micrograms a day. This is also the approximate amount found in the urine. In balance studies carried out at the Kettering Laboratory, it was found that over a period of many months the excretion of lead exceeded the ingestion even when the levels of blood lead and presumably of body burden had not altered.[25] From this it was deduced that the excess must have been based on absorption from inhaled air. However, measurements of the amount of lead in inhaled air concurrent with these experiments were not reported. It has been estimated that the absorption from inhalation was approximately 20 micrograms per day. This figure might have resulted if there had been 2 micrograms per cubic meter of ambient air, 50 percent absorption, and 20 cubic meters of respiration per day, but these figures all seem slightly higher than would have been expected. There may have been a contribution from cigarette smoking.

Gusev reports investigations of children from five to seven years of age who were in a nursery for eight hours a day in the vicinity of lead smelter and cable plants in the Soviet Union.[43] They were exposed to approximately 1 microgram per cubic meter of average lead concentration and had an apparently significant increase in coproporphyrin excretion (8.2 micrograms per eight hours compared to 6.5 micrograms per eight hours for children exposed to less than 0.01 microgram per cubic meter of average lead concentration). A similar group of children in a nursery near a pewter factory were exposed to approximately 2.5 micrograms of lead per cubic meter; they had an average coproporphyrin excretion of approximately 10.5 micrograms per eight hours. Of course, the children might have had exposure to lead other than by inhalation; for example, to lead paint or to vegetables grown in the vicinity or there may have been other exposures or conditions leading to porphyria; nevertheless, this finding has raised questions which deserve to be investigated in other locations. The report has also been influential in setting air quality criteria in the Soviet Union.

3. Lead Absorption from Cigarette Smoking

In the study of occupational exposure to lead no attention was paid until recently to the possibility that cigarette smoking was important. Cogbill and Hobbs in 1957 reported a systematic study of the amount of lead (and other metals) in cigarette tobacco and the fractional transfer of lead to the smoke inhaled by the smoker.[44] At the time the Department set its Air Quality Standards in 1959 there were no systematic data on the consequences of lead being present. Since that time, studies, particularly the Three-City Study, have documented the importance of cigarette smoking as a factor in producing differences in blood lead levels.

Cogbill and Hobbs suggested that the lead in cigarette smoking represents the transfer into leaf tobacco of lead arsenate spray residues in soils. These sprays had been used for many years but are no longer used on tobacco. The increased absorption of lead also strongly suggests an increase in the absorption of arsenic as well. Cogbill and Hobbs showed that the lead-arsenic ratios were what would be expected if lead arsenate was in fact the source of the lead. There has been a downward trend in arsenic content in cigarettes and cigarette smoke. Accordingly, the lead content should also drop or has already done so.[45,46,47] It would also follow from these considerations that younger cigarette smokers should be less likely to show differences than older smokers. The smaller differences between women smokers and nonsmokers as compared with the differences between men smokers and nonsmokers might be explained by the fact that on the average the women smokers started the habit more recently.

On the basis of the available estimates, it would seem that the absorption from inhalation of cigarette smoke is of the magnitude of 0.5 microgram per cigarette; thus, a heavy cigarette smoker might have an absorption of ten or more micrograms. It is likely that some of the 20 micrograms excess referred to above in the Kettering Laboratory balance studies represents absorption from cigarettes. But the differences between cigarette smokers and nonsmokers are small.

While cigarette and pipe or cigar tobacco may all contain lead, the absorption from these latter forms of smoking is likely to be less because the cigar and pipe smokers are not likely to inhale.

4. Transport, Storage and Excretion of Lead

The largest proportion of lead in the human body is stored in bones.[4,25] Even lead compounds which are relatively insoluble can be presumed to be in equilibrium with the body fluids though the period of time required for equilibrium to develop with a fixed intake may be fairly long. It is known that lead may be absorbed and act upon the surface of the red cell; lead may be found both in plasma and in red cells as they are normally collected with much the greater portion carried by the red blood cells.[25] The form in which lead is carried in the body is not entirely understood but presumably it competes for sites normally occupied by calcium and other bivalent ions. When changes of lead exposure occur over a relatively short period of time, they are likely to be reflected in changes in urinary lead.[4,25] Over longer periods of time the storage of lead in the body tends to be reflected in blood lead; these considerations, however, apply only to inorganic lead. Organic lead is readily absorbed by the skin, has its characteristic toxicity on the nervous system, and does not tend to be reflected in blood lead but is reflected in urine lead levels. Accordingly, highly variable and/or organic lead exposure might be expected to show themselves in increased urinary lead earlier than in blood lead level.

Because of these considerations and because of the general association, it is assumed that blood lead reflects body storage. Over long periods of time (years to decades), if the exposure is continuous at a given level, there does not seem to be a steady increase in blood lead; rather, in healthy individuals studied, it has seemed as though the body slowly increases its capacity to excrete the excess to which it is exposed.[4,25] Nevertheless, the body storage of lead tends to reflect the amount to which exposure has occurred in a general way and the blood lead is generally accepted as a crude reflection of this.

There is some disagreement on the question of whether the storage of lead in adults increases with age. Some studies have indicated that it does, but in other studies the evidence did not favor increased body lead with age.[48,49,50,51]

Where the exposure is predominantly respiratory and in small particle sizes, a larger fraction of the body storage may occur in the lungs from which absorption may continue to occur than in the case of larger particle sizes or with oral ingestion. Accordingly, it would be important to obtain systematic data on lung lead levels in Los Angeles.

Excretion of absorbed lead is primarily via the urine. Values for urinary lead of 0.01 to 0.08 milligram of lead per liter are considered normal, with a total excretion of about 0.03 milligram per day.[4,25] This is approximately the amount of lead estimated to be absorbed from the average diet in the United States.[4] Some lead is also excreted in the bile but most of this is probably reabsorbed.[25] The concentration of lead in sweat is thought to approximate that in the urine.[25]

5. Lead in Human Tissues

A number of studies of lead in human tissues have been made, including two studies which were financed in part by the Department.[51,52]

Studies utilizing human tissue gathered under a variety of environmental conditions have shown substantial differences among tissues in their lead burden. Unfortunately, different studies have used different tissues and have used different bases for reporting results, so that direct comparisons are hard to make. Nevertheless, these studies do show reasonable agreement and permit a few general conclusions.

a. Lead is not distributed evenly throughout the tissues. The aortic arch, liver, and kidney carry much higher concentrations of lead than other soft

tissues while the brain, heart, and muscles carry somewhat less. Long bones carry a substantially greater burden than flat bones. The concentration in the liver may be ten times that in muscles and may approach that in flat bones.[25,53,54,55]

b. Blood lead is often taken as an indicator of total body burden, but repeated samples from the same individuals may show substantial shifts over a period when it does not seem likely that total body burden has undergone much change.[25,56]

c. Most studies have shown differences by sex, with males carrying substantially greater burdens.[5,25,51]

d. Even very young infants carry substantial body burdens of lead. The total increases with age, reaching a maximum at about the fifth or sixth decade for most tissues. However, the total is near its maximum by twenty years of age.[49,50,53]

e. Geographic differences exist. Higher levels are generally observed in urban areas, particularly if industrialized. The lowest levels are generally reported from rural, underdeveloped areas. Several studies have reported lower values from areas with higher altitudes, but this may be because of the association of urbanization with altitude.

Relatively low values have been reported from Mexico, Peru, Central Africa and mountain areas in California; high values have been reported from New York City, Los Angeles, Cincinnati, Hong Kong, and Cairo, with values for Switzerland intermediate.[5,25,50,53,55]

Some representative findings are shown in Table 12.

In a study of adult autopsies in Los Angeles, male smokers were found to have higher concentrations of lead in bone and lung tissue than male nonsmokers and females (Table 13); no relation was observed for age or length of residence in Los Angeles.[51] In another study in Los Angeles of adult blood donors and hospital patients and employees, age, sex, auto driving, and length of residence had no apparent effect upon mean serum values for lead.[52]

Analyses are usually performed on 5 to 20 grams of tissue or whole blood or on 100 milliliters of urine.[57] The analytic error rarely exceeds 0.001 milligram, but when results are expressed in milligrams per 100 grams of tissue or whole blood this analytic

error may be of the order of one-third the observed value.[25,57] For this reason (and because contaimation of samples may occur despite all precautions) the reported values are often the average of duplicate analyses.

Repeated samples of urine from the same individuals taken over a span of a few hours may vary widely in lead concentration while the concentrations in samples of blood taken at the same times remain relatively constant.[25] However, samples of blood taken from the same individuals after a lapse of several weeks or months may show substantial shifts well beyond the variability expected from analytic error and when it does not seem likely that total body burden has undergone much change. (Table 14)

This indicates that blood lead reflects varying physiological states, which include not only body burden and exposure to lead but also other factors, about which little or nothing is known. It is for this reason that blood lead cannot be depended upon as a reliable indicator of body burden for an individual, although it may be suitable for such use in population studies where individual variations may be expected to average out.

Most reports of tissue lead are based on a very few samples drawn from easily available sources; for example, autopsy material from teaching hospitals. These sources are indicative of "normal" ranges but cannot be regarded as necessarily representative of the populations of these areas.

Current analytic methods require substantial quantities of tissue, so autopsy material must continue to be the major source. As long as this remains true, it will be impossible to obtain samples which are unquestionably representative of a living population. However, it should be possible to obtain random samples from routine autopsies with enough additional information to make better inferences about the living populations from which they came.

Such studies are urgently needed to answer questions concerning the relationship between body burden and such variables as water quality, exposure to atmospheric pollution, socio-economic status, and smoking habits.

C. Lead Exposure As a Public Health Problem

1. Hazards to the Population

In high doses, unlikely to be associated with community air pollution, nerve palsies and gastro-intestinal symptoms occur.[4,31,32] With lower doses a low-grade anemia may occur, and possibly some impairment of fertility.[4] Associated with the anemia is interference with red blood cell metabolism and increased excretion of Type 3

coproporphyrin and delta-aminolevulinic acid.[33,37] The biochemical pathway is shown in Appendix A. Increased excretion of these substances occurs at blood lead levels substantially below those at which anemias or other symptoms are usually observed; this indicates that some alteration of the metabolism must be occurring at these lower levels even though nothing of provable medical importance has occurred. The public health significance of this is unknown.

Most statements concerning the innocuousness of blood or urine lead levels below stipulated points make no mention of the possibility that there may be sensitive individuals in occupationally exposed populations.[4] It should be assumed that there are, since congenital disorders of porphyrin metabolism are well known. Also, small children seem to have increased sensitivity. Blood and urine specimens of persons with chronic respiratory, kidney, and liver diseases in the Three-City Study (only two of the three cities had collections made) did now show any unusually high values of lead in blood or urine. The question of whether the observed levels are a greater health hazard to individuals with chronic disease is an important and as yet unanswered question.

Among lead workers, Lane has shown increased probability of death due to vascular disease.[58] However, the relevant exposures occurred during periods in which adequate industrial controls of lead exposures were not in existence and Lane does not feel that the presently permitted industrial exposure levels are likely to produce excess mortality. Studies in the U.S.S.R. have suggested that lead may be associated with the development of atherosclerosis.[59] Effects of high level exposures on chronic kidney diseases and on kidney function are well documented.

While these considerations are important as possible long-term effects of continuous lead exposure on the public health, there have not been any cases of characteristic lead toxicity reported in the literature which could reasonably be ascribed to community air pollution.

2. Evidence Derived from Occupational Exposures

In the report of the American Conference for Governmental Industrial Hygienists entitled "Threshold Limit Values for 1966" is found the following statement:

> "These limits are intended for use in the field of industrial hygiene and should be interpreted and applied only by persons trained in this field. They are not intended for use, or for modification for use (1) as a relative index of toxicity by making a ratio of two units, (2) in the evaluation or control of community air pollution or air pollution nuisances, (3) in estimating the toxic potential of continuous uninterrupted exposures, (4)

as proof or disproof of an existing disease or physical condition, or (5) adoption by countries whose working conditions differ from those in the United States."[60]

Nevertheless, it is the collected experience in industrial hygiene which provides the perspective for the evaluation of lead hazards. The detection of early reactions has provided a great deal of information of benefit in the evaluation of community air pollution exposures. Industrial hygienists have been primarily concerned with the avoidance of risks of acute toxicity from lead. It seems well established that blood lead levels between 0.07 and 0.0 milligram per 100 grams and urinary excretion of lead between 0.10 and 0.15 milligram per liter are levels below which manifestations of lead poisoning in employed adults are not likely; it is for this purpose that the Threshold Limit Value for occuptational exposure to lead of 200 micrograms per cubic meter of air has been set. Many statements are made concerning the application of stipulated levels to long-term toxicity. There have in fact been very few studies of such long-term exposure effects, as on longevity or on increasing incidence of certain chronic conditions when exposed individuals are followed throughout their lives.

