METABOLISM AND DISTRIBUTION OF RADIOACTIVE AND STABLE LEAD IN MAN

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Abstract

The literature concerning the metabolism and distribution of radioactive and stable lead in animal and human organisms was reviewed. All the available data have been summarized in tables so that a comparison between results obtained using either radioisotopes of lead or stable lead could be made. The purpose of such comparison was to ascertain whether the information obtained with radiolead could clarify the metabolic processes of stable lead in man. The usefulness of the experiments performed with radioactive tracers seems unquestionable : the results of the experiments performed in order to study the retention and excretion of radiolead in animals and in humans are, in general, confirmed by direct observations made on the behaviour of stable lead in man. Some inconsistencies might be due to differences in the experimental conditions. However, the critical examination of the literature on both radioactive and stable lead reveals that the mechanism of lead absorption in man is not completely known. Precise information, for instance, on transfer coefficients of lead through the respiratory and gastro-intestinal tracts is not reported in the literature. The analysis of the various studies on metabolism of lead has permitted to discover where additional research is needed. Some specific points to be clarified, also through experiments with radiolead, are suggested.

The present paper was prepared on the basis of published information on the metabolism and distribution of radioactive and stable lead in man and experimental animals.
The objective of this review was to perform a comparative analysis of the available data and ascertain whether and to what extent results obtained for very small concentrations of radiolead are also valid for stable lead. Furthermore it was aimed at pointing out which aspects of the problem of environmental lead contamination require additional research.

RADIOACTIVE LEAD

Horiuchi and Horiuchi[1] studied the fate of ^{210}Pb in the organism of rats which had already been poisoned with lead acetate. Radiolead was given by means of subcutaneous injection, parenteral administration and inhalation. The level of ^{210}Pb in the urine and feces was measured daily. Twenty days after subcutaneous injection, about 20 % of the

radiolead was excreted and 24 % absorbed within the body. After parenteral administration excretion was about 87 % and absorption 5 %, while an excretion of 46 % and an absorption of 32 % was observed after inhalation. Most of the absorbed ^{210}Pb was accumulated in bones and teeth. Regardless of the mode of administration, lead circulating in blood was found in greater amounts in red cells than in plasma.

Holtzman[2,3] determined the ^{210}Po and the ^{210}Pb content of bone samples from professionally unexposed people. The average ratio $^{210}Pb/^{210}Po$ was found to be equal to unity. The distribution of ^{210}Pb was as follows :

Tissue	% of body burden
Liver	1.7
Muscle	17.0
Other tissues	18.0
Bone (Rib)	63.0

According to Holtzman most of the radiolead in bone, comes from potable water (0.022 pCi/g ash) and from the atmosphere (0.073 pCi/g ash).

He reports also the fractions of the daily ingested lead retained by the organs (fw) and the fractions of lead entering the organs from blood (f'_2) obtained by other authors for rats injected with ^{203}Pb.

Tissue	fw	f'_2
Bone	0.022	0.28
Liver	0.0064	0.08
Kidney	0.013	0.14

Castellino and Aloj[4] studied the kinetics of the distribution and excretion of lead in rats for 14 days following single intravenous injections of lead acetate with an activity of about 1 μCi of ^{210}Pb. The highest concentrations were found in the kidneys and, in decreasing order, in liver, bone, whole blood, lung, spleen, muscle and heart. In bone tissue the concentration did not wary, or at least very little, with time, while in all the other tissues the disappearance of lead was very rapid during the first three days and slowed down afterwards. During the whole period lead in the blood was bound mostly to the red cells (96 %) while only 4 % was in the plasma. At the end of the experiment, fourteen days after injection, 44.8 % of the injected dose was still retained. Excretion occurred through feces and urine. Over the whole 14 day period, the fecal excretion of ^{210}Pb was 36 % of initial dose, while 16 % was excreted with the urine. The excretion curves show that the ratio Feces/Urine was approaching unity in the final stage of the experiment.

Jaworowski[5] in a study on stable and radioactive lead, reports data of his own and of other authors on the distribution of ^{210}Pb in human organism.

