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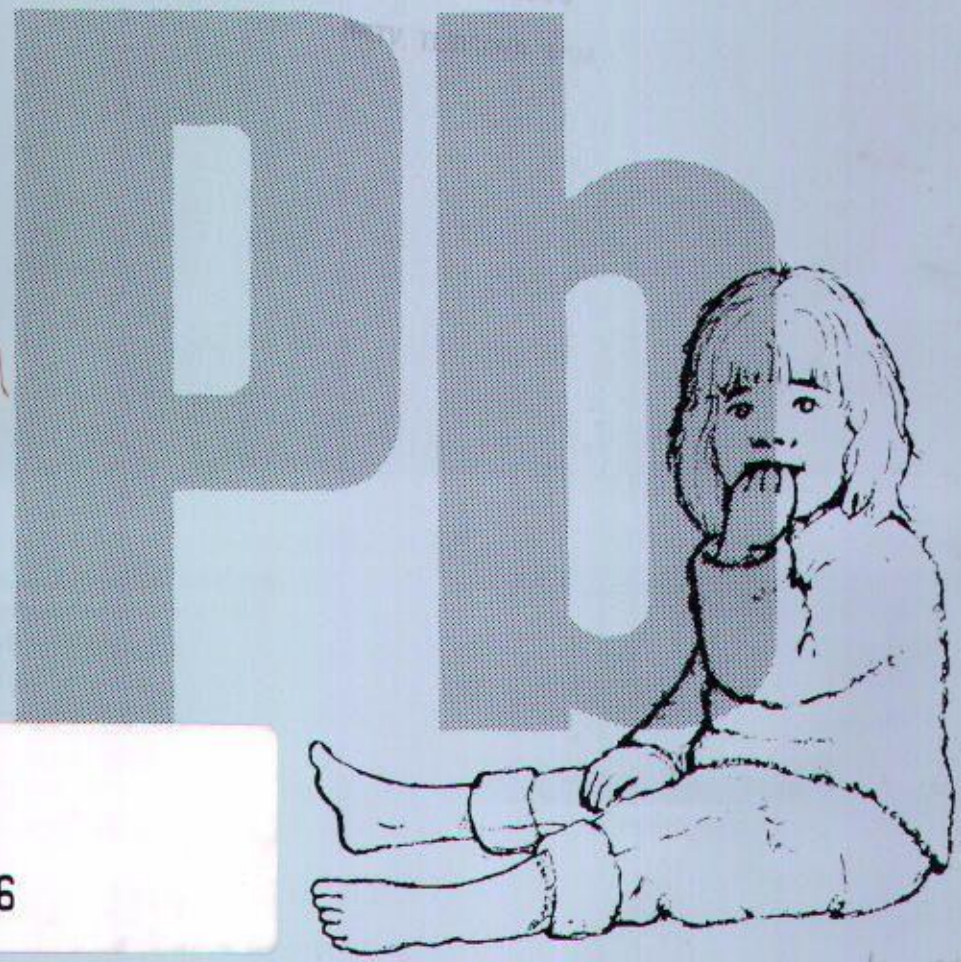
a study in environmental epidemiology

bert brunekreef



THE RELATIONSHIP BETWEEN ENVIRONMENTAL LEAD AND BLOOD LEAD IN CHILDREN - A STUDY IN ENVIRONMENTAL EPIDEMIOLOGY

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The relationship between environmental lead and blood lead in children: a study in environmental epidemiology.

Proefschrift

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"De wagen ging de heirweg,
een stroom van lood door het land.
De chauffeur liet hem uitlopen,
met geweldig ontploffen."

F. Bordewijk
"Knorrende beesten", 1933

0. INTRODUCTION

0.1. Aim and structure of report

Although the concentrations of lead in the air and in man have declined in most industrialized countries in recent years, the hazards of environmental lead pollution continue to raise interest and concern.
Several recent studies have documented or suggested that adverse health effects of lead occur at blood lead levels which were considered safe only a few years ago. Other studies have emphasized the importance of ingestion of soil and dust particles as a mode of lead intake for young children, who form a population at risk for lead for other reasons too.
The above-mentioned developments call for a re-evaluation of environmental quality standards for lead. The key elements of such standards are the blood lead threshold and the impact of environmental lead exposure on blood lead concentrations of children. It may be necessary to adopt a lower blood lead threshold whereas at the same time, the impact of environmental lead exposure on children's blood lead is probably greater than was assumed previously.
In The Netherlands, the national Health Council has already proposed a guideline for the long term average concentration of lead in air of 0.5 $\mu g/m^3$ (Health Council 1984). This guideline is 3-4 times lower than comparable guidelines used in the United States, the Federal Republic of Germany and the United Kingdom. In the U.S., the Ambient Air Quality Standard for lead is currently under revision (EPA 1983, 1984).
In this report, the impact of environmental lead exposure on children's blood lead is subjected to a detailed study. Chapter 1 provides a summary of the environmental health aspects of lead. In chapter 2, methodological issues in studies on correlations between environmental lead and blood lead in children are discussed. The report further proceeds along two lines: it contains a critical review of studies from which quantitative estimates of the impact of environmental lead exposure on children's blood lead can be obtained (chapter 3), and it gives an account of a study on the association between blood lead and lead in the environment which was performed among a population of Dutch

children living in Rotterdam, The Hague and Zoetermeer in 1981 (chapter 4).

0.2. Motivation for a review of studies on the relationship between environmental lead and blood lead in children

The relationship between environmental lead exposure and the concentration of lead in blood has been reviewed recently by several authors (Hammond et al. 1981, Ratcliffe 1981, Snee 1981, Chamberlain 1983a, Jones and Stephens 1983). These reviews have concentrated on the relationship between air lead and blood lead in adults and only limited attention was paid to studies among children. The focus was on air lead in these reviews, and minimal attention was paid to the role of ingestion of soil and dust particles by children as a mode of lead intake from the environment. As a result, most reviews have assumed that the impact of environmental lead on blood lead is not much larger for children than it is for adults. When it was suggested that this point of view should serve as a basis for the development of air quality standards for lead (Snee 1982a), the author has commented that a re-evaluation of childhood blood lead studies might result in a higher estimate of the impact of environmental lead on children's blood lead (Brunekreef 1983). Subsequently, it was decided to review the relationship between environmental lead and blood lead for children in detail, stressing the importance of non-inhalation modes of lead intake from the environment by children.

0.3. Background of environmental impact study in Rotterdam, The Hague and Zoetermeer

In the spring of 1979, blood lead levels were measured in a number of Dutch child populations of nursery school age, within the framework of the First E.C. Blood Lead Survey (Ligeon et al. 1981). In the city centers of Rotterdam and The Hague, children were found to have blood lead levels which slightly exceeded a guideline which was used by the Dutch Department of Public Health to evaluate the results of the Survey. In this guideline, it was

stated that at least 50% of blood lead levels found in any population of children had to be less than 20 µg/100 ml, 90% less than 25 µg/100 ml and 98% less than 30 µg/100 ml. The 90- and 98-percentiles of this guideline are 5 µg/100 ml lower than the Biological Quality Guide for the concentration of lead in blood proposed by Zielhuis (1974) and adopted by the E.C. (E.C. 1977) for the general population; the fact that children are more susceptible to lead than adults was the main reason to use a lower guideline.

In the spring of 1981, a Second E.C. Blood Lead Survey was to be held. At the request of the Department of Public Health, an environmental exposure study was conducted in conjunction with the Survey, to investigate to what extent the elevated blood lead levels in inner city children could be explained by exposure to lead in the environment. The study was designed on the basis of our earlier work in Arnhem, where the surroundings of a secondary lead smelter were studied in 1978, to assess the intake routes of lead from the environment by preschool children (Brunekreef et al. 1978, 1981, Diemel et al. 1981).

In the Arnhem study, significant associations between some lead exposure variables and children's blood lead levels were found although the general level of environmental lead exposure was low in the study area (when compared to results from smelter studies performed abroad), and although blood lead levels were not higher than in Dutch inner city children in 1979. It was therefore considered possible that the elevated blood lead levels in the inner city children of Rotterdam and The Hague were also related to exposure to lead in the environment.

1. ENVIRONMENTAL HEALTH ASPECTS OF LEAD

1.1. Lead in the environment and in man

From prehistoric times, lead has been used by mankind. The low melting point of lead makes it easy to mine, and lead is a workable and durable metal. Its uses for water pipes and as wine conservation and sweetening agent in the Roman Empire are well known, and have led to interesting speculations about the role that lead poisoning of Rome's upper classes may have played in the decline of the Empire (Gilfillan 1965, Nriagu 1983).

For hundreds of years the toxic properties of lead have been known. A classical example is the "Devonshire Colic", caused by the consumption of cider in which lead was dissolved due to the grinding of apples with lead-filled grinding stones, and during storage in lead-glazed vessels. The hazards of lead smelting operations for the environment have also already been appraised in the past centuries (Meiklejohn 1954, Beritic 1984). Meiklejohn, for example, cites the article "an account of the disease called Mill-Reek" written by J. Wilson, which appeared in 1754 in the Scots Magazine:

> "All the inhabitants at Leadhills are subject to this disease; but it mostly seizes and violently affects the men whose daily business it is to melt down the lead. The reek or smoake rising from the melting is believed to be the cause of the disease; because the melters, who are most subject to it, are most exposed to the smoake, which comes out often full in their faces."

And an account by the Rev. C. Crutwell of the same area runs as follows:

> "The appearance of Leadhills is disagreeable in the extreme: rocky, rude and barren, every vegetable is raised with difficulty, and seldom brought to perfection. Spring water is to be obtained of excellent quality, but that which is below the smelting mills is poisonous. The lead ore, before smelting, is broke very small and washed from filth, which frequently contains arsenic. Fowls of any kind do not live many days at Leadhills;

horses, cows, dogs and cats often find ill effects of this poisonous mineral."

Although lead has been used for thousands of years, it took the industrial revolution to exponentially increase the amount of lead mined and used to its high, present-day levels (figures 1.1 and 1.2).

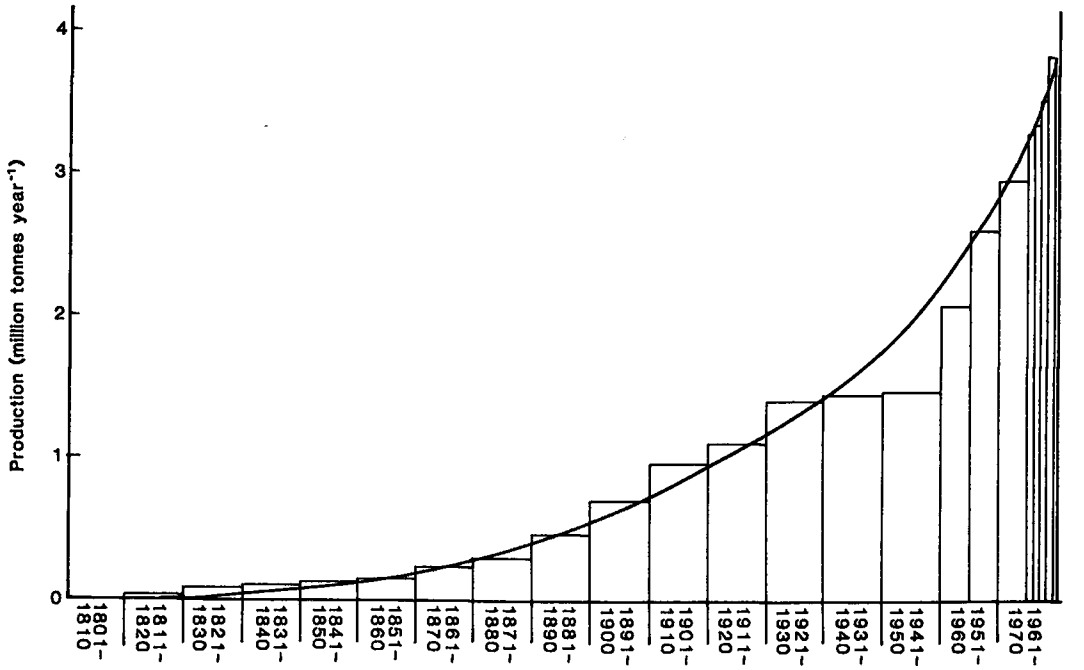


Figure 1.1. Smelting of lead in the world
(Reprinted with permission from Harrison and Laxen 1984).

Half of the world production of refined lead is being used for the fabrication of storage batteries (Harrison and Laxen 1984). About 15 percent goes into pigments and chemicals, and another 10 percent into the production of tetra-alkyllead which is almost exclusively used as anti-knock agent in gasoline. It is this latter use, however, which is to a large extent responsible for the global emission of lead into the atmosphere. For the US the relative contribution of vehicular emissions to total atmospheric emissions has been estimated at more than 90% (Harrison and Laxen 1984) for the year 1975, and this is not different in other

countries where tetra-alkyllead is being used as a gasoline additive including The Netherlands (Department of Health and Social Security 1980, Anonymus 1982d). In industrialized areas, the relative contribution of industrial lead sources locally outweighs vehicular traffic.

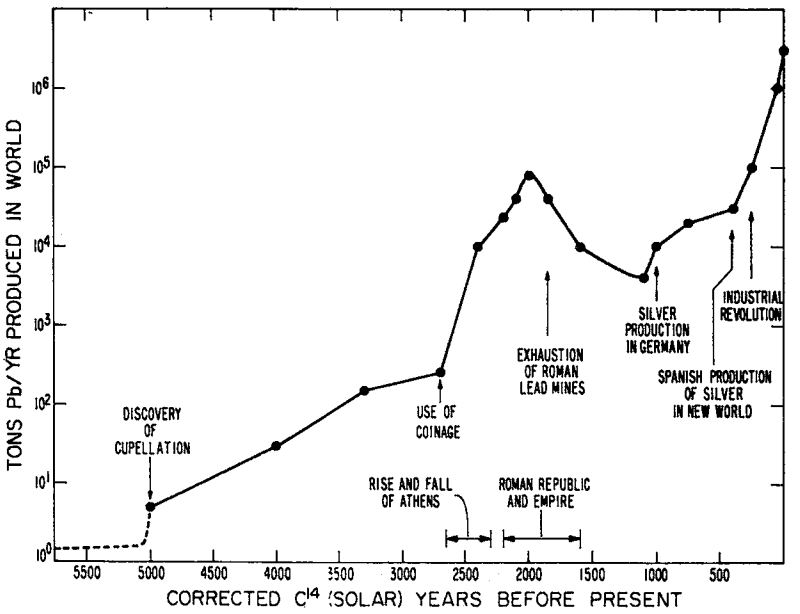


Figure 1.2. World lead production during the last 5500 years. (Reprinted with permission from Patterson 1982).

Lantzy and Mackenzie (1979) have calculated the ratio between anthropogenic and natural emissions of 20 different trace elements into the atmosphere, and their ratio of 346 for lead is the highest of all.

As a result of worldwide emissions of lead into the atmosphere, lead pollution has increased in even the remotest areas of the world. The lead concentration of Greenland snow has been shown to have increased about 200-fold in the past 3000 years, with most of the increase happening after 1945, i.e. after the use of tetra-alkyllead in gasoline became widespread (Patterson 1982).

Even though global lead emissions into the atmosphere are mainly

restricted to the northern hemisphere, the lead concentration of Antarctic snow has also increased more than 10-fold over the past century (Boutron and Patterson 1983).

The concentrations of lead in prehistoric samples of snow and other materials are often extremely low, and extreme precautions are necessary to avoid contamination of samples during handling and analysis (Murozumi et al. 1969, Patterson 1982, Boutron and Patterson 1983).

Although it is now beyond dispute that the lead concentrations of certain media like polar ice and snow have considerably increased due to atmospheric pollution, it is less clear whether this is also true for the body burden of man.

Lead is a normal constituent of soils in rather high concentrations of 10-200 mg/kg (Khan 1980, Harrison and Laxen 1984). Even though most plants do not efficiently take up lead from the soil, lead is naturally present in plants and animals to a certain extent, and must always have been a constituent of man's diet. Information on body burdens of prehistoric man mainly relies on analyses of the lead content of bones, and these have produced conflicting results. Drasch (1982) for example has maintained that present-day body burdens are at most 20 times higher than they were in prehistoric Peruvian indians. Ericson et al. (1979) have argued, on the contrary, that the difference between present-day and prehistoric, uncontaminated man is at least 1000-fold. Part of the difference between Drasch and Ericson et al. is caused by the selection of a representative, present-day body burden which was higher in the Ericson et al. paper. The number of prehistoric samples has usually been small in these and other investigations, and it is impossible to assess their representativeness.

It is also difficult to be certain that no post-mortem contamination of bone samples from the burial soil has occurred (cf. Waldron 1982 and Knutti 1984), and another part of the difference in the conclusions reached by Drasch (1982) and Ericson et al. (1979) is due to a different evaluation of the extent to which the Peruvian samples were contaminated after death.

Blood lead levels of isolated, non-industrialized present-day populations have been found to be lower than those of populations living in industrial countries, but not by a factor of more than 5-15 (Hecker et al. 1974, Piomelli et al. 1980, Poole et al. 1980) (cf. also section 2.6). It is not clear, however, whether

these populations can be compared to prehistoric, uncontaminated populations.
It should be noted that the acceptability of the present level of lead contamination from the view point of human health depends not on our knowledge of the size of the increase of man's body burden of lead, but on our knowledge of the adverse health effects of lead, and of the exposure levels where these adverse effects begin to manifest themselves (Budiansky 1981).
At present levels of exposure in industrialized countries, adverse effects of lead on human health are subtle and hard to detect - if present at all. One of the most important questions today is whether low doses of lead are able to permanently damage the central nervous system of children, affecting various CNS functions including intelligence (Anonymus 1980a, 1982a, 1982b, 1982c, Rutter 1980, Bornschein et al. 1980a, 1980b, Rostron 1982a, 1982b, Needleman 1983).
To date, this question has not been fully answered, and one can only state that there may or may not be subtle effects of lead on children's brains at levels of exposure currently considered safe. Even if future research would prove the current no-adverse-effect levels to be safe indeed, there would still be only a narrow margin of safety between current exposure and exposure levels where adverse effects would become likely.

1.2. Children as a population at risk for lead

There is general agreement that within the non-occupationally exposed population, children of 0-6 years old constitute the population most at risk for lead (WHO 1977a, EPA 1978, National Research Council 1980, Rostron 1982a, 1982b).
The main reasons for this are that (1) children are more susceptible to lead than adults, (2) they take in more lead, with food, per kg body weight than adults, (3) they exhibit mouthing which exposes them to lead in dust and dirt more than adults and (4) they absorb more lead from the gut than adults.

ad 1
It is well established that at a given level of lead in the blood (PbB), children suffer more strongly from ill effects than

adults. The level of free erythrocyte protoporphyrin in blood begins to rise at lower PbB levels in children than in adults (Roels et al. 1976, 1978b, Cavalleri et al. 1981, Piomelli et al. 1982); adverse effects on central nervous system functioning (as measured by various tests of mental ability) have been suggested to occur at PbB levels well below those at which CNS-effects in adults can be detected (Needleman (et al.) 1979, 1983, Yule et al. 1981, Winneke et al. 1982, 1983, for reviews cf. Rutter 1980, Bornschein et al. 1980a, 1980b, Rostron 1982a, 1982b) although it is still a hotly debated issue from what level of blood lead these effects start to manifest themselves (Anonymus 1982a, 1982b, 1982c, Jones et al. 1983). Previously, it was thought that adverse CNS-effects did not occur in children who had PbB levels below 30 µg/100 ml, but at present, some authors even begin to doubt whether a threshold exists below which adverse effects do not occur.
It has been suggested that acceptable levels of lead in blood should be lower for children than for adults (Roels et al. 1978b, Zielhuis 1981, Grandjean 1981, Piomelli et al. 1982).

ad 2
Children take in more lead per kg body weight with their food than adults, for the simple reason that they consume more food per kg body weight. The difference may very well be two- to threefold (Barltrop 1972, ICRP 1975) depending on the age of the child. Expressed per unit volume of blood, the intake in children has been asserted to be 1.5 times greater than in adult women (Duggan 1983a). The inhalation rate per kg body weight is also greater (Knelson 1974) due to the higher metabolism in children.

ad 3
During some period in early life, the normal child will investigate its surroundings by hands and mouth (Lepow et al. 1974, Sayre et al. 1974, Charney et al. 1980). The amount of dust and dirt ingested as a consequence of mouthing has never been directly measured. It has been suggested that the amount of ingested dust could be in the order of about 20-50 mg/day (Duggan and Williams 1977) but this figure should not be taken as more than an 'educated guess'. Regardless of how large the ingested quantity actually is, it will be larger than the relative amounts of dust and dirt ingested by adults, although one recent study has

suggested that for adults as well, lead in dust and dirt represents a pathway of lead intake (Gallacher et al. 1984b, 1984c).

ad 4

Limited evidence suggests that the absorption of lead from the gut is more efficient in children than in adults (Alexander et al. 1972, 1974, Ziegler et al. 1978). In animal studies, it has been documented clearly that very young animals absorb more lead from the gut than adult animals (Jugo 1977, Quarterman and Morrison 1978, Mahaffey 1983).

A higher absorption rate does not necessarily mean, however, that more lead is being retained as well; a number of children in the study by Ziegler et al. (1978) actually excreted more lead than they absorbed, indicating that lead excretion may also be higher in children than in adults. It has been pointed out, however, that this may only be so at low levels of exposure, and that at somewhat higher levels, lead is actually being retained in children more than in adults (Ryu et al. 1983).

The mechanisms 2-4 would lead one to expect that in general, children should have higher blood lead levels than adults. This, however, is not the case (Chamberlain 1983a, Duggan 1983b, 1983c). Children living in not heavily polluted environments have repeatedly been shown to have blood lead levels slightly higher than those of their mothers, and more or less equal to those of their fathers (Billick et al. 1979, Landrigan and Baker 1981, Mahaffey et al. 1982a).

Various explanations can be proposed for this phenomenon. The additional intake through mouthing activity could be negligible compared to lead intake with food (Chamberlain 1981); however, the intake of lead from food alone is already so much larger in children than in adults, on a per kg body weight basis, that some difference in metabolism between children and adults has to be assumed anyway - and in absence of knowledge about the size of the difference, it seems not possible to draw conclusions on the amount of lead ingested through mouthing from the absence of considerable differences between blood lead levels in children and adults in non-polluted areas alone.

Another explanation would be that the distribution of lead over the various body tissues is different in children than in adults (Duggan 1983a). It is indeed true that in children, relatively more lead is in the soft tissues than in adults, for whom lead in

the skeleton constitutes 90-95% of the total body burden (Schroeder and Tipton 1968, WHO 1977a). This probably reflects mainly the fact that the lead concentration in children's bones is much lower than in adult bones; limited evidence from a study by Barry (1981) does not support the hypothesis that the lead concentration in soft tissues in children - including the brain - is higher than it is in adult soft tissues.

A more likely explanation would be that although uptake from the gut is higher in children than in adults (both through the higher food intake and the greater absorption efficiency), retention is not necessarily higher because the uptake may be balanced, to a certain extent, by a higher excretion rate (Duggan 1983a). As mentioned, the Ziegler et al. (1978) study supports this; a recent study by Ryu et al. (1983) in addition has demonstrated that at levels of lead intake which are low - but still higher than in adults on a per kg body weight basis - children's blood lead levels in the first half year after birth remained below those of their mothers, and even decreased somewhat during the first months of life. A subsequent higher intake in some of the children resulted in a doubling of the children's blood lead levels within a few months, suggesting that only at low levels of intake, excretion is able to balance uptake. The Ryu et al. (1983) study shows a similarity with a study from the Federal Republic of Germany (Haas et al. 1972) in which it was shown that blood lead levels in hospitalized children aged 0-6 yrs were lower than at birth. For some more examples cf. Duggan (1983b, 1983c).

It is well established that a child is born with a blood lead level which is somewhat lower (10-20%) than that of its mother (Haas et al. 1972, Schaller et al. 1976, Kuhnert et al. 1977, Buchet et al. 1978, Roels et al. 1978a, Alexander and Delves 1981, Kaul et al. 1983, Zarembski et al. 1983, Tsuchiya et al. 1984). Over 90% of the lead in blood is in the erythrocytes (Zielhuis 1974). At birth, children have a haematocrite value which is about twice that of their mothers (Zielhuis 1974, ICRP 1975) and it has been argued that this protects new-born children from the adverse effects of lead, as at a certain blood lead level, the concentration in the erythrocytes as well as in plasma is lower in new-born children than in their mothers. It has to be pointed out, however, that the haematocrite decreases rapidly after birth and that between 0.5-2 yrs, it is actually lower in

children than in their mothers (ICRP 1975). Up to a certain level of exposure, the blood lead level in children apparently does not rise above its initial level. Still, this does not necessarily mean that the child excretes as much lead as it absorbs. A child grows, and builds up a body burden of lead which may very well be about 50 mg when the child has reached adulthood (Schroeder and Tipton 1968, Barry 1978). If in the course of 20 years 35 mg of lead have been added to the body burden, this constitutes an average retention of 35 mg/(20 * 365) = 5 µg/day (approximately). In recent years, it has become clear that lead intake with food for young children in many countries is probably only about a few tens of micrograms per day (cf. section 2.7 for further details) of which 50% at most is being absorbed from the gut.
It could be argued that quite a large part of the absorbed lead simply goes into the formation of the total body burden over the years. The body burden figures used to arrive at this tentative conclusion may be too high for present-day situations, as levels of lead in blood and in food seem to have been declining (cf. Diehl 1982, Oxley 1982, Annest et al. 1983, Brunekreef et al. 1983, Elwood 1983a, Sherlock 1983). At least part of the reduction of lead in food has been ascribed to analytical artifacts (Sherlock 1983, Bloom and Smythe 1984); as the body burden of lead is mainly determined by the lead content of bones which is relatively high and therefore somewhat easier to measure without bias, it is possible that total body burden data as measured 10-20 years ago still have relevance for present-day situations.
Lack of specific data makes it difficult to arrive at reliable estimates of how much of the absorbed lead actually goes into the formation of the body burden; it is certainly not a negligible part, and it is remarkable that this point is usually not given much attention in the literature.

1.3. The exposure system

After having been released into the environment, lead can reach children through a number of different pathways. The major sources and pathways are shown in figure 1.3.

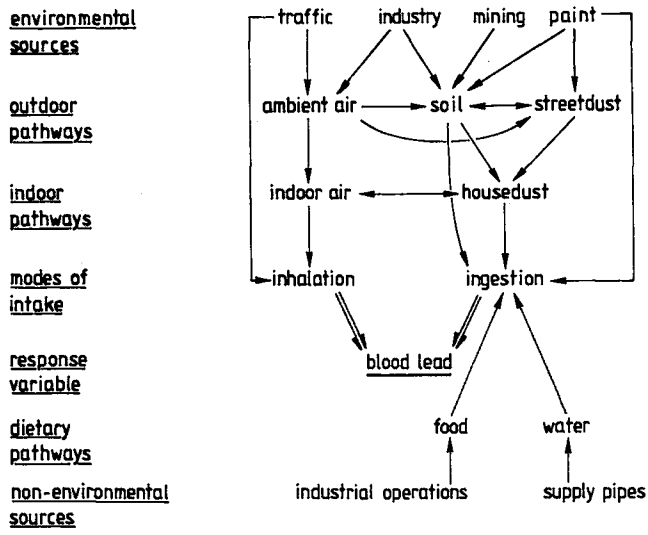


Figure 1.3. Sources of environmental lead and pathways to children.

Although the figure looks complex it is in fact a simplification. A comparable flow chart in the NAS-report (National Research Council 1980) "Lead in the human environment" has over one hundred arrows and interactions; Billick (1983) has aptly remarked that that flow chart certainly illustrates the complexity of the system, "but whether it clarifies or confuses the understanding of what is happening is questionable".

Figure 1.3 hopefully clarifies more than it confuses; it mostly contains variables which conceivably can be measured in a single study. Four main categories of environmental sources have been discerned. Of these, vehicular traffic is the single largest source of environmental lead pollution in the industrialized nations, which accounts for over 90% of all emissions into the atmosphere (WHO 1977a, National Research Council 1980, Harrison and Laxen 1984).

The organolead compounds tetra-ethyllead and tetra-methyllead

have been added to gasoline as an anti-knock agent in concentrations up to 1 g/l in the past. At present, the maximum concentration is limited to .15 to .40 g/l in most advanced nations, and lead-free gasoline is used in Japan and increasing its market share in the United States. In the future, lead will probably be removed from gasoline in the countries of the European Communities as well (Anonymus 1984). In The Netherlands, the lead content of petrol will be reduced to a maximum of 0.15 g/l in 1986 (Zielhuis 1984) and by the end of 1984, one manufacturer had actually started to offer lead free gasoline for sale.

It is estimated that some 75% of gasoline lead is released from a driving car into the atmosphere, mostly in the form of inorganic lead compounds (Habibi 1970, Chamberlain et al. 1978). Part of this is deposited near the road, part of it remains airborne for long periods of time and contributes to global lead pollution (Daines et al. 1970, Chamberlain et al. 1978).

Industrial lead emissions are quantitatively less important, but have led to very high pollution levels near industrial sources in a number of countries (Roberts et al. 1974a, 1974b, Landrigan et al. 1975, Einbrodt et al. 1975, Rosmanith et al. 1975a, 1975b, 1976, Roels et al. 1976, 1978b, 1980, Yankel et al. 1977, Schmitt et al. 1979, Zielhuis et al. 1979, Walter et al. 1980, Cavalleri et al. 1981, Popovac et al. 1982, Prpic-Majic et al. 1983). In mining districts, large quantities of lead can be found in the soil (Barltrop et al. 1974, Davies et al. 1978, 1981a, 1981b, 1981c, Davies 1983, Culbard et al. 1983a, 1983b). From there, it can move into the food chain and pollute house dust.

In the past, lead was a major constituent of paint in many countries (Chisholm 1973). Especially in the United States, the combination of flaking high-lead paints and adverse social conditions in inner city areas has led to a large number of fatal poisonings among children (Ingalls et al. 1961, Anderson and Clark 1974, Chisholm 1982).

Similar experiences have not been reported from other countries, although this does not mean that crumbling paint locally does not contribute heavily to lead pollution of dust and dirt inside and outside dwellings (Reeves et al. 1982, Millar and Cooney 1982).

The three major outdoor pathways are air, soil and dust.

