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Environmental health aspects of lead

Die gesundheitlichen Aspekte der Umweltverschmutzung durch Blei

Les problèmes sanitaires posés par le plomb présent dans l'environnement

INTESTINAL LEAD ABSORPTION

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INTESTINAL LEAD ABSORPTION

Lead has been known to be toxic for more than two thousand years and it continues to be the cause of numerous episodes of chemical intoxication of industrial and accidental origin as well as it remains a main problem of pbulic health.

Lead ingestion

Lead ingestion results from the contamination of food during its production, its preparation and during the storage of food; air contamination from motor exhaust gases may deposit dry particles of lead on foods, or on other objects which may be brought to the mouth especially in children. Drinking water may be rich in lead from the use of lead piping, particularly when combined with the use of a water-softener which usually decrease the pH of water. Finally there are multiple circumstances which may increase the amount of ingested lead: glazed ceramic often release much lead when used for keeping acid beverages like fruit juices or cola-drinks. The paint covering of most pencils is a health hazard for pencil chewers (33). Some popular brands of toothpaste are potentially hazardous as a result of the lead content in the tube, the tube-coating and in the toothpaste itself (19).

Lead intake: some values

	Mean (mg/d)
Kehoe, 1961 (23)(24)	0.30
Imamura, 1957 (18)	0.15 (0.09-0.18)
Jaworowski, 1967 (20)	
Kehoe, 1962 (27)	0.30 (0.05-2.00)
Patterson, 1965 (32)	0.33 (0.23-30)
Schroeder, 1961 (36)	0.33
Schroeder, 1968 (35)	0.1-0,54
Parry-Howells, 1971 (30)	0.44
Thompson, 1971 (38)	0.27
Bogen, 1968 (3)	0.27

The values for lead intake are obtained by different methods, measurement of the actual content of foods, measurement of the lead content of feces with appropriate corrections to get back to intake.

The amount ingested in food and in water has been studied by some authors:

	Lead content (mg/d)	Food (mg/d)	Water (mg/d)	
	0.280	0.260	0.020	Schroeder 1968 (35)
	0.410	0.400	0.010	Patterson 1965 (32)
Total:	0.093-0.187	0.089-0.127	0.004-0.033 (water)	
			0.027 (tea)	Imamura 1957 (18)

Lead intake: infants

Lead intake in infants without evidence of picy, have been estimated by measuring fecal output of lead. If one uses an absorption coefficient of 25% instead of 8% as for adults, one gets approximately the following values:

References	Fecal output	Estimated intake
Kehoe 1933 (21)	0.080 mg/d	0.100 mg/d
Barltrop 1967 (2)	0.123	0.150
Chisholm 1956 (5)	0.132	0.165

GASTROINTESTINAL ABSORPTION OF LEAD

Methods of study

Different methods have been used to estimate the fraction of absorbed lead which would correspond to the f_1 factor of ICRP.

1 Intake and output studies (12) (8)

One measures the amount of lead in urine and in stools and one calculates the ratio $\frac{\text{Urinary lead}}{\text{Fecal + urinary lead}}$

This method supposes that the equilibrium is reached i.e. that intake=output; that no lead is accumulated in the body; that the amount of lead lost through sweat and hair is negligible.

Measurement of oral intake (food and water) as well as fecal output permits to calculate the ratio $\frac{\text{Fecal outpu}}{\text{Oral intake}}$

Finally, the urinary excretion of lead is a rough estimate of the amount absorbed. These different methods do not allow to estimate how much lead is actually absorbed, how much is actually secreted by the liver and how much is secreted by the intestinal wall. It permits only to know the net result of absorption and secretion.

2 Measurement of f_1 with Pb212 (16)

An oral dose of Pb212 is administered and fecal and urinary excretion are measured.

3 Measurement of the amount excreted vi

Measurement of the elimination of Pb210 in the bile after IV injection of 100 ug of lead.

