THE ROUTES AND MECHANISMS OF THE ELIMINATION OF LEAD ABSORBED BY MAN

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Introduction

In his report of 1933, Prof. Kehoe[1] was the first to demonstrate that lead was an inevitable component of all living matter, by virtue of the ubiquitous presence of this metal on the surface of the earth. Since that time much has been learned of the physiological and toxicological behaviour of lead in the animal organism from intensive research studies carried out in many countries of the world. Indeed it is probable that more active study has been devoted to this one element than to any other.

It is my brief in this report to consider the various routes by which lead is eliminated from the body, together with circumstances of pathology and body burden which may influence excretary mechanisms.

The lead balance studies of Kehoe,[2] reported in his Harben Lectures of 1961, established a clear relationship between the intake and output of lead in man in which the intake is very largely balanced by the output, resulting in a state of dynamic equilibrium of lead in body tissues.

Lead in Faeces

Kehoe[2] established that on average among the U.S.A. population about 300 µg. of lead is ingested daily (range 100 to 400 µg.) from food and beverages, of which 5-10% is absorbed into the body and the remainder excreted in the faeces unchanged. In his lead balance studies he determined that the quantities of lead ingested in food and beverages were substantially equivalent to the quantities of lead found in faeces. Some of the lead in faeces has probably been absorbed and re-excreted into the gastro-intestinal tract by biliary and pancreatic secretion, by gut resorption and from saliva. Also pulmonary muco-ciliary action may account for a return of lead from the pulmonary system, to add further to the total faecal content.

The report of the Swiss Leaded Gasoline Commission of 1961[3] provides evidence which supports the findings of Kehoe with respect to the quantity of lead ingested in the diet. Their estimate of 340 µg. per day is also close to that of Monier Williams who in 1949[4] reported a dietary intake of lead in Great Britain of 320 µg. per day, compared to an estimated daily intake of 500 µg. reported by him in 1938.[5] Horiuchi[6] estimated, in a report published in 1970, that the amount of lead ingested by Japanese adults varies between 230 and 320 ug. per day; the faecal lead content was determined at about 250 µg. per day.

The lead balance studies of Thompson[7], reported in 1971, reveal a mean daily lead intake from the diet of 274 ug. with a daily excretion in the faeces of 240 µg. in a small group of subjects in Northern England. These figures are a little lower than those reported by Kehoe and indicate a small negative imbalance in the faecal output compared to intake by ingestion.

Lead in Urine

The quantity of lead eliminated from the body in the urine has been estimated as approximately 10% of that found in faeces.[2,7] Kehoe's lead balance work[2] indicates a mean daily urinary excretion of 30 µg. Pb with a daily range of 10 to 80 µg. Thompson[7] showed a mean daily excretion in the urine of her subjects of 24.4 ug. Pb. The United States Public Health Service report of 1965[8] on a study involving 1700 subjects in three cities in the U.S.A., revealed a mean urinary lead excretion of 27 µg/litre, a figure comparable to that of kehoe[2], Thompson[7] and other investigators including Stopps[9], Goldwater[10], Lehnert[11], Barry and Oxley[12], and Niculescu et al.[13]

It has been reported that excessive exposure to lead may result in renal and vascular disease.

In an extensive review of the effects of lead on renal function, Goyer[14] discusses his findings and those of numerous other investigators. He makes the point that there is no evidence that current levels of lead in our present day environment results in any particular problem with regard to renal function.

In clinically overt acute lead poisoning it has been shown that the kidney undergoes a number of abnormal changes which include the development of intranuclear inclusion bodies, mitochondrial changes and altered renal tubular function, which are generally believed to be reversible, although there may be exceptions. The question remains whether a form of diffuse chronic renal disease may occur as a sequel to acute lead poisoning or prolonged excessive exposure to lead.

Renal excretion of lead is presumed to involve two routes, glomerular filtration and transtubular flow or excretion. The comparative importance of the two routes is not clear from the data. Teisinger (1966)[15] suggests that only a very small amount of ultrafilterable or diffusable lead in the plasma, estimated at 5% of the total lead in blood, is actually excreted by the kidneys into the urine. It has been suggested that some filtered lead may be reabsorbed as well as secreted by the tubular lining cells and with normal or low blood lead levels there is a net transfer of lead from the filtrate to the tubular lining cells.