When airborne lead is inhaled, the smaller particles (less than about 1-2 µm in diameter) penetrate deep into the lungs, and experiments with radioactive lead have shown that lead is quanti-

tatively absorbed (Knelson et al. 1972, Chamberlain (et al.) 1975, 1978, 1983a, Gross 1981). It has been argued that in these experiments, more soluble forms of lead were used than are commonly encountered in the atmosphere (Lawther et al. 1972). On autopsy the lead concentration in the lung of adults was, however, not found to be elevated (Barry 1978) which reinforces the conclusion that no retention of lead in the lung occurs. Larger particles are trapped in the upper airways, from where they can be ingested, thereby contributing to total exposure through another mode of intake. Soil and street dust may contribute to total exposure mainly when lead bearing particles are ingested by children.

The main indoor pathways are indoor air and house dust; the respective modes of intake are the same as for the outdoor pathways, i.e. inhalation and ingestion. Food and drinking water constitute the main dietary pathways. Lead in drinking water mainly originates from lead solved in water supply systems, but for food the picture is less clear (for further details cf. section 2.6).

It must be stressed that it is generally not possible to derive fixed transfer coefficients indicating how large the transport of lead through some pathway is, irrespective of the situation which is being studied. Quite a number of "transfer modifying variables" exist, and some knowledge of their value is necessary when studying lead intake from the environment by children in a specific environment. Some examples are: the frequency of hand-to-mouth movements, which is an obvious determinant of the amount of dust which is being ingested, and a child's nutritional status which is a determinant of the blood lead concentration given a certain intake of lead.

In chapter 2, the major "transfer modifying variables" will be listed.

2. METHODOLOGICAL ISSUES IN STUDIES ON RELATIONSHIPS BETWEEN ENVIRONMENTAL LEAD AND BLOOD LEAD IN CHILDREN

2.1. Preface

Experimental studies on lead intake from the environment by children have not been performed. To investigate the associations between environmental lead and blood lead in children, we therefore have to rely mainly on observational studies (although it is sometimes possible to take advantage of changes like emission reductions, clean up operations, opening of new roads or factories etc.).

Such studies are of an epidemiological nature, as epidemiology is concerned with the patterns of disease occurrence in human populations and of the factors that influence these patterns (Lilienfeld and Lilienfeld 1980). If the determinants of disease are environmental pollutants, environmental epidemiology is the study of exposure to and health effects of these pollutants in the non-occupationally exposed population (WHO 1983). The methodological problems in studying the relationship between environmental lead and blood lead in children are those of environmental epidemiology in general.

The potential health effects of environmental pollutants are usually not unique; the main difference between environmental epidemiology and epidemiology in general lies therefore in the determinants which are being studied, whereas the general methodology concerning study designs, data analysis etc. is more or less the same (WHO 1983). One further observation is that relatively often, studies in environmental epidemiology are "agent-oriented" in the sense that studies are prompted by concern over the potential health effects of agents which are present in the environment, and not by observations of unusual distributions of disease in a given population (Janerich et al. 1981, Strehlow and Barltrop 1981, Philip and Hughes 1982). In the past 20 years, concern over the potential health effects of environmental pollutants has reached a high level in most advanced countries. The resulting pressure to do agent-oriented epidemiological studies has emphasized the general problem of how to decide that an agent-oriented study has any chance of detecting a specified

health effect in environmental epidemiology particularly (Stebbings 1981, Stinett et al. 1981, Lyon et al. 1981).
In this chapter, a number of specific methodological issues will be addressed which are of particular interest in studies on blood lead/environmental lead relationships. These include the definition of environmental pathways (2.2) and lead transfer modifying variables (2.3); the characteristics of the outcome variable (2.4) and outcome modifying variables (2.5); the definition of confounding variables (2.6) and the analysis of the data (2.7).

2.2. Environmental pathways of lead to children

The main environmental pathways of lead to children are air and soil, dust, dirt and paint.

Air lead
The main sources of lead in outdoor air are vehicular traffic and industrial emissions (WHO 1977a, National Research Council 1980, Chamberlain 1983a, Harrison and Laxen 1984). Consequently, the concentration of lead in air varies with distance from roads and industrial sources (Daines et al. 1970, Little and Wiffen 1977). Near roads, a variation with elevation has also been reported, with higher levels at street level than at rooftop level (Darrow and Schroeder 1974, Lioy et al. 1980). The traffic-generated lead aerosol is mostly in the submicron range (Chamberlain et al. 1978) so that upon inhalation, it can penetrate deeply into the lung. Near industrial sources, more of the lead is in particles larger than one µm (Roberts et al. 1974a, Landrigan et al. 1975, Paciga et al. 1975), and less of it will penetrate to the deeper regions of the lung.
Usually, lead in outdoor air is sampled with High Volume samplers; these devices are known to sample particles up to about 10 µm relatively efficiently (Wedding et al. 1977, Meulen et al. 1984). Consequently, the amount of lead which can actually reach the alveoli in the lung is being over-estimated by Hi-Vol measurements, and the bias will be most probably larger near industrial lead sources than near roads.
Other devices, sampling lower volumes of air, are sometimes used, and the resulting air lead concentrations are usually lower than

those measured by Hi-Vol samplers at the same spot and time (Lieback and Rüden 1983).
Indoors, the concentration of lead in the air is typically lower than outdoors (Daines et al. 1972, Johnson et al. 1978, Alzona et al. 1979, Cohen and Cohen 1980).
It has been shown that large particles in outdoor air penetrate less well into buildings than small ones (Cohen and Cohen 1980). Presumably, the indoor/outdoor ratio therefore differs in areas where air lead is predominantly of industrial origin from that in areas where vehicular traffic is the main source.
Inside driving cars, the concentration of air lead has been shown to be equal to or lower than the concentration of outdoor air lead measured on the street where the car was driving (Bevan et al. 1974, Chamberlain et al. 1978), but higher than the concentrations measured at nearby fixed monitoring sites (Rohbock 1981, Den Tonkelaar 1983). This is due to the rapid decrease of the Pb-concentration in the air next to the road.
Due to the many sources of variability mentioned above, the concentration of lead in the air which is actually being inhaled by people cannot be well estimated from measurements at fixed sites in outdoor air; a correlation of only 0.20 (Spearman's r) has been reported between the concentration of lead in air as measured with personal samplers and the concentration of lead in air measured at fixed outdoor sites (Tosteson et al. 1982). The range of outdoor air lead concentrations in this particular study was low, 0.40 $\mu g/m^3$; when larger ranges of air lead are being studied, the correlation between the concentrations of lead in inhaled and outdoor air will be higher, especially when there are systematic, large differences in outdoor air lead between areas where people spend most of their time.

Wet and dry deposition
From the air, lead is transferred to the earth's surface by dry and wet deposition (Galloway et al. 1982). The dry deposition flux is related to the concentration of lead in air; the relationship has been expressed in the following equation:

$$F = Vg * C \qquad \text{(Chamberlain et al. 1978)}$$

F = flux (mass per surface unit per time unit)
Vg = deposition velocity (distance units per time unit)
C = concentration of lead in air (mass per volume unit)

The deposition velocity is a unit which depends on the structure of the surface to which deposition takes place; if the surface is rough, more mass is being transferred to it, per surface unit, from the air at a given air lead concentration than when the surface is smooth. For different types of grass fields, the deposition velocity was shown to range from 0.05-1 cm s^{-1} for example (Davidson et al. 1982).
As a result there may be large differences of dry deposition fluxes in areas with comparable outdoor air lead concentrations.
Wet deposition of lead occurs when lead particles are trapped by rain and snow, and thereby transferred to the earth's surface. It depends on precipitation volume, intensity and duration (Lindberg 1982). The ratio between wet and dry deposition is not fixed, but depends on climatic factors. For a deciduous forest in the eastern US which had a yearly precipitation of 1400 mm, it was shown that wet deposition accounted for 45% of the total atmospheric deposition of lead (Lindberg and Harris 1981). For New York City, a value of 56% has been reported (Nriagu 1978a). The input of lead from the air into other environmental pathways is thus not a fixed function of the air lead concentration.

Lead in soil
The soil lead concentration has been shown to be high in or near mining areas (Barltrop et al. 1974, Nriagu 1978b, Davies 1983, Culbard et al. 1983a), near industrial lead sources (Roberts et al. 1974a, Landrigan et al. 1975, Yankel et al. 1977. Cf. also section 3.2), and near (mostly wooden) houses painted with high-lead paints (Ter Haar and Chadzynski 1979, Reeves et al. 1982). Vehicular traffic causes elevated soil lead concentrations within about 100 m from busy roads (Page et al. 1970, 1971, Healy and Aslam 1980, Fergusson et al. 1980, Garcia-Miragaya et al. 1981, Agrawal et al. 1981, Byrd et al. 1983) and adds only slightly to soil lead concentrations away from roads (> 150 m).
In most soils, lead is highly immobile (Scokart et al. 1983, Khan 1980); as the pollution usually arrives on the toplayer, the concentration of lead in soil in polluted areas may vary sharply with depth (Roberts et al. 1974a, Farmer and Lyon 1977, Steinnes 1983). The amount of lead recovered from a soil sample varies with the extraction method used (Köster and Merkel 1982, Khan 1980). It is possible to recover virtually all lead from samples by using strong digesting acids, but the use of less strong

methods causes different proportions of total lead to be recovered from different soil samples (Köster and Merkel 1982, Harrison and Laxen 1977). Consequently, extraction methods and sampling depths should be reported when studying soil lead concentrations.
The accessibility of soils determines their potential as a pathway of lead to children; it is obvious that if soils are unaccessible because they have been paved, they cannot contribute much to exposure. In gardens and playgrounds, type and density of vegetation may influence the possibility of direct contact with the soil (Barltrop et al. 1974, Seifert et al. 1984). It has not yet been tried before to develop "measures of accessibility".

Lead in street dust
The lead concentration in street dust was shown to be elevated in inner city areas with high traffic densities (Graf et al. 1980, Cool et al. 1980, Fergusson et al. 1980, 1984, Anagnostopoulos 1983) and near industrial lead sources (Roberts et al. 1974a, Yankel et al. 1977) as a consequence of wet and dry deposition. In addition, crumbling paint may contribute to lead in street dust (Ter Haar and Aronow 1974, Reeves et al. 1982). Paint on street curbs and bridges has also been implicated as a source of lead in street dust (Franz and Hadly 1981, Landrigan et al. 1982). As with lead in soil, the extraction method used to recover lead from street dust determines which proportion of lead will actually be recovered (Day et al. 1979, Ellis and Revitt 1982, Jones and McDonald 1983, Gibson and Farmer 1984).
The variety of sampling methods which have been used is great; these may include sweeping a certain area with brooms (Elwood et al. 1977, Harrison 1979) or using a specially designed vacuum cleaner (Brunekreef et al. 1983).
The concentration of lead in the dust has been shown to depend on the particle size (Rameau 1972, Linton et al. 1980, Ellis and Revitt 1982). As a consequence, the results of measurements pertaining to different size fractions of the dust cannot be directly compared.
The concentration of lead in the dust also depends on whether the samples were taken from the pavement, the gutter or from the road surface itself (Cool et al. 1980). The variability of dust lead concentrations in time and space has only been assessed on a limited basis (Duggan 1984, Hamilton et al. 1984, Gallacher et

al. 1984a); it is probably rather large, suggesting that collection of large area samples, and some repetition of sampling are needed to reduce the variability in estimates of exposure to dust lead. Usually, lead in street dust is expressed as weight ratio, mg lead/kg of dust; sometimes, lead loadings are used (µg of lead per m^2 of pavement) which are thought to reflect total available lead better than the lead concentration in the dust itself (Brunekreef et al. 1983), but which are probably even more variable than the lead concentrations in the dust (Hamilton et al. 1984). There is a definite need for standardization of street dust sampling procedures and methods; at present, the results of different studies can only be compared with care, and not without some reference to the sampling methods and procedures.

Lead in house dust

For lead in house dust, the same major sources have been identified as for lead in street dust. In addition it has been shown that the house dust in lead workers' homes may contain very high levels of lead (Baker et al. 1977, Elwood et al. 1977, Rice et al. 1978, Fergusson 1981, Kawai et al. 1983). This was found in spite of changing of work clothes and showering by the lead workers in the factory (Rice et al. 1978) and it has been suggested that lead is being transported home on shoes, socks etc. (Elwood et al. 1977).

The same problems in sampling and analysis exist as with street dust. Sometimes, samples are taken from the vacuum cleaner of the house (Yankel et al. 1977, Culbard et al. 1983a, 1983b). As vacuum cleaners and vacuum cleaning practices vary across houses, the dust inside the cleaners is ill-defined.

Specially designed vacuum cleaners have been used to standardize sampling across homes (Solomon and Hartford 1976, Brunekreef et al. 1981, 1983). In house dust as well as street dust the lead concentration varies with particle size (Johnson et al. 1982). Sometimes, sampling has therefore been restricted to the smaller particles, as these tend to have the higher lead concentrations and are presumed to stick to children's hands better than large particles (Duggan and Williams 1977, Brunekreef et al. 1983). For house dust also, there is consequently a need for standardization of sampling procedures and methods. One method which has been used to evade the variability associated with sampling floor dust is to measure lead deposition in homes (Brunekreef et al. 1981,

1983, Aurand et al. 1983, Seifert et al. 1984). Sampling periods of one week to a few months have been used when this method was applied, thereby giving a somewhat more integrated picture than is obtained when spot samples of floor dust are taken.

For soil and dusts in general, it has not been clearly established which are the most relevant characteristics that one should measure for estimating exposure of children. All that can be said at present is that lead should be measured on surfaces which are accessible to children - but accessibility as such is not a clearly defined item either, as mentioned earlier. At best, the various measures of lead in soil and dust are crude approximations of actual lead intake, and this should be borne in mind when analysing the data from studies on the relationship between environmental lead and blood lead, as will be argued further in section 2.7.
The transfer of environmental lead into the food chain will be discussed in section 2.6.
An important aspect of studying environmental pathways for lead is the absence or presence of a steady-state situation.
The concentration of lead in air will quickly respond to changes of lead emissions into the air in the area under study, but this is not true for the concentration of lead in most other pathways. The concentration of lead in surface soil will slowly increase for years after emission has started - and may take years to decrease after emission has stopped as lead is persistent in most soils. Street dust is subject to removal in periods of rainfall and due to street cleaning; house dust is being moved by cleaning practices as well. Therefore, the concentration of lead in street and house dust probably responds quicker to emission changes, but here also, time lags of uncertain lengths are likely. It is thus of importance to obtain historical information on emission changes when studying a particular environment.

2.3. Exposure-dose relationships

The main modes of intake of lead from the environment by children are inhalation and ingestion.
Children inhale more air per kg bodyweight than adults (Knelson

1974). For persons in rest, the difference is about 2-fold for very young children (< 3 years); when children grow older, the difference gradually decreases. Between boys and girls, there is not much difference until they have reached puberty. From about 12-13 years of age, ventilation in boys is somewhat higher than in girls.

In addition to the higher inhalation rate per kg body weight at rest, children tend to be more active than adults. To an unknown extent, the real volume of inhaled air per kg body weight will thus be higher again. If the same proportion of inhaled lead is deposited in the lungs, and if the same proportion of the deposited lead is absorbed from the lungs in children as in adults, the uptake from air in the first 3-5 years of life is probably larger by a factor of at least 2. Depending on air lead concentrations, this may be important as part of total uptake.

The ingestion of soil and dust by children is extremely hard to quantify. It depends on the frequency with which hands and objects are mouthed, on the amount of dust removed from hands and objects by mouthing, and on the concentration of lead in the dust.

Mouthing frequencies of children have been observed, and may range from 2.4-6.4 times per hour (Lepow et al. 1974, Brunekreef et al. 1978). There are no observations of the amount of lead or dust on children's hands just before and after mouthing.

Mouthing is considered to be an aspect of normal child development (Charney 1982) and it is reported to occur at least until children are 5 or 6 years of age (Barltrop 1966, Vostal et al. 1974, Charney 1982).

Mouthing frequency appears to depend on a number of social factors like inadequate child care, quality of play environment, presence of siblings who "teach" each other the habit etc. (Green et al. 1976, Stark et al. 1978, 1982a, 1982b, Madden et al. 1980, O'Hara 1982, Hunt et al. 1982).

Pica (Latin for "Magpie") which is the tendency to actually chew and eat non-food items on a regular basis, usually in excessive amounts, is considered an abnormality (Barltrop 1966, Palmer and Ekvall 1978, Charney 1982).

The etiology of pica is not well understood; exaggerated mouthing behaviour, addiction, personality disturbances, emotional factors and nutritional status have all been mentioned as possible causes (Mooty et al. 1975, Palmer and Ekvall 1978). Due to the fact that

pica itself is inconsistently defined in the literature, it is also difficult to estimate its prevalence reliably. Barltrop (1966), for example, has estimated its prevalence as high as 48% for 1 year old children living in Boston. This figure was based on the results from a questionnaire sent to the parents of a random sample of all children living in Boston, and 'pica' was defined as placing non-food objects into the mouth rather than actually swallowing them, as the objects which were allegedly ingested included blankets, shoes and tooth brushes which one would not expect a young child to swallow with ease. It would seem that the prevalence of mouthing rather than pica has been estimated in this particular study.
The amount of lead on children's hands has been measured by several investigators. In table 2.1, the findings are listed and details about the circumstances of measurement are given. From the results it appears that in urban environments, up to about 20-30 µg of lead can be found on a child's hand during normal play. Near industrial sources, or in homes where the lead content of dust is high through paint or other causes, the levels can be much higher and may exceed 100 µg/hand.

Table 2.1. Lead on children's hands in a number of investigations

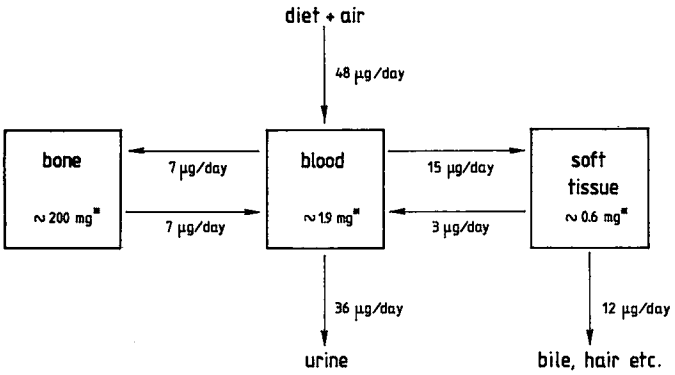
reference	lead on hands in µg/hand	remarks
Vostal	20	median in urban children (2-6 yr)
et al. 1974	5	median in suburban children (2-6 yr)
Roels	244-436	school-age children near smelter (10-14 yr)
et al. 1980	13- 20	urban children (10-14 yr)
Brunekreef	12	inner city children (4-6 yr)
et al. 1983		
(cf. chapter 4)	5	suburban children (4-6 yr)
Charney	49	children with PbB 40-70 µg/100 ml (1-6 yr)
et al. 1980	21	children with PbB ≤ 29 µg/100 ml (1-6 yr)

The amount of dust which may stick to a child's hand has been determined experimentally by Duggan and Williams (1977). It appears that 2 mg of dust may easily stick to each finger of a moisty hand of a child. No information is available about the average amount of lead and/or dust present on a child's hand during the day, as the data, mentioned in table 2.1, essentially are based on spot samples of unknown representativity.
At present, only rough estimates are possible about the amount of lead which can be ingested by mouthing children. If 10 mg of dust with a lead content of 300 mg/kg is ingested daily, this would contribute 3 µg to daily intake. If, however, 100 mg of dust with a lead content of 1000 mg/kg is ingested daily, the contribution would be 100 µg. In other words, the contribution may be small or large compared to the food contribution which will be discussed later (section 2.6).
The available data on mouthing frequency, hand lead levels and hand dust levels suggest that ingestion of soil and dust particles may be an important pathway of environmental lead to children. To assess its importance, we have to rely on indirect evidence; this evidence consists of associations between blood lead and soil, dust or hand lead, which will be discussed in chapter 3.
Most probably, the between-person variability of the factors which influence the ingestion of soil and dust particles is large; at a certain level of environmental pollution, some children may ingest much larger amounts of lead than others. Although several of these factors are hard to quantify, an attempt should be made to incorporate them into the design of studies on lead intake from the environment by children.

2.4. The concentration of lead in blood as dependent variable

The concentration of lead in blood (PbB) is widely regarded to be the most relevant indicator of biologically active lead in the human body (Zielhuis 1974, 1975, Zielhuis and Wibowo 1978, WHO 1977a, National Research Council 1980, Ratcliffe 1981).
In adults, PbB half life has been estimated to be about 20 days in studies of an experimental nature (Rabinowitz et al. 1973, 1974, 1976, 1977, Chamberlain et al. 1975, 1978, Gross 1981).

After continuous, heavy exposure, however, the half life seems to be prolonged due to the slow release of lead from bone into blood (Hammond 1982, O'Flaherty et al. 1982, Kang et al. 1983).
A three-compartment model for the metabolic behaviour of lead in the adult human body has been proposed by Rabinowitz et al. (1976). The model is shown in figure 2.1.



* total amount of lead in compartment

Figure 2.1. Three-compartment model for metabolic behaviour of lead in the adult human body according to Rabinowitz et al. (1976)

The model was derived from an experiment in which subjects ingested 300-360 µg of lead daily.
In adults, who are in steady state, more than 90% of the total body burden of lead is in the skeleton where it has an extremely long half life of approximately 20 years. In children, the concentration of lead in the skeleton is much lower than in adults (Barry 1981). There are no direct data on the blood lead half life in children. David et al.(1982) measured blood lead in 29 children aged 4.3-11.6 years, on 4 occasions spaced one month apart to evaluate the stability of the blood lead concentration. The differences in the average blood lead concentrations were generally insignificant, and the correlations between measure-

ments were from .72 to .81, indicating a reasonable stability of blood lead over time in these children. The average blood lead concentration in these children was 25 µg/100 ml, which indicates that the daily intake of lead was rather high.
A recent study by Rabinowitz et al. (1984a) on blood lead concentrations of children aged less than two years showed that at this age, the correlation between serial blood lead determinations was low (less than .5). Only the correlation between blood lead levels determined at 1.5 years, and 2.0 years of age was higher at .61, although this is still lower than David's findings. The blood lead levels of the children in this study were generally below 10 µg/100 ml and this may mean that the relative error in the blood lead determinations was larger than in David's study. Comparison of the results of these two studies suggests that at very young ages and/or at low levels of exposure, the measured concentration of lead in children's blood is more variable than at higher ages and/or higher levels of exposure. More specific data are necessary before conclusions can be reached concerning the use of single blood lead determinations as an index of internal exposure in studies on very young child populations.

It is important to express the short-term, within-subjects variability of blood lead as a percentage of total variability, as Lucas (1981) has pointed out.
If within-subjects variability is large compared to total variability, there is not much between-subjects variability left which could be explained by differences in lead exposure.
Using data from four studies performed between 1965 and 1975 Lucas (1981) has asserted that within-subjects variability is usually more than 50 percent of total variability of blood lead, and that this more or less invalidates the use of blood lead as a health effect indicator of internal exposure in environmental exposure or health effect studies. Angle and McIntire (1979) reported that in their study, more than 60% of observed blood lead variability was true, between-subjects variability; this study was performed in the years 1971-1977.
The correlation coefficients reported by David et al. (1982) can be used to estimate the proportion of total variability which is taken up by between-subjects variability (cf. section 2.7). This is consequently 72 to 81 percent. A recent study by Delves et al. (1984) has shown that PbB values in adults who were only exposed

to environmental lead, were very stable over a period of 7 - 11 months. In men who had an average PbB value of 12.2 µg/100 ml, the within-subjects variance of about .3 was small relative to a total variance of 5.0, and even in women who had an average PbB value of 8.5 µg/100 ml and a total variance of only 1.5, the within-subjects variance of about .3 was small. The most recent study used by Lucas was the Southern California Study performed in 1974 by Johnson et al. (1975). In this study, a second blood sample was taken from the same subjects one week after the first sample. In 1976, the same investigators studied a population living in Dallas using the same protocol, and in this study, the within-subjects variance of the blood lead concentrations was much smaller than in the first, leading the investigators themselves to doubt the quality of their own blood lead analyses in the first study (Johnson et al. 1978). It would seem that the recent studies just cited prove the blood lead concentration to be a much more usable variable than Lucas (1981) suggested.

Part of the within-subjects variability of blood lead is associated with the error of sampling and analysis. As the concentration of lead in blood is low, care should be taken to obtain uncontaminated samples; venous blood samples generally offer better opportunities for avoiding contamination than capillary samples (Angle and McIntire 1979, Johnson et al. 1978, Mahaffey et al. 1979). The chemical analysis of the samples requires skill and experience; participation in some blind inter-laboratory control program is necessary to maintain a high standard of performance (Maher et al. 1979, Hunter 1980, Vahter 1982, Berlin 1982, Colinet 1983, Zwennis 1984). In recent years, much effort has been devoted to improvement of the quality of sampling and analysis of blood lead, and within the same laboratory, the relative standard deviation (coefficient of variation) of sampling and analysis may be below 10% (Saltzman et al. 1983).

Compared to the effort devoted to improving sampling and analysis practices (which, in itself, is completely justified), surprisingly little work has been done to define total, within-subjects variability of blood lead concentrations over a given period of time. As will be argued more fully in section 2.7, it is the ratio between within-subjects variability over time and between-subjects variability, and not the analytical error alone, which determines the usefulness of PbB as an indicator of internal exposure in environmental exposure and health effect studies.

Few studies have attempted to establish a quantitative relationship between lead intake and blood lead in children. Ryu et al. (1983) studied the relationship between dietary lead intake and blood lead in 29 children of 0-6 months of age. Judged from the average blood lead level of the mothers of the study children, which was 9.6 µg/100 ml, prenatal exposure had been low. Dietary lead intake was established by measuring lead in human milk for 4 breast fed infants, and by supplying infant formula of a known and repeatedly checked lead content to the parents of the remaining 25 children for a period of 4 months after birth. On average, dietary lead intake was only 17 µg/day. After 4 months, the average blood lead level was 6.1 µg/100 ml. For another period of 2 months, 17 children remained in the study, 10 of which were kept at a dietary lead intake of 16 µg/day. Their blood lead level was 7.2 µg/100 ml at the end of the study period. The remaining 7 children received canned infant formula and/or milk in this period, and their average dietary lead intake was 61 µg/day. At the end of the study period, their blood lead level had increased to 14.4 µg/100 ml. These data suggest a distinct curvilinearity of the PbB/lead intake relationship, as a fourfold increase in intake only doubled the resulting PbB level. In a study performed in Scotland, bottle-fed infants were shown to have an average blood lead level of 14 µg/100 ml at a dietary intake of only about 10 µg/day. The average blood lead level was 23 µg/100 ml at intakes of 50-70 µg/day, and 30 µg/100 ml at an intake of 160 µg/day (Dept. of the Environment 1982). At comparable levels of lead intake, the PbB levels in the Scottish study were higher than in the study by Ryu et al. (1983). There is no ready explanation for this difference.

2.5. Factors other than lead intake which affect the concentration of lead in blood

It has already been argued that lead absorption from the gut is higher in children than in adults, but that the concentration of lead in blood is not necessarily higher in children than in adults indicating that the excretion of lead and/or the transfer to bone are also higher in children than in adults.
There is a number of factors which potentially affect the concen-

tration of lead in blood in children at a given lead intake.
Absorption, excretion and distribution patterns vary with age, which makes age a prime selection variable in studies concerning environmental lead and blood lead in children.
Various nutritional factors have been implicated as determinants of PbB. The intake of calcium and phosphorus are inversely related to PbB and/or to lead uptake from the gut (Barton et al. 1978, Heard et al. 1982, 1983, Blake et al. 1983a, 1983b); a high intake of fat seems to cause a higher absorption of lead from the gut (Barltrop and Khoo 1976, Bell and Spickett 1983); milk consumption was shown to be inversely related to PbB in two observational studies (Johnson and Tenuta 1979, Brunekreef et al. 1983) and in one human experiment (Blake et al. 1983a). This probably indicates the importance of milk(products) in the diet as a source of calcium. In animal experiments the milk component lactose has been shown to actually enhance lead uptake from the gut, when lead and milk are consumed together (Bell and Spickett 1981, Bushnell and De Luca 1981). The experiments by Bushnell and Deluca (1981) were done, however, at unrealistic levels of lactose consumption, and recent data suggest that at normal levels of intake, lactose does not increase lead uptake from the gut (Bushnell and De Luca 1983).
A study by Kostial and Kello (1979) has suggested that the retention of lead administered in the stomach by tube is greater in rats fed cow's milk than in rats fed 'solid' human diets. This may be due to the greater absorption of lead administered in fluids than with solid food (cf. below). As mentioned earlier, milk consumption has been shown to decrease lead retention in a human experiment (Blake et al. 1983a).
Iron and zinc deficiency have also been associated with increased lead absorption from the gut (Watson et al. 1980).
In the US, 65% of all 2-3 yr old children were reported to receive less than the recommended dietary allowance (RDA) of calcium, and 98% were reported to receive less than the RDA for iron (McCabe 1979, Babich and Davis 1981). It is not clear, however, whether all of these children were "deficient" to an extent that the absorption and/or toxicity of ingested lead is being enhanced.
Recent evidence suggests that lead compounds, ingested in water by fasting individuals are absorbed much more efficiently than when taken with solid food (Rabinowitz et al. 1980, Heard et al.

1983). After fasting for 12 hours, about 50% of lead, ingested in water, was absorbed. When taken with a meal, absorption was only 3-7%. Other studies (Blake 1976, Moore et al. 1979c) suggest that even after 2 hours of fasting, absorption is still about 4 times greater than when lead is ingested with a meal. The important tentative implication of this is that lead consumed with drinking water and dust is more important than equal amounts of lead consumed with solid food - if these results are valid for children as well, and in so far as drinking water and dust are ingested in between meals.

There does not seem to be a large influence of the chemical form in which (inorganic) lead is administered on the uptake from the gut (Karhausen 1972, Barltrop and Meek 1975, Mahaffey 1983); the size of the lead particles seems to be more relevant (Barltrop and Meek 1979), with the small particles being more effectively absorbed than the large ones. This is particularly of relevance for the exposure to paint lead, as it implies that ingested paint flakes do not contribute as heavily to intestinal absorption as their lead content would suggest.

