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METABOLISM OF INORGANIC LEAD IN OCCUPATIONALLY EXPOSED HUMANS

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Decay rates of blood lead levels in 29 lead workers after end of exposure were analysed mathematically with an exponential two-compartment model. The slow pool had a median half-time of about 5 years, the fast one about one month, but with a considerable inter-individual variation. Lead levels in finger-bone, as determined in 73 active and retired workers by an X-ray fluorescence method, ranged from less than 20 up to 135 mg/kg. There was an increase of finger-bone lead level with increasing exposure time (maximum about 10 mg/kg/year), but the variation between individuals was considerable. In retired workers there was an association between lead levels in finger-bone and blood; an increase of 100-150 mg/kg corresponded to about 1.5 μmol/l. Bone lead levels in biopsies from vertebral spinous processes of 28 lead workers were often lower or higher than in finger-bone, suggesting at least two bone lead pools. Lead level in bone may be practically useful to determine the extent of »internal« lead exposure by mobilization from the skeleton.

Exposure to inorganic lead is still important in the occupational setting. In Sweden the number of exposed subjects has been estimated at about 5 000. Cases of classical clinical lead poisoning are rare nowadays. However, in the last years subclinical adverse effects have been found at exposure levels earlier believed to be harmless.

There is thus a need for information on the metabolism of lead in man. However, many important aspects of human lead metabolism are not well understood. We here present some data from studies on this issue. Kinetics of blood lead as well as lead levels in the skeleton have been investigated.

KINETICS OF BLOOD LEAD

A group of 29 lead workers was examined. They had been exposed either in a secondary smelter, in metal scrapping, in a storage battery

plant, in a plant coating wire with lead, or at spray-painting. Blood lead (B-Pb) was measured after removal of workers from occupational lead exposure.

B-Pb was analysed with a method of atomic absorption spectroscopy after wet digestion and extraction with dithizone in methyl isobutyl ketone (1). The detection limit was 0.05 μmol/l and the method error 4 per cent. The accuracy was continuously checked in a Nordic inter-laboratory calibration programme and was always within ±10 per cent of the mean of about ten participating laboratories.

The elimination pattern first displayed a rapid decrease and then a slower decay (Fig. 1). The sum of two exponential functions could be fitted to the data. Thus half-time of one slow and one fast compartment could be calculated.

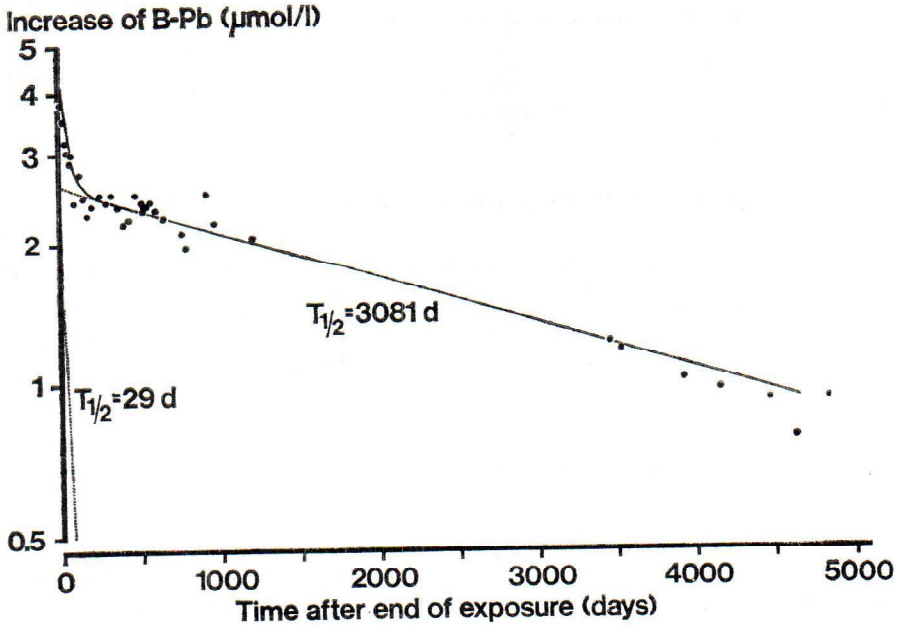

Fig. 1 — *Decay of blood lead level (logarithmic) after end of exposure in an ex-lead worker. A two-compartment model was fitted to the data. Biological half-times ($T^1/_2$) for the compartments are given.*

The decay rate of the slow compartment was calculated in 13 retired subjects followed for up to 11 years. The half-time of the slow compartment ranged 2—11 years, with a median of about 5 years. An

accurate estimate of decay rates needs a lot of data covering a long time period. Therefore we are not sure that the full range found is correct. However, the median should be a fairly good estimate.

