Occupational lead exposure in Denmark: screening with the haematofluorometer

P. GRANDJEAN¹

From the Institute of Hygiene, University of Copenhagen, Denmark

ABSTRACT The zinc protoporphyrin/haemoglobin (ZPP/Hb) ratio was measured in the field with a haematofluorometer. A significant increase in ZPP/Hb ratio with advancing age was found in 1295 men who denied any excess exposure to lead. Ninety-seven per cent of the results were below 110 $\mu\text{mol ZPP/mol Hb(Fe)}$ (4.4 $\mu\text{g ZPP/g Hb}$). The ZPP/Hb ratio was determined in a lead-exposed population of 2275 men, and in 305 a blood lead analysis was also performed. A blood lead limit of 2.9 $\mu\text{mol/l}$ (60 $\mu\text{g/100 ml}$) corresponds to about 500 $\mu\text{mol ZPP/mol Hb(Fe)}$ (20 $\mu\text{g/g}$). This limit was exceeded in workers engaged in secondary lead smelting, storage battery manufacture, car radiator repair, crystal glass manufacture, storage battery repair, ship breaking, metal foundries, the ceramic industry, scrap metal handling, and PVC plastic manufacture. Other occupations caused lower lead exposures with ZPP/Hb ratios between 110 and 500 $\mu\text{mol ZPP/mol Hb(Fe)}$: such ratios were found in men from shooting ranges, in leaded pane manufacturers, gunsmiths, car paint sprayers, type setters, steel rolling mill workers, shipbuilders and welders, car mechanics, lead pigment handlers, and solderers. Increased ZPP/Hb ratios and blood lead levels in 210 workers were associated with a decrease in haemoglobin concentration in the blood. Thus, the haematofluorometer has proved to be very useful for screening purposes. A blood lead determination should be performed if the ZPP/Hb ratio exceeds 300 $\mu\text{mol ZPP/mol Hb(Fe)}$ (12 $\mu\text{g/g}$).

The incidence and severity of lead poisoning have decreased substantially during recent years, but much still remains to be done to eliminate lead poisoning completely as an occupational disease (World Health Organization, 1977). Lead and lead compounds are used in a very wide range of industries, and the US Public Health Service (1964) has listed 113 occupations with potential lead exposure. Cases of lead poisoning occur mainly within a limited number of occupations. Thus, in Denmark, poisoning has been notified in industries manufacturing electric storage batteries, a secondary lead smelter, metal foundries, and industries producing polyvinyl chloride plastic. In this regard Denmark resembles other countries from which official statistics have been published (Popper and Raber, 1966; Quaas and Naas, 1971; Tola *et al.*, 1976). It has been estimated that about 1% of the workforce in Finland has a blood lead level in excess

of 1.9 $\mu\text{mol/l}$ (40 $\mu\text{g/100 ml}$) because of occupational lead exposure (Tola *et al.*, 1976). Forty years ago a survey in the USA showed that about 1.5% of the workers were exposed to large quantities of lead (Bloomfield *et al.*, 1940). The major hazard today seems to be in the small workshops, but high exposures also occur in some large companies with inadequate industrial hygiene programmes (National Academy of Sciences Committee on Biological Effects of Atmospheric Pollutants, 1972; Hernberg, 1973). Under these circumstances, extensive exposure control is necessary.

Blood lead levels are, under certain conditions, a useful indicator of the exposure to lead in groups of workers (World Health Organization, 1977). Cases of lead poisoning have, however, occurred below a safety limit for blood lead concentration of 3.9 $\mu\text{mol/l}$ (Waldron, 1974; Federal Register, 1975). Alternatively, measurements of biological effects of lead have been recommended (Baloh, 1974; Tomokuni and Ogata, 1976; Beritić *et al.*, 1977; Joselow and Flores, 1977). An international working group has recently recommended the use of protoporphyrin analysis in screening for occupational lead exposure (Zielhuis, 1977). Protoporphyrin accumu-

¹Present address: Environmental Sciences Laboratory, Mount Sinai Hospital, Fifth Avenue and 100th Street, New York, NY 10029, USA

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lates in the erythrocytes during their maturation in the bone marrow because lead interferes with the function of ferrochelatase (Piomelli *et al.*, 1973; Sassa *et al.*, 1975). It has been shown that this protoporphyrin is mainly chelated with zinc (Lamola and Yamane, 1974), and a special front surface fluorometer, the haematofluorometer, has been designed to measure zinc protoporphyrin (ZPP) rapidly in the field (Blumberg *et al.*, 1977). The ZPP measurement, however, has two drawbacks: it is not sufficiently sensitive to recent, sudden, or mild increases in lead exposure, and it is not specific for lead, as increased levels may be attributable to iron deficiency anaemia (Lamola and Yamane, 1974; Beritić *et al.*, 1977). The purpose of the investigation described here was to evaluate the use of a haematofluorometer in a screening programme for occupational lead exposure in male workers in Denmark.

