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Lead

Guideline

The maximum acceptable concentration (MAC) for lead in drinking water is 0.010 mg/L (10 µg/L). It is recommended that faucets be flushed before water is taken for analysis or consumption.

Identity, Use and Sources in the Environment

Lead is the most common of the heavy elements. Several stable isotopes exist in nature, ^{208}Pb being the most abundant. The average molecular weight is 207.2. Lead is a soft metal that resists corrosion and has a low melting point (327°C). It has therefore been used extensively since Roman times and, as a result, has become widely distributed throughout the environment.[1]

In 1984, 264 300 tonnes of lead in all forms, including recycled lead, were produced in Canada, and 130 550 tonnes of refined lead were consumed.[2] In the same year, 67 000 tonnes were used in the production of lead acid storage batteries, and less than 50 000 tonnes (10 000 tonnes from each of the following categories) were used in the production of tetraethyl lead, pigments and chemicals, solder, other alloys and cables.[3] From a drinking water perspective, the almost universal use of lead compounds in plumbing fittings and as solder in water distribution systems is important. Distribution systems and plumbing installed before 1945 may be made from lead pipe.[4]

Solid and liquid (sludge) wastes account for about 81% of the lead discharged into the Canadian environment, usually into landfills,[5] but lead has been dispersed more widely in the general environment through atmospheric emissions. In 1982, leaded gasoline additives accounted for 63% of all atmospheric emissions.[5] With the introduction of unleaded fuel, emissions from this source declined from a peak of 14 360 tonnes in 1973 to 6500 tonnes in 1983.[3] Emissions have declined to virtually nil in 1991[6] as a result of the phaseout of leaded gasoline in December 1990 under the Gasoline Regulations of the Canadian Environmental Protection Act.[7]

Exposure

Lead is present in tap water as a result of dissolution from natural sources or from household plumbing systems containing lead in pipes, solder or service connections to homes. The amount of lead from the plumbing system that may be dissolved depends upon several factors, including the acidity (pH), water softness and standing time of the water, with soft, acidic water being most plumbosolvent.[8] Lead concentrations in untreated water were generally less than 1 µg/L in 71 Canadian municipalities in two national surveys conducted in 1976 and 1977.[9,10] Mean levels in tap water samples taken after three to five minutes of flushing (to remove any standing water) were below 1 µg/L (range ≤1 to 65 µg/L) in the two national surveys and 4 µg/L (range ≤1 to 48 µ/L) in 64 municipalities in surveys conducted in Ontario between 1981 and 1985.[11] The concentration of lead determined from integrated monitoring of all tap water used in the kitchens of 18 homes in Montreal ranged from 0.25 to 2.76 µg/L, with a median of 0.65 µg/L.[12] The median level of lead in drinking water samples collected in five Canadian cities during a duplicate diet study was 2.0 µg/L.13

In a recent study in Ontario, the concentration of lead in water actually consumed was determined using a composite sampler in 40 homes at seven locations.[14] The average concentration of lead over a one-week sampling period ranged from 1.1 to 30.7 µg/L, with a median level of 4.8 µg/L. The results of this study are considered to be the most realistic estimate of the intake of lead from drinking water. Using the median concentration of 4.8 µg/L and daily drinking water consumption of 1.5 L for an adult and 0.6 L for a child, the average daily consumption of lead from drinking water is 7.2 µg for an adult and 2.9 µg for a child.

Food can be contaminated by naturally occurring lead in soil as well as by lead from sources such as atmospheric fallout, water used for cooking or the use of lead-soldered cans. The use of lead-soldered cans has been estimated to contribute 13 to 22% of the total dietary intake of lead.[15] Intake of lead from this source has declined markedly in Canada in recent years as the

use of cans with lead solder has been phased down by the food processing industry. Based on recent analyses of lead in food in a national market basket study, the intakes of lead from food have been estimated to be 1.1 µg/kg bw per day for children aged one to four years and 0.75 µg/kg bw per day for adults.[16] This represents a drop of 56% between 1985 and 1989 for children.

Annual geometric mean concentrations measured at more than 100 National Air Pollution Surveillance (NAPS) stations across Canada have declined steadily from 0.74 µg/m^3 in 1973 to <0.1 µg/m^3 (the detection limit) in 1991,[6,17] paralleling the decrease in the use of lead additives in gasoline to their phaseout in December 1990. Some sampling stations in a few Canadian cities still record measurable concentrations of lead in air (e.g., Vancouver, Edmonton, Calgary, Toronto, Hamilton, Montreal), but average concentrations in these cities are not above 0.1 µg/m^3. It is difficult to estimate the current average intake of lead from air, as geometric mean concentrations, although well below the detection limit, are not measurable. Intakes for a two-year-old child and an adult have been estimated to be 0.36 and 1.2 µg/d, respectively, based on NAPS data using one-third the detection limit with a sampling height correction factor of 2.*

Soils and household dust are significant sources of lead exposure for small children.[20,21] In 1973, in Toronto homes not near point sources, average lead concentrations were 110 µg/g in garden soil and 845 µg/g in household dust.[22] There are no recent data for lead concentrations in household dust in urban Canadian homes. Lead in soil and lead in outdoor air are the main contributors to lead in household dust in Canada. Based on Toronto data, average concentrations of lead in soil and air have declined by 43% and 76%, respectively, between 1973 and 1984, or 3.9% and 6.9% per year, respectively.[17,23,24] Using these data,** the concentration of lead in household dust in urban communities can be estimated to be 350 µg/g in 1984 and 140 µg/g in 1990, assuming no airborne lead and a further reduction of 24% for lead in soil between 1984 and 1990.