Occupational exposures are customarily for an eight-hour working day or approximately 40 hours of the 168-hour week. Community exposures, however, are likely to be continuous in nature even though fluctuating in magnitude. Other factors are not similar; for example, it seems very likely that the particle size of many occupational exposures is substantially greater than the particle size for community air pollution exposures. The effect of this is particularly important since particles larger than one micron are more likely to impinge on the portions of the respiratory tract which are lined with mucus; this mucus is transported to the pharynx and is likely to be swallowed. Smaller particles, those more common in community air pollution, are likely to impinge on the deeper portions of the alveoli and bronchioles from which they may be directly absorbed. (Table 15)

In addition, the exposure of the community to organic lead represents a much less well-studied problem than exposure to inorganic lead and a much less well-studied problem than the exposure to organic lead in occupational circumstances. However, community exposure to organic lead is probably only a small fraction of the total lead exposure.

The Technical Report of California Standards for Ambient Air Quality and Motor Vehicle Exhaust reviews the nature of lead toxicity, routes of exposure, and the bases available in 1959 for estimating the effects of additional absorption.[41] At that time the excretion of porphyrins was felt to be a sensitive method for use in a study of possible exposure to lead in the community. Since that time an additional index has been widely accepted which reflects alterations in the same metabolic pattern. This is delta-aminolevulunic acid.

Delta-aminolevulinic acid is now felt to appear consistently and earlier in exposed workers and in experimental animals than the evidence of increased porphyrin secretion and it is not necessarily parallel with urinary lead levels.[33,36] Elevations in concentrations of this substance are also observed under circumstances in which the blood lead level is thought to be within the "normal" range, that is, less than 0.08 milligram per 100 grams of blood. But lead is not the only substance which may interfere with porphyrin metabolism or with excretion of delta-aminolevulinic acid. There have not been, to the best of our knowledge, any studies made of the effects of exposures to community air pollution on either of these substances.

3. The Geochemical Point of View

In hearings before the Senate Subcommittee on Air and Water Pollution, Eighty-ninth Congress,[61] and in a previous article in the Archives of Environmental Health,[62] the geochemical point of view was expressed that the natural level of lead exposure prior to the mining and processing of this substance was very substantially lower than the present exposure in most parts of the world. While these data seem sound from a geochemical point of view, they raise the difficult question of what health consequences may be associated with the very wide distribution of this increased amount of lead.

Another set of questions is related to policies for public health protection, which could be based (a) on arbitrary increments above the "natural" level, (b) on manifest toxic reactions, or (c) on the earliest unfavorable effects on the most sensitive group in the population. The Department in considering ambient air quality standards has based them on the likelihood of specified effects occurring among the most sensitive groups in the State, provided the groups are definable in terms of age and medical status. Thus widespread occurrence of increased lead exposures which could not be shown to produce any deleterious effects would not be reflected in the standards. However, where interference with hemoglobin synthesis for example can be shown to result from a body burden of lead without overt toxicity this would be relevant.

The basis for air quality standards is under periodic review and all relevant data are considered at the time of such review. The geochemical data will be among the sets considered at the appropriate time. If previous policies are again followed, data on effects at low dosage or body burdens, will be of decisive importance.

So far the Department has not indicated that any specified levels are safe or harmless.

Finally, the standards, if any are adopted, will reflect the multiple sources of lead exposure, and not only that from community air pollution.

D. Studies of Lead Burden in Population Groups

1. The Three-City Study

To establish a baseline estimate of lead body burden in the public, the lead content of blood and urine of selected population groups totaling 2,342 individuals was determined in the Survey of Lead in the Atmosphere of Three Urban Communities (The Three-City Study).[5] A social and medical history, including smoking habits, was obtained from each individual. Subjects were selected who had no known industrial lead exposure. Some groups were selected who had opportunity for occupational lead exposure, mostly working close to motor traffic. All subjects had lived in the survey area at least five years. Several groups totaling 126 individuals with various chronic diseases were selected. Data on 478 individuals were from a prior (1956) study in Cincinnati and on 2[illegible] individuals from prior pilot studies in California. In general, the results were as follows:

a. Men had higher blood levels than women.

b. Cigarette smokers had slightly higher blood and urine lead levels than nonsmokers, or pipe or cigar smokers.

c. Urban dwellers had higher blood and urine lead levels than suburban dwellers. Rural dwellers had the lowest levels.

d. No relationship was found between blood lead level and age, and there were no unusual findings in the chronic disease groups. The Los Angeles data showed no relation between blood lead and commuting time.

e. As variables, sex, smoking habits, and exposure to automobile exhaust seemed to be independent of each other.

f. For each of the three cities considered separately, lead levels in both blood and urine appeared to follow the likely degree of exposure to atmospheric lead from automobile exhaust.

A portion of the data is shown in Table 16.

2. The Los Angeles Freeway Study

In 1966, the Department undertook a study with the Los Angeles County Health Department to determine whether people living near a freeway had higher concentrations of blood lead than people living at some distance from a freeway. Samples of blood were taken from two groups of 50 persons each. The homes of the first group were adjacent to a heavily traveled freeway; homes of the second group were near the coast in an area with substantially less atmospheric lead. Table 17 shows the concentrations of lead in the blood of the two groups as well as in some of the groups previously studied by the Department.

The average concentration of lead in the blood of the people near the freeway was higher than that of the people living near the coast. This was true for both men and women. Other factors were also examined, including age, occupation, and smoking habits, but no other statistically significant differences were found. It is particularly worth noting that the blood levels of the people near the freeway were as high as or higher than that of any other nonoccupationally exposed group measured in California. These data can be explained in several ways, but we believe the most likely reason is exposure to atmospheric lead.

3. Urban-Rural Gradients

Since the largest differences observed in the recent studies of blood lead in various populations in the country, including California, have been between urban and rural residents, it is possible that the differences are largely the reflection of exposure to airborne lead. If it could be demonstrated that the differences were not due to the contributions of food and water, then it could be deduced that the increase in blood lead levels was due to atmospheric lead. The determination of such differences would not require a formidable research effort.

The low values in all studies of blood lead in California are from 0 to 0.006 milligram per 100 grams among nonsmokers. Repeated determinations on blood from the same person show variability substantially greater than that associated with analytic methods, which suggests some of these low values may be merely temporary fluctuations from a higher level. (Table 14) The average values among rural residents in Alpine County are one-half those of the residents of urban areas and other studies have also shown an urban-rural gradient. Data in Table 17 for populations who live adjacent to freeways and on the coast show that residence near freeways is associated with a significant increase compared with residence near the coast. Residence near freeways is not, however, associated with a significant increase compared with many other urban

groups. All groups of urban residents show higher blood lead levels than rural residents in Alpine County. Thus, it is correct to say that rural residents have the lowest levels, Los Angeles coastal residents have the next lowest, with other groups higher. These differences are small.

4. Relationship between Atmospheric Exposure and Blood Level

Table 18 indicates the environmental exposures associated with blood lead levels from the data collected mostly in the Three-City Study. In Figure 1 these data are plotted (the logarithmic scales used are generally more appropriate for biologic data than arithmetic scales[63,64,65]) and a regression fitted to show an approximate dose-response relationship. Table 19 gives expected blood lead levels for various exposures, based on this regression.

It must be emphasized that most sets of blood lead levels were not taken of individuals who had actually been breathing the air samples with which they are matched. Atmospheric sampling and measurement of blood of residents in the same area may be at different times. There are seasonal fluctuations in exposure and there are also substantial variations from time to time which do not show any systematic pattern. No seasonal fluctuations have been shown for blood lead levels in community studies, though some do appear in the Kettering experimental studies.

No data have been obtained on the response of California children and no data have been obtained which might make it possible to compare porphyrin and delta-aminolevulinic acid excretion or levels. In California, data on both of these are needed. Thus, it can be concluded that the presently available data do not indicate any levels at which classical toxicity could be predicted, but the data are not adequate to evaluate the major criteria relevent to possible public health consequences at atmospheric lead pollution.

E. The Basis Available for Judgment of Health Hazards from Atmospheric Lead

A reasonable interpretation of the presently available data on blood lead levels indicate that there are distinct rural-urban patterns, but rather less striking patterns for differences within urban areas of the State. The urban-rural differences are consistent with the contribution of air pollution, but in the absence of studies of diet and water supply it is premature to draw a cause-and-effect conclusion. In the Three-City Study, observed differences of between 0.002 and 0.004 milligram of lead per 100 grams of blood, which appear to be associated with cigarette smoking, are consistent with the estimates of airborne exposure and with the general tendency of cigarette smokers to excrete slightly more lead in the urine.

One must note the lack of unusually high lead values for freeway residents. Exposures for these people may differ by a small amount from that of those living in other parts of the metropolitan areas because the concentration of lead decreases rapidly with distance from the freeway. This is consistent with what is known about the gradients of pollutants, such as carbon monoxide, with comparable distances from the freeway. One must also note the lack of high blood lead values in traffic policemen, though in the Three-City Study there appeared to be slightly higher urine lead to blood lead ratios in policemen in Los Angeles and decidedly higher ratios in Cincinnati. This suggests increased excretion of lead by these groups.

Much additional data are needed to have an adequate basis for judgment of health hazards; in particular, this would include measurements of lead in the diet and water supplies in rural and urban areas, measurement of lead in tobacco smoke, and contemporaneous measurement of lead exposures with blood and urine levels in exposed populations using 24-hour urine specimens.

In addition, aminolevulinic acid and porphyrin concentrations should be determined in the blood and urine of adults and children from exposed populations and compared with values for healthy individuals who live in relatively lead-free environments. Correlation of these tests with blood and urine lead levels, the survival time of red cells and decreases in red cell aminolevulinic acid dehydrase should establish the scientific value of aminolevulinic measurements as indicative of subclinical lead exposures. Also, they will determine if another pathological symptom - decreased red cell survival time - can be shown prior to other clinical observations and high blood or urine lead levels. Data presently available do not permit an assessment of metabolic damage from lead slowly released from reserves such as bone. With increasing environmental contamination there is every reason to expect increasing body burdens of lead. If so, increases in blood and urine aminolevulinic acid levels can be used in setting environmental limits on lead concentration.

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Table 1

LEAD CONSUMPTION IN THE UNITED STATES AND CALIFORNIA, 1964

USE	TONS
Total United States	1,155,785
Metal Products	353,952
Storage Batteries	429,898
Pigments	99,946
Chemicals	233,917
Misc. & Unclassified	38,072
Total California	108,980
California, Percent of U.S. Total	9.43%

Source: U.S. Bureau of Mines, Minerals Year Book, v. 1, 1964.

Table 2

LEAD CONTENT OF SOILS, DUSTS AND PARTICULATE MATTER

SOURCE	PERCENT LEAD
Average in earth's crust	0.0016
Old residential soils	0.0360
New York City street sweepings	0.2650
Airborne particles, Philadelphia average	1.5
Airborne particles, Cincinnati, average	1.7
Airborne particles, Los Angeles, Average	2.3

Source: U.S. Public Health Service, Symposium on Environmental Lead Contamination, Publication No. 1440, March 1966.

U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965.

Table 3

LEAD FURNACES AND CONTROL METHODS
LOS ANGELES COUNTY, 1966

TYPE OF FURNACE	NUMBER	LEAD PROCESSED (annual tons)	CONTROL METHOD	REMARKS
Total	160	816,600		
Cupola	3	16,250	baghouse	about 98% emission control
Reverberatory and Sweating	13	20,950	afterburner & baghouse	about 99% emission control
Pot (uncontrolled)	95	672,000	...e	low temperature; emissions very low
Pot (controlled)	49	107,400	baghouse	about 98% emission control

Source: Los Angeles County Air Pollution Control District.

Table 4

LEAD CONTENT OF GASOLINE IN
THREE CALIFORNIA AREAS, 1964-1965
(Grams of lead per gallon)[1]

AREA	TYPE AND YEAR			
	Premium		Regular	
	1964	1965	1964	1965
Los Angeles	2.85	3.00	1.93	2.12
San Francisco Bay	2.72	2.76	1.96	2.18
Bakersfield	3.25	3.28	2.27	2.46

[1] Unweighted average of all brands reported.