Seasonal variation of children's blood lead is sometimes observed, and it has been suggested that exposure to sunlight is its main cause (Hunter 1977). One proposed mechanism is that in summer vitamin D is synthesized in the body, and that vitamin D increases the absorption of lead from the gut. It has, however, been demonstrated that the active vitamin D metabolite in this respect is 1,25 dihydroxycholecalciferol, which has no seasonal variation, and that the metabolite 25 hydroxycholecalciferol, which does show seasonal variation, does not affect lead metabolism (Rosen et al. 1980, Chesney et al. 1981, Mahaffey et al. 1982b). Other explanations for seasonal variations of blood lead have been proposed, like increased exposure to pollution during outdoor play or through seasonal variations in gasoline lead consumption (Einbrodt et al. 1975, Billick et al. 1980). In some studies, seasonal variation of blood lead was absent (McCusker 1979).

It is not easy to decide which meaningful variables should be - and could be - incorporated in the design of studies on blood lead/environmental lead relationships. Age in itself is important, and age is also related to many of the factors mentioned in this section. Selection of a specific age category, or incorporation of the age variable in the analysis of the data seems a

necessity in any study. Some consideration of nutritional factors would further be useful. In addition, it would be better to conduct studies within a short period of time, to avoid seasonality effects on the outcome of the study.

2.6. Identification of confounding factors

A confounder is a determinant of the dependent variable under study - but not the determinant that one would like to investigate primarily - which is related to the determinant of interest to an extent that adjustment for it reduces or eliminates bias when estimating the 'true' relationship between the dependent variable and the determinant of interest (Breslow and Day 1978, Kleinbaum et al. 1982).
As potential confounders, all factors which in earlier investigations were shown to bias the estimate of the 'true' relationship between the determinant and the dependent variable of interest need to be identified. What is a confounder and what is the determinant of interest in a specific study depends largely on the hypotheses one would like to test. If one would like to investigate the influence of air lead on blood lead, tapwater lead and food lead are (potential) confounders, whereas air lead would be a (potential) confounder in a study on the relationship between dietary lead intake and blood lead. If one would like to evaluate the impact of traffic emissions on blood lead, all lead in the environment which does not originate from traffic is a (potential) confounder of the traffic lead - blood lead relationship, and attempts should be made to design and/or analyse the study so that the effects of traffic lead and lead from other sources can be separated.
Theoretically, all sources and pathways, mentioned in figure 1.3 should be considered in the design phase of a study either as determinant, potential confounder or selection variable (by this we mean that studies can be restricted to areas where one or more sources are uninfluential). The various environmental sources and pathways have already been described in sections 2.2. and 2.3. Food lead, tap water lead and other factors will be treated here.

Presence and origin of lead in food

Lead in food is a potential confounder of associations between environmental lead and blood lead in a limited sense only. As will be discussed later, some lead in food originates from environmental pollution. In industrialized countries, however, the food that people consume is usually not grown at or near the places where people live and where people may be exposed to environmental pollution. It is consequently defendable to assume that associations between food lead and environmental lead are non-causal if these are found to exist in an urban study area.

As mentioned in section 1.2, a child is born with a blood lead level somewhat lower than its mother's. After birth, breast milk, bottled milk and children's formulae are the main sources of lead in the first months of life.

A recent review on chemical contaminants in human milk suggests that the concentration of lead in breast milk is mostly in the range of 5-20 µg/l in women living in industrialized countries (Jensen 1983). A more recent study in a British urban population has shown that at maternal PbB levels of about 10 µg/100 ml, the lead content of breast milk was only 2 µg/liter (Kovar et al. 1984) and in a study among urban and rural women living in Arizona, US, it was only 3 µg/liter (Rockway et al. 1984).

Recent data on lead intake through food by young children are compiled in table 2.2. Most estimates are based on market basket studies, i.e. studies in which the lead content of individual food items of a representative diet is being measured. There are some indications that market basket studies tend to over-estimate 'real' lead intake, as estimated by duplicate diet studies. In a study in the UK, Sherlock et al. (1983) estimated the dietary lead intake of adults in the area under study at 770 µg/week, whereas a duplicate diet study in the same area resulted in an estimated lead intake of 500 µg/week (a duplicate diet study is a study in which during some period of time, duplicate meals are sampled in which the amount of lead is being measured).

A recent market basket study from Belgium even estimated total daily lead intake for adults to be 282 µg/day (Fouassin and Fondu 1981) whereas a duplicate diet study, performed at the same time, resulted in an estimated daily lead intake of 96 µg (Buchet et al. 1981, 1983).

In The Netherlands, one market basket study performed in 1974-1975 resulted in an estimated daily lead intake for adults of 135

µg (Ellen 1977). In a later publication containing data on the period 1974-1978, this figure was reduced to 92 µg/day. Both estimates did not take lead intake with drinking water into account. A duplicate meal study was performed in the years 1976-1978, and resulted in an average intake of 107 µg/day, including drinking water (Anonymus 1980b).

The data in table 2.2 range from a very low intake of only a few µg per day for breast-fed infants to somewhat over 100 µg/day for children of ages well into their teens from the FRG. The other 11 studies all indicate daily lead intakes of about 20-80 µg/day.

At present, it is not difficult to find child populations in industrial countries with an average blood lead level below 10 µg/100 ml (Taskinen et al. 1981, Rabinowitz and Needleman 1984; cf. also results for control population in chapter 4). Although this is a matter of speculation in view of the limited available evidence, the data from the studies by Ryu et al. (1983) and by the (UK) Department of the Environment (1982) suggest that in these populations, dietary lead intake may even be well below 50 µg/day.

Whether lead in food is an actual confounder in studies on the relationship between environmental lead and blood lead in children depends on its association with environmental lead. To the author's knowledge, no study has ever systematically compared the lead contents of diets consumed in urban and suburban areas. In The Netherlands, food consumption patterns have been compared for different categories of workers' families (Centraal Bureau voor de Statistiek 1979). In the years 1974/1975, workers' families tended to buy more food per person in the major lead containing food groups when their level of income was higher. According to Anonymus (1980b), almost 80% of total dietary lead intake in The Netherlands came from bread, cereals, potatoes, vegetables, fruits, wine and spirits, meat, milk and milk products.

When it is assumed that wine and spirits are not consumed by preschool children, the differences in the amounts of lead, bought with food per person, would amount to 10 percent at most between income strata of workers' families, with the higher amounts of lead bought in the higher income categories.

In a more recent survey, differences between food consumption patterns in areas with different levels of urbanization have been investigated (Centraal Bureau voor de Statistiek 1982, 1984) but the results published so far do not permit evaluation of food

consumption patterns per person for different areas.
On the basis of the above-mentioned, limited data, it is not considered likely that differences in food consumption patterns would explain differences in PbB levels in children living in urban and suburban areas in The Netherlands. There is not much doubt that food lead is an important determinant of blood lead, and for this reason, we felt that it needed to be discussed in some detail in the framework of this report, even though it is not clear whether it is an actual confounder.

Table 2.2. Daily lead intake with food by young children

Reference	Daily dietary lead intake (µg/day)	Remarks
Bander et al. 1983	49 ± 38	children less than 1 year old, US, ± S.D.
	55 ± 21	1-2 years old
	56 ± 22	2-3 years old
	65 ± 24	3-4 years old
	65 ± 29	4-5 years old
	74 ± 33	5 years old
		market basket study
Biddle 1982	21 - 36	infants, US, 1975-1980
	28 - 46	toddlers, US 1975-1980
		market basket studies
Boppel 1975	45	infant formulae, FRG
Department of the Environment 1982	10 - 160	bottle fed infants, intake depends on water lead concentration in area under study Glasgow, UK
Haschke and Steffan 1981	50 - 80	Children 1-6 months of age, Austria

Table 2.2. (continued)

Reference	Daily dietary lead intake (µg/day)	Remarks
Johnson et al. 1981, 1984	20 - 30	infants and toddlers, US market basket studies, 1975-1977
Kirkpatrick et al. 1980	17 - 81	children of < 1 yr market basket study, Canada
Larsson et al. 1981 Kovar et al. 1984	2 - 3	on the basis of lead in breastmilk (± 2 µg/kg) in Sweden and U.K.
Reith et al. 1974	42	1-4 year olds, Netherlands market basket study
Stolley et al. 1981	95 - 142	children of 2-14 years old, FRG market basket study
Woidich and Pfannhauser 1980	6 - 80	infants and toddlers, FRG
Ryu et al. 1983	16 - 17	infants less than one year of age, USA infant formulae and cow's milk
	61	canned formulae and canned milk

The origins of lead in food have not been quantified in detail. Chamberlain (1983b) has argued that on the basis of ^{210}Pb/stable Pb ratios of outdoor lead deposition and human diets, probably

only 13 µg of lead per day in an adult, human diet in the UK comes from vehicular traffic. For children, this would then probably amount to no more than 7 µg/day, and the relative contribution of traffic lead to dietary lead for children would then come to depend on how much lead a child actually ingests with food. As will be discussed in section 3.7, a study from Italy has recently suggested that at least 46% of the lead in children's blood originates from automobile traffic.

Human populations living in remote, non-industrial areas have been shown to have average blood lead levels between 1 and 5 µg/100 ml, although in one study the PbB value was much higher. Hecker et al. (1974) studied a number of Yanomamö Indians living in the area drained by the Upper Orinoco River and its tributuaries in southern Venezuela. Their average blood lead concentration was only 0.83 µg/100 ml, and significantly lower than the average blood lead concentration (14.6 µg/100 ml) of a control population living in the US which was studied with the same methods of sampling and analysis.

Poole et al. (1980) studied a population of 7-10 yr old children living in the remote Eastern Highlands Province of Papua New Guinea; the children's diet contained small quantities of canned food, and their average blood lead concentration was 5.2 µg/100 ml.

Piomelli et al. (1980) studied a population of children and adults living in the remote Manang district of Nepal and found a mean blood lead concentration of 3.4 µg/100 ml without apparent differences between children and adults.

Hansen et al. (1983) studied a population living in the isolated district of Angmagssalik in East Greenland; males were found to have an average PbB value of 14.8 µg/100 ml, and females an average of 12.8 µg/100 ml. For Danes living in the Århus (urban) area, values of 10.5 and 7.7 µg/100 ml were found, using the same methods. There was no explanation for this unexpected finding.

For at least some remote populations, PbB values were so low that it is most probable that their food contained much less lead than the food of people living in industrialized countries.

Other sources than vehicular traffic contribute to lead in food, notably lead soldered cans (Crowell 1980, Schaffner 1981, Ludwigsen 1982, Moore 1984). These, however, are now being replaced by cans which do not contribute lead to the food so much in most countries. It is unclear to what extent other industrial food

preparation processes contribute to lead in food. Scattered references indicate that the contribution is negligible from mechanical deboning of meat (Forschner and Wolff 1981) and other industrial meat handling processes (Hecht et al. 1981) and that some processes may even decrease the lead content of food (Bielig and Hofsommer 1980). In urban areas, food may become polluted with lead during transport, handling, storage and display (Beaud et al. 1982), or during preparation (Gallacher et al. 1984c) and cooking (Moore et al. 1979b, Little et al. 1981, Smart et al. 1981, 1983, Haring 1984) when the cooking water contains lead; if the lead concentration of cooking water is not elevated, cooking does not change the lead content of food (Schelenz and Boppel 1982) or may even decrease the lead content if soft water is being used (Haring 1984) (soft water contains less than 3 milliequivalents of cations per liter).
All of this means that the proportion of lead in the diet originating from traffic will vary from situation to situation, and that it is probably naive to try to attribute any precise number to this proportion, as Moore (1983) has aptly pointed out.

Lead in tap water
If lead is present in a water supply system, the concentration of lead in tap water may be greatly elevated (Beattie et al. 1972, Goldberg 1974, Elwood et al. 1976, 1984, Moore (et al.) 1977, 1978, 1979, 1981, 1982, 1983, Pocock 1980, Pocock et al. 1983, Haring 1978, 1984, Thomas (et al.) 1979, 1980, 1981, Sartor et al. 1980, 1981a, 1981b, 1983, Sharrett et al. 1982a, 1982b, McIntosh et al. 1982).
Studies from Belgium and the UK especially, have shown that in some areas, blood lead levels in adults as well as children may rise well above accepted standards due to a high tap water lead concentration (Sartor et al. studies, Moore et al. studies).
The plumbosolvency of drinking water has been shown to depend largely on pH (Moore 1973, 1983, Haring 1983, 1984), so that in areas where pH is low, much lead is being dissolved from pipes and storage tanks. Alterations of pH by adding lime have been shown to greatly reduce the lead content of tap water even if lead pipes are not being replaced and it has been shown that these alterations produced marked reductions in blood lead levels as well (Moore 1983).
It has been suggested that the reduction in blood lead levels was

partly caused by the increased Ca-intake with the water, and that this has led to some over-estimation of the contribution of water lead to total lead intake (Bryce Smith and Stephens 1981, Elwood and Gallacher 1984). In the Glasgow study, lime was increased to a concentration of about 5 mg/liter. At a normal Ca-intake of about 500-800 mg/day, this would, however, not seem to make a significant contribution to total Ca-intake (Mahaffey 1974, Wijn en Van Staveren 1980, Koivistonen 1980). In The Netherlands, the Ca-content of drinking water was shown to range from 20-117 mg/l in a survey conducted in 19 different communities (Haring 1984). In Glasgow, however, the Ca-content of drinking water was originally only 0.33 mg/l (Moore 1973). It is interesting that in The Netherlands, a negative correlation between calcium and pH in drinking water has been observed, and a positive correlation between lead and calcium, which is opposite to the situation in Glasgow (Haring 1984). Reduction of tap water lead therefore requires other measures than lime addition in The Netherlands.
The higher absorption rate of lead administered with water, compared to lead administered with food makes tap water lead a potentially much more important contributor to total lead uptake, even at relatively low levels of water lead, than seems to have been realized; Elwood (1984) has remarked that the omission of water lead from epidemiological studies on blood lead/environmental lead relationships in children raises serious questions about the validity of the resulting equations.

Other potential confounders

Alcohol consumption and tobacco smoking have been shown to be related to blood lead levels of adults (Wibowo et al. 1977, Ducoffre et al. 1980, Grandjean et al. 1981, Awad et al. 1981, Shaper et al. 1982, Pocock et al. 1983, Bortoli et al. 1983, Brockhaus et al. 1983, Perelli et al. 1984).
Both habits are not generally present in young children, however, and the fact that the smoking effect on adult blood lead levels has been small in the majority of studies suggests that "passive smoking" by children is not an important pathway.
Objects like glazed pottery (Acra et al. 1981), printed matter (Bogden et al. 1975, Eaton et al. 1975), household articles in general (Horiguchi et al. 1982), electric kettles (Wigle and Charlebois 1978), toothpaste (Berman and McKiel 1972) and cosmetics (Anonymus 1979) have been mentioned as potential sources of

lead for children. Do-it-yourself enthousiasts have been warned that, for example, improper removing of old paint layers in old homes may cause elevated air lead and dust lead concentrations (Inskip and Atterbury 1983). On average, these factors do not usually seem to have a detectable influence on population blood lead levels, however.

In the US, children of a different race have repeatedly been shown to have different blood lead levels (Billick et al. 1979, 1980, Quah et al. 1982, Stark et al. 1982a, Mahaffey et al. 1982a, Annest 1983). As race, socio-economic status and living conditions in general are related, it is not clear whether these PbB differences are caused by innate factors or mostly by external factors. In the UK as well, higher blood lead levels have been reported in children of Asian origin, compared to Caucasian children (Josephs 1977, Archer et al. 1980, Strehlow and Barltrop 1982). It has been suggested that the use of surma, a lead-containing cosmetic, by Asian women may contribute to this (Josephs 1977) but dietary factors may be more important (Strehlow and Barltrop 1982).

Shortly after birth, children of different gender generally do not have different PbB levels (cf. for example Rabinowitz and Needleman 1984), but when children grow older, boys and girls may have different blood lead levels. Age is related to a number of factors which influence blood lead levels, and as a consequence, PbB levels exhibit a peak at ages of about 3-6 yrs in some populations, but not in others (Duggan 1983a).

Several factors which tend to increase the blood lead concentration at a given exposure level like mouthing, Ca-deficiency, inadequate child care etc. may very well be more prevalent in areas where lead pollution is also more severe, as people of low socio-economic status will have less opportunity to move away from polluted living areas near industrial lead sources or in inner cities with high traffic densities.

The impact of a given amount of lead in the environment on children's blood lead may consequently be larger in inner cities than in suburbs.

2.7. Mathematical issues

2.7.1. Curvilinearity of the relationship between environmental lead and blood lead

For children as well as adults, the relationship between blood lead and environmental lead has repeatedly been shown to be curvilinear in the sense that ΔPbB/Δexposure is smaller at high levels of PbB than at low levels of PbB (Hammond et al. 1981, Laxen 1983, Chamberlain 1983a, cf. figure 2.2). The mechanisms behind this are not fully understood, and could include reduced absorption from the gut, altered distribution within the body and increased excretion (Hammond et al. 1981).
It has been suggested that the departure from linearity is not great at low levels of PbB (Chamberlain 1983a) but the recent results of the study by Ryu et al. (1983) seem to contradict this, as discussed in section 2.4. The curvilinearity of the relationship can be taken into account by relating log PbB to log (exposure), or by relating PbB to some exponential of the exposure variables (Moore et al. 1982).
If downward curvilinearity is present in the data, a log/log relationship results in which the regression coefficient of log PbB on log (exposure variable) is less than one.

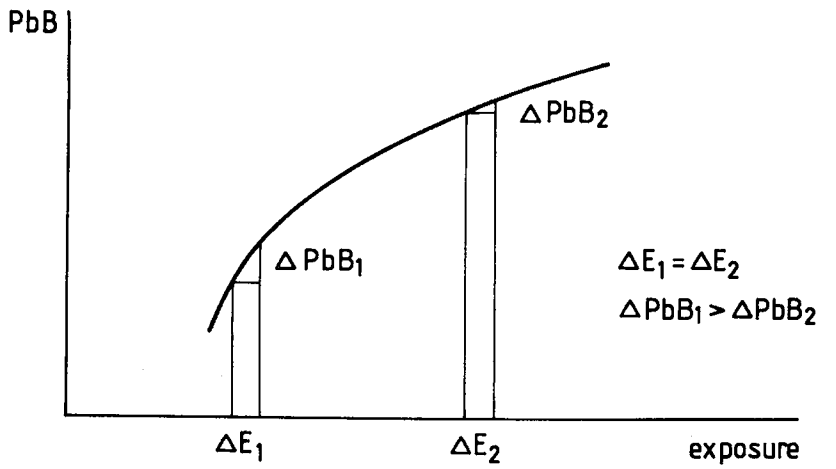


Figure 2.2. Curvilinear dependence of blood lead on lead exposure.

A straight line relationship results in a log/log relationship with a regression coefficient of exactly one, and a curvilinear upward relationship results in a regression coefficient > 1. The general consequence of the downward curvilinearity is that ΔPbB/Δexposure relationships obtained at different levels of PbB cannot be directly compared; one may expect a stronger effect of a given exposure change at low levels of PbB than at high levels of PbB.

2.7.2. The causal structure of the exposure-response system

From the preceding sections it is clear that many variables potentially influence the concentration of lead in blood, and that many of these are interrelated. In the analysis of the data, the presumed causal ordering of the variables must be carefully taken into account. If, for example, in old homes more lead piping is present than in new ones, the age of the home and the concentration of lead in tap water will be related. If both are evaluated together as determinants of blood lead, one may find that water lead becomes insignificant after adjustment for home age. This is an artifact, as it does not mean that water lead has no influence; it is merely represented already by home age. Usually, some environmental exposure variables will also be correlated with each other. Sometimes, several exposure variables are entered into an equation as explanatory variables together (Angle and McIntire 1979, Snee 1982b, EPA 1983). This is justifiable as an attempt to separate their respective effects on blood lead, but the partial regression coefficients obtained do not adequately describe what will happen to the blood lead concentration when the input of lead into the system is changed. If, for example, air lead changes due to e.g. a reduction of petrol lead, in the long run dust lead will be reduced as well. The partial regression coefficients of blood lead on air lead cannot be used to predict the effect on blood lead of such a petrol lead reduction without evaluating also the pathway through dust. The partial ΔPbB/ΔPbA under-estimates, in other words, the ΔPbB/Δpetrol lead relationship. It is therefore questionable to use partial ΔPbB/ΔPbA relationships for setting air lead standards (as, for example, was done in the US, cf. EPA 1978), as such a

procedure tacitly assumes that air lead can be manipulated without affecting lead in other environmental pathways.
It should be emphasized that evaluating the structure of the exposure response system is a largely non-statistical issue which requires detailed knowledge of the specific research area. In chapter 4, an attempt will be made to separate determinants of environmental lead, which should not be used as adjustment variables for the ΔPbB/Δexposure relationship, from 'true' confounders. The different environmental lead exposure variables will also be evaluated one at a time, to avoid over-adjustment of the ΔPbB/Δexposure relationship.

2.7.3. Variability of exposure and outcome variables

It is well known from regression theory that the results of regression analyses are affected by random errors in both the exposure and the outcome variables (Snedecor and Cochran 1967, Cochran 1968, Draper and Smith 1981). Generally, random errors in the outcome variable reduce the correlation coefficient, but not the regression coefficient of the outcome variable on some predictor. In other words, an association which is significant in reality may go undetected, but the size of the regression coefficient is still an unbiased though unstable estimate of the size of the effect.
Random errors in an explanatory variable do not only decrease the correlation coefficient, but bias the regression coefficient toward zero as well (Cochran 1968, Draper and Smith 1981).
It is therefore of interest to reduce as much as possible random errors in both the outcome and the explanatory variables.
An interesting observation at this point is that in the past, considerable effort has been devoted especially to reducing the error of the blood lead determination - but that this error has been rather narrowly defined as the error associated with sampling and analysis.
Likewise, in lead exposure studies the error analysed and reported (if at all) is usually the error associated with sampling and analysis.
A typical exposure-response study may thus consist (for each subject) of a single blood lead determination, an air lead study

of some duration and single or duplicate samples of soil, dust, drinking water etc. taken on one occasion only. Still one assumes that the obtained values are representative for periods of one to a few months, as the outcome variable, blood lead, is usually taken to represent recent exposure in terms of one to a few months (cf. section 2.4).

It would therefore be more useful to define the "random error" of the outcome and the explanatory variables as the within-person variability over some period of time. In order to obtain an estimate of this type of error in the exposure variables, it is necessary to repeat the exposure measurements for at least a number of individuals, at least once in space, or in time, or in both. The type of exposure information which is required determines which is the best way to repeat the measurements. If, for example, variations in time are of less interest because some time-integrated measurement like long-term outdoor deposition has been performed, it is most useful to perform the measurements in the locations most frequently visited by the study subjects. For outdoor deposition, the measurements might then be performed in a few locations near the homes of the study subjects. An analysis of variance can be performed then, to estimate the within-subjects and between-subjects variance of the exposure indicator under study (Snedecor and Cochran 1967). The correlation coefficient between repeated measurements (cf. correlations between serial blood lead levels in children in papers by David et al. 1982 and Rabinowitz et al. 1984a) can also be used to estimate the between-subjects variance relative to total variance (Cochran 1968). In section 2.4 it has already been shown that the available, limited evidence suggests that this type of error may very well be 20-40% of total blood lead variance.

Although some information on variability of environmental lead exposure variables over space and time has recently become available, systematic evaluation of within- and between-person variability of lead exposure variables in epidemiological studies has not been performed to date.

This is unfortunate as regression coefficients from environmental exposure-response studies are currently being used as basic information for the derivation of air lead standards (EPA 1978, 1983), and it would not seem in the interest of public health to use systematic under-estimates of the 'true' blood lead/environmental lead relationship.

In Appendix 1, a brief mathematical treatment is given of this type of error, and the required analysis to estimate it.

3. LITERATURE REVIEW OF STUDIES ON RELATIONSHIPS BETWEEN ENVIRONMENTAL LEAD AND BLOOD LEAD IN CHILDREN

3.1. Introductory remarks

In this chapter published studies will be reviewed which permit an estimate of relationships between environmental lead and blood lead in children. The preceding chapter suggests a number of criteria which can be used to evaluate these studies:

a. the variables used for classifying exposure (section 2.2). Which pathways were investigated, was exposure measured on an individual basis or for groups only etc.;
b. the variables used for assessing the exposure-dose relationship (section 2.3); was mouthing taken into account etc;
c. method of blood sampling, presence of information on quality control, frequency of blood sampling (section 2.4);
d. assessment of dietary and other non-exposure factors affecting the concentration of lead in blood (section 2.5);
e. investigation of lead intake through food and water; investigation of other potential confounders of the relationship between environmental lead and blood lead (section 2.6);
f. statistical analysis of study results (section 2.7).

Three different categories of studies will be reviewed:

- studies performed near industrial sources of lead pollution (section 3.2);
- studies performed in urban areas where lead pollution is mainly caused by vehicular traffic (section 3.3);
- other studies, predominantly studies on relationships between lead in soil and dust and lead in blood, performed in areas where the lead in soil and dust originates from mining, paint etc. and not from air (section 3.4).

In section 2.7, it has been argued that the relationship between environmental lead and blood lead is curvilinear in the sense that a given exposure increment results in a larger increase of the blood lead concentration at low levels of exposure than at high levels of exposure. In principle, we would therefore like to compare curves rather than linear relationships. From most studies, curvilinear relationships could not be calculated, however, and it was decided to express the relationship between environ-

mental lead and blood lead on a linear scale.
The consequence of this is that results from studies performed at widely differing levels of exposure cannot be readily compared. Where appropriate, the reader will be reminded of this when study results are likely to have been heavily influenced by unusually high or low overall exposure conditions. The relationship between environmental lead and blood lead will be expressed as α when the concentration of lead in air is the prime indicator of environmental lead pollution; α will be expressed as µg per 100 ml (PbB) per µg per m^3 (lead in air, PbA). If lead in dust or soil is the prime lead exposure indicator, the relationship between blood lead and environmental lead will be expressed as β. Usually, β will be expressed as µg per 100 ml (PbB) per gram per kg (lead in soil, dust), although occasionally the mg per m^2 unit will be used for lead in dust. The units were chosen such that the α- as well as the β-values would mostly fall in the 1 - 10 range.

3.2. Studies performed near industrial lead sources

1. Cavalleri et al. (1981) studied 110 children 3-6 years old and 143 children of 8-11 living near a lead smelter (exposed population) or more than 4 km away (control population). The smelter underwent emission reduction prior to the study, and as a consequence air lead levels may have been relatively low compared to soil and dust lead levels. Air lead was measured close to the smelter (150-300 m) and in the control area. The average values were 2.9 and .6 µg/m^3 respectively (method of sampling not given).
   Venous blood was sampled once, and was found to contain 15.9 and 16.1 µg Pb/100 ml (geometric mean for exposed children) and 8.2 and 7.0 µg Pb/100 ml (geometric mean for control children) respectively. To calculate the geometric mean, the mean of the log-transformed data is determined, which is then transformed back into natural units again.
   The α-values calculated from these data are consequently 3.3 for 3-6 year olds and 4.0 for 8-11 year olds.
   No information was given on lead levels in dust and soil. Paint, food and tap water were not investigated as other potential sources of lead intake. According to the published

study results, the quality of the blood lead analyses was checked and found to be adequate. No data on potential confounders were reported.

2. A complicated study was carried out in 1973/1974 in a heavily contaminated industrial area in Nordrhein-Westfalen, Western Germany (Einbrodt et al. 1975, Rosmanith et al. 1975a, 1975b, 1976). The yearly average air lead concentration in this area was reported to be 5.6 $\mu g/m^3$, and extreme lead deposition values of 500->10000 $\mu g\ m^{-2}d^{-1}$ were found. In a control area an average air lead value of 1.1 $\mu g/m^3$ was found. Methods of sampling were not reported.
   In the exposed area PbB of 404 randomly chosen 2-14 year old children was measured in March and May 1973 (method of sampling not given, reference to small inter-laboratory study), and an average PbB of 16.7 µg/100 ml (arithmetic mean) was reported; the parents of 29 additional children volunteered to have the PbB of their children determined in May 1973, and these blood lead levels averaged 21.9 µg/100 ml. This was interpreted by the authors as evidence of a selection effect on PbB values in the sense that children who were presented voluntarily for blood sampling had higher PbB levels than children who were invited to participate at random. However, when the March and May results for the first group were reported separately, a large difference became evident (arithmetic average PbB 12.6 and 21.2 µg/100 ml respectively). A seasonal influence rather than a selection effect would seem to be present in the data. Some children had their blood lead level determined again in August and October, and the results were even more striking: 40.4 µg/100 ml in August, and 20.9 µg/100 ml in October. Analytical procedures were checked and not found responsible. Thus, an extreme seasonality was present in these data which was attributed by the authors to outdoor play in spring and summer. Increases were largest in the 4-5 year olds who had the highest blood lead levels in May. The seasonality in this study is much more extreme than the seasonality noted in some US-studies (Hunter 1977, Billick et al. 1980, Billick 1983). In the recent EC survey of 1981 in the UK, no difference between children's blood lead levels in samples taken in March, April and May was found (Department of the Environment 1983).

In the control area 393 children were sampled at random, and 293 were presented by their parents voluntarily for blood lead analysis. They were also aged 2-14. All samples were taken in December 1973 and January 1974, and the arithmetic average 'random' results (7.8 µg/100 ml) were clearly lower than the 'voluntary' results (12.5 µg/100 ml). In the control area, the children who were presented voluntarily for blood sampling do not seem to have been representative for the complete control population then.

α-Estimates based on the 'random' results from both areas and based on an air lead difference of 4.5 $\mu g/m^3$, would give different results for different seasons: 1.1 in March, 3.0 in May, 7.2 in August and 2.9 in October.

If indeed, in heavily contaminated areas, fluctuations of PbB as large as noted in this study occur regularly, exact knowledge about the date of blood sampling is required to facilitate interpretation.

β-Estimates based on lead deposition values would be 0.4 - 2.5 µg (per 100 ml) per mg (per m^2 per day) for the different seasons.

The α- and β-estimates from this study have to be interpreted with care, as no data were presented on any of the relevant covariables mentioned in section 3.1.

