In-vivo determination of lead in the skeleton after occupational exposure to lead

L AHLGREN,[1] BIRGITTA HAEGER-ARONSEN,[2] S MATTSSON,[1] AND A SCHÜTZ[3]

From the Radiation Physics Department,[1] University of Lund, Lund, Department of Occupational Medicine,[2] Malmö General Hospital, Malmö, and Department of Occupational Medicine,[3] University Hospital, Lund, Sweden

ABSTRACT The concentrations of lead in the phalanges and in the blood were determined in 22 subjects who had formerly been exposed to lead in a storage battery plant, which had been closed for seven years. The bone lead concentration was measured in vivo using an x-ray fluorescence technique in which two ^{57}Co γ-ray sources were used for generating the characteristic x-rays of lead, which were measured with a Ge(Li) detector. In three subjects the variation of the lead concentration along the forefinger was measured together with the lead concentration in the tibia. The measured lead concentrations in the phalanges were between 20 μg/g (our detection limit) and 118 μg/g. The lead concentration in the phalanges was found to increase with the length of employment, but no simple relation was found between the lead concentrations in the blood and in the phalanges. The decrease in the blood lead concentration after the cessation of exposure was followed in four subjects. Seven years after exposure had ended, the blood lead concentration was found to be more dependent on the daily intake of lead than on the release of lead from the skeleton. These experimental results could be explained by a two-compartment model using exchange rates given in publications. This model has also been used to calculate the blood lead concentration that could be achieved after a sudden release of lead from the skeleton.

The skeleton contains about 90-95% of the total body burden of lead.[1][2] Measurements of the lead concentration in the skeleton are therefore of fundamental importance for estimating the total body burden of lead. In earlier publications[3-5] we have reported the in-vivo detection of lead in the skeleton of lead workers using x-ray fluorescence analysis. This paper deals with a comparison between the lead concentrations in the blood and in the skeleton as determined in the phalanges by x-ray fluorescence analysis in vivo. The determinations were carried out on subjects whose occupational exposure to lead had ended seven years before the study.

Materials and methods

Twenty-two men aged between 27 and 75 years (mean 57), who had earlier worked in a storage

battery plant for periods from 0·8 to 45 years (mean 22) were studied. At the time of the measurements the factory had been closed for seven years, since which time none of the subjects studied had been occupationally exposed to lead. Blood samples for determination of the lead content were collected at the time of the in-vivo measurement and analysed by atomic absorption spectrophotometry.[6] For some of the subjects studied, the variation in the blood lead concentration had also been followed during the first year after the closing down of the factory.

In our determination of lead in the skeleton the lowest detection limit (20 μg Pb/g fresh weight) is reached when the measurements are carried out on the fingers. The lead concentration in the second phalanx of the left forefinger was therefore determined for all the participants in this study. The fingers were carefully washed with water and detergent before measurement to remove any lead which might have been contaminating the skin. For three of the subjects, the proximal and distal joints of the left forefinger as well as the upper part of the tibia

were also measured. In normal measurements a small volume (about 1 cm³) of the second phalanx of the left forefinger was irradiated for 40 minutes with two collimated ^{57}Co sources (0·6 and 0·2 GBq) as shown in fig 1. The count rates of characteristic *x* rays emitted from lead in the irradiated bone volume were measured with a Ge(Li) spectrometer (16 mm diameter × 5·2 mm; energy resolution: FWHM = 750 eV at 75 keV). The angle between the incident and measured radiation was about 90°. The collimator in front of the detector and the radiation shield was made of high purity tin partly covered with gold (fig 1). The mean diameter of the bone measured was calculated from two radiographs taken in orthogonal projections. To relate the count rates of the characteristic lead *x* rays to the lead concentration in the bones of the finger, measurements on finger-like phantoms with known concentrations of lead in their bony part and with various bone diameters were carried out as described by Ahlgren and Mattsson.[5]