Source: Derived from Ethyl Corporation data by State of California, Department of Public Health, Bureau of Air Sanitation

Table 5

LEAD CONSUMPTION AND EMISSION BY MOTOR VEHICLES IN CALIFORNIA, 1965

AREA	PERCENT OF MOTOR VEHICLES [2]	LEAD CONSUMPTION (tons)	LEAD EMISSION (tons)
California, Total	100.0	21,300	16,000
Los Angeles County	37.0	7,880	5,910
San Francisco Bay Area Air Pollution Control District[1]	19.8	4,220	3,170
Orange County	6.0	1,280	960
San Diego County	5.5	1,170	880
Sacramento County	3.4	725	545
San Bernardino County	3.2	680	510
Riverside County	2.2	470	350
Remainder of California	22.9	4,875	3,675

1 Includes Alameda, Contra Costa, Marin, San Francisco, San Mateo, and Santa Clara Counties.

2 Derived from State of California, Department of Motor Vehicles, Gross Report.

Source: State of California, Department of Public Health, Bureau of Air Sanitation.

Table 6

LEAD CONCENTRATIONS IN THE ATMOSPHERE
AT FOUR CALIFORNIA LOCATIONS, 1957-58 and 1965-66

LOCATION OF SAMPLING AND YEAR[1]	NUMBER OF SAMPLES	LEAD CONCENTRATION (micrograms per cubic meter)	
		Range	Average
Berkeley[2]			
1957-58	25	.02- 3.2	1.04
1965-66	24	.09- 1.48	.41
Los Angeles[2]			
1957-58	26	.45-12.7	4.30
1965-66	26	.16- 4.90	2.88
San Diego			
1957-58	27	.28- 3.17	1.34
1965-66	22	.51- 4.64	1.44
Mt. Hamilton			
1957-58	24	.02- .28	.12

1 All samples at each location were taken at a single site.

2 Sampling sites in Berkeley and Los Angeles were changed between 1957-58 and 1965-66.

Source: State of California, Department of Public Health, Bureau of Air Sanitation

Table 7

LEAD CONTENT OF ATMOSPHERIC PARTICLES BY SIZE
BERKELEY, 1960

MEDIAN EQUIVALENT DIAMETER (microns)	PERCENT OF TOTAL ATMOSPHERIC LEAD (by weight)
Total, all sizes	100
20	2-4
9	2-6
4	3-6
3	1-6
1.5	4-25
1	2-15
< 1	50-80

Source: State of California, Department of Public Health, Air and Industrial Hygiene Laboratory

Table 8

LEAD CONCENTRATIONS IN WASHED AND UNWASHED LETTUCE
(Parts per million by weight)

WASHING AND DISTANCE FROM ROAD	NUMBER OF SAMPLES	LEAD CONCENTRATION	
		Range	Mean
Washed			
less than 100 yds.	7	.27-1.45	.48
100 yds. or more	5	.04- .33	.12
Unwashed			
less than 100 yds.	7	.43-1.62	.91
100 yds. or more	5	.13-1.15	.51

Source: State of California, Department of Public Health, Bureau of Air Sanitation (1965)

Table 9

LEAD CONTENT OF SOME FOODS AND BEVERAGES
(Milligrams of lead per kilogram of food)

FOOD	SOURCE	NUMBER OF SAMPLES	LEAD CONTENT
Cabbage	Market	4	.10 - .24
Wheat Bread	Market	8	.02 - .16
Bran Flakes	Market	2	.14 - .15
Spaghetti(prepared)	na	2	.06 - .21
Cornstarch	na	4	.75 - 1.83
Cocoa	Market(20 brands)	25	.40 -11.5
Beef bone(fresh)	Western U.S.A.	1	3.60
Beef liver	Western U.S.A.	2	.29 - .40
Beef kidney	Western U.S.A.	2	.12 - .38
Beef cooked	Market	9	.003- .63
Eggs	Market	6	.003- .12
Lobster	U.S.A.	na	2.5
Lobster	India	na	.08
Coffee(prepared)	na	2	.01 - .03
Beer	na	3	.13 - .29
Grape juice	na	7	.04 - .40
Wine	na	10	.05 - 1.51
Milk	U.S.A.--1936	na	.02 - .04
Milk	Japan---1936	na	.01 - .06
Milk	Cincinnati, recent	na	.04 ± .017
Milk	Northern and Eastern U.S.A., recent	na	.05 ± .025

na Not available.

Source: U.S. Public Health Service, Symposium on Environmental Lead Contamination, Publication No. 1440, March 1966.

U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965.

Kehoe, R.A., "The Harben Lectures, 1960--The Metabolism of Lead in Man in Health and Disease," J. Roy. Inst. Public Health, 1961.

Table 10

MEAN LEAD CONCENTRATIONS AND
SAMPLING LOCATIONS, LOS ANGELES, 1961-1962
(Micrograms per cubic meter)

SITE	SITE CLASSIFICATION	LOCATION	MEAN LEAD CONCENTRATION
All			2.5
1	Commercial	Downtown Los Angeles	2.7
2	Commercial	West Los Angeles	3.0
3[a]	Rural	Arcadia	2.8
4	Residential	Pasadena	2.4
5	Residential	Pasadena	2.1
6	Residential	Westwood	1.5
7	Industrial	Vernon	2.3
8	Commercial	Downtown Los Angeles	2.9

[a] Site 3 was at the Los Angeles County Arboretum, a large sylvan park between two heavily traveled thoroughfares, and near the Santa Anita Racetrack.

Source: U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965.

Table 11

ATMOSPHERIC LEAD CONCENTRATIONS
IN THREE CITIES, JUNE 1961-MAY 1962
(Micrograms per cubic meter)

DATA INTERVAL	CITY		
	Cincinnati	Philadelphia	Los Angeles
Number of Sites	4	8	8
Annual Mean at All Sites	1.4	1.6	2.5
Maximum Monthly Mean For a Single Site	3.1	4.4	6.4
Month of Maximum Mean, Single Site	October	October	December
Maximum For a Single Sample	6.4	7.6	11.4

Source: U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965.

Table 12

LEAD CONCENTRATIONS IN HUMAN TISSUES
(Micrograms of lead per gram of dry ash)

TISSUE	SOURCE			
	United States	Africa	Near East	Far East
Aorta	170	76	140	92
Brain	5	5	23	11
Heart	5	5	21	21
Kidney	110	37	70	84
Liver	150	60	77	110
Lung	51	26	47	48
Pancreas	56	17	33	42
Skin	46	na	na	na
Spleen	30	22	58	41
Testis	12	29	28	33

na Not available

Source: Tipton, I.H., et al., "Trace Elements in Human Tissue," Health Physics, 1963,1965.

Table 13

MEAN LEAD CONCENTRATIONS IN BODY TISSUES FOR SMOKERS AND NON-SMOKERS, LOS ANGELES

TISSUE AND SMOKING STATUS	MALE			FEMALE		
	Number of Cases	Lead Concentration[1]		Number of Cases	Lead Concentration[1]	
		Mean	S.E.		Mean	S.E.
Calvarium						
Smoker	23	76	5	15	63	5
Nonsmoker	9	59	4	23	58	4
Rib						
Smoker	24	84	5	15	59	4
Nonsmoker	9	66	7	23	63	4
Lung						
Smoker	24	0.423	0.052	15	0.238	0.030
Nonsmoker	8	0.241	0.049	21	0.244	0.030

S.E. Standard error

1 Calvarium and Rib: Micrograms of lead per gram of dry ash.
Lung: Milligrams of lead per 100 grams of dry tissue.

Source: Nusbaum, R.E., et al.: "Relation of Air Pollutants to Trace Metals in Bone," Arch. Env. Health, 10:227-232 (1965).

Table 14

BLOOD LEAD LEVELS ON TEST AND RETEST FOR
PERSONS IN PASADENA FOLLOW-UP STUDY
LOS ANGELES LEAD FIELD STUDY, 1961
(Micrograms of lead per 100 grams of blood)

MALE			FEMALE		
June 1961	March 1962	Change	June 1961	March 1962	Change
19	12	- 7	37	17	-20
0	26	+26	0	4	+ 4
37	17	-20	8	9	+ 1
20	9	-11	26	17	- 9
19	20	+ 1	5	12	+ 7
38	15	-23	12	30	+18
13	12	- 1	14	14	0
22	18	- 4	18	21	+ 3
19	7	-12	12	11	- 1
25	34	+ 9	2	24	+22
0	33	+33	14	24	+10
9	0	- 9	0	9	+ 9
36	0	-36	14	5	- 9
0	0	0	0	10	+10
21	13	- 8			
5	33	+28			
23	19	- 4			

Source: State of California, Department of Public Health, Bureau of Chronic Diseases.

Table 15

SOME CHARACTERISTICS OF ATMOSPHERIC PARTICLES BY SIZE

EQUIVALENT DIAMETER OF PARTICLES (Microns)	REMARKS
$> 5.$	Settle rapidly; not a large part of airborne lead.
$> 2.$	Trapped out high in respiratory tree; cleansed out normally and expectorated or swallowed
≤ 0.6	Reach the alveoli, past normal cleansing defenses of respiratory system.
< 0.45	60% of Los Angeles atmospheric lead.
< 0.90	75% of Los Angeles atmospheric lead.
< 1.60	90% of Los Angeles atmospheric lead.

Source: U.S. Public Health Service, Symposium on Environmental Lead Contamination, Publication No. 1440, March 1966.
U.S. Public Health Service, Survey of Lead in The Atmosphere of Three Urban Communities, Publication No. 999-A P -12 January 1965.

Table 16

MEAN CONCENTRATION OF LEAD IN
BLOOD AND URINE OF SELECTED POPULATIONS

POPULATION	FEMALE	MALE	
	Blood Lead (milligrams per 100 grams)	Blood Lead (milligrams per 100 grams)	Urine Lead (milligrams per liter)
Alpine County, Calif. (rural)	0.009	0.012	na
Philadelphia			
Suburban	0.013	0.013	0.020
Commuters	0.015	0.019	0.028
Downtown	0.018	0.024	0.030
Police	na	0.026	0.033
Oakland			
Non-smokers	0.015	0.019	na
Cigarette Smokers	0.023	0.029	na
Other Smokers	na	0.023	na
Los Angeles			
Aircraft Workers			
Non-smokers	0.014	0.018	0.013
Cigarette Smokers	0.019	0.022	0.015
Other Smokers	na	0.017	0.015
Police			
Non-smokers	na	0.020	0.020
Cigarette Smokers	na	0,022	0.022
Other Smokers	na	0.016	0.017
Motorcycle	na	0.020	0.019
Parking and Intersection	na	0.022	0.022
Pasadena, City Employees			
Non-smokers	0.012	0.018	0.012
Cigarette Smokers	0.012	0.020	0.020
Other Smokers	na	0.021	0.026
Cincinnati,			
All Police	na	0.025	0.038
Service Station Attendants (1956)	na	0.028	0.027
Traffic Police	na	0.030	0.039
Traffic Police (1956)	na	0.031	0.023
Car Drivers	na	0.031	0.036
Car Drivers (1956)	na	0.033	0.020
Parking Lot Attendants (1956)	na	0.034	0.028
Garage Mechanics (1956)	na	0.038	0.040

na Not available; not applicable.

Source: U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965.

Table 17

COMPARISON OF MEAN BLOOD LEAD FOUND IN LOS ANGELES FREEWAY STUDY WITH MEAN BLOOD LEAD FOUND IN THREE CALIFORNIA COUNTIES

POPULATION SURVEYED	NUMBER IN SURVEY	BLOOD LEAD (micrograms/100 g)		PROBABILITY OF DIFFERENCE[1]	
		Mean	Standard Deviation	Residence Near Freeway	Residence Not Near Freeway
	MALE				
Los Angeles Freeway Study (1966)					
Near freeway	15	22.7	5.6	--	<.006
Not near freeway	20	16.0	8.4	<.006	--
Los Angeles County (1961)					
Pasadena city employees	88	19	11	<.06	nss
Aircraft employees	291	19	10	<.03	nss
Traffic policemen	155	21	6	nss	<.02
Alameda County (1960)					
Oakland and vicinity residents	81	21	8	nss	<.02
Alpine County (1960)					
Rural residents	16	12	na	na	na
	FEMALE				
Los Angeles Freeway Study (1966)					
Near freeway	35	16.7	7.0	--	<.00006
Not near freeway	30	9.9	4.9	<.00006	--
Los Angeles County (1961)					
Pasadena city employees	52	12	9	<.007	nss
Aircraft employees	87	17	9	nss	<.00006
Alameda County (1960)					
Oakland and vicinity residents	93	17	8	nss	<.00006
Alpine County (1960)					
Rural residents	11	9	na	na	na

[1] Statistical Significance of Difference between sex-residence-specific mean blood lead of the Los Angeles Freeway study and mean blood lead of previously surveyed population shown on same line.

na Not available.

nss Difference between means is not statistically significant ($p>.1$).

