LEAD AND INORGANIC COMPOUNDS

CAS number: 7439-92-1 (Elemental lead)

Molecular formula: Pb (Elemental lead)

TLV–TWA, 0.05 mg/m^3, as Pb

A3 — Confirmed Animal Carcinogen with Unknown Relevance to Humans

Summary

A TLV–TWA of 0.05 mg/m^3, measured as lead (Pb), is recommended for occupational exposure to elemental lead and its inorganic compounds based on the BEI® for lead (see current BEI *Documentation* for Lead). This value is intended to minimize the potential for adverse health effects that may include blood dyscrasias, reduced nerve conduction velocities, peripheral neuropathies, a possible kidney dysfunction, spermatogenesis, impaired intellectual development in children exposed to lead during gestation, and carcinogenicity (as reported from animal studies with soluble lead compounds).

Identifying a blood lead level in workers that will be protective during a working lifetime is necessary for recommending an airborne TLV concentration because blood values, rather than work environment air lead concentrations, are most strongly related to health effects. Taken in total, the toxicity data expressed in this TLV *Documentation* suggest that long-term lead exposure in adults below levels that do not produce blood lead concentrations above 40 µg lead/dl blood should minimize the potential for adverse health effects. Consequently the TLV–TWA is intended to maintain worker blood lead levels below the BEI of 30 µg/dl. Maintaining blood levels at or below this level must also focus on control of exposure to non-airborne sources of lead, such as by meticulous plant environment housekeeping, strict personal cleanliness, and prohibition of eating, drinking, and smoking in lead-contaminated areas.

Based on the demonstrated carcinogenicity of soluble lead compounds in animals, an A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans, notation is designated for elemental lead and its inorganic compounds. Sufficient data were not available to recommend Skin or SEN notations or a TLV–STEL.

Chemical and Physical Properties

Elemental lead is a heavy, ductile, bluish-white, metallic element in Group IVB of the periodic table. Chemical and physical properties include:[1]

Atomic number: 82
Atomic weight: 207.2
Specific gravity: 11.35 at 20°C
Melting point: 327.5°C
Boiling point: 1740°C
Vapor pressure: significant above 500°C (1.77 torr at 1000°C)
Solubility: only a few lead compounds are appreciably soluble in water; many are dissolved by acids and most are sufficiently soluble in body fluids to be toxic, especially when inhaled as fume or in finely divided form

Major Uses

Metallic lead has found wide industrial use where its properties of high density, softness, low melting point, resistance to corrosion, and opacity to gamma and X-rays have been needed. It has been a major component of many alloys such as solder, type metal, brass, and many bronzes. Lead compounds have had a wide variety of uses, especially as paint pigments, in lead–acid storage batteries, glass, plastics, and ceramics. Smelting and refining, scrap recovery, automobile radiator repair, construction and demolition, and firing range operations have resulted in significant exposure of workers.

Overview of Biologic Effects

Once absorbed into the body, lead becomes widely distributed and interacts with a number of enzyme systems, of which the enzymes associated with heme synthesis appear to be the most sensitive. Lead content in animals is also associated with decreased production or decreased activity of a number of heme-containing enzymes, including microsomal mixed-function oxygenases and cytochrome *c*.[1–3] Because the enzymes sensitive to lead are present in all organ systems of the mammalian body, the following discussion of biologic effects in the human will focus on the dose–response relationships of those organ systems that are the most frequently observed targets of lead toxicity. For thorough reviews of the adverse effects of lead on the health of animals and humans, the reader is referred to the publications by the U.S. Environmental Protection Agency (EPA), *Air Quality Criteria for Lead*[4] and the U.S. Agency for Toxic

Substances and Disease Registry, *Toxicological Profile for Lead*.[5]

Human Studies: Dose–Response Relationships

Organ System Toxicity

Much information in the open literature concerning human lead toxicity relates the degree of effect to blood lead level and to duration of exposure. The following information is presented to relate workplace air lead exposures to blood lead levels in derivation of the TLV.

HEME BIOSYNTHESIS AND ERYTHROPOIESIS

Although a number of enzyme systems involved in heme synthesis may be affected by lead, those involved in lead worker monitoring are δ-amino-levulinic acid dehydrase (ALA-D) and ferrochelatase. ALA-D catalyzes the condensation of two units of δ-aminolevulinic acid (ALA) to form porphobilinogen, and ferrochelatase catalyzes the insertion of iron into the protoporphyrin ring to form heme.

In the Griffin et al.[6] study of human male volunteers exposed 23 hours/day for 3 months at 3.2 μg/m^3, blood lead concentrations increased from 20 to 27 μg/dl with a 20% decrease in ALA-D activity. Exposures at 10.9 μg/m^3 increased blood Pb levels from 20 to 37 μg/dl, decreasing ALA-D activity by 47% in the fourth week of exposure. Other work found no threshold for inhibition of ALA-D activity down to a blood lead level of 12 μg/dl. Secchi et al.[7] and Meredith et al.[8] found that inhibition of ALA-D resulted in exponential increases in blood and urine ALA concentrations.