3. The surroundings of a secondary lead smelter located in Arnhem, The Netherlands, have been investigated repeatedly in the period 1976-1978 (Kranjc et al. 1977, Zielhuis et al. 1979, Brunekreef et al. 1981, Diemel et al. 1981). The smelter had been in operation since World War II, and emissions were restricted during the seventies, for the last time in 1977, i.e. in the midst of the investigations.

Venous blood samples were taken from 108 (1976), 690 (1977) and 95 (1978) children respectively. Quality control data were presented. The arithmetic average results for the 2-3 year olds are shown in table 3.1, according to distance from the smelter. This age category was chosen for comparison, as it was the only category sampled in each year. In 1976 and 1978, blood lead analyses were performed by the same laboratory. In 1977, a different laboratory did the analyses.

Table 3.1. Blood lead in 2-3 year olds according to distance from the Arnhem smelter (Kranjc et al. 1977, Zielhuis et al. 1979, Brunekreef et al. 1981)

	400-1000m	1000-2000m	>2000m
	PbB (µg/100 ml, n in parentheses)		
1976	19.7 (17)	14.7 (53)	11.8 (36)
1977	18.2 (88)	14.6 (96)	---------
1978	16.6 (67)	---------	---------

Air lead was measured at 6 sites using High Volume samplers during the 1978 study and was found to be uniformly low (.3-.5 µg/m^3).

In 1977, air lead varied between .4 and 1.6 µg/m^3, and in 1976 between .5 and 2.5 µg/m^3 (Provinciale Waterstaat Gelderland 1978, Zielhuis et al. 1979). Although measuring sites and periods have not been completely comparable through the years, an influence of the emission reduction that was enforced in the spring of 1977, can be detected in the data.

A decline of PbB seems also present in the most exposed group. For estimating α in 1976, an air lead difference of 2.0 µg/m^3 has been assumed between the highest and lowest PbB group. An α of 4.0 results. The PbB difference between children living at less than 1000 m from the source and those living at more than 2000 m from it (about 8 µg/100 ml) decreased to 7.2 µg/100 ml after adjustment for parental education, resulting in a slightly lower adjusted α-estimate (3.6). For 1977, an air lead difference of 1.0 µg/m^3 has been assumed between exposed and control children of 2-3 years old and who had average PbB values of 18.2 and 14.6 µg/100 ml respectively. An α-estimate of 3.6 results. In 1978, a direct estimate of α was not possible as air lead did not correlate with PbB within the exposed population and no control population was investigated.

Soil lead was measured in composite samples of garden top soil (0-5 cm) obtained from the gardens next to the homes of the 1978 study population. Lead was extracted using 3 M HCl, for three hours at 100^{o}C. This procedure was shown to have

the same efficiency as digestion with $HClO_4$:HNO_3 in a 1:4 ratio by volume (Keizer et al. 1982), which means that practically all lead was extracted from the samples. After adjustment for parental education, soil lead was significantly correlated with blood lead, and the estimated β was 12.6 µg (/100 ml) per g/kg for the 100-600 mg/kg range. Tap water lead, use of self-grown vegetables, age of the home, mouthing behaviour, exposure through parental occupation or hobbies and house dustiness were all evaluated and not found to be confounders of the blood lead/soil lead relationship in this study.

The absence of a significant blood lead/air lead relationship in this study may reflect the fact that within the study area, air lead had become low and more or less uniform as a result of prior emission reductions.

Other environmental pathways which were evaluated were outdoor deposition, street dust and house dust. Of these, indoor lead deposition was significantly correlated with blood lead in those children who lived in homes without gardens, and who were consequently not exposed to soil lead but to lead in street dust, house dust, etc.

4. A large number of 1-19 year old children were studied in the surroundings of a lead smelter located in El Paso, Texas, in 1972 (Landrigan et al. 1975, Landrigan and Baker 1981). The immediate surroundings of the smelter were extremely polluted, with annual average air lead values of 8-10 µg/m^3 as measured by High Volume samplers. Surface soil (upper 1-2 cms) was sampled and was shown to contain 1791 mg/kg on average within 1.6 km of the smelter. The extraction procedure was not reported. Soil lead levels were reported to decrease with depth over a range of only 7.5 cm. This is an interesting observation, as it shows that soil samples, taken at different depths in different studies will yield results which are not readily comparable. Within 1.6 km from the smelter, house dust contained the extremely high level of 22191 mg/kg on average. The methods of sampling and extraction were not reported. The early reports from this study concentrated on specifying the percentage of children per area with venous PbB values above a given level (e.g. 40 µg/100 ml or 60 µg/100 ml) and did not supply sufficient information to derive quantitative relationships between

environmental lead and blood lead. Quality control information was not given.

In 1977, a small follow-up study was carried out to ascertain whether emission reductions which were introduced in the preceding years, had been effective in reducing environmental lead and blood lead (Morse et al. 1979). From this study, table 3.2 has been compiled.

Table 3.2. Reduction of environmental lead and blood lead in El Paso, Texas between 1972 and 1977 (Landrigan et al. 1975, Morse et al. 1979)

	1972		1977	
	<0.8 km from source	0.8-1.6 km from source	<0.8 km from source	0.8-1.6 km from source
PbB (µg/100 ml, ar.m.)	41.4	31.2	17.7	20.2
number of children studied	160	96	3	137
mean age (years)	8.9	9.7	13.3	9.1
air lead (µg/m^3)	10.0	6.0 (est.)	5.5	3.0 (est.)
house dust lead (mg/kg)	22191		1479	
soil lead (mg/kg)	1791		427	

The reduction of PbB within 0.8 km of the smelter is not well documented, in view of the small number of children studied in this area in 1977. Between 0.8 and 1.6 km from the smelter the reduction of PbB was clear. Air lead values for this particular area were not given and had to be obtained by interpolation of air lead values reported at 0.4 and 4 km from the source respectively.

α-Estimates of 2.6 (1972) and 3.7 (based on reduction of PbA and PbB at 0.8-1.6 km from the source) are thus obtained.

The unweighted average PbB value for the 0-1.6 km area for 1972 is 36.6 µg/100 ml. If we put the average reduction of PbB between 1972 and 1977 at 16 µg/100 ml, a β-estimate for house dust lead would be 0.8 µg/100 ml per g/kg. For soil lead, the β-estimate would be 11.7 µg/100 ml per g/kg. There

are many uncertainties in the representativity of the exposure data for the populations of children who were studied. The environmental data from this study are unusual in showing a rapid reduction of lead levels in soil and house dust. The extremely arid climate with its accompanying wind erosion has been held responsible for this phenomenon.
No statistical correction for confounders is possible on the basis of the reported data. Family income, paint lead exposure, lead in drinking water and lead release from pottery were shown to be reasonably uncorrelated with distance from the smelter. Water samples were taken from 13 homes only, however, and the limit of detection was at the rather high value of 50 µg/liter.

5. A large lead smelter located in Kosovska Mitrovica, Yugoslavia, has caused one of the gravest lead pollution problems mentioned in the literature (Popovac et al. 1982). Citywide average air lead values of 14.3 $\mu g/m^3$ and 23.8 $\mu g/m^3$ were reported for the years 1978 and 1980 respectively. PbB was measured in a control group of 73 children in 1978, and in 179 exposed children in 1980. There was reference to a small inter-laboratory control program for blood lead determinations.
For 0-3 year olds arithmetic mean venous PbB levels were 46.3 and 6.8 µg/100 ml for exposed and control children respectively. For 3-5 year olds, the values were 44.4 vs 7.5 µg/100 ml, for 5-10 year olds 45.9 vs 8.7 µg/100 ml and for 10-15 year olds 46.8 vs 8.7 µg/100 ml.
Assuming an air lead difference of 23.5 $\mu g/m^3$ between exposed and unexposed children, α can be estimated at 1.6 to 1.7, depending on age. Considering the large exposure range over which these α's were calculated, it is quite conceivable that their comparatively low value is at least partly related to the presumed curvilinearity of the blood lead/environmental lead relationship. The reported increase in PbA levels between 1978 and 1980 further indicates a non-steady state; it is conceivable that the PbB values, which have been shown to lag behind changes in environmental exposure (Prpic-Majic et al. 1983), were still increasing.
Here again, no data on covariates were reported.

6. Another heavily polluted area in Yugoslavia is the Meza Valley (Prpic-Majic et al. 1983, 1984). In the years 1974-

1976, an average air lead value of 20.8 µg/m^3 was recorded without an indication of change over time. In 1978, a bag filter system was introduced and air lead values declined to 1.6-1.9 µg/m^3 over the years 1979-1982. Table 3.3 shows the results of blood lead level determinations in children in different years (method of blood sampling not given).

Table 3.3. PbB values in children in the Meza Valley, Yugoslavia, for the years 1976-1982. PbB in µg/100 ml (arithmetic means) (Prpic-Majic et al. 1983, 1984)

	1976	1979	1982
preschool children, exposed	46.7 (30)*		
school children, exposed	49.2 (30)	52.3 (28)	31.2 (54)
preschool children, control	10.3 (19)		
school children, control	10.5 (11)		
air lead (µg/m^3), exposed	20.8	1.6	1.9
air lead, control	0.1		

* number of children in parentheses

A number of different α-estimates can be derived from these data. First of all in 1976, α-values of 1.8 (preschool) and 1.9 (schoolage) can be derived for the prevailing presumed steady state conditions. Here again, the values seem to have been forced downward in view of the large range of exposures studied. For 1979, an α of 26.7 can be calculated - an obviously inflated value caused by the persistence of high PbB values despite a radical drop in PbA values. Taking the drop in PbB values of school children between 1976 and 1982, an α of 1.0 is calculated. This is most probably an underestimate as it is quite likely that in the future the PbB values will continue to decline when children grow up who have been born after the emission reduction of 1978, and lead levels in house dust, street dirt and eventually top soil decline.

No data were reported on covariates, so that the α-estimates again have to be interpreted with care.

An interesting comparison can be made between this study and

the study reported by Morse et al. (1979). Apparently, the rate of decline of PbB values is more or less comparable, although the climate in north western Yugoslavia is almost certainly less arid than in El Paso. One is led to wonder what changes in lead in soil, house dust and dustfall have occurred in the Meza Valley over the years, and how these compare to the values cited from El Paso.

7. An extensive study was carried out in 1973 in Toronto, Canada, in an area near two large lead smelters and in an urban control area (Roberts et al. 1974a, 1974b, 1975). Air lead averaged 3.0 $\mu g/m^3$ in the smelter area and 0.8 $\mu g/m^3$ in the urban control area. High Volume samplers were used. On one spot in the smelter area indoor air lead was measured (method not given). It was found to be about 30% of outdoor air lead. Surface soil (0-2 cm) was sampled at more than 100 locations, and the samples were digested with a 1:4 $HClO_4$: HNO_3 mixture. Concentrations up to 40000 mg/kg were found close to one of the smelters, but in exposed residential areas the geometric mean garden soil lead level was 1715 mg/kg. There was a decrease of lead content with depth. In the urban control area, the soil lead concentration was 99 mg/kg. In street dust, the levels were 2416 vs 924 mg/kg (geometric means) respectively. In house dust, they were 1550 vs 713 mg/kg (geometric means). Methods of sampling for house dust and street dust were not reported.
Heavy lead deposition occurred near the smelters, with a geometric mean of 5267 $\mu g\ m^{-2}d^{-1}$ in the smelter area vs 767 $\mu g\ m^{-2}d^{-1}$ in the urban control area.
Tap water lead was low in both areas, at 5.9 and 1.34 $\mu g/l$ on average respectively. Paint lead was measured and appeared to be not different between areas.
Capillary blood was analysed for lead and was found to average 27.0 and 28.0 $\mu g/100$ ml in children aged 0-15 yrs living within 300 m from the respective smelters, and 19.0 $\mu g/100$ ml in an urban control population of similar socio-economic background. The average PbB for children in this group was not reported; it was only stated that less than 1% of 0-14 year olds in the control group had PbB > 40 $\mu g/100$ ml. When it is assumed that the average PbB of control children was 19.0 $\mu g/100$ ml as well, and an air lead difference of 2.2 $\mu g/m^3$ is assumed between exposed and control

children, an α-estimate of 3.9 results. No blood lead quality control data were reported.
The β-estimates from this study would be:
5.3 µg/100 ml per g/kg for surface soil lead;
5.7 µg/100 ml per g/kg for street dust lead;
10.2 µg/100 ml per g/kg for house dust lead, and
1.9 µg/100 ml per mg $m^{-2}d^{-1}$ for lead deposition.
It will be clear that the use of capillary blood may have inflated these estimates; that the absence of separately reported data for control children adds uncertainty; and that the age range was too wide to cover only the age category at the highest risk.

8. A large lead smelter and its surroundings in Hoboken near Antwerp, Belgium, have been repeatedly studied between 1973 and 1978 (Roels et al. 1976, 1978b, 1980). School children in the age category of 10-15 years were studied in an area at less than 1 km from the smelter in the 5 consecutive years 1974-1978. An intermediately exposed group with its school at 2.5 km from the smelter was studied in the same years.
Rural controls were investigated in 1974-1976 and 1978, urban controls in 1976 and 1978. Lead emission of the smelter was reduced in 1975 and the study can thus be compared to the earlier discussed ones (studies 3, 4 and 6) in which such non-steady state conditions were present as well.
All blood samples were venous, and there was reference to several quality control programmes. Air lead was sampled by low volume methods in the different areas, and the air lead values might thus be lower than those that would have been found by High Volume sampling, especially near the smelter where more of the lead will have been concentrated in the larger particles.
The results of the different surveys are summarized in table 3.4 (Roels et al. 1980).
Playground dust was sampled at the schools and was found to contain 3541 and 5466 mg lead per kg at the schools near the smelter, 397 mg/kg at the school at 2.5 km from the smelter and 152 mg/kg at the school in the rural area. The method of sampling was not given, the samples were digested with a 1:3 mixture of nitric/hydrochloric acid.

Table 3.4. Air lead and blood lead in different populations of school age children in Belgium, 1974-1978 (Roels et al. 1980)

year	population	air lead ($\mu g/m^3$)	PbB ($\mu g/100$ ml, arithmetic mean)	n
1974	< 1 km from smelter	4.06	30.1	37
	2.5 km from smelter	1.00	21.1	14
	rural	0.29	9.4	92
1975	< 1 km from smelter	2.94	26.4	40
	2.5 km from smelter	0.74	13.6	29
	rural	0.31	9.1	45
1976	< 1 km from smelter	3.67	24.6	38
	2.5 km from smelter	0.80	13.3	40
	urban	0.45	10.4	26
	rural	0.30	9.0	44
1977	< 1 km from smelter	3.42	28.9	56
	2.5 km from smelter	0.49	14.8	50
1978	< 1 km from smelter	2.68	27.8	43
	2.5 km from smelter	0.54	16.0	36
	urban	0.56	12.7	29
	rural	0.37	10.7	42

A regression analysis on the combined survey data which was performed by the authors resulted in an α-estimate of 5.3 (5.8 for boys, 5.0 for girls). A β-estimate for playground dust would be 3.5 $\mu g/100$ ml per g/kg. The authors have, on the basis of children's hand lead levels, argued that most of the lead was probably ingested and not inhaled. It is arguable whether mouthing behaviour can still be expected to be prevalent in this age category; the α-values, however, exceed those usually found in adults to a large extent and a predominant route of intake other than inhalation, be it mouthing behaviour or not, will have to be assumed.

On the basis of PbB group means for girls and boys in 4 different areas in 1978, the authors performed a multiple regression analysis with air lead and hand lead as independent variables. The analysis resulted in a significant contribution of hand lead but not of air lead to PbB after the other independent variable had been taken into account. However, air lead and hand lead were shown to be extremely correlated in both girls and boys ($r = 0.995$ and 0.999 respectively). This collinearity prevents meaningful interpretation of the multiple regression analysis and it does not seem valid to conclude from the result that the quantitative contribution of air lead to the children's blood lead is negligible compared to that of hand lead.

The method of air sampling under-estimated air lead levels probably especially in the most heavily exposed area, which would mean that the α-estimates from this study are inflated. Children of 3 - 8 yrs were studied in the area between 1978 and 1984, and a group average PbB value of 45.2 µg/100 ml was found in 1978 in children living at less than 800 m from the smelter. In 1984, the PbB levels in this age category were on average still above 30 µg/100 ml (Schrijver 1984). For young children the α- and β-values were consequently higher than for the older children.

Tap water lead and parental education were measured in this study and were not found to confound the PbB/PbA relationship. Other covariates were not studied.

Interesting in this study is also that PbB levels remained elevated despite an emission reduction in 1975. However, judging from the air lead levels which were measured through the years, the reduction must have been far less efficient than the ones cited from Arnhem (The Netherlands), El Paso (US) and Meza Valley (Yugoslavia).

9. Another smelter study was carried out in Trail, Canada in 1975 (Neri et al. 1978, Schmitt et al. 1979). Children aged 1-6 and 13-14 yrs (grade 9) were investigated in Trail and in Nelson, a control town. Air lead levels averaged 2.0 and 0.5 $\mu g/m^3$ respectively (method of sampling not given).
Surface soil (0-2.5 cm) was sampled from 245 100 cm^2 areas; the samples were predigested with concentrated HNO_3 and digested with 70% $HClO_4$. The median soil lead level in Trail was 800 mg/kg and it was 83 mg/kg in Nelson.

In young children, PbB levels (method of sampling not given) were higher in Trail (22 µg/100 ml) than in Nelson (14 µg/100 ml), a difference which was not observed in the older age group (11 vs 10 µg/100 ml). α-Values of 5.3 and 0.7 can be calculated for the respective age groups; especially the low value for the oldest age group is in marked contrast with the results of the Belgian study (Roels et al. 1980), which covered the same age range. An explanation cannot easily be given. For the young children, lead in soil was shown to be closely related to PbB.

The difference in PbB and soil lead levels between Trail and Nelson suggests a β-value of 11.2 µg/100 ml per g/kg soil lead. A detailed breakdown of the data from Trail only suggests β-values of 8.3 and 4.8 µg/100 ml per g/kg for children aged 1-3 and 6 yrs respectively. No data were given on potential confounders.

10. A smelter study from Czechoslovakia was reported by Wagner et al. (1981). Air lead near a secondary smelter was reported to average 1.5 µg/m^3, compared to 0.5 µg/m^3 in a control area. In 1976, blood was sampled from children aged 10-15 yrs by venous puncture and their PbB values were found to be markedly different between exposed and control groups, especially in boys (38.7 vs 21.0 µg/100 ml, arithmetic mean). For girls, the difference was 31.6 vs 19.1 µg/100 ml. α-Estimates on the basis of these results would be as high as 17.7 (boys) and 12.5 (girls) respectively. No information was published on lead levels in other environmental media, which might explain this finding. Data on blood lead analysis quality were not given; information on covariates was not reported either.

11. The last industrial study to be discussed in this review is perhaps the most frequently cited in the literature: the Silver Valley Lead Study (Yankel et al. 1977, Walter et al. 1980). In 1974 1149 children aged 1-9 yrs were studied and in 1975, another 781 children aged 1-10, all living at varying distances from a large lead smelter located in Kellogg, Idaho (US).

Air lead was measured by High Volume samplers and averaged 16.7 µg/m^3 close to the smelter in 1974, having risen rapidly since 1971 when it was only 6.1 µg/m^3 and slightly lower than in the period 1966-1970 (Anonymus 1976). Contributing

to the extremely high air lead levels in 1974 was a fire in a bag house within the smelter; after replacing the unit, air lead levels were lower again in 1975, averaging 10.3 $\mu g/m^3$ close to the smelter. Geometric mean venous PbB levels (no quality control data) ranged from 18 to the extreme of 77 µg/100 ml, depending on age and exposure category. It has been suggested that an upward error could have been present in the 1974 PbB data due to contamination of samples taken in the field (Anonymus 1976, Snee 1982b). The 1975 survey was performed under circumstances which make comparison between the 1974 and the 1975 population samples invalid (Walter et al. 1980): selective outmigration had occurred of children with high PbB living close to the smelter; in the lesser exposed areas, only children whose blood lead had been greater than 40 µg/100 ml in 1974 were studied again in 1975; some children with high PbB values in 1974 had subsequently been treated by chelation therapy; an extensive home hygiene campaign had taken place in the community and schools; people were more aware of the problem in 1975 than in 1974; top soil had been replaced in some badly polluted places; and emissions had been reduced.

Analysis of the data by the original investigators yielded adjusted α-estimates of 1-2.5, depending on exposure level. For the 0.5-1.5 $\mu g/m^3$ range, the author's equation as mentioned in Yankel et al. (1977) predicts an α-value of 1.1 at a soil lead level of 1000 mg/kg and average values for 3 modifier variables (socio-economic status, house dustiness and age) in the equation. Unadjusted estimates were not given. The single log model which was used was unusual in predicting larger PbB increases at high PbA levels than at low PbA levels; adjustment for lead in soil must have led to an under-estimate of the 'true' impact of environmental lead on blood lead.

A reanalysis of the data by Snee (1982b) has suggested that the α-estimates from this study were more likely to be in the 0.8-1.7 range. This particular reanalysis has many shortcomings, however, making its results questionable (Brunekreef 1984).

Comparing the groups with highest and lowest PbB values in 1974 yields unadjusted α-estimates of 2.4-3.3. As mentioned, contamination problems may have resulted in an upward bias

of the PbB values of the children with the heaviest exposure especially, and if this was the case, the mentioned α-values are biased upward as well. Group average PbB values of over 70 µg/100 ml have never been found in children living near other lead smelters, although exposure conditions were sometimes at least as severe as near the Kellogg smelter (cf. studies 4-6).

Soil lead levels ranged from 300 to 7600 mg/kg (area wide averages); methods of sampling and analysis were not reported. Comparing groups with highest and lowest PbB values in 1974 yields unadjusted β-estimates of 5.2 -7.3 µg/100 ml per g/kg soil lead. At an air lead level of 1 µg/m^3, the equation mentioned in Yankel et al. (1977) yields an adjusted β-estimate of 0.6 µg/100 ml per g/kg, showing that the adjustment procedure reduced the soil lead impact estimate more than 10-fold in this case. No analyses have been published in which the impact of individual lead exposure indicators was adjusted for confounders only, and not for other lead exposure indicators as well.

Summary of results from smelter studies

Table 3.5 contains a summary of the findings from the different smelter studies.

Table 3.5. Summary of findings from smelter studies

study nr	α-estimate[1]	β-estimate	Remarks
1	3.3		unadjusted; 3-6 yr olds
	4.0		unadjusted; 8-11 yr olds
2	1.1-7.2		unadjusted; 2-14 yr olds; depending on season
		0.4 - 2.5 (1d)[2]	unadjusted, depending on season

Table 3.5. (continued)

study nr	α-estimate[1]	β-estimate	Remarks
3	4.0		unadjusted; 2-3 yr olds
	3.6		adjusted for parental education
		12.6 (s)	1-3 yr olds, adjusted for parental education
4	2.6-3.7	11.7 (s)	1-19 yr olds; unadjusted;
		0.8 (hd)	based on reduction of PbB and PbA over time
5	1.7		0-10 yr olds; unadjusted
	1.6		10-15 yr olds; unadjusted
6	1.8		preschool age; unadjusted
	1.9		school age; unadjusted
7	3.9	5.3 (s)	0-15 yr olds; unadjusted
		5.7 (sd)	
		10.2 (hd)	
		1.9 (ld)	
8	5.3	3.5 (pd)	10-15 yr olds; adjusted for tap water lead and parental education
9	5.3	11.2 (s)	0-6 yr olds; unadjusted
	0.7	1.4 (s)	13-14 yr olds; unadjusted
		8.3 (s)	0-3 yr olds; Trail only
		4.8 (s)	6 yr olds; Trail only
10	12.5		10-15 yr old girls; unadjusted
	17.6		10-15 yr old boys; unadjusted

Table 3.5. (continued)

study nr	α-estimate[1]	β-estimate	Remarks
11	2.4-3.3	5.2 - 7.3 (s)	1-9 yr olds; unadjusted
	1.0-2.5	0.6 (s)	1-9 yr olds; adjusted for parental occupation, house dustiness, age and one other lead exposure variable

1 α = µg/100 ml (PbB) per µg/m^3 (Pb air)
2 ld = lead deposition β = µg/100 ml per mg $m^{-2}d^{-1}$

s = soil
hd = house dust β = µg/100 ml per g/kg
sd = street dust
pd = playground dust

From the data in the table it is clear that a wide range of α-values can be calculated from the different studies. Adjustment for confounders has been weak or absent in most studies. In studies 3 and 8, adjustment for at least some confounders did not reduce the α-estimates much, but in view of the many differences between studies, it cannot be assumed that this is the general rule. Unadjusted α-values below 2 generally stem from areas where PbB values were high (studies 5, 6, 11) or from older children (study 9). The majority of values is in the 2.4-5.3 range; the results of the Wagner et al. study (nr. 10) are evidently out of range.
For soil lead, the unadjusted β-values range from 4.8 - 12.6 µg/100 ml per g/kg, if we exclude the low 1.4 value for 13-14 yr olds in study 9. For house dust, the two available β-values are very different (10.2 vs 0.8 µg/100 ml per g/kg). The two street and playground dust β's on the contrary are close to each other (5.7 and 3.5 µg/100 ml per g/kg respectively) and only somewhat lower than the soil lead β's.

3.3. Studies performed in urban areas where lead pollution is mainly caused by vehicular traffic

12. The Omaha study (Angle et al. 1974, 1984, Angle and McIntire 1979) is an analysis of more than 1000 blood lead values obtained from 831 children between 1971 and 1977 in Omaha, Nebraska. Some samples were taken by venous puncture, most were capillary. On some individuals both methods were used and it was found that capillary PbB was on average 4 µg/100 ml higher than venous PbB. All venous PbB's were subsequently corrected to capillary PbB values - a rather unusual procedure in view of the afore mentioned problems with capillary blood lead analyses. Quality control data were not reported. The population was mostly of school age and not further subdivided by age within the two classes used (1-5, 6-18 yrs). Children came from 3 areas: suburban, mixed urban/commercial and commercial. Some industrial lead sources were present in the commercial district. Suburban children were white, children from both other groups predominantly black, introducing a cultural and probably socio-economic difference which was not accounted for in the analysis of the data. Air was sampled with High Volume samplers on one spot within each area, and geometric mean Pb-air levels in a range of 0.02-1.69 µg/m^3 were assigned to the more than 1000 PbB values for further analysis.

Soil (0-5 cm) was sampled near 37 homes and 20 schools within the 3 areas, and levels with a geometric mean of 227 mg/kg and a 95-percentile of 843 mg/kg were assigned to the individual PbB values on the basis of the school values, or, if present, the home values. House dust was sampled (usually from the vacuum cleaner bag) at the same sites as soil, and levels with a geometric mean of 337 mg/kg and a 95-percentile of 894 mg/kg were assigned to the PbB values, in the same way as the soil levels. Extraction methods for soil and house dust were not reported.

Milk and water were analysed and found to be uniformly low in lead. Food was not analysed as the major grocery chains were equally distributed in the three areas.

The analysis of the data was mainly restricted to the influence of air lead, soil lead and house dust lead on blood lead, and is thus of limited value in view of the probable

influence of the earlier mentioned confounders like race.
All variables were log-transformed before further analysis. Unadjusted regression analyses yielded α-values of 1.0 (all children), -3.4 (1-5 yr olds)(!) and 2.6 (6-18 yr olds) for the air lead range of .5-1.0 $\mu g/m^3$.
The respective unadjusted β-values for soil lead were 10.5, 15.5 and 10.6 $\mu g/100$ ml per g/kg for the 100-750 mg/kg range.
For house dust lead, the β-values were 10.8, 12.8 and 12.6 $\mu g/100$ ml per g/kg for the 100-750 mg/kg range.
Soil lead correlated best with blood lead and explained 19.4% of variance of PbB for the 6-18 yr olds. A multiple regression of blood lead on air lead, soil lead and house dust lead only increased the percentage of explained variance to 21%. Due to the inter-correlation of the three lead exposure indicators, the regression coefficients were only about 36% of their unadjusted values for air lead and house dust lead, and 64% of the unadjusted value for soil lead.
For the years 1970, 1972 and 1973 only, air lead values were reported for each of the three study areas. Soil and house dust samples were taken in 1972 only. As blood samples were taken in the spring of 1971, in the winter of 1972/1973, in the spring of 1973, in winter and spring in 1975, in spring and late autumn in 1976 and in the spring of 1977, a definite problem of this study is the allocation of exposure data to individual blood lead data. The average values of blood lead and lead exposure variables per area were reported and are shown in Table 3.6.
This tabulation shows that surprisingly, the trend for blood lead and soil lead was not the same although soil lead was the best predictor of blood lead in the regression analysis. If we estimate unadjusted α's and β's from the differences in group averages between the suburban and the commercial area, the results are: $\alpha = 15.8$ for air lead, $\beta = 37.6$ for soil lead and 25.4 for house dust lead. These values are much larger than the unadjusted regression coefficients, and one is tempted to speculate that in view of the divergence in periods in which environmental and blood samples were taken, and in view of the low correlations between environmental lead and blood lead, the regression coefficients were systematically under-estimated due to misclassification in

the allocation of exposure values. This is not to imply that the latter values would be more realistic; the absence of adjustment for race and other potential confounders prevents such a conclusion.

Table 3.6. Blood lead and environmental lead in Omaha, Nebraska, 1971-1977 (Angle and McIntire 1979)

	area		
	suburban	mixed urban/ commercial	commercial
PbB[1] 1971-1977 (all children, µg/100 ml)	18.0	22.0	24.8
air lead 1970,1972,1973 (µg/m^3)	.40	.69	.83
soil lead[1] 1972 (mg/kg)	81	339	262
house dust lead[1] (mg/kg)	211	300	479

1 geometric means

Another reanalysis of the same data was reported by Angle et al. (1984). A linear exposure model for all children now resulted in an α-value of 1.92 µg/100 ml per µg/m^3 (adjusted for soil lead and house dust lead) and in β-values of 6.8 and 7.2 µg/100 ml per g/kg for soil lead and house dust lead respectively, adjusted for the other two lead exposure variables in the equation. The data reported for environmental lead were arithmetic rather than geometric means, and by exclusion of some high values in the mixed urban/commercial area, the soil lead levels in this area were now intermediate between those of the suburban and the commercial area. An unadjusted α was now given variously as 4-5 (abstract) and 6.94 (text) µg/100 ml per µg/m^3.
The changes in α- and β-estimates from reanalysis to reanalysis were large and have not been adequately explained.