Source: U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965

State of California, Department of Public Health, Air and Industrial Hygiene Laboratory.

Table 18

BLOOD LEAD LEVELS AND ESTIMATED AMBIENT AIR AND OCCUPATIONAL EXPOSURES OF SELECTED POPULATIONS

TYPE OF POPULATION	ESTIMATED EXPOSURE (micrograms/m^3)			MEAN BLOOD LEAD (micrograms/100 g)	
	Occupational	Ambient	Average[1]	Male	Female
Populations Without Known Occupational Exposures					
Remote California mountain residents		0.12		12	9
Composite rural U.S.		0.5		16	10
Suburban Philadelphia		1.0		13	13
Composite urban U.S.		1.0		21	16
L.A. Aircraft workers		1.9		19	17
Pasadena City employees		2.2		19	12
Downtown Philadelphia		2.4		24	18
Populations With Known Occupational Exposures					
Cincinnati policemen (all)	4.7	1.4	2.2	25	
Cincinnati traffic policemen	12.8	1.4	3.8	30	
Cincinnati auto test lane inspectors	14.8	1.4	4.2	31	
L.A. traffic policemen	16.5	2.2	5.2	21	
Cincinnati garage workers	21.1	1.4	5.5	31	
Boston Sumner tunnel employees	44.5	1.1	6.3	30	

[1] For populations with known occupational exposures, the average is a weighted average of presumed occupational and ambient exposure. Ambient exposures are estimates only and were not necessarily measured at the same times and places at which the populations were exposed.

Source: U.S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12, January 1965.
State of California, Department of Public Health, Environmental Hazards Evaluation Unit.

Table 19

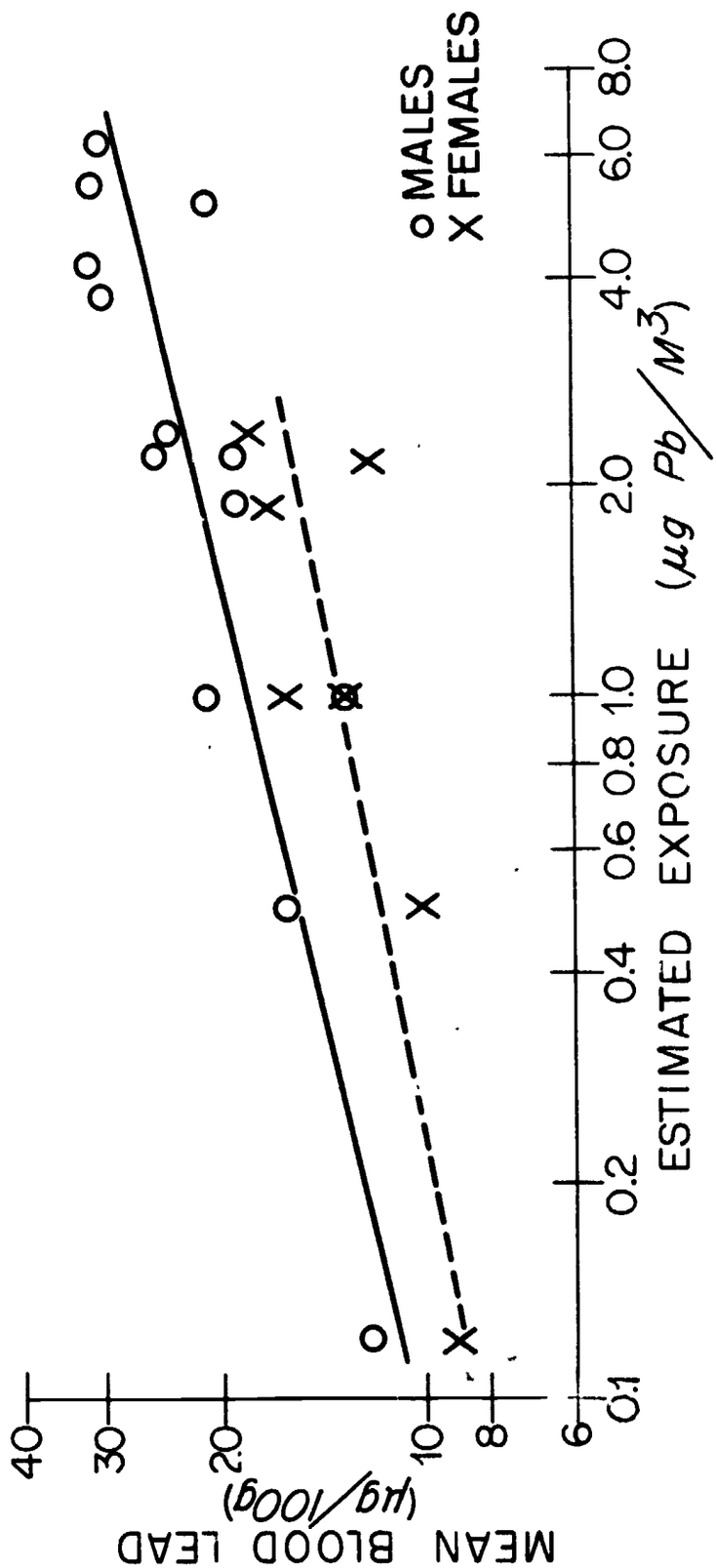
EXPECTED BLOOD LEAD LEVELS BY SEX AND ATMOSPHERIC CONCENTRATIONS OF LEAD

ATMOSPHERIC CONCENTRATION OF LEAD (micrograms/m^3)	EXPECTED BLOOD LEAD LEVEL (micrograms/100 g)	
	Male	Female
0.5	15.5	11.6
1.0	18.4	13.4
1.5	20.3	14.5
2.0	21.8	15.4
2.5	23.0	16.1
3.0	24.0	16.7
3.5	25.0	17.2
4.0	25.8	17.7

Source: State of California, Department of Public Health, Environmental Hazards Evaluation Unit.

FIGURE 1

BLOOD LEAD LEVELS BY ESTIMATED AMBIENT AND OCCUPATIONAL AIR EXPOSURE FOR SELECTED POPULATIONS



References

1. U.S. Bureau of Mines, Minerals Year Book, 1964.

2. State of California, Department of Agriculture, Division of Chemistry, Verbal Communication.

3. Chevron Chemical Company (Ortho Div.), Verbal Communication.

4. U.S. Public Health Service, "Symposium on Environmental Lead Contamination," Publication No. 1440, 1966.

5. U.S. Public Health Service, "Survey of Lead in the Atmosphere of Three Urban Communities," Publication No. 999-AP-12, 1965.

6. Los Angeles County Air Pollution Control District, Verbal Communication.

7. Bay Area Air Pollution Control District, Verbal Communication.

8. Ethyl Corporation, "Gasoline Quality Survey," 12 monthly reports each for 1964 and 1965; 7 monthly reports, January through July, 1966.

9. Western Oil and Gas Association, Verbal Communication

10. State Board of Equalization, signed by Richard B. West, Associate Statistician, letter to Harmon Wong-Woo, Bureau of Air Sanitation, March 3, 1966.

11. State of California, Department of Public Health, "The Oxides of Nitrogen in Air Pollution," 1966.

12. Hirschler, D. A., et al., "Particulate Lead Compounds in Automobile Exhaust Gas," IEC 49, July, 1957.

13. State of California, Department of Motor Vehicles, Gross Report for 1965.

14. Brief, R. S., et al, "Lead, Carbon Monoxide and Traffic, a Correlation Study," JAPCA, 10, pp. 384-8, October, 1960.

15. U.S. Public Health Service, "Proceedings of a Conference to Determine Whether or Not There is a Public Health Question in the Manufacture, Distribution or Use of Tetraethyl-Lead Gasolines," Public Health Bulletin No. 158, 1925.

16. U.S. Public Health Service, "The Use of Tetraethyl Lead and Its Relation to Public Health," Public Health Bulletin, No. 163, 1926.

17. U.S. Public Health Service, "Public Health Aspects of Increasing Tetraethyl Lead Content in Motor Fuel," Publication No. 712, 1959.

18. U.S. Public Health Service, "Air Pollution Measurements of the National Air Sampling Network," 1958, 1962, and 1963.

19. State of California, Department of Public Health, Bureau of Air Sanitation, "The Clean Air Quarterly," Vol. 2, No. 2, June, 1958.

20. State of California, Department of Public Health, Air and Industrial Hygiene Laboratory, "Interim Report of Metals in Air in Berkeley, Los Angeles, and San Diego in 1965-66," unpublished data transmitted to Bureau of Air Sanitation, September 26, 1966.

21. Mueller, P. K., et al., "Concentration of Fine Particles and Lead in Auto Exhaust," paper presented at Fourth Pacific Area National Meeting, American Society for Testing Materials, Los Angeles, California, October 5, 1962.

22. Mueller, P. K., "Lead Content of Airborne Particulates as a Function of Size, Evaluation of Sampling Devices," California Department of Public Health, Air and Industrial Hygiene Laboratory, Research Report, January 27, 1961.

23. Robinson, E., et al., "Variations of Atmospheric Lead Concentrations and Type with Particle Size," Stanford Research Institute, Menlo Park, California, November 1, 1963, 92pp.

24. Intra-Bureau Memos, Bureau of Air Sanitation, California Department of Public Health, Monterey County File: H. F. Droege to J. A. Maga, "Lead Concentrations in Lettuce," May 18, 1965 and July 23, 1965.

25. Kehoe, R. A., "The Metabolism of Lead in Man in Health and Disease, The Harben Lectures, 1960," J. Royal Institute of Public Health and Hygiene, 1961.

26. "U.S. Public Health Service Drinking Water Standards - 1962," U.S. Public Health Service, Publication No. 956.

27. Johnson, R. E., et al., "Dustfall as a Source of Water Quality Impairment," Proc. Am. Soc. Civ. Engrs., 92, J. San. Eng. Div: #SA-1-February, 1966, Paper 4694, pp. 245-267.

28. Intra-Department Memo, California Department of Public Health, Clarence L. Young, Bureau of Sanitary Engineering, to George J. Taylor, Bureau of Air Sanitation, October 18, 1966.

29. Idem, "Lead Content of Water Supplies," October 26, 1966.

30. Brief, R. S., "Air Lead Concentrations from Automotive Engines," Arch. Env. Health, 5, pp. 527-31, December, 1962.

31. Thienes, C. H. and Haley, T. J., "Clinical Toxicology," Lea and Febiger, Philadelphia, 1964.

32. Cecil, R. L. and Loeb, R. F. (editors), "A Textbook of Medicine," W. B. Saunders, Philadelphia, 1959.

33. Efe, S., "Studies on Urinary Excretion on Delta-Aminolevulinic Acid in Cases of Saturnism and in Plumb Workers," New Istanbul Contribution to Clinical Science, 7, pp. 209-26, 1964.

34. Westerman, M. P., et al., "Concentrations of Lead in Bone in Plumbism," New England Journal of Medicine, 273, pp. 1246-50, 1965.

35. Albahary, C., et al., "Toxic Effect of Lead on Blood, Report on 40 Hospital Patients with Occupational Lead Poisoning," Nouvelle Revue Francaise d'Hématologie, 5, pp. 689-706, 1965.

36. Schepers, G. W. H., "Tetraethyllead and Tetramethyllead, Comparative Experimental Pathology: Part I. Lead Absorption and Pathology," Arch, Env. Health, 8, pp. 277-95, 1964.

37. Saita, G. and Moreo, L., "Determination of Blood and Urinary Delta-Aminolevulinic Acid in the Diagnosis of Past Lead Poisoning," Medicina del Lavoro, 55, pp. 357-64, 1964.

38. Selye, H., et al., "Effect of Lead Acetate on the Susceptibility of Rats to Bacterial Endotoxins," J. Bacteriology, 91, pp. 884-90, 1966.