Erythrocyte protoporphyrin measured as either zinc protoporphyrin or free erythrocyte protoporphyrin increased as blood lead concentrations increased. A threshold for this relationship appeared to be between 25 and 30 μg/dl.[9,10] In women, the protoporphyrin threshold appeared to be somewhat lower, i.e., 15 to 20 μg/dl.[9,11] Despite the sensitivity of these systems to absorbed lead, frank anemia does not appear below blood lead concentrations of 80 μg/dl.[4]

Cardiovascular Toxicity

Although the search for a cause and effect relationship between occupational lead exposure and myocardial pathology was unsuccessful, some inferential evidence can be drawn from cases of childhood lead poisoning where, at high levels of exposure, the human myocardial function was adversely effected by lead. In studies of childhood poisoning cases, frequently present electrocardiographic abnormalities were reversed by chelation therapy while signs of encephalopathy persist. These observations may infer independent action of lead for the myocardium and the brain.[12–14]

EPA[4] cited the study by Kosmider and Petelenz as supporting a relationship between chronic lead poisoning in workers and myocardial damage. In this study, 25 of 38 workers over the age of 46 years with chronic lead poisoning had electrocardiographic changes where only 6 cases were expected.

In a study by Kirkby and Gyntelberg[15] of 95 workers at a large lead smelter with employment for more than 9 years, 20% were found to have ischemic electrocardiographic changes, while only 6% of a referent population had such changes. Although the lead smelter workers with electrocardiographic changes had significantly higher blood pressures than their referents, no statistically significant correlations were observed between blood pressure values and the zinc protoporphyrin or blood lead levels. In addition to lead exposures, the authors[15] cite concurrent exposures to antimony, smoke and dust, and the lifting of heavy burdens as possible coronary risk factors.

CEREBROVASCULAR DISEASE

A significant excess of cerebrovascular accidents occurred in a cohort of workers who became pensioners between 1926 and 1961 and who had mean lead-in-urine values between 100 and 250 μg/L between 1941 and 1961 but whose values "not infrequently exceeded 250 μg/L."[16] These workers were employed in the lead industry at a time when exposures were poorly controlled, compared to current occupational hygiene practice. No similar increase in the mortality rate has been reported for workers subsequently employed, according to EPA.[4]

HYPERTENSION

Hypertension and lead exposure have been the focus of much attention. Analyses of the U.S. National Health and Nutrition Examination Survey data[17–19] led to conclusions that lead absorption causes a statistically significant but small increase in both systolic and diastolic blood pressure. The blood pressure relationship with lead appears to be more strongly related at low exposure levels than at high levels, according to Pirkle et al.[18] An increase in mean diastolic pressure of 4 to 5 millimeters of mercury (mm Hg) in the highly exposed (mean blood lead = 51) lead smelter workers studied by Kirkby and Gyntelberg[15] was found to be statistically significant. They found no significant elevation in systolic pressure.

At the Symposium on Lead-Blood Pressure Relationships, Victery et al.[20] summarized the generally agreed upon conclusion ". . . that there is a broad consistency in the results across studies, that the coefficient relating blood lead to blood pressure on the log scale indicated that a doubling of blood lead was associated with a 1 to 2 mm change in mercury."

Renal Toxicity

The classic description of lead nephropathy was reviewed by Tsuchiya.[21] Chronic lead nephropathy

is characterized by interstitial fibrosis, tubular atrophy, and dilatation. The degenerative changes in the proximal tubular lining cells, involving mitochondrial swelling and eosinophilic dense-staining nuclear inclusion bodies with characteristic outer fibrillar margins, were reversible when treated with ethylenediamine tetraacetic acid (EDTA). These reversible changes may be more characteristic of acute or short-term exposures than of the slowly progressive chronic lead nephropathy associated with industrial lead exposure.[22]

The levels of lead exposure capable of causing kidney disease appear to be a function of exposure duration. This, together with the fact that current blood lead concentration in a worker may not reflect past lead exposure, makes the interpretation of the occupational literature difficult. In a population of lead workers with blood lead concentrations averaging 80 µg/dl (range, 42–141 µg/dl), Lilis et al.[23] found nephropathy more frequently in workers exposed to lead for more than 10 years than in those with shorter exposures. In a study[24] of Scottish households having long-term exposure to elevated lead concentrations in drinking water, the frequency of renal dysfunction was elevated in those having blood lead concentrations in excess of 41 µg/dl. This study[24] does not present a strong association between lead exposure and lead nephropathy because of the small number of cases identified and the use of serum urea as the basis of diagnosis. Serum urea is a very insensitive indicator of renal dysfunction; the fact that any association was found gives importance to the observation. The U.S. EPA[4] summarized its review of the occupational literature by stating: ". . . Numerous studies of occupationally exposed workers have provided evidence for lead-induced chronic nephropathy being associated with blood lead levels ranging from 40 to more than 100 µg/dl, and some are suggestive of renal effects possibly occurring even at levels as low as 30 µg/dl." Nephropathy reported at levels as low as 30 µg/dl, however, occurred in workers who had been diagnosed as symptomatic lead-poisoning cases. Low blood lead levels in workers with symptomatic lead poisoning may be the result of a considerable interval between last exposure to lead and the point in time when blood lead was measured.

Reproductive Toxicity

The U.S. EPA[4] further summarized the information on the effects of lead on reproduction and development stating, ". . . Studies of humans and animals indicate that lead may exert gameto-oxic, embryotoxic, and teratogenic effects that could influence the survival and development of the fetus and newborn. It appears that prenatal viability and development may also be indirectly affected by lead through its effects on the health of the expectant mother. The vulnerability of the conceptus to such effects has contributed to concern that the unborn may constitute a group at risk for the effects of lead on health. Also, certain information regarding male reproductive functions has led to concern regarding the impact of lead on men."