Material and methods

REFERENCE POPULATION

Free ZPP tests were offered to the visitors at the Working Environment Foundation exhibitions in Copenhagen and in 33 provincial and country towns. An experienced occupational health nurse noted the name, age, occupation and possible sources of lead exposure in each case. A total number of 1295 men without known excess exposure to lead were examined.

EXPOSED POPULATION

At the same exhibitions, 340 men with potential occupational exposure to lead were tested for ZPP (21% of the total number examined at the exhibitions).

In co-operation with the Danish Labour Inspectorate, 171 enterprises were visited, and 1935 male workers with lead exposure lasting for at least six months were examined. Not all employees could be included in the study because of shift work, sickness or other reasons for absence during our visits. It is probable, however, that the workers examined are representative of the individual firms, but that the firms are not necessarily representative of the respective branches of industry. The companies were identified from the register of notified cases of lead poisoning and from the files of the district offices of the Labour Inspectorate. It is believed that all Danish secondary lead smelters, storage battery manufacturers, ship breakers, crystal glass manufacturers, paint manufacturers and steel rolling mills were visited. Moreover, because of a recent report on high lead exposure among car workers (Clausen and Rastogi, 1977), special emphasis was laid on garages.

ANALYTICAL METHODS

ZPP was measured with an Aviv Haematofluorometer, Model ZPP meter. The instrument has proved to be reliable and rapid, and the measured ratio between zinc protoporphyrin and haemoglobin concentrations is expressed in $\mu\text{mol ZPP/mol Hb(Fe)}$ (Grandjean and Lintrup, 1978). This unit corresponds to approximately $25 \mu\text{g ZPP/g Hb}$.

If the ZPP/Hb molar ratio was in excess of 300, a venous blood sample was drawn into a 10 ml Vacutainer tube for lead analysis. Previous investigations have indicated that blood lead levels higher than $2.9 \mu\text{mol/l}$ ($60 \mu\text{g/100 ml}$) rarely occur below this ZPP limit (Beritić *et al.*, 1977; Blumberg *et al.*, 1977; Grandjean *et al.*, 1978). Blood samples were also drawn from individuals at their workplaces, if their birth dates were the 2nd, 15th, or 24th of the month. Of these blood samples, 305 were analysed by the National Institute of Occupational Hygiene, Copenhagen, by the method described by Hessel (1968). This laboratory has participated in several comparative programmes, and its performance has proved to be reliable with a coefficient of variation less than 10% (Grandjean, 1978).

Haemoglobin was measured in 210 of the venous blood samples by means of a Coulter S or a Hemalog 8/90, both standardised by comparison with a cyanhaemoglobin standard (Baker 3061) in a Zeiss spectrophotometer. One mmol Hb(Fe)/l blood corresponds to 1.6 g/100 ml .

Results

REFERENCE INTERVAL FOR ZPP

The normal ZPP/Hb ratio in the reference population was found to be age-dependent (Fig. 1). The Spearman rank correlation coefficient was 0.23 ($p < 0.001$). The total median was $71 \mu\text{mol ZPP/mol Hb(Fe)}$. The increase in ZPP with advancing age was apparently linear (Fig. 1). For practical purposes the upper cut-off limit of the reference interval was set at $110 \mu\text{mol ZPP/mol Hb(Fe)}$. This level is the 97th percentile; it was exceeded by 22 of the subjects aged over 50 years (7%), and by 19 aged 15–49 years (2%). Excess exposure to lead could explain a few high results found in the reference group, although such exposure was denied by all of them.