Other sources of lead intake include ceramic ware, activities involving arts and crafts, peeling paint and renovations resulting in dust or fumes from paint.[25] No allowance has been made for the contribution of lead from these sources, because they occur on a highly sporadic basis and because no quantitative data are available. It has been pointed out[25] that old paint has been an important source of excess lead intake for inner-city children living in older housing stock in the United States. This may not be as important in Canada as in the United States, because Canada's stock of older housing is smaller relative to the total stock available. However, these sources, as well as occurrences of high lead concentrations in drinking water in some older houses, can be extremely important for a small number of children.

Total intakes and uptakes of lead from all sources are shown in Table 1 for children and adults in urban areas. The relative contribution of water to average intake is estimated to be 9.8% and 11.3% for children and adults, respectively. Total intake of lead from three of the four major sources—air, food and dust—appears to have dropped significantly since the mid-1980s as a result of regulatory and voluntary actions to control lead from air (via gasoline) and food (via cans). For young children, average daily intake is calculated to be about 29 µg/d, down from 70 µg/d calculated on the basis of 1984 to 1986 data, and is now below the intake of 48 µg/d for a two-year-old based on the World Health Organization's (WHO) provisional tolerable weekly intake (PTWI) of 25 µg/kg bw, equivalent to approximately 3.5 µg/kg bw per day.[26]

Table 1. Total intake[a] and uptake[b] of lead (µg/d)

		Child (two years old, 13.6 kg)		Adult (70 kg)	
Medium	Concentration	Intake (%)	Uptake (%)	Intake (%)	Uptake (%)
Air	0.06 µg/m^3	0.36 (1.2)	0.14 (1.1)	1.2 (1.9)	0.48 (7.1)
Water	4.8 µg/L	2.9 (9.8)	1.45 (11.6)	7.2 (11.3)	0.72 (10.7)
Food	Various	15.0 (50.9)	7.5 (60.2)	52.5 (82.4)	5.25 (78.0)
Dust, dirt	140 µg/g	11.2 (38.0)	3.36 (27.0)	2.8 (4.4)	0.28 (4.2)
Total		**29.5**	**12.5**	**63.7**	**6.7**

[a] Assumed volume of air inhaled per day is 20 m^3 for adults and 6 m^3 for children. Assumed drinking water consumption is 1.5 L/d for adults and 0.6 L/d for children. Intake of lead estimated to be 1.1 µg/kg bw per day for children and 0.75 µg/kg bw per day for adults.[16] Assumed quantity of dirt ingested is 20 mg/d for adults and 80 mg/d for young children.[27,28] Numbers may not be exact due to rounding.

[b] Absorption of inhaled lead is assumed to be 40% for adults and children. Absorption of lead in food and drinking water is assumed to be 50% for children and 10% for adults. Absorption of lead from dirt and dust is assumed to be 30% for children and 10% for adults.[21]

* Curbside lead concentrations are two to four times higher than those measured by NAPS samplers, which are generally located on rooftops.[18,19] Assumed volume of air inhaled per day is 20 m^3 for adults and 6 m^3 for children.

** See previous data; a 50% contribution from dirt and air was assumed for household dust.

Analytical Methods and Treatment Technology

Atomic absorption spectrometry (AAS) may be used to determine concentrations of lead and other metals in water. Detection limits of less than 1 µg/L can be achieved;[12] however, practical quantitation limits (PQLs) are usually 1 to 3 µg/L during routine monitoring studies.[11] Inductively coupled plasma atomic emission spectrometry (ICP–AES) is frequently used in routine monitoring analyses, because of speed, relative freedom from interference by other components in the sample and lower cost per analysis. This technique is preferable to AAS when multi-element analysis is required. The detection limit is 1 to 2 µg/L and the PQL is about 7 to 10 µg/L.[29]

Because the maximum acceptable concentration (MAC) for lead in drinking water is intended to apply to average concentrations in distributed water, sampling should be carried out on flushed samples at the point of consumption.