Of the six major prospective studies that reported measures of prenatal lead exposure and postnatal cognitive development, three[25–27] found Bayley Mental Development Index deficits associated with increasing lead exposure (maternal or umbilical cord blood lead levels up to 25 µg/dl). Assessment of cognitive function at 2 years of age in one study,[26] at 1, 2, 3, and 4 years of age in another,[27] and at 5 years of age in a third,[28] indicated no association between cognitive development and prenatal measures of lead exposure. Three other prospective studies[29–31] failed to find any association between cognitive function and prenatal lead exposure when maternal or cord blood lead levels were as high as 20 or 30 µg/dl.

Lancranjan et al.[32] reported that effects on spermatogenesis may occur in workers with mean blood lead levels of 52.8 but not in a group with a mean blood lead level of 41 µg/dl. Wildt et al.[33] found changes in spermatogenesis in men who had mean blood lead levels of 46.1 and 44.6 µg/dl, but they did not find such changes in men with blood lead levels up to 39 µg/dl. Telisman et al.[34] presented preliminary results on 101 workers with blood lead levels ranging from 11.9 to 104 µg/dl that show oligospermia and an increase in the numbers of pathological sperm when compared with 51 workers without lead exposure.

Neurologic and Neurobehavioral Toxicity

Much attention has been given to the nerve conduction velocity of peripheral nerves of lead exposed workers, often with conflicting results. Seppalainen et al.[35] found decreased sensory and motor conduction velocities in the median and ulnar nerves of workers with blood lead concentrations in the 30 to 50 µg/dl range, as compared to a control population. Spivey et al.[36] found no significant reduction in conduction velocities in ulnar and peroneal nerves of workers with blood lead levels in the 60 to 80 µg/dl range. Triebig et al.[37] found decreased conduction velocities of sensory ulnar and motor median nerves at blood lead concentrations greater than 70 µg/dl. Nerve conduction velocities of workers with mean blood lead concentrations of 52 µg/dl were improved with EDTA chelation therapy,[38] supporting the association between lead absorption and nerve conduction velocity. The question of whether reduced nerve conduction velocity has clinical significance is still not answered. This may be an early warning signal of more serious neuropathy as believed by Feldman et al.[39] The U.S. EPA[4] takes the position that reduced nerve conduction velocity represents a departure from normal neurological

function. Such departures "should be seriously considered for their potential health significance."[4] Neither the EPA assessment nor the epidemiological literature on lead reports an excess of clinically apparent peripheral neuropathies in lead workers with prolonged exposures to lead in amounts that produce blood lead concentrations less than 70 µg/dl.

Dramatic neurotoxic events such as fulminant encephalopathy and wrist drop are infrequently seen in workers because blood levels in the 100 to 120 range, which are capable of producing overt neuropathy, are rare.[40] Their rarity may lead to misdiagnosis in the clinical situation because of a lowering of an index of suspicion.

Genotoxicity

The U.S. EPA[4] summarized the human data for genotoxicity as being contradictory by tabulating studies that support and those that fail to support genotoxicity. The report[4] points out that human studies were difficult to evaluate because of deficiencies in exposure information and, in the case of lymphocyte studies, absence of culture-time data.

Carcinogenicity

Carcinogenicity in animals was demonstrated by the parenteral and oral administration of soluble lead compounds such as basic lead acetate and lead phosphate. The International Agency for Research on Cancer (IARC)[41] considered evidence for carcinogenicity of inorganic lead in animals to be sufficient; thus, a 2B IARC carcinogenicity classification.

In an epidemiologic study of workers exposed to lead in U.S. smelters and battery plants, Cooper et al.[42] reported significant excesses of stomach cancer (34 observed versus 20.2 expected) and of respiratory cancer (116 observed and 93.5 expected). They found, however, a decreasing trend in standardized mortality ratios by number of years employed. Selevan et al.[43] studied U.S. smelters and found a nonsignificant excess of respiratory cancer (41 observed and 36.9 expected) but an excess of kidney (6 observed and 2.9 expected) and bladder cancers (6 observed and 4.2 expected). Such epidemiological studies, however, were confounded by mixed exposures. In their 1987 review, IARC[41] considered evidence for human carcinogenicity of lead and lead compounds to be inadequate.

Pharmacokinetics

Absorption

Pulmonary deposition of lead particles, as with other particles suspended in air, varies as a function of particle size distribution and respiratory rate. Within the range where Brownian diffusion predominates, as particle size increases, deposition decreases until a mass median aerodynamic diameter of 0.5 is reached. With particle size increases above this value, deposition increases as impaction and sedimentation become the main deposition factors.[44] Mehani[45] measured total deposition rates of 28% to 70% in battery workers and in marine scrap yard workers.

Pulmonary absorption from the lower respiratory tract takes place directly, while particles deposited in the upper airways are cleared by mucocilliary movement and swallowed, where absorption takes place through the gastrointestinal tract. From radioactive and stable isotope studies, it can be concluded that lead deposited in the deep lung is completely absorbed.[46] This appears to be true for all forms of lead.[44,46] Barry[47] found, however, that lead does not accumulate in lungs of workers.

Gastrointestinal absorption of lead to the extent of 19% was measured in a classic 1961 study of human volunteers.[40] Subsequently, similar results (6%–15%) were obtained.[48,49] Rabinowitz et al.[49] and Heard and Chamberlain[50] found that fasting adults absorb lead at rates up to 63.3%.