VALIDITY OF ZPP ANALYSIS

Because of the cumulative characteristics of lead, the ZPP level may depend on the length of exposure. Ninety-four employees from a company which manufactures electric storage batteries comprised the largest exposed group from the same firm. Thus, the possible association between ZPP level and exposure time could be evaluated. After the

Fig. 1 Median and 95% confidence limits to median of zinc protoporphyrin/haemoglobin ratio in different age groups ($N = 1295$; Spearman rank correlation coefficient, $r_s = 0.23$; $P < 0.001$). The dashed line is the regression line (y on x).

first six months of exposure, no further increase in ZPP was apparent (Table 1).

Individuals with high ZPP/Hb ratios almost invariably had a concomitant increase in the blood lead level (Fig. 2). The correlation between the two measures is highly significant ($r_s = 0.86$; $P < 0.001$). The data shown in Fig. 2 indicate an exponential increase in ZPP with increased lead exposure. The regression lines indicate that the upper limit of the reference interval, $110 \mu\text{mol ZPP/mol Hb}$, would correspond to about $1.2 \mu\text{mol Pb/l blood}$ ($25 \mu\text{g}/100 \text{ ml}$). Almost all subjects (98%) with a ZPP/Hb ratio within the reference interval had a blood lead level of $1.5 \mu\text{mol/l}$ or less. The recommended permissible limit for lead in blood, $2.9 \mu\text{mol/l}$, would correspond to about $500 \mu\text{mol ZPP/mol Hb(Fe)}$. However, several individuals with a blood lead level in excess of the limit had a comparatively low ZPP/Hb ratio. The validity of different cut-off levels for ZPP/Hb ratios is shown in Table 2. It appears that very few subjects with high blood lead levels also had a ZPP/Hb ratio below the $300 \mu\text{mol/mol}$ limit used in this screening study.

In 210 males from the exposed population, the haemoglobin concentration was determined and was found to be significantly associated with the ZPP/Hb ratio ($r_s = -0.42$; $P < 0.001$) (Fig. 3).

Table 1 ZPP/Hb ratios ($\mu\text{mol/mol}$) in relation to duration of lead exposure in 94 workers manufacturing electric storage batteries

Duration of exposure (yr)	Number of workers	ZPP/Hb ratio		
		Median	95% confidence limits to median	Range
0.5-1.0	18	616	176-754	125-901
1.1-2.0	19	640	172-770	72-1227
2.1-5.0	23	492	309-646	114-1197
5.1-10.0	19	412	271-718	112-1188
>10	15	513	356-953	97-1282

The blood lead level, assessed in the same blood samples in 202 of these individuals, was significantly associated with haemoglobin ($r_s = -0.31$; $P < 0.001$) (Fig. 4). With increasing levels of ZPP and lead in the blood, the haemoglobin concentration decreases, and the proportion of haemoglobin values in the lower normal range increases. The cut-off limits for ZPP are more effective than blood lead limits in distinguishing low from high haemoglobin concentrations (Tables 3 and 4).

ZPP LEVELS IN DIFFERENT OCCUPATIONS

The ZPP/Hb ratio seems to be a convenient measure of lead exposure, and it was not possible to find any difference between different occupations in the relationship between ZPP and blood lead levels. Thus,

Fig. 2 Relationship between zinc protoporphyrin/haemoglobin ratio and lead concentration in the blood of 305 men with occupational lead exposure. The two regression lines are shown.

Table 2 Validity of ZPP determinations with different cut-off points compared with a blood lead limit of $2.9 \mu\text{mol/l}$

ZPP limit ($\mu\text{mol/mol Hb}$ (Fe))	Sensitivity (% true positives)	Specificity (% true negatives)	Validity (sensitivity + specificity)
750	62	87	149
500	56	92	148
300	45	98	143

Table 3 Haemoglobin concentrations (mmol/l) compared with ZPP/Hb ratios ($\mu\text{mol/mol}$) in 210 lead-exposed workers

ZPP/Hb ratio	Number of workers	Haemoglobin	
		Median	% lower than 9.0
<110	76	9.7	13
110-500	71	9.2†	30‡
>500	63	9.0†	46‡

† $P < 0.05$ and ‡ $P < 0.001$ compared with the preceding group by a two-tailed Mann-Whitney U-test.

§ $P < 0.05$ compared with the preceding group by a two-tailed χ^2 test.

Fig. 3 Relationship between haemoglobin concentration and zinc protoporphyrin/haemoglobin ratio in the blood of 210 men with occupational lead exposure. The two regression lines are shown.