Conventional water treatments, including settling, aluminum sulphate (alum) or ferric sulphate coagulation and filtration are reasonably effective in removing lead from treated drinking water. Lime softening at elevated pH is also effective in removal of lead. However, because the majority of lead in drinking water is introduced after leaving the treatment plant as a result of leaching from materials in the distribution system or household plumbing, corrosion control is a more effective method of preventing high concentrations of lead at the point of consumption. Adjustment of the pH from less than 7 to 8 or 9 and moderate increases in alkalinity, measured as carbonate, to more than 30 mg/L reduce the plumbosolvency of acidic waters and minimize leaching.[30,31] Corrosion inhibitors such as zinc orthophosphate or silicate-based inhibitors may also be added. Although water treatment can reduce tap water lead concentrations substantially, water treatment alone may be inadequate to reduce lead to concentrations below 10 µg/L when water is supplied through leaded distribution systems and lead concentrations are high.[32]

Other effective methods of treatment, which are also suitable for home use, include reverse osmosis and ion exchange using a strong acid cation resin; activated adsorption has also been reported to be effective in some cases.

Health Effects

Absorption and Distribution

Lead can be absorbed by the body through inhalation, ingestion, dermal contact (mainly as a result of occupational exposure)[33] or transfer via the placenta.[34] In adults, approximately 10% of ingested lead is absorbed into the body.[20] Young children absorb from 40% to 53% of lead ingested from food.[35,36] For lead in soil and dust, the gastrointestinal absorption rate in children has been estimated as 30%.[21] Absorption of lead is greatly increased after fasting and when the intakes of dietary calcium and phosphorus are low.[37,38] The relationship between blood lead levels of children and adults and the concentration of lead in water and in food appears to be curvilinear overall, with the curve at low doses near-linear.[39–42] The amount of airborne lead deposited and absorbed in the lungs of adults ranges from 30% to 50%.[20] No data on absorption following inhalation in children are available; however, their respiratory uptake of lead is likely to be comparatively greater than that of adults on a body weight basis.[20]

Placental transfer of lead occurs in humans as early as the twelfth week of gestation, and uptake of lead by the foetus continues throughout development.[43] The concentration of lead in umbilical cord blood is correlated with maternal blood lead levels in ratios that range from 0.8 to 1.0.[34,39,44,45] The ratio of foetal blood lead level to maternal blood lead level is also about 0.8 to 1.0.[34,44]

Once lead is absorbed, it enters either a “rapid turnover” biological pool with distribution to the soft tissues (blood, liver, lung, spleen, kidney and bone marrow) or a “slow turnover” pool with distribution mainly to the skeleton.[46] Of total body lead, approximately 80 to 95% in adults and about 73% in children accumulate in the skeleton.[47,48] The biological half-life of lead is approximately 16 to 40 days in blood[46,49] and about 17 to 27 years in bones.[46,50]

Metabolic balance studies in infants and young children indicated that net retention of lead averaged 32% of intake above intakes of 5 µg/kg bw per day, whereas retention was negative (i.e., excretion exceeded intake) below 5 µg/kg bw per day. Regression analysis indicated a balance point of 4.1 µg/kg bw per day.[36] No increases in blood lead were observed in infants with low exposure to other sources of lead and mean dietary intakes of 3 to 4 µg/kg bw per day,[51] thus confirming the metabolic data.

Although blood lead concentrations reflect only recent intake (about 40 days), there is a steady state distribution of lead between various organs and systems under conditions of chronic exposure.[20] The blood lead concentration is, therefore, a reasonably good indicator of exposure from all sources[25] and is commonly used for this purpose.

Acute and Chronic Exposure

Lead is a cumulative general poison, with foetuses, infants, children up to six years of age and pregnant women (because of their foetuses) being most susceptible to adverse health effects. Lead can severely affect the central nervous system. Overt signs of acute

intoxication include dullness, restlessness, irritability, poor attention span, headaches, muscle tremor, hallucinations and loss of memory,[52] with encephalopathy occurring at blood lead levels of 100 to 120 µg/dL in adults and 80 to 100 µg/dL in children.[20]

Signs of chronic lead toxicity, including tiredness, sleeplessness, irritability, headaches, joint pain and gastrointestinal symptoms, may appear in adults with blood lead levels of 50 to 80 µg/dL.[53] After one or two years of exposure, muscle weakness, gastrointestinal symptoms, lower scores on psychometric tests, disturbances in mood and symptoms of peripheral neuropathy were observed in occupationally exposed populations at blood lead levels of 40 to 60 µg/dL.[54,55] At levels of 30 to 50 µg/dL, there were significant reductions in nerve conduction velocity.[56]

Renal disease has long been associated with lead poisoning; however, chronic nephropathy in adults and children has not been detected below blood lead levels of 40 µg/dL.[57,58] In a recent epidemiological study, there was no evidence of an association between hypertension and lead-induced renal effects in men with blood lead concentrations below 35 µg/dL, but there was some suggestion (not statistically significant) of increased hypertension at blood lead concentrations above 37 µg/dL.[59]

A significant ($p \leq 0.01$) association has been established, without evidence of a threshold, between blood lead levels in the range 7 to 34 µg/dL and high diastolic blood pressure in people aged 21 to 55, and particularly for white men aged 40 to 49 years, using data from the second U.S. National Health and Nutrition Examination Survey (NHANES II).[60,61] The significance of these results has since been questioned, following further analysis of the same data using a different statistical method.[62]

Lead interferes with the activity of several of the major enzymes involved in the biosynthesis of haem.[20] As haem is a constituent of several haemoproteins, interference with its biosynthesis would be expected to result in multi-organ toxicity; however, the only clinically well-defined symptom is anaemia,[63] which occurs only at blood lead levels in excess of 40 µg/dL in children.[64] In children, inhibition of the activity of d-aminolevulinic acid dehydrase has been noted at blood lead concentrations as low as 5 µg/dL.[20,65] However, no adverse health consequences are associated with inhibition at this level.