13. The study reported from Lausanne, Switzerland, by Berode et al. (1980) included 287 children from a few months to 10 yrs old living in different parts of Lausanne. The study was carried out from October-December 1975. Blood was sampled by venous puncture, and extensive quality control data concerning the blood lead analysis were published. There was no concomitant environmental sampling, but air lead levels of about 2.5 $\mu g/m^3$ were said to prevail in the central urban zone.

    Lead in drinking water was uniformly low (1-5 µg/l). Information concerning nationality, age, dietary habits, season, proximity to roadways, population density of residential area, parental occupation, mouthing behaviour and presence of pets was gathered by means of a questionnaire. The results showed an increase of PbB values from about 11 µg/100 ml at age 1 to about 15 µg/100 ml at ages 4 and 5, and a subsequent decrease to about 11 µg/100 ml at age 10. Among others, traffic density (numbers not given) was shown to be related to PbB. Geographic analysis yielded geometric mean PbB levels in 5 different zones ranging from 11.3 to 15.2 µg/100 ml. When it is assumed that the maximum between-area difference in air lead was 2 $\mu g/m^3$, an unadjusted α of 2.0 can be calculated from these figures. Adjustment for father's profession and mouthing behaviour probably would not change this estimate to any great extent, as can be deduced from the fact that the influence of traffic density upon PbB remained largely unaffected by adjustment for these two factors. The unavailability of actual air lead data within the areas of interest in the months preceding blood sampling makes the α-estimate from this study uncertain.

14. The studies published by Billick (et al.) (1979, 1980, 1983) cover the extremely large number of over 175000 venous blood samples obtained from New York children mostly in the range of 0-6 years of age, over the years 1970-1976. Quality control data were presented.

    PbB depended on age and race, with the highest values in black children of 2-4 years of age. Interestingly, the highest PbB values in white children occurred at age 5. There was a clear seasonal influence, and an overall decline of PbB values between 1970 and 1976.

    There was no clear dependence of PbB on geographic area for

blacks, and a dependence of PbB on area for hispanics that decreased over the years. Air was sampled with High Volume samplers at an elevated site over the years, and the resulting air lead values were incorporated in a multiple regression analysis with quarterly geometric mean PbB as dependent variable and age and race as other independents. A highly significant correlation with air lead was found with an (adjusted) regression coefficient of 5.16.

Subsequent analyses showed an even higher dependence of PbB on gasoline lead consumption, suggesting vehicular traffic as an important source of lead in the blood of these children. Later, the analysis was extended to Chicago and again the same pattern arose, giving further support for the conclusions reached.

Some comments, however, can be made. Air lead was measured at an elevated site, and a later comparison showed that, at the same site, air lead levels at street level were about 45% higher (Lioy et al. 1980). Adjustment for this difference would reduce the α-estimate to about 2.9.

By taking quarterly geometric mean blood lead levels as a dependent variable, any factor that varies seasonally will correlate well with blood lead. Seasonal variation of blood lead levels in children has been observed before (cf. chapter 2) and has been ascribed to other causes like sunlight, increased exposure to outdoor pollution by playing outdoors etc. Adjustment for these factors was not attempted, and would reduce the α-estimate.

A reduction of PbB values over time in children seen in screening programmes has also been observed before (Sachs 1974) and has been ascribed to the concentration of early screening efforts to the presumed 'worst' areas, and to increasing awareness of the public for lead paint hazards due to the accompanying publicity. Especially in the central districts of large US cities, elevated blood lead levels have customarily been thought to be mainly related to lead in paint (Lin-Fu 1973) and lead paint hazard abatement programmes cannot be dismissed as possible causes of a reduction of childhood PbB values.

Nevertheless, the data presented by Billick et al. have also shown that irregularities in seasonal gasoline lead consumption have been closely mirrored by irregularities in the

seasonal variation of PbB, a phenomenon that cannot easily be accounted for by other putative causes of seasonality of PbB or of PbB decreases.

15. In september 1974, 38 children aged 1-16 year living near the San Diego Freeway in Los Angeles, were studied and compared with 46 children of the same age, living in the desert town of Lancaster, 40 miles from Los Angeles (Johnson et al. 1975, 1976). Venous blood samples were taken twice, one week apart from each participant; quality control data were presented. Two different reports, including one by the investigators themselves, later suggested that the accuracy of the blood lead analyses from this particular study was limited (Johnson et al. 1978, Lucas 1981). Air lead was sampled for two weeks only in Lancaster backyards and also 80 feet down (prevailing) winds from the San Diego Freeway, using High Volume samplers. Two samples from Los Angeles gave an average reading of 6.3 $\mu g/m^3$ and were compared to 13 samples from Lancaster, giving an average value of 0.6 $\mu g/m^3$. No information was given on prevailing wind directions during this short sampling period, making it impossible to judge whether the high Los Angeles air lead value was representative for the long term average air lead concentration at the sampling site. The housing complex from which most volunteers for this study were recruited, was reported to be located between 100 and 300 feet from the Freeway. It is well known that the concentration of lead in air decreases rapidly within short distances of busy roads. Thus, there is a distinct possibility that the personal air lead exposure of Los Angeles children was significantly overestimated by using air lead values that were obtained at only 80 feet from the Freeway.

The age range was broad (1-16) and in view of the limited number of children studied, only few children in the proper risk category (0-6 years of age) were incorporated. In an appendix to the original report it was shown that PbB values were higher in preschool children (19.6 µg/100 ml) than in older children (16.4 µg/100 ml) in Los Angeles but not in Lancaster. This also was not taken into account, probably because the difference was not statistically significant due to the small number of children involved. It was mentioned that the older children visited schools well away from the

Freeway. Without doubt, their personal exposure was lower than the air lead values measured close to the Freeway. This, again, was not taken into account in any of the analyses of the data from this study.

In the study area, PbB values were clearly higher in male children (20.8 µg/100 ml) than in female children (14.9 µg/100 ml). α-Estimates based on the results of this study are different for males (1.8) and females (0.9) as a result.

16. A study on the relationship between automobile traffic and blood lead levels was carried out in Dallas in the summer of 1976 (Johnson et al. 1978).

Included were 116 children aged 1-8, living in 4 areas characterized by different levels of traffic density.

Capillary blood was sampled in about 2/3 of the children; in the rest venous blood was sampled. Capillary samples were stated to give more variable results; from 8 children venous and capillary samples were obtained. Capillary PbB's were higher than venous PbB's but not significantly so - most probably due to the small number of pairs and the large spread in capillary values. Quality control data were given. The investigators chose to pool venous and capillary data, to avoid data loss for the subsequent statistical analysis.

Air lead was measured with High Volume samplers for a total of 152 days at 17 different sites, located 15 m downwind of the road used for classifying the traffic density of the area. The results for the four different categories of roads are shown in table 3.7.

Table 3.7. Traffic density, air lead and geometric mean blood lead in Dallas (Johnson et al. 1978)

site		1	2	3	4
traffic density (cars/day)		250	8000	17000	30000
air lead (µg/m^3)		.67	.89	1.07	1.54
blood lead	male	12.9	16.5	11.7	15.1
(µg/100 ml)	female	14.9	18.6	14.9	13.6

No relationship between air lead (or traffic density) and blood lead is evident from these figures. Multiple regression analysis, performed by the authors, also did not show a significant effect of traffic density on children's blood lead after taking a number of confounding factors into account.

It is possible that the greater analytical variability associated with capillary PbB determinations has contributed to this negative finding. It is also possible that actual exposure of the study children simply was not different. Indoor air lead values were extremely low and there was no association between traffic density and soil lead and house dust lead, which gives support to the latter explanation.

There is one other study in the literature in which only a very weak relationship between traffic density and children's PbB has been found (Ter Haar and Chadzynski 1979), and another study which has established a clear relationship between the two measures (Caprio et al. 1974). Absence of environmental lead determinations in these studies makes it impossible to obtain α- or β-estimates from them.

Another related study was done in London in 1980 along a road carrying 25000 gasoline powered vehicles per day (Millar 1979, Millar and Cooney 1982). Air lead was measured but only at the very short distances of 2 and 5 m from the curb, and it was found to be between 1.4 and 2.1 $\mu g/m^3$. Blood lead was measured in 221 nursery and junior school children who had either their school, their home or both located adjacent to the road. Exposure contrasts were thus minimized in this study, and no conclusions can be drawn concerning a PbB/PbA relationship.

17. Another urban study was performed in a German town with some zinc and cadmium pollution, but without specific industrial lead sources (Rosmanith et al. 1977a, 1977b). Children of 2-14 years old were divided into three groups: close to the zinc/cadmium source (n=84), intermediate (n=36) and city center (n=293) where some lead pollution by traffic was stated to be present.

PbB values were low, averaging 5.0 µg/100 ml (industrial), 5.7 µg/100 ml (intermediate) and 7.6 µg/100 ml (urban) respectively.

No information on type of blood sampling and the quality of

the blood lead analysis was presented. The PbB values in the industrial area were very low, approaching the levels found in isolated, non-industrialized populations (section 2.6), but low PbB values have been reported from Western Germany before (Haas et al. 1972) and in the absence of further information, it is not possible to form a judgement on the quality of the blood lead analysis in this study.
Air lead was reported at 0.5 $\mu g/m^3$ for the urban area, and not reported for the other 2 areas. Assuming an air lead difference of 0.4 $\mu g/m^3$ between the highest and the lowest group, an α-estimate of 6.5 results.

18. In Tokyo, Japan, air lead has been measured since about 1970, and children's blood lead levels were determined in the years 1975-1980 in urban as well as suburban areas (Okubo et al. 1978, 1983).
In the urban area, air lead was above 1 $\mu g/m^3$ until about 1972. From 1975 onwards, air lead in the urban and suburban areas has been uniformly below 0.5 $\mu g/m^3$.
Blood lead levels (method of sampling not given although quality control data were presented) of children have been declining also, but interestingly, differences between urban and suburban children have persisted long after differences in air lead had virtually ceased to exist. PbB differences remained generally above 1 $\mu g/100$ ml until 1980, despite air lead differences of only about 0.1 $\mu g/m^3$. Group comparisons would yield α-values above 10. Information on possible confounders was not presented although it was stated that paint lead is not known to present problems in Japan. If indeed the differences in PbB between the urban and suburban children are indirectly caused by the historical differences in PbA, this would indicate an important time lag of over 5 years, emphasizing once more the problems associated with studying environments in which there is no equilibrium between the concentrations of lead in air and in other environmental media.

Summary of results from urban studies

Table 3.8 contains a summary of the findings from the different urban studies.

Table 3.8. Summary of findings from urban studies

study nr.	α-estimate[1]	β-estimate	remarks
12	-3.4	15.5 (s)[2]	1-5 yr olds; unexplained
		12.8 (hd)	negative α-result of un-
			adjusted analysis
	2.6	10.6 (s)	6-18 yr olds; unadjusted
		12.6 (hd)	
	1.0	10.5 (s)	1-18 yr olds combined;
		10.8 (hd)	unadjusted
	1.92	6.8 (s)	1-18 yr olds, linear
		7.2 (hd)	model, adjusted for
			other exposure variables
	4 - 7		1-18 yr olds, unadjusted
13	2.0		0-10 yr olds; unadjusted
14	2.9		0-6 yr olds; adjusted
			for age and race
15	1.8		1-16 yr olds, boys, un-
			adjusted
	0.9		1-16 yr olds, girls,
			unadjusted
16	-		no association between
			PbB and air lead
17	6.5		2-14 yr olds, unadjusted
18	> 10		4-18 yr olds, unadjusted
			time lag not taken into
			account

1,2 cf. table 3.5.

The available information on city environments is even more scant than on smelter areas.
Air lead determinations in these studies were more restricted

than in the smelter studies with only one or a few sites, or practically useless due to selection of sampling location and period (study 15). Estimates of β for soil and house dust could be obtained from one study only (study 12). Although these estimates are reasonably in line with those from the smelter studies, the instability of the α- and β-estimates from this study and the remarkable difference between the regression analyses results and the group comparisons do not lead one to trust the size of the various estimates much. The range of α-values from urban studies would be about 2-6.5 if we exclude the more obvious outliers. This range is somewhat larger than the range obtained from smelter studies, and probably reflects the scantness of exposure information in urban studies.

3.4. Other studies

19. Baker et al. (1977) compared 20 1-6 year old children of lead workers with 17 children of the same age from control families. House dust was sampled by wiping surfaces with a moist tissue. The samples were digested in acid of unreported pH. In lead workers' homes, house dust was found to contain up to 80000 mg lead per kg, whereas in the control homes, the geometric mean dust lead concentration was 404 mg/kg. A tabulation of blood lead levels (method of sampling not given, no quality control data) and dust lead concentration permits estimation of β-values. These range from 8.6 to 19.8 µg/100 ml per g/kg for the dust lead range of 0-6000 mg/kg and the blood lead range of 20-65 µg/100 ml.
    The concentration of lead in paint was checked in both groups of homes and was not found to be different.
20. Barltrop et al. (1974, 1975), Barltrop (1975) studied children 2-3 years old living in an old mining area, and compared them to children living in villages situated in an area without history of mining. Air lead and dustfall lead were low in both areas.
    Surface soil samples of 0-5 cm were taken from gardens near the homes of the children. In addition, house dust samples were collected (method not given). The samples were digested in nitric acid of unreported pH before analysis with AAS.

Venous blood samples were taken (no quality control data), and the results were grouped according to soil lead levels < 1000 mg/kg, 1000-10000 mg/kg and > 10000 mg/kg.
In the most exposed area, blood lead, soil lead and house dust lead were 29.0 µg/100 ml, 13969 mg/kg and 2582 mg/kg respectively. In the least exposed area, they were 20.7 µg/100 ml, 420 mg/kg and 531 mg/kg.
On the basis of these data, β for soil lead would be 0.6 µg/100 ml per g/kg. For house dust lead, β would be 4.0 µg/100 ml per g/kg.
In this study, fecal lead excretion was measured also; it was found to be unremarkable at about 50 µg/day which suggests that in this particular group of children, ingestion of dust and soil did not happen to a great extent.

21. Galke et al. (1975) studied 187 black preschool children living in Charleston, SC, US. Paint lead in the home, soil lead at the child's chief play location, and traffic density of the street were measured as well as venous blood lead (no quality control data). The depth of the soil samples and the extraction methods were not given. Soil lead ranged from 9-7890 mg/kg, blood lead from 18-77 µg/100 ml. Soil lead was found to be related to both paint lead and traffic density. Two groups of soil lead levels were constructed using the median as a cut-off point. The resulting "low soil lead" group had a median soil lead level of 173 mg/kg, the "high soil lead" group had a median of 1400 mg/kg. The corresponding blood lead levels were 35 and 41 µg/100 ml respectively; this suggests a β-value of 4.9 µg/100 ml per g/kg. Within different categories of paint lead exposure and traffic density, the blood lead differences between the "high soil lead" and "low soil lead" group ranged from 2-7 µg/100 ml, indicating that probably some of the unadjusted soil lead effect was due to paint ingestion.

22. Reeves et al. (1982) studied 4 groups of 1-3 year old children living in areas of Auckland, New Zealand, with presumed differences in paint lead exposure. Capillary blood samples were taken after extensive measures to avoid contamination. Geometric mean PbB values ranged from 11.4 µg/100 ml in a control area to 18.0 µg/100 ml in the most exposed area. Exterior paint contained 0.19 and 3.6% of lead by weight respectively.

For soil and interior dust lead, the values were 24 vs 842 mg/kg and 63 vs 233 $\mu g/m^2$.
Surface soil (0-1 or 2 cm) was sampled, and for sampling house dust, 0.09 m^2 areas on floors or windowsills that children could easily reach were wiped with a damp paper tissue. The samples were digested in concentrated nitric acid before analysis.
Comparison of the children most exposed to those living in the control area results in β-estimates of 8.1 µg/100 ml per g/kg for soil, and 38.8 µg/100 ml per mg/m^2 for house dust.
By questionnaire, information was gathered on a number of potential confounders: parental occupation, years since repainting, years since replacement of top soil, pica, distance from nearest road and traffic density of this road and others; a multivariate analysis has not yet been published, however.

23. Shellshear et al. (1975) studied 136 1-5 year old children living in Christchurch, New Zealand. Another group of 34 1-5 year olds, living in homes with gardens which contained more than 300 mg/kg of lead in the soil, was studied as well. The sampling depth was not reported; the samples were boiled in 0.6% hydrochloric acid before analysis. Of those who had lived at the same address for more than one year, 21 inner city children were compared to 47 suburban children. The blood lead levels (method of sampling not given, no quality control data) in these two groups were 25.4 vs 18.3 µg/100 ml. The soil lead levels of the gardens near the homes of these children averaged 1950 vs 150 mg/kg. Paint was suggested to be the main source of lead in the inner city soils. On the basis of these data, β would be estimated at 3.9 µg/100 ml per g/kg soil lead.
24. Watson et al. (1978) compared 27 lead workers' children with an average age of 4 years to 30 control children aged 3.3 years on average. Capillary blood samples (no quality control data) were taken, and house dust was sampled by wiping surfaces with cotton gauze swabs (method of extraction not reported). In addition, paint lead and water lead were measured. Blood lead levels were higher in children of lead workers (31.8 µg/100 ml, arithmetic mean) than in control children (21.4 µg/100 ml, ar.m.). The lead in dust levels were 2239 mg/kg and 718 mg/kg respectively. A β-estimate of

6.8 µg/100 ml per g/kg results.
Lead in paint and drinking water lead were not found to be different between homes of lead worker and control children.

25. Stark et al. (1982b) studied 377 children aged 0-6 years living in New Haven, Ct, US. The homes and gardens of these children were polluted with lead due to the presence of paint layers containing high concentrations of lead. Capillary blood samples were taken, and there was reference to quality control data. Pre-weighed cotton gauzes were used to sample house dust. Soil was sampled near the home, but the sampling depth was not given. Extraction methods for soil and house dust samples were not reported either. The geometric mean blood lead levels of the children ranged from 22.3-28.9 µg/100 ml, depending on age and housing category. Soil lead levels ranged from 300-1200 mg/kg, and house dust lead levels from 240-760 mg/kg, depending on the age of the home. Bivariate regressions of log PbB on log house dust lead and log soil lead were calculated, and resulted in β-estimates of 11.0 µg/100 ml per g/kg for house dust over the range of 0-750 mg/kg, and 10.2 µg/100 ml per g/kg for soil lead, over the range of 0-1000 mg/kg. These figures may contain some direct contribution of paint ingestion. A reanalysis of this study was performed by EPA (1983) and a multiple regression analysis now suggested a β for soil lead of only 2.0; this estimate was adjusted, however, for house dust lead.

Summary of results from other studies

Table 3.9 contains a summary of the findings from the studies just cited.

The results of these studies indicate a β for soil lead between 0.6 and 10.2 µg/100 ml per g/kg. The low 0.6 value is evidently out of line with the other values which range from 3.9 to 10.2 and which are only somewhat lower than those reported in tables 3.5 and 3.8.

For house dust lead, the β-estimates in table 3.9 range from 4.0 to 19.8. This is in line with the results in tables 3.5 and 3.8. Only in one study (nr. 22) was house dust lead reported as $\mu g/m^2$ in stead of mg/kg. The results of this study cannot be compared to those of others.

Table 3.9. Summary of findings from other studies

study nr.	β-estimate[1]	remarks
19	8.6 - 19.8 (hd)	1-6 yr olds; lead worker children;
20	0.6 (s) 4.0 (hd)	2-3 yr old children from high soil lead area (mining) compared to controls fecal lead suggested little ingestion of dust and soil
21	4.9 (s)	black preschool children; soil lead related to paint lead and traffic density; unadjusted estimate
22	8.1 (s) 38.8 (hd)	1-3 yr old children; soil and house dust contaminated by paint lead; house dust lead expressed as $\mu g/m^2$
23	3.9 (s)	1-5 yr old children; soils contaminated by paint lead
24	6.8 (hd)	lead worker children of preschool age
25	11.0 (hd) 10.2 (s)	0-6 year old children, living in high-lead paint homes

1 for units cf. table 3.5.

3.5. Summary of pathway impact estimates

It must be stressed that none of the 25 reviewed studies had as

its primary goal to establish quantitatively the relationship between environmental lead and blood lead in children. As a consequence, most studies do not permit straightforward calculation of α- and β-values, which are properly adjusted for the relevant confounders.

In the preceding sections, we have noted the central tendency of the α- and β-values rather than trying to separate acceptable from unacceptable studies. The criteria to do so must necessarily remain arbitrary to a certain extent, if only because published study results often do not permit clear-cut application of even well-defined criteria. If we were to apply the six criteria mentioned in section 3.1 strictly, no study would meet all of them as, for example, no study has tried to measure individual exposure to air lead. If any discrimination is to be made, some of the criteria have to be relaxed therefore. As minimum criteria we would like to propose:

a. environmental lead and blood lead measured at the same time and place; for soil and house dust, sampling at individual homes;
b. venous blood samples, with some reference to a quality control program.

Of the 11 industrial studies, this would leave the studies 1, 3, 5 and 8 with α-values of 1.7 (measured at a high level of exposure) and 3.3-5.3 µg/100 ml per $\mu g/m^3$ for lower levels of exposure, a playground dust β of 3.5 µg/100 ml per g/kg, and a soil lead β of 12.6 µg/100 ml per g/kg. Of the urban studies only study 14 would remain, with an α-value of 2.9.

No other studies fulfilled even these relatively lenient criteria.

When we drop the requirement of reference to a quality control program for the blood lead analysis, studies 4, 10, 11, 20 and 21 would become acceptable too. This would add α-values of 2.4-3.7, and 12.5-17.6 (from the study by Wagner et al. 1981), and β-values of 0.6 (from Barltrop's study) and 4.9 - 11.7 for soil, and 0.8 and 4.0 for house dust.

Application of these criteria evidently does not change the general picture, which puts most α-values between 3 and 5 µg/100 ml per $\mu g/m^3$, with some clear outliers on both sides of this range, and which puts β for soil lead between 5.0 and 10.0 µg/100 ml per g/kg.

For adults, who do not generally ingest dust or soil particles,

experimental studies have sufficiently demonstrated that α is about 1-2 µg/100 ml per µg/m^3 (Griffin et al. 1975, Azar et al. 1975, Chamberlain et al. 1978, Gross 1981). Earlier reviews have suggested that α may be somewhat larger in children than in adults (Ratcliffe 1981, Snee 1981, Hammond et al. 1981, Jones and Stephens 1983, Chamberlain 1983a) and the present review suggests that the difference may be as much as 2-3 fold. It must be stressed that probably the major part of this difference is caused by the fact that for children, additional pathways like dust and soil are much more important than for adults. The α-values consequently represent total lead intake from the environment rather than inhalation alone, as we avoided adjustment for other environmental pathways.

For soil lead, the unadjusted β's range from 0.6 - 15.5 µg/100 ml per g/kg. The 0.6 value is evidently an outlier as the remaining values are all between 3.9 and 15.5.
The 0.6 value comes from the only study area where soils were polluted by historical mining activities whereas in all other cases, contamination of the soil surface was actually going on or had only been stopped or reduced shortly before the study. It may be that the surface soil particles which were actually available for intake had a different lead content, compared to the lead content in the sample actually taken, in this study. This seems to be supported by the observation that the β for house dust in this study was much less out of line with the results from other studies.
Studies performed in areas where soils were predominantly contaminated by paint gave β-estimates for soil between 3.9 and 8.1 whereas studies near industrial sources in urban areas gave β-estimates for soil between 4.8 and 15.5. It may be that in the latter two types of studies, the influence of other pathways like air, which were more or less absent in the 'paint'studies, were reflected in the β-estimates.

For house dust lead, β-values ranged from 0.8 to 19.8 µg/100 ml per g/kg. The 0.8 value is an outlier, as the rest of the values was between 4.0 and 19.8. The 4.0 value was from the Barltrop et al. study which also gave a low β for soil lead, and in which, judging from the fecal lead data that where reported, children with a low intake of dust and soil were studied. The next lowest

value was 6.8.
Excluding some outlying values, the β's for soil and house dust lead are generally within a range of 3-4 from each other. All differences between groups in age, race, mouthing, exposure through other pathways, sampling and analysis methods, etc. evidently were not able to push the β-estimates further apart. The few β's derived for street and playground dust are also within the general range for soil and house dust lead.
For soil lead, β-values clearly above 10.0 come from the Omaha study (nr. 12), in which lack of adjustment for race probably inflated this estimate; from the Arnhem study (nr. 3), in which the overall level of exposure was low; from the Trail study but only when Trail was compared to a control town (within Trail, β-values were lower); and from the El Paso Study (nr. 4) in which the β-values were estimated from a reduction of PbB and lead in soil over time which was probably not yet completed. Nine other β-estimates from 7 different studies were all in the 3.9 - 10.2 range.
For house dust lead, β-values above 10.0 again come from the Omaha study (nr. 12); from one of the lead worker children studies (nr. 19) in which, however, only few children were studied and from which β's had to be estimated from exposure categories rather than averages; and from one of the paint studies (nr. 25). Generally, the 5.0 - 10.0 range is where most of the β-values for lead in soil, house dust, street dust and playground dust can be found.
Earlier reviews by Duggan (1980, 1983b) have suggested that a reasonable mid-point for β might be 5.0. These reviews have relied, however, more heavily on studies in which one or more of the other pathways were excluded, and in some cases, adjusted rather than unadjusted β-values were calculated.
As mentioned earlier, the size of the α-values was more or less unrelated to age, blood lead level and type of blood sampling. For the β-estimates, the presented evidence suggests the same.
This is not to imply that the blood lead/lead exposure relationship is independent of age, that curvilinearity does not exist and/or that type of blood sampling is irrelevant to blood lead level; it merely indicates that within the scatter of values found, the influence of age, blood lead level and method of blood sampling cannot be detected.

3.6. The scientific basis of standards for environmental lead

From the previous sections it will be clear that it is not easy to give an exact, quantitative picture of the impact of environmental lead pollution on children's blood lead. It is equally clear that public health authorities would like to have such a picture to derive standards for lead in air, soil, dust or other environmental media. The ambient air quality standard for lead as adopted in the US (EPA 1978) can be used to illustrate the complications involved.

The 1978 standard uses an α-estimate of 2, which is mainly based on the Silver Valley Lead Study, and which was derived after adjustment for soil lead. Apart from the various difficulties involved in the interpretation of the Silver Valley Lead Study (cf. section 3.2), this in fact means that a standard was adopted which under-estimates what will happen to children's blood lead when the concentration of lead in air is changed - as this will ultimately change the concentration of lead in other media as well, which is assumed not to happen by the adjustment procedure (cf. section 2.7.2).

Currently, the Standard is under revision; drafts of the Criteria Document issued in 1983 have emphasized three studies, i.e. the Silver Valley Lead Study, the Omaha Study (Angle and McIntire 1979) and the Belgian Smelter Study (Roels et al. 1980). In the drafts, secondary analyses of the data from these studies were presented in which the blood lead/air lead relationship was adjusted for soil lead and/or hand lead; the resulting α was now correctly interpreted as representing an inhalation slope; again however, the impossibility of manipulating air lead without affecting lead in soil, dust etc. was not adequately discussed - although it was correctly remarked that once soil and dust are polluted, other methods of control might be necessary apart from reducing lead in the air (Charney et al. 1983, Marcus 1984). If this remark might be interpreted that one is willing to keep soil lead and dust lead not only statistically, but also factually constant in areas where air lead is allowed to increase up to the standard, the adjusted relationship can indeed be used to predict the resulting blood lead rise. It is obvious, however, that this would be a rather impractical procedure.

An update of the review draft issued in September 1984 (EPA 1984) suggests that it may be better to adopt an aggregate approach,

which would emphasize air lead as an indicator of general multi-media environmental pollution. If this approach would be accepted, α would have to be approximately doubled. At present, it is not yet clear which approach EPA will adopt when it will finally publish its new air lead standard.

In the new draft, a β for soil and house dust of 2.0 µg/100 ml per g/kg is suggested, which is rather lower than the 5.0 - 10.0 range mentioned in this chapter. The review draft mixes adjusted and unadjusted β-values, however, and uses an adjusted value from the Stark et al. (1982b) study as an 'acceptable' mid-point value. As mentioned earlier, unadjusted β-values from the same study are in the order of 10.0 µg/100 ml per g/kg.

The scatter in the α- as well as the β-values further stresses the importance of using safety factors. One single mid-point value is evidently not sufficient to protect specific population groups which may differ in important ways from the average. In other areas of the Environmental Health field, it is more or less common practice to use safety factors of 2 or more when using epidemiological data, applied to the lowest exposure level where insult has been demonstrated (or to the highest where it was not), to derive a standard (WHO 1977b, 1978). It is quite remarkable that such a line of reasoning has seldom been applied to the environmental exposure impact estimate of lead. It is evident that a safety factor of two, applied to, for example, the 90-percentile of the α- or β-estimates alone would be sufficient to arrive at standards which are at least four times lower than the one currently in use in the US. This is even more important when it is realized that in establishing currently accepted safe levels of lead in blood, safety factors were not or only marginally used (cf. chapter 1).

On the basis of the observation that the current level of exposure to lead is quite close to the level where adverse health effects have been demonstrated in man and in animal experiments, Rostron (1982b) has remarked that if we were to decide now to which levels lead could be introduced in our environment, these levels would preferably be rather lower than the ones currently encountered. I would like to stress this point, from the observation that safety factors were not applied to the α-estimates used in most existing standards for air lead.

3.7. Urban/suburban differences in blood lead, associations between gasoline lead and blood lead, and the Turin Isotopic Lead Experiment

Urban/suburban or urban/rural differences of PbB in children were investigated in a number of studies in which environmental lead determinations were absent. Urban/suburban PbB differences were small in Germany (Anonymus 1981), larger in The Netherlands (Ligeon et al. 1981, Brunekreef et al. 1983) and in the US (Mahaffey et al. 1982a) and as large as 9.3 µg/100 ml in Ireland (Richardson 1982, Richardson et al. 1982). Urban/rural differences were absent in a Finnish study (Taskinen et al. 1982) and even negative in some German comparisons (Anonymus 1981).
Urban/suburban and urban/rural differences in PbB differ widely in size (or even sign) and this emphasizes the complexity of the lead exposure problem.
Studies on the association between gasoline lead consumption and children's blood lead have been performed in the US (Billick et al. 1979, 1980, Billick 1983, Annest et al. 1983, Pirkle 1983, Schwartz 1983, Rabinowitz and Needleman 1983, Rabinowitz et al. 1984b). In these studies, a significant association between blood lead and gasoline lead consumption was found. These associations have been disputed by representatives of the lead industry (Lynam et al. 1983, Pierrard et al. 1983) but an independent panel of biostatisticians has found them to be valid (Rosenblatt et al. 1983).
The Turin Isotopic Lead Experiment (Facchetti and Garibaldi 1972, Facchetti 1979, Facchetti and Geiss 1982) is a large scale enterprise which consisted of changing the isotopic ratio of lead in gasoline in the Turin area for a number of years with the explicit goal to evaluate the importance of gasoline lead as a source of lead in human blood. Samples of air, food, blood etc. were taken to evaluate the contribution of gasoline lead to blood lead. On the basis of the available evidence, this contribution was estimated to range from at least 28% for adults to at least 46% for children, for the area under investigation. Preschool children became only involved in the study when it was already halfway, however, and numbered less than ten (Elwood 1983b). For this reason, the estimated percentage for children cannot be considered as very reliable.
For a further discussion, cf. Brunekreef 1984.

