Environmental Lead in Perspective

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1 Lead Pollution:—The Nature of the Problem

Lead naturally occurs in the form of mineral deposits, mainly as galena (lead sulphide). The finely ground ore may be concentrated by the process of flotation and lead subsequently extracted by smelting. This simple isolation procedure, together with the fact that lead does not readily corrode, has a low melting point, and is malleable and relatively inert, make it an ideal material for many applications. Indeed lead has been used to the benefit of man since pre-Christian times. However, it was recognized as long ago as the second century B.C.[1] that working with lead was a health hazard. Nevertheless this knowledge did little to protect the slaves in the mines of ancient Rome, as public concern was not aroused. Later during the technological revolution of the 18th and 19th centuries, the increased widespread use of lead in manufacturing processes, resulted in industrial lead poisoning becoming a serious cause of ill health and death. Subsequently a more enlightened approach to the problems of public health brought about the improved techniques of fume and dust control at work places; recent legal requirements including regular medical examination of employees have helped to virtually eliminate the incidence of fatal occupational lead poisoning.[2]

Modern day consumer use of lead throughout the industrialized world has more than doubled during the last thirty years (Table 1).[3,4,5] America today produces approximately a million tons of lead annually, or about 10 lbs per inhabitant. The battery industry is one of the biggest single users of lead, but leaded petrol accounts for more than 20% of the total lead consumed per year.[5] [Tetraethyl lead (TEL), tetramethyl lead (TML) and mixed lead alkyls are used as anti-knock additives to improve the combustion characteristics of petroleum.] In Britain, the metallic uses of lead, with the exception of battery production, have marginally decreased whereas the manufacture of lead alkyls has significantly increased (Table 2).[4,5] The total lead alkyl figure is somewhat misleading however as three quarters of the production is exported.

Biological interest in lead was initiated as a result of its pronounced toxic properties as an industrial hazard to man. The concentration of lead necessary

[1] Nicander, *Alexipharmacia*.
[2] Ann. Reports of H.M. Insp. Factories on Ind. Health.
[3] *Metallgelellschaft*, 1938—1959.
[4] World Bureau of Metal Statistics, 1942—61.
[5] World Metal Statistics, 1961—78.

Table 1 *World Refined Consumption*/(Thousand Metric Tons)[3–5]

	U.K.	*Europe*	*U.S.A.*	*World Total*
1940	348	747	563	1653
1945	240	374	704	1325
1950	236	640	803	1856
1955	285	880	735	2262
1960	286	1061	647	2633
1965	312	1197	753	3179
1970	262	1358	826	3805
1975	238	1169	811	3878
1977	241	1380	988	4436

Table 2 *U.K. Uses of Lead*/(Thousand Metric Tons)[4,5]

	1951	1961	1971	1977
Batteries	62	68	101	68
Tetraethyl	5	25	44	55
Sheet and Pipe	72	73	54	47
Cables	92	97	52	31
Oxide and Other Compounds	34	23	31	31
Alloys	15	21	17	13
Solder	12	16	14	14
Shot	6	6	6	8
White Lead	21	8	3	2
Collapsible Tube	6	4	2	1
Rolled and Extruded Products	—	7	2	1
Miscellaneous	17	20	20	19
TOTAL*	341	369	346	290
Refined Lead	236	276	277	241

*Total includes refined lead plus scrap and remelted lead.

to produce frank lead poisoning is well documented.[6–9] It still remains a controversial question however, whether or not the levels of lead found in our modern environment, to which the general public are exposed, are entirely

[6] R. A. Goyer, *Amer. J. Path.*, 1971, **64**, 167.
[7] R. A. Goyer and J. J. Chisolm, 'Metallic Contaminants and Human Health', ed. D. H. Lee, Acad. Press, 1972, 57.
[8] R. A. Kehoe, *Pharmac. Ther.*, 1976, **1**, 161.
[9] H. S. Posner, *Envir. Health Pers.*, 1977, **19**, 261.

safe.[10–14] Attention has more recently therefore been confined to the biological consequences of long term exposure to lesser amounts of lead present in our environment, and the chemical factors that influence the retention of lead in man.

2 Atmospheric Lead

In the early part of this century smelting and refining were the main sources of atmospheric lead. Today the combustion of leaded petrol is the greatest single contribution to lead in our atmosphere. Approximately 90% of airborne lead in the United States, that can be traced to its source comes from the combustion of petrol.[15] When subjected to elevated temperatures and pressure of combustion, the lead alkyl compounds in petrol are converted to lead oxides which inhibit 'engine knock'. The lead oxides react with other fuel additives and are subsequently emitted in the car exhaust. The chemical composition of exhaust particles appears to be related to particle size. The major lead products emitted in particles of 2—10 μm equivalent diameter are, lead bromochloride ($PbCl \cdot Br$), the alpha and beta forms of ammonium chloride and lead bromochloride ($NH_4Cl \cdot 2PbCl \cdot Br$; $2NH_4Cl \cdot PbCl \cdot Br$) together with minor quantities of lead sulphate ($PbSO_4$) and the mixed oxide ($PbO \cdot PbCl \cdot Br \cdot H_2O$). The particles subsequently lose halogens, (a process which appears to be photochemically enhanced), and become smaller and more soluble (especially in the presence of SO_2). Several reports have suggested that the lead halogen compounds are then converted to oxides and/or carbonates.[16,17]

The phased reduction in the lead content of petrol in the U.K. from the 1971 limit of 0.84 gl^{-1} to 0.46 gl^{-1} today has coincided with an increase in traffic density. Therefore despite the fact that the potential hazard from industrial exposure and emissions has decreased over the last fifty years, the total amount of atmospheric lead man is subjected to from day to day has not diminished. The concentration of lead in ambient air is closely related to traffic density.[18,19] It is highest in cities and towns and decreases towards the suburbs and rural districts. These concentration gradients are subjected to daily as well as seasonal cycles.[20,21] The precipitation of lead from the atmosphere depends on its physiochemical form and on meteorological factors that help to dissipate it. About half the lead containing particulate matter from car exhausts is removed from the air by

[10] C. Patterson, *Arch. Envir. Health*, 1965, **11**, 344.
[11] D. Bryce-Smith, *Chem. in Brit.*, 1971, **7**, 54.
[12] D. Bryce-Smith, *J. Roy. Soc. Arts.*, 1973, **121**, 120.
[13] A. Mills, *Chem. in Brit.*, 1971, **7**, 160.
[14] A. Beattie, M. Moore. A. Goldberg, M. Finlayson, J. Graham, E. Mackie, J. Main, D. McClaren, R. Murdoch, and G. Stewart, *Lancet*, 1975, i, 589.
[15] Data from Nat. Inventory Air Pol. Emission and Control 1972.
[16] Report. Inter-Deptal Working Gp. Heavy Metals. HMSO 1974.
[17] G. Ter Haar and M. Bayard, *Nature*, 1971, **232**, 553.
[18] R. Daines, H. Motto, and D. Chilko, *Envir. Sci. and Tech.*, 1970, **4**, 318.
[19] L. Tepper, *Internat. Symp. Envir. Lead Res. Zagreb Arhiv. Za. Higijenu I Toksikologiju*, 1976, **26**, 139.
[20] T. Chow and J. Earl, *Science*, 1970, **169**, 577.
[21] P. Lawther, B. Commins, J. Ellison, and B. Biles, 'Lead in the Environment', ed. P. Hepple, Inst. of Petroleum, London, 1972, 8.

gravity within a few hundred feet of roadways.[18] The remaining lead is present in aerosols, which are largely airborne until removed by precipitation.[22] The mean residue time of lead in the atmosphere is between 7—30 days[23] (mean residue time is the interval required for the concentration of lead to drop to half its original value). The different microclimate conditions in the vicinity of traffic are therefore of potential significance to the health of the people, who spend their working day in them.