Table 4 Haemoglobin concentrations (mmol/l) compared with blood lead levels ($\mu\text{mol/l}$) in 202 lead-exposed workers

Blood lead	Number of workers	Haemoglobin	
		Median	% lower than 9.0
<1.2	66	9.6	17
1.2-2.9	80	9.2†	26
>2.9	56	9.1	45‡

† $P < 0.05$ compared with the preceding group by a two-tailed Mann-Whitney U-test.

§ $P < 0.05$ compared with the preceding group by a two-tailed χ^2 test.

a comparison between ZPP values found in different occupations is permissible.

Table 5 lists the industries which employ workers with ZPP/Hb ratios above $500 \mu\text{mol/mol}$. The lead hazard in most of these industries is well known. Several other industrial facilities showed increased ZPP levels below $500 \mu\text{mol/mol Hb(Fe)}$ (Table 6).

Discussion

Determination of the ZPP/Hb ratio represents the easiest and quickest method available for the assessment of lead exposure. The haematofluorometer provides the result in a few seconds, and this makes immediate action possible when excessive ZPP levels are found. Some hundred blood lead determinations are performed each year by the National Institute of Occupational Hygiene, but the haematofluorometer has made it possible to examine several thousand individuals in a year. However, before the haematofluorometer is accepted as a screening method, its validity should be carefully checked.

It has been shown in this study that the ZPP/Hb ratio increases significantly with advancing age. This could be related to impaired iron absorption or reduced iron intake in the older individuals. Thus, in the elderly, an increased incidence of iron de-

Fig. 4 Relationship between haemoglobin and lead concentration in the blood of 202 men with occupational lead exposure. The two regression lines are shown.

Table 5 ZPP/Hb ratios ($\mu\text{mol/mol}$) in different occupations with high lead exposure

Industry	Number of firms visited	Number of employees examined	ZPP/Hb ratio		
			Median	% in excess of 110	% in excess of 500
Secondary lead smelter	1	67	479	96	45
Storage battery plant	4	264	302	87	34
Car radiator repair	15	45†	208	78	22
Crystal glass manufacture	2	16	259	88	19
Storage battery repair	10	21†	116	52	14
Ship breaking	2	31	154	61	10
Metal foundry	30	205†	107	48	10
Ceramic industry	19	48†	77	23	6
Scrap metal handling	4	21	144	57	5
PVC plastic manufacture	6	32	102	41	3

†Number includes subjects examined at the Working Environment Foundation exhibitions (see text).

Table 6 ZPP/Hb ratios ($\mu\text{mol/mol}$) in occupations with low lead exposure (no employees with more than 500 $\mu\text{mol ZPP/mol Hb(Fe)}$)

Occupation	Number of concerns visited	Number of employees examined	ZPP/Hb ratio	
			Median	% in excess of 110
Shooting range instruction	3	9	90	44
Leaded pane manufacturing	6	18†	75	39
Gunsmiths	4	7	84	29
Car paint-spraying	5	26†	92	23
Type setting	23	278†	74	11
Steel rolling	1	380	86	10
Shipbuilding and welding	4	105†	82	10
Car repair	18	479†	82	9
Lead pigment handling	7	97	71	8
Soldering	14	126†	78	6

†Number includes subjects examined at the Working Environment Foundation exhibitions (see text).

iciency anaemia (Bowering *et al.*, 1976) could lead to higher mean protoporphyrin concentrations (Lamola and Yamane, 1974; McLaren *et al.*, 1975). On the other hand, the mean haemoglobin level is constant in adult male populations until old age, and the evidence of impaired iron absorption with advancing age is only suggestive (Bowering *et al.*, 1976). It may therefore be of significance that the body burden of lead increases with age (World Health Organization, 1977). The increase in ZPP (Fig. 1) would correspond to an increase in blood lead of about 0.003 $\mu\text{mol Pb/l}$ blood per year. Although some authors have found no increase in blood lead with age (World Health Organization, 1977), a Danish study of 63 males showed a mean annual increase of 0.005 $\mu\text{mol Pb/l}$ blood (Nygaard *et al.*, 1977). A similar increase was apparent in 136 males with low-level lead exposure in Belgium, and the age-dependent increase was even steeper in 265 males with exposure to lead-contaminated drinking water (De Graeve *et al.*, 1975). The possible accumulation of lead in the blood and increased lead toxicity with advancing age, therefore, call for further studies.