The only organ containing an amount of lead sufficiently large to cover the slow compartment is the skeleton, which is known to harbour more than 90 per cent of the body burden of lead (Table 1). The two-compartment model thus may involve one large skeletal pool and one small one, probably mainly representing the soft tissues.

Table 1

Lead levels in organs from a dead lead smelter worker. Analyses were made by atomic absorption spectroscopy.

Organ	Lead level (mg/kg)
Blood	0.47 (2.3 μmol/l)
Liver	1.2
Kidney	1.0
Heart	0.07
Muscle	0.17
Bone marrow	0.77
Brain	
White matter	1.3
Gray matter	6.3
Nerve	0.36
Skeleton	
Femur	180
Finger	120
Vertebra	110

The half-time for lead in the skeletal pool is considerably shorter than has been estimated earlier by different indirect methods (2).

In 18 subjects, mostly removed from work with lead because of high B-Pb (3.5 μmol/l or more), the half-time of the fast compartment was calculated. In 16 cases the time studied (240 days or less) was not enough to permit an accurate estimate of the slow compartment. Thus the median half-time obtained in the retired workers was applied (Fig. 2). There was a considerable variation in half-time between different subjects. The shortest half-time was 7 days and the longest one 69 days (Fig. 3). The median value was 31 days. This is in accordance with our earlier findings in 2 subjects exposed to a single heavy lead dose (1). Also, it fits remarkably well with other data, obtained in subjects exposed to much lower lead doses (3, 4).

The inter-individual variation in half-time probably implies a different risk at a certain lead absorption. However, it is not known

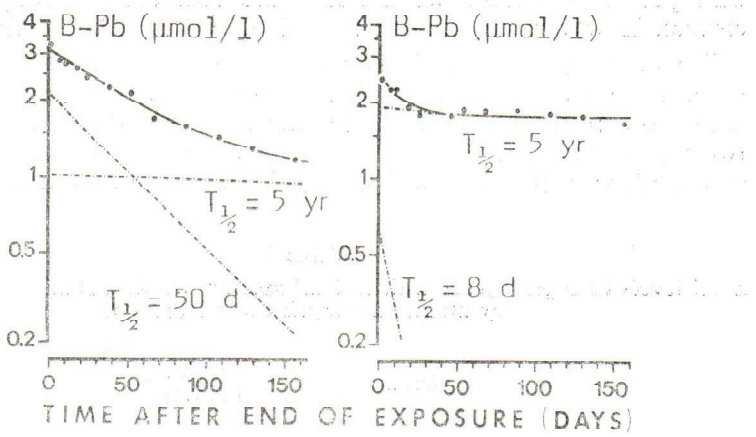

Fig. 2 — *Decline of blood lead level (logarithmic) in lead workers temporarily removed from exposure. A two-compartment model was fitted to the data. Biological half-time ($T^1/_2$) of the slow compartment was set at 5 years. $T^1/_2$ for the fast compartment is given.*

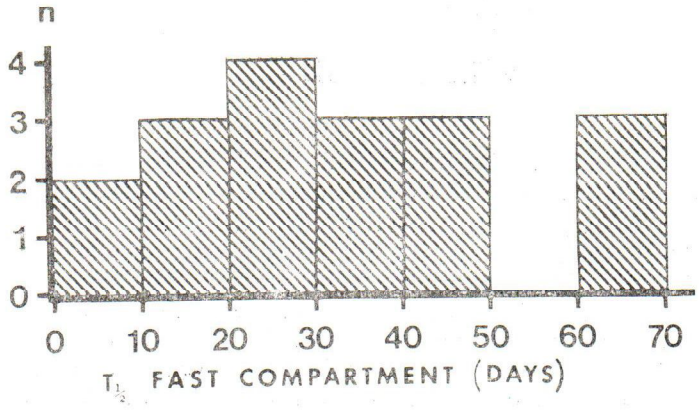

Fig. 3 — *Half-times ($T^1/_2$) of the fast compartment of lead in blood in 18 lead workers removed from exposure.*