4. THE RELATIONSHIP BETWEEN ENVIRONMENTAL LEAD AND BLOOD LEAD IN DUTCH CITY CHILDREN

4.1. Preface

In this chapter, our study on the relationship between environmental lead and children's blood lead performed in 1981 is described in detail.
The background of this study was discussed in the Introduction. Briefly, the study was meant to investigate to what extent the differences in blood lead levels between Dutch urban and suburban children which had been observed in the First E.C. Blood Lead Survey in 1979 could be explained by differences in environmental exposure to lead.

4.2. General design of the study

As a Second EC Blood Lead Survey was planned in the spring of 1981, it was decided to do a detailed environmental exposure study in a group of urban and in a group of suburban children. The design of the study was cross-sectional, which means that exposure measurements were performed shortly before or at the time of the blood sampling.
According to the "Guidelines on Studies in Environmental Epidemiology" (WHO 1983), the cross-sectional design is one of several possible design options for environmental epidemiological studies. A major advantage of a cross sectional study is that it can be performed quickly and relatively easily, and that one can actually measure exposure and response within the same, short period of time. A disadvantage is that changes in exposure and response cannot be monitored, and that hence, inferences of causality from the results of cross-sectional studies are inherently weaker than those from, for example, prospective or follow-up studies.
Table 4.1 lists the various designs with their problems and advantages, as given in the "Guidelines".

Table 4.1. Major features of various study designs in environmental epidemiology (reprinted with permission from WHO 1983).

Study design	Population	Exposure	Health effect	Confounders are:	Problems	Advantages
Descriptive study	Various sub-populations	Records of past measurements	Mortality and morbidity statistics, case registries, etc.	Difficult to sort out	Hard to establish cause-result and exposure-effect relationships	Cheap, useful to formulate hypothesis
Cross-sectional study	Community or special groups; exposed vs. non-exposed groups	Current	Current	Usually easy to measure	Hard to establish cause-relationship; current exposure may be irrelevant to current disease	Can be done quickly; can use large populations; can estimate extent of problem (prevalence)
Prospective study	Community or special groups; exposed vs. non-exposed groups	Defined at outset of study (can change during course of study)	To be determined during course of study	Usually easy to measure	Expensive and time consuming; exposure categories can change; high dropout rate	Can estimate incidence and relative risk; can study many diseases; can infer cause-result relationship
Retrospective cohort study	Special groups such as occupational groups, patients, and insured persons	Occurred in past - need records of past measurements	Occurred in past - need records of past diagnosis and measurements	Often difficult to measure because of retrospective nature (e.g., past smoking habits)	Changes in exposure/effect over time of study; need to rely on records that may not be accurate enough	Less expensive and quicker than cohort prospective study giving similar response, if sufficient past records are available
Time-series study	Large community with several million people; susceptible groups such as asthmatics	Current, e.g., daily changes in exposure	Current, e.g., daily variations in mortality	Often difficult to sort out, e.g., effects of influenza	Many confounding facters, often difficult to measure	Useful for studies on acute effects
Case-control study	Usually small groups; diseased (cases) vs. non-diseased (controls)	Occurred in past and determined by records or interview	Known at start of study	Possible to eliminate by matching for them	Difficult to generalize due to small study group; some incorporated biases	Relatively cheap and quick; useful for studying rare diseases
Experimental (intervention) study	Community or special groups	Controlled/known	To be measured during course of study	Can be measured; can be controlled by randomization of subjects	Expensive; ethical consideration; study subjects' compliance required; drop-outs	Well accepted results; strong evidence for causality
Monitoring and surveillance	Community or special groups	Current	Current	Difficult to sort out	Difficult to relate exposure data with effects	Cheap when using existing monitoring and surveillance data

4.3. Choice of population

As study population, children of 4-6 years old were chosen. Children of this age are part of the population most at risk (cf. chapter 2). In The Netherlands, virtually all children of this age attend nursery schools and it was consequently decided to use nursery schools as the principal unit of selection in this study. The areas of study chosen were the inner city of Rotterdam (1) where children of 5 nursery schools in 2 different areas were invited to participate; the suburb Ommoord of Rotterdam (2) where 2 schools were selected; one area in the inner city of The Hague (3) where the local health authorities preferred not to use schools as a unit of selection but rather to draw a random sample from the population registry; two areas in Zoetermeer (4) which is a suburb of The Hague. Here, 4 schools were selected.
The inner cities of Rotterdam and The Hague were chosen for the obvious reason that in 1979, this was where the highest blood lead levels had been found. As suburban areas, suburbs of these two cities were chosen to minimize the influence of inter-city differences.
The use of nursery schools as a unit of selection has as disadvantage that the study results may not be representative for the general population of children living in the study areas. All schools were selected after careful consultation with the local health authorities to ensure that they were typical for nursery schools in the area under study. The investigation of differences of study results between schools within areas is a means to gain insight in the consequences of this selection procedure. The use of a different method of selection in one area (The Hague) constituted another problem.
Only children of Dutch nationality were invited to participate to avoid language problems when interviewing the parents and to avoid difficulties in the interpretation of the study results due to differences in dietary habits etc. between Dutch children and children of other nationalities.
The parents of the children were invited by letter to let their children participate in the study. In the EC blood lead survey, larger numbers of children needed to participate than the maximum number that could, for practical reasons, participate in the environmental study. For this reason the parents were given the choice whether they would like to have their children participate

in the blood lead study alone or in the environmental study as well. This may have introduced a selection bias, and therefore the PbB results of the complete study population will be compared to those of the population participating in the environmental study (section 4.6). The original study plan was to have 50 children from each of the 4 areas participate in the combined environmental-blood lead study, and to have an additional 50 children per area participate in the blood lead study only. Table 4.2 shows the number of children invited and the response figures.

Table 4.2. Response figures

area	number of children invited	non-response	blood sample taken (% of children invited)	participant in environmental exposure study (% of children invited)
Rotterdam	296	105	191 (65%)	126 (43%)
The Hague (June 1981)	100	83	17 (17%)	16 (16%)
The Hague (Sept.1981)	200	129	71 (36%)	--
Zoetermeer	200	108	92 (46%)	53 (27%)

In The Hague, communication problems with the local health authorities led to delays in the mailing of the requests; it was decided to invite only the parents who could be reached before the summer to let their child participate in the environmental as well as in the blood lead study.
Table 4.2 shows that the projected study sample size was reasonably attained in Rotterdam and Zoetermeer, but not in The Hague.

4.4. Assessment of exposure - methods

4.4.1. General description of exposure assessment efforts

Chapter 2 has already discussed the problems associated with measuring exposure of children to environmental lead. The inadvertent ingestion of dust and dirt is hard to quantify and at present, only crude approximations are possible.
The number of potential pathways is great, and there are no studies in the published literature in which all potential pathways have been adequately quantified (cf. chapter 3).
In our study too, choices had to be made about how, with the available resources, exposure could be assessed most efficiently. Table 4.3 summarizes the exposure pathways that we decided to quantify in our study. Exposure was measured in the month prior to blood sampling, for the reasons given in chapter 2.

Table 4.3. Lead exposure variables

Outdoor environment:	lead deposition
	lead in soil
	lead in sidewalk dust
	lead in school playground
Indoor environment:	lead deposition (homes and schools)
	lead in floor dust (homes and schools)
	lead in drinking water (homes and schools)
Personal:	lead on hands

In the outdoor environment, lead deposition was measured to assess the transfer of lead into the study areas from the air; lead in garden soil and school sand pits, in school playgrounds and on sidewalks was measured to assess ingestible lead.
The concentration of lead in air was not measured. The Rijnmond Central Environmental Agency monitors lead in air continuously on three locations in the Rotterdam area, and the results showed that long term average concentrations had been below 0.5 $\mu g/m^3$ for several years before the start of the study already, and that

urban-suburban differences were in the order of 0.1-0.2 $\mu g/m^3$. At these concentrations, inhalation could not be expected to explain urban-suburban differences of blood lead in children.
In the homes and schools of the children, lead deposition and lead in floor dust were measured, to assess ingestible lead. Lead in drinking water was measured also in homes and schools, as urban-suburban differences in blood lead could conceivably be caused by differences in drinking water lead as well as by differences in environmental lead.
The lead concentration in indoor air was not monitored, for reasons mentioned above, and because one could expect it to be even lower than in outdoor air (cf. section 2.2). As a result, differences in indoor air lead concentration between inner city and suburbs were supposedly very small.
To assess whether indeed ingestion of dust and dirt could contribute to blood lead differences, it was decided to measure lead on the hands of the children as well. Exposure modifying factors were assessed by asking specific questions to the parents of the children.

4.4.2. Exposure to lead in the outdoor environment

Lead deposition
Lead deposition was measured for one month at 5-10 locations per study area using standard deposit gauges which were set up at 2 m height. The gauges had an internal diameter of 18.9 cm. The location of sampling was mostly the playground of the schools from which the children were participants in the study. This enabled us to assess not only the between-area differences in lead deposition, but to some extent also the within-area differences. To each individual child, the lead deposition value was assigned which was measured on its school playground or nearest to its home. Alltogether, 8 different lead deposition values were thus assigned to the 195 children of the study population. In this study, repeated measurements per location were not performed. From our earlier work in Arnhem, where we used the same method of measurement, we were able to make some estimate of within-location variability.

Lead in soil

Soil was sampled in the gardens of each home of the study population, if a garden was present and the soil was not completely unaccessible due to pavements. All samples were composite, i.e. a mixture of a number of samples taken from different locations within the garden. Soil samples were also taken from the sand pits on the school playgrounds. Only the top 0-5 cm was sampled. The samples were extracted with 3 M HCl for 3 hours in a boiling water bath. The efficiency of this method was checked against digestion with a 1:4 $HClO_4/HNO_3$ mixture, and it was found that digestion did not yield significantly higher contents of Pb than this extraction method (Keizer et al. 1982). To each individual child, a lead in garden-soil value was assigned on the basis of the sample taken in its own garden. For the majority of inner-city children, this meant that no soil lead value could be assigned to them, because they lived in homes without gardens. To each individual child a value for the concentration of lead in the school sand pit was assigned. This was not possible for the The Hague children, as they were not selected from schools.
Repeated measurements per location were not performed. Lead in soil is very immobile, and it is not to be expected that composite samples, taken within a few months from the same location, will show large differences in concentration.

Lead in sidewalk dust and playground dust

Street dust was sampled on street sidewalks near the homes of the study population, on about 10-40 locations per study area. A specially designed vacuum cleaner was used to sample particles of less than 0.3 mm in diameter as these can be expected to stick to hands, objects etc. better than the larger particles. The samples were extracted with 10 M HCl for 30 minutes at room temperature. The efficiency of this method was checked against digestion with a 1:3 $HClO_4/HNO_3$ mixture, and was found to be adequate (Brunekreef et al. 1978).
It was decided to measure the load per area rather than the concentration of lead in the dust, as it was felt that this would give a better indication of the amount of available lead per surface unit. On each location, 2 separate samples from adjacent 1 m^2 areas were taken. After about 4 weeks, each location was visited again to take repeat samples. Samples were taken in dry weather from dry sidewalks only. To each individual child, an

average lead in street dust value was assigned if a sampling location was sufficiently near. For 104 children, this was the case.
From paved areas of school playgrounds, dust samples were also taken, using the same method. To each child, a school playground dust lead value was assigned if samples had been taken at its school.

4.4.3. Exposure to lead in the indoor environment

Lead deposition indoors
In each home of the study population, indoor deposition of lead was measured during one month. Two samples per home were taken. If possible, these were taken in the livingroom and in the child's bedroom. If this was not possible, two samplers were usually placed in the livingroom. The samplers were plastic plates of 30 x 40 cm which were greased with paraffin (110 cP viscosity at 20 °C) to make the deposited dust stick. In the laboratory, the paraffin was removed with petroleumether and the dust particles were collected on a filter for further handling. The extraction method was the same as described for sidewalk dust. To each child, the average value of the samples taken in its home was assigned. The fact that duplicate samples were taken in each home enabled us to evaluate the within-home variability of the lead deposition values.
In our earlier study in Arnhem, 3 consecutive samples of one month were taken using this method. The within-home variability over time of the lead deposition values can be calculated from these results, and will be reported.
In the schools, lead deposition was measured in two different classrooms per school, on two different locations per classroom. The average of these values was assigned to the children visiting the school.

Lead in floor dust
Dust was sampled from the floors in each home of the study population using the same equipment which was used to measure lead on sidewalks.
In each home, a sample was taken from 2 different 1 m^2 surfaces,

which were either both in the livingroom or in the livingroom and one other room (usually the child's bedroom). After about 4 weeks, two repeat samples were taken. The extraction method was the same as for pavement dust. To each child, the average value of all samples, taken in its home, was assigned.
In the schools, duplicate samples were taken from 2 classrooms per school. Here also, repeat samples were taken after about 4 weeks. To each child, the average of all values obtained in its school was assigned.

Lead in drinking water
In each home, one sample of tap water was collected in the early morning before flushing using acid-rinsed containers. In the schools, samples could not be taken before flushing, so only flush samples were available from the schools.
The lead concentration in first-flush samples appears to be well correlated with the lead concentration of integrated samples over a period of one week. Haring (1984) found a correlation coefficient of 0.69.
Repeat samples were not taken. A recent study from Seattle (Sharrett et al. 1982a, 1982b) has established that within-home variability of lead in tap water over time can be appreciable.

4.4.4. Lead on children's hands

After playing in the school playground for at least 15 minutes on a dry day, the dominant hand of each child was rinsed with slightly acidic water to remove the lead from it. Plastic containers containing 0.5 liters of water were used, and the children were invited to stir the water with their hand for about 10 seconds. This was only done once. Consequently, no information was obtained on the variability over time of the lead-on-hand values.

4.4.5. Chemical analysis

All analyses were performed with atomic absorption spectrophoto-

metry. The flame technique was used for all analyses except the analysis of lead in drinking water, and the analysis of lead in the water used to take the hand samples. These were analysed using flameless electrothermal atomization. The soil samples were analysed by the Oosterbeek Laboratory for Soil and Plant Research. To obtain data on the quality of the flameless analyses, 20 samples were sent to the National Institute for Water Supply (dr. BJA Haring) in Voorburg. In a regression analysis of the results, slope and intercept of the regression line were not significantly different from one and zero respectively.

4.5. Assessment of exposure - results

4.5.1. Results of outdoor measurements

Lead deposition outdoors

In table 4.4, the lead deposition values are given for each study area. There was a clear difference between the urban and the suburban results, the lowest value in the urban areas being higher than the highest value in the suburban areas.

Tabel 4.4. Lead deposition outdoors per area

area	arithmetic mean lead deposition ($\mu g.m^{-2}.d^{-1}$)	range	n of samples
Rotterdam, inner city	643	394-957	9
Rotterdam, suburb	220	144-315	6
The Hague, inner city	369	317-439	5
Zoetermeer, suburb	125	73-278	10

Lead in soil

In table 4.5, the soil lead values for home gardens are given. The distribution for the garden soil values was positively skewed, so the geometric mean rather than the arithmetic mean is reported. The concentrations in the urban areas were much higher than in the suburban areas, but this observation rests on a limited number of samples in the urban areas.

Table 4.5. Lead in soils in gardens per area

area	geometric mean soil lead in gardens (mg/kg)	range	n of samples
Rotterdam, inner city	(336)	-	1
Rotterdam, suburb	34	6-184	56
The Hague, inner city	176	35-527	6
Zoetermeer, suburb	16	3- 75	33

The school sand pit soils contained very little lead in both the urban and the suburban areas (5-6 mg/kg). This was probably caused by the fact that the top layer of sand in these sand pits is regularly being replaced.

Lead in sidewalk and school playground dust

In table 4.6, the values for lead in sidewalk dust are given. Again, the urban areas had higher amounts of lead on the sidewalks than the suburban areas, although the difference was less pronounced than for lead deposition outdoors, as can be seen from

the overlapping ranges.
On school playgrounds, 337 $\mu g/m^2$ (Zoetermeer), 364 $\mu g/m^2$ (Rotterdam suburb) and 1120 $\mu g/m^2$ (Rotterdam inner city) was found respectively.

Table 4.6. Lead in sidewalk dust per area

area	geometric mean lead in sidewalk dust ($\mu g/m^2$)	range	n of samples
Rotterdam, inner city	532	168-2304	37
Rotterdam, suburb	318	113-1155	36
The Hague, inner city	428	81-1339	10
Zoetermeer, suburb	126	46- 497	21

4.5.2. Results of indoor measurements

Table 4.7 shows the results of the indoor lead deposition measurements. Table 4.8 contains the results of the floor dust measurements. In schools, a deposition of 4.59 $\mu g\ m^{-2}d^{-1}$ (Zoetermeer), 4.29 $\mu g\ m^{-2}d^{-1}$ (Rotterdam suburb) and 11.74 $\mu g\ m^{-2}d^{-1}$ (Rotterdam inner city) was found. The amount of lead on school floors was 40 $\mu g/m^2$ (Zoetermeer), 29 $\mu g/m^2$ (Rotterdam suburb) and 100 $\mu g/m^2$ (Rotterdam inner city) on average respectively. Table 4.9 gives the tap water lead concentrations. For all of these variables, the urban concentrations were higher than the suburban concentrations again.

Tabel 4.7. Indoor lead deposition per area in homes

area	geometric mean lead deposition in homes ($\mu g\ m^{-2} d^{-1}$)	range	n of samples
Rotterdam, inner city	2.86	0.10-20.86	48
Rotterdam, suburb	0.99	0.10- 8.40	67
The Hague, inner city	4.32	1.95-27.05	13
Zoetermeer, suburb	1.51	0.48- 4.40	49

Table 4.8. Lead in floor dust in homes per area

area	geometric mean amount of lead ($\mu g/m^2$)	range	n of samples
Rotterdam, inner city	81	5-740	43
Rotterdam, suburb	30	1-410	62
The Hague, inner city	58	22-166	11
Zoetermeer, suburb	32	3-201	50

Table 4.9. Lead in tap water in homes per area

area	geometric mean tap water lead conc. in homes (µg/l)	range	n of samples
Rotterdam, inner city	20	1-126	46
Rotterdam, suburb	2	1- 50	60
The Hague, inner city	21	1- 85	16
Zoetermeer, suburb	1	1- 4	53

In schools, 1 µg/l (Zoetermeer and Rotterdam suburb) and 6 µg/l (Rotterdam inner city) was found.
The lead on hands data are summarized in table 4.10. Again, the urban values were clearly higher than the suburban values.

Table 4.10. Lead on hands of children, per area

area	geometric mean amount of lead on dominant hand (µg)	range	n of samples
Rotterdam, inner city	12	1-96	44
Rotterdam, suburb	5	1-21	65
The Hague, inner city	--	--	
Zoetermeer, suburb	4	1-18	37

4.5.3. Variability of lead exposure measurements

Following the reasoning developed in section 2.7.3, calculations were performed to establish the within- and between-subjects variability of the lead exposure measurements which were used.
In Appendix 1 it is being argued that in epidemiological studies, a relevant indicator of the quality of an exposure variable is the reliability coefficient, which has been defined as within-subjects variance divided by between-subjects variance (σ^2e/σ^2t). If this index is zero, reliability is perfect; if it becomes large, reliability is poor.
For most exposure variables, repeated measurements were available from this study or from our former work. These repeated measurements allow calculation of two types of reliability coefficients: first, an index for the average of all repeated measurements; second, an index for the reliability associated with individual measurements.
The first index is necessarily smaller than the second, as the average of a number of variable measurements is less uncertain than the individual measurements from which it was calculated.
The SPSS program RELIABILITY was used to perform the necessary calculations. In the following tables, the reliability coefficients for most of the exposure variables are given. For lead in soil, tap water and on children's hands they could not be calculated. Most probably, the coefficients are close to unity for soil lead, but not for tap water and hand lead.
The coefficients were calculated for the ln-transformed variables, as these were used in the further analysis of the data. Also, the coefficients were calculated for exactly those groups for which adjusted associations between blood lead and the respective exposure indices were investigated (section 4.10).
In table 4.11, the results of the reliability calculations are given for a number of outdoor variables. For outdoor deposition, repeated measurements were only available from our earlier study in Arnhem. For lead on sidewalks and playgrounds, data were available from the present study.

Table 4.11. Reliability of outdoor exposure variables

variable	reliability coefficient for average value	number of repetitions	number of children	reliability coefficient for single measurements
outdoor deposition Arnhem	0.89	2*	91**	1.85
lead on sidewalks (this study)	1.49	2*	91	3.16
lead on playgrounds (this study)	0.84	2*	156***	1.72

* repetitions in time

** exposure estimates obtained from interpolation from data from 13 locations

*** exposure data assigned on the basis of measurements performed at 11 different schools

In table 4.12, reliability coefficients are presented for indoor exposure variables. For indoor lead deposition and lead on home floors, data were available from our earlier study in Arnhem as well as from the present study. For lead on school floors, data were only available from the present study.

Table 4.12. Reliability of indoor exposure variables

variable	reliability coefficient for average value	number of repetitions	number of children	reliability coefficient for single measurements
indoor lead deposition in homes (Arnhem)	0.24	3*	91	0.74
indoor lead deposition in homes (this study)	0.75	2**	157	1.54
lead on home floors (Arnhem)	0.14	4***	91	0.59
lead on home floors (this study)	0.33	4***	148	1.45
lead on school floors (this study)	0.35	2*	156****	0.70

* repetitions in time
** repetitions in space
*** repetitions in time and space
**** exposure data assigned on the basis of measurements at 11 different schools

Theoretically, the reliability coefficient for single measurements is exactly equal to the coefficient for the average value times the number of repetitions (Liu et al. 1978), but the RELIABILITY program calculates a coefficient which is corrected acccording to Kristof (1969). It can be seen from the tables that this

correction leads to a small reduction of the reliability coefficients for the average value.

4.5.4. General discussion of exposure assessment results

From the results of the exposure assessment it is clear that relatively large differences exist between inner city areas and the suburbs. For most exposure variables, the difference is about two- or three-fold; for lead in soil, the difference appears to be larger but this is based on very few inner city samples only. Lead in tap water is very low in the suburbs, whereas in the inner cities, it is present in higher quantities.
The lead deposition outdoors in the inner city of Rotterdam was slightly higher than the values found in Arnhem in 1978. In some other large European cities deposition values were found which were somewhat lower (Lahman and Seifert 1981, Chamberlain 1983b) or equal (Scholl et al. 1983) to the values found in Rotterdam.
Lead in street and sidewalk dust has not frequently been reported as the amount of lead per area unit; Hamilton et al. (1984) have reported an average value of 56000 $\mu g/m^2$ for a residential street in the UK. This value is much higher than even our highest inner city value, and probably reflects differences in methodology.
Indoor deposition was lower than previously found in Arnhem, using the same method. Recently, Seifert et al. (1984) reported results obtained with a comparable method; for city areas, the values were comparable to ours whereas in the immediate vicinity of a lead smelter, much higher values up to 100 $\mu g\ m^{-2}d^{-1}$ and above were found. On floors, the values were again somewhat lower than those previously found in Arnhem. In homes polluted by paint lead, Reeves et al. found an average value of 233 $\mu g/m^2$, using moist tissues for sampling. The urban control value of 63 $\mu g/m^2$ was comparable to our inner city values.
Lead in drinking water was clearly different between inner cities and the suburbs. The inner city geometric mean levels remain, however, well below recognized standards which usually aim at keeping the lead concentration in drinking water below 50 µg/liter. Nevertheless, tap water lead could be an important confounder of relationships between environmental lead and blood lead even at these levels, as Elwood (1984) has pointed out.
The amount of lead found on the children's hands after playing

outdoors was not excessive. Using a comparable method, Roels et al. (1980) found levels of 244-436 µg per hand in children living and playing close to a large lead smelter. In city areas, they found an average of 12.7-20.4 µg per hand. The Belgian city values are in close agreement with ours, whereas near the smelter much higher values were found.
On the school playgrounds, generally larger amounts of lead were found than on sidewalks and streets in the same area. Indoor lead deposition in schools was also clearly larger than in homes in the same area; lead on school class floors, however, was not different from lead on home floors.
It could be argued that the presence of a group of children in and near the school increases movement and resuspension of dust; in a study in the United States, it has been found that the dust load of indoor air was increased in homes of families with young children (Moschandreas et al. 1978).

The reliability coefficients shown in tables 4.11 and 4.12 indicate that for most variables, within-subjects or within-locations variance was relatively large compared to total variance. For several variables, the reliability coefficient for single measurements was greater than 1, indicating that appreciable underestimation of the effect of environmental lead on blood lead will occur when these variables are measured only once for a study population, and when the results are entered into a regression analysis. Replication of measurements in time and space leads to a better quality of the data, as can be judged from the difference between the two types of reliability coefficients.
The observed variance of outdoor deposition was about 6 times as large in this study as it was in the Arnhem study. Most probably, this indicates that the actual reliability coefficient for the deposition data in this study was much smaller than for the Arnhem deposition data.
Interestingly, reliability was better for the home indoor variables measured in Arnhem than in this study. In this study more emphasis was laid upon obtaining data from different rooms in the home, whereas in Arnhem, repeat samples were usually taken from the same room. Calculations not reported here show that for the data obtained in this study as well, reliability is better when the repeat samples were taken from the same room.

The "Guidelines" (WHO 1983) stress the importance of obtaining representative exposure estimates. In this study, an effort was made to sample the micro-environments in which the individual children who participated in the study actually live and play. It should nevertheless be noted that the actual exposure variable of interest - ingestion of dust and dirt - has not been measured directly and it is doubtful whether direct measurement is possible at all. It is interesting that in the "Guidelines", the example of environmental exposure of children to lead is used to emphasize the difficulties involved in obtaining a reliable environmental exposure assessment. The "Guidelines" then proceed to evaluate the usefulness of biological monitoring for lead in blood, as a measure of integrated exposure to lead from all sources. There can indeed be no doubt that it is quite difficult to make an accurate quantitative estimate of the amount of lead which is actually entering the body by environmental monitoring alone. The goal of our study, however, was to evaluate the relative importance of environmental lead exposure for the explanation of urban-suburban differences in children's blood lead levels (i.e., in integrated exposure to lead from all sources).

4.6. Assessment of the concentration of lead in blood

As mentioned in previous sections already, the "effect" or outcome variable used in this study was the concentration of lead in blood. In section 2.4, the usefulness of measuring lead in blood as an indicator of recent, integrated exposure has been discussed.
In this study, blood sampling and analysis were performed within the framework of the second EC blood lead survey (Ligeon et al. 1981, Brunekreef et al. 1983, Noij et al. 1984).
All samples were taken by a trained nurse using venous puncture; only in The Hague, physicians of the School Health Service preferred to do the blood sampling themselves. All materials were supplied and tested by the National Institute of Public Health where the analyses were carried out. During the study, the National Institute of Public Health participated in a European Quality Assurance Programme for blood lead analyses. The standard deviation of the method was found to be 1.8 µg/100 ml in the range of

10-60 µg/100 ml. Within this range, the NIPH-results were at the median of the results of the collective of laboratories which participated in the Quality Assurance Programme (Brunekreef et al. 1983, Noij et al. 1984).
All samples were taken in May and June 1981. For a group of children living in The Hague, samples were taken in September 1981; none of these participated in the environmental exposure study.
The results of the blood lead measurements are given in tables 4.13-4.15. The 50-, 90- and 98-percentiles are given to allow direct comparison with the standard for lead in blood discussed earlier (cf. Introduction).
The results indicate a consistent difference between urban and suburban children. The differences were statistically significant (t-test on geometric means, $p < .001$).
The differences of geometric mean blood lead levels between suburbs and between schools within suburbs were small. The differences between inner city areas, subareas, and schools within (sub)areas were somewhat larger, indicating less homogeneity within inner city areas than within suburbs. Partly, the small number of children sampled in some schools may be responsible for this finding. Even in inner city areas, blood lead levels were below existing standards.
For the evaluation of the EC Blood Lead Survey results, the Dutch Department of Public Health has used a stricter Guideline than the official EC-Guideline; a 50-percentile of 20 µg/100 ml, a 90-percentile of 25 µg/100 ml and a 98-percentile of 30 µg/100 ml was used for children in The Netherlands.
From the tables, it is clear that in no area these values were exceeded in the children who were examined. This indicates that a rather large drop in children's blood lead values had taken place between 1979 and 1981, in at least the inner cities of Rotterdam and The Hague. In 1979, study population selection procedures were equal to those used in 1981 in both cities. It was not considered likely that laboratory practices had shifted enough to explain even a limited part of the blood lead reduction. Petrol lead had been reduced in The Netherlands by January 1, 1978, and this could lead one to speculate that a delayed effect of this reduction has manifested itself in the blood lead data. There are no specific data available, however, to give firm ground to this speculation (Brunekreef et al. 1983).