Percutaneous absorption was studied in eight adult volunteers with topical application of labeled lead acetate in a cosmetic preparation.[51] Absorption of 0% to 0.3% was observed. The highest absorption rate was obtained after skin abrasion.

Distribution

The distribution of lead between various tissues within the body and the rates at which lead transfers from one compartment to another are important to the design of medical surveillance programs, to decisions concerning exposure control, and to diagnosis and treatment. An extensive treatment of this subject is available.[52,53]

Elimination

A review of lead excretion rates from a number of studies and a series of plots of lead urinary excretion rates versus blood lead are available.[54,55] Renal clearance of lead appears to be positively related to blood lead in at least the range studied (i.e., 25 to 80 µg/dl).

Air Concentration–Blood Lead Relationships

The relationship of blood lead to air lead exposure concentrations is important as the bridge between workplace atmospheric lead exposure and possible damage to the health of workers.

In humans, the relationship between blood lead and air lead has been studied under experimental conditions where airborne exposures varied from 0.2 to 36 µg/m^3 and blood leads varied from 14 to 43 µg/dl.[44,48,54–56] At exposure levels of 3.2 µg/m^3 or less and blood lead levels less than 30 µg/dl in the clean surroundings of the experimental setting, slope beta of the regression line is typically in the range of 1.64.

Studies of the relationship between work exposure to airborne lead and blood lead levels were summarized in the EPA review.[4] The relationship (beta slope) varied from 0.03 to 0.19 µg/dl blood per µg/m^3 air. The much lower slope for occupational exposures[57–60] was recognized and ascribed to a nonlinear blood lead response to increasing concentrations of airborne lead. A possible explanation rests in the behavior of workers who have learned methods of limiting lead intake and the incidental ingestion of lead. Avoidance behavior such as breath-holding during short peak exposures was not reflected in measurements obtained by personal air samplers. Chamberlain[54] pointed out that, in occupational settings, a curvilinear relationship between workplace airborne lead and blood lead concentration resulted at least partly from particle size changes (i.e., with increasing dust concentration, with increasing particle aggregation rate, and as the effective fraction of submicron particles [those penetrating to the deep lung where complete absorption is likely] compared to total particles lessens). Steeper slopes found in community lead studies can be explained, in part, by the fact that measured exposure concentrations continued throughout 24-hour periods rather than extending only during a working shift as is the case with worker population studies.

Bishop and Hill[60] conducted a cross-sectional analysis of the dose–response relationship of 233 workers in six plants in 1978. The year 1978 was chosen because it was the last full year prior to the introduction of the 50 µg/m^3 U.S. Occupational Safety and Health Administration[61] Permissible Exposure Limit. Only workers with maximum air lead levels below 200 µg/m^3 were studied. Thus, the effect of respirator wear was minimized if not eliminated. The authors[60] used the Snee model[56] for fitting a curve to their data, believing that this gave them a better fit than linear models. When results were plotted for each of the six plants, they found large variations between plants and concluded that air lead levels were not the only, and not necessarily even the major, determinant of blood lead levels. Their estimate of blood lead versus air lead slopes ranged from 0.02 to 0.06 with an average of 0.04. The Y-axis intercept at the theoretical plant zero-lead-in-air exposure level ranged from 24 to 47 µg/dl for the lowest and highest plant, giving further evidence that blood lead values were significantly elevated by sources of lead exposure other than workplace air.

In a study of 972 battery factory workers, Gartside et al.[59] identified a sub-cohort of 94 workers for whom personal air sampling results, together with blood lead measures taken within a month of the air sample, were available. The partial regression of blood lead (Y) on air lead (X) is described by the relation Y = 38.33 + 0.0536(X). In this plant, if the Y-axis intercept was considered the blood lead level of workers that cannot be ascribed to inhalation exposure, then control of air concentration of lead could not directly reduce blood lead levels below 38.33 µg/dl with upper and lower 95% confidence limits being approximately 58 and 18 µg/dl, respectively.

It was reasonable to assume that blood-lead/air-lead points which were below the regression line represented workers with good personal hygiene and personal habits that did not foster ingestion of lead, while those points above the line needed significant improvement. The beta slope of 0.0536 by Gartside et al.[59] and the similar slopes by Bishop and Hill[60] and King et al.[58] underline the relatively small contribution of atmospheric lead levels in the workplace to blood lead levels.

TLV Recommendation

Identifying a blood lead level in workers that would be protective during a working lifetime was necessary for recommending a TLV, because blood values, rather than air lead concentrations, were most strongly related to health effects.

The preceding review of the experimental and epidemiological literature identified reduced ALA-D activity at blood lead levels as low as 18 µg/dl in animals and no threshold in humans down to 12 µg/dl. The threshold for free erythrocyte protoporphyrin was between 25 and 30 µg/dl in men and 15 and 20 µg/dl in women, but there was no reduction in hemoglobin or hematocrit levels below 75 µg/dl in animals or below 80 µg/dl in humans. Neurologic changes in adult animals exposed to lead have not been observed below 258 µg/dl, while reports of human changes in nerve conduction velocities below 52 µg/dl were conflicting. Clinically apparent peripheral neuropathies were not seen at blood lead concentrations below 70 µg/dl in lead workers with long employment histories. Cardiovascular toxicity has been seen in experimental animals only at circulating lead levels above 100 µg/dl. There were no data relating cardiovascular changes in humans to blood lead levels. However, an excess of cases with electrocardiographic changes has been reported among workers with diagnosed lead poisoning. Cerebrovascular accident excesses associated with occupational lead exposures have not been reported since modern occupational hygiene and control measures have been in place. Nevertheless, there has been much concern that a relationship between blood lead levels and hypertension exists. In adults, the relationship appears to be a 1 to 2 mm Hg increase in diastolic blood pressure for each doubling of blood lead.[20] Kidney changes due to lead have been studied widely in animals, but little or no information relating blood lead levels in experimental animals to such changes is available. The studies of the effects of lead on the kidney in