The upper limit of the reference interval is higher than that established by other authors (Piomelli *et al.*, 1973; Roels *et al.*, 1975; Sassa *et al.*, 1975). This is explained by the fact that the haematofluorometer gives higher readings than the extraction methods, especially in the low concentration range (Blumberg *et al.*, 1977; Grandjean and Lintrup, 1978).

The ZPP level in the erythrocytes is not determined by lead alone (Lamola and Yamane, 1974), and it is therefore not surprising that the relationship between ZPP and lead in blood is scattered (Fig. 2). However, it is probable that a closer relationship can be obtained in subjects with constant lead exposure (Sassa *et al.*, 1975). The linear relationship between log ZPP/Hb and blood lead is a reasonable approximation (Piomelli *et al.*, 1973; Sassa *et al.*, 1975; Grandjean and Lintrup, 1978). A no-detectable-effect level in adult males was identified at about 1.2–1.7 $\mu\text{mol Pb/l}$ blood (Roels *et al.*, 1975), and this is in accordance with Fig. 2 in this study.

Anaemia is a well-known sign of lead poisoning, but it is not normally found until the blood lead level exceeds 5 $\mu\text{mol/l}$ (Williams, 1966; Cooper *et al.*,

1973). Two cross-sectional studies, similar to the study described here, have shown a significantly negative association of blood haemoglobin levels with blood lead concentrations in workers exposed to lead (Wada, 1976; Lilis *et al.*, 1977), but such a relationship could not be found in a large-scale study in Finland (Tola, 1973). A prospective study of new male lead workers showed, however, that the mean haemoglobin decreased in 100 days from 8.9 mmol/l to 8.3 mmol/l, while the blood lead level increased to a mean of about 2.4 $\mu\text{mol/l}$ (Tola *et al.*, 1973). The accumulation of ZPP in the erythrocytes is several times lower than the associated decrease in Hb (Fig. 3). Thus, interference with other steps of haem metabolism must be partly responsible for this decrease. Almost all haemoglobin values found in this study were within the normal range (above 8.0 mmol/l), and there is little evidence of any harmful effect of a low haemoglobin level as such (Elwood, 1973). However, a concomitant lead-induced decrease in other haem proteins has been demonstrated (Alvares *et al.*, 1976; Goldberg *et al.*, 1977). Thus, the decreased synthesis of haem should not be evaluated on the basis of haemoglobin levels only.

Hernberg (1973) reviewed the literature on the incidence of occupational lead poisoning, and distinguished between occupations with high risk and those with moderate or slight risk. These two groups are very similar to the groups listed in Tables 5 and 6, respectively. A large-scale Finnish screening study for blood lead levels concluded that the highest lead exposures occurred in the same industries as those mentioned in Table 5 (Tola *et al.*, 1976). Shooting instructors and fingerprint experts handling lead pigment were not mentioned in the Finnish reports, but cases of poisoning have occurred in these occupations as well (Winge, 1931; Nyfeldt, 1937). By far the most extensive lead exposure is found in secondary lead smelters and in electric storage battery manufacturers (Williams *et al.*, 1969; Lilis *et al.*, 1977; World Health Organization, 1977). Thus the results of the present survey are in accordance with most other reports. However, one recent study of 216 workers from 10 garages in Denmark showed that 9% of the workers had a blood lead level in excess of 3.9 $\mu\text{mol/l}$, and that motor mechanics had higher levels than the platemiths and the paint sprayers (Clausen and Rastogi, 1977). Our study, carried out two years later, included two of the garages studied by Clausen and Rastogi (1977) but it was not possible to confirm their findings. Our results are in accordance with findings in Finland (Tola *et al.*, 1972); it appears, therefore, that in most instances car repair results in only a limited lead exposure.

A significant proportion of the work-force is

exposed to lead, so that extensive monitoring is necessary. The haematofluorometer has proved very efficient for screening purposes, but an increased ZPP level is not specific for lead (Lamola and Yamane, 1974; Grandjean and Lintrup, 1978). An increased ZPP/Hb ratio should therefore be controlled by blood lead determination. A screening limit of 300 $\mu\text{mol ZPP/mol Hb(Fe)}$ is convenient, as almost all subjects with a blood lead level in excess of 2.9 $\mu\text{mol/l}$ (60 $\mu\text{g/100 ml}$) also exceed this limit for the ZPP/Hb ratio.