Despite the rapid rise in the consumption of lead alkyls, the dispersion and rapid precipitation of airborne lead has generally resulted in only a relatively slow rise in the concentration of lead in urban atmospheres. The Gravelly Hill motorway interchange near Birmingham (Spaghetti Junction) is of particular interest as almost a million vehicles a week pass through this area and emit about 9.5 kg of lead over a radius of a quarter of a mile. The airborne lead concentrations at Gravelly Hill in 1971 were within the range 0.99—2.19 $\mu g/m^3$ with a mean of 1.5 $\mu g/m^3$;[24,25] these levels have not substantially changed over the last five years. The values are similar to other Birmingham city street measurements and indicate the beneficial effect of elevated motorways with sufficient ventilation to disperse the lead.

Many investigators have published measurements of the concentration of airborne particulate lead, but the figures are not comparable to one another because the measurements are critically dependent on the sampling site, the period in the day and the season in which the samples were collected as well as the length of time of sampling[21] (see Table 3). Generally in Britain there appears to have been little change in airborne lead levels over the last five years. At the kerbside of busy city streets (10 000+ vehicles per day) the concentration of airborne particulate lead lies within the range 2—5 $\mu g/m^3$; city areas not immediately influenced by traffic have mean levels less than 1 $\mu g/m^3$.

3 Inhalation of Lead

The expected atmospheric contribution to the total intake of lead by an average man engaged in light activity will be extremely variable and will depend upon his rate of inhalation and the concentration of lead in his working and domestic environment (see Table 4).[28] The potential respiratory intake for infants is greater than for adults on a body weight basis;[29] the significance of this finding remains in doubt due to lack of information concerning the metabolism of lead in infants.

[22] A. Lazrus, E. Lorange, and J. Lodge, *Envir. Sci. and Tech.*, 1970, **4**, 55.
[23] C. Francis, G. Chesters, and L. Haskin, *Envir. Sci. and Tech.*, 1970, **4**, 586.
[24] A. Archer and R. Barratt, *Roy. Soc. Health J.*, 1976, **96**, 173.
[25] J. Butler, S. Macmurdo, and D. Middleton, *Envir. Health.*, 1975, **1**, 24.
[26] P. Robinson, Lanchester Poly., Personal Communication, 1977.
[27] A. Apling, Warren Spring Lab. Herts., Personal Communication, 1977.
[28] 'Biological Effects of Atmospheric Pollutants—Lead', Nat. Acad. of Science, Washington D.C., 1972.
[29] W. Spector, 'Handbook of Biological Data', 1956, 267.

Table 3 *Air Lead Concentrations*/(μg/m^3)

	Mean	*Range*
[a]Birmingham Airborne 1975[24]	0.75	0.41—1.40
[b]Bart's Medical College Roof London 1971[19]	1.2	0.9 —2.3
Coventry Airborne 1976[26]	0.47	—
[c]Birmingham Roadside Site 1975[24]	2.3	12.1 maximum
[d]Fleet Street, London 1971[21]	6.3	4.9 —8.7
[e]Warren Springs 5-Town Survey 1977[27]		2.0 —5.0
[f]Gravelly Hill Interchange Birmingham 1971[25]	1.5	0.99—2.19

[a] Mean value estimated from weekly mean concentrations at 16 sites not exposed predominantly to road traffic emissions.
[b] Pb concentration measured between April—October 1971 on weekdays between 8 am—7 pm.
[c] Mean daily value from one roadside site in Birmingham; part of Warren Springs Five-Town Survey.
[d] As for *b*
[e] Selected roadside sites at London (× 2), Birmingham, Cardiff, Glasgow, and Cambridge.
[f] Samples collected at 12-hourly intervals. Measurements between 1971 and 1976showed both seasonal and diurnal variation; however the mean air concentration has not substantially altered over this period (J. Butler, Aston University. Personal Communication).

Table 4 *Potential Daily Intake of Lead by Inhalation*[28]

	Air Inhaled	*Concentration of lead in air*		
		0.1 μg/m^3	0.5 μg/m^3	2.5 μg/m^3
8 hr working, light activity	9.6 m^3	0.96	4.8	24.0
8 hr non-occupational activity	9.6 m^3	0.96	4.8	24.0
8 hr resting	3.6 m^3	0.36	1.8	9.0
TOTAL*	22.8 m^3	2.28	11.4	57.0

*Of a 'standard man' weighing 70 kg, 20—30 years old. 175 cm tall, and having a surface area of 1.8 m^2

n.b. A 1-year old child inhales approx. 6 m^3 of air per day[29]

The fraction of lead retained by the human body will vary according to the particle size and the solubility of the inhaled lead. The size of particulate lead in urban atmospheres is usually in the order of 0.15—0.4 microns with a mean of approximately 0.25 microns.[30,31] A proportion of inhaled lead of large diameter (> 0.5 microns) will be trapped in the upper respiratory tract, cleared by ciliary action and swallowed. Lung deposition has been estimated to be approximately 35—50%.[28,31] However the concentration of lead used to make these laboratory determinations was greatly in excess of real atmospheric conditions (for example

[30] R. Lee, R. Paterson, and J. Wagman, *Envir. Sci. and Tech.*, 1968, **2**, 288.
[31] H. Waldron and D. Stofen, 'Sub-clinical Lead Poisoning', Acad. Press, 1974.

see Table 5). The amount of lead absorbed is also difficult to estimate. In the case of aerosols generated in the laboratory approximately half the retained lead

Table 5 *Deposition of Lead Inhaled by Man*

10 Respirations/min 1350 cc Tidal Air		30 Respirations/min 450 cc Tidal Air	
Particle Diameter (μm)	*Particle Deposition* (%)	*Particle Diameter* (μm)	*Particle Deposition* (%)
1.0	63.2	1.0	35.5
0.6	59.0	0.6	33.5
0.4	50.9	0.4	33.0
0.2	48.1	0.2	29.9
0.1	39.3	0.1	27.9
0.08	40.0	0.08	26.5
0.05	42.5	0.05	21.0

Adapted from K. Nozaki, *Ind. Health* (*Japan*), 1966, **4**, 118.
(*n.b.* Lead Concentration 10 mg/m^3)

is absorbed.[32,33] Nevertheless, in 1974 the Working Group on Heavy Metals[16] considered that in urban areas of Britain the amount of lead absorbed following inhalation would not be expected to exceed 13 μg a day. More recently Chamberlain *et al.*[34] estimated that the lead deposition from motor exhausts was 35% for a 15 breaths per minute cycle. The same authors also predicted that continuous exposure to 1 μg/m^3 of exhaust lead over a period of months will give an average contribution of approximately 1 μg of lead to 100 ml of blood. Experimental observations suggest that clinically evident poisoning due to inhalation of inorganic lead does not usually occur unless the concentration of lead is several times the maximum concentration reported in urban atmospheres at present.

An air quality standard of 2 μg Pb/m^3 is currently proposed by the Commission of the European Communities. In a recent evaluation of EEC sponsored research, Prof. R. Zielhuis[35] concluded that research findings do not support an air quality standard of $\leqslant$ 2 μg Pb/m^3 in ambient air. However the same author indicated that more data was required to evaluate the relationship between ambient air exposure levels and the uptake by pre-school age children.