39. Koumidis, O., "Lead Poisoning as a Cause of Mental Retardation in Children," in Forensic Immunology, Medicine, Pathology and Toxicology, Report of the Third International Meeting (1963). International Congress Series No. 80, Amsterdam Excerpta Medica Foundation, p. 97, 1964.

40. Goldsmith, J. R., "The Body Burden and Air Quality Standards," Arch. Env. Health, 8, pp. 39-43, 1964.

41. State of California, Department of Public Health, "Technical Report of California Standards for Ambient Air Quality and Motor Vehicle Exhaust," 1960.

42. Kehoe, R. A., "Criteria for Human Safety from the Contamination of the Ambient Atmosphere with Lead," Proc. XV Congres Internationale de Medicine du Travail, Vienna, September 19-24, 1966, Vol. III, 83pp.

43. Gusev, M. E., "Effects of Small Concentrations of Lead on the Urinary Excretion of Coproporphyrins in Children," Gigiena i Sanitariya, 24(No. 7), pp. 6-9, 1959.

44. Cogbill, E. C. and Hobbs, M. E. "Transfer of Metallic Constituents of Cigarettes to the Main-Stream Smoke," Tobacco Science, 69, p. 24, 1957.

45. Saterlee, H. S., "The Problem of Arsenic in American Cigarette Tobacco," New England Journal of Medicine, 254, p. 1149, 1956.

46. Oliver, J. H., "Arsenic and Tobacco," letter to the editor, Lancet, 2, p. 603, 1957.

47. Guthrie, F. E., et al., "Arsenic Content of Commercial Tobacco, 1917-1958," Tobacco Science, 3, pp. 62-4, 1959.

48. Kehoe, R. A., et al., "A Spectrochemical Study of the Normal Ranges of Concentration of Certain Trace Metals in Biological Materials," J. Nutrition, 19, p. 579, 1940.

49. Robinson, M. J., et al., "The Concentration of Lead in Plasma, Whole Blood and Erythrocytes of Infants and Children," Pediatrics, 21, pp. 793-796, 1958.

50. Tipton, I. H., "Metal Binding in Medicine," Chapter 4, Lippincott, Philadelphia, 1960.

51. Nusbaum, R. E., et al., "Relation of Air Pollutants to Trace Metals in Bone," Arch. Env. Health, 10, pp. 227-232, 1965.

52. Butt, E. M., et al., "Trace Metal Levels in Human Serum and Blood," Arch. Env. Health, 8, pp. 52-7, 1964.

53. Schroeder, H. A. and Balassa, J. J., "Abnormal Trace Metals in Man: Lead," J. Chron. Dis., 14, pp. 408-25. 1961.

54. Tipton, I. H. and Cook, M. J., "Trace Elements in Human Tissue. Part II. Adult Subjects from the United States," Health Physics, 9, pp. 103-45, 1963.

55. Tipton, I. H., et al., "Trace Elements in Human Tissue. Part III. Subjects from Africa, the Near and Far East and Europe," Health Physics, 11. pp. 403-51, 1965.

56. State of California, Department of Public Health, Bureau of Chronic Diseases, "Health Effects of Atmospheric Lead in Los Angeles, Final Report to the United States Public Health Service," 1963.

57. Cholak, J., "Analytical Methods for Determination of Lead," Arch. Env. Health, 8, pp. 222-31, 1964.

58. Lane, R. E., "The Care of the Lead Worker," Brit. J. Industr. Med., 6, pp. 125-43, 1949.

59. Kovnatskii, M. A., et al., "Influence of Lead on the Development of Atherosclerosis," Gigiena Truda: Prof. Zabolevaniya, 8, pp. 6-12, 1964.

60. American Conference of Governmental Industrial Hygienists, "Threshold Limit Values for 1966," available from the Conference Office, Cincinnati, Ohio.

61. Air Pollution - 1966, Hearings before a Subcommittee on Air and Water Pollution of the Committee on Public Works, United States Senate, Eighty-Ninth Congress, U.S. Government Printing Office, Washington, D.C., 1966.

62. Patterson, C. C., "Contaminated and Natural Lead Environments of Man," Arch. Env. Health, 8, pp. 344-60, 1965.

63. Finney, D. J., "Statistical Method in Biological Assay," Hafner Publishing Company, New York, 1952.

64. Finney, D. J., "Probit Analysis," Cambridge University Press, Cambridge, England, 1952.

65. Rustagi, J. S., "Stochastic Behavior of Trace Substances," Arch. Env. Health, 8, pp. 68-76, 1964.

APPENDIX A

SYNOPSIS OF RELEVANT ABSTRACTS

Following a reading of the Kettering Abstracts an attempt has been made to collect and evaluate the information on known effects of exposure to inorganic and organic lead compounds. In many cases the original papers were reviewed. Data which include quantitated exposures are listed in Table A-1 in order of increasing exposure concentrations to the extent this was possible. Data obtained from nonquantitated exposure situations are listed in Table A-2. These are grouped mainly by effects measured in occupational situations. In addition, there is a table listing several metabolites which figure prominently in lead poisoning together with the concentrations expected in normal persons and those suffering from lead absorption. Finally, a chart is provided concerning porphyrin synthesis which delineates known sites of lead attack. These explain the increase of certain metabolic intermediates in body fluids after lead exposure.

Table A-1

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
1.	Approx 0.0043 to 0.043 mg/kg (0.3, 1.0, 2.0, 3.0 mg and food contained 0.3 mg/day)	$Pb(NO_3)_2$ or $PbCl_2$	Orally each day	For 0.3 mg/day, 420 days, no change in blood lead, little change in urine lead (0.025-0.036 mg/l). Change in body burden about 12 mg. For 1.0 mg/day, 4 yrs, 0.046 mg Pb/100 gm blood; 0.08 mg Pb/l urine. Change in body burden 118 mg. For 2.0 mg/day, 2 yrs, 0.065 mg Pb/100 g blood; 0.11 mg Pb/l urine. For 3.0 mg/day, 4 mos, 0.05 mg Pb/100 g blood; 0.08 mg Pb/l urine. The normal upper limit for urine-Pb is stated as 0.15 mg/l. The normal upper limit for blood-Pb is stated as 0.08 mg/100 ml.		I-57
2.	0.1 to 0.4 mg/kg	$Pb(Ac)_2$	Subcutaneously		Rabbits: Losses in ALA dehydrase activity. Some recovery in 24 hr; full activity recovered in 10 days, with the low dosage of Pb. Urinary excretion of heme metabolites requires 10 x the dosages used and they do not appear for several days after treatment.	I-347
3.	Approx 0.5 to 2.5 mg/kg (0.1 to 0.5 mg/rat)	$Pb(Ac)_2$	Intravenously or orally		Rats: EDTA does not remove Pb from bones.	I-227
4.	Approx 0.6 to 1.2 mg/kg (30 to 60 mg)	$Pb(Ac)_2$	In food daily		Wethers: High loss of reserve Ca^{++}. Considerable increase of excreted P; decreased bone strength. Effects most pronounced in animals fed higher Pb conc.	I-357

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
5.	17 or 1.7 mg/kg	TEL	Single dose by intragastric intubation		Rats: Oral lethal doses - TEL - 17 mg/kg TML - 108 mg/kg	I-26
	108 or 10.8 mg/kg	TML	Single dose by intragastric intubation		TEL - enhanced sensorimotor neurological activity; TML opposite effect.	
	0.17 or 0.0017 mg/kg	TEL	Dosed 5x/week by intragastric intubation to 100 doses.		Generally, multiple doses equivalent to 1 single dose are more injurious. Male rats somewhat less prone to severe injury. Both alkyls severe on nerves with TML more destructive to neurons. Severe reaction with liver, panoreas, endocrine and renal systems and hypertrophy of left ventricle. Absence of symptoms may occur but organs show lesions.	
	1.08 or 0.001 mg/kg	TML	Dosed 5 x/week by intragastric intubation to 100 doses.			
6.	3 mg/kg	$Pb(Ac)_2$	Intraperitoneally every 8 to 10 days for 75 days		Rats: RBC lactic dehydrogenase activity increased 88% by day 15 to 262% by day 75.	I-359
7.	4 mg/kg	$Pb(Ac)_2$	Intravenously every other day for a month		Rabbits: Pb caused a definite shortening of life span of RBC which was noticeably alleviated with EDTA treatment.	I-246
8.	4 mg/kg	$Pb(Ac)_2$	Intravenously daily for 6 mos.		Rabbits: RBC catalase activity increased up to 170%.	I-28
9.	4 mg/kg	$Pb(Ac)_2$	Intravenously every other day for a month		Rabbits: RBC survival time was greatly shortened. Alterations in Fe metabolism cannot be explained by hemolysis but suggest an inhibition of Fe incorporation into porphyrins.	I-365
10.	4.7 mg/kg (3 mg Pb/kg)	$Pb(Ac)_2$	Subcutaneous injection from single to multiple administrations		Rabbits: Within 24 hr after single injection there was always a high Pb increase in bone. With other series of injections Pb appears in various organs, but decreases before it does in bone. The content of Pb in blood does not always indicate Pb accumulation in organs and this is of importance in diagnosing Pb poisoning.	II-15

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
11.	Approx 4 to 5 mg/kg (1 ml, 8% soln)	$Pb(OAc)_2$			Dogs: Increase of blood acetylcholine occurred more rapidly as the extent of poisoning increased.	I-249
12.	5 to 50 mg/kg	$Pb(OAc)_2$	Subcutaneously		Rabbits: 5 mg/kg - ALA dehydrase activity decreased within 1 hr. Loss was 70%, recovered in 1-6 days then decreased to low value for at least 20 days. 25 mg/kg - As with the 5 mg dose. 50 mg/kg - Same, but loss was about 100%.	I-347
13.	5, 15, 50, 400 100 mg/kg	TML	Subcutaneously and by inhalation		Rabbits: TML doses which produce acute or subacute intoxication affect nervous system mainly. With lower doses neurotoxic effects are not constant or evident but blood changes and alterations of liver and kidney function are produced.	I-230
14.	6 mg/kg	$Pb(OAc)_2$	Intravenously each day for 12 days		Rabbits: Enzymes of gingival mucosa - Decreased activity in: NADH diaphorase, alkaline phosphatase, ATPase. Increased activity in acid phosphatase.	II-97
15.	6 mg/kg	$Pb(OAc)_2$	Intravenously daily for 12 days		Chinchilla rabbits: In skeletal and heart muscle ATPase, diaphorase and alkaline phosphatase activities decreased, while acid phosphatase activity increased. In walls of small blood vessels alkaline phosphatase and ATPase activities decreased.	I-22
16.	10 to 100 mg/kg	TEL	Intramuscular injection		Rabbits: 6 of 16 showed some increase in serum glutamic oxalacetic transaminase but with 1 exception little change in serum glutamic pyruvic transaminase.	I-255

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
17.	20 mg/kg	$Pb(OAc)_2$	Intraperitoneally, twice a week		Rats: No noted change in glomeruli of kidney from 1 to 18 weeks but after 4 weeks there were many alterations in the kidney tubules. The experimental findings resemble those found in children usually at the subacute to subchronic level of poisoning. In such poisoning children apparently die before kidney vascular changes have had time to develop.	II-107
18.	Approx 25 mg/kg (5 mg)	$Pb(OAc)_2$	Intravenously		Rats: A strain generally not susceptible to a number of bacterial endotoxins became very sensitive following Pb treatment befow the level producing organ lesions. Some endotoxins then caused 100% mortality. Symptoms - spleen hemorrhage, hemorrhagic necrosis in the arterioles of the kidney, renal cortical necrosis, hepatic hemorrhages. The endotoxin effect is most serious when Pb and endotoxin are injected together but the effect is still pronounced when the endotoxin is given from 1 hr before to 7 hr following the Pb. Pb-sensitized rats tolerated endotoxins at 0.001 to 0.010 µg no better than controls at 100 µg.	II-402
19.	25 mg/kg	$Pb(OAc)_2$	Injected 4 to 5 months		Rats: Following Pb intoxication P^{32} was administered orally. Less P^{32} was eliminated in the feces and more deposited in the bones compared with controls.	I-23
20.	Approx 25 mg/kg (5 mg)	$Pb(OAc)_2$	Intravenously		Rats: When Pb and histamine (20 mg) used together, 87-88% incidence of Ca^{++} deposits in vagi and sympathetic nerves. Antihistamines prevent this effect.	I-241 and I-243

