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Blood Lead and Blood Pressure: Some Implications for the Situation in the Netherlands

by Wim L. A. M. de Kort* and Wim C. M. Zwennis†

Studies performed earlier have shown a positive relation between blood lead (a parameter for lead body burden) and blood pressure, whereas such a relation between urine cadmium (a parameter for cadmium body burden) and blood pressure could not be shown. Median (i.e., 50th percentile, P50) blood levels in the general population in the Netherlands are in the range of 80 to 150 μg/L. Persons occupationally exposed to lead show median blood lead levels that may exceed 400 μg/L. To study causality, a prospective study among lead workers is desired.

Introduction

In the literature, a positive, rather than a negative, relation between lead and blood pressure is more often cited. Furthermore, experimental (animal) studies render some support to this relation, although a satisfactory explanation by some underlying mechanism is not yet at hand. Recently, the U.S. Environmental Protection Agency published an extensive report on lead, which contained a review on this topic (*1*). Apart from the fact that positive results are more easily reported than negative results, the actual existence of a positive relation should be seriously considered.

The relation between occupational lead exposure and blood pressure was studied in the Netherlands (*2*). After a brief review of this study, some results are presented of studies on the blood lead values in the general population in the Netherlands. An attempt will be made to evaluate the consequences of these results.

Lead Worker Study

A group of 53 occupationally exposed workers (from a plant processing lead and cadmium compounds) was compared with a group of 52 workers not occupationally exposed (from a plant where insulation materials are produced). For the results to be included in the analysis, the worker had to have been employed for more than 1 year and not be under treatment for hypertension. Further details concerning the methods used in this study have been described previously (*2*). The groups were comparable with regard to their socioeconomic background, physical exertion, workplace conditions (apart from exposure), place of residence, and some lifestyle characteristics. A statistically significant difference existed concerning their age and their duration of employment (Table 1).

The average values of systolic and diastolic blood pressure were found to be higher in the exposed group (Table 2). Because the workers were exposed to both lead and cadmium and because the exposed group was on

Table 1. Ages and duration of employment.[a]

	Pb-exposed	Controls	Significance
n	53	52	
Age	42.1 ± 1.2[b]	38.2 ± 1.1	$p < 0.05$
Years at work	12.5 ± 1.2	8.6 ± 0.8	$p < 0.01$

[a]From de Kort et al. (*2*)
[b]Values are means ± SEM.

Table 2. Blood pressure and heart rate.[a]

	Pb-exposed	Controls	Significance
n	53	52	
Systolic blood pressure, mm Hg	140 ± 3[b]	131 ± 3	$p = 0.01$
Diastolic blood pressure, mm Hg	86 ± 2	80 ± 2	$p = 0.01$
Heart rate, beats/min	78 ± 2	81 ± 2	NS[c]

[a]From de Kort et al. (*2*).
[b]Values are means ± SEM.
[c]NS, nonsignificant.

*Directorate-General of Labour, Ministry of Social Affairs and Employment, P.O. Box 69, 2270 MA Voorburg, the Netherlands.
†Medical Biological Laboratory TNO, Rijswijk, the Netherlands.

the average older than the control group, further statistical analyses were performed. Calculation of the correlation coefficients revealed significant results for the correlation between blood lead and blood pressure while controlling for age and heart rate; additional controlling for urine cadmium (only feasible for a smaller number of complete data sets) revealed a nonsignificant result at the 0.05 level. On the other hand, no significant result was obtained for the correlation between cadmium and blood pressure if age effects were controlled for (Tables 3 and 4).

The following regression equation was obtained for systolic blood pressure using multiple linear regression analysis:

$$P_{syst}\ (\text{mm Hg}) = 73.8 + 0.018 \times \text{PbB}\ (\mu\text{g/L}) + 0.52 \times \text{age (years)} + 0.45 \times \text{heart rate/min}$$

The regression equation for diastolic blood pressure contained no significant contribution from blood lead (the coefficient in the equation being 0.010, $p > 0.10$).

Kidney function parameters (serum creatinine, blood urea nitrogen, retinol binding protein in urine, relative uric acid clearance, and total protein) revealed no significant differences between the groups. From the study, which had its limitations (small groups, insufficient data on body mass index), it was concluded that a positive relationship may exist between blood lead level and blood pressure (notably systolic blood pressure). A relationship between urine cadmium and blood pressure appeared to be linked with age.