Radiation dosimetry—The absorbed dose rate to the finger was measured with small (2 × 2 × 1 mm³) extruded LiF dosimeters. The absorbed dose at the surface of the skin was 5·5 mGy (550 mrad) and to the centre of the finger it was 2·5 mGy (250 mrad) per 40 minutes. Since the total volume of the finger (bone and soft tissue) irradiated was always less than 3·5 cm³, the total absorbed energy was much
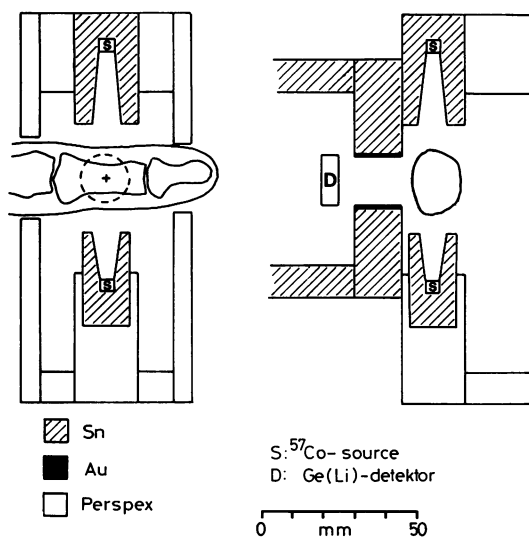
Table 1 *Mean absorbed dose and absorbed energy*

Type of investigation	Mean absorbed dose mGy	Absorbed energy mJ
x-ray fluorescence analysis of finger	2·5	10^{-2}
x-ray examination of hand	0·65	$(10\text{-}25) \times 10^{-2}$

smaller than in an ordinary radiograph of the hand (table 1).

Results and discussion

It is important to know how well the lead concentration in the phalanges represents the mean lead concentration in the skeleton and thus the total body burden of lead. Figure 2 shows the results of measurements of the lead concentration in different parts of the skeletons of three highly contaminated subjects. The concentrations in three different regions of the left forefinger are not significantly different, and a significant difference between the lead concentration in phalanx and the tibia could be detected only for one person (No 1, fig 2). It must, however, be pointed out that the uncertainty in the tibia measurements was considerably larger than that in the finger measurements. This means that differences of up to 50% between the lead concentration in the phalanx and the tibia could be present without their being registered as being significant.

Of the 22 men studied, 15 (70%) had lead concentrations in the phalanx above 20 μg/g, which was the limit of detection. The lead concentration in the phalanges increased with the length of employment in the battery factory (fig 3). The variation of the exposure to lead, with time, and from worker to worker, is only very poorly known, although increased health care certainly lowered the exposure to lead during the last years of the exposure period. The shortest period of exposure giving a measurable lead concentration in the fingerbones was three

Fig 1 *Arrangement for determination of lead in phalanx by x-ray fluorescence analysis. Radiation shield, two ^{57}Co sources, detector collimator with its gold-covered opening, and perspex-holder for finger are shown.*

Sn
Au
Perspex

S: ^{57}Co- source
D: Ge(Li)-detektor

0   mm   50

Subject No				Tibia
1	117± 9	118±12	135±12	62±19
2	59±7	65±10	89±9·	85±18
3	81 ± 10	94 ± 13	85±11	84±21

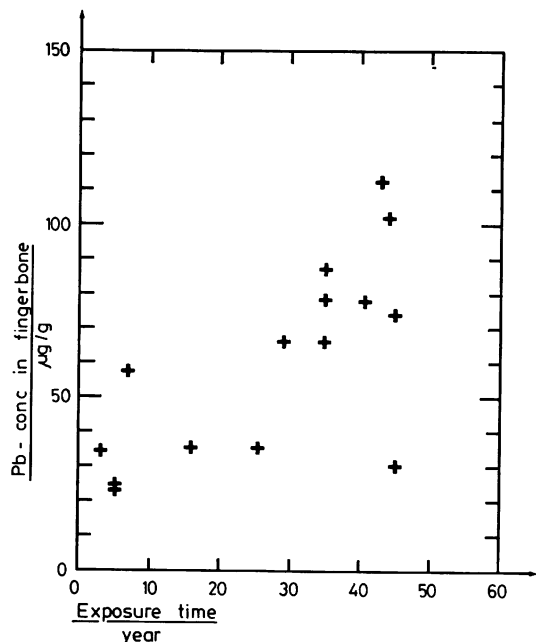Fig 2 *Lead concentrations (μg/g ± 1 SD) in phalanx and tibia.*