[32] J. Hursh, A. Schraub, E. Sattler, and H. Hoffman, *Health Physics*, 1969, **16**, 257.
[33] D. Booker, A. Chamberlain, D. Newton, and A. Stott, *Brit. J. Radiology*, 1969, **42**, 457.
[34] A. Chamberlain, W. Clough, M. Heard, D. Newton, A. Stott, and A. Wells, *Proc. Roy. Soc. London*, B. 1975, **192**, 77.
[35] R. Zielhius, A. Wibowo, and A. de Bruin, Evaluation of ECE-Sponsored Research in view of ECE-Directives', 1977.

4 Inhalation of Tobacco Smoke

The contribution of lead from smoking, to the total daily intake of lead is expected to be small. After 1952 leaded pesticides were no longer used on tobacco crops. As a result the concentration of lead in American tobacco has decreased from a high of about 130 p.p.m. during the early fifties to 20 p.p.m. in 1965. Today tobaccos vary in their lead content, but cigars tend to have a greater amount than cigarettes or pipe tobaccos. A large percentage of this lead remains in the ash and only a small quantity is available in the smoke for inhalation. Some investigators[40] have claimed an association between smoking habits and blood lead content. More recent findings[36] have failed to demonstrate this effect. Tola *et al.*[36] have pointed out that, as lead has been shown to decrease the number of alveolar macrophages[37,38] and thereby impair lung clearance, the combined effect of smoking and lead exposure would be more severe than that of lead exposure alone.

5 Ingestion of Lead

The diet is the major source of lead in man. Clinically evident lead poisoning most frequently results from the absorption of lead through the gastrointestinal rather than the respiratory tract. Chronic lead poisoning was a major cause of illness throughout the period of the Roman Empire. One of the most damaging effects of lead was due to its presence in a sweet syrup called 'sapa'. Sapa was produced by simmering fresh grapes in a leaden vessel and added to flavour, colour, and preserve food. It is estimated that sapa contained 1 mg/ml of lead.[39] Later in the Middle Ages the practice of adulterating inferior wines with concoctions containing lead was responsible for the outbreak of colic epidemics. Legislation to prohibit the addition of lead to wine was only introduced at the end of the 17th century.

For many centuries the daily diet was considerably contaminated with lead, both from the vessels used in food preparation and by the practice of adulterating food with lead (Table 6).[41–45] Lead compounds were added as colouring matter to spices, sweets, cakes, and cheese. In 1820 in a best selling book of the day, Accum[43] exposed this malpractice. He went on to postulate that lead, present in the glaze of storage jars, dissolved in the acid of fruits, marmalades, and pickles and consequently constituted a danger to health. More recently manufacturing processes in the food industry have been the cause of additional contamination

[36] S. Tola and C. Nordham, *Envir. Res.*, 1977, **13**, 250.
[37] E. Bingham, E. Pfitzer, W. Barkley, and E. Radford, *Science*, 1968, **162**, 1297.
[38] J. Bruch, A. Brockhaus, and W. Dehnen, *Internat. Symp.* 'Recent Advances—Health Effects of Environmental Pollution', Paris, 1974.
[39] J. Eisinger, *TIBS*, 1977, **2**, 147.
[40] L. Tepper and L. Levin, Dept. Envir. Health Uni., Cincinnati, 1972.
[41] R. Mead 'A Mechanical Effect of Poisons', 1702.
[42] G. Baker, 'An Essay Concerning the Cause of the Endemial Colic of Devonshire', 1757.
[43] F. Accum, 'A Treatise on Adulterations of Foods and Culinary Poisons', 1820.
[44] J. Mitchell, 'A Treatise on the Falsifications of Food and the Chemical Means Employed to Detect Them', 1848.
[45] A. Hassall, *Lancet*, 1855.

Table 6 *Early References to the Contamination of Foodstuffs by Lead*

Source	*Use or Effect*	*Ref.*	
Lead from pipes and vessels	Contamination of Cider and Rum	Dr. Richard Mead Sir George Baker	1702[41] 1767[42]
Lead oxide	Glaze for storage jars	F. Accum	1820[43]
Lead oxide	Sweeten wine	F. Accum	
Lead oxide	Clear cloudy white wine	F. Accum	
Lead oxide	Colour cheese	F. Accum	
Black lead	Food colouring	John Mitchell	1848[44]
Lead chromate	Improve colour of mustard, Cayenne pepper, turmeric and snuff	Dr. A. Hassall	1855[45]
Lead carbonate and Lead acetate	Colour sweets and cakes	Dr. A. Hassall	1855[45]

of lead. In 1954 the Food Standards Committee[46] reported that lead was one of the most widespread and serious of metallic contaminants in food and drink. The principal source of contamination was the use of lead compounds in the manufacture, storage, transport, and cooking of foodstuffs as well as from agricultural insecticides. In 1961 regulations were introduced for the first time to control the limits of lead in food and beverages.[47] Similarly another potential source of excessive lead ingestion, namely that from glazes used in domestic cooking-ware, has been restricted by the introduction of British Standards and regulations. Metallic coatings on cooking utensils are required to contain no more than 0.2% of lead.[16] As a result of these measures contamination from lead in the course of food processing and cooking is now far less frequent.[48]

6 Lead in Water

Today lead compounds are widely distributed throughout surface soils and aquatic systems and as a result can be detected in most animal and plant tissues. Precipitation from the atmosphere tends to increase the lead content of soil and aquatic systems gradually, although much of the inorganic lead entering aquatic systems is not water soluble and is removed by sedimentation.

The daily intake of lead from drinking water for an adult is usually 15—20 μg.[49,50] Drinking water, however, has long been suspected of being a source of excessive dietary lead. Where domestic lead plumbing is still in use, and the water is soft and acid, more than one-third of the total lead intake could be

[46] Report on Lead, Ministry of Food, H.M.S.O., 1954.
[47] Lead in Food Regulations No. 1931, 1961.
[48] B. Oser, *Food Cosmet. Toxicol.*, 1970, **9**, 245.
[49] H. Egan, 'Lead in the Environment', ed. P. Hepple, Inst. of Petroleum, London, 1972, 34.
[50] MAFF., Survey of Lead in Food, HMSO, 1972.

from water.[49–53] In some areas of Scotland where plumbosolvent water is not treated, the daily intake of lead from the drinking water, cooking water, and the water used for mixing infant feeds may be excessive, particularly for infants.[54–57] (In Birmingham plumbosolvency was recognized at the beginning of this century by the then Medical Officer of Health who considered it prudent to introduce 1½ grains of powdered chalk per gallon to harden the water.[58]) The practice of installing lead piping has now been superseded by the use of copper or plastic piping, hence most municipal water supplies measured at the tap are below the W.H.O. recommended limits (100 μg/litre).[59]

7 Lead in Food

Plants absorb soluble lead through their roots. Hence there is a natural content of lead in plants related to the lead content of the soil. In general, differing concentrations of lead in the soil have little effect on the lead content of a plant.[60] Airborne lead does not appear to measurably increase the lead content in the edible root portion of plants,[61] neither is rainwater a significant source of lead for crops. On the other hand close to major highways, the leafy portion of vegetation has an increased lead concentration, up to half of which can be removed by washing. The possible role of micro-organisms in the transfer of lead has not been investigated thoroughly.