Averaged values are :

Tissue	% of body burden
Kidney	0.13
Spleen	0.14
Liver	2.00
Muscle	13.00
Blood	2.00
Soft tissues (all)	30.00
Bone	70.00

It must be noted that the soft tissue data were derived from a limited number of analysis. The contribution of the non-osseous portion of the organism to the total burden of lead-210 is, therefore, estimated with less certainty than of bone tissue, which, on the contrary, has been frequently analyzed.

The data presented by Jaworowski indicate that an increase in the ^{210}Pb levels of human bone occurred between 1952 and 1964 to reach a mean concentration of 0.04 pCi/g wet bone. A possible correlation between ^{210}Pb in bone and age suggested by some authors was not confirmed. On the basis of data from other authors, Jaworowski also states that in normal and contaminated humans, excretion of lead-210 through feces and urine is roughly equal. In experimental animals excretion rates were more than twice as high in feces as in urine shortly after administration, but the ratio approached unity with time. Another route of excretion is hair in which the concentration of radiolead, according to Jaworowski's experiments with animals, is related to the amount administered and reflects blood concentration at the time of its formation.

Cohen and Howells[6] in reviewing the literature from 1947 to 1968 concerning the metabolism of ^{210}Pb, have realized that little information was available on the absorption, distribution, retention and excretion of trace quantities of carrier-free ^{210}Pb in the animal and human organisms. Some studies have been performed in an attempt to characterize those parameters, but only for abnormal intakes leading to toxicity. Cohen and Howells present a model, valid also for stable lead, of the metabolic pathways of ^{210}Pb (Fig.1) in which the main steps are :

1) intake,
2) absorption, i.e. transport of ingested lead across the intestinal mucosa or direct passage of inhaled lead into the blood stream,
3) transport in the body fluids from the sites of absorption to the tissues and then to excretory sites,
4) lead uptake by various tissues, including deposition in bone,
5) removal from sites of uptake and deposition including bone resorption
6) excretion via the kidney, the intestine and other routes such as hair and sweat glands.

Several investigations of these various steps, especially those numbered 2 through 5, have been made by using radioisotopes of lead in various chemical forms, but, according to Cohen and Howells, results for a particular animal species have been inconsistent and, therefore, further studies are required. The use of trace quantities of ^{210}Pb would also help in the study of the movement and fate of stable lead in the environ-

ment. Several studies have also been performed by various authors in the attempt to find out whether analyses of blood could provide an indication of exposure levels or of body burden. The data are unfortunately still insufficient to establish the type of relationship that may exist. The same thing can be said for excreta, especially urine samples, in which the concentration of radiolead may vary according to mode of intake.

Schubert and White[7] and Lucas and Stanford[8], whose studies are reported in Cohen and Howells' review, obtained urine to fecal ratios of about 1 for rats injected with carrier-free ^{210}Pb. Lucas and Stanford in their experiment also found, in agreement with other authors, that 90 % of the lead in blood was in the red cells.

Cohen, Howells, Wrenn and Eisenbud[9] have studied the metabolism of injected ^{210}Pb in the adult baboon in the hope that extrapolation of data to man might be more reliable. Most of the experiments are still under way. Excretion studies have revealed that after an initial period during which some differences were observed, the ratio of total ^{210}Pb excreted in urine and feces was about 1.

Hursh[10] performed an experiment with three beagle dogs which were made to inhale ^{210}Pb aerosols with a stable lead content of 0.006 to 0.018 µg per liter air. The particles had a mean diameter of 0.25 µ. Retentions of 25 and 15 % were measured on two dogs. Complete excreta collection was made yielding a fecal to urinary lead ratio of about 1.25. The dogs were sacrificed at 2, 11 and 31 days ; and the tissues and blood were analyzed. The higher fractions of the lead absorbed were found in bone, liver and red cells.