whether the rapid decrease in some individuals is due to fast excretion, efficient incorporation in the skeleton, or both. If the lead is mainly accumulated in the skeleton, the rapid decay of B—Pb may not be entirely advantageous, as lead in the skeleton causes a source of »internal« lead exposure, as will be shown in the following.

Lead is not the only heavy metal displaying remarkable inter-individual variations in kinetics. We have earlier made similar findings for methylmercury (5) and cadmium (6). Recently, a considerable range was seen in the excretion rate of chromium (7).

The slow compartment made up 33—83 per cent of the combined slow and fast compartments, the average was 60 per cent. Thus the impact of the lead pool present in the skeleton upon B-Pb is considerable. If this is not realised, at biological monitoring of exposure, a raised B-Pb, which is really due to »historical« exposure, may be misinterpreted as caused by present lead absorption. Also, significant »internal« exposure of e. g. the nervous system may occur, not only during exposure, but long after retirement. It has sometimes been claimed that the lead pool in the skeleton constitutes a risk for acute lead poisoning if it is rapidly released. However, although theoretically possible, e.g. when lying in bed with high fever, in hyperparathyreoidism or osteolytic bone tumours, there are no convincing case reports on such events. But it is obvious that it is worthwhile to study the lead burden in the skeleton. However, information on this important issue is limited.

LEAD IN THE SKELETON

The lead content in bone may be estimated by an X-ray fluorescence (XRF) method (8, 9). The interphalanx of the left forefinger is irradiated by low energy photons from two 57-Co sources. This causes an emission of characteristic X-ray from lead in the bone, which is measured. Each measurement takes 40 minutes. The detection limit of the method is 20 mg/kg and the method error about 30 per cent. A good accuracy of the method has been established by measurements in the same forefinger *in vivo* with XRF and *post mortem* with XRF and chemically by atomic absorption spectroscopy. The XRF method was applied on lead workers. In addition to the occupations studied in the blood lead kinetics investigation, a few metal moulders were included.

Finger-bone lead concentrations were measured in a total of 40 active lead workers, who had been exposed for an average of 13 years. The levels ranged from less than 20 up to 122 mg/kg. The average was 59 mg/kg. In 33 retired lead workers, who had a mean exposure time of 23 years and who had been retired for an average of 4 years, the finger-bone lead level ranged from less than 20 up to 135 mg/kg. The

average was 65 mg/kg. There was an increase of bone lead levels with increasing time of employment, but the variation was considerable (Fig. 4). The maximum accumulation rate was about 10 mg/kg/year. Retired workers may have high levels, which indicates a slow decay after end of exposure.

The levels encountered are in agreement with a limited number of earlier reported values on skeletal lead levels in lead workers, mainly measured *post mortem* (10—14). The variation of bone lead with time is not surprising. The intensity of exposure may have varied. Also, differences in the kinetics of metabolism would expand the range.