humans are difficult to evaluate because blood lead levels taken at the time of the study may not reflect past blood levels. An increase in renal dysfunction was seen in adult householders in Scotland where lead-contaminated drinking water resulted in blood lead levels in excess of 41 µg/dl. Reproductive effects, such as changes in spermatogenesis, have been reported at levels above 40 µg/dl. Developmental effects such as depressed intellectual development in children exposed during gestation to blood lead levels in excess of 10 µg/dl (as estimated by placental cord blood measurements) have been reported. Taken in total, these data suggest that long-term lead exposure in adults to amounts below levels that do not produce blood lead concentrations above 40 µg/dl will minimize the potential for adverse health effects.

Carcinogenicity in animals has been demonstrated by the administration of soluble lead compounds. IARC[43] considered the evidence for carcinogenicity of inorganic lead in animals to be sufficient. Epidemiological studies have been confounded by mixed exposures; consequently, IARC[43] considered evidence for human carcinogenicity of lead and its compounds to be inadequate.

Because TLVs are intended to protect workers from impairment of functional capacity and from disease, effects of gestational lead exposure affecting the capacity for producing a child with normal cognitive capability must be considered. There is some,[26–28] but conflicting[30,31] evidence that elevated prenatal lead exposure causes detectable impairment in cognitive ability during postnatal and early childhood at either maternal or umbilical cord blood lead levels in the 20 to 30 µg/dl range. Concern about prenatal exposures below 20 µg/dl maternal blood lead is tempered by the observation that all studies reporting lead-associated impairment in cognitive measures find reversal of early postnatal findings by 12 to 58 months.

The U.S. Centers for Disease Control (CDC)[62] issued a statement in October 1991 that reviewed the effects of low levels of blood lead on young children and recommended different intervention strategies, depending on the child's blood lead concentration. The CDC noted several studies, including those cited above, which suggested that children with blood lead levels between 10 and 20 µg/dl were at increased risk for decreases in IQ and other subtle effects and recommended that the environments of such children should be evaluated with efforts made to reduce the blood lead levels to below 10 µg/dl.

A child who was exposed to lead *in utero* in the workplace is largely removed from that exposure at birth. After birth and certainly after the second year of life, other sources of lead in the general environment and the social environment are more significant determinants of intellectual development than prenatal lead exposure. Accordingly, ACGIH believes that workplace conditions that keep a woman's blood lead level below the BEI of 30 µg/dl will protect her ability to bear children that can develop normally (see the BEI *Documentation* for Lead). However, the 30 µg/dl BEI will be re-evaluated by the ACGIH as new data become available from new or current prospective studies because presently available studies did not test the cognitive function of children that had experienced intrauterine lead exposure in the range of 20 to 30 µg/dl.

A worker, male or female, can bring workplace lead contamination home on clothing. Only the strictest standards of sanitation and personal hygiene at work can assure that a child is not adversely affected by contamination originating in the parent's workplace.

Control of blood lead at or below 30 µg/dl requires careful consideration of all sources that contribute to lead absorption. For the U.S. population, the geometric mean blood lead level between 1988 and 1991 was 2.8 µg/dl (95% confidence interval = 2.7 to 3.0), a 78% decline from the levels measured during the period 1976 to 1980 by the Second U.S. National Health and Nutrition Examination Survey.[63] Lead industry blood lead levels above this range are the result of both inhalation and ingestion at the workplace. Analysis of the Bishop and Hill[60] data indicate that nonairborne (hand to mouth) lead absorption can be controlled to amounts that will increase the blood lead level by as little as 5 to 10 µg/dl.

The slope of the regression line relating blood lead to airborne lead in workplaces varied from 0.03 to 0.19 µg/dl of lead in blood per µg/m^3 of airborne lead.[58–60,64] The correlation coefficients were also quite variable, ranging from 0.14 to 0.90. The lower values occurred at lower airborne lead exposures.

If the steepest slope representing the relationship between blood lead and air lead concentrations in the workplace (0.19 µg/dl blood per µg/m^3 air) is used for judging the contribution of airborne lead to blood lead levels, a major reduction in air lead concentrations such as from 0.05 to 0.025 mg/m^3 would only result in a reduction of blood lead concentration by 4.5 µg/dl. A TLV–TWA of 0.05 mg/m^3 would contribute an airborne, work-related fraction of blood lead concentration of 9.5 µg/dl; contributions from community sources and from nonairborne workplace contamination should be controllable such that total blood lead concentrations could be kept below the BEI of 30 µg/dl. Thus, the occupational hygienist must keep in mind that blood lead concentration, rather than air lead concentration, is the principal means for monitoring lead exposure control.

A TLV of 0.05 mg/m^3, with an A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans, designation, is recommended for airborne

lead. However, in order to prevent blood lead levels from exceeding 30 µg/dl, nonairborne absorption of lead must be controlled by meticulous plant housekeeping, strict personal cleanliness, and prohibiting eating, drinking, and smoking in lead-contaminated areas. The level of attention to these measures must far exceed that currently practiced in the lead industry and will have to approach that degree of cleanliness encountered in the food processing industry if the recommended exposure limitations are to be met. Workers considering reproduction should consult their personal physicians for guidance on the reproductive effects of lead exposure.