Dinischiotu and co-workers (196)[16] have shown that urinary lead exists in two chemical forms, organic and inorganic. At normal blood lead levels nearly all urinary lead is in the form of inorganic sulphates and phosphates (Teisinger 1966)[15], suggesting that organically bound lead is reabsorbed by the tubules. However, as lead excretion is increased, particularly to levels associated with lead intoxication, as much as 40% of urinary lead may be bound to organic ligands (Dinischiotu et al 1960)[16].

Teisinger (1966)[15] found a linear correlation between blood lead and urinary lead levels in persons, when blood lead levels are in the normal range without known excessive exposure to lead. A similar relationship has been confirmed in lead workers with blood lead levels in excess of 40 µg/100 ml. (Selander and Cramer 1970[17], Barry and Oxley 1972[12]).

In the study by Barry and Oxley[12], over 500 adult males with no previous occupational exposure to lead and over 400 male adults with current occupational exposure were investigated. A crude correlation was determined between lead concentrations in blood and urine, but for a given blood lead level the urinary excretion rate was generally higher for occupationally exposed subjects than for those not occupationally exposed. When these results were subjected to linear regression analysis, however, the correlation coefficients, as expected, were low ($r = 0.18$ for the unexposed group and 0.30 for the exposed group). This study provides no more than a broad indication of a trend, when comparison is made of blood and urine lead concentrations among population groups.

It has been noted that increasingly excessive lead intake does not produce a proportionate increase in urinary excretion (Goyer)[14] and it is suggested that this indicates an increased retention of lead in body stores. From his experimental work on rats, fed on a diet containing 1% lead acetate for 10 weeks, Goyer[14] showed a progressive increase in renal lead content and intranuclear inclusion bodies. These bodies have been identified as lead-protein complexes and are found in the nuclei of proximal renal tubular lining cells in the presence of toxic blood lead levels. At very high levels of lead ingestion urinary lead does increase further. It is suggested that a maximal physiological renal excretion of lead may exist which is only exceeded by levels associated with severe renal tubular injury.

In acute lead poisoning the cells of the proximal convoluted tubules are most severely affected and demonstrate cloudy swelling and some degree of cellular necrosis. There is little evidence that the glomerulus is affected, although a recent report suggests that ultrastructural changes in basement membrane of epithelial cells may occur (Macadam 1969)[18].

Lead induced intranuclear inclusion bodies in renal rubular lining cells appear to be a response to excessive body burden of lead. Direct chemical analysis of isolated inclusion bodies confirms that they are composed of a lead-protein complex containing approximately 50 µg. of lead per milligram of protein. Lead within the inclusion bodies is 60 to 100 times more concentrated than whole kidney lead (Goyer 1970 b,[19] Horn 1970[20]).

Even in the kidneys of control animals, i.e. rats, most of the lead is contained in the cell nuclei and in lead poisoned rats is concentrated in the inclusion bodies. In the course of transtubular flow a portion of lead enters the cell nucleus where it becomes bound to the inclusion body in a non-diffusible form. It is suggested by Goyer[14] that this mechanism must serve to reduce the cytoplasmic concentration of lead and toxic effects on cellular metabolism and so may be relevant to man's adaptation to his chronic body burden of lead, as well as providing a useful index in the diagnosis of lead poisoning, by renal biopsy.

Goyer et al (1968)[21] have postulated that the renal tubular dysfunction observed in lead poisoning is related to the mitochondrial effect of lead. The increase in lead content of mitochondria is small, but in lead poisoned rats the mitochondria in the basilar portion of proximal renal tubular lining cells are swollen and distorted in shape and orientation. On isolation they also show impairment of respiration and phosphorylation. Similar changes have been noted in liver cells (Watrach 1964)[22] and reticulocytes in bone marrow (Bessis and Jenson 1965)[23] in lead-poisoned animals, and it is suggested that this is a factor in producing the clinical symptoms of lead poisoning.

Several investigators have demonstrated aminoaciduria, glycosuria and hypophosphataemia to be associated with clinical lead-poisoning. (Wilson et al 1953,[24] Marsden and Wilson 1955,[25] Chisolm 1962,[26] Goyer et al 1970 a).[27]

These defects might be anticipated in lead poisoning because of the morphological changes observed in the proximal tubular lining cells where resorption of these substances from glomerular filtrate normally occurs. Restoration to normal function has been noted following treatment with chelating agents and the abatement of clinical symptoms, which implies restoration of normal morphology. This is an important observation relative to the long-term or chronic effects of lead on the kidney, which has yet to be confirmed experimentally. (Goyer 1971)[14]

Chronic lead nephropathy in man following many years of excessive exposure to lead, has been reported in the medical literature on numerous occasions in the past. (Oliver 1914,[28] Aub et al 1925[29] and Purdy 1886.[30]). Renal pathology includes tubular atrophy and dilatation with interstitial fibrosis and progressive contraction of kidney size with subsequent sclerosis of glomeruli. These findings are not specific to lead intoxication and the role of lead remains uncertain.