The total amount of lead in fresh and uncontaminated processed food has fallen over the last 30 years (Table 7). It was reported in 1949 that the average daily intake was between 200—250 μg.[62]. Subsequently in 1975 The Food Additives and Contaminants Committee[51] recommended that the maximum permitted lead level for food, other than specified food, should be reduced from 2.0 mg/kg to 1.0 mg/kg. It is estimated that the present daily intake of lead in food by the average person in the United Kingdom is approaching 140 μg (Table 8).[53] Infants are estimated to ingest proportionally more than adults on a body weight basis, but not on the basis of metabolic rate or calorific requirements.[63,64] Up until 1973 canned baby foods, which may form the major part of the diet of some infants, contained twice the lead content of corresponding fresh foods. This was voiced as a cause of concern.[65] The compulsory replacement of lead

[51] MAFF., Review of Lead in Food Regulations, HMSO, 1975.
[52] B. Cambell, A. Beattie, M. Moore, A. Goldberg, and A. Reid, *Brit. Med. J.*, 1977, **1**, 482.
[53] MAFF., Survey of Lead in Food, HMSO, 1975.
[54] A. Beattie, J. Dagg, A. Goldberg, I. Wang, and J. Ronald, *Brit. Med. J.*, 1972, **2**, 488.
[55] A. Beattie, M. Moore, W. Devenay, A. Miller, and A. Goldberg, *Brit. Med. J.*, 1972, **2**, 491.
[56] A. Goldberg, *Envir. Health Pers.*, 1974, **7**, 103.
[57] A. Goldberg, *Post Grad. Med. J.*, 1975, **51**, 747.
[58] *Brit. Assoc. Advancement of Science*, 1913.
[59] WHO European Studies for Drinking Water, Geneva, 1970.
[60] G. Ter Haar, *Envir. Sci. Tech.*, 1970, **4**, 226.
[61] R. Dedolph, G. Ter Haar, R. Holtzman, and H. Lucas, *Envir. Sci. Tech.*, 1970, **4**, 217.
[62] G. Monier-Williams, 'Trace Elements in Food', Chapman and Hall, 1949.
[63] J. Chisolm and H. Harrison, *Pediatrics*, 1956, **18**, 943.
[64] D. Barltrop and N. Killala, *Lancet*, 1967, **2**, 1017.
[65] D. Bryce-Smith and H. Waldron, *Chem. in Brit.*, 1974, **10**, 202.

Table 7 *Daily Lead Intake in Food*

	U.K.	*U.S.A.*	
Monier-Williams (1938)[67]	500 μg	400 μg	Patterson (1965)[10]
Monier-Williams (1949)[62]	250 μg	337 μg	F.D.A. (1970)[68]
M.A.F.F. (1972)[50]	200 μg	233 μg	Kolbye (1974)[69]
M.A.F.F. (1975)[53]	140 μg		

Table 8 *Estimation of the Average Daily Intake of Lead from Food*[53]

Food Group	*Mean Lead Content* (mg/kg)	*Weight of Food Eaten* (kg)	*Lead Intake Per Person* (μg/day)
Cereals	0.12	0.27	32
Meat and Fish	0.16	0.18	29
Fats	0.08	0.08	6
Fruits and Preserves	0.11	0.25	28
Root vegetables	0.09	0.21	19
Green vegetables	0.19	0.11	21
Milk	0.02	0.40	8
Total	0.09*	1.5	about 140
Previous total 1972 Survey[50]	0.13*	1.5	about 200

*Weighted according to the proportions of the food groups consumed.

solder by tin solder[66] has now reduced any possible risk. Recent recommendations have proposed that infant foods sold ready for consumption should be subject to a limit of 0.2 mg/kg (previously 0.5 mg/kg).[51]

8 Lead in Dust and Paint

Street dust is a potential source of ingested lead, especially by children. The lead content of city dust represents both an accumulation of lead over centuries of industrial emissions, as well as the more recent deposition of lead from the exhausts of motor cars. Measurements in Birmingham indicate that the lead content of the dust is related to traffic flow and the proximity of the roadway.[24]

The association between lead poisoning in children with pica (the repetitive ingestion of non-food items) and old deteriorating urban housing in Britain is well documented.[28,70] In the U.K. in 1961, the Ministry of Health and the Paintmakers Association agreed that paint containers with lead content of more

[66] Lead in Food Amendment Regulation, HMSO, 1973.
[67] G. Monier-Williams, 'Lead in Food', Min. of Health Report, No. 88, HMSO, 1938.
[68] FDA (U.S.A.) Status Report on Lead, 1970.
[69] A. Kolbye, K. Mahaffey, J. Fiorino, P. Corneliussen, and C. Jelinek, *Envir. Health Pers.*, 1974, 7, 65.
[70] D. Barltrop and N. Killala, *Arch. Dis. Child.*, 1969, **44**, 476.

than 1.5% (later reduced to 1%) should be specially labelled. Paints used on toys are limited to 0.5% and that used on pencils to 0.025%.[16]

9 Absorption of Lead from the Gastrointestinal Tract

Inorganic lead compounds are absorbed poorly from the alimentary tract of man[71–74] Approximately 10% of the ingested lead, from whatever source, is absorbed by adults, the remainder is excreted in the faeces.[75–78] The physiological processes involved in the transport of substances from the lumen of the gut to the intestinal serosal compartment are complex. Simple diffusion appears to be the mechanism of absorption of some water soluble vitamins and nucleic acid derivatives (passive transport). Most nutrients (glucose, amino acids, fats, and sodium chloride) are absorbed by active transport and other special mechanisms, whereby they move across the intestinal membrane barrier against an electrochemical gradient. Such a process requires energy to be supplied by cellular metabolism. Studies designed to provide information about the mechanism of transport of lead compounds across the small intestine and the effect of lead ions on the transport of other substances and physiological processes of the intestine are being sponsored by the European Economic Community and the City of Birmingham Environmental Department.[79]

Kinetic data[79,80] indicates that lead ions are transported at similar rates across all regions of the rat intestine by a process of passive diffusion, linked to water movement. It has also been suggested that the main reason why such a small proportion of ingested lead permeates the intestinal membrane barrier is because of the interaction of lead ions with tissue phosphate ions, effectively removing up to 95% of lead from transport.[79,81] Chelation of lead by dietary constituents, to form neutral species reduces the interaction with intestinal tissue and thereby promotes transport.

In vitro studies with laboratory animals have investigated the effect of nutritional factors, age, and chelating agents on the absorption of lead ions from the gastrointestinal tract, and the partition of lead between bone and soft tissues. Low intake of calcium,[82,83] phosphorus,[72] and iron,[73] both low and high protein diets, low dietary vitamin C, added vitamin D, and high fat diets[74] have all been claimed to increase lead absorption. Conflicting evidence concerning the possible effects of chelating agents on the transport of lead across the gastrointestinal

[71] D. Kello and K. Kostial, *Envir. Res.*, 1973, **6**, 355.
[72] K. Six and R. Goyer, *J. Lab. Clin. Med.*, 1970, **76**, 933.
[73] K. Six and R. Goyer, *J. Lab. Clin. Med.*, 1972, **79**, 128.
[74] D. Barltrop and H. Koo, *Sci. Total Envir.*, 1976, **6**, 265.
[75] R. Kehoe, *Roy. Inst. Pub. Health Hyg.*, 1961, **24**, 81.
[76] J. Thompson, *Brit. J. Ind. Med.*, 1971, **28**, 195.
[77] M. Rabinowitz, G. Wetherrill, and J. Kopple, *Envir. Health Pers.*, 1974, **7**, 145.
[78] M. Rabinowitz, G. Wetherrill, and J. Kopple, *J. Clin. Invest.*, 1976, **58**, 260.
[79] J. Blair, I. Coleman, and M. Hilburn, *J. Physiology*, 1979, **286**, 343.
[80] I. Coleman J. Blair, and M. Hilburn, *Biochem. Soc. Trans.*, **6**, 915.
[81] J. Blair, I. Coleman, and M. Hilburn, Aston University, Unpublished Data.
[82] J. Barton, M. Conrad, L. Harrison, and S. Nuby, *J. Lab. Clin. Med.*, 1978, **91**, 366.
[83] R. Goyer, *J. Lab. Clin. Med.*, 1978, **91**, 363.