Sufficient data were not available to recommend Skin or SEN notations or a TLV–STEL. The reader is expected to be familiar with the section on *Excursion Limits* in the "Introduction to the Chemical Substance TLVs" of the current edition of the *Documentation of the TLVs and BEIs* for the guidance and control of excursions above the TLV–TWA, even when the 8-hour TWA is within the recommended limit. Lead is a substance for which Biological Exposure Indices (BEIs) have been recommended (see *BEI Documentation* for Lead).

Historical TLVs

1946: MAC–TWA, 0.15 mg/m^3 — Lead
1948–1956: TLV–TWA, 0.15 mg/m^3 — Lead
1957–1972: TLV–TWA, 0.2 mg/m^3 — Lead and inorganic compounds
1971: *Proposed:* TLV–TWA, 0.15 mg/m^3 — Lead, inorganic compounds, dusts & fumes
1973–1994: TLV–TWA, 0.15 mg/m^3, as Pb — Lead, inorganic dusts & fumes
1976–1985: TLV–STEL, 0.45 mg/m^3, as Pb — Lead, inorganic dusts & fumes
1984: *Proposed:* Withdraw TLV–STEL
1986: TLV–STEL withdrawn
1993: *Proposed:* TLV–TWA, 0.05 mg/m^3, as Pb; A3, Confirmed Animal Carcinogen with Unknown Relevance to Humans — Lead, elemental and inorganic compounds
1995: TLV–TWA, 0.05 mg/m^3, as Pb; A3

References

1. Goldberg, A.M.; Meredith, P.A.; Miller, S.; et al.: Hepatic Drug Metabolism and Heme Biosynthesis in Lead-Poisoned Rats. Br. J. Pharmacol. 62:529–536 (1978).
2. Meredith, P.A.; Moore, M.R.: The Influence of Lead on Heme Biosynthesis and Biodegradation in the Rat. Biochem. Soc. Trans. 7:637–639 (1979).
3. Bull, R.J.; Lutkenhoff, S.D.; McCarty, G.E.; Miller, R.G.: Delays in the Postnatal Increase of Cerebral Cytochrome Concentrations in Lead-Exposed Rats. Neuropharmacology 18:83–92 (1979).
4. U.S. Environmental Protection Agency: Air Quality Criteria for Lead. Vol. I–IV. EPA Assessment Office, Research Triangle Park, NC (1986).
5. U.S. Agency for Toxic Substances and Disease Registry: Toxicological Profile for Lead. ATSDR/TP-88/17. U.S. Public Health Service, ATSDR, Atlanta, GA (June 1990).
6. Griffin, T.B.; Coulston, F.; Goldberg, L.; et al.: Clinical Studies on Men Continuously Exposed to Airborne Particulate Lead. In: Lead, pp. 221–240. T.B. Griffin and J.G. Knelson, Eds. Georg Thieme Publishers, Stuttgart, FRG (1975).
7. Secchi, G.C.; Erba, L.; Cambiaghi, G.: δ-Aminolevulinic Acid Dehydratase Activity of Erythrocytes and Liver Tissue in Man: Relationship to Lead Exposure. Arch. Environ. Health 28:130–132 (1974).
8. Meredith, P.A.; Moore, M.R.; Campbell, B.C.; et al.: δ-Aminolaevulinic Acid Metabolism in Normal and Lead-Exposed Humans. Toxicology 9:1–9 (1978).
9. Roels, H.A.; Lauwerys, R.R.; Buchet, J.P.; Vrelust, M.T.: Response of Free Erythrocyte Porphyrin and Urinary-Aminolevulinic Acid in Men and Women Moderately Exposed to Lead. Int. Arch. Arbeitsmed. 34:97–108 (1975).
10. Grandjean, P.; Lintrup, J.: Erythrocyte-ZN-Protoporphyrin as an Indicator of Lead Exposure. Scand. J. Clin. Lab. Invest. 38:669–675 (1978).
11. Stuik, E.J.: Biological Response of Male and Female Volunteers to Inorganic Lead. Int. Arch. Arbeitsmed. 33:83–97 (1974).
12. Freeman, R.: Reversible Myocarditis Due to Chronic Lead Poisoning in Childhood. Arch. Dis. Child. 40:389–393 (1965).
13. Myerson, R.M.; Eisenhauer, J.H.: Atrioventricular Conduction Defects in Lead Poisoning. Am. J. Cardiol. 11:409–412 (1963).
14. Silver, W.; Rodriquez–Torres, R.: Electrocardiographic Studies in Children with Lead Poisoning. Pediatrics 41:1124–1127 (1968).
15. Kirkby, H.; Gyntelberg, F.: Blood Pressure and Other Cardiovascular Risk Factors of Long-Term Exposure to Lead. Scand. J. Work Environ. Health 11:15–19 (1985).
16. Dingwall–Fordyce, I.; Lane, R.E.: A Follow-Up Study of Lead Workers. Br. J. Ind. Med. 20:313–315 (1963).
17. Harlan, W.R.; Landis, J.R.; Schmouder, R.L.; et al.: Blood Lead and Blood Pressure: Relationship in the Adolescent and Adult U.S. Population. JAMA 253:530–534 (1985).
18. Pirkel, J.L.; Schwartz, J.; Landis, J.R.; Harlan, W.R.: The Relationship Between Blood Levels and Blood Pressure, and Its Cardiovascular Risk Implications. Am. J. Epidemiol. 121:246–258 (1985).
19. Landis, J.R.; Flegal, K.M.: A Generalized Mantel–Haenszel Analysis of the Regression of Blood Pressure on Blood Lead Using NHANES II Data. Environ. Health Prospect. 78:35–41 (1988).
20. Victery, W.; Tyroler, H.A.; Volpe, R.; Grant, L.D.: Summary of Discussion Sessions: Symposium on Lead-Blood Pressure Relationships. Environ. Health Perspect. 78:139–155 (1988).
21. Tsuchiya, K.: Lead. In: Handbook on the Toxicology of Metals, Chap. 14. L. Freiberg, G.F. Nordberg, and V.B. Vouk, Eds. Elsevier, Amsterdam, The Netherlands (1986).
22. Cramer, K.; Goyer, R.A.; Jagenburg, R.; Wilson, M.H.: Renal Ultrastructure, Renal Function, and Parameters of Lead Toxicity in Workers with Different Periods of Lead Exposure. Br. J. Ind. Med. 31:113–127 (1974).
23. Lillis, R.; Covrilescu, N.; Nestorescu, B.; et al.: Nephropathy in Chronic Lead Poisoning. Br. J. Ind. Med. 25:196–202 (1968).