Impairment of the insertion of iron(II) into the porphyrin ring to form haem results in an accumulation of erythrocyte protoporphyrin (EP). No-observed-adverse-effect levels (NOAELs) for increases in EP levels occurred in infants and children at about 15 to 17 µg/dL,[66–69] whereas elevated EP levels were significantly ($p \leq 0.02$) correlated with blood lead levels above 15 and 20 µg/dL, with 50% of children showing elevations of two standard deviations above "normal" values at blood lead concentrations of 25 and 35 µg/dL.[66,68] In adults, the NOAEL for increases in EP levels ranged from 25 to 30 µg/dL;[70] for females alone, the NOAEL ranged from 20 to 25 µg/dL, which is closer to that observed for children.[68,71] Anaemia results from both lead-induced inhibition of haem synthesis and shortening of erythrocyte survival.[72] The NOAEL for changes in haemoglobin concentration in blood has been suggested to be 50 µg/dL in adults and 40 µg/dL in children.[64,73] Changes in growth patterns in infants less than 42 months old have been associated with increased levels of EP, with persistent increases in high blood EP levels leading initially to a rapid gain in weight but subsequently to a retardation of growth.[74] An analysis of the NHANES II data showed a highly significant negative correlation between the stature of children aged seven years and younger and blood lead levels in the range 5 to 35 µg/dL.[75]

Lead has also been shown to interfere with calcium metabolism, both directly and by perturbation of the haem-mediated generation of the vitamin D precursor 1,25-dihydroxycholecalciferol. The vitamin D–endocrine system plays a major role in the maintenance of extra- and intracellular calcium homeostasis,[76,77] bone remodelling, intestinal absorption of minerals, cell differentiation and immunoregulatory capacity.[20] Dose-related significant decreases ($p \leq 0.001$) in circulating 1,25-dihydroxyvitamin D levels were observed in children with blood lead concentrations ranging from 33 to 55 µg/dL compared with children with blood lead levels ranging from 10 to 26 µg/dL.[78] A regression analysis indicated that significant decreases were associated ($r = -0.88$) over the entire range of blood lead concentrations from 12 to 120 µg/dL, with no evidence of a threshold.[79] Tissue lead content is increased in calcium-deficient persons, a fact that assumes great importance when considering the increased propensity to lead exposure that could result from the calcium-deficient status of the pregnant woman. Finally, it has been demonstrated that interactions between calcium and lead were responsible for a significant portion of the variance in the scores on general intelligence ratings, and that calcium had a significant effect on the deleterious effect of lead.[80]

Several lines of evidence demonstrate that both the central and peripheral nervous systems are principal targets for lead toxicity. These include subencephalopathic neurological and behavioural effects in adults and electrophysiological evidence of both central and peripheral effects on the nervous system in children with blood lead levels well below 30 µg/dL. Aberrant electroencephalograph readings were significantly correlated ($p < 0.05$) with blood lead levels down to 15 µg/dL, with

effects at non-significant levels noted down to 6 µ/dL.[81,82] Significant reductions in maximal motor nerve conduction velocity (MNCV) have been observed in five- to nine-year-old children living near a smelter, with a threshold occurring at a blood lead level around 20 µg/dL. A 2% decrease in the MNCV was seen for every 10 µg/dL increase in the blood lead level.[83]

The auditory nerve may be a target for lead toxicity, based on reports of reduced hearing acuity in children.[84] In the NHANES II survey in the United States, the association with blood lead was highly significant at all blood lead levels from 5 to 45 µg/dL ($p < 0.0001$) for children four to 19 years old, with a 10 to 20% increased likelihood of an elevated hearing threshold for persons with a blood lead level of 20 µg/dL compared with 4 µ/dL.[85] The NHANES II data also revealed that blood lead levels were significantly associated with the age at which infants first sat up, first walked and first started to speak. Although no threshold existed for the age at which the children first walked, thresholds existed at the 29th and 28th percentile of lead rank for the age at which the children sat up and spoke, respectively.[85]