Lloyd, Mays and Atherton[11] also studied the distribution and retention of ^{210}Pb in beagle dogs. The percentage of radiolead retained at different times after intravenous injection, was indirectly calculated on the basis of lead blood removal and excretion data. After three weeks the retention was about 49 % of the injected dose. The excretion values obtained during the first three weeks give a ratio F/U = 3 with no apparent tendency toward equal fecal and urine excretions of radiolead. This fact is in contrast with the observations of other authors who, at later stages of experiments on animals of different species, found the excretion ratio equal or close to unity. A total retention of 37.6 % of injected ^{210}Pb was found for one dog sacrificed 28 days after injection. The distribution values were the following :

Tissue	% of body burden
Bone	63
Liver	20
Blood	8
Other tissues	9

The retention data, calculated from excreta measurements were confirmed by tissue analysis performed at sacrifice.

Another study on the retention and excretion of ^{210}Pb in dogs had been previously performed by Black[12]. The animals were exposed to an atmos-

phere containing radon and its daughters. The fraction of the calculated ^{210}Pb body burden retained after one year was about 25 %. The ratio of the daily fecal excretion to the daily urinary excretion radio varied from 2 to 8.7 for a period of about two years after exposure. This is another case of higher fecal excretion at late stages of experiment.

Blanchard and Moore[13] have analyzed tissues of 41 uranium miners and 11 unexposed people for the ^{210}Po content. The concentrations for exposed people were 5 to 50 times higher than in normal population.
Distribution studies gave the following results :

Tissue	% of body burden	
	^{210}Po	^{210}Pb
Bone	77.0	79.0
Lungs	5.6	4.9
Muscle	4.0	4.4
Kidney	1.3	-
Liver	-	2.2
Blood	-	1.6

The average value of the $^{210}Po/^{210}Pb$ body ratio was 0.74 in both exposed and non-exposed subjects. In general the relative distribution of the two nuclides in the body is similar among individuals of a population group. For some tissues though, due to differences in the degree and avenue of exposure, the relative concentrations may vary within a group. For instance, the concentrations of radiolead and polonium found in the lungs of miners were much higher than those observed for unexposed people in relation to the concentrations of other tissues. Good correlations seem to exist between the ^{210}Pb concentration in blood and that in bone and liver and between the ^{210}Po concentration in blood and that in bone, liver kidney and spleen. The results indicate that in this case blood concentrations were a good index of the ^{210}Po and ^{210}Pb body burdens. In the case of miners, when the exposure is interrupted, there is a removal from bone of ^{210}Po and ^{210}Pb which pass into other body compartments until an equilibrium is established between skeleton, blood and soft tissues.

Hursh and Suomela[14] administered carrier-free ^{212}Pb to three human subjects to determine the fraction of radiolead taken into the alimentary canal that enters the blood. The retention of ^{212}Pb was calculated by comparing the amount excreted in the urine during the first 24 hours with that of two subjects who received the radiolead by intravenous injection. The validity of this indirect method depends on the assumption that the fraction of the systemic ^{212}Pb excreted in the urine is the same whether the mode of administration is by ingestion or intravenous injection. The retention values found by Hursh and Suomela for the three subjects were : 1.3, 8.1 and 16.0 % of the administered dose with an average value of 8 % which is equal to that used by ICRP[15]. The results seem indicate a decrease in absorption with age. Excretion values given by the authors for experiments in which ^{212}Pb was injected intravenously indicate a higher excretion in urine in relation to that in feces : 4.9 and 3.4 % of the dose appeared in the 24 hr urine collection of two subjects, while the fecal excretions during the first

48 hrs were only 0.29 and 0.25 %. This might due to the fact that Hursh and Suomela carried out a short-term experiment because of the short half-life of ^{212}Pb and therefore the observations had to be made within the first two days following administration.
An "in vitro" experiment conducted by the same authors with heparinized blood incubated in the presence of ^{212}Pb, showed that after 16 minutes the uptake by the red cells was 99 %.

Hursh, Schraub, Sattler and Hoffmann[16] performed a study on the deposition, translocation and excretion of inhaled ^{212}Pb in humans. An average total lung retention of 25 % of the amount inhaled was found with a subsequent recovery of 3 % in the feces. The average 24 hr urinary excretion of radiolead was 2.8 %. The authors estimated that 50 % of the lung burden was distributed to systemic tissues in 6.5 hrs.