24. Campbell, B.C.; Beattie, A.D.; Moore, M.R.; et al.: Renal Insufficiency Associated with Excessive Lead Exposure. Br. Med. J. 1:482–485 (1977).
25. Bellinger, D.C.; Leviton, A.; Waternaux, C.; et al.: Longitudinal Analyses of Prenatal and Postnatal Lead Exposure and Early Cognitive Development. N. Eng. J. Med. 316:1037–1043 (1987).
26. Ernhart, C.B.; Greene, T.: Low-Level Lead Exposure in the Prenatal and Early Pre-School Periods: Language Development. Arch. Environ. Health 45:342–354 (1990).
27. Dietrich, K.N.; Krafft, K.M.; Bier, M.; et al.: Neurobehavioral Effects of Foetal Lead Exposure: The First Year of Life. In: Lead Exposure and Child Development. M.A. Smith, L.D. Grant, and A.L. Sors, Eds. Dordrecht, Kluwer, The Netherlands (1989).
28. Bellinger, D.; Leviton, A.; Sloman, J.: Antecedents and Correlates of Improved Cognitive Performance in Children Exposed *in utero* to Low Levels of Lead. Environ. Health Perspect. 89:5–11 (1990).
29. Moore, M.R.; Bushnell, I.W.R.; Goldberg, A.: A Prospective Study of the Results of Changes in Lead Exposure in Children in Glasgow. In: Lead Exposure and Child Development. M.A. Smith, L.D. Brant, and A.L. Sors, Eds. Dordrecht, Kluwer, The Netherlands (1989).
30. McMichael, A.J.; Baghurst, P.A.; Wigg, N.R.; et al.: Port Pirie Cohort Study: Environmental Exposure to Lead and Children's Abilities at the Age of 4 Years. N. Engl. J. Med. 319:468–475 (1988).
31. Coonin, G.H.; Bell, A.; McBride, W.; Carter, C.: Low-Level Exposures to Lead: The Sydney Study. Devel. Med. Child. Neurol. 31:640–649 (1989).
32. Lancranjan, I.; Popescu, H.I.; Gavanescu, O.; et al.: Reproductive Ability of Workmen Occupationally Exposed to Lead. Arch. Environ. Health 30:396–401 (1975).
33. Wildt, K.; Eliasson, R.; Berlin, M.: Effects of Occupational Exposure to Lead on Sperm and Semen. In: Reproductive and Developmental Toxicity of Metals, pp. 279–300. Proceedings of a joint meeting, May 1982, Rochester, NY. T.W. Clarkson, G.F. Nordberg, and P.R. Sager, Eds. Plenum Press, New York (1983).
34. Telisman, S.; Cvitkovic, P.; Gavella, M.; Pongracic, J.: Semen Quality in Men with Respect to Blood Lead and Cadmium Levels. Institute for Medical Research and Occupational Health. Mose Pijade 158, 41000, Zagreb, Yugoslavia (1990).
35. Seppalainen, A.M.; Hernberg, S.; Vesanto, R.; Kock, B.: Early Neurotoxic Effects of Occupational Lead Exposure: A Prospective Study. Neurotoxicology 4:181–192 (1983).
36. Spivey, G.H.; Baloh, R.W.; Brown, C.P.; et al.: Subclinical Effects of Chronic Increased Lead Absorption. A Prospective Study: III. Neurologic Findings at Follow-Up Examination. J. Occup. Med. 22:607–612 (1980).
37. Triebig, G.; Weltle, D.; Valentin, H.: Investigations on Neurotoxicity of Chemical Substances at the Workplace: V. Determination of the Motor and Sensory Nerve Conduction Velocity in Persons Occupationally Exposed to Lead. Int. Arch. Occup. Environ. Health 53:189–204 (1984).
38. Araki, S.; Honma, T.; Yanagihara, S.; Ushio, K.: Recovery of Slowed Nerve Conduction Velocity in Lead-Exposed Workers. Int. Arch. Occup. Environ. Health 46:151–157 (1980).
39. Feldman, R.G.; Hayes, M.K.; Younes, R.; Aldrich, F.D.: Lead Neuropathy in Adults and Children. Arch. Neurol. 34:481–488 (1977).
40. Kehoe, R.A.: The Metabolism of Lead in Man in Health and Disease: The Normal Metabolism of Lead. (The Harben Lectures, 1960). J. Research Inst. Public Health Hyg. 24:81–97, 129–143, 177–203 (1961).
41. International Agency for Research on Cancer: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Suppl. 7, pp. 230–232. IARC, Lyon, France (1987).
42. Cooper, W.C.; Wong, O.; Kheifets, L.: Mortality Among Employees of Lead Battery Plants and Lead Producing Plants, 1947–1980. Scand. J. Work Environ. Health 11:331–345 (1986).
43. Selevan, S.G.; Landrigan, P.J.; Stern, F.B.; Jones, J.H.: Mortality of Lead Smelter Workers. Am. J. Epidemiol. 122:673–683 (1984).
44. Chamberlain, A.C.; Heard, M.J.: Lead Tracers and Lead Balances. In: Environmental Lead: Proceedings of the Second International Symposium on Environmental Lead Research, pp. 175–198. D.R. Lynam, L.G. Piantanida, and J.F. Cole, Eds. Academic Press, New York (1981).
45. Mehani, S.: Lead Retention by the Lungs of Exposed Workers. Ann. Occup. Hyg. 9:165–171 (1966).
46. Morrow, P.E.; Beiter, H.; Amato, F.; Gibb, F.R.: Pulmonary Retention of Lead: An Experimental Study in Man. Environ. Res. 21:373–384 (1980).
47. Barry, P.S.I.: A Comparison of Concentrations of Lead in Human Tissues. Br. J. Ind. Med. 32:119–139 (1975).
48. Gross, S.B.: Human Oral and Inhalation Exposures to Lead: Summary of Kehoe Balance Experiments. J. Toxicol. Environ. Health 8:333–377 (1981).
49. Rabinowitz, M.B.; Kopple, J.D.; Wetherill, G.W.: Effect of Food Intake and Fasting on Gastrointestinal Lead Absorption in Humans. Am. J. Clin. Nutr. 33:1784–1788 (1980).
50. Heard, M.J.; Chamberlain, A.C.: Effect of Minerals and Food on Uptake of Lead from the Gastrointestinal Tract in Humans. Human Toxicol. 1:411–415 (1982).
51. Moore, M.R.; Meredith, P.A.; Watson, W.S.; et al.: The Percutaneous Absorption of Lead-203 in Humans from Cosmetic Preparations Containing Lead Acetate, as Assessed by Whole-Body Counting and Other Techniques. Food Cosmet. Toxicol. 18:399–405 (1980).
52. Marcus, A.H.: Multicompartment Kinetic Models for Lead: I. Bone Diffusion Models for Long-Term Retention. Environ. Res. 36:441–489 (1985).
53. Marcus, A.H.: Testing Alternative Nonlinear Kinetic Models in Compartmental Analysis. In: Mathematics and Computers in Biomedical Applications, pp. 259–267. J. Eisenfeld and C. Delisi, Eds. Elsevier, Amsterdam, The Netherlands (1985).
54. Chamberlain, A.C.: Effect of Airborne Lead on Blood Lead. Atmos. Environ. 17:677–692 (1983).
55. Rabinowitz, M.; Wetherill, G.W.; Kopple, J.D.: Studies of Human Lead Metabolism by Use of Stable Isotope Tracers. Environ. Health Perspect. 7:145–153 (1974).
56. Snee, R.D.: Evaluation of Studies of the Relationship Between Blood Lead and Air Lead. Int. Arch. Occup. Environ. Health 48:219–242 (1981).
57. Ashford, N.A.; Geicht, R.D.; Hattis, D.B.; Katz, J.I.: The Effects of OSHA Medical Removal Protection on Labor Costs of Selected Lead Industries. Massachusetts