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
21.	31 to 69 mg/kg	$Pb(OAc)_2$	Subcutaneously 7 to 14 days		Rabbits: Examined blood about 24 days later. Free porphyrinogen synthesis and incorporation of glycine and δ-ALA into heme decreased. All porphyrinogens synthesized from ALA decreased. No significant decreases in porphyrins synthesized from porphobilinogen or uroporphyrinogen. Comparable amounts of uroporphyrinogen III and phyriaporphyrinogen III were metabolized. Results show a principal block by Pb in porphyrin synthesis occurs at ALA dehydrase with a less important block between phyriaporphyrinogen III and coproporphyrinogen III. Pb may also impair the transport of Fe or other metabolites through the metochondial membrane.	II-99
22.	Approx 38 mg/kg (7.5 mg)	$Pb(OAc)_2$	Intravenously		Rats: Pb plus various mast-cell dischargers on some mast-cell components produce topical connective tissue calcification at the sites of injection.	I-244
23.	40 mg/kg	$Pb(NO_3)_2$	Subcutaneously daily for 10 days		Rabbits: Ages 2, 12, 30 to 36 mos. All showed decreased total blood proteins.	II-100
24.	50 mg/kg	$Pb(OAc)_2$	Intravenously		Rats: Repeated injections induce osteomyeloselerosis similar to that in man.	I-242
25.	50 mg/kg	$Pb(OAc)_2$	Intravenously		Rats: When $Pb(OAc)_2$ and methoxamine used together - 80% of animals have thrombosis of the auricle while 100% show renal lesions.	I-231
26.	50 mg/kg	$Pb(OAc)_2$	Stomach tube		Rabbits: Slight decreases in platelets and agglutin-ability rule out these factors in alterations of blood clotting in Pb poisoning.	I-361

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
27.	50 mg/kg (0.5 ml 10% soln/kg)	$Pb(OAc)_2$	Stomach tube		Rabbits: Bilirubin in blood increased. Decrease in blood albumin but total blood protein did not change by much. β and γ globulins increased. Conclude: hepatic functions impaired which are important to whole organism.	I-360
28.	50 mg/kg	$Pb(NO_3)_2$	Subcutaneously every other day for 18 days		Rats: 1 mo in age died in 9 days; 5 to 6 mos in age lived up to 26 days; 20 mos in age lived up to 18 days.	II-100
29.	50 mg/kg	TEL	Intramuscular each day		Rabbits: Serotonin or hydroxy-tryptophan injected. TEL inhibits catabolism of hydroxy-indole acetic acid in brain. Urine passed HIAA in rabbits treated with serotonin. (Abstract comments do not back the conclusion.)	I-15
30.	50 mg/kg	TEL	Injected daily		Rabbits: HIAA in urine decreased significantly suggested monoamine oxidase is inhibited in the reaction, serotonin → HIAA.	I-20
31.	50 mg/kg	$PbCl_2$	Subcutaneously 2 x each week for 2 mos.		Chickens: No stippling, fewer vacuoles produced from mitochondria compared with guinea pigs. These manifestations reflect on lowered heme synthesis in Pb poisoning. (In part, the results reflect species variations.)	I-238
32.	Approx 66 mg/kg (200 mg/day as 2 ml of 10% soln)	$Pb(OAc)_2$	Orally for 10 days		Rabbits: propoporphyrin chelates Pb.	I-225
33.	66 mg/kg (200 mg)	$Pb(OAc)_2$	Orally each day		Rabbits: Pb inhibits the synthesis of pyridine nucleotides in RBC with or without the administration of nicotinic acid.	I-364

Table A-1, (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
34.	Approx 10 [illegible]/kg (20 mg)	$Pb(OAc)_2$	Orally each day for 9 weeks		Guinea pigs: In Pb poisoning there is an increased need for vit. C. (In man Pb exposures increase need 2-3 fold.)	I-352
35.	100 mg/kg	$Pb(OAc)_2$	Single intraperitoneal injection		Rabbits and rats: Mitochondria of liver - little ALA synthetase activity. Same for controls. Urinary ALA, PBG showed increases. Thus increased synthesis is not the reason for urine values. Rather they depend on an inhibition of porphyrin synthesis.	I-19
36.	Approx 200 mg/kg (4 ml, 1% soln)	$Pb(OAc)_2$	Intraperitoneally		Rats: Pb causes interference in mobilization or deposition of P in the exchangeable fraction of bone.	I-229
37.	200 to 400 mg/kg	$Pb(OAc)_2$	Subcutaneously as single dose or multiple series		Guinea pigs, rabbits and rats: The multiplicity of results regarding basophilic stippling may be due to preparation of samples. Here, only ribosomal aggregates seen by E M in young red cells constitute basophilic stipple.	I-353
38.	Approx 250 to 300 mg/kg (50-60 mg)	$Pb(NO_3)_2$	Esophageal catheter daily		Guinea pigs: In 3-4 weeks, 2,000-30,000 stippled RBC per million. Vacuoles, vesicle clusters and other formations developed. No noted changes in leucocytes.	I-238
39.	Approx 300 mg/kg (3 ml 30% soln)	$Pb(OAc)_2$	Gastric administration daily for 4 days		Rabbits: Highest normal value / Pb poisoning average value ALA dehydrase of RBC: 0.29 μM/hr/ml / 0.31 μM/hr/ml ALA Plasma: 0.034 mg/100 ml / 0.063 mg/100 ml ALA Urine: 0.021 mg/24 hr / 0.71 mg/24 hr PBG Plasma: 0.022 mg/100 ml / 0.023 mg/100 ml PBG Urine: 0.058 mg/24 hr / 0.18 mg/24 hr	I-66

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
40.	Approx 5,000 mg/kg (1 g/rat)	$Pb(NO_3)_2$	Orally each day		Rats: Impairment of synthesis of N-acetylsulfanilamide could reflect a decreased synthesis of CoA (or decreased transacetylation).	II-12
41.	0.06 to 0.32 mg/m^3	From atmosphere in place of work (Yugoslavia)	Inhalation	Workers showed normal concentrations of RBC, reticulocyt , hemoglobin, stippled RBC, blood Pb. All showed significantly raised urine ALA. MAC in Yugoslavia is 0.15 mg/m^3.		II-118
42.	0.075 and 0.15 mg/m^3	Pb_2O_3	Inhalation	Mean part. size 0.05μ, and 0.095 to 1.2μ, 7½ hr/day/5 day week/130 week max. Retention 35% at 0.05μ Retention 54% at 0.75μ Retention 43-53% at 0.9-1.2μ At 0.075 mg Pb/m^3, urine 0.048 mg/l at 0.15 mg Pb/m^3, urine 0.071 mg/l In both, blood same at 0.04 mg/100g > 1 μ particles absorbed in upper tract and transferred to alimentary tract where they were ingested. Ingestion causes progressive body burden while particles < 1 μ, intermittently inhaled caused a balance of intake to output.		I-57
43.	0.08 to 0.12 mg/m^3 (Calc'd. TLV)	From atmosphere in place of work	Inhalation	At this Pb level 5% show urinary coproporphyrin > 0.050 mg/l. Normal upper limit is 0.0531 mg/l.		I-286
44.	5 mg/m^3 (0.005 mg/l)	$Pb(OAc)_2$	Drinking water		Rats: Followed life span - with Pb, life span shortened, fewer tumors than controls. Pb at concentrations found in organs of humans exerted a continuously toxic effect at all ages and both sexes in terms of mortality and life span. Pb-treated rats are more susceptible to infection.	I-240

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
45.	Approx 1 g/m^3 air (1 mg/l air)	TEL	Inhalation 30 min/day for 12 days		Rabbits: TEL does not affect tryptophan → nicotinic acid at monoamine oxidase step but later in the sequence.	I-129
46.	Approx 1 g/m^3 air (1 mg/l air)	TEL	Inhalation 1 hr/day for 3 days		Rabbits: Acute poisoning, lung serotonic < 0.004 mg/g.	I-17
		TEL	Inhalation ½ hr/day for 44 days		Subacute poisoning, some decrease in lung serotonin.	I-17
47.	5×10^{-9} to 5×10^{-5} M	$Pb(OAc)_2$	Nonbiological observation		Pb in the presence of 1.3 mM Ca^{++} and 0.5 to 4mM $PO_4^{\equiv}$ has an activating effect on $Ca_3(PO_4)_2$ crystal formation.	I-123
48.	10^{-7} to 10^{-11}M	$Pb(OAc)_2$	In vitro, bone marrow preparations		Rabbits: Protoporphyrin synthesis stimulated 31% at 10^{-7}M and 80% at 10^{-11}M.	I-218
49.	5×10^{-6} to 2×10^{-5}M	$Pb(OAc)_2$	In vitro	RBC lactic dehydrogenase was inhibited by as little as 5×10^{-6}M. (Compare with ref. I-359 above.)		I-345
50.	$> 5 \times 10^{-6}$M	$Pb(OAc)_2$	In vitro	Serum phosphomonoesterase was inhibited.		I-124
51.	8.26×10^{-6}M				Roaches: There was a 50% inhibition of B-glucosidase.	I-122
52.	3.08×10^{-5}M to 3.08×10^{-4}M (10 to 100 µg/ml blood)	$Pb(OAc)_2$	In vitro	Alterations in the mechanical fragility of RBC plays little, if any, part in the production of anemia in Pb poisoning.		
53.	5×10^{-5}M	$Pb(OAc)_2$	In vitro, erythrocytes	After inhibition of ALA dehydrase, 60% recovery obtained by 2.5×10^{-2}M cystine. The inhibition constant was 1×10^{-6} mole.		II-85

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
54.	10^{-6}M	$Pb(Et)_3$	In vitro		Rats: Inhibits active transport of glutamate into brain cortex slices.	I-125
	10^{-4}M	TEL	In vitro		Largely suppresses energy-dependent transport of amino-acids into rat brain slices.	I-125
55.	10^{-3}M	$Pb(Ac)_2$	In vitro	Succinic dehydrogenase - partially inhibited, and alkaline phosphatase-not inhibited in kidney tissue.		I-215
56.	3×10^{-3}M (0.1% soln)	$Pb(NO_3)_2$	5 to 30 min in vitro		Mice: Thorax immersed in the solution. Pb localizes at the myoneural junctions in post-synaptic membrane, where acetylcholinesterase is located.	I-214
57.	2×10^{-2}M	$Pb(NO_3)_2$	In vitro		Rats: Mast cell leucine aminopeptidase exhibited a 25% loss in activity while neither esterase nor ATPase showed inhibition.	I-216
58.	3×10^{-6}M	$Pb(Ac)_2$	Drinking water for 20.5 to 25 mos. or for 19 to 23 mos.		Rats: Dilation of tubules - up to cysts formation. Prominent nuclear inclusions in cells of proximal tubule. Inflammation, interstitial fibrosis, vascular changes, adenoma. Blood pigment in cytoplasm of tubular epithelia. Crystals and calculi in tubules. Decreased dye transport. Only cells with large nuclear inclusions and swollen granular cytoplasm transported dyes poorly or not at all. Possible correlation of chronic Pb poisoning and renal tumors was noted.	I-350
59.	10^{-1} to 10^{-4}	$Pb(Ac)_2$	In vitro, bone marrow preparation		Rabbits: Protoporphyrin synthesis inhibited 38% at 10^{-1}M and 61% at 10^{-4}M. (Compare with results of lower Pb conc. I-218 above.)	I-218
60.	1.5×10^{-1}M	$Pb(Ac)_2$	Orally for 181 days		Rabbits: Continued ALA increases in urine.	I-234

Table A-1 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER QUANTITATED EXPOSURES

ITEM	Pb CONCENTRATION	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE		KETTERING ABSTRACT REFERENCE
				Man	Other Organisms	
61.	1% of diet	$Pb(OAc)_2$	Orally 3 - 12 weeks		Rats: Aminoaciduria - disrupted renal mitochondria, cytoplasmic vacuoles.	I-233
62.	25 x levels found in blood	$Pb(NO_3)_2$ (in mixture with Cu, Ni, Zn as nitrates)	Single intravenous dose		Rabbits: Dose was well tolerated.	I-235
63.	0.05 to 31.25 mg/kg nutrient solution	$Pb(OAc)_2$ or $Pb(NO_3)_2$	Supplied as nutrients, 10 mos.		Sweet orange seedlings: At pH 4.5 and 5.5 root growth stimulated at intermediate levels and inhibited by higher Pb levels. Shoot root growth increased. At pH 6.5 root and shoot root growth inhibited by all but lowest levels. Organic constituents o tissues did not change much. Pb inhibited water absorption; seedlings were often wilted.	I-219