Booker, Chamberlain, Newton and Stott[17] studied the fate of inhaled and injected ^{212}Pb in two human volunteers. The inhalation experiment was performed with ^{212}Pb generated from a source of ^{228}Th and administered either attached to submicron particles or as vapour. For the particulate lead-212, initial retentions of 60 % and 34 % were observed for the two subjects respectively. After 24 hrs, 75 % of the activity passed into the blood with a subsequent slow removal from it. An excretion of only 2-3 % in the feces was observed after 72 hrs. When ^{212}Pb was inhaled as a vapour, in one experiment, the fecal excretion was 37 % of retained dose, after 72 hrs. This was due to vapour deposited in the upper respiratory tract and subsequent passage, through swallowing, into the gastro-intestinal tract.
In the experiment in which ^{212}Pb, was injected with 10 µg of $Pb(NO_3)_2$ as carrier, an increase in the activity of blood, with more than 90 % of it associated with the red cells, occurred during the first few hours. A similar observation was made by Hursh and Suomela[14] in the experiment with humans already mentioned and by Stover[18] who injected ^{212}Pb in dogs. In their experiment Booker et al. could not ascertain the ultimate fate of inhaled and injected lead-212. An increasing activity in the legs of one subject between 24 and 60 hrs after administration (injection and inhalation), seems to suggest an accumulation of ^{212}Pb in bone. An excretion in urine of 4.4 and 5.6 % of dose was observed in the first 24 hrs after injection which is in good agreement with the figures of 4.9 and 3.4 % found by Hursh and Suomela[14]. Because of slow transfer from the lungs, excretion of inhaled ^{212}Pb was lower.

STABLE LEAD

Holtzman[2] gives the following values for the distribution of stable lead in human body :

Tissue	% of body burden
Bone	83.2
Muscle	4.6
Liver	3.1
Blood	1.4

He calculated a total body burden of 111 mg for unexposed people. At equilibrium the daily intake of lead acquired through alimentary and respiratory absorption is equal to the daily urinary and fecal excretion. Holtzman calculated an intake of 0.46 mg/day of Pb. He gives a value of 0.08 for the fraction of the daily ingested lead entering the blood.

Kehoe[19,20] studied the metabolism of lead in man under normal and abnormal conditions. Considering a normal daily intake of 0.33 mg, he states that the output of lead in the feces corresponds to the lead in food, 0.3 mg/day, while the output of lead in the urine is about 0.03 mg/day. Somewhat less than 10 % of the normally ingested Pb is absorbed ; some of this may go back to alimentary canal and excreted. Of the inhaled Pb, 70-75 % is discharged in the expired air, 25-30 % is retained. According to Kehoe, there is little evidence of retention or accumulation of lead in the body of the normal individual even though lead is found in all human tissues. Most of it is found in the skeleton. A progressive increase of lead body burden with age under normal environmental conditions is excluded by Kehoe.
In order to get information on absorption, excretion and retention of lead under occupational or abnormal conditions, Kehoe carried out experiments in humans with ingested and inhaled lead. With daily intake varying from 0.3 to 3.0 mg, added to the amount of lead normally introduced in the organism, he observed a prompt increase in the Pb concentration of urine. A smaller and more gradual increase was also observed in the lead concentration of blood and of all tissues. The increase would continue at a steady rate as long as the alimentary absorption of lead was being maintained at a constant rate. At the termination of the experimental ingestion of lead, there was a decrease in the concentration of lead in urine and blood. Kehoe found that the loss of lead accumulated in the body depended more upon the length of time over which the accumulation occurred than upon the quantity accumulated.
The inhalation experiments were carried out with particles of diameter varying from 0.05 to 1.2 μ. The retention of lead ranged from 35 to 54 % according to particle dimensions. A prompt increase in the lead concentration of urine was observed, but the most significant result was that the increase reached a peak above which it did not go subsequently. When most of the particles had diameters above 1 μ, the quantity of lead excreted in the feces increased, because of deposition in the upper respiratory tract and passage into the gastrointestinal tract. Kehoe states that the severity of occupational exposure is related to the concentration of lead in blood which, therefore, may be an index of body burden, in agreement with Blanchard's[13] observations.