Institute of Technology, Center for Policy Alternatives, Cambridge, MA. CPA Report No. CPA-77/11; NTIS Pub. No PB-278-653. U.S. National Technical Information Service, Springfield, VA (1977).
58. King, E.; Conchie, A.; Hiett, D.; Milligan, B.: Industrial Lead Absorption. Ann. Occup. Hyg. 22:213–239 (1979).
59. Gartside, P.S.; Buncher, C.R.; Lerner, S.: Relationship of Air Lead and Blood Lead for Workers at an Automobile Battery Factory. Int. Arch. Occup. Environ. Health 50:1–10 (1982).
60. Bishop, L.; Hill, W.J.: A Study of the Relationship Between Blood Levels and Occupational Air Lead Levels. Am. Stat. 37:471–475 (1983).
61. U.S. Department of Labor: Occupational Exposure to Lead; Final Standard, 29 CFR 1910-1025. Fed. Reg. 43:54354. Washington, DC (1978).
62. U.S. Centers for Disease Control: Preventing Lead Poisoning in Young Children. U.S. Department of Health and Human Services, Public Health Service. Atlanta, GA (1991).
63. U.S. Centers for Disease Control: Blood Lead Levels — United States, 1988–1991. MMWR 43(30):545–548 (August 5, 1994).
64. Williams, M.K.; King, E.; Walford, J.: An Investigation of Lead Absorption in an Electric Accumulator Factory with the Use of Personal Samplers. Br. J. Ind. Med. 26:202–216 (1969).