Table A-2

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
1.		Occupational	Increased ALA in urine rather specific for Pb poisoning. It is the earliest sign of poisoning. Three workers with only 10 to 15 days exposure showed ALA at 5 to 10 x normal.	I-41
2.		Occupational	Urinary ALA increases when (or before) porphobilinogen and coproporphyrin increase.	I-61
3.	TEL and inorganic Pb	Occupational	TEL - 13 patients showed urine protoporphyrins in normal range (21.12 ± 2 µg/100 ml). Pb - 5 patients showed elevated values (312 ± 2 µg/100 ml).	I-53
4.		Occupational		I-66

	Highest normal value	Pb poisoning average value
ALA dehydrase of RBC	1.03 µM/hr/ml	1.08 µM/hr/ml
Plasma ALA	0.046 mg/100 ml	126.73 mg/100 ml
Urine ALA	2.5 mg/24 hr	19.07 mg/24 hr
Plasma PBG	0.030 mg/100 ml	0.0291 mg/100 ml
Urine PBG	1.5 mg/24 hr	1.94 mg/24 hr

5.		Occupational		I-75

Time elapsed past exposure	ALA in blood	ALA in urine	Free protoporphyrin IX in RBC
3 mos to 1 yr	0.065 mg/100 ml	29 mg/24 hr	0.232 mg/100 ml
1 to 3 yrs	0.043	15	0.225
3 to 9 yrs	0.032	4.56	0.159
Normal	0.026 (max.)	1.3 to 2.8	0.035 to 0.055

6.		Occupational	Correlated degree of poisoning in 15 workers, judged clinically, with urinary excretion of: Pb - poor correlation Coproporphyrin - poor correlation ALA - good correlation Stippled RBC - no correlation Since concentration of excreted creatinine is fairly constant, amounts of other excreted substances are related to creatinine rather than to volume or time. This eliminates errors due to inadequate urine collection or to diuresis.	I-372

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
7.			10 normal subjects - urine ammonacetone (AA) 0.59 to 1.03 mg/g creatinine and ALA 0.85 to 2.40 mg/g creatinine. In all Pb patients ALA > 2.4 mg/g creatinine while AA within limits of controls.	I-259
8.		Occupational	Normal group; ALA excreted in 24 hr up to 4 mg (literature shows 2.1 to 4.0 and 0.29 ± 0.140 mg/100 ml). Patients with Pb exposures excreted up to 110 mg/24 hr. Stippling of RBC is not as sensitive a test for poisoning.	I-260
9.		Occupational	Normal persons, 15; exposed workers not showing signs of intoxication, 20; and 20 showing clinical signs of poisoning. Nonprecipitable urine Pb was negligible in normal persons, total Pb higher than precipitable in exposed persons. Normal: Total Pb 0.049 mg/l; Precipitable Pb 0.047 mg/l; Nonprecipitable Pb 0.002 mg/l Increased absorption: 0.127; 0.100; 0.027 Pb poisoning: 0.300; 0.204; 0.096	II-117
10.		Occupational	In chronic poisoning; 20 adults RBC: 3.45 to 5.36 x $10^6/mm^3$, av 4.21 x $10^6/mm^3$ Hemoglobin: 8.1 to 12.8 g/100 ml, av 10.7 g/100 ml Hematocrit: 28.8 to 43.0%, av 35% Mean corpuscular volume: 70 to 92 µl, av 79 µl Mean corpuscular hemoglobin conc: 27 to 36 per 100 ml, av 31 per 100 ml Reticulocytes: 1.5 to 11.6%, av 4.4% Stippled cells: 0.1 to 7.5%, av 1.8% Icterus index: 4 to 10, av 6.5 Stippling is not a reliable index of poisoning.	I-263
11.	TEL		In man and other mammals TEL does not appear to interfere with heme synthesis and the usual tests applied for inorganic Pb exposure in relation to porphyrins do not reflect TEL exposures.	II-125
12.	General (but probably not TEL or TML)	Occupational	If increases in Pb absorption are left to clinical diagnosis, considerable Pb accumulation results before symptoms appear. Two methods now detect increases in Pb before poisoning is evident. Blood Pb of 50 to 60 µg/100 ml should denote an unallowable exposure. Urinary ALA increases occur only in acute intermittent porphyria and in Pb poisoning. A very close correlation existed between blood Pb and urinary ALA excretion in 15 Pb poisoned workers removed from exposure at least one week. A value of 1.50 mg ALA/100 ml urine considered indicative that harmful Pb exposure had occurred.	II-116

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES *

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTEPING ABSTPACT REFERENCE
13.	General (inorganic)	Occupational	The most reliable criterion for diagnosing chronic Pb poisoning is an increase of ALA in the presence of normal porphobilinogen (PBG) which indicates a blockage of ALA dehydrase. In contrast, non-Pb-induced anemia and liver damage will almost always be accompanied by a significant increase of PBG. Normal blood ALA given as 0.026 mg %, and normal urinary ALA given as 2.8 mg/24 hr.	II-137
14.		Occupational (Yugoslavia)	Subjects: 40 healthy persons and 80 exposed to Pb. Urine ALA of controls av 4.53 mg/liter (as against 5.64 mg/liter in chronic alcoholics). Av normal coproporphyrin was 150 mg/liter (no increase in the alcoholics). Among the Pb exposed, 27 of 37 without objective or subjective disturbances had urinary ALA up to 30 mg but coproporphyrins up to 450 mg in only 6. Pb excretion was normal in all cases. 21 men with high exposure and early signs of poisoning all showed increased ALA - up to 50 mg/liter while coproporphyrins increased in 16 persons - up to 1,000 mg/liter. In 22 men with clinical Pb poisoning all showed ALA increases up to 80 mg/liter with coproporphyrins up to 1,500 mg/liter.	II-118
15.	TEL	Occupational	Approximate permissible concentration in air of work areas used 40 hr/week is 0.075 mg/m^3.	I-76
16.		Occupational and nonoccupational exposure to Pb-minerals	Toxic and possible carcinogenic effect by repeated exposure and absorption.	I-211
17.		Occupational	Refers to a study by Dingwall-Fordyce & Lane (1963) on 425 pensioners of a storage battery factory. No evidence found that malignant disease is associated with Pb absorption.	II-101
18.			Pb claimed to be one of the most potent carcinogens.	I-121
19.		Occupational	Limits - England: Blood Pb < 0.08 mg/100 ml Urine Pb < 0.15 mg/l Hemoglobin > 13 g (90%) Punctate basophils < $10,000/10^6$ Coproporphyrin 500 µg/l	I-63
20.		Occupational	Limits for detection of possible poisoning - England: Hemoglobin > 13 g Stippled RBC < $200/10^6$ RBC Urinary porptryrin < 100 µg/l	I-152

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
21.		Occupational	Pb excretion follows that of creatinine and specific gravity of urine - highest at 2 to 4 p.m., lowest midnight to 3 a.m.	I-270
22.		Occupational	Stippled RBC, > $200/10^6$ cells indicative of Pb poisoning. Normal values for coproporphyrins < 100 µg/24 hr urine.	I-271
23.		Occupational	Workers using Pb alloys experience much less hazard if Pb conc is < 75% of alloy.	I-275
24.	Environment	Ingested and inhaled	Pb levels of various groups given (Hofreuter):	I-282
			City dwellers 0.003 to 0.060, av 0.019 mg/100 ml Rural dwellers 0.001 to 0.38, av 0.014 mg/100 ml Urban males 0.005 to 0.059, av 0.021 mg/100 ml Urban females 0.003 to 0.060, av 0.016 mg/100 ml Rural males 0.005 to 0.038, av 0.016 mg/100 ml Rural females 0.001 to 0.018, av 0.010 mg/100 ml Urban nonsmokers 0.003 to 0.044, av 0.017 mg/100 ml Urban smokers 0.005 to 0.060, av 0.021 mg/100 ml Rural nonsmokers 0.001 to 0.036, av 0.011 mg/100 ml Rural smokers 0.010 to 0.038, av 0.017 mg/100 ml	
25.	PbO	Occupational	Working atmosphere contained 0.2 to several mg Pb/m^3. Significant correlation between atmospheric Pb and urinary Pb and coproporphyrinuria.	I-286
26.			Criteria of lead poisoning in Japan: positive urinary coproporphyrins, increase in stippled RBC > 0.5% and reduction in specific gravity blood < 1.0540.	I-387
27.			Serum globulins is the protein fraction containing the greatest quantity of bound Pb.	I-396
28.			Normal level of blood Pb in the population is 0.025 mg/100g, range (0.005 - 0.040).	I-392
29.		Occupational	Workers with symptoms of poisoning had decreased number of thrombocytes while speed of coagulation and clot retraction was increased.	I-402
30.		Occupational	Pb inhibits: ALA dehydrase, coproporphyrinogen decarboxylase, heme chetalase. Excretion of ALA is highly specific for Pb poisoning. Amounts > 3.0 mg/24 hr are definitely pathologic.	I-261
31.		Occupational	Noticeable correlation of increase of urinary Pb and serum aldolase activity.	I-288

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
32.	TEL	Occupational	Serum enzymes - glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase showed no significant increases in activity after exposure to TEL. Increases in serum transaminase levels are good indications of organic damage.	I-255
33.		Occupational	As physical condition decreased in Pb poisoning so did activity of carbonic anhydrase. This effect of Pb on the enzyme has been noted <u>in vitro</u> also.	II-110
34.			Pb inhibits, particularly, enzymes containing --SH groups.	II-108
35.			Man and other mammals: at a relatively small concentration, Pb acts as a poison for dehydrogenases.	I-165
36.	TEL	Occupational	Patients chosen to include only those with TEL-induced cochleovestibular disfunction. They exhibited subacute poisoning. Slight hearing alterations. All showed nucleoreticular lesions.	I-141
37.		Occupational	50 men with poisoning studied. Functional disturbances of circulatory system more prevalent in 20 to 30 yr age group than in 30 to 45 yr group. Organic damage prevailed in the older group suggesting Pb accelerated arthrosclerosis.	I-388
38.		Occupational	Arthrosclerosis may occur relatively early and assume a severe course in persons exposed to Pb for an extended time.	I-389
39.			Whereas 0.08 mg Pb/100g blood is considered a normal upper limit for adults, 0.04 mg Pb/100g is the upper limit for children. 200 normal children showed blood Pb of 0.014 to 0.03 mg/100g while 100 mentally defective children showed 0.040 to 0.080 mg/100g blood. Normal children showed 0.20 to 0.26 mg ALA/100 ml urine while mentally defective children showed 0.38.	I-290
40.			Pb is much more toxic to children than to adults.	USPHS Symposium 12/13-15/65
41.			25% of the children with Pb encephalopathy succumb.	I-168
42.			Blood Pb levels in mentally retarded children and those with behavioral disorders are frequently higher than in normal children.	I-91
43.			Treatment of Pb poisoning in children does not prevent a 25% fatality in cases with encephalopathy nor prevent development of neurologic or behavioral sequelae.	I-89

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
55.	Environment	Inhalation and ingestion	In Cincinnati - human soft tissues - liver. 0.04 to 0.28 mg Pb/100 g Skeleton - 0.67 to 3.59 mg Pb/100 g	I-56
56.		Occupational	In contrast to Pb levels in blood and soft tissues, levels in bone are very high (biopsy specimens). To be considered is the possibility of health hazard from Pb mobilized from bone, even if blood and urine levels are presumably low.	I-408
57.			Man and other animals: Pb causes the most significant destruction in the radial nerve and to a slightly less extent in the median and ulnar nerves.	I-399
58.	(Concerns nerves)		In chronic intoxication axonal degeneration and muscular damage occurs.	I-151
59.	TEL	Occupational	Hearing impaired, particularly at high frequencies.	I-62
60.	TEL		Blood Pb not unduly raised by TEL.	I-36
61.	TEL		TEL at 2 ml/U.S. gal. or less involves no hazard by contact or inhalation.	I-44
62.		Occupational	Untoward effects of Pb on pregnancy and on the fetus do not appear until the woman shows an excessive Pb absorption.	I-391
63.		Occupational	Compared to those not exposed, Pb exposure of women led to a much higher rate of abortions and stillbirths. Actual data were collected prior to time of occupational safety procedure.	I-112
64.			Statistics show that the percentage of poisonings by Pb or benzene is higher in women than men.	II-166
65.		Occupational	At least 2 times daily normal vit. C requirement needed by Pb workers.	I-49
66.		Occupational	There are cases of poisoning by inhaled or ingested Pb - plasticizers such as Pb-stearate used in manufacturing certain plastics.	I-55
67.		Occupational	In cases of chronic poisoning there was little or no HCl secretion and decreased pepsin secretion. Some cases showed decreased secretion of intrinsic factor and thus exhaustion of vitamin B_{12} stored in liver.	I-140
68.			Inhalation of Pb results in 10 to 20 times more absorption than by ingestion. Normal individuals have approx 18 µg/100 ml spiral fluid. In nonfatal Pb encephalopathy it is 25 to 50 µg/100 ml. In fatal cases it is approx 100 µg/100 ml.	I-256