Patterson[21] describing the contaminated and natural environments of man, states that toxic tresholds of lead concentrations in the blood may be better defined than toxic tresholds for total body burdens. The amount of lead present in the blood reflects that absorbed during a very short period ; over longer periods the blood concentration of lead tends to increase only with increased rates of absorption. Lead content of urine reflects better short-term fluctuations in lead ab-

sorption.
Patterson estimated that in the USA, because of industrial contamination, absorption rates are about 30 times higher than natural rates, yielding body burdens of about 200 mg/70 kg and blood concentrations of 0.25 ppm.

Mehani[22] performed an experimental study on the retention of lead in workers exposed to a contaminated atmosphere. The average percentages of lead retained in relation to the amount inhaled were 39 and 47 % for two different types of workers. The values are not much different from those given by Kehoe[19]. Despite the rather good agreement between results of different, eventthough similar, experiments, Mehani affirms that the percentages of lead retention represent only approximate orders of magnitude because of difficulty in the measurements. The interaction of various factors (e.g. : particle size and density, respiratory frequency, exposure, duration...), might affect the results.

Schroeder and Tipton[23] analyzed human tissues collected between 1952 and 1957 in various localities of the United States and other countries in order to determine the lead content. Concentrations in U.S. subjects were, in general, higher than in those from Africa and the Far East. The lead concentration of some tissues, e.g. : aorta, kidney, liver, lung, bone, appeared to increase with age in Americans. For non-Americans lead increased with age only in aorta.
The analysis of bone revealed that the skeletal content was higher for American subjects, about 91 % of total body burden. The authors affirm that lead exposures from food and water probably declined in recent years, while those from air increased. Correlations of concentrations of lead in lungs and in other tissues indicate that soft tissue lead reflects pulmonary lead and that lead deposited in the lungs is absorbed into the rest of the body.

Jaworowski[4] in his study on stable and radioactive lead in the environment and in the human body, on the basis of data of his own and from other authors, estimates that the world mean body burden for stable lead is 240 mg/70 kg. He reports the following fractions of total body burden (source ICRP) :

Tissue	% of body burden
Bone	69.5
Muscle	7.7
Skin and subcutaneous tissue	5.1
Liver	5.1
Fat	3.0
Blood	2.4
Lungs	1.1
G.I. tract	0.9
Bone marrow	0.9
Brain	0.9
Kidneys	0.6
Lymphoid tissue	0.2
Heart	0.2
Spleen	0.2
Other	2.1
Total body	100.0

Data of Hofreuter et al.[24] are also reported in Jaworowski's review as an indication of existing differences in blood lead concentration in relation to residential area, sex and smoking habits.

Group	Mean blood concentration ppm Pb	
	Urban areas	Rural areas
Male	0.21	0.16
Female	0.16	0.10
Smokers	0.21	0.17
Nonsmokers	0.17	0.11

No correlation between blood levels and age was observed ; however, according to other authors, there is such a correlation for the lead content of bone and of some other organs (e.g. liver). Jaworowski calculated the mean concentration of lead in bone of professionally exposed humans :

Bone	ppm Pb
Cortical	24.2
Trabecular	7.4

He suggests the use of hair, which reflects the blood levels of lead existing during its growth, for the detection and evaluation of internal contamination. He gives a mean concentration of 8.9 µg/g hair for unexposed people and 79.7 µg/g hair for professionally exposed people and found an average hair/bone concentration ratio of 3.84 analyzing samples from the same individuals.

Hammond[25] in describing the metabolism of lead mentions the two principal routes of entry into the organism : gastrointestinal tract and lungs. Absorption through the skin is insignificant for inorganic lead, quite important on the contrary for alkyl lead compounds. It is known that under conditions of normal intake, absorption of ingested lead in humans is less than 10 % but, acoording to Hammond, knowledge is lacking about the transfer mechanism of lead across the gut mucosa into the blood. Calcium in the diet plays an important role on the degree of absorption.
Retention of inhaled lead, estimated by different authors not to exceed the 50 % of the amount introduced in the organism, is influenced by particle size.
The affinity of lead for bone is also known, (90 % of total body burden) but Hammond points out that the mechanism of deposition and removal of lead in bone requires further investigations. Studies on the distribution of lead in soft tissues revealed a considerable range of concentrations. Hammond, on the basis of the findings of other authors, confirms an increase in lead concentration of bone and of various soft tissues with age at least through the fifth decade of life. He reports results of the "Three-city study" [26] performed in USA in 1961-1962 from which it is evident that 1) the concentration of lead in blood and urine did not increase over a period of 5 years, 2) the concentration of lead increases in relation to automobile traffic, 3) smoking habits influence blood and urine concentration of lead 4) levels of lead observed are well within the accepted range of concentrations considered non-dangerous for humans.