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Lead seems to be more readily absorbed from water than from food and Patterson (32) suggests the following factors:

Absorption fraction	%
Food	5
Water	10

Some physiological factors are probably relevant, like the fraction secreted by the liver and the fraction secreted by the intestinal wall (15). There have been some contradicting reports in the literature as to whether bile or intestinal wall are a more significant pathway of lead excretion. In sheep and in rats about 8% of the IV dose of lead acetate was excreted through the biliary tract which was about one hundred times more than through the walls of the intestines (4).

Two human subjects who received an IV injection of Pb212 excreted 0.29 and 0.25 per cent dose in the 0 to 48h fecal collection (16).

Inhalation of particulate lead-212 was followed by a fecal excretion of 2-3% in the 0 to 72 hours collection, while inhalation of lead-212 as a vapour showed an excretion of 37% during the same period. It is not known whether the swallowed fraction differed in the two situations (34).

Constipation increased the absorbed fraction (21).

The chemical form of the ingested lead is probably very important. Table 1, from Kehoe (27) shows some of the chemcial and physical chemical characters of the main compounds of lead. However, solubility is not the whole story. For instance, lead sulphide is not absorbed in the lungs but is readily absorbed in the gastrointestinal tract if gastric acidity is present. Lead sulphide is converted to lead chloride which is readily absorbed before it reached the colon, where it reverses back to sulphide. The lead compounds which are absorbed are those which are soluble or which are converted to absorbable compounds.

Experimental ingestion of lead arsenate showed that the arsenate was completely broken down in the body and the lead was poorly absorbed: 1.3% to 3.2% of the ingested lead appeared in the urine (8).

The following compou-ds are readily absorbed through the gastrointestinal tract: Lead acetate, Lead chloride, Lead oxide and Lead tetraethyl; less soluble but still absorbed are other compounds like Chromate, Sulphide, Sulphate and Carbonate.

Nothing is know regarding the mechanism of absorption through the intestinal wall. Is there a protein which limits the amount absorbed (like iron)? What is the role of complexants and ligands?

All the known biological ligands contain dissociable protons which may be replaced by heavy metals in complex formation.

Metal binding by biological ligands is not specific; the order of affinities and the relative concentrations of the different ligands only count. On the other hand chelation may be highly specific and introduces exceptions to the rule of relative affinities (31).

The effect of lead on epithelial membranes is restricted, as far as we know, to the effect on the cells of the renal tubule, where it produces a pattern of aminoaciduria which is rather specific (alaninuria) (31).

The load of lead may probably raise the value of the absorbed fraction (41) (23) (24) (25) (26).

The size of the lead particles which is very important in inhalation is probably irrelevant in the case of oral intake.

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Measurement of fecal elimination of RaD after IV administration of a carrier-free tracer dose, taking account if necessary of bile excretion.

Urinary lead as an estimate of absorbed lead

Usually 5-10% of dietary lead is absorbed and the following values have been reported for lead in 24-hour urine output:

Lead in 24h urine collection		authors
0.030 mg	(0.010-0.080)	Parry Howells (30)
	(0.00 -0.290)	Horiuchi (13)
0.030	(0.010-0.080)	Kehoe (27)
0.044	(activation analysis)	Kopito (28)

In children the 24h urinary excretion in subjects presumably free from pica was
0.026 mg — Webster (40)

Incidentally it may be mentioned that an international study of urinary lead concentration was published by Kehoe et al, 1940 (22) which showed the following values: (see also (9))

Country	Lead concentration (µg/litre)
France	0.020
Mexico	0.022
USA	0.029
Germany	0.027
UK	0.050 (35)

In we find a value of
but the methods, the authors and the time being different it is difficult to draw firm conclusions. Anyway, lead concentration in urine in the basence of values for urinary volumes should be interpreted with caution.

Urine and fecal lead as an estimate of absorbed lead

Holtzman (16) calculates the ratio of the daily urinary output (which he gives as 0.037 mg) to the fecal output: $f_1 = 0.037/0.33 = 0.11$.

