Diethyllead as a specific indicator of occupational exposure to tetraethyllead

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ABSTRACT In a group of 26 workers exposed to tetraethyllead a correlation was found between the concentration of tetraethyllead in the air and the concentration of diethyllead ($r = 0.70$) and total lead ($r = 0.84$) in the urine and also between the excretion of diethyllead and total lead ($r = 0.68$). The results obtained indicate that diethyllead may be used as a specific indicator of occupational exposure to tetraethyllead.

The evaluation of occupational exposure to neurotoxic compounds such as tetraethyllead (Et_4Pb), which is still used in some countries as an antiknock agent in petrol, demands an urgent solution. Biochemical tests used in evaluating exposure to inorganic lead compounds are not specific for these compounds.¹⁻⁶

Tetraethyllead is metabolised to triethyllead (Et_3Pb^+), diethyllead ($\text{Et}_2\text{Pb}^{+2}$), and ionic lead (Pb^{+2}).⁷⁻¹⁰ Some data have shown that in the case of acute Et_4Pb poisoning in man the predominant metabolite excreted in the urine is $\text{Et}_2\text{Pb}^{+2}$.^{9,10} The main problem in establishing the use of this metabolite in evaluating occupational exposure has been the lack of specific analytical methods. It has been suggested by Chiesura that $\text{Et}_2\text{Pb}^{+2}$ could be used as a specific indicator of occupational exposure to Et_4Pb ⁷ and our initial research using the modified method of Yamamuchi¹⁰ also indicates this.

The aim of the present work was to study a group of people occupationally exposed to Et_4Pb to establish whether the excretion of $\text{Et}_2\text{Pb}^{+2}$ in the urine may be used as a specific indicator of occupational exposure.

Materials and methods

A group of 26 men employed by a petrol company and a control group of men not exposed to Et_4Pb were studied.

Et_4Pb in the atmosphere was evaluated by a modified spectrophotometric dithizone method. The

principle of this method depends on the absorption of Et_4Pb on to carbon and the deabsorption and mineralisation of the sample followed by spectrophotometric determination of the dithizonate complex. The limits of detection through this method are $2.5 \mu\text{gEt}_4\text{Pb}/\text{m}^3$ air (M Dobecki, unpublished data).

Test samples of air were obtained from an area where the workers were respiring using personal samplers. The total lead blood concentration (Pb-B) in the exposed and control group was evaluated by flameless AAS.*

After evaluating the concentration of creatinine and the specific gravity of the urine, the level of total lead (Pb-U) was determined using a flameless AAS method, whereas $\text{Et}_2\text{Pb}^{+2}$ was evaluated using our modified flameless AAS method.¹⁰ The results of Pb-U and $\text{Et}_2\text{Pb}^{+2}$ were adjusted to the average specific gravity of urine (1.024).

Results

Table 1 and fig 1 present the data on the degree of occupational exposure to Et_4Pb , depending on the workplace. The results obtained indicate that the magnitude of exposure to Et_4Pb in the population studied, as defined by the modal value, varied greatly. The workers exposed to the highest concentration of Et_4Pb were those adding Et_4Pb to petrol (workplace No 3). Workers servicing rail tankers (petrol) were less exposed (workplace No 2)

*Our laboratory participates in the United Kingdom External Assessment Scheme.

Table 1 Concentrations of Et_4Pb in the air (mg/m^3) by workplace (8 h – TWA)

No of workplace and occupation	No of workers	Mean	Median	Mode	Range
1 Loading petrol into tankers	7	0.015	0.007	0.009	0.004–0.050
2 Loading petrol into rail tankers	14	0.012	0.009	0.016	0.004–0.026
3 Adding Et_4Pb to petrol	5	0.205	0.140	0.480	0.050–0.810

Fig 1 Cumulative frequency: percentage of workers exposed to Et_4Pb . ○—○ Workplaces Nos 1 and 2, ●—● workplace No 3.

and those with the least exposure were loading petrol into tankers (workplace No 1).

Table 2 includes a description of the men occupationally exposed to Et_4Pb , and their concentrations of total lead (Pb-U) and $\text{Et}_2\text{Pb}^{+2}$ in urine and also the concentration of total lead in the

blood (Pb-B). Similar data for the control group are in table 3.

The cumulative frequency graph shows the excretion of Pb-U (fig 2a) and $\text{Et}_2\text{Pb}^{+2}$ (fig 2b) in the urine of the test workers, according to their workplace. In the workers exposed to the lowest concentrations of Et_4Pb (workplace Nos 1 and 2) the excretion of Pb-U was not greater than $60 \mu\text{g}/\text{l}$. In 50% of these workers no urinary excretion of $\text{Et}_2\text{Pb}^{+2}$ was found. In the remainder the amount excreted in the urine did not exceed $8 \mu\text{g} \text{Et}_2\text{Pb}^{+2}/\text{l}$. In the workers exposed to the highest concentration of Et_4Pb (workplace No 3) the amount of metabolite excreted in the urine was significantly higher than in the less exposed workers. The concentration of Pb-U in the urine ranged from 35 to $230 \mu\text{g}/\text{l}$ and the concentration of $\text{Et}_2\text{Pb}^{+2}$ in the urine ranged from 2.5 to $27 \mu\text{g}/\text{l}$; in 50% of the workers at workplace No 3 the excretion of this metabolite was in excess of $7 \mu\text{g} \text{Et}_2\text{Pb}^{+2}/\text{l}$.