Fig 3 *Measured lead concentration in phalanx of subjects with different periods of occupational exposure.*

years. Figure 4 shows the lead concentrations in the skeleton and the blood for 15 workers, the periods of employment being roughly indicated in the figure.
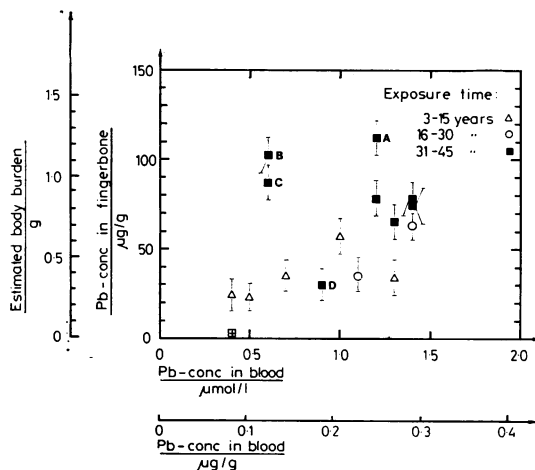
The mean blood lead concentration for men from the same part of Sweden but with no known occupational exposure to lead is 0·4 μmol/l (range 0·2-0·9 μmol/l).[7] From lead concentrations in the skeleton derived from necropsy samples taken from 126 non-occupationally exposed Danes, the total body burden of lead has been estimated to be 22 mg.[8] Assuming that the lead concentration in the phalanx reflects the body burden, fig 4 indicates that even seven years after the end of exposure to lead there is no simple relation between the total body burden of lead and the blood lead concentration.

Three subjects (A, B, and C) deviated from the rest of the group in having ratios between the lead concentrations in the skeleton and in the blood which are two to three times greater than for the other subjects. Subject A had been exposed to lead oxide dust for 43 years, while B had been highly exposed to the same dust during the first 20 years of his employment. During this period he had several times shown acute symptoms of lead poisoning, but for the last 20 years of employment his exposure to lead had been very low. Subject C was exposed for 35 years, but the degree of his exposure cannot be reliably estimated. The last of this group, (D), worked for 45 years, being mainly concerned with the melting of metallic lead. Figure 5 shows the variation in the blood lead concentration of A, B, C, and D after their exposure was discontinued. The rapid decrease in the blood lead concentration may represent the washout of lead from the pools of soft tissue. The figure suggests that seven years after exposure had ended the blood lead concentration of these highly contaminated people was dependent
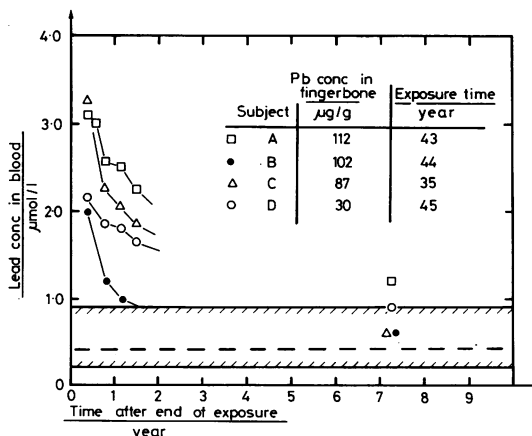

Fig 4 *Measured lead concentrations in phalanx and blood for occupationally exposed subjects. Total body burden of lead is estimated assuming that lead concentration in phalanx represents lead concentration in whole skeleton. ⊞ represents these values for non-occupationally exposed people. Indicated uncertainty is due to counting statistics.*

Fig 5 *Measured blood lead concentrations at different times after end of occupational exposure. Mean value and range of lead concentration in blood for non-occupationally exposed subjects is indicated.*
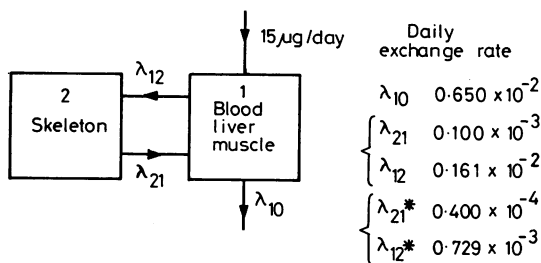
Daily exchange rate