The work of Nye (1929),[31] Henderson (1954)[32] and Emmerson (1963)[33] in Queensland, Australia, indicates that chronic renal disease can occur following overt childhood lead poisoning.

In 1929 Nye[31] reported that of 34 persons with a history of severe childhood lead poisoning with central nervous system symptoms, 29 developed chronic nephritis in young adulthood.

In a follow-up study of 401 children from Queensland, Australia, who had suffered from lead poisoning, Henderson[32] reported in 1954 that 108 were found to have died in later life, between the ages of 5 and 40 years, from disease of renal and vascular cause. Of this number 94 died from chronic nephritis. These figures far exceed the expected mortality from vascular and renal disease in the population of Queensland, by an approximate ratio of 25 to one.

In his study reported in 1963, Emmerson[33] determined that 32 patients with chronic renal disease, which he attributed to childhood lead poisoning, showed increased lead excretion following the administration of the chelating agent calcium disodium ethylene diamine tetra-acetic acid, suggesting evidence of increased residual body lead burden.

Research workers in the U.S.A. have been unable to confirm the findings of the Australian investigators. In a follow-up study of 139 subjects in Massachusetts, U.S.A., with histories of well-documented plumbism in childhood 20 to 35 years previously, Tepper[34] found only one to have died from chronic renal disease. He concludes that the different conditions existing in Massachusetts and Queensland may account for this discrepancy.

In another follow-up study by Chisolm[35] reported in 1970, among 62 subjects who had suffered lead poisoning in childhood in Baltimore, none showed evidence of renal disease or increased lead excretion following the EDTA mobilisation test. Chisolm[35] suggests that lead toxicity in the Australian children must have been of a different type, with a more protracted course, than that experienced by the American children.

In a study by Radosevic et al[36], reported in 1961 of 53 patients suffering from lead poisoning with histories of exposure varying from two months to 35 years, two cases, in which exposure to lead was the longest and the most intense, developed permanent changes of chronic nephropathy. A further 23 patients showed temporary functional renal lesions, one showed a persistently raised blood pressure, and two a temporarily raised blood pressure in the acute stage of poisoning. These investigators did not record the level of lead in the urine of their subjects. They concluded that lead intoxication can cause renal lesions which are for the most part functional and temporary, but in cases of long and severe exposure, and repeated lead intoxication, irreversible organic renal lesions seem possible. They ascribed the disturbance of renal function observed

in their series of cases to disordered intrarenal circulation due to the spastic effect of lead on intrarenal blood vessels and to a direct toxic or indirect hypoxic effect of lead on the tubules.

An association between excessive lead exposure and gout has been cited by a number of investigators in the past. Several case reports of the 19th century linking lead with gout are summarised by Ludwig in his report of 1957.[37] In 1886 Lorimer[38] associated gout with lead poisoning. A review by Aub et al (1925)[29] questions the lead-gout relationship, but a report by Emmerson[39] (1968) indicated that 16 individuals out of a group of 33 with lead nephropathy, suffered from gout. Morgan et al (1966)[40] reported that in 13 adults suffering from chronic lead poisoning and unexplained renal failure, following the consumption of illicitly distilled alcohol, six had hyperuricaemia and gout. However it could not be proven unequivocally that lead present in the alcoholic beverage was responsible for the observed pathological changes.

Several studies of workers in lead industries have suggested a correlation between excessive lead exposure and renal hypertension. Cantarow and Trumper[41] reported in 1944 that an increased incidence of hypertension appeared to correlate with lead exposure. However, relationship of hypertension to renal disease was not established.

Dingwall-Fordyce and Lane[42] in 1963 reviewed causes of death among men eligible for pension (65 years of age) who had worked in an accumulator factory in England between 1926 and 1960. They found an excess of deaths from cerebro-vascular lesions, about twice the normal expectancy, in workers heavily exposed to lead for more than 25 years, who had consistently excreted lead in their urine in excess of 200 µg/litre. No renal basis for the hypertension was demonstrated and no difference in deaths from the normal expectancy was noted in workers whose excretion of lead in urine was less than 200 µg/litre.