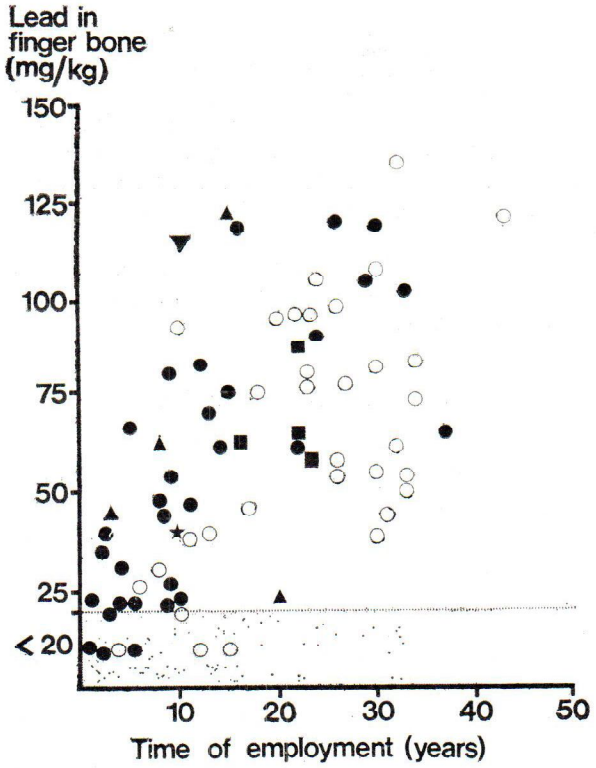

Fig. 4 — *Relation between lead level in finger-bone and time of lead exposure. Closed symbols denote 40 subjects exposed in the last year, open symbols 33 subjects not exposed in the last year. Round symbols indicate smelter workers, squares metal scrappers, triangles metal moulders (point upwards) and a storage battery worker (point downwards), and a star a spray-painter. Area below detection limit is shadowed.*

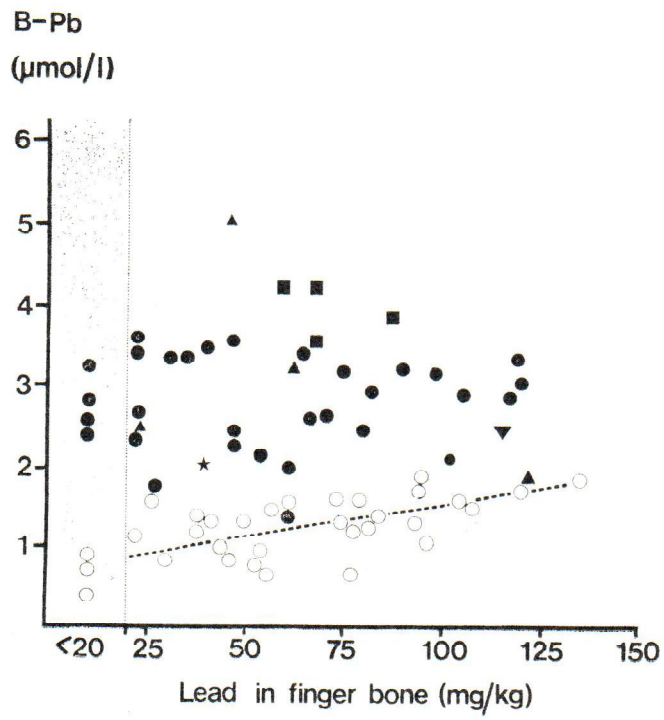

Fig. 5 — *Relation between lead level in finger-bone and blood in lead workers. Numbers and symbols as in Figure 4. The regression line (Y = 0.0077X + 0.82) denotes open symbols above the detection limit.*

In presently exposed lead workers no association between bone lead levels and B-Pb was observed (Fig. 5). However, in retired workers there was an increase of B-Pb with rising bone lead. At a skeletal lead level of 100—150 mg/kg, the corresponding B-Pb was 1.5—2 μmol/l of which about 0.5 μmol/l is the »normal« background B-Pb concentration in Sweden. The lack of correlation between lead levels in the finger-bone and blood in active lead workers is not surprising as the lead absorption during the last period should cover efficiently any association. After retirement, when the absorption decreases, the association is revealed.

The finger-bone tissue analysed by XRF is mainly of the cortical type. The skeleton in addition contains trabecular bone, which in many aspects differs from the cortical bone. Thus it was of interest also to study the lead levels in trabecular bone. One part of the