λ_{10} 0.650×10^{-2}

λ_{21} 0.100×10^{-3}

λ_{12} 0.161×10^{-2}

$\lambda_{21}*$ 0.400×10^{-4}

$\lambda_{12}*$ 0.729×10^{-3}

Fig 6 *Two-compartment model used to describe kinetics of lead transfer between skeleton and blood. Two different exchange rates λ_{21} and $\lambda_{21}*$ for transfer of lead from skeleton to soft tissue pool correspond to yearly turnover rates for skeleton of 3·5% and 1·5% respectively.*

more on their normal daily intake of lead than on the total body burdens. This result can also be predicted using a two-compartment model describing the kinetics of lead in the body as shown in fig 6. Compartment 1 represents the blood, liver, and muscles and compartment 2 the skeleton. The exchange rates λ_{12} (from compartment 1 to 2) and λ_{10} have been calculated assuming the steady state condition described by the ICRP[9] with 110 mg lead in the skeleton, 6·2 mg lead in the blood, liver and muscles (of which 1·40 mg is in the blood), and a daily absorption of 40 μg. Two different exchange
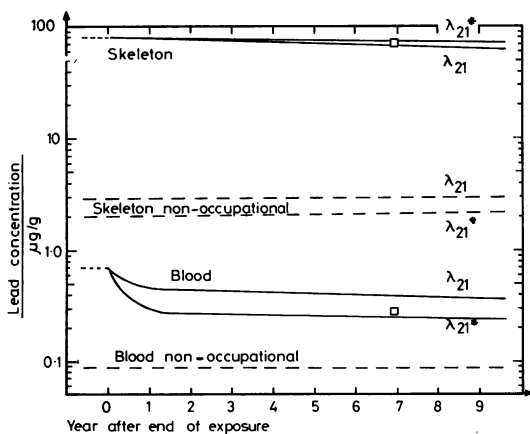

Fig 7 *Lead concentrations in skeleton and blood at different times after end of occupational exposure as calculated from two-compartment model.* □ *represents mean value of measured blood concentration of five people having about 70 μg/g in their skeletons seven years after end of exposure. Calculated lead concentrations in skeleton and blood for non-occupationally exposed people are also given.*

rates (λ_{21}) from the skeleton to the blood have been used, one being taken as the mean skeletal turnover rate of 3·5% a year[10] and the other as the turnover rate for femur-like bones, 1·5% a year.[10]

Using these calculated exchange rates and a daily absorption of 15 μg, it can be shown that after 55 years the blood will reach a value of 0·43 μmol/l (0·09 μg/g) and that the skeleton will contain between 2 and 3 μg/g (fig 7). These values are in good agreement with the corresponding values for non-occupationally exposed subjects in Sweden. These results further indicate the validity of the calculated exchange rates. The same kinetic model has been used to predict the decrease in the lead concentration in the blood after the end of a long occupational exposure. For this calculation, the lead concentration in the skeleton at the end of the exposure was taken to be 80 μg/g, with a blood lead of 3·4 μmol/l (0·7 μg/g). These values are typical for the most highly exposed subjects in our study. Our kinetic model predicts that seven years after the end of exposure the lead concentration in the skeleton will be 68-74 μg/g and in the blood between 1·9 and 1·2 μmol/l, assuming transfer rates of lead from skeleton to the blood of 3·5% and 1·5% a year respectively.

In fig 7 the mean value (□) is shown for the measured blood lead concentration for five people having about 70 μg/g in the skeleton seven years after the exposure. The blood lead concentration that originates from the skeletal pool is very dependent on the exchange rate from the skeleton. The low concentrations in the blood of these formerly occupationally exposed subjects indicates an exchange rate from the skeleton of 1-2% a year. This low exchange rate can be explained by the fact that most of the lead in the skeleton of the subjects was acquired during the first part of their 30-year exposure, when lead exposure in the factory was very intense. The lead in the more easily exchangeable parts of the skeleton may therefore already have been released.