tract has been reported.[84,85] It has been suggested, although not proven, that the absorption of lead from the gastrointestinal tract, as well as the partitioning of lead in the various body compartments, is regulated by the same physiological mechanism which controls the metabolism of calcium and phosphorus.[72]

There are three possible mechanisms by which nutritional factors could affect the absorption and retention of lead. Firstly, lead compounds could bind to a poorly absorbed nutritional moeity, rendering lead unavailable for transport. Conversely, the interaction with lead and a dietary component could produce a more lipid soluble product, thereby increasing absorption. Secondly, a dietary factor could interact with a cellular process regulating lead absorption, either increasing or inhibiting lead absorption. The data of Blair *et al.*[81] suggests that if intestinal cell to cell adhesion is reduced, for instance by reduced calcium ion concentration, the absorption of lead *via* an extracellular route is increased. Thirdly, dietary factors could modify the metabolic status of tissues that have a particular affinity for lead.

The significance of interactions between lead and other possible dietary constituents is less clear. It is believed that alcoholism increases susceptibility to the toxic effects of lead. Both lead and alcohol can produce mitochondrial injury, giving rise to decreased oxidative properties and increased membrane permeability.[86]

However it is equally possible that nutritional deficiencies such as low protein, vitamin, and calcium intake, associated with alcoholism indirectly enhance the toxicity of lead.

The young of a given species appear to be more prone to nutritional factors,[87,88] and it has been suggested that a mechanism is acquired during growth which enables the adult to avoid undue accumulation of certain elements normally present in the diet, yet no evidence for such a mechanism has been reported.

10 Retention and Distribution of Lead

Continuous exposure to lead results in its gradual accumulation in the body. The absorbed lead is distributed throughout the body *via* the blood stream, and subsequently excreted, mainly in the urine[76–78] although a small amount is secreted in the bile, sweat, and hair. Biliary lead may subsequently be reabsorbed from the small intestine or eliminated in the faeces.[89] Retention of lead by adults is variable (6—33 μg/day)[28] with a mean value about 10 μg/day (about 4% ingested lead). Estimates of the total body burden of lead for adults range from 50—400 mg with a mean of less than 200 mg.[75,89–91] It has been suggested that children with higher absorption rates, could retain approximately 18% of in-

[84] B. Garber and E. Wei, *Tox. App. Pharm.*, 1974, **27**, 685.
[85] S. Jugo, T. Maljkovic, and K. Kostial, *Tox. App. Pharm.*, 1975, **34**, 259.
[86] S. French and T. Todoroff, *Arch. Pathol.*, 1970, **89**, 329.
[87] G. Forbes and J. Reino, *J. Nutrit.*, 1972, **102**, 647.
[88] K. Kostial, J. Simonovic, and M. Pisonic, *Nature*, 1971, **233**, 564.
[89] H. Schroeder and I. Tipton, *Arch. Envir. Health*, 1968, **17**, 965.
[90] P. S. Barry and D. Mossman, *Brit. J. Ind. Med.*, 1970, **27**, 339.
[91] P. S. Barry, *Brit. J. Ind. Med.*, 1975. **32**, 119.

gested lead[92] (2.03 μg/kg/day), and therefore could have a ten-fold greater body burden of lead compared with that of an adult; recent measurements by Barry[91] indicate that this is not so. The observed differences of retention between the sexes, is probably due to the greater consumption of food and greater variety of occupational exposure to lead by adult males.

The concentration of lead in various soft tissues and blood remains relatively stable, throughout adult life.[93,94] The highest concentrations of lead are found in the aorta, liver, and kidneys, but small amounts are found in all the major organs of the body. Analysis of post mortem tissue for lead indicates that more than 95% of the total body burden in man is stored in the bone[89,91] as the relatively insoluble triphosphate.

The concentration of lead in the bones of children is about 1 mg/kg and rises to 40 mg/kg at 50 years of age and continues to increase.[91]

These observations are consistent with the theory that the total body burden of lead can be divided into three major pools. (i) A relatively slow non-diffusible pool of dense bone and teeth. (ii) Lead accumulated in skin, muscle, and bone marrow which has an intermediate exchange rate. (iii) Lead found in soft tissues and blood which is relatively rapidly exchanged with other storage areas. Large increases in the concentration of the relatively mobile fraction of lead in soft tissue are associated with the known toxic effects of this metal.

Blood contains about 2% of the total body burden of lead.[94] The blood lead content of urban dwellers is normally higher than that of rural dwellers and may reflect the contribution of atmospheric lead to the total body burden. Perhaps surprisingly the blood lead content of people from industrial and motorized countries is not always greater than that of populations from less developed countries. For instance, it has been found that the blood lead content of New Guinea natives is comparable with that of Western Europeans.[95] This observation may reflect a difference in the ability of different populations to absorb lead, or more likely indicate the importance of domestic diet and habits as regulators of both absorption and retention of inorganic lead.

Approximately 90% of the lead in blood is bound to the red blood cells.[96,97] The remainder, the plasma-protein bound fraction, is thought to constitute the diffusible metabolically active portion of lead. The partition of lead between the red blood cells and plasma portion of blood may be a decisive factor in the development of the associated toxic effects of high concentrations of lead ions. Although plasma lead may offer the best method to monitor the biologically effective portion of lead, such small amounts are beyond the routine resolution of most analytical instruments, used in epidemilogical surveys.[98] Whole blood lead

[92] F. Alexander, H. Delves, and B. Clayton, *Internat. Symp. Envir. Health*, Aspects of Lead, Amsterdam, 1972, 319.
[93] R. Nusbuam, E. Butt, T. Gilmour, and S. DiDio, *Arch. Envir. Health.* 1965, **10**, 227.
[94] R. Baloh, *Arch. Envir. Health*, 1974, **28**, 198.
[95] L. Goldwater and A. Hoover, *Arch. Envir. Health*, 1967, **15**, 60.
[96] T. Davies and S. Rainsford, *Lancet*, 1967, **2**, 834.
[97] Air Quality Criteria for Lead, EPA U.S.A., 1977.
[98] J. Pierce, S. Koirtyohann, T. Clevenger, and F. Lichte, 'The Determination of Lead in Blood, A Review and Critiquee of the State of the Art', I.L.Z.O., 1976.

Table 9 *Birmingham Blood Lead Survey*[100] *Variation with Age Group/(μg/100 ml)*

	Age Range, Years							
Males	15—19	20—24	25—29	30—34	35—39	40—44	45—49	50—64
Mean	19.8	21.2	21.6	23.8	23.8	22.3	22.4	21.3
Standard Error	1.3	1.2	0.9	1.1	1.3	1.2	1.1	1.5
No.	12	40	53	39	23	15	22	20
Females								
Mean	13.7	13.5	13.8	14.8	13.7	17.2	19.0	18.5
Standard Error	0.9	0.6	0.7	0.9	1.1	1.6	1.8	1.0
No.	25	68	44	20	15	10	13	24

contents on the other hand are relatively convenient to measure and provide an appropriate index of the small rapidly diffusible fraction within the total body burden. It is undoubtedly the parameter most studied and quoted at present.[97] A 'typical' blood lead content for adults in Britain is 15—25 μg/100 ml.