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References

- Alvares, A. P., Fischbein, A., Sassa, S., Anderson, K. E., and Kappas, A. (1976). Lead intoxication: effects on cytochrome P-450-mediated hepatic oxidations. *Clinical Pharmacology and Therapeutics*, **19**, 183-190.
- Baloh, R. W. (1974). Laboratory diagnosis of increased lead absorption. *Archives of Environmental Health*, **28**, 198-208.
- Beritić, T., Prpić-Majić, D., Karačić, V., and Telisman, S. (1977). ALAD/EP ratio as a measure of lead toxicity. *Journal of Occupational Medicine*, **19**, 551-557.
- Bloomfield, J. J., Trasko, V. M., Sayers, R. R., Page, R. T., and Peyton, M. F. (1940). *A Preliminary Survey of the Industrial Hygiene Problem in the United States*. Public Health Bulletin No. 259. US Public Health Service: Washington.
- Blumberg, W. E., Eisinger, J., Lamola, A. A., and Zuckerman, D. M. (1977). Zinc protoporphyrin level in blood determined by a portable hematofluorometer: a screening device for lead poisoning. *Journal of Laboratory and Clinical Medicine*, **89**, 712-723.
- Bowering, J., Sanchez, A. M., and Irwin, M. I. (1976). A conspectus of research on iron requirements of man. *Journal of Nutrition*, **106**, 985-1074.
- Clausen, J., and Rastogi, S. C. (1977). Heavy metal pollution among autoworkers. I. Lead. *British Journal of Industrial Medicine*, **34**, 208-215.
- Cooper, W. C., Tabershaw, I. R., and Nelson, K. W. (1973). Laboratory studies of workers in lead smelting and refining. In *Proceedings of an International Symposium on Environmental Health Aspects of Lead*, pp. 517-529. Commission of the European Communities: Luxembourg.
- De Graeve, J., Jamin, P., and Rondia, D. (1975). Plombémie d'une population adulte de l'Est de la Belgique. *Revue d'Epidémiologie et de Santé Publique*, **25**, 131-152.
- Elwood, P. C. (1973). Evaluation of the clinical importance of anemia. *American Journal of Clinical Nutrition*, **26**, 959-964.
- Federal Register (1975). *Occupational Exposure to Lead. Proposed Rulemaking*. October 3, 45934-45948.
- Goldberg, A., Meredith, P. A., Miller, S., Moore, M. R., and Thompson, G. G. (1977). Haem biosynthesis and hepatic drug metabolism in lead poisoned rats. *British Journal of Pharmacology*, **61**, 134P-135P.