Neurological Effects in Infants and Children

A number of cross-sectional and longitudinal epidemiological studies have been published that have considered the possible detrimental effects that exposure of young children to lead might have on their intellectual abilities and behaviour. These studies have been concerned with documenting effects arising from exposure to "low" levels of lead (i.e., <40 µg/dL), at which overt clinical symptoms are absent. Interpretation of these epidemiological data has often been contentious for a number of reasons, many of which have been discussed in the literature.[86,87] The validity of the conclusions made by the authors of these epidemio-logical studies has been shown to depend upon a number of factors,[87] including: 1) the statistical power of the study, 2) the effect of bias in the selection of the study and control populations, 3) the choice of the parameter used to evaluate the exposure to lead, 4) the temporal relation between exposure measurement and psychological evaluations, 5) the extent to which the tests utilized for evaluating neurological and behavioural parameters can be quantified accurately and reproducibly, and the extent to which the test results are strictly comparable with those from other studies, 6) which confounding covariates have been included or excluded in any multiple regression analysis, and whether it has been considered that some of these covariates may be interlinked, and 7) the effect of various nutritional and dietary factors such as iron and calcium intake.[88]

A number of cross-sectional studies exist in which due account has been taken of many of the above factors. In one of the earliest studies, by Needleman and colleagues, a group of 58 six- and seven-year-old children with "high" dentine lead levels (i.e., above 24 µg/g dentine; blood lead level 30 to 50 µg/dL) taken from a cohort of about 2100 American children performed significantly less well than 100 children from a "low" dentine lead group (i.e., below 6 µg/g dentine; mean blood lead level 24 µg/dL). The children's performance was measured using the Wechsler Intelligence Test in addition to other visual and auditory tests and teachers' behavioural ratings.[89] There was a significant difference ($p < 0.03$) of four points and a uniform downward shift in IQ scores between the "low" and "high" dentine lead groups. A child in the group with "high" dentine lead was three times more likely to have an IQ of 80 or lower than a child in the "low" dentine lead group. The results on IQ remained almost unchanged after further reanalysis using multiple regression rather than analysis of covariance and using the father's education instead of his socioeconomic status;[90] however, in a more recent review, the effect was claimed to be statistically significant only for children with the highest lead levels in dentine (blood lead level above 40 µg/dL).[20] In a follow-up study of these children 11 years later, children in the original "high" dentine lead group were significantly more likely than those in the "low" dentine lead group to have been involved in juvenile delinquency, to have quit school early and to have had other behavioural problems.[91]

The Needleman study served as a stimulus for a number of cross-sectional studies on lead and neuro-behavioural effects in children. A similar study in which dentine was also used as the indicator of exposure was carried out using a cohort of 400 British children.[92] There were several consistent but non-significant differences between the high and low dentine lead groups similar to those observed in the American study, with IQ decrements of about two points and poorer scores in behaviour indices. In the British study, mean blood lead levels in the "high" exposure group (15.1 µg/dL) were lower than the mean of the "low" group (24 µg/dL) in the American study, a possible explanation for the lack of statistical significance of the results. Results from studies on German children[93–95] were similar to those of the British study, in that the effect of lead on behaviour had only borderline significance ($p < 0.10$).

Another study[96] involving 500 Edinburgh school children aged six to nine years demonstrated a small (up to five points in the British Ability Scales) but significant ($p < 0.003$) negative relationship between blood lead levels and intelligence scores, reading skills

and number skills. There was a dose–response relationship in the range 5.6 to 22.1 µg/dL. The effect of lead was small (less than 1% of variance was due to lead) compared with several other of the 33 variables considered (including birth history and the mother's and father's socioeconomic status and general intelligence). Blood lead levels averaged 11.5 µg/dL (range 3.3 to 34.0 µg/dL). In contrast, a series of studies[97–99] on a total of about 800 British children with blood lead levels between 4 and 32 µg/dL showed no significant associations between blood lead levels and indices of intelligence and behaviour after socioeconomic and family characteristics had been taken into account. In accounting for their negative results[98] compared with results from an earlier study,[100] the authors pointed out that lead might have a noticeable effect only when other factors (particularly socioeconomic or home environment) leading to disadvantage are present.[98,101]

In a cross-sectional study in Lavrion, Greece, involving 509 primary school children living near a lead smelter, blood lead levels of between 7.4 and 63.9 µg/dL (mean level 23.7 µg/dL) were recorded.[102] When the IQ was measured using the revised Wechsler Intelligence Scale for Children and due account taken of 17 potential confounders, it was found that there was a significant association between blood lead levels and IQ, with a threshold at about 25 µg/dL. Attentional performance was also associated with blood lead levels using two different tests; in this case, however, no threshold level was found.

This study was part of a multi-centre collaborative international study with school-aged children sponsored by the WHO and the Commission of European Communities.[103] A more or less common protocol was adopted, and quality assurance procedures were followed for the exposure analyses. The Wechsler Intelligence Scale for Children for verbal and performance testing, the "trail-making test" and the German form of the Bender Gestalt test for visual–motor integration, the Vienna Reaction Device for delayed reaction time and general behaviour ratings were employed by some or all of the eight centres. Psychometric intelligence was negatively affected in five of the eight studies. The association with blood lead level was marginal, except in the Greek study (above) in which blood lead concentrations were high and a Danish study in which they were quite low. The most consistent associations were for visual–motor integration as measured by the Bender Gestalt test and for reaction performance as measured by the Vienna Reaction Device. Six of seven centres reported increased error scores on the Bender Gestalt test in association with increased lead burden (but statistically significant in only one case). Three of four centres reported disruption of serial choice reaction performance in the Vienna reaction test. The results of the remaining tests were inconsistent. The degree of association between lead exposure and outcome was very weak even in the statistically significant cases. (The complete report of this study was not available at the time of this analysis.)