Blood Lead Levels in the Netherlands

Several studies have been performed to gain a clearer insight into the average blood lead levels in the Dutch population (*3*). Some studies were particularly aimed at assessing blood lead levels in children (*4,5*). In other studies, samples from draftees, which are being gathered at regular intervals, were examined for heavy metal contents such as lead and cadmium (*6*). Another study reported on blood lead levels and other trace metal levels in elderly men (*7*). Occupationally exposed persons frequently have been the subject of epidemiological studies. Some of the results are presented here.

Table 3. Zero-order correlation coefficients for systolic blood pressure.[a]

Parameter	r	p
Blood lead	0.29	0.003
Urine cadmium	0.22	0.04
Age	0.34	0.001
Heart rate	0.34	0.001

[a]From de Kort et al. (*2*).

Table 4. Partial correlation coefficients for systolic blood pressure.[a]

Parameter	r	p
Blood lead, adjusted for age, heart rate	0.22	0.02
Urine cadmium, adjusted for age, heart rate	0.13	0.22
Blood lead, adjusted for age, heart rate, urine cadmium	0.20	0.07

[a]From de Kort et al. (*2*).

Blood Lead Levels in Children

In 1984, a committee of the Public Health Council in the Netherlands has published recommendations for air quality criteria for lead (*3*). The committee has also taken into consideration accepted limits for blood lead levels in children as recommended by Zielhuis (Table 5) (*5*). In cooperation with the European community, blood lead levels were assessed in children under the age of 6 years, in several small and large cities, in 1979 and in 1981 (*4*). The results showed that the limit values were generally not exceeded, with median (50th percentile, P50) values declining over the years, being at a level of 130 μg/L in 1981 (Table 6).

Blood Lead Levels in Draftees

The Government Institute for Public Health and Environmental Hygiene in the Netherlands has reported on blood lead levels in draftees (*6*). In random samples (of at least 1% of all draftees in 1 year) blood lead levels of draftees in several years have been assessed (Table 7). The results in 1980 and 1981 showed markedly lower values when compared with those of earlier years (1976). Furthermore, trend analyses showed a significant downward trend over time within the 1980/1981 groups. The investigators suggested that reducing the gasoline lead content in 1978 might have played a role.

Table 5. Dutch public health standards for children.[a]

Percentile	Blood lead, μg/L
P50	200
P90	250
P98	300

[a]From Zielhuis et al. (*5*).

Table 6. Blood lead levels in children, age 6 years.[a]

	Blood lead, μg/L, P50/P98	
City	1979	1981
Rotterdam-centre ($n \pm 99$)	160/330	130/220
The Hague ($n \pm 88$)	180/320	130/230

[a]From Ligeon et al. (*4*).

Blood Lead Levels in Lead Workers

It is estimated that in the Netherlands (14.5 million inhabitants) less than 10,000 and probably approximately 5000 workers are occupationally exposed to lead, a figure that is expected to become smaller. In the near future, a directive from the European community will be implemented in Dutch legislation, including action levels and limit values for blood lead levels of occupationally exposed workers (Table 8). Supported by the Directorate-General of Labour, the Medical Biological Laboratory TNO performed a Health and Health Hazard Survey in branches of industry, where occupational exposure to lead is an important factor. The blood lead levels obtained in this survey were pooled, and the results (Table 9 and Fig. 1) show that median (P50) values vary between 288 μg/L and 340 μg/L for Dutch workers and between 381 μg/L and 452 μg/L for workers of Mediterranean origin. However, it must be emphasized that the workers examined in this survey probably do not constitute a group that is representative for all lead workers. More likely they represent those who are exposed to relatively high levels of lead, as the survey was preferentially performed in workplaces with levels of exposure expected to be higher than average.

Discussion

The study of lead workers indicates the possibility of a positive relation between blood lead and blood pressure. The effect on systolic blood pressure is in the order of magnitude of an 1.8 mm Hg increase per 100 μg/L increase in blood lead level when a linear relation is assumed. If a relationship between blood lead level and diastolic blood pressure exists, then here the increase per 100 μg/L increase in blood lead level would amount to approximately 1.0 mm Hg. These figures are lower than those found in the NHANES II study (*8*), but well in concordance with results from the Kirkby and Gyntelberg study (*9*). However, it must be kept in mind that linearity of a relation is merely an assumption, provided an effect does exist. In particular, at lower blood lead levels (i.e., values < 100 μg/L), deviation from linearity would not be a surprising result. Nevertheless, since median blood lead levels of persons not occupationally exposed in general do not exceed 200 μg/L, reducing this level to zero could imply an average lowering of systolic blood pressure with 3.6 mm Hg and perhaps an average lowering of diastolic blood pressure of 2.0 mm Hg.