Figure 3 shows a regression graph for the correlation between the concentration of Et_4Pb in the air and the excretion of its metabolites in the urine (Pb-U fig 3a, $\text{Et}_2\text{Pb}^{+2}$ fig 3b). The data for

Table 2 Characteristics of the 26 workers exposed to Et_4Pb

Parameters	Mean	Median	Mode	Range
Age (years)	35.6	30.0	30.0	26.0–58.0
Years of employment	8.1	7.5	10.0	0.5–22.0
Pb-B ($\mu\text{g}/\text{l}$)	256.3	240.0	325.0	190.0–535.0
Pb-U ($\mu\text{g}/\text{l}$)	73.8	72.8	78.4	16.8–229.6
Pb-U ($\mu\text{g}/\text{mean spec grav}$)	84.6	83.3	117.6	22.1–165.6
Pb-U ($\mu\text{g}/\text{g creatinine}$)	42.2	36.2	56.0	9.0–128.0
$\text{Et}_2\text{Pb}^{+2}$ ($\mu\text{g}/\text{l}$)	6.6	5.5	4.0	3.0–25.0
$\text{Et}_2\text{Pb}^{+2}$ (mean spec grav)	8.6	6.3	8.0	2.7–27.2
$\text{Et}_2\text{Pb}^{+2}$ ($\mu\text{g}/\text{g creatinine}$)	4.4	3.4	4.0	1.1–24.3
Specific gravity of urine	1.021	1.022	1.025	1.005–1.030
Creatinine (mg/ml)	2.00	1.87	1.50	0.55–4.50

Table 3 Characteristics of the control group ($n = 26$)

Parameters	Mean	Median	Mode	Range
Age (years)	34.2	34.0	30.0	24.0–47.0
Pb-B ($\mu\text{g}/\text{l}$)	105.7	90.0	100.0	55.0–160.0
Pb-U ($\mu\text{g}/\text{l}$)	24.9	25.0	27.5	7.5–55.0
Pb-U ($\mu\text{g}/\text{mean spec grav}$)	31.8	28.4	30.0	9.3–72.0
Pb-U ($\mu\text{g}/\text{g creatinine}$)	19.3	15.4	25.0	6.7–44.5
$\text{Et}_2\text{Pb}^{+2}$ ($\mu\text{g}/\text{l}$)	—	—	—	—
Specific gravity of urine	1.020	1.020	1.624	1.005–1.030
Creatinine (mg/ml)	1.63	1.40	1.20	0.9–5.5

* $\text{Et}_2\text{Pb}^{+2}$ — undetected.

Fig 2 Cumulative frequency: urinary excretion of (a) Pb-U and (b) $\text{Et}_2\text{Pb}^{+2}$. ○—○ Workplaces Nos 1 and 2, ●—● workplace No 3. (Results adjusted to average specific gravity of urine.)

Fig 3 Correlation between concentrations of Et_4Pb in air and (a) concentration of Pb-U and (b) concentration of $\text{Et}_2\text{Pb}^{+2}$ in urine. (Results adjusted to average specific gravity of urine - 1.024.)

Fig 4 Correlation between concentrations of $\text{Et}_2\text{Pb}^{+2}$ and total lead in urine. ((a) Results adjusted to average specific gravity of urine - 1.024; (b) Results calculated per gram of creatinine.)

those workers in whom the Pb-U concentration was less or equal to that of the control group have not been included. The results obtained show a positive correlation between the concentration of Et_4Pb in air and the amount of Pb-U and $\text{Et}_2\text{Pb}^{+2}$ in the urine ($r = 0.84$ and $r = 0.70$ respectively). A positive correlation (fig 4) was also found between the excretion of Pb-U and $\text{Et}_2\text{Pb}^{+2}$ in the urine.

A small positive correlation was found between the concentration of Et_4Pb in the air and Pb-B ($r = 0.11$) but no correlation was found between Pb-B and the concentrations of Pb-U and $\text{Et}_2\text{Pb}^{+2}$ in the urine.

Discussion

The concentrations of Pb-B in people with clinical symptoms of Et_4Pb poisoning have been found to be higher than $500 \mu\text{g/l}$.⁴⁻⁶ Observations made by Robinson showed that the concentration of Pb-B in people who had been exposed to Et_4Pb for 20 years ranged from 200 to $500 \mu\text{g/l}$ ¹¹ but that none suffered any detectable impairment in health. Millar *et al* showed that in people occupationally exposed to

Et₄Pb the mean concentration of Pb-B rose to 425 µg/l and the activity of ALA-dehydratase (ALA-D) was significantly reduced.³ Studies made by Piotrowski and O'Brien, however, have shown that the activity of ALA-D is a subcritical indicator for the evaluation of lead poisoning.¹²

These results and those of our studies indicate that the evaluation of Pb-B is of little use in estimating the extent of occupational exposure to Et₄Pb.