Blood lead levels have been used to monitor the retention of lead in Birmingham residents. The blood lead levels of residents living near to the newly opened Gravelly Hill motorway interchange in Birmingham were monitored during the period May 1972 to October 1973.[99] The blood lead levels of both men and women initially rose by a little over 0.1 μg/week. The data indicated that the blood lead levels gradually came into balance with the new atmospheric lead levels. The mean blood lead of adults living in Birmingham is shown in Table 9.[100] The blood lead levels of Birmingham children aged between eight and fourteen years is, as may be expected, highest in the inner city areas and decreases towards the outer suburbs.[101]

Blood lead determinations have been used to assess the absorption of lead by two groups of patients with known disorders of the intestine, *viz.* Coeliac disease and Crohn's disease. The values may be compared to that of a group with no known history of intestinal malfunction, as well as with those values reported from the Birmingham survey.[100] Although the number of measurements was small, both Crohn and Coeliac patients had significantly higher blood-leads than those of a small group of hospital staff. However, compared to the figures obtained from a group of hospital outpatients and the Birmingham lead survey there was no statistical difference between the groups (Table 10). Neither was there any correlation between the severity of the disease and the blood lead values; nor any difference in blood lead levels of those Coeliac patients on a gluten free diet. The fact that there is no obvious trend implies that the morphological disorder of the intestine associated with Coeliac and Crohn's diseases does not cause either a significant increase or decrease in the absorption of lead.

The exercise did however underline the known association between blood lead levels and working conditions. The mean blood lead level of a small group of young healthy hospital laboratory staff was significantly lower than the mean level found from hospital outpatients and from the Birmingham survey (Table 10). It was also evident from the results that there was a correlation between red blood cell count from young healthy individuals and their blood lead level (Figure). The same relationship does not exist in anaemic patients or in the group of hospital outpatients, both of which were older age groups. The blood leads of a small group of anaemic patients (defined by their statistically lowered red blood cell count) was found to be significantly lower than that reported for a similar age group in the Birmingham survey (Table 10). The result emphasizes the inadequacy of quoting blood leads without some correction for haematocrit value (number of RBC in a blood sample).

[99] H. Waldron, *Nature*, 1975, **253**, 345.
[100] 'Lead Pollution in Birmingham, Report of the Joint Working Party on Lead Pollution around Gravelly Hill', HMSO, 1978.
[101] R. Stephens and H. Waldron, *Roy. Soc. Health J.*, Birmingham Conf., 18th March, 1976.

Table 10 *Blood Lead Levels/(μg/100 ml)*

	Male			
	No.	*Mean*	*S.D.*	*p*
Birmingham Survey	225	22.1	6.4	
Outpatients	22	26.2	12.4	N.S.
Crohn's	12	23.7	6.7	N.S.
Coeliac	12	19.6	5.5	N.S.
Birmingham Survey (aged under 25 yrs)	52	20.6	6.6	
				0.001
Hospital Staff (aged under 25 yrs)	16	14.7	3.4	
Birmingham Survey (55 yrs +)	10	19.2	4.8	
				0.001
Anaemics (55 yrs +)	11	10.0	5.6	
	Female			
	No.	*Mean*	*S.D.*	*p*
Birmingham Survey	221	14.7	5.0	
Outpatients	20	18.0	9.4	N.S.
Crohn's	38	16.2	6.4	N.S.
Coeliac	37	16.7	6.2	N.S.
Birmingham Survey (aged under 25 yrs)	94	13.5	4.6	
				0.02
Hospital Staff (aged under 25 yrs)	24	11.7	3.7	
Birmingham Survey (55 yrs +)	13	19.8	5.8	
				0.001
Anaemics (55 yrs +)	15	8.3	4.0	

Analytical measurements were carried out by A. Coombes, City Analyst Department, Birmingham.

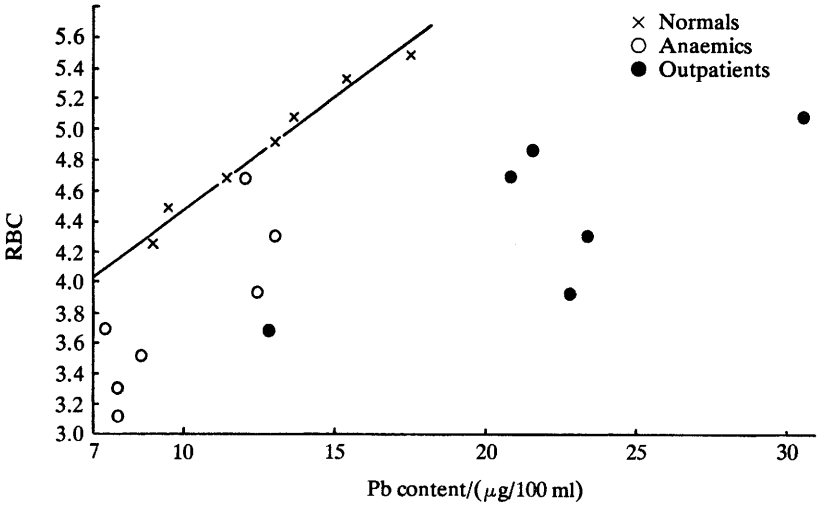

Figure *Relationship between RBC and blood lead levels*

11 A Model Relating the Blood Lead Content to Dietary Intake of Lead and Red Blood Cell Count

Absorption studies[79,80] have demonstrated that lead is absorbed slowly from the intestinal lumen by a passive process, and that most ingested lead is excreted in the faeces and only a small percentage in the urine.[77] The daily intake of lead compounds in food and drink approaches 160—200 μg/day. If the gut fluid volume is approximately 500 ml, the concentration of lead in the lumen will be 32—40 μg/100 ml. In fact over 90% of the lead is attached to the intestinal mucosal surface; hence the free lead concentration is probably only in the order 2 μg/100 ml. The mean blood lead level of adult males in Birmingham is approximately 21 μg/100 ml whole blood; however the concentration of unbound lead is again only 2 μg/100 ml. Hence when a person is in equilibrium with his environment, the concentration of 'free lead' in the intestinal lumen appears to equal the concentration of 'free lead' in the blood serum. The correlation suggests that the level of ingested lead therefore controls the level of lead in whole blood and soft tissues. The model could also explain why the blood lead values of women during the years of menstruation are significantly lower than for males, but rises after the menopause to approximately the same level.

12 Biochemical Considerations

Ideally the body exists in a physiological steady-state whereby the uptake of lead ions is in balance with the excretion and deposition in storage areas. Above a certain threshold, however, the ability of an organism to adapt to further intake breaks down. At this point toxic effects become apparent. The total intake of lead which can be considered safe, *i.e.* below the level where adverse biochemical effects occur, is still open to considerable debate. Therefore great uncertainties still remain concerning the relationship between any possible subclinical effects of lead compounds and the observed effects of lead cations on biochemical pathways.