Barry and Mossman[27] have determined lead concentrations in human tissues of 69 individuals from an area characterized by increasing industrialization over a period of more than 100 years. A consistent difference was observed in the Pb concentration of bones from individuals of both sexes. Adult male bones were found to contain concentrations as high as 30 times that in females.
This was not valid for soft tissues. The concentrations of lead appeared to increase with age only for bone samples. Total body burdens presented great variations. Ninety five % of lead content was in bone (70 % in cortical bone). In some occupationally exposed subjects lead content of bones was higher than in unexposed subjects, but no difference was observed in soft tissues. Examples of Pb mean concentrations of tissues from unexposed and exposed people are :

Tissue	occupational exposure ppm Pb	non-occupational exposure ppm Pb
Bone (Tibia)	59.20	32.65
Liver	1.17	1.11
Lung	0.29	0.30
Blood	0.17	0.22
Muscle	0.04	0.06

Values found for lead body burdens, whose non-occupational range is 108-352 mg, are comparable to those of earlier investigators. They indicate, therefore, according to Barry and Mossman, that the present population is not exposed to higher levels of lead.

Blokker[28] in a very recent review concerning the health aspects of lead emissions from gasoline engines, has studied, among other topics, the presence of lead in the human organism. He states that the main hazard resulting from exposure to small amounts of lead resides in its gradual accumulation in the body of exposed people during their lifetime. Data gathered by the California Public Health Department[29] and by Patterson[21], reported in Blokker's review, indicate that for urban residents the total quantity of lead absorbed from the respiratory tract is of the same order of magnitude as that absorbed from the gastrointestinal tract.

Goldsmith and Hexter[30] confirm this fact. According to them, increasing respiratory exposure may cause an increased storage of lead in the body. Kehoe[31] in a recent study denies this possibility. In regard to the use of blood lead as indication of total body burden, Blokker reports what is stated in a publication of the California Public Health Dept.[29], that repeated blood analyses from the same individual may give quite different results, while total body burden does not change. However, blood may be a reliable indicator of body burden in population studies where individual variations average out. Blokker includes in his review also some results of the "Three-city study"[26], already mentioned by Hammond[25], and "The Los-Angeles Free-way study"[32]. Such results clearly indicate that a correlation exists between lead air levels and blood concentrations of lead. For instance, to an exposure of 2.2 µg/m3 for employees of Pasadena corresponds a mean blood lead of 19 µg/100 g. A correlation between inhaled lead and lead concentration in bone was observed during experiments with animals.

Blokker reports the results of Lutmer et al.[33] who in mice exposed to auto-exhausts found a bone content 40 % higher than in unexposed animals.

CONCLUSIONS

The analysis of various studies has revealed that many experiments have been performed to investigate the problem of radioactive and stable lead contamination of humans. Despite the relative abundance of data the literature, transfer coefficients of lead through the respiratory and gastro-intestinal tracts, are not known with a sufficient degree of precision. Data on storage of lead in the different compartments of the organism are also far from being consistent. The absorption and retention values given by some authors have always a range of variation, sometimes rather large ; they do not provide, therefore, a completely satisfactory basis for the establishment of permissible levels of exposure.
With regard to the principal aim of the present review which was to ascertain whether experiments performed with radioisotopes of lead in animals and humans, may provide useful information on the metabolism of stable lead in man, recapitulative tables with data on radioactive and stable lead are presented (see Tables 1 and 2). It seems evident, in general, that the results of experiments performed with radioactive tracers are confirmed by those on the behaviour of stable lead in man. However, metabolic differences may occur for carrier-free radiolead and for stable lead introduced into the organism at normal or abnormal levels. Yet, many important questions concerning the toxicological aspects of environmental contamination due to lead are still without satisfactory answer. The experiments with lead radioisotopes which in the past were performed with the aim of estimating the degree of exposure to radiolead for the establishment of radioprotective rules, might be usefully continued to fill in the subsisting gaps concerning stable lead.
The choice of the radioisotope and the experimental conditions should be, of course, carefully studied in order to obtain results and conclusions which give a valid contribution to the elucidation of the toxicity mechanism of lead.
The analysis of the different studies on metabolism of lead, has shown where additional research is required. The following list includes the main subjects to be further studied also with the use of radiolead :