The concentration of Pb-U in 80% of workers exposed to Et₄Pb for 20 years ranged from 30 to 120 µg/l.¹¹ In our studies on workers exposed for 10 years the level of Pb-U ranged from 16 to 229 µg/l. The mean concentration of Pb-U (73.8 µg/l) was lower than those (150 µg Pb/l¹³ and 110 µg Pb/l¹⁴) which have been recognised as being without hazard for workers occupationally exposed to Et₄Pb. As shown by fig. 2a, despite high concentrations of Et₄Pb in the air only three workers of the test group exhibited Pb-U excretion higher than the one quoted above.

With respect to the above, it seems that the concentration of Pb-U is also of little use as an indicator of occupational exposure to Et₄Pb.

On the other hand, Et₂Pb⁺² was found in the urine of workers exposed to both high and low concentrations of Et₄Pb. A significant correlation was found between the concentration of Et₄Pb in the air and excretion of Et₂Pb⁺² in the urine ($r = 0.70$). These show that this metabolite could be a specific indicator for occupational exposure to Et₄Pb.

The concentrations ratios between Et₂Pb⁺²/total Pb in the urine of exposed workers differed. For workers employed at workplaces Nos 1 and 3 (table 1) the mean ratios were 0.093 (from 0.04 to 0.19) and 0.085 (from 0.049 to 0.14), respectively. On the other hand, in cases of acute poisoning the mean ratio was 0.35 (from 0.08 to 0.72).^{9, 10}

These results would make us surmise that the metabolism of Et₄Pb to Et₂Pb⁺² depends on the dose or the extent of exposure.

In people occupationally exposed to Et₄Pb the urinary level of Pb-U of 110 µg/g creatinine has been assumed as safe.¹⁵ Figure 4b shows the correlation between the excretion of Pb-U and Et₂Pb⁺² in

the urine (per gram creatinine): these data indicate that the permissible level of Et₂Pb⁺² in the urine of workers occupationally exposed is about 8 µg. Hence it would seem that the detection of this metabolite at a concentration greater than 8 µg could indicate that the exposure may be hazardous to health.

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References

- Crept M, Chiesura P. Porphyrins in tetraethyl lead poisoning. *Panminerva Medica* 1966;7-8:295-301.
- Foa V, Cavagna G, Manfredi M. Evaluation of urinary lead in the diagnosis of tetraethyl lead poisoning. *Med Lav* 1970;10:491-501.
- Millar JA, Thomson GG, Goldberg A, Barry PSI, Lowe EH. S-Aminolevulinic acid dehydratase activity in the blood of men working with lead alkyls. *Br J Ind Med* 1972;29:317-20.
- Beattie AD, Morre MR. Tetraethyl-lead poisoning. *Lancet* 1971;i:12-5.
- Robinson TR, Rouge B. Delta-aminolevulinic acid and lead in urine of lead antiknock workers. *Arch Environ Health* 1974;28:133-6.
- Yamamura Y, Takakura J, Hirayama F, Yamauchi H, Yohida M. Tetraethyl lead poisoning caused by cleaning work in the aviation fuel tank. *Jap J Ind Health* 1975;17:223-35.
- Chiesura P. Urinary excretion of lead tetraethyl catabolites in man. *Med Lav* 1970;61:437-41.
- Bolanowska W, Piotrowski J, Garczyński H. Triethyllead in the biological material in cases of acute tetraethyllead poisoning. *Archiv für Toxikologie* 1967;22:276-82.
- Yamamura Y, Arai F, Yamauchi H. Urinary excretion pattern of triethyllead, diethyllead and inorganic lead in the tetraethyllead poisoning. *Ind Health* 1981;19:125-31.
- Turlakiewicz Z, Jakubowski M, Chmielnicka J. Determination of diethyllead in urine by flameless atomic absorption spectrometry. *Br J Ind Med* 1985;42:63-5.
- Robinson TR. The health of long service tetraethyllead lead workers. *J Occup Med* 1976;18:31-49.
- Piotrowski JK, O'Brien BJ. Analysis of the effects of lead in tissue upon human health using dose-response relationship. *Progress Reports in Environmental Monitoring and Assessment* 1980;1:72-88.
- Kehoe RA. *Lead, alkyl compounds*. Geneva: Occupational Health and Safety ILO, 1972:765.
- Chiesura P, Danielli A. Urinary lead and judgment of tetraethyl poisoning. Investigation among workers engaged in production. *Med Lav* 1969;60:129-37.
- Lauwerys R, Buchet JP, Roels H. *Caharien de Medicine du Travail* 1980;17:91-7.