No beneficial biological role for lead has yet been demonstrated and there is no substantial evidence to suggest that it is an essential trace element. On the contrary, at the cellular level lead is found to interfere with the respiratory pigment,[102–105] energy production[106] and membrane function.[107] Organs with the greatest uptake of lead form intranuclear inclusion bodies, which are composed of a lead–protein complex. When bound in this non-diffusible complex, cellular function can continue in the presence of large amounts of intracellular lead. Membranes of the mitochondria, however, appear to be particularly sensitive to intracellular lead, and decreased phosphorylative and respiratory or enzymic

[102] M. Bessis and W. Jensen, *Brit. J. Haematol.*, 1965, **11**, 49.
[103] J. Granick, S. Sassa, and A. Kappas, *Adv. Clin. Chem.*, 1978, **20**, 287.
[104] D. Ulmer and B. Vallee, 'Trace Substances in Environmental Health' II, ed. D. Hemphill, University of Missouri Press, 1969, 7.
[105] H. Waldron, *Brit. J. Ind. Med.*, 1966, **23**, 83.
[106] R. Goyer, *Lab. Invest.*, 1968, **19**, 71.
[107] R. Goyer and B. Rhyne, In 'Pathologic Aspects of Cell Membranes', ed. B. Trumps and A. Arstila. Acad. Press, New York, 1972.

ability results.[108] *In vitro* experiments have demonstrated that low concentration of lead cations inhibit a number of enzyme systems.[102,104] Low levels of lead can partially inhibit lipoamide dehydrogenase, an enzyme which plays an essential role in the oxidation of pyruvic and ketoglutaric acids in the mitochondria and plays an essential role in the metabolism of almost all cells.[104] ATPases which are involved in the transport of sodium and potassium ions are also inhibited by low levels of lead.[109] Inhibition of this group of enzymes may interfere with the generation and transmission of nervous impulses. The effects of lead on protein synthesis are less well understood.[97,103,110]

Lead can reduce red blood cell survival, inhibit the biosynthesis of haem, and the utilization of iron.[105] A sustained blood lead level in excess of 80 μg/100 ml interferes with haem synthesis and will result in a microcytic hypochromic anaemia. It is postulated that lead can inhibit the formation of haem at several points in its synthesis. It has been clearly established[111] that lead interferes with the conversion of aminolaevulinic acid (ALA) to porphobilinogen (PBG) by the inhibition of the enzyme aminolaevulinic acid dehydrase (ALA-d). Increases in blood lead content above approximately 40 μg/100 ml of whole blood have been correlated with an exponential increase in 'chelatable' lead, an exponential decrease in ALA-d activity in blood and an exponential increase in urinary ALA excretion.

Observed accumulation of free erythrocyte protoporphyrin (FEP) as a result of lead poisoning, is another example of lead interfering with haem synthesis. Therefore measurement of the inhibition of either ALA-d or urinary ALA or FEP offer a convenient method of indexing and correlating observed clinical effects with a biochemical parameter. Whole blood lead content alone is not regarded as a good indicator of internal effects of absorbed lead, rather a combination of blood lead content and ALA-d inhibition or FEP measurements is preferred. Humans are unable to compensate for small increases in blood lead concentrations by increasing their production of red cells. However people who already suffer from iron deficiency, haemolytic anaemias, certain renal malfunctions and disease[107] or are deficient in glucose-6-phosphate dehydrogenase,[112] will be less able to compensate for increased lead absorption and hence show an increased susceptibility to lead.

13 Clinical Considerations

Evaluation of the effects due to exposure to high quantities of lead and sustained high blood and tissue lead contents has been largely based on data derived from clinical studies of industrial workers in the lead trades,[97,113] and imbibers of lead-contaminated illicitly distilled whisky in the United States.[114] Lead poisoning

[108] R. Goyer, P. May, M. Cates, and M. Krigman, *Lab. Invest.*, 1970, **22**, 245.
[109] J. Hasan, V. Vihko, and S. Hernberg, *Arch. Envir. Health*, 1967, **14**, 313.
[110] L. Muro and R. Goyer, *Arch. Path.*, 1969, **87**, 660.
[111] S. Hernberg, J. Nikkanen, G. Mellin, and H. Lilius, *Arch. Envir. Health*, 1970, **21**, 140.
[112] M. McIntire and C. Angle, *Science*, 1972, **177**, 520.
[113] W. Gafafer, 'Occupational Diseases. A Guide to their Recognition', US Govt. Printing Office, 1964, 375.
[114] J. Morgan, M. Hartley, and R. Miller, *Arch. Internat. Med.*, 1966, **118**, 17.

can give rise to several well known, but non-specific, clinical syndromes, including anaemia, abdominal colic, encephalopathy, and nephropathy.[115] Clear cut clinical signs of acute lead-poisoning in adults appear to be associated with blood lead concentrations greater than 80 μg/100 ml.[116] There is however, conflicting evidence for a possible correlation between increased incidence of hypertension and exposure to industrial levels of lead.[117,118]

The long term consequences of small but sustained increases in soft-tissue lead content are not well understood. Some physiological mechanisms may be able to compensate temporarily for small increases of lead. Certainly, permanent impairment of the renal system is unlikely in persons whose blood lead does not exceed 30 μg/100 ml. It remains a controversial point whether adults with blood lead content between 30—60 μg/100 ml may be said to have symptoms compatible with lead poisoning. It is also clear that at present the biological significance of blood lead concentrations between 30—60 μg/100 ml cannot be evaluated by reference to routine clinical studies alone.

Epidemiological data suggests that children living in deteriorated inner city housing are liable to possess higher blood lead concentrations than normal.[119,120] The extent to which lead bearing dust contributes to the problem is not clear. The ingestion of old paint, containing up to 40% lead, has been implicated in many areas. The use of the eye cosmetic 'surma' containing almost 90% lead sulphide by children of Asiatic origin constitutes an unusual hazard. Between 1966—1971, of 38 reported cases of children from the Birmingham area with high blood leads, 15 were Asian.[121] (The EEC have subsequently issued a directive to prohibit the use of lead in cosmetics). The more frequent occurrence of lead poisoning in children than in adults is not proof of an increased biological susceptibility of children to lead toxicity. It probably only indicates that children are more often exposed to lead, and that their smaller body size makes them more susceptible to a particular dose of lead. Barltrop[122] has suggested that lead may affect different tissues at various stages of development, and affect a particular tissue in different ways according to its state of maturation. It has also been suggested that a greater proportion of 'mobile' lead may be able to transfer into and out of the growing bones of infants, which in turn may influence biological effects. This postulation is disputed by some investigators in the field today.

It has been suggested that there is an association between raised body burdens of lead and hyperactivity in children. David *et al.*[123] compared hyperactive children with a control group, using blood lead levels and urine levels, after oral

[115] 'Diseases of Occupations', ed. D. Hunter, Eng. University Press, 1971, 234.
[116] R. Kehoe, *J. Occ. Med.*, 1972, **14**, 390.
[117] K. Cramer and L. Dahlberg, *Brit. J. Ind. Med.*, 1966, **23**, 101.
[118] D. Beevers, E. Erskine, M. Robertson, A. Beattie, B. Campbell, A. Goldberg, M. Moore, and V. Hawthorne, *Lancet*, 1976, ii, 1.
[119] J. Lin-Fu, *New Eng. J. Med.*, 1972, **286**, 702.
[120] L. Blanksma, H. Sachs, E. Murray, and M. O'Connell, *Pediatrics*, 1969, **44**, 661.
[121] P. Betts, R. Astley, and D. Raine, *Brit. Med. J.*, 1973, **1**, 402.
[122] D. Barltrop, 'Lead in the Environment', ed. P. Hepple, Inst. of Petroleum, London, 1972, 52.
[123] O. David, J. Clark, and K. Voeller, *Lancet*, 1972, **2**, 900.

administration of the chelating agent penicillamine, as a measure of total body lead. The data indicates that hyperactive children have raised body lead burdens. An association between high blood lead levels and mental retardation has also been reported.[14,124,125] Although other investigators have found no correlation.[126–128] Beattie *et al.*[14] suggest an association between high water-lead exposure during pregnancy and the development of mental retardation in the newborn.