In a study by Lilis et al[43] in Bucharest, reported in 1968, renal failure was found in 17 patients who had had several episodes of abdominal colic and occupational exposure for more than 10 years. Thirteen of these patients had arterial hypertension with evidence of renal disease preceding the rise in blood pressure by several years. In a report by Cramer and Dahlberg[44] in 1966, however, no excessive incidence of hypertension was noted among workers in a Swedish accumulator factory in which 265 workers had been employed for more than 10 years. It has been suggested (Goyer,[14] Malcolm[45]) that the surveillance of workers and improved working conditions may account for the failure of these and other investigators, including Belknap[46] in 1936 and Lane[47] in 1949, to find an increase in frequency of hypertensive and chronic renal disease.

It has been reasoned that if lead poisoning can produce hypertension in man it should also occur in lead poisoning in experimental animals. Such studies, however, have yielded inconsistent results. Fouts and Page[48] in 1942 failed to produce hypertension in lead poisoned dogs; Griffith and Lindauer[49] in 1948 showed a progressive increase in systolic blood pressure of rats over a two-month period, but these results were not confirmed with similar studies by Pardoe,[50] reported in 1952, and Padilla et al[51] in 1969.

The development of renal adeno-carcinoma has been reported by a number of investigators in rats fed for prolonged periods, of one year's duration, on a diet containing high concentrations of lead (1% lead acetate). (Goyer 1971,[14] Zollinger 1953,[52] Kilham et al[53] 1962, Boyland et al[54] 1962, Van Esch et al[55] 1962, Hass et al[56] 1967, Mao and Molnar[57] 1967). Lead induced renal tumours have not been observed in experimental animals other than the rat, and less frequently the mouse (Van Esch and Kroes[58] 1969). The tumours do not appear to have any obvious or immediate relevance to man, since renal tumours have not been noted in industrial workers with chronic lead exposure (Dingwall-Fordyce and Lane,[42] 1963).

Lead in Sweat

The elimination of lead from the body in sweat has not been studied to any great extent. In his lead balance studies Kehoe[2] (1961) found the lead content in the urine of his subjects to diminish in the Summer months and to increase in Winter. In explanation he suggested the difference might be accounted for by loss of lead in sweat and has estimated that the total loss of lead by this route may be roughly equivalent to that excreted in urine. Shiels[59] (1954), from experimental work on human subjects in Australia, deduced that the quantity of lead eliminated in the sweat is dependent on climatic conditions and in hot climates, with profuse sweating, may greatly exceed that removed by the urine. The loss of lead in surface skin desquamation is not considered to be an avenue of excretion of any importance.

Lead in Hair and Nails

Hair and nails have been found to contain varying concentrations of lead, considerably in excess of those of body soft tissues. From a series of post-mortem subjects[60] we have found wide differences in the lead concentrations in hair between individuals, which do not reflect the concentrations found in the soft tissues. In 53 hair samples from adults, 34 of which were from male subjects, we found the range of lead concentrations to lie between 0.70 and 1,000 ppm with a mean value of 34.46 ppm. If two samples of the highest values, of 325 ppm in a female and 1,000 ppm in a male, are withdrawn from the total

number of samples, the range becomes 0.70 - 83 ppm and the mean value 9,83 ppm. The 33 males represented in the total showed a mean value of lead in hair of 8.92 ppm (range 1.00 - 83.00 ppm) and the 18 females a mean value of 11.49 ppm (range 0.70 - 55.00 ppm). On the basis of these findings male and female subjects do not appear to show a significant difference in the concentrations of lead found in hair. In another series involving 32 male lead workers, we found a mean lead concentration in hair distal to the scalp to be 517 ppm (range 24-1880 ppm) and in hair proximal to the scalp to be 402 ppm (range 24-1830 ppm). The mean blood lead concentration of this group was 30 µg/100 grams and the mean urinary lead concentration was 81.70 µg/l.

The results from our occupationally exposed group suggests that much of the lead found in hair is from sources external to that which might be attributable to body elimination, and so does not reflect the body burden of lead. The sulphydril groups, of which an abundance are present in hair, have a strong affinity for lead and it seems likely that the lead present in the atmosphere, much greater in a lead industry than in the general ambient air, is contributing directly to the concentrations of lead found in hair.

The concentrations of lead found in nails are generally less divergent and of a lower order of magnitude than those found in hair. Among a group of 40 adult subjects at post-mortem, with no occupational exposure to lead, of which 11 were female, we found a mean value of lead in nails of 4.96 ppm with a range of 0.65 - 15.00 ppm. The mean value for the 29 male subjects was 4.73 ppm and the 11 female subjects 5.50 ppm.