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
44.			Emphasizing the danger to children of Pb levels that appear to be less than those affecting adults, three children with marked hypochromic anemia had urinary Pb at 0.060 to 0.182 mg/l.	I-88
45.			Care is needed in noting Pb poisoning in children since mental impairment may result as a sequel even though it was not initially noticed.	I-85
46.			In children Pb-anemia is usually more severe than in adults and is hypochromic.	II-145
47.			An increase of iron in the blood is an earlier symptom of Pb poisoning than the appearance of stippled erythrocytes.	II-135
48.		Occupational	Five men with poisoning from Pb exposure, 4 of them 2 to 6 mos., 1 for 8 yrs. All removed from work 10 days. RBC volume markedly reduced in all. Blood Fe increased in four. RBC survival time reduced 37-69% in cases of increased blood Fe, and 70 to 72% in 2 cases with little or no blood Fe increase. Pb anemia is caused by hyperhemolysis and defective hemoglobin formation. In the stage of regression the anemia is characterized by hyperplasia and erythiopoietic hyperactivity.	I-39
49.		Occupational	The survival time of blood cells is shortened in cases of Pb poisoning.	II-108
50.		Occupational	In three persons with no symptoms specifically suggesting Pb poisoning, RBC survivals were 21, 24 and 41 days against a normal time of 45 to 55 days. Blood Pb was high.	I-408
51.			Kidney function disturbed wherein the frequency and degree of disturbances increased with the severity of poisoning. With 99 cases of mild Pb poisoning, 52 showed decreased urea clearance, 43 of 93 showed an increased Anbar constant, 37 of 90 showed decreased blood flow through kidneys, 25 of 90 showed decreased canalicular filtration and 4 of 14 showed decreased canalicular reabsorption of water.	I-378
52.		Occupational	Renal malfunction allows amino aciduria.	I-64
53.		Occupational	Mild chronic poisoning, 99 patients. Produces spasms of abducent (efferent) blood vessels of kidney.	I-142
54.		Occupational	Microscopic examination - kidney biopsies, voluminous intranuclear inclusions, glomerular lesion, tubular cell lesions, increased uric acid excretion (or faulty metabolism), faulty urea clearance. Caution against accepting some toxic thresholds in vivo, such as blood Pb at 0.08 mg/100 ml, as indicative of poisoning. Some individuals show abnormal function when their blood Pb is less than the established threshold.	I-137

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
69.			In 40 patients with Pb poisoning, majority showed decreased hypothalamic-pituitary-adrenal activity. Patients also showed decreased urinary 17 ketosteroids and some showed a reversed ephedrine effect.	I-395
70.	TEL	Occupational	TEL may have caused diabetes insipidus.	I-370
71.			Lead has a damaging effect upon fertility, pregnancy and fetal development. Young women appear to suffer harmful effects at lower doses than men of comparable age. Both male and female germ cells are injured by Pb.	USPHS Symposium 12/13-15/65
72.		Occupational	Based on control of Pb absorption for established levels in various tests, atmospheric Pb TLV and MAC values are, for 48-60 hr/week:	I-287

Test	Upper normal level	TLV, mg/m^3	MAC, mg/m^3
Urinary [illegible]	0.15 mg/l	0.16	0.10
Urinary Pb	0.20 mg/l	0.20	0.12
Urinary coproporphyrin	50 µg/l	0.9	0.12
Urinary coproporphyrin	100 µg/l	0.22	0.13
Basophilic stippling	0.3/1,000	0.27	0.14
Anemia	Sp. gr. 1.053	0.28	0.14
Overall considerations		0.12	0.19

73.	Proprietary engine oil additive	Paint skin 1-2 times weekly for 12 months with additive fraction of base oil, additive concentrate, Pb naphthenate	Mice: The Pb naphthenate did not lead to any significant carcinoma development but caused marked kidney damage.	I-14
74.	TML, TEL		Rats: Rats are relatively insensitive to inorganic Pb but show TEL poisoning similar to man. It is triethyl Pb that appears to be the toxic metabolite. TML found less than 1/10 as toxic as TEL by inhalation. It is decomposed very slowly to trimethyl Pb. Both TEL, TML affect central nervous system. Neither can be chelated as can inorganic Pb.	I-373

Table A-2 (continued)

SOME RESULTS ILLUSTRATING THE BIOLOGICAL EFFECTS OF LEAD (Pb) AFTER NONQUANTITATED EXPOSURES

ITEM	Pb SOURCE	METHOD OF Pb EXPOSURE	RESULTS OF EXPOSURE	KETTERING ABSTRACT REFERENCE
75.			Rats: In acute poisoning, thyroid epithelium is flattened and follicles enlarged, reducing secretory action.	I-368
76.			Rats: Rats exposed intratracheally once to dusts from Pb and baryta concentrates. Dusts from Pb baryta and Pb-Zn mines caused proliferation of connective tissue in lungs but marked fibrosis only after 12 mos.	I-358
77.	TEL or $Pb(OAc)_2$	Orally	Sheep: Before treatment had 13 to 17 µg Pb/100 ml blood. With $Pb(OAc)_2$, or TEL at the same Pb conc., tolerance to TEL was less than to $Pb(OAc)_2$. Inhibition by TEL occurred much more rapidly and it took a little more time to recover full activity when treatment ceased.	I-247
78.			Plants: Pb in orchard soils has increased where Pb-As insecticides have been used. Some damage to trees and cover crops results as well as increased levels of Pb in some plants.	II-55
79.	Environment		Plants: Increasing air and plant contamination by Pb is due to auto exhausts almost exclusively. U.S. grasses along traffic-bearing roads have up to 0.3 mg Pb/gm dry grass. This would render cows' milk unfit and the rearing of offspring impossible.	I-99

Table A-3

VALUES REFLECTING LEAD (Pb) INTOXICATION IN HUMANS

CRITERION	ACCEPTED NORMAL VALUES	LEVEL FOUND AFTER Pb EXPOSURE	KETTERING ABSTRACT REFERENCE
Urine			
δ Aminolevulinic acid			
after 10 to 20 days exposure		5 to 10 times normal	I-41
	2.5 mg/24 hr (max)	19.07 mg/24 hr	I-66
< 1 yr post exposure		29 mg/24 hr	I-75
1 to 3 yr post exposure		15 mg/24 hr	I-75
3 to 9 yr post exposure		4.56 mg/24 hr	I-75
	1.3 to 2.8 mg/24 hr		I-75
based on creatinine excretion	0.85 to 2.40 mg/g creatinine	> 2.4 mg/g creatinine	I-254
	up to 4 mg/24 hr	up to 110 mg/24 hr	I-260
	2.1 to 4.0 mg/24 hr		I-260
	0.29 ± 0.140 mg/100 ml		I-260
		> 1.5 mg/100 ml (harmful)	II-116
	4.53 mg/l	~ 30 mg/l	II-118
children, normal	0.20 to 0.26 mg/100 ml		I-290
children, mentally defective		0.38 mg/100 ml	I-290
Coproporphyrin	150 mg/l	up to 450 mg/l	II-118
	0.053 mg/l		I-286
	< 0.1 mg/24 hr		I-271
Porphobilinogen	1.5 mg/24 hr	1.94 mg/24 hr	I-66
Urinary aminoacetone	0.59 to 1.03 mg/g	within normal limits	I-259
Urinary Pb			
non-precipitable, adults	0.002 mg/l	0.027 mg/l	II-117
precipitable, adults	0.047 mg/l	0.100 mg/l	II-117
		0.204 mg/l (intox'd)	II-117
Total Pb - urine, adults	0.049 mg/l	0.127 mg/l	II-117
		0.300 mg/l (intox'd)	II-117
Urinary Pb - children		0.06 to 0.182 mg/l	I-88

Table A-3 (continued)

VALUES REFLECTING LEAD (Pb) INTOXICATION IN HUMANS

CRITERION	ACCEPTED NORMAL VALUES	LEVEL FOUND AFTER Pb EXPOSURE	KETTERING ABSTRACT REFERENCE
		Blood	
δ Aminolevulinic acid			
< 1 yr post exposure		0.065 mg/100 ml	I-75
1 to 3 yr post exposure		0.043 mg/100 ml	I-75
3 to 9 yr post exposure		0.032 mg/100 ml	I-75
	0.026 mg/100 ml (max)		I-75
	0.026 mg/100 ml		II-116
	0.046 mg/100 ml	126.7 mg/100 ml	I-66
Protoporphyrin IX			
TEL exposed	0.021 mg/100 ml		I-53
Pb exposed		0.312 mg/100 ml	I-53
	0.035 to 0.055 mg/100 ml		I-75
< 1 yr post exposure		0.232 mg/100 ml	I-75
1 to 3 yr post exposure		0.225 mg/100 ml	I-75
3 to 9 yr post exposure		0.159 mg/100 ml	I-75
Porphobilinogen			
nonexposed patient	0.030 mg/100 ml		
Pb exposed patient		0.029 mg/100 ml	I-66
RBC Survival Time		reduced 37 to 69%	I-39
	45 to 55 days	21 to 41 days	I-408
Lead			
adult, maximum	0.08 mg/100 gm (max)		I-290
adult, average	0.025 mg/100 gm		
adult, range	(0.005 to 0.040)		
children, normal	0.04 mg/100 gm		I-290
children, mentally defective		0.04 to 0.08 mg/100 gm	I-290

Table A-3 (continued)

VALUES REFLECTING LEAD (Pb) INTOXICATION IN HUMANS

CRITERION	ACCEPTED NORMAL VALUES	LEVEL FOUND AFTER Pb EXPOSURE	KETTERING ABSTRACT REFERENCE
Blood			
Lead, continued			
RBC volume	$5 \times 10^6/mm^3$	3.5 to $5.4 \times 10^6/mm^3$	I-263
Hgb	14.5 g%	8 to 12.8 g%	I-263
Hct	43%	28.8 to 43% (35% av)	I-263
MCV	80 to 94 μ^3	70 to 92 (79 av)	I-263
MC Hgb conc	33 to 38 g/100 ml	27 to 36 g/100 ml (31 av)	I-263
Reticulocytes	0.5 to 1.5%	1.5 to 11.6% (4.4% av)	I-263
Stippled cells - RBC		0.1 to 7.5% (1.8% av)	I-263
Isteric Index	3 to 5	4 to 10 (6.5 av)	I-263
Stippled cells - RBC		> $200/10^6$ cells	I-271
Stippled cells - RBC		> 0.5%	I-387
Specific gravity (blood)	1.057 (1.052 to 1.063)	< 1.054	I-387
Miscellaneous			
Tissue Pb, adults			
soft	0.04 to 0.28 mg/100 g		I-56
skeleton	0.67 to 3.59 mg/100 g		
Pb inhalation	10 to 20 x more absorption than by ingestion		I-256
Spinal fluid	~ 18 µg/100 ml	~ 25 to 50 µg/100 ml	I-256
		fatal cases: ~ 100 ml	

Table A-4

NOMENCLATURE

ALA	Aminolevulinic Acid	MC	Mean Corpuscular
Av	Average	MC Hgb Conc	Mean Corpuscular Hemoglobin Concentration
EDTA	Ethylene Diamine Tetraacetic Acid	MCV	Mean Corpuscular Volume
g	Gram	μ	Micron
Hct	Hematocrit	μ^3	Cubic Micron
Hgb	Hemoglobin	μg	Microgram
m^3	Cubic Meter	μm	Micro Mol
mg	Milligram	μM	Micro Molar
ml	Milliliter	PBG	Porphobilinogen
mm^3	Cubic Millimeter	RBC	Red Blood Cells
mM	Millimolar	TEL	Tetraethyl Lead
M	Molar	TML	Tetramethyl Lead
MAC	Maximum Allowable Concentration	Vit	Vitamin

Figure A-1. PATHWAY OF PORPHYRIN SYNTHESIS