The cross-sectional studies are on balance consistent in demonstrating statistically significant associations between blood lead levels of 30 µg/dL or more and IQ deficits of about four points. Although there were associations between lower blood lead levels and IQ deficits of about two points, these relationships were marginally statistically significant, except for the Edinburgh study, in which they were significant. It is particularly difficult to determine minimum levels (as measured in blood) above which significant effects occur.

A number of prospective (longitudinal) studies have also been described in the literature. Longitudinal studies have the advantage over cross-sectional studies in that more precise estimates of exposure can be made; in addition, the question of whether the effects are reversible can be investigated as well as the temporal sequence of causality. However, longitudinal studies also have certain disadvantages: for example, repeated psychometric testing may introduce artefactual results, and there may also be problems of bias associated with attrition within the study population.

The possible relationship of low-level lead exposure during the foetal period and in early childhood with later effects on infant and child development has been investigated in at least six prospective studies, in the United States (Boston, Cincinnati, and Cleveland), Australia (Port Pirie, Sydney) and Scotland (Glasgow). Broadly similar methodologies were used in all studies in order to facilitate comparisons. The Bailey Scales of Infant Development or subsets of the test were used to evaluate early cognitive development in verbal and performance skills in infants and young children, whereas the McCarthy Scales of Children's Abilities were used in most studies for older children. In all cases except Glasgow, the average maternal and/or umbilical cord blood lead concentration was less than 10 µg/dL (range 6.0 to 9.5 µg/dL).

In the Boston Lead Study, which was the earliest to report its results, three groups of infants and young children were selected from over 11 000 births and classified according to umbilical cord blood lead concentrations. The levels in the low, middle and high lead groups were less than 3 µg/dL, 6 to 7 µg/dL and 10 to 25 µg/dL (mean 14.6 µg/dL), respectively. Children were tested semi-annually from age six months to almost five years.[104,105] When 12 potential confounders were controlled for, a significant ($p = 0.006$) inverse relationship was demonstrated between foetal exposure, measured as lead levels in cord blood, and mental

development at age two, as measured using the Bailey Mental Development Index (MDI). There was no significant correlation with the infants' current blood lead levels, which were below 8.8 µg/dL in all cases. However, results of testing at almost five years, using the McCarthy Scales, showed an attenuation of this association. At 57 months, only the association between intelligence scores and blood lead three years previously, at age two, remained significant after controlling for confounding variables.[105]

In a longitudinal study involving 305 pregnant women in Cincinnati,[106] it was shown that, for both male infants and infants from the poorest families, there was an inverse relationship between either prenatal or neonatal blood levels and performance on both the Bailey Psychomotor Developmental Index (PDI) and the Bailey MDI at the ages of three and six months. The mean blood lead levels for newborns and their mothers were 4.6 and 8.2 µg/dL, respectively, and all blood lead levels were below 30 µg/dL. Multiple regression analysis for boys only showed that for every increment of 1 µg/dL in the prenatal blood lead level, the covariate-adjusted Bailey MDI at six months of age decreased by 0.84 points ($p \leq 0.01$). The inverse relationship of Bailey MDI with prenatal blood lead level disappeared at age one, because it was accounted for, and mediated through, the effect of lead on birth weight, but the Bailey PDI was still related significantly to maternal blood lead level.[107]

In a prospective study similar in design to the Boston study, undertaken at Port Pirie, a lead smelter town in Australia, a cohort of 537 children was studied from birth to four years.[108] The cohort was divided into four groups on the basis of maternal and umbilical blood lead levels, which ranged from a (geometric) mean of 4.3 to 14.9 µg/dL. The mean blood lead level ranged from 9.1 µg/dL at mid-pregnancy to 21.3 and 19 µg/dL at two and four years, respectively. The integrated postnatal average blood lead level was 19.1 µg/dL. At six, 15, 24 and 36 months, the developmental status of the child was assessed using the Bailey MDI; the McCarthy Scales of Children's Abilities was used at four years. At each age, a consistent but weak inverse relationship was shown between concurrent postnatal blood lead levels and McCarthy Scales scores, without consideration for confounding factors. Perinatal blood lead level was not associated in this way. Following the incorporation of 18 covariates that were considered potential confounders in the multivariate analysis, the integrated blood lead level showed the strongest inverse relation with the General Cognitive Index score (a subset of the McCarthy Scales) at age four years, which suggests that the detrimental effect of lead on child development is cumulative during early childhood. Repeated analysis restricted to children whose blood lead levels were below 25 µg/dL showed that the inverse relationship with the General Cognitive Index score was as strong for this group as for the cohort as a whole, demonstrating that there is no clear threshold below which a detrimental effect of lead on child development does not occur.