In most studies median blood lead levels are lower than 200 μg/L, and reducing this level to zero will probably not be possible. As a result, detecting an effect of the lowering of blood lead levels will not be an easy task: population standard deviation in blood pressure measurements can vary from 15 to 25 mm Hg (for systolic

Table 7. Blood lead levels in draftees.[a]

	1976	1981	1982
n	1170	175	150
Blood lead, μg/L, P50/P98	140/350	90/210	80/200

[a]From Ellen et al. (*6*).

Table 8. Proposed action levels and threshold levels for occupationally exposed persons.

Blood lead level, μg/L	Requirements
> 300	Information to workers Hygienic measurements Opportunity to undergo medical examination
> 500	Medical surveillance Information to workers Hygienic measurements
> 700, but ZPP < 20 μg/g Hgb[a]	Medical surveillance Information to workers Hygienic measurements
> 700 and ZPP > 20 μg/g Hb or > 800	If occurring twice within 3 months, withdrawal from exposure

[a]ZPP, blood zinc protoporphyrine content.

Table 9. Blood lead levels in male lead workers in the Netherlands.[a]

	Dutch workers				Mediterranean workers			
Age	*n*	P50	P90	P98	*n*	P50	P90	P98
< 30	149	302	725	929	81	381	662	762
30–39	136	288	588	795	75	451	689	772
40–49	128	339	635	774	65	389	704	863
> 50	138	292	675	886	24	424	710	927

[a]Blood lead levels in μg/L.

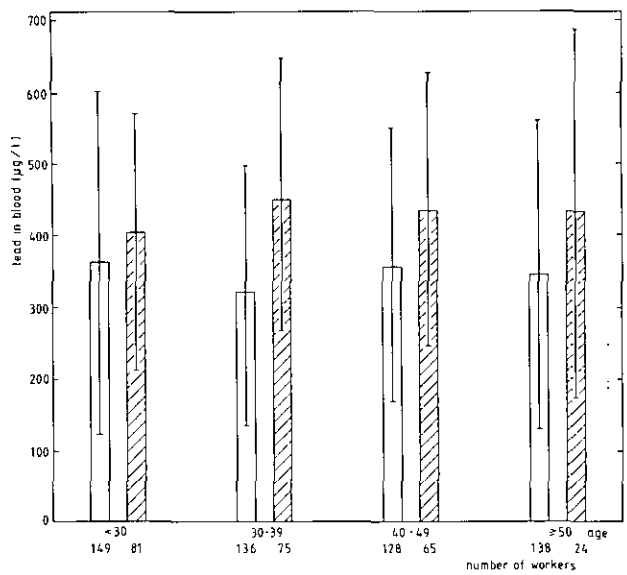

FIGURE 1. Average blood lead values ± SD of Dutch lead workers (open bars) and Mediterranean lead workers (hatched bars) in the Netherlands.

blood pressure). Thus, if a difference of 1.8 mm Hg is to be detected, using first and second type error probabilities of 0.05 (two-sided and one-sided, respectively), groups of at least 3200 persons each have to be examined. The detection of such differences will be further impaired because of the many factors (lifestyle, genetic, environmental, etc.), which may influence the outcome of blood pressure measurements. In statistical terms, the stability of blood pressure measurements might even decrease further if many factors are controlled for, demanding even larger groups to be examined.

Because the half-life of blood lead is rather long, a follow-up study will necessarily have to be performed over several years if one chooses to use a longitudinal study. Also, it is not known if a blood pressure-raising effect of lead is at all reversible. If cross-sectional studies are preferred, one might have to take into account the additional disadvantage of a cohort effect, which could hide an effect or erroneously reveal one. A prospective study of lead workers may yield more conclusive results, because the occupational level of lead exposure is higher than the level of exposure in the general population.

In conclusion, the expected reduction of environmental pollution with lead due to the reduction of the gasoline lead content and the expected reduction of occupational exposure due to hygienic measurements make a reduction of lead body burden in the general population, as well as in the occupationally exposed population, likely. In the Dutch situation, further epidemiologic evaluation of an effect on blood pressure will be difficult to perform. Prospective studies, e.g., in an occupational setting, are desired.

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