1) Form of Pb circulating in plasma ("in vivo" studies not performed). Nature of binding to plasma constituents.
2) Relationship between Pb in blood and in soft tissues and between Pb in blood and in total exchangeable Pb pool.
   Factors influencing the relation of Pb in blood to Pb in soft tissues e.g. age, sex, blood type, etc...
3) Mechanism of Pb transportation across the intestinal mucosa into systemic circulation.
4) Mechanism of deposition of Pb in bone or metabolic factors modyifing interaction of Pb with bone.
5) Effects of interruption of Pb absorption on reduction of Pb body burden. Factors influencing mobilization of Pb in the body.
6) Fate of inhaled Pb. Absorption rates for particles of less than 1 μ (radioisotopes of lead could be particularly useful).
7) Effects of lead on enzymatic systems.

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FIGURE : 1

Metabolic pathways of radiolead in human organism

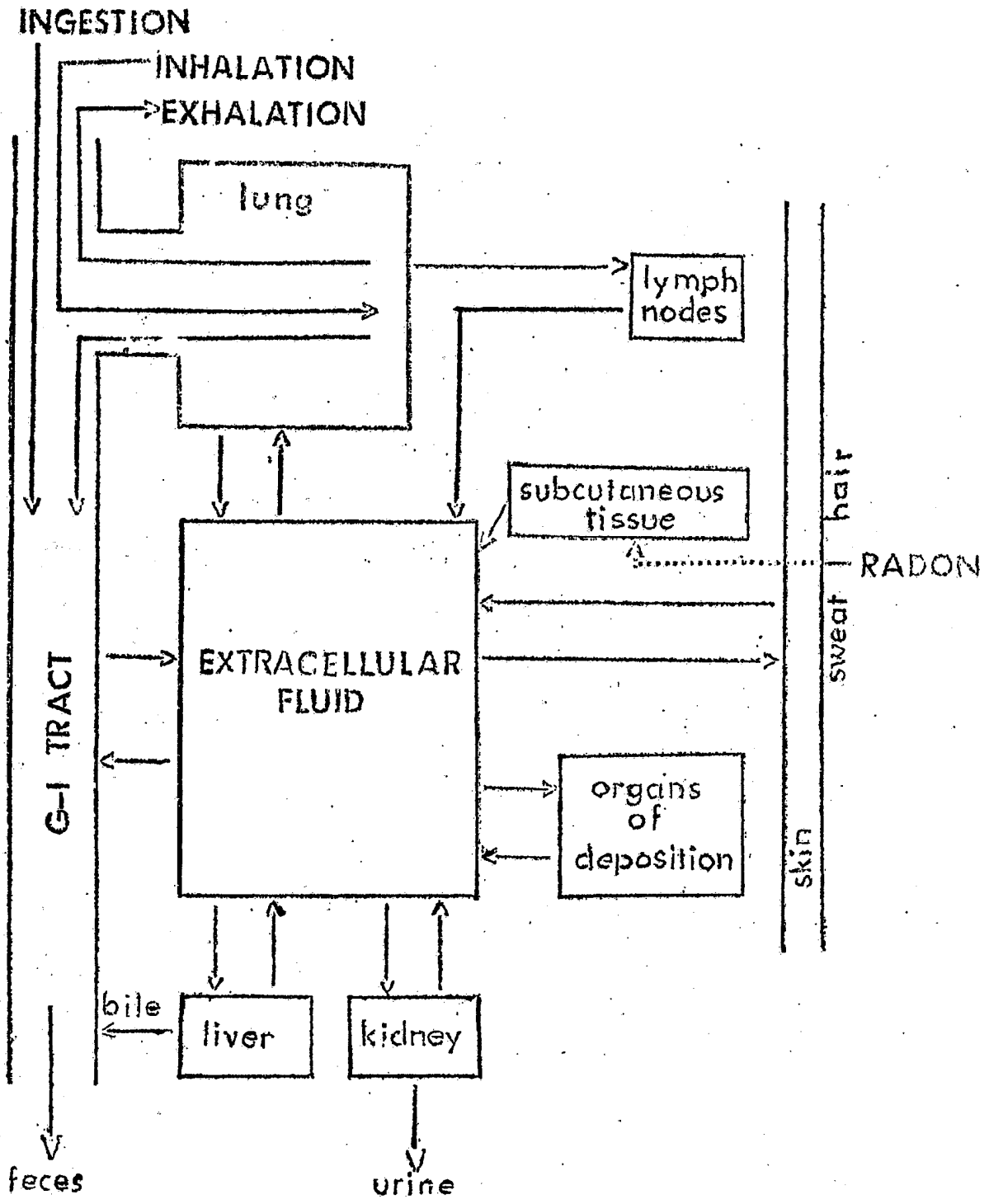

TABLE I

Distribution of radioactive and stable lead in man

Tissue	% of body burden		N° reference (see list)
	^{210}Pb	Stable Pb	
Bone	63.0	83.0	2, 3
	58.0		5
	80.0		5 (other authors)
	79.0		13
	80.0		13 (other author)
		70.0	5 (ICRP)
		90.0	12 (other author)
		91.0	23
		95.0	27
Liver	1.7	3.1	2, 3
	2.8		5 (other author)
	1.5		5 (other author)
	2.2		13
		5.1	5 (ICRP)
Spleen	0.14		5
		0.2	5 (ICRP)
Muscle	17.0		2
	13.0		5 (other authors)