- Grandjean, P. (1978). Lead concentration in single hairs as a monitor of occupational lead exposure. *International Archives of Occupational and Environmental Health*, **42**, 69-81.
- Grandjean, P., Fogh, A., and Petersen, R. (1978). Zink-protoporfyrin koncentrationen i erythrocytter hos blyeksponerede mænd. *Ugeskrift for Læger*. (In press.)
- Grandjean, P., and Lintrup, J. (1978). Erythrocyte-Zn-protoporphyrin as an indicator of lead exposure. *Scandinavian Journal of Clinical and Laboratory Investigation*, **38**, 669-675.
- Hernberg, S. (1973). Prevention of occupational poisoning from inorganic lead. *Work-Environment-Health*, **10**, 53-61.
- Hessel, W. (1968). Simple and rapid quantitative determination of lead in blood. *Atomic Absorption Newsletters*, **7**, 55-56.
- Joselow, M. M., and Flores, J. (1977). Application of the zinc protoporphyrin test as a monitor of occupational exposure to lead. *American Industrial Hygiene Association Journal*, **38**, 63-66.
- Lamola, A. A., and Yamane, T. (1974). Zinc protoporphyrin in the erythrocytes of patients with lead poisoning and iron deficiency anemia. *Science*, **186**, 936-938.
- Lilis, R., Fischbein, A., Eisinger, J., Blumberg, W. E., Diamond, S., Anderson, H. A., Rom, W., Rice, C., Sarkozi, L., Kon, S., and Selikoff, I. J. (1977). Prevalence of lead disease among secondary lead smelter workers and biological indicators of lead exposure. *Environmental Research*, **14**, 255-285.
- McLaren, G. D., Carpenter, J. T., Jr., and Nino, H. V. (1975). Erythrocyte protoporphyrin in the detection of iron deficiency. *Clinical Chemistry*, **21**, 1121-1127.
- National Academy of Sciences Committee on Biological Effects of Atmospheric Pollutants (1972). *Lead: Airborne Lead in Perspective*. National Academy of Sciences: Washington, D.C.
- Nyfeldt, A. (1937). Et tilfælde af kronisk blyforgiftning. *Ugeskrift for Læger*, **99**, 283-284.
- Nygaard, S.-P., Ottosen, J., and Hansen, J. C. (1977). Whole-blood lead concentration in Danes: relation to age and environment. *Danish Medical Bulletin*, **24**, 49-51.
- Piomelli, S., Young, P., and Gay, G. (1973). A micromethod for free erythrocyte porphyrins: the FEP test. *Journal of Laboratory and Clinical Medicine*, **81**, 932-940.
- Popper, L., and Raber, A. (1966). Saturnismus in Austria. In *XVth International Congress on Occupational Health*, Suppl. 1. Verlag der Wiener Medizinischen Akademie: Wien.
- Quaas, M., and Naas, W. (1971). Zur Epidemiologie beruflicher Bleiintoxikationen. *Deutsche Gesundheitswesen*, **26**, 2139-2144.
- Roels, H. A., Lauwerys, R. R., Buchet, J. P., and Vrelost, M.-Th. (1975). Response of free erythrocyte porphyrin and urinary δ -aminolevulinic acid in men and women moderately exposed to lead. *Internationales Archiv für Arbeitsmedizin*, **34**, 97-108.
- Sassa, S., Granick, S., and Kappas, A. (1975). Effect of lead and genetic factors on heme biosynthesis in the human red cell. *Annals of the New York Academy of Sciences*, **244**, 419-440.
- Tola, S. (1973). The effect of blood lead concentration, age, sex and time of exposure upon erythrocyte δ -aminolevulinic acid dehydratase activity. *Work-Environment-Health*, **10**, 26-35.
- Tola, S., Hernberg, S., Asp, S., and Nikkanen, J. (1973). Parameters indicative of absorption and biological effect in new lead exposure: a prospective study. *British Journal of Industrial Medicine*, **30**, 134-141.
- Tola, S., Hernberg, S., and Nikkanen, J. (1972). Occupational lead exposure in Finland. II. Service stations and garages. *Work-Environment-Health*, **9**, 102-105.
- Tola, S., Hernberg, S., and Vesanto, R. (1976). Occupational lead exposure in Finland. VI. Final report. *Scandinavian Journal of Work, Environment and Health*, **2**, 115-127.
- Tomokuni, K., and Ogata, M. (1976). Relationship between lead concentration in blood and biological response for porphyrin metabolism in workers occupationally exposed to lead. *Archives of Toxicology*, **35**, 239-246.
- US Public Health Service (1964). Publication 1097. *Occupational Diseases, A Guide to their Recognition*. Edited by W. M. Gafafer. USPHS: Washington, D.C.
- Wada, O. (1976). Human responses to lead and their background with special reference to porphyrin metabolism. In *Effects and Dose-response Relationships of Toxic Metals*, pp. 446-454. Edited by G. F. Nordberg. Elsevier: Amsterdam.
- Waldron, H. A. (1974). The blood lead threshold. *Archives of Environmental Health*, **29**, 271-273.
- Williams, M. K. (1966). Blood lead and haemoglobin in lead absorption. *British Journal of Industrial Medicine*, **23**, 105-111.
- Williams, M. K., King, E., and Walford, J. (1969). An investigation of lead absorption in an electric accumulator factory with the use of personal samplers. *British Journal of Industrial Medicine*, **26**, 202-216.
- Winge, K. (1931). Et tilfælde af blyforgiftning med ejendommelig ætiologi. *Ugeskrift for Læger*, **93**, 1154-1155.
- World Health Organization (1977). *Environmental Health Criteria*. 3. Lead. WHO: Geneva.
- Zielhuis, R. L. (1977). Second International Workshop on permissible levels for occupational exposure to inorganic lead. *International Archives of Occupational and Environmental Health*, **39**, 59-72.