Table 4.13. PbB (µg/100 ml) in complete study population (n=371)

area	50 percentile	90 percentile	98 percentile	range	n of children
Rotterdam, inner city	13	18	22	4-31	99
Rotterdam, suburb	8	11	13	4-15	92
The Hague, inner city	13	19	23	5-23	88
Zoetermeer, suburb	8	11	15	4-16	92
Guideline	20	25	30		

Table 4.14. PbB (µg/100 ml) in participants in environmental exposure study only (n=195)

area	50 percentile	90 percentile	98 percentile	range	n of children
Rotterdam, inner city	13	19	23	7-31	54
Rotterdam, suburb	8	11	14	5-15	72
The Hague, inner city	11	19	21	7-21	16
Zoetermeer, suburb	8	11	14	4-15	53
Guideline	20	25	30		

Table 4.15. PbB levels in urban and suburban children, participating in the environmental exposure study, per sub-area and school

area	subarea	school	geometric mean blood lead level (µg/100 ml)		n
Rotterdam, inner city	Spangen		11.6		20[1]
		1		11.0	13
		2		13.0	6
	Oude Westen		14.0		34[1]
		3		13.2	21
		4		15.1	7
		5		14.8	7
Rotterdam, suburb	Ommoord		8.2		72
		6		8.0	33
		7		8.3	39
The Hague, inner city	Regentesse-wijk		11.5		16
Zoetermeer, suburb	Buitenwegh	8	7.9		29
	Meerzicht		8.0		22
		9		8.4	6
		10		8.7	9
		11		6.8	7

1. Some children visited schools outside their living area

4.7. Factors affecting lead levels in the environment

The levels of lead in the environment are affected by various factors. If environmental lead were found to be a determinant of blood lead in this study, it would be of interest to find out which were the main determinants of environmental lead.
As the areas of study did not contain major lead emitting industries, it was fairly certain that lead deposition was mainly a

function of traffic-related lead pollution. For lead in other media, other sources were conceivable, however.
Flaking paint is a potential source of lead in street dirt, soil and lead in floor dust and indoor deposition. The investigators in the field recorded the visual presence of flaking paint indoors and outdoors when visiting the homes of the study population, as it was considered possible that in some old homes in the inner city areas, paint layers containing high levels of lead could still be present, as we found in Arnhem in our earlier investigations (Brunekreef et al. 1978).
Hobbies and parental occupations involving the use of lead are potential determinants of indoor lead pollution. Questions were asked about these factors (cf. Appendix 2). Small neighbourhood businesses like garages conceivably pollute their immediate surroundings with lead; their presence was recorded.
The pollution level on streets may have been influenced by recent re-paving of the street; the parents of the study children were questioned about this.
It was noted whether the streets were transformed into residential precincts (with restricted rights to traffic flow), as this tends to reduce the amount of traffic in a street, and thereby possibly reduces lead pollution levels as well. Dogs (and some other pets) may introduce dust and dirt into the home, and may increase indoor lead pollution this way; their presence was recorded as well.

4.8. Factors affecting ingestion and internal exposure

As mentioned in section 2.3, the amount of lead inadvertently ingested depends on mouthing habits and personal cleanliness. One of the parents of the child (usually the mother) was interviewed on mouthing activity and personal cleanliness of the child. The questions are given in Appendix 2.
There are indications in the literature that milk consumption is inversely related to the concentration of lead in blood (section 2.5). For this reason, questions were asked about the consumption of milk and milk products, and the volume of the child's "favourite cup" was measured.

4.9. Confounding factors

A confounder is a known determinant of the outcome variable under study, which is related to the determinant of interest to an extent that adjustment for it reduces or eliminates a bias in the estimation of the 'true' relationship between the outcome variable and the determinant of interest (section 2.6).
In the case of environmental exposure to lead, many potential confounders exist. They were listed in section 2.6.
In the framework of this study, the following main potential confounders were measured:

a. lead in tap water (already discussed in section 4.5)
b. age and sex of the child
c. crowding (number of persons living in the home divided by the number of rooms)
d. incompleteness of family
e. consumption of self grown vegetables from polluted gardens
f. consumption of canned food
g. use of self-glazed pottery
h. education of parents.

Although some attention was paid to specific sources of dietary lead (a and e-g), the amount of lead consumed with food as such was not measured.
In The Netherlands, the main grocery chains are distributed through urban as well as suburban areas, and it is not likely that there are large systematic differences in the lead contents of the same food items offered for sale in different areas. It is assumed that by adjustment for socio-economic indicators, potential S.E.S. dependent differences in the choice of dietary components are adjusted for as well.
To the author's knowledge, no study has ever systematically compared the lead content of diets consumed in urban and suburban areas in The Netherlands (cf. section 2.6), so that it remains to be proven that it is an actual confounder of the relationship between environmental lead and blood lead in children. As indicated in section 2.6, the available data on food consumption patterns in The Netherlands do not suggest that elevated blood lead levels, found in inner city areas, are likely to be caused by dietary lead intake (tap water excluded).
Most confounders mentioned in this chapter were measured by questionnaire. For the phrasing of the questions, the reader is

again referred to Appendix 2.

4.10. The relationship between environmental lead and blood lead

4.10.1. General description of data analysis procedure

From sections 4.5 and 4.6 it was already clear that the concentrations of lead in children's blood and in the environment were different between urban and suburban areas in this study. The main purpose of the statistical analysis of the data was therefore to establish whether this difference would remain after adjustment for a number of potentially relevant factors. If the difference remained, it would be of interest to find out which were the main determinants of environmental lead in this study.
First, a set of 12 adjustment variables was selected; a backward elimination procedure was used to reduce this set to a smaller set of significant predictors of blood lead, which was further to be used as a fixed set of adjustment variables in the analysis of the associations between environmental lead and blood lead.
Then the associations between environmental lead and blood lead were analysed. Eight different indicators of general environmental lead pollution were used and each was tested separately.

4.10.2. Selection of adjustment variables

Of the potential confounders mentioned in section 4.9, the consumption of self-grown vegetables and the use of self-glazed pottery for food preparation or storage were not considered for further analysis, as both were virtually absent in the study population (positive answers in 2 and 6 individual cases respectively).
This left lead in tap water, age and sex of the child, crowding, incompleteness of family, parental education (for which maternal education was chosen as an index as this may more closely reflect relevant aspects of child care than paternal education) and consumption of canned food as potential confounders.
Selected for consideration as adjustment variables were also the

factors affecting ingestion and internal exposure (section 4.8). These were hand-to-mouth activity, hand dirtiness, mouthing of unedible objects, frequency of hand washing and milk consumption. The factors affecting lead levels in the environment (section 4.7) were not considered as adjustment variables, as this would potentially lead to over-adjustment of the associations between environmental lead and blood lead. If, for example, traffic flow affects lead levels in the environment, and lead levels in the environment affect blood lead, the association between environmental lead and blood lead will be weakened or extinguished by adjustment for traffic flow, and this would not mean that children are not affected by environmental lead, but that environmental lead is merely well represented by (c.q. a good representative of) traffic flow (cf. also section 2.7).

There were 174 out of 195 children who had data on all of these adjustment variables. Missing data on lead in tap water were the main cause for this reduction in sample size. Lead in tap water was considered to be an important potential confounder, and it was decided to retain it at the cost of a small reduction in sample size.

A backward elimination regression procedure was used to produce a smaller set of adjustment variables to be used in further analysis. The standard option of the SPSS NEW REGRESSION program was used, which is that variables are not removed from the equation if their significance level is <.100.

Both the concentration of lead in blood (PbB) and its logarithmic transformation (Ln PbB) were used as dependent variable, to assess whether this would result in different resulting sets of adjustment variables.

The backward elimination procedure resulted in a set of 9 adjustment variables which were all significantly related to PbB. For the logarithm of PbB, the set was about the same. These variables were:

1. lead in tap water	(positive association with blood lead)
2. mouthing behaviour	(positive)
3. hand dirtiness	(positive) (only significant for Ln PbB)

4. milk consumption	(negative)
5. sex of the child	(PbB higher in boys)
6. crowding	(positive)
7. frequency of hand washing	(negative) (only significant for PbB)
8. incompleteness of family	(PbB higher in children from incomplete families)
9. mother's education	(higher blood leads with lower education)

The interpretation for most of these variables is fairly straight-forward: lead in tap water is a known determinant of blood lead; increasing PbB levels with increased mouthing activity, hand dirtiness and low frequency of hand washing point to the importance of hand-to-mouth activity; milk consumption has been shown to be negatively related with blood lead in children before; a crowded home is potentially more dusty than a non-crowded home; the educational level of the mother and the incompleteness of the family may have served as a general representative of play habits, personal hygiene etc. related to blood lead; and the somewhat higher blood lead levels in boys may reflect greater activity.

All factors were conceivably related to environmental lead as well. Lead in tap water is related to the age of the home, which was higher in the urban area. Factors 2-4 and 6-9 are all related to the socio-economic status which was also different between participants from the urban and suburban areas. In the urban areas, slightly more boys were investigated than in the suburban areas (urban sex ratio 1.25 times suburban sex ratio).

It was decided to use the 8 variables which were significantly related to Ln PbB as adjustment variables for equations in which Ln PbB was used as the dependent variable.

4.10.3. Associations between environmental lead and blood lead, adjusted for confounders and exposure modifying variables

As the distributions of the environmental lead exposure variables were positively skewed, they were transformed into their natural logarithm (ln) before further analysis. A ln-transformation of both the blood lead variable and the environmental lead exposure variables further serves to accommodate the curvilinearity of the blood lead/environmental lead relationship, as mentioned in section 2.7.

Ten different environmental lead exposure variables were available for further analysis:

1. lead deposition outdoors
2. lead on sidewalks near the homes of the children
3. lead in garden soil
4. lead on the hands of the children
5. lead deposition indoors in homes
6. lead deposition indoors in schools
7. lead on floors in homes
8. lead on floors in schools
9. lead on school playground pavements
10. lead in school sand pit soils

Lead in school sand pit soils was found to be uniformly low; and gardens were almost absent in the inner city study populations. For these reasons, both soil lead variables could not be expected to contribute to our understanding of the urban-suburban differences in blood lead, and it was decided to omit them from further analysis.

The remaining 8 variables represent different aspects of general environmental lead exposure.

They can be expected to be correlated, as the different environmental media in which lead is present are not isolated from each other. The correlation matrix in table 4.16 shows that indeed, relatively high correlations were found between most environmental lead exposure variables.

Table. 4.16. Pearson correlations between Ln-transformed environmental lead variables

lead exposure variable (natural logarithm)	1	2	3	4	5	6	7
1. lead deposition outdoors							
2. lead on sidewalks	.552* (.000)						
3. lead on hands	.537 (.000)	.297 (.004)					
4. lead deposition in homes	.341 (.000)	-.002 (.491)	.254 (.002)				
5. lead on home floors	.344 (.000)	.431 (.000)	.325 (.000)	.331 (.000)			
6. lead deposition in schools	.634 (.000)	.302 (.002)	.429 (.000)	.295 (.000)	.306 (.000)		
7. lead on school floors	.521 (.000)	.136 (.095)	.331 (.000)	.222 (.002)	.245 (.001)	.143 (.029)	
8. lead on school playgrounds	.482 (.000)	.345 (.000)	.426 (.000)	.252 (.001)	.420 (.000)	.380 (.000)	.595 (.000)

* pairwise deletion of missing data; n=79-177;
in parentheses: significance level

The implication of this is that these variables to some extent represent each other. It was decided to evaluate each lead exposure variable separately. As mentioned in section 3.6, the practice of entering more than one lead exposure variable into regression equations of blood lead on environmental lead and confounders has led to under-estimates of the impact of environ-

mental lead on blood lead whenever it was implied that the adjusted coefficients could be interpreted as representing the integrated impact of environmental lead on blood lead. The wish to avoid such misinterpretations was an argument for a separate evaluation of each exposure variable. As mentioned in section 4.10.2, a fixed set of adjustment variables was chosen to be incorporated in the equations. Alltogether, 8 equations were calculated to evaluate the impact of environmental lead exposure. A summary of the results can be found in table 4.17; it shows the regression coefficients (and their significance levels) of the various lead exposure variables. The complete equations are given in Appendix 3. In the Appendix, plots of the adjusted and unadjusted associations between blood lead and environmental lead are shown as well.

The results displayed in table 4.17 show that all environmental lead exposure variables were positively associated with blood lead after adjustment for the confounders. Most of the associations were statistically significant ($p < .05$).

These findings suggest that environmental lead pollution is partly responsible for the differences in blood lead between urban and suburban children.

The association between lead deposition outdoors and blood lead was the most significant of the calculated associations between environmental lead and blood lead; although this suggests that lead deposition outdoors is the most important lead exposure variable, it could be argued that this in part also reflects differences in reliability of the respective lead exposure variables. The reliability coefficient calculated earlier in this chapter does not suggest that lead deposition outdoors was the most reliable lead exposure variable. This reliability coefficient was based on our data from Arnhem, however, where total variance of lead deposition was about six times smaller than in this study, and where the fact that a point source area rather than a generally polluted area was studied may have contributed to within-location variance. The actual reliability coefficient for lead deposition in the present study may therefore have been closer to zero.

From table 4.16 it is also clear that lead deposition outdoors shows generally the highest correlation with the other lead exposure variables. It consequently represents the other lead exposure variables better than the others, so that effects of

Table 4.17. Summary of adjusted associations between environmental lead and the natural logarithm of the blood lead concentration (µg/100 ml)

lead exposure variable (natural logarithm)	regression coefficients and significance level*	
1. lead deposition outdoors ($\mu g\ m^{-2}d^{-1}$)	.1923 (.000)	n=172
2. lead on sidewalks ($\mu g\ m^{-2}$)	.0228 (.564)	n= 91
3. lead on hands (µg/hand)	.0358 (.240)	n=127
4. lead deposition in homes ($\mu g\ m^{-2}d^{-1}$)	.0218 (.362)	n=157
5. lead on home floors ($\mu g\ m^{-2}$)	.0474 (.035)	n=148
6. lead deposition in schools ($\mu g\ m^{-2}d^{-1}$)	.0603 (.027)	n=156
7. lead on school floors ($\mu g\ m^{-2}$)	.1182 (.006)	n=156
8. lead on school playgrounds ($\mu g\ m^{-2}$)	.0943 (.026)	n=156

* adjustment variables: ln lead in tap water, hand dirtiness, incompleteness of family, sex, crowding, milk consumption, mouthing behaviour, maternal education

other pathways show up more effectively when lead deposition outdoors is used as exposure indicator.
Insignificant associations were found with lead on sidewalks, lead deposition in homes and lead on hands. Reliability was poor for the first two variables (tables 4.11 and 4.12) and unknown

for lead on hands. All school exposure variables were significant.

If we use lead deposition outdoors as an indicator of general environmental lead pollution, the adjusted effect of environmental pollution on blood lead can be estimated by substituting population-average confounder values, and area-specific lead deposition values into the equation. The results are shown in table 4.18. It is clear that a major part of the difference in blood lead between areas is related to environmental lead pollution; the unadjusted PbB difference between the 'worst' and the 'best' area in this study was about 5 µg/100 ml for 50-percentiles, and after adjustment, 3.0 µg/100 ml is explained by lead deposition outdoors as a measure of general environmental lead pollution.

Table 4.18. Unadjusted and ajusted differences between blood lead levels in urban and suburban children

area	observed PbB value (µg/100 ml, geometric mean)	adjusted PbB value (µg/100 ml) as calculated from equation*
Rotterdam, inner city	13.1	11.2
Rotterdam, suburb	8.2	9.1
The Hague, inner city	11.5	10.0
Zoetermeer, suburb	7.9	8.2

* adjusted for variables mentioned in table 4.17; for equation cf. Appendix 3

The size of this effect may still be an under-estimate due to the imperfectness of our knowledge of the true exposure (cf. Appendix 1).

It should be noted that random errors are present in at least some of the adjustment variables as well, which in its turn would lead to under-estimation of their effect. The presence of more than one independent error-bearing variable in the equation makes the calculation of the 'true' regression coefficients rather complicated (Cochran 1968). Assuming that the difference in out-

door air lead between the 'worst' and the 'best' area were no larger than .2 $\mu g/m^3$, these results suggest a large influence of environmental lead, as characterized by outdoor air lead.

4.11. The origins of lead in the environment

Having established the associations between environmental lead and blood lead, the question remained which were the origins of environmental lead in the study areas.
In the previous section, lead deposition outdoors emerged as the most influential environmental lead exposure variable among 7 others; it was suggested that this partly reflected the rather high correlations between lead deposition outdoors and the other lead exposure variables.
Lead deposition outdoors is not likely to be caused by any other sources than vehicular and industrial emissions; in so far as lead deposition outdoors is a determinant of blood lead, this most probably represents the genuine influence of these two emission sources, of which vehicular traffic is dominant in the study areas.
We proceeded to investigate whether the other lead exposure variables are mainly related to lead deposition outdoors - and hence to vehicular traffic predominantly - or to other sources of lead as well. This was done for lead on sidewalks, lead on home floors and lead deposition in homes, as potential determinants of these variables were gathered by questionnaire. No potential determinants of the school lead variables - all of which were significantly related to blood lead - were recorded, so that the results of the analyses in this section need to be interpreted with care.
For lead on sidewalks, the following potential determinants were used in the analysis: time passed since (re)pavement of the street, presence of a lead emitting neighbourhood facility nearby, presence of obstacles reducing traffic flow, and the presence of cracking or flaking paint on the outside of the home. All variables were entered into the equation at the same time.
The results are shown in table 4.19.

Table 4.19. The association between lead on sidewalks and potential determinants of lead on sidewalks (n=78)

independent variables	regression coefficents (in parentheses: standard deviation)	significance level
lead deposition outdoors	.675 (.215)	.002
time since (re)pavement (3 categories)	-.127 (.104)	.228
presence of lead emitting neighbourhood facility (0=no; 1=yes)	-.017 (.212)	.938
residential precinct with restricted rights for traffic flow (0=no; 1=yes)	-.495 (.201)	.016
presence of cracking or flaking outdoor paint (0=no; 1=yes)	.187 (.247)	.451
constant	1.458 (1.281)	

From the table it is clear that lead deposition outdoors and the presence of obstacles to traffic flow in the street are the main determinants of lead on sidewalks. The predominant sources of lead on sidewalks are then most probably not different from those of lead deposition outdoors.
For lead on home floors, the following variables were investigated as potential determinants: lead deposition outdoors, lead hobbies, presence of pets, presence of cracking or flaking paint indoors, parental occupational lead exposure, lead on sidewalks and construction year of the home. The results are shown in table 4.20.

Table 4.20. The association between lead on home floors and potential determinants of lead on home floors (n=80)

independent variables	regression coefficients (in parentheses: standard deviation)	significance level
lead deposition outdoors	.177 (.311)	.572
lead hobbies (0=no; 1=yes)	.355 (.258)	.173
presence of pets (0=no; 1=yes)	.264 (.220)	.236
presence of cracking or flaking paint indoors (0=no; 1=yes)	.005 (.571)	.993
parental occupational exposure to lead (0=no; 1=yes)	-.464 (.446)	.302
lead on sidewalks	.503 (.157)	.002
costruction year of the home	-.003 (.007)	.619
constant	2.962 (7.761)	

Lead on sidewalks was associated most closely with lead on home floors. This is in line with our earlier findings in Arnhem (Diemel et al. 1981) where lead in soil and lead on home floors were closely related, and it suggests that much of the lead on home floors originated from dust and dirt transported into the home from the street.
As lead on sidewalks was shown to be mainly related to lead

deposition outdoors, the main source of lead on home floors is also suggested to be vehicular traffic.
For lead deposition indoors, the same potential determinants were investigated as for lead on home floors. The results are shown in table 4.21.

Table 4.21. The association between lead deposition in homes and potential determinants of lead deposition in homes (n=86)

independent variables	regression coefficients (in parentheses: standard deviation)	significance level
lead deposition outdoors	.133 (.267)	.620
lead hobbies	-.231 (.206)	.267
presence of pets	.433 (.190)	.025
presence of cracking or flaking paint indoors	.202 (.435)	.645
parental occupational exposure to lead	.217 (.320)	.500
lead on sidewalks	-.270 (.129)	.040
construction year of the home	-.015 (.006)	.008
constant	15.772 (6.413)	

Lead deposition indoors appeared to be related to the construction year of the home and to the presence of pets, which presumably bring dust and dirt into the home or contribute to resuspension of it. There was even an unexpected, negative association

between lead on sidewalks and lead deposition indoors. The bivariate correlation between lead deposition indoors and lead on sidewalks was only -.002 and not significant, so probably we should not attach too much value to the unexpected negative adjusted relationship (correlation matrices concerning tables 4.19 - 4.21 are shown in Appendix 3 for further inspection).
For both indoor lead exposure variables, the influence of parental occupational exposure to lead was insignificant. All occupations in which some exposure to lead was likely were considered as positive in this analysis (13 cases). This may mean that in several cases, exposure was only slight and not comparable to the exposures encoutered inside lead smelters, battery factories etc. The effect of the construction year of the home on lead deposition indoors might reflect some paint influence, although the presence of cracking or flaking paint itself was not significant at all; it might also reflect that in older homes, more dust has accumulated over the years which is available for resuspension, or that in older homes, more airborne dust enters the home through cracks and joints.

In general, these results do not suggest that other sources than vehicular traffic contributed heavily to the lead levels in the home and street environment. For schools, this is less clear as no information was available on eventual determinants of lead levels in the schools.

4.12. General discussion

4.12.1. Selection and response rate

In Rotterdam and Zoetermeer, nursery schools were used as selection unit. Although the schools were selected after consultation with the local school health services, there is no direct information on the representativity of the selected children for the complete population of the same age, living in the same area. Within areas, there was no large difference between the average blood lead levels found in children from different schools. This suggests that either every selected school was representative for

the area, or that all schools were not representative. There is no reason which should lead us to believe in the latter possibility.
The response rates of 65% (Rotterdam), 17% and 36% (The Hague) and 46% (Zoetermeer) make clear that from a considerable part of the invited children blood lead data were not obtained (cf. table 4.2). In the First E.C. Blood Lead Survey in 1979, the response rates were 69% in Rotterdam, and 46% in The Hague, which was somewhat higher than the present response rates (Ligeon et al. 1981). No information was obtained on the characteristics of the non-responders, and it cannot be assumed that the children investigated were completely representative for the population of children living in the areas under investigation. The average blood lead levels can only be compared between areas with this reservation in mind.
The subpopulation of children that participated in the environmental survey had blood lead levels which followed those of the complete study population closely in each of the different study areas (tables 4.13-4.14). For this reason it can be assumed that the subpopulation which participated in the environmental survey was representative for the complete study population.
The main purpose of this study was to establish to what extent blood lead levels were related to lead in the environment, and blood lead as well as most environmental lead variables were measured for each individual child. It is not considered likely that selection and/or non-response in this study have exerted a large influence on the results of the statistical analyses presented in section 4.10.

4.12.2. Errors in exposure and outcome variables

For most exposure variables, it was possible to estimate the ratio between the within-subjects variance and the between-subjects variance. It was shown that for most exposure variables, within-subjects variance was not negligible compared to between-subjects variance. In principle, this decreases the chance of finding a significant association between exposure and outcome variables, and it may also reduce the size of the regression coefficient in a regression analysis. Although it is possible to

calculate adjusted regression coefficients using the ratio of within- and between-subjects variances, it was decided not to do so. In a multiple regression analysis in which more than one independent variable are subject to error, the calculations become complicated and require knowledge of the size of the error in each of these variables. One of the confounding variables in the analysis about which such information was not obtained was the concentration of lead in drinking water which varies in time to a certain extent in areas where lead piping is present. The error associated with the outcome variable (the concentration of lead in blood) was about 15-20%, expressed as coefficient of variation due to errors in sampling and analysis. The children's blood was sampled only once, and it is not possible to calculate the ratio of the within- and between-subjects variance for this population. Errors in the outcome variable decrease the chance of finding a significant association, but they do not affect the size of the regression coefficient in a regression analysis. In our statistical analyses, up to 50% of the variance of blood lead concentrations could be explained by the independent variables in the equations. This indicates that the within-subjects variance of blood lead concentrations - which cannot be explained by independent variables having only one value per subject - must have been smaller than the between-subjects variance of blood lead concentrations in this particular study population.

4.12.3. Errors in adjustment variables

If the error in adjustment variables is large compared to the error in exposure variables, a multiple regression analysis may result in regression coefficients for the exposure variable of interest, which are larger, and not smaller than the 'true' coefficients (assuming positive confounding).
As indicated in the previous section, the concentration of lead in tap water varies in time, especially in homes with leaden water supply pipes. A large part of our study population was, however, living in suburban areas where the lead concentration in tap water was uniformly low, and therefore much less variable than in the urban areas. As a result, one would expect that on a population basis, the between-subjects variability of tap water

lead is still an appreciable part of total variablity.
Questions about mouthing behaviour and hand dirtiness were asked once; it cannot be estimated to what extent misclassification has occurred in the two broad categories used in the analysis. The amount of milk and (liquid) milk products consumed was entered into the analysis as a continuous variable. Here also, the questions were asked once, so that it is not known how reliable the data on milk consumption are. The same holds for the questions on maternal education, sex of the child, crowding and incompleteness of the family, although it is not considered likely that for these variables, serious misclassification has occurred.

4.12.4. The importance of environmental lead for the explanation of urban/suburban differences in children's blood lead

The results of our study indicate that after adjustment for various confounders and transfer modifying variables, more than half of the urban/suburban PbB difference could be explained by differences in total environmental lead exposure. It was not possible to measure the actual dietary lead intake in the study population; as indicated in sections 2.6 and 4.9, it was not considered likely, however, that differences in food consumption patterns existed between areas and between socio-economic strata which would lead to a significantly higher dietary lead intake in inner city children.
No emphasis has been laid on the identification of the major environmental pathways. Lead deposition outdoors correlated best with blood lead, but this exposure variable also showed relatively high correlations with most other exposure variables, so that it represented other pathways to a certain extent.
Insignificant associations were found between PbB and lead on sidewalks, lead deposition in homes and lead on hands. The reliability of the first two variables was shown to be poor. Lead on hands was only measured once, and it is considered likely that the reliability of this variable was poor as well. The different school lead variables were all significantly associated with blood lead. In view of the relatively high pollution levels in the inner city schools, lead intake from the environment by the investigated children probably took place partly when they were at school.

The concentration of lead in air as measured by the Rijnmond Central Environmental Agency was low in urban as well as in suburban areas. Recently, a study was conducted in the Dutch city of Nijmegen (Bakker and van Pul 1983); at a lead deposition difference of about 200 $\mu g\ m^{-2}\ d^{-1}$ an air lead difference as measured by High Volume samplers of 0.3 $\mu g/m^3$ was found between measuring locations near and away from busy roads. This suggests that the air lead differences between the areas studied by us in 1981 may have been somewhat larger than was assumed originally. This still does not make it likely, however, that the observed PbB differences had been caused by inhalation alone. The study results thus stress the importance of non-inhalation modes of intake of lead from the environment by children. The results also reinforce the conclusions reached in section 3.6 on the proper formulation of standards for environmental lead: if the intake of lead from the environment by children were only different for the inhalation mode between areas with differing pollution levels (as was assumed in the 1978 US Air Quality Standard for Lead), the PbB levels encountered in urban and suburban areas would have to be much more alike than they actually were. If it is considered necessary to adopt standards for lead in the environment, total intake must be considered, and not intake by one mode and/or pathway only.

4.12.5. The size of the environmental exposure impact estimates compared

It is difficult to compare the size of the exposure impact estimates from our study with those of others. Few studies have been performed in a general city environment at relatively low levels of exposure, and in only one other urban study, other exposure variables than air lead were measured (cf. section 3.3).
Table 4.22 lists a number of exposure impact estimates from our and other studies.
For lead deposition outdoors and lead on home floors, our results indicate higher β-values than the few that were found in the literature. The limited information on soil lead in our study is in line with the majority of β-values obtained from the literature on the impact of soil lead. The size of the difference for lead deposition outdoors and lead on home floors is not such that

it could not conceivably be explained by differences in study areas, population groups and methodologies.

Table 4.22. Comparison of exposure impact estimates between the present study and literature data

exposure variable	β this study	β literature	study nr	table nr
lead deposition outdoors ($\mu g\ m^{-2}d^{-1}$)	5.8	0.4 - 2.5	2	3.5
		1.9	7	3.5
lead on home floors ($\mu g/m^2$)	61.2	38.8	22	3.8
soil lead[1] (mg/kg)	11.3	5.0 - 15.0	many	3.5 3.7 3.8

1 comparison of The Hague with Zoetermeer, assuming adjusted PbB difference of 1.8 µg/100 ml on the basis of table 4.18

As indicated in chapter 3, a three- to fourfold range of α- and β-values is in general the outcome of the reviewed studies. Furthermore, our study was performed at blood lead levels lower than in most other studies, so that our results are consistent with the curvilinearity of the blood lead/lead exposure relationship. We conclude, therefore, that the size of the exposure impact estimates in our study is not out of line with the estimates from other studies.

4.12.6. The origins of lead in the study areas

The areas studied in The Netherlands in 1981 did not contain major industrial lead sources so vehicular traffic was the main source of lead in the air and of the lead deposited from the air.

It was assumed that lead in the environment also originated mainly from leaded gasoline when variations of the lead concentrations in other media were found to vary directly or indirectly with lead deposition outdoors.
The amount of lead found on sidewalks was indeed shown to depend mainly on lead deposition outdoors; the amount of lead on home floors was shown to depend mainly on the amount of lead found on sidewalks nearby. For sidewalk dust and floor dust, it was concluded therefore that they were mainly polluted by lead from gasoline as well.
The amount of lead deposited inside homes was found to depend mainly on the construction year of the home. This may indicate that old homes are dustier than new homes. The presence of flaking paint was not related to the amount of lead deposited inside homes, so the relationship with the age of the home was most probably not caused by the influence of deteriorating, lead-containing paint layers.
The results of the calculations presented in section 4.11 suggest consequently, that the lead found in different environmental media in the areas we studied in The Netherlands in 1981, originated mainly from the use of leaded gasoline in motor powered vehicles, and not from other sources.

5. CONCLUDING REMARKS

Despite the great research effort which has been devoted to the environmental health aspects of lead in the past, it is still difficult to give an exact description of the relationship between environmental lead and blood lead in children. Partly, this is due to the differences in circumstances under which different child populations grow up: there is no unique relationship between concentrations of lead in the environment and of lead in children's blood. Depending on local circumstances like accessibility of environmental media, play habits and nutritional status of the involved populations, the blood lead levels of children are more or less affected by a given level of lead in the environment.

Also, there has been no standardization of the methods used for investigating exposure of children to lead in the environment.

In addition, there are several key topics which have not been investigated in detail. These include the relationship between total lead intake and blood lead in children, and the amounts of dust and dirt which are ingested during normal play.

Quantitative estimates of relationships between environmental lead and blood lead in children - including the ones given in this report - therefore need to be interpreted with care.