There does not appear to be a correlation between the concentration of lead in nails and the total body burden of lead in subjects with no occupational exposure, either for groups or in individuals. In our post-mortem series we have compared the lead concentrations in nails with the total soft tissue body burden and with individual body tissues, including bone, liver, kidney and blood, and been unable to determine any correlation of statistical significance. We obtained nail samples from three of our six subjects with occupational exposure to lead and found the concentrations of lead in their nails to be 14, 28 and 44 ppm respectively. These concentrations exceed, for the most part, the concentrations we found in non-occupationally exposed individuals.

In our view the lead found in hair and nails is not a good perameter for the accurate estimation of lead absorption. It may provide broad evidence of environmental exposure of relatively recent origin, but because of the real possibility of external contamination and the activity of SH groups, it cannot be regarded as a reliable measure of lead intake which could supersede the measurement of lead in blood and urine or of coproporphyrins and ALA in urine.

Lead in Bone

A further route for the elimination of lead, in the context of its availability for physiological participation in bodily functions, lies in the ca acity of bone to retain lead within its matrix. Post-mortem studies[60,61] have shown that lead accumulates in bone, particularly in the dense tubular areas, with age. In our series we examined four types of bone, rib, tibia, calvarium and petrous temporal. The lowest concentrations of lead were found in rib, of high vascularity, and the highest concentrations in the almost avascular dense petrous temporal bone. The mean values of the lead concentrations in 45 samples of petrous temporal bone and 94 samples of rib, from adults with no occupational exposure to lead, were 32 ppm and 8,7 ppm respectively. Seven male adults in our series with histories of occupational exposure to lead, two samples of petrous temporal bone showed a mean lead value of 85.5 ppm and six samples of rib a mean value of 36.8 ppm.

The concentrations of lead in the soft tissues remained substantially constant with age in both the occupationally exposed and unexposed subjects, and did not reflect the concentrations found in bone. The occupationally exposed group showed marginally higher concentrations of lead in their soft tissues than those of the non-occupationally exposed group.

The lead retained in the deep matrix of bone, would seem to be fixed and not available to other body tissues, other than at a rate of release which is inconsequential in relation to the soft tissue equilibrium.

In our post-mortem studies we found the mean value of the total body burden of lead in men aged over 50 years to be 222 mg. of which 214 mg. was in bone. Thompson[6] has calculated that over 60 years the amount of lead retained daily would have been approximately 10 ug, which is very close to the average amount of lead which was retained daily by the individuals in her lead balance studies. Her findings indicated that the daily retention is normally less than 10 % of the total lead intake and more than 90 % is effectively eliminated from the body. Any accumulation of lead in bone will depend upon past exposure, which may fluctuate widely in the course of a life span, and it is unlikely that a quantitative assessment of retention can be accurately determined on a day to day basis.

Pulmonary Lead

Knowledge concerning the contribution of respired air to the total amount of lead entering the body is insufficient to allow anything better than general approximations. This is the opinion stated in the report of the National Research Council of the National Academy of Sciences[62] (1971). The report continues as follows:-

"A reasonably good estimate can be provided for the fraction of the inhaled lead that is deposited in the airways, but very little is known concerning its fate once deposited. Lead particles in the nasopharyngeal region may be swallowed or ejected by nose-blowing or expectoration. Particles deposited in the trachea and bronchi may migrate up to the pharynx by muco-ciliary transport to be swallowed or expectorated later, or they may enter the systemic circulation. Even particles deposited in the alveolar bed may be phagocytised by migratory macrophages and conveyed back up the airways to be swallowed and passed through the gastro-intestinal tract, largely unabsorbed."

Observations by Mehani[63], Kehoe[2] and Nozaki[64] suggest that the deposition in the respiratory tract of lead from the air is approximately 37%. These studies were undertaken at concentrations of lead in air greatly in excess of these in the general range to which the public is currently being exposed.