An equal number of prospective studies have shown no consistent association between mental development and blood lead levels, either in the perinatal period or in early childhood. A study carried out with extremely socially disadvantaged mothers and infants in Cleveland did not show any relationship between blood lead levels at any time and language development, the Bailey MDI or the Stanford-Binet IQ test at age three years after confounding factors were considered, the most important of which was the care-giving environment. In this cohort, half the mothers had alcohol-related problems, and the average maternal IQ was 79.[109]

A second Australian study has been carried out in Sydney on a relatively advantaged population of 318 mothers and children. No association was found between blood lead levels in the mother or the child at any age with mental or motor deficits at age four years after six covariates, including the HOME score (a measure of the care-giving environment), were considered. Moreover, there was no consistency with regard to the direction of the coefficients.[110] The third negative study was carried out in Glasgow, where the primary exposure was to high water lead, which was reduced dramatically by corrosion control measures shortly after the children were born. The cohort was divided into high, medium and low groups on the basis of maternal blood lead levels, with means of 33.1, 17.7 and 7.0 µg/dL, respectively. Although the expected decrements in scores in the Bailey MDI and PDI were observed at ages one and two years as lead exposure increased, they could be better explained by birth weight, home environment and socioeconomic status, as analysed by stepwise multiple regression analysis. This was true even when birth weight was removed from the analysis (it was lower in the high lead group).[111]

Results from the prospective studies have been somewhat inconsistent after the initial Boston study. It appears that prenatal exposure may have early effects on mental development, but that these effects do not persist to age four, at least not using the tests so far employed. There are indications that these early effects may be mediated through birth weight or other factors. Several studies indicated that the generally higher exposures of children in the 18- to 36-month age range may be negatively associated with mental development, but this, too, has not been confirmed in other studies.

Neurological Effects in Animals

Research on young primates also supports the view that significant ($p \leq 0.05$) behavioural impairment of the same type as that observed in children (measures of activity, attention, memory, distractibility, adaptability and learning ability) occurs at doses of lead given postnatally (for 29 weeks) that resulted in blood lead concentrations from 10.9 to 33 µg/dL.[112] These effects persisted into young adulthood after concentrations in the blood returned to 11 to 13 µg/dL and were maintained for the next eight to nine years.[113]

Carcinogenicity, Genotoxicity and Reproductive Effects

The carcinogenicity of lead in humans has been investigated in several epidemiological studies of occupationally exposed workers.[114–117] There was no excess of overall cancer deaths in two small studies, one with an observed:expected ratio of 0.87 on a total of 337 deaths from all causes[115] and the other with an observed:expected ratio of 0.59 on a total of 140 deaths from 1930 to 1977.[116] In the latter, however, there was a substantial excess of deaths from chronic renal disease (standardized proportional mortality ratio was 3.06 for 1930 to 1977, $p \leq 0.05$). A study on 7000 smelter and battery factory workers employed between 1946 and 1970 for one or more years indicated a slight but not statistically significant excess of deaths from cancer of the digestive and respiratory systems. Mean blood lead levels were 79.7 µg/dL for smelter workers and 62.7 µg/dL for battery workers.[118] A follow-up study[117] reported an excess of respiratory cancer deaths (observed:expected ratio of 1.14) in battery plant workers, but the potential confounding effect of smoking was not considered. The International Agency for Research on Cancer considered the overall evidence for the carcinogenicity of lead to humans to be inadequate.[114]

Renal tumours have been induced in rats exposed orally to high levels, 1000 ppm or more in the diet (approximately 50 mg/kg bw per day), of certain lead salts (lead acetate, subacetate and phosphate); tests on other salts were inadequate. Lead acetate also caused renal tumours in mice at 1000 ppm in the diet.[114,115,119] In one study, lead concentrations of 5, 8, 62, 141, 500, 1000 or 2000 ppm in the diet (approximately 0.3, 0.9, 3, 7, 27, 56 and 105 mg/kg bw per day) were fed to rats for two years. Renal tumours developed in male rats at 500 ppm (approximately 27 mg/kg bw per day) and above but only at 2000 ppm (105 mg/kg bw per day) in female rats.[120] As a detailed description of this experiment, including histopathology and systemic toxicity, has never been published, no further evaluation of it is possible; the U.S. Environmental Protection Agency[32] did not find this study adequate for developing a quantitative risk assessment for carcinogenicity.