The large amounts of lead stored in the skeletons of these subjects represents a potential risk should it be suddenly released. In table 2 we have calculated the blood lead concentration after a release of 1-10% of the lead in the skeleton during one, six, or 12 months. The calculations have been carried out using the kinetic model in fig 6 with $\lambda_{12} = 0$ and with values for λ_{21} and λ_{10} as given in table 2. The calculated blood level after a sudden release is high in comparison with the limit value for occupational exposure, 3·4 μmol/l (0·7 μg/g). These values are theoretical calculations and may represent an upper limit for lead concentration in blood. The exponential increase in lead excretion in urine with increasing

Table 2 *Calculated blood lead concentrations after release of part of total skeletal lead. Calculations have been carried out for a person with an initial lead concentration of 70 $\mu g/g$ in the skeleton, and 1·4 $\mu mol/l$ in the blood, with an excretion rate (λ_{10}) of 0·650 $\times$ 10^{-2} a day*

Percentage of total lead released	Period during which the lead is released (d)	Excretion rate λ_{21} (a day)	Maximal calculated blood lead concentration ($\mu mol/l$)
1	30	0·330 $\pm$ 10^{-3}	2·5
5	30	0·167 $\pm$ 10^{-2}	7·3
10	30	0·330 $\pm$ 10^{-2}	12·8
10	180	0·556 $\pm$ 10^{-3}	8·2
10	360	0·278 $\pm$ 10^{-3}	5·4

concentration of lead in the blood noted by Schütz and Skerfving[6] indicates that the excretion rate, λ_{10}, increases with increasing blood lead concentration, thus lowering the real blood lead concentration.

Conclusion

The concentration of lead in the skeleton of 22 occupationally exposed men was determined in vivo in the phalanges and compared with the blood lead concentration seven years after their exposure to lead had ended. In three subjects, the concentration of lead along the finger and in the tibia was also studied. No statistically significant variation of the concentration along the phalanx bone could be detected.

Fifteen of the 22 men had a lead concentration in the phalanx exceeding the detection limit of 20 $\mu g/g$, and the concentration was found to increase with the length of employment in the lead factory. No simple relation between the concentrations in the blood and skeleton was found.

A two-compartment model describing the kinetics of lead in the body has been used to verify the measured lead concentrations in the blood and skeleton several years after the end of an occupational exposure.

The results of this work indicate the necessity of carrying out in-vivo measurements of skeletal lead concentrations in order to have a valid estimate of the total body burden of lead and hence information on the potential risk associated with a particular degree of lead contamination.

References

[1] Barry PSI, Mossman DB. Lead concentrations in human tissues. *Br J Ind Med* 1970;27:339-51.

[2] Schroeder HA, Tipton IH. The human body burden of lead. *Arch Environ Health* 1968;17:965-78.

[3] Ahlgren L, Liden K, Mattsson S, Tejning S. X-ray fluorescence analysis of lead in human skeleton *in vivo*. *Scand J Work Environ Health* 1976;2:82-6.

[4] Ahlgren L, Liden K, Mattsson S. *In vivo* X-ray fluorescence analysis of lead in human bone. *Digest of the ninth Nordic meeting on clinical physics, Gothenburg, Sweden.* 1977:155-7.

[5] Ahlgren L, Mattsson S. An X-ray fluorescence technique for *in vivo* determination of lead concentration in a bone matrix. *Phys Biol* 1979;24:136-45.

[6] Schutz A, Skerfving S. Effect of a short heavy exposure to lead dust upon blood lead level, erythrocyte δ-aminolevulinic acid dehydratase activity and urinary excretion of lead, δ-aminolevulinic acid and coproporphyrin. *Scand J Work Environ Health* 1976;3:176-84.

[7] Haeger-Aronsen B, Schutz A. Zinc protoporphyrin in the blood—A new variable for assessment of the influence of lead. *Lakartidningen* 1978;75:3427-30.

[8] Grandjean P. *Bly i danskere, en historisk-toksikologisk undersøgelse.* Copenhagen: Trykteknik A/S, 1973. (Summary in English.)

[9] International Commission on Radiological Protection. *Report of the task group on reference man.* Oxford: Pergamon Press, 1975.

[10] Rivera J. Human bone metabolism inferred from fall-out investigations. *Nature* 1965;207:1330-2.