In a very recent report by Lawther et al[65] (1972) electron microscope studies of lead particles in automobile exhausts indicate that the shape of the particles are far from well-defined. They are for the most part notably smaller than has previously been thought probable and form aggregates of extreme and diverse shape, ranging in size of less than 0.01 μm. to greater than 1 μm. The effective density of these aggregates for aerodynamic purposes is quite unknown, as is their behaviour with respect to diffusion, although it seems possible that their Brownian diffusion rates will be lower, because of greater surface area, than for those of compact particles of the same volume. These authors consider that diffusion is probably the most important mechanism by which particles may be propelled to the surface of the lung, from where they can be taken up and absorbed into the blood. There is no agreement as to what fraction of inhaled lead is deposited in the various parts of the respiratory tract. It is considered by Lawther et al[65] that the most reliable data produced so far on the deposition of inhaled particles are probably those of Davies and Muir[66] who reported in 1967 to find the deposition of spherical particles of diameter 0.5 um to be 10-12%, under conditions of light physical exertion.

More extensive studies are needed in which the particle size, the nature of the lead compounds involved and varying rates and depths of respiration are considered, in respect of concentrations of lead in present day ambient atmospheres. The percentage of lead absorbed from the pulmonary system, of the lead that may be deposited following inhalation, is not known. Tentative estimates have been made of very considerable variation, but none of the studies

so far undertaken provide clear and reliable evidence of the absorptive capability of lung tissue for lead in the various forms in which it may occur. Lawther (1972)[65] has stressed the need to extend work on the sources and biological availability of airborne lead and on the variations in body burden with exposure to it. Until such time as more definitive answers are available, estimates of the contribution of intake via the pulmonary system to the body burden of lead can only be speculative.

Biological half-time of lead

Information from published data relating to the biological half-time of lead in the body seems to be scanty. Roach[67] in a report in 1966 estimated the biological half-time of lead to be six months, based on calculations from Kehoe's lead balance studies (Harben lectures).[2] His estimate was based on a conservate lowest conceivable limit, to ensure a maximum margin of safety. When the half-time of a substance is very long, as in the case of lead, the body burden is directly proportional to time as well as concentration - that is, to the total dose of the substance - and varies very little around its average value. If the dose remains the same per day the mean body burden at equilibrium is the same, whether the concentration is held constant or varies. Roach indicates that when the duration of exposure is large the rate of elimination equals the rate of intake.

For substances with short biological half-times, the body burden is directly proportional to the concentration and does not increase with the duration of exposure.

Roach[67] maintains that for substances with a long biological half-time the body burden depends merely on dose. This allows for greater variation in concentration to be tolerated without change in the body burden. He has estimated that an optimum air sampling period for any substance is one-tenth the biological half-time for that substance. With respect to lead, air sampling periods totalling 2½ weeks in 6 months would therefore be appropriate.

The risk of exceeding the body burden, on exposure to a variable air concentration, can be predicted if the steady concentration and the body burden half-time are known. A range of constant concentrations exists for any substance, any one of which will not produce adverse effects from continued exposure for 24 hours per day. The highest of these concentrations might be called a threshold concentration, which could be of use in studies of community air pollution.

Roach[67] has shown that, provided the duration of the individual sampling is no more than one-tenth the half-time, the coefficient of variation of man's body burden will be no more than one-fifth the coefficient of variation of the

air concentration. No matter what the nature of the size frequency distribution of the air concentration, the fluctuations of the body burden from time to time tend to have a normal distribution as the time scale of the fluctuations becomes small in comparison with the biological half-time. This means that the risk of exceeding the threshold body burden at any time would be less than one in a million.

It is reasonable to infer from Roach's study, as was indicated by Williams[68] in 1971, that the long biological half-time of lead in the body renders it less hazardous than if the half-time were of shorter duration, for it allows time for measurement, assessment and suitable action if necessary, both in the individual and the group.

Summary

To summarise, it does appear that the main avenue of excretion of lead is through the intestinal tract, where the bulk of the intake by ingestion, up to 90%, is excreted unabsorbed. Excretion via the kidneys accounts for up to a further 10% and sweat may account for a similar amount, depending upon climatic conditions. Hair and nails are also significant avenues of elimination, but may not represent a true picture of the lead that has been absorbed. Bone retention may account for a further 10 µg. Pb/day of the lead absorbed, based upon the results of long-term absorption studies. The contribution of the pulmonary route of absorption and possible elimination, has yet to be resolved. The half-time of lead in the body has been conservatively estimated at 6 months and more studies of this aspect of the body burden of lead would be of value.

High level lead absorption resulting in overt poisoning has been shown to be conducive to renal disease and hypertension. There is no evidence that current levels of lead in the present day environment are a cause of ill-health, but more studies relevant to low level exposure, as experienced by the general population, are desirable towards the definition of a level of lead at or below which no conceivable harm could occur in any section of the population.

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