The effects of lead exposure on a variety of neurochemical substances have been studied.[129,130] The approaches employed include the biochemical assay of steady state levels of neurotransmitters, and the measurement of activity of enzymes responsible for transmitter synthesis or degradation. The published data suggests that lead appears to resemble other divalent cations in that it interferes with the calcium-mediated release of neurotransmissions in the peripheral nervous system.[97] The effect however has only been demonstrated after exposure to large quantities of lead and many studies showed growth retardation, which may affect the metabolism of the neurotransmitters.

There is also good evidence that perinatal exposure to moderate levels of lead, produces delays in neurological and sexual development.[133–135] The nature and significance of these alterations have not been determined, and it is clear that animal investigations have confused the interpretation of human data. It has been repeatedly indicated that serious methodological problems exist in many animal studies.[97]

In our laboratory[131] the effect of lead on tetrahydrobiopterin metabolism has been investigated. Tetrahydrobiopterin functions as a co-factor in the metabolism of phenylalanine to tyrosine and the hydroxylation of tyrosine to hydroxyphenylalanine (dopa) and tryptophan to 5-hydroxytryptophan. A defect in tetrahydrobiopterin metabolism would therefore interfere with the synthesis of the neurotransmitters dopamine, noradrenaline, adrenaline, and serotonin.

Rats were injected intraperitoneally every 48 hours with 300 μg Pb/kg body weight and their serum biopterin levels determined using a *Crithidia fasciculata* assay.[132] Typical experimental data indicates that the serum biopterin levels were significantly reduced after each injection (Table 11). This result needs to be interpreted with care, as the dose given to the animals was probably fifty times in excess of that normally encountered by humans in their diet.

[124] O. David, S. Hoffman, B. McGann, J. Sverd, and J. Clark, *Lancet*, 1976, **2**, 1376.
[125] M. Moore, R. Meredith, and A. Goldberg, *Lancet*, 1977, **1**, 717.
[126] R. Lansdown, J. Shepherd, B. Clayton, H. Delves, P. Graham, and W. Turner, *Lancet*, 1974, **1**, 538
[127] J. McNeil and J. Ptasnik, 'Recent Advances in the Assessment of the Health Effects of Environmental Pollution', CEC, Luxembourg, 1975, **2**, 571.
[128] J. Hebel, D. Kinch, and E. Armstrong, *Brit. J. Prev. Soc. Med.*, 1976, **30**, 170.
[129] E. Silbergeld and A. Goldberg, *Neuropharmacol.*, 1975, **19**, 431.
[130] M. Sauerhoff and I. Michaelson, *Science*, 1974, **182**, 1022.
[131] R. Leeming, J. Blair, and M. Hilburn, Birmingham Gen. Hosp.
[132] R. Leeming, J. Blair, V. Melikian, and D. O'Gorman. *J. Clin. Path.*, 1976, **29**, 444.
[133] D. Brown, *Toxicol. Appl. Pharmacol.*, 1974, **32**, 628.
[134] C. Snowdon, *Pharmacol. Biochem. Behav.*, 1973, **1**, 599.
[135] T. Damstra, *Envir. Health Pers.*, 1977, **19**, 297.

Table 11 *Serum Biopterin and Lead Values**

	Biopterin/(μg/ml) *Control*		*Test*			Pb/(μg/100 ml)	
		S.E		S.E.	p		S.E.
Day 2	18.0	0.98	14.8	0.97	0.05	3.1	0.9
Day 4	18.6	0.80	10.0	1.17	0.001	4.7	0.9
Day 6	18.2	0.59	7.6	1.77	0.001	6.3	1.2

*Mean of 4 samples

Analytical measurements were carried out by R. Leeming, General Hospital, Birmingham.

14 Conclusions

It is clear that man has substantially contaminated his environment with lead. It is important to recognize however that more lead is added to the total environment in the form of paint pigments and metallic products than in the form of lead alkyls. Yet the proportion of contamination that results from combustion and dispersion of lead compounds is increasing. The contribution of inhaled lead to the total body burden varies considerably, during occupational exposure respiratory uptake of lead may exceed oral uptake. Outside of industrial conditions oral uptake of lead will exceed respiratory uptake. In general, the amount of lead inhaled is less than one third the amount that comes from the diet (Table 12). Recent evidence suggests that the amount of lead in our diet is decreasing.

Table 12 *Average Daily Uptake of Lead*

	Average Daily Intake	*Approx. Lead Conc.*	*Approx. % Absorbed*	*Average Daily Uptake* (μg)	*Normal Range* (μg)
Food	1.5 Kg	0.09 μg/g	10	14	9—18[a]
Water	1.5 Kg	0.01 μg/g	10	1.5	1—3[b]
Urban air	15—20 m^3	2.0 μg/m^3	50	6	1—13[c]
Rural air	15—20 m^3	0.1 μg/m^3	50	0.6	0.1—3.0
		Total Uptake Urban Man		22	10—34

[a] Intake of lead from food will depend upon the diet of the person and the quantity of food eaten. Meat and green vegetables have a higher lead content than cereals and root vegetables. Canned items have a higher lead content than fresh foods.[51]

[b] Lead content of water is relatively low if copper pipes are used.[51]

[c] The concentration of lead and volume of air inhaled will depend upon the particular domestic and occupational activity of a person. The percentage of lead deposited in the lungs was estimated by Chamberlain *et al.*[34] to be 35%, of which 50% is absorbed.[16]

The most prominent pathological effects of lead are observed in haematopoietic,

renal, and nervous systems. Most adults in Britain have blood lead levels below that which is known to be associated with a risk of clinical lead poisoning. However the safety margin appears to be decreasing as more evidence concerning the clinical and biochemical effect of lead is published. Certainly no other chemical pollutant has accumulated in humans to average levels so close to the threshold of potential poisoning. It has long been thought that exposure to low concentrations of lead might produce some subtle effects on the health and behaviour of small minority groups within the general population. However it has not been possible to link unequivocally the incidence of human diseases, other than lead poisoning, to lead exposure. Further the concentration of lead in the atmosphere which constitutes a long term threat to health is yet to be established.

Based on present knowledge and levels of lead pollution the concentration of lead in the air of our cities does not appear to pose any threat to the health of the general population. However three categories appear to be more at risk. The first is those who are continuously exposed to unusually high concentrations of lead in their working environment, for example workers in the lead trade, traffic policemen, and garage employees. The second group at risk consist of young children, particularly those living in old, dilapidated inner city housing. It has yet to be established whether the threshold for a given effect of lead is lower in the immature nervous system than that observed in an adult. The third group who give rise for concern is the unborn. The risk cannot be expressed quantitatively, but it is known that lead crosses the placental barrier at an early stage in embryonic development.

In this technological era, the use of lead compounds must be regulated to prevent possible toxicological effects to man and his environment. The problem of lead pollution will ultimately be solved by economic and political means rather then scientific means. The extent of the regulation can only be determined after a comprehensive chemical understanding of the clinical and biological response of man to lead compounds is achieved.

I would like to record my thanks to Prof. J. A. Blair, for his advice and encouragement throughout the preparation of this review.