However, by accounting for the atmospheric lead contribution of 0.009 mg/d we obtain, says Holtzman, $f_1 = 0.08$. The intake proposed by the authro is 0.46 mg/d. The value calculated corresponds to the 8% of ICRP (17). It seems preferable to me to use the ratio U/U + F. This method can be criticised since it does not take account of sweat and hair loss which in basal conditions amount to about 0.1 mg/day.

Absorbed fraction in adults

Authors	f_1	Method
Kehoe (26)	0.10	Intake output
Kehoe (27)	0.08-0.10	Same
Patterson (32)	soluble (in water): 0.10 insoluble (food): 0.05	Same
Schroeder (35)	0.10	
Imamura (18)	0.20 to 0.40	Intake output
Hursh (15)	0.01, 0.08 & 0.16	Absorption of Pb
Harrison (11)	0.06. 0.16 & 0.18	Absorption of Pb
Horiuchi (13)(14)	0.06	Intake output
Thompson (38)	0.08	Intake output:Food
	0.13	Intake output:U/U
Fairhall (8)	0.01 to 0.03	Intake output

Absorbed fraction in infants and children

The data are very scarce. It is generally known that the absorbed fraction is higher in infants for heavy metals like Sr or Ca. Moreover it has been shown that the absorbed fraction in the intestine is increased in the early stages of life (29)

Applying the Intake-output method to Kehoe's data (21) yields a ratio of 0.25. If calculated by age there are some variations but it does not seem there is an age trend.

Variability of the absorption fraction

There are many factors of variation of the absorption fraction. Some are known, others are suspected or may reasonably be supposed to modify the intestinal absorption

Such studies must take account of the magnitude of salivary excretion of lead which adds up to the oral intake (34)

There are good reasons to believe that some of the factors which regulate Ca (and Sr) absorption may play a role. It is not unlikely that the amount of vitamin D of phosphate and of some complexant agents like inositohexaphosphate in food are relevant. It has been shown that rats and men on a low Calcium diet absorb more lead, since their fecal output of lead was higher and the urinary output was lower than the controls. It is likely that pregnant women, growing children particularly in populations showing dietary deficiencies, are critical groups with a higher risk of increased absorption (37)(8).

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SUMMARY

1 Oral intake of lead amounts to about 0.44 mg in adults and 0.15 mg in children.

2 The coefficient of intestinal absorption is around 0.08 in adults and 0.25 in children. However the value for children is questionable and needs confirmation.

3 Absorption in the intestine depends on known factors (chemical form, dietary Ca) and presumably significant factors (vitamin D intake, diet composition, load of lead, gastric acidity).

4 Inhaled lead contributes a significant part to lead intake. It varies mainly with the atmospheric concentration of lead, the size of the particles and some physiological factors.

5 Further studies, if necessary, should concentrate on the fractions absorbed and secreted at the different levels of the GI tract, on the effect of biological complexants and ligands in the intestinal lumen and on the mechanism of transfer through the intestinal wall.

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TABLE II

Retention and excretion of stable and radioactive lead in animal and human organism.

% retention		excretion
stable lead	radiolead	
Ingestion		
Pb in humans: <10% Ref. 16,17. Pb in humans: 8% Ref. 2.	Pb-210 in rats: 5% (parent. admin.) Ref. 1. Pb-212 in humans:1.3-16% Ref. 6.	Pb-212 in huma urine: 4.9% and Ref. 6. Pb-210 in human excret.ratio F/ Ref. 4.
Inhalation		
Pb in humans: 25-30% experim.with Pb particl. of 0.05-1.2 u: 35-54% Ref. 16,17.	Pb-212 in humans: 60% and 34% Ref. 10 Pb-210 in rats: 32% Ref. 1. Pb-210 in dogs: 26-32% Ref. 14.	
Injection		
	Pb-210 in rats: 24% Ref. 1. Pb-210 in rats: 38% Ref. 12 Pb-210 in dogs: 40% Ref. 12.	Pb-210 in rats: Ref. 7 and 8. Pb-210 in baboon Ref. 9. Pb-212 in humans urine: 4.4% and Ref. 10. Pb-210 in dogs faeces: 70-75% Ref. 12.

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