The evidence for an effect of lead on genetic material is conflicting, but the weight of evidence suggests that some salts of lead are genotoxic. Lead chloride, lead acetate, lead oxide and lead tetroxide were inactive in mutation tests on a number of procaryotes and fungi, including *Salmonella typhimurium* and *Saccharomyces cerevisiae*. *In vitro* tests on human cells were positive for chromosomal damage in one case and negative in two others. *In vivo* short-term tests on mice, rats, cattle and monkeys were positive in three cases (dominant lethal test and chromosomal damage to bone marrow cells) but negative in five others. Cytogenetic studies in humans exposed to lead, usually with blood lead levels above 40 µg/dL, are also conflicting, with seven negative reports and nine positive reports of chromatid and chromosomal aberrations, breaks and gaps.[114,115]

Gonadal dysfunction in men has been associated with blood lead levels of 40 to 50 µg/dL,[121,122] and there may also be reproductive dysfunction in females occupationally exposed to lead.[20,115] Increased spontaneous abortion and rates of stillbirths have been associated with lead intoxication of workers in the lead industry.[115] A link has also been suggested for lower, environmentally encountered levels. Miscarriage and stillbirth rates were elevated in the Australian lead smelter town of Port Pirie in comparison with a rural area matched for other variables. Blood lead levels averaged 10.6 µg/dL for Port Pirie women and 7.6 µg/dL for the controls.[123] Exposure of pregnant women to lead also increases the risk of pre-term delivery. In the study of 774 pregnant women in Port Pirie who were followed to the completion of their pregnancy, multivariate analysis revealed that the relative risk of pre-term delivery rose more than fourfold when blood lead levels rose from 8 to >14 µg/dL. If cases of late foetal death were excluded from the analysis, the association became even stronger, with the relative risk due to lead exposure increasing to 8.9 when blood lead levels exceeded 14 µg/dL.[123]

Animal studies in rats lend support to the findings in humans, with effects at blood lead levels above 30 µg/dL on sperm counts and testicular atrophy in males and on oestrous cycles in females.[124,125]

In a survey of more than 4000 consecutive births, elevated cord blood lead levels were associated with minor malformations, such as angiomas, syndactylism and hydrocele in about 10% of all babies. The covariate-adjusted relative risk of malformation doubled at blood lead levels of about 7 to 10 µg/dL, and the incidence of

any defect increased with increasing cord lead levels across the range in the population, from 0.7 to 35.1 µg/dL.[126]

Classification and Assessment

The evidence for the carcinogenicity of lead in humans is inconclusive, because of the limited number of studies, the use of small cohorts leading to lack of statistical power and a lack of consideration of confounding variables. An association has been shown in animals between the ingestion of lead salts at high doses and renal tumours. Lead has been classified in Group IIIB—possibly carcinogenic to humans (inadequate data in humans, limited evidence in animals), according to the classification scheme of the Environmental Health Directorate of the Department of National Health and Welfare.

For compounds classified in Group IIIB, the acceptable daily intake (ADI) is derived on the basis of division of the NOAEL or LOAEL in humans or in animals by appropriate uncertainty factors, taking into account the equivocal evidence of carcinogenicity. For lead, there is also evidence from human studies that adverse effects other than cancer may occur at very low levels, and that a guideline derived for these effects would also be protective for the risk of carcinogenic effects.

The WHO[26] established a provisional tolerable weekly intake (PTWI) for lead for children of 25 µg/kg bw, equivalent to an ADI of approximately 3.5 µg/kg bw per day. This PTWI was established on the premise that lead is a cumulative poison and that there should be no increase in the body burden of lead from any source, thus avoiding the possibility of adverse biochemical and neurobehavioural effects in infants and young children. It was based on metabolic studies in infants[36,51] showing that a mean daily lead intake of 3 to 4 µg/kg bw was a NOAEL and was not associated with an increase in blood lead levels or in the body burden of lead, whereas a daily intake of 5 µg/kg bw or more resulted in lead retention. An unusually small uncertainty factor (less than 2) reflected the conservatism of the end point, the quality of the metabolic data and use of one of the most susceptible groups in the population.

Rationale

Because lead is classified in Group IIIB, the MAC for lead in drinking water is derived from the ADI as follows:

$$\text{MAC} = \frac{0.0035 \text{ mg/kg bw per day} \times 13.6 \text{ kg bw} \times 0.098}{0.6 \text{ L/d}} \approx 0.008 \text{ mg/L}$$

where:

- 0.0035 mg/kg bw per day is the ADI, as derived above
- 13.6 kg bw is the average body weight of a two-year-old child
- 0.098 is the proportion of total daily intake allocated to drinking water, taken from Table 1, showing recent average intake data.[14] Intake of lead from sources other than water has decreased substantially over the last few years because of the phasedown of the use of lead-soldered cans in the food industry and the phaseout of lead additives in gasoline, processes that are now almost complete
- 0.6 L/d is the average daily water consumption for a two-year-old child.[127]

The PQL for routine analysis of lead in drinking water is 1 to 10 µg/L, depending on other compounds that may also be present in some water supplies. Because the MAC should be measurable and achievable at reasonable cost, the MAC selected is 10 µg/L, or 0.010 mg/L, based on this PQL.

Because the MAC for lead is based on chronic effects, it is intended to apply to average concentrations in water consumed for extended periods; short-term consumption of water containing lead at concentrations above the MAC does not necessarily pose undue risk to health.

In order to minimize exposure to lead introduced into drinking water from plumbing systems, it is also recommended that only the cold water supply be used, after an appropriate period of flushing to rid the system of standing water, for analytical sampling, drinking, beverage preparation and cooking.

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