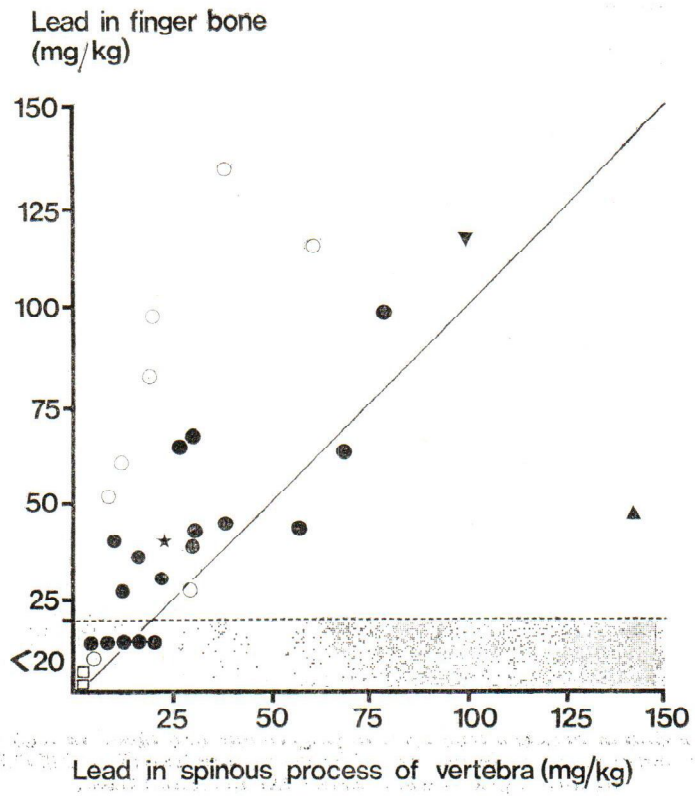

Fig. 6 — ***Relation between lead levels in finger-bone and in spinous process of*** *vertebra. Open squares denote 2 occupationally non-exposed subjects. Other symbols (as in Figure 4) indicate 28 lead workers. The line shows identity.*

skeleton, which contains that kind of bone, is the vertebra. Samples of about 10 mg of vertebral bone tissue may be obtained from the spinous process of lumbar vertebrae by bone biopsy using Radner's instrument (15). The samples were analysed by a method of atomic absorption spectroscopy similar to that employed for blood. The detection limit is considerably below that of XRF, less than 1 mg/kg. Good accuracy has been ascertained by analysis of biopsy samples and larger samples obtained from the same spinous process.

Biopsy samples were obtained from 30 subjects examined earlier also by XRF (Fig. 6), of whom 28 were active or retired lead workers and 2 occupationally nonexposed persons. The levels found in the

spinous process biopses were often considerably different — lower or higher — from the level in finger-bone as analysed by XRF. It is interesting to note that retired lead workers have relatively lower levels in the vertebrae than in the finger-bone.

One possible explanation of the lack of association may be that the cortical finger-bone and the trabecular vertebral bone represent two different skeletal lead pools. Indeed, this was suggested by animal experiments many years ago (16). Also, three-compartment models have been applied to lead metabolism on the basis of animal data in several studies. It must be realized, however, that it is easy to fit data to a complicated model but difficult to produce firm evidence that a certain multi-compartment model is better than any other.

As already mentioned, determination of lead levels in bone, whether analysed by XRF or chemically in biopsy material, may have practical importance in surveillance of exposure, as it allows conclusions on to what extent a raised B-Pb is due to earlier or present exposure. Moreover, it may be used as a time-integrated dose index in studies of the relation between long-term exposure and effects or response in cross-sectional studies.

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Sažetak

METABOLIZAM ANORGANSKOG OLOVA U PROFESIONALNO EKSPONIRANIH LJUDI

Napravljena je matematička analiza smanjenja razine olova u 29 radnika pomoću modela s dva kompartmenta. Spori dio kompartmenta imao je vrijeme poluvičnog nestanka od otprilike pet godina, a brzi od otprilike jedan mjesec. Postojale su značajne individualne varijacije. Razina olova u falangama kretala se između 20 i 135 mg/kg, kao što je utvrđeno fluorescentnom metodom s X-zrakama u 73 aktivna i umirovljena radnika. Razina olova u kosti rasla je s vremenom ekspozicije s maksimumom od 10 mg/kg. U umirovljenih radnika postojala je povezanost između koncentracije olova u kosti i one u krvi. Povećanje od 100 do 150 mg/kg u kosti odgovaralo je otprilike 1,5 μmol/L. Koncentracija olova u spinalnim nastavcima kralješaka bila je često veća ili manja od one u falangama, što upućuje na postojanje barem dvaju kompartmenta. Razina olova u kosti može poslužiti u praktične svrhe za procjenu moguće interne ekspozicije olovu mobiliziranjem iz skeleta.

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