	4.4		13
		4.6	2
		7.7	5 (ICRP)
Soft tissues(all)	30.0		5
		30.0	5 (ICRP)
Blood	2.0		5
	1.6		13
		2.4	5 (ICRP)

TABLE II

Retention and excretion of radioactive and stable lead

Mode of administration	Retention (% of dose)	Excretion (ratio Feces/Urine or %
Ingestion	^{210}Pb in rats : 5% (Ref.1) (parenteral administr.) ^{212}Pb in humans : 1.3%, 8.1%, 16.0% (Ref.14) Stable Pb in humans : 8% (Ref.2) Stable Pb in humans : 10% (Ref.19)	^{210}Pb in humans : Feces/Urine =
Inhalation	^{210}Pb in rats : 32% (Ref.1) ^{210}Pb in dogs : 25%, 15% (Ref.10) ^{210}Pb in dogs : 25% (Ref.12) ^{212}Pb in humans : 25% (Ref16)+ ^{212}Pb in humans : 60%, 34% (Ref.17)+ (initial retention) Stable Pb in humans : 25-30% (Ref.19) Stable Pb in humans : 35-54% (Ref.20) (Pb particles:0.05-1.2 μ) Stable Pb in humans : 39%, 47% (Ref.22)+	^{210}Pb in dogs : Feces/Urine = 1. ^{210}Pb in dogs : Feces/Urine = 5 ^{212}Pb in humans : Urine = 2.8% (24 hrs) ^{212}Pb in humans : Feces = 2-3% (72 hrs after administr.)
Injection	^{210}Pb in rats : 24% (Ref.1) ^{210}Pb in rats : 45% (Ref.4) ^{210}Pb in dogs : 49%, 38% (Ref.11)	^{210}Pb in rats : Feces/Urine = 1 ^{210}Pb in baboon : Feces/Urine = ^{210}Pb in dogs : Feces/Urine = 3 ^{212}Pb in humans : Urine = 4.9%, (0 - 24 hrs) Feces = 0.29%, (0 - 48 hrs) ^{212}Pb in humans : Urine = 4.4%, (0 - 24 hrs)

+ lung deposition = inhalation minus exhalation, as specified by authors