At present, it is not yet possible to predict blood lead levels of children precisely from their exposure to lead in the environment. As a consequence, it will remain necessary to measure blood lead if an adequate assessment of health risks is desired in any situation in which environmental lead concentrations are elevated.

The uncertainty which surrounds the estimates of the impact of environmental lead exposure on children's blood lead emphasizes the necessity of using a margin of safety when establishing environmental quality standards for lead. In the interest of public health it seems more sensible to rely on reduction or elimination of lead in gasoline than to establish detailed quality standards for the concentration of lead in different environmental media.

SUMMARY

This study deals with the relationship between environmental lead and blood lead in children.

Chapter 1 provides a summary of the environmental health aspects of lead. The occurrence of lead in the environment and in man is described; children are discussed as a population at risk for undue lead absorption, and the exposure-response system is briefly outlined.

Chapter 2 discusses a number of methodological issues in studies on the relationship between environmental lead and blood lead in children. Lead is present in various environmental media like air, soil and dust. From all these media, lead intake by children may occur, by inhalation or ingestion. The inhalation rate per kg body weight is larger in children than in adults, due to a higher metabolism. The ingestion of dust and dirt cannot be easily quantified; at present, measurement of the lead concentration in dust and dirt usually serves as a surrogate. The concentration of lead in blood has been the major dependent variable in studies on the relationship between environmental lead exposure and internal lead exposure. The concentration of lead in blood does not only depend on intake but also on the fractional absorption of lead from the gut, and on distribution and excretion patterns within the body. All of these vary with age. Nutritional factors are important as well, for example dietary calcium, iron, phosphorus and fat. Lead is not only present in the general environment but also in food and drinking water, both of which may act as predominant sources of lead intake. Lead in food originates in part from environmental pollution, and it is still debated how large this part actually is. Lead in drinking water usually originates from pipes or storage facilities. In the United States especially, lead from crumbling paint is an important source for children; paint lead does not seem to be of general importance in The Netherlands, however.

The relationship between total lead intake and the concentration of lead in blood is usually given as a curvilinear downward function. The implication of this is that at low levels of exposure, a given increase of intake is expected to result in a stronger increase in blood lead concentrations than at high levels of exposure. In some studies, it has been customary to adjust relationships between air lead and blood lead for lead in

other media. As lead in the air and lead in other media like soil and dust often originate from the same source or sources, such a procedure may under-estimate the impact of environmental lead on children's blood lead.

It is difficult to measure the intake of lead from the environment by children exactly. Instead, the concentration of lead in one or more environmental media is usually measured as an index of exposure.

Apart from being only approximations of actual lead intake from the environment, these concentrations also tend to have large temporal and spatial variations. A decomposition of total variation into within-subjects and between-subjects variation is a means to estimate the reliability of exposure indicators. If the within-subjects variation of exposure indicators is large compared to the between-subjects variation, the impact of environmental lead exposure on blood lead will usually be underestimated in a regression analysis.

Chapter 3 reviews a number of studies from which estimates of relationships between environmental lead and children's blood lead can be obtained. Aggregate relationships are emphasized, i.e. it is not attempted to estimate the separate contributions of inhalation, ingestion of soil, dust etc. as the available data usually do not permit such an analysis. Aggregate relationships are relationships in which different indicators of lead exposure are thought to represent all environmental exposure. When the concentration of lead in air is taken as an indicator, a blood lead/air lead slope of about 3-5 µg/100 ml per $\mu g/m^3$ is obtained. When the concentration of lead in soil, street dust or house dust is taken as an indicator, most blood lead/soil (dust) lead slopes are in the order of 5.0 - 10.0 µg/100 ml per g/kg.

Although the ranges of the different types of estimates are wide, the review suggests that for children, lead intake from the environment constitutes a major part of total lead intake in quite a number of situations.

Chapter 4 is a description of our study on environmental lead and blood lead in children living in Rotterdam, The Hague and Zoetermeer which was performed in 1981.

Blood lead concentrations in children were different between city centers and suburbs. After adjustment for a number of confounders, more than half of the difference remained. Most probably, this was caused by differences in environmental lead pollution as

most indicators of lead exposure were clearly different between city centers and suburbs. In a multiple regression analysis, most exposure indicators were significantly associated with the concentration of lead in blood, after adjustment for a number of confounders. Further analysis of the origins of lead in the environment suggested that in the area under investigation, vehicular traffic was the main source.

When our study results were compared with those of others, the estimated impact of environmental lead on children's blood lead was somewhat higher than in most other studies, but the difference was not great, considering the wide range in estimates which was reported in chapter 3. Theoretically, the differences can be explained by the low level of exposure which was studied, and by the use of repeated exposure measurements. As indicated in chapter 2, a given exposure difference is expected to result in a larger blood lead difference at low overall levels of PbB than at a high overall level of PbB. Also, repetition of exposure measurements leads to a more precise estimate of exposure, and can theoretically be expected to result in a higher exposure impact estimate than when exposure is only measured once, as was the case in most studies reviewed in chapter 3.

SAMENVATTING

In dit onderzoeksrapport wordt de relatie tussen lood in het milieu en lood in het bloed van kinderen besproken.
Hoofdstuk 1 bevat een samenvatting van de gezondheidsaspecten van lood in het milieu. Het vóórkomen van lood in het milieu en in de mens wordt besproken; kinderen worden ten tonele gevoerd als belangrijke risicogroep voor lood, en er wordt een overzicht gegeven van de verschillende wijzen waarop kinderen aan lood kunnen zijn blootgesteld.
Hoofdstuk 2 bespreekt een aantal methodologische facetten van het bestuderen van de relatie tussen lood in het milieu en lood in het bloed van kinderen. Lood is aanwezig in diverse milieucompartimenten, zoals lucht, de bodem, huisstof e.d. Kinderen kunnen lood vanuit al deze media binnenkrijgen, door inhalatie of ingestie. Kinderen ademen per kg lichaamsgewicht méér lucht in dan volwassenen, vanwege een hoger metabolisme. Het is niet eenvoudig de ingestie van bodem- en stofdeeltjes goed te kwantificeren; het meten van de loodconcentratie van bodem- en stofdeeltjes wordt gewoonlijk als surrogaat gebruikt. De concentratie van lood in het bloed wordt geacht een goede maat voor de inwendige blootstelling aan lood te zijn, en wordt gewoonlijk als afhankelijke variabele bepaald in studies van de relatie tussen uit- en inwendige blootstelling. Behalve door de uitwendige blootstelling wordt de bloedloodconcentratie ook bepaald door de mate van absorptie van lood uit het maagdarmkanaal, en door de distributie van lood in, en de excretie van lood uit het lichaam. Al deze zaken variëren met de leeftijd. Voedingsfactoren zijn eveneens van belang, zoals bijvoorbeeld de hoeveelheden calcium, ijzer, fosfor en vet in het dieet.
Lood is niet alleen in het milieu aanwezig, maar ook in het voedsel en in drinkwater, die in bepaalde gevallen de belangrijkste bron van loodinname voor kinderen vormen. Het voedsellood is ten dele afkomstig van milieuverontreiniging, waarbij het nog steeds een punt van discussie is hoe groot dit gedeelte precies is. Lood in drinkwater is gewoonlijk afkomstig uit loden drinkwaterleidingen of opslagsystemen. In de Verenigde Staten is afbladderende, loodhoudende verf in het verleden steeds een belangrijke bron van loodinname door kinderen geweest; in ons land lijkt dit probleem zich echter nauwelijks voor te doen. De relatie tussen de totale loodinname en de bloedloodconcentratie wordt

gewoonlijk als curvilineair beschouwd, in die zin dat bij geringe totale inname de bloedloodconcentratie sterker op een gegeven verandering van de inname reageert dan bij een hoge totale inname.
In sommige studies is men gewoon geweest de relatie tussen lood in de lucht en lood in het bloed van kinderen te standaardiseren voor lood in andere milieucompartimenten. Aangezien lood in de lucht en lood in andere milieucompartimenten zoals bodem, huisstof, e.d. echter gewoonlijk tot op zekere hoogte van dezelfde bron(nen) afkomstig zijn, kan een dergelijke standaardisatie ertoe leiden dat de totale invloed van lood in het milieu op lood in het bloed van kinderen wordt onderschat.
De werkelijke inname van lood vanuit het milieu door kinderen is zeer moeilijk te meten. Als blootstellingsindex wordt daarom gewoonlijk de loodconcentratie in een of meer milieucompartimenten bepaald. Deze loodconcentraties zijn slechts benaderingen van de werkelijke loodinname vanuit het milieu; daarnaast vertonen deze concentraties niet zelden een aanzienlijke variatie in ruimte en tijd. Ontleding van de totale variatie in een binnen-persoons component en een tussen-persoons component is een methode om de reproduceerbaarheid van de gebruikte indices te bepalen. Als de binnen-persoons component groot is ten opzichte van de tussen-persoons component, dan zal het totale effect van lood in het milieu op de loodconcentratie in het bloed gewoonlijk worden onderschat in een regressie-analyse.
In hoofdstuk 3 wordt een aantal studies besproken die een schatting van de relatie tussen lood in het milieu en lood in het bloed van kinderen mogelijk maken. De nadruk wordt gelegd op geaggregeerde relaties waarin de diverse blootstellingsindices steeds geacht worden de totale blootstelling aan lood in het milieu te representeren. Er wordt niet getracht de afzonderlijke bijdragen van inhalatie, ingestie van bodemdeeltjes, ingestie van huisstofdeeltjes etc. te achterhalen, omdat de beschikbare gegevens hiervoor niet voldoende betrouwbaar worden geacht.
Wanneer de loodconcentratie in de lucht als blootstellingsindex wordt gebruikt, kan er uit de diverse studies een gemiddelde bloed lood/lucht lood relatie van ongeveer 3-5 µg/100 ml per $\mu g/m^3$ worden berekend. Wanneer de loodconcentratie in bodem-, straatstof- en huisstofdeeltjes als blootstellingsindex wordt gebruikt, leidt de berekening tot een gemiddelde bloed lood/bodem (stof) lood relatie van ongeveer 5.0-10.0 µg/100 ml per g/kg. De

spreidingsbreedte van de schattingen is over het algemeen groot; toch suggereert de analyse in dit hoofdstuk dat in diverse situaties een belangrijk deel van de totale loodinname door kinderen heeft bestaan uit loodinname vanuit het milieu.
Hoofdstuk 4 beschrijft de studie die wij in 1981 in Rotterdam, Den Haag en Zoetermeer uitvoerden met betrekking tot de relatie tussen lood in het milieu en lood in het bloed bij kinderen. De bloedloodconcentraties bleken duidelijk te verschillen tussen kinderen, wonend in binnensteden en kinderen, wonend in buitenwijken. Meer dan de helft van dit verschil bleef bestaan na standaardisatie voor een aantal verstorende variabelen. Vermoedelijk werd het resterend verschil veroorzaakt door verschillen in blootstelling aan lood in het milieu aangezien verreweg de meeste blootstellingsindices duidelijk verschilden tussen binnensteden en buitenwijken. In meervoudige regressie-analyses bleken de meeste indices bovendien statistisch significant geassocieerd met de concentratie van lood in het bloed, na standaardisatie voor een aantal verstorende variabelen. Een analyse van de samenhang tussen de loodconcentraties in de diverse milieucompartimenten suggereerde verder dat het verkeer de voornaamste bron van lood in het onderzochte gebied vormde.
Vergeleken met de resultaten van ander onderzoek bleken de geschatte effecten van lood in het milieu op de bloedloodconcentratie in onze studie wat groter. De verschillen waren echter niet groot, gezien de spreidingsbreedte die reeds in hoofdstuk 3 werd opgemerkt. Theoretisch kunnen de verschillen worden verklaard door het lage blootstellingsniveau in onze studie, en door het toepassen van herhaalde blootstellingsmetingen. Zoals in hoofdstuk 2 werd aangegeven, kan bij een laag blootstellingsniveau worden verwacht dat een gegeven verschil in blootstelling leidt tot een groter verschil in bloedloodconcentratie dan bij een hoog blootstellingsniveau. Herhaling van blootstellingsmetingen leidt er verder toe dat de blootstelling preciezer wordt geschat, en men kan op theoretische gronden verwachten dat een preciezere schatting van de blootstelling leidt tot een hogere schatting van het effect van de blootstelling op de bloedloodconcentratie dan wanneer slechts éénmalig de blootstelling is bepaald, zoals het geval was in de meeste studies die in hoofdstuk 3 werden besproken.

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APPENDIX 1.

Variability of exposure measurements and what it does to regression analyses in epidemiology

A common assumption in regression analysis is that the X or independent variable is measured without error. In environmental epidemiology, however, it is usually not possible to do so. In measuring exposure to environmental agents, a sometimes large variability in time and space may be encountered which makes it difficult to define exactly the exposure level of each individual of a study population. If we define, for example, the relevant house dust lead exposure of an individual child as the average amount of lead on the floor of the livingroom over the month prior to blood sampling, it will be clear that one sample from one spot at one point in time within that month yields an estimate of the relevant exposure the reliability of which depends on the variability of the amount of lead on livingroom floors in time and space.

It is well known that a random error in the X or independent variable leads to a biased estimate of the regression coefficient of the Y or dependent variable on X (Cochran 1968, Draper and Smith 1981). In the bivariate case, the bias is consistently towards zero, and one of the methods to estimate the size of the bias is to obtain estimates of the error variance and the true variance of the X variable.

These estimates can be obtained from an analysis of variance; an analysis of variance can be performed when there has been some repetition of the exposure measurements in time and/or space. A correction of the observed regression coefficient of Y on X may then be defined as $b = B\ (1+\lambda)^{-1}$

with b = observed regression coefficient
B = 'true' regression coefficient
$\lambda = \sigma^2_e/\sigma^2_t$
σ^2_e = error variance
σ^2_t = true variance

From an analysis of variance, estimates of the error variance and true variance can be obtained as the within-subjects variance and the between-subjects variance respectively. From a standard ana-

lysis of variance table, these can be obtained from the within-subjects Mean Square and the between-subjects Mean Square (Snedecor and Cochran 1967).

Sum of Squares	Degrees of freedom	Mean Square
Between Subjects	n-1	$SS_b/n-1$
Within Subjects	k	SS_w/k
Total	n + k-1	$SS_t/n+k-1$

n is the number of subjects; n+k is the total number of observations, which is equal to n.q, in which q is the number of repetitions of the exposure measurements.
SS_w/k is an estimate of the error variance;
$SS_b/n-1$ is an estimate of the (error variance + q.true variance).
We may now define λ as a reliability coefficient.
If it is zero, there is no error variance, and the regression coefficient of Y on X is not biased. If it deviates much from zero (because σ_e^2 is large compared to σ_t^2) the bias in the regression coefficient becomes large.
The SPSS programme Reliability (Parallel option) can be used to obtain the required analysis of variance table. The programme has the property that it estimates the error variance and true variance after adjustment for systematic differences between measurements due to time sequence effects etc. The analysis of variance table which is produced also permits calculation of unadjusted components of variance. The programme also produces a reliability coefficient, defined as
σ_e^2/σ_t^2 , for the sum of the repeated measurements.
The variance of the sum of q measurements is equal to q^2 times the variance of the mean of these q measurements. This is also true for the components of variance σ_e^2 and σ_t^2 so that σ_e^2/σ_t^2 for the sum is equal to σ_e^2/σ_t^2 for the mean.
The latter reliability coefficient can thus be used to establish how much better the exposure was estimated by the mean of q measurements than by one single measurement, by comparing this reliability coefficient to the one based on single measurements.
In multivariate regression analyses, the simple correction formula for obtaining the 'true' regression coefficient no longer holds (Cochran 1968).
The calculations become complicated, and depending on the size of the error in the different independent variables, the bias in the regression coefficients may be away from as well as toward zero.

APPENDIX 2.

Excerpt from questionnaire and questionnaire results

question		frequency of answers/ average and range
What is the child's sex?	male=1	119
	female=2	76
What is the child's age? (in years)	4	97
	5	98
How long does the child live at its present address? (in years)	less than 1	5
	less than 2	23
	more than 2	167
How often does the child put its hands or fingers into the mouth?		
seldom or never = 0		78
sometimes/often = 1		117
How often does the child chew inedible objects?		
seldom or never = 0		142
sometimes/often = 1		53
How often does the child have dirty hands?		
seldom or never = 0		26
sometimes/often = 1		169
How often does the child wash its hands?		
..... times/day	less than 5	62
	more than 5	133
How many people live in the childs home?		
2		3
3		23
4		131
5		31
6		5
7		2
Is the childs father part of the family?	no=2	9
	yes=1	186
Is the childs mother part of the family?	no=2	0
	yes=1	195
When was the home built?		1958 (1880-1981)

Appendix 2 (continued)

How many rooms are there in the home (excluding kitchen, bathroom etc.)?		
2		5
3		17
4		81
5		74
6		15
7		3
What is the condition of the paint layers indoors?		
good	=1	177
beginning to crack and flake	=2	7
much flaking paint	=3	2
missing		9
What is the condition of the paint layers outdoors?		
good	=1	131
beginning to crack and flake	=2	36
much flaking paint	=3	10
missing		18
Do you have pets?	no=0	111
	yes=1	84
When was the street next to the home paved last?		
less than one year ago	=1	39
1-3 years ago	=2	51
more than 3 years ago	=3	72
don't know	=0	33
Are there detector-pads in the street? (residential precinct with resticted rights to traffic flow)	no=0	92
	yes=1	76
	missing	27
Are there lead emitting neighboorhood facilities (garages etc.) in the street near the home?	no=0	161
	yes=1	33
	missing	1
How much water does the child consume per day? (content of 'favourite cup' measured)	(liters)	0.45
coke, seven-up etc.		0.20
yoghurt and milk		0.71
Does the child often consume canned food?	seldom	131
	often	64

Appendix 2 (continued)

Do you grow your own vegetables?	no=0	183
	yes=1	12
If yes, is the garden located near a busy road?	no=0	9
	yes=1	3
If yes, do you regularly consume food from your own garden?	no=0	10
	yes=1	2
Is lead used in the home for hobbies or handicrafts?	no=0	151
	yes=1	44
Do you use self-glazed pottery?	no=0	175
	yes=1	20
If yes, do you use it for food preparation or storage?	no=0	14
	yes=1	6
Does the childs mother have a job?	no=0	145
	yes=1	50
If yes, what job does she have?		
Does the childs father have a job?	no=0	14
	yes=1	181
If yes, what job does he have?		
What education does the childs mother have?		
never been to school	=1	1
primary school	=2	41
lower professional education	=3	43
intermediate general education	=4	41
intermediate professional education	=5	34
higher general education	=6	15
higher professional education	=7	17
university	=8	2
missing		1

Appendix 2 (continued)

What education does the childs father have?

never been to school	=1	1
primary school	=2	27
lower professional education	=3	41
intermediate general education	=4	28
intermediate professional education	=5	31
higher general education	=6	14
higher professional education	=7	26
university	=8	14
missing		4
father not present in family		9

APPENDIX 3.

Regression equations showing the adjusted associations between the natural logarithm of the concentration of lead in blood and the natural logarithm of lead in the environment.

The adjustment variables were:

Ln PbW = natural logarithm of lead in drinking water (µg/liter)
Sex (0=male, 1=female)
Mouthing (0=never, 1=sometimes/often)
Father (0=father present, 1=father not present)
Crowding (no of people in home divided by no of rooms)
Handdirt (0=never, 1=sometimes/often)
Milkcon (liters of milk and milk products consumed per day)
Motheduc (0=low education, 1=intermediate/high education of mother)

Equation 1. Association between Ln PbB and Ln lead deposition outdoors, adjusted (n=172)

	B (regression coefficient)		(standard deviation)
Ln PbB =	1.1185	(constant)	0.2843
	+ 0.0302	Ln PbW	0.0150
	- 0.0711	Sex	0.0407
	+ 0.1161	Mouthing	0.0411
R^2 = 0.487	+ 0.1722	Father	0.0964
	+ 0.1610	Crowding	0.0860
	+ 0.1136	Handdirt	0.0574
	- 0.3691	Milkcon	0.1023
	- 0.0562	Motheduc	0.0475
	+ 0.1923	Ln lead dep outdoors	0.0483

Equation 2. Association between Ln PbB and Ln lead on sidewalks, adjusted (n=91)

	B (regression coefficient)	(standard deviation)
Ln PbB =	2.0877 (constant)	0.364
	+ 0.0454 Ln PbW	0.0176
	- 0.1320 Sex	0.0596
	+ 0.2147 Mouthing	0.0620
R^2 = 0.476	+ 0.7327 Father	0.2071
	+ 0.2402 Crowding	0.1087
	+ 0.0050 Handdirt	0.0923
	- 0.3256 Milkcon	0.1463
	- 0.1632 Motheduc	0.0603
	+ 0.0228 Ln Lead on sidewalks	0.0393

Equation 3. Association between Ln PbB and Ln lead on hands, adjusted (n=127)

	B (regression coefficient)	(standard deviation)
Ln PbB =	1.9042 (constant)	0.2067
	+ 0.0615 Ln PbW	0.0152
	- 0.0682 Sex	0.0504
	+ 0.1300 Mouthing	0.0491
R^2 = 0.497	+ 0.1831 Father	0.1060
	+ 0.2909 Crowding	0.1059
	+ 0.1331 Handdirt	0.0793
	- 0.2915 Milkcon	0.1249
	- 0.1526 Motheduc	0.0533
	+ 0.0358 Ln lead on hands	0.0303

Equation 4. Association between Ln PbB and Ln Pb deposition indoors in homes, adjusted (n=157)

	B (regression coefficient)	(standard deviation)
Ln PbB =	2.0708(constant)	0.1791
	+ 0.0629 Ln PbW	0.0132
	- 0.0570 Sex	0.0436
	+ 0.1471 Mouthing	0.0453
R^2 = 0.430	+ 0.1677 Father	0.1043
	+ 0.1793 Crowding	0.0927
	+ 0.1031 Handdirt	0.0650
	- 0.2503 Milkcon	0.1094
	- 0.1544 Motheduc	0.0460
	+ 0.0218 Ln Pb dep in homes	0.0238

Equation 5. Association between Ln PbB and Ln lead on home floors, adjusted (n=148)

	B (regression coefficient)	(standard deviation)
Ln PbB =	1.7966 (constant)	0.2027
	+ 0.0602 Ln PbW	0.0139
R^2 = 0.462	- 0.1053 Sex	0.0443
	+ 0.1180 Mouthing	0.0455
	+ 0.2152 Father	0.1055
	+ 0.3009 Crowding	0.1091
	+ 0.1441 Handdirt	0.0671
	- 0.2805 Milkcon	0.1107
	- 0.1180 Motheduc	0.0476
	+ 0.0474 Ln Pb homefloors	0.0223

Equation 6. Association between Ln PbB and Ln lead deposition in schools, adjusted (n=156)

	B (regression coefficient)	(standard deviation)
Ln PbB =	1.9338 (constant)	0.1803
	+ 0.0482 Ln PbW	0.0145
	- 0.0677 Sex	0.0429
	+ 0.1211 Mouthing	0.0434
R^2 = 0.475	+ 0.1519 Father	0.1025
	+ 0.2826 Crowding	0.0968
	+ 0.1403 Handdirt	0.0625
	- 0.3021 Milkcon	0.1083
	- 0.1557 Motheduc	0.0458
	+ 0.0603 Ln Pb dep in schools	0.0269

Equation 7. Association between Ln PbB and Ln lead on school floors, adjusted (n=156)

	B (regression coefficient)	(standard deviation)
Ln PbB =	1.5942 (constant)	0.2280
	+ 0.0411 Ln PbW	0.0150
	- 0.0845 Sex	0.0423
	+ 0.1114 Mouthing	0.0432
R^2 = 0.484	+ 0.1665 Father	0.1013
	+ 0.3056 Crowding	0.0953
	+ 0.1310 Handdirt	0.0619
	- 0.3008 Milkcon	0.1073
	- 0.1521 Motheduc	0.0455
	+ 0.1182 Ln Pb school floors	0.0425

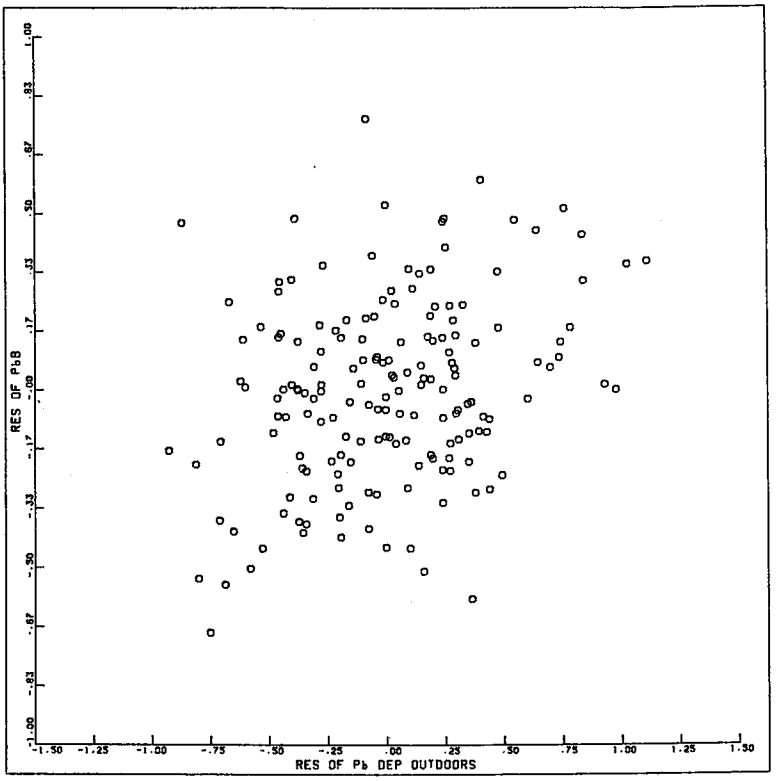
Equation 8. Association between Ln PbB and Ln lead on school playgrounds, adjusted (n=156)

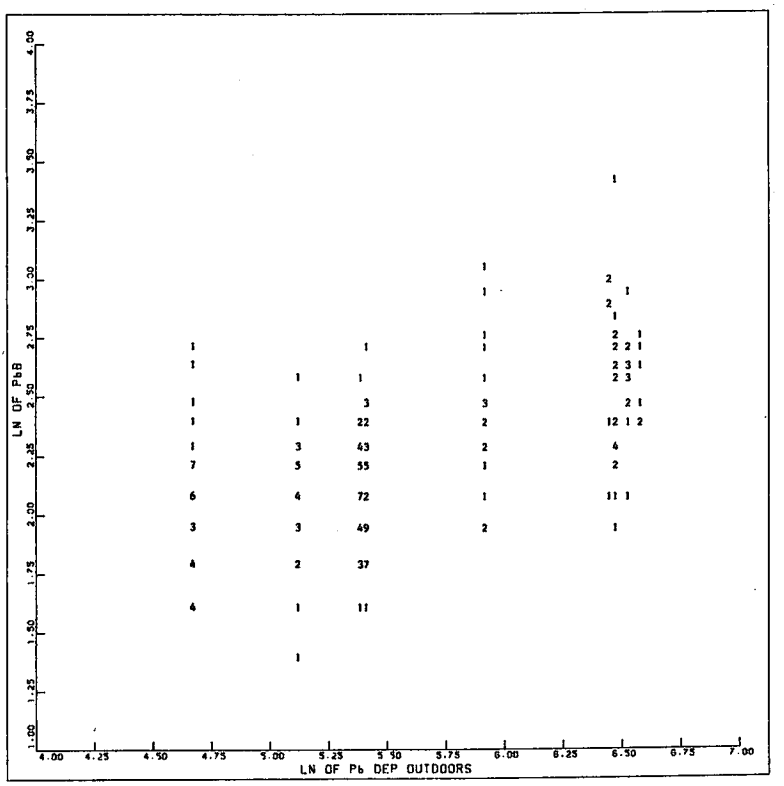
	B (regression coefficient)		(standard deviation)
Ln PbB =	1.5278	(constant)	0.2993
	+ 0.0454	Ln PbW	0.0149
	- 0.0784	Sex	0.0426
	+ 0.1297	Mouthing	0.0434
R^2 = 0.475	+ 0.1339	Father	0.1033
	+ 0.3148	Crowding	0.0962
	+ 0.1147	Handdirt	0.0629
	- 0.2938	Milkcon	0.1083
	- 0.1590	Motheduc	0.0457
	+ 0.0943	Ln lead on school playgrounds	0.0419

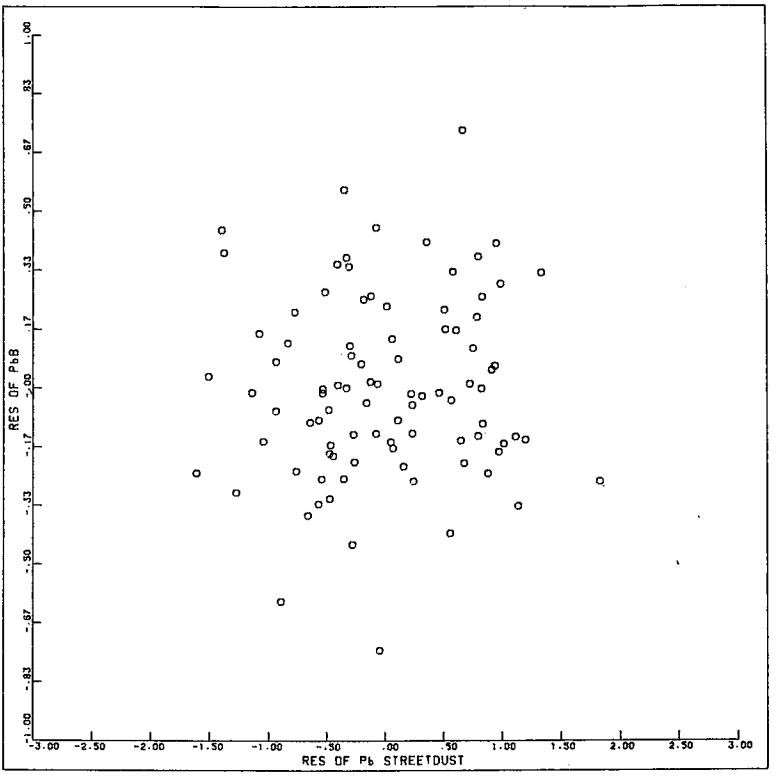
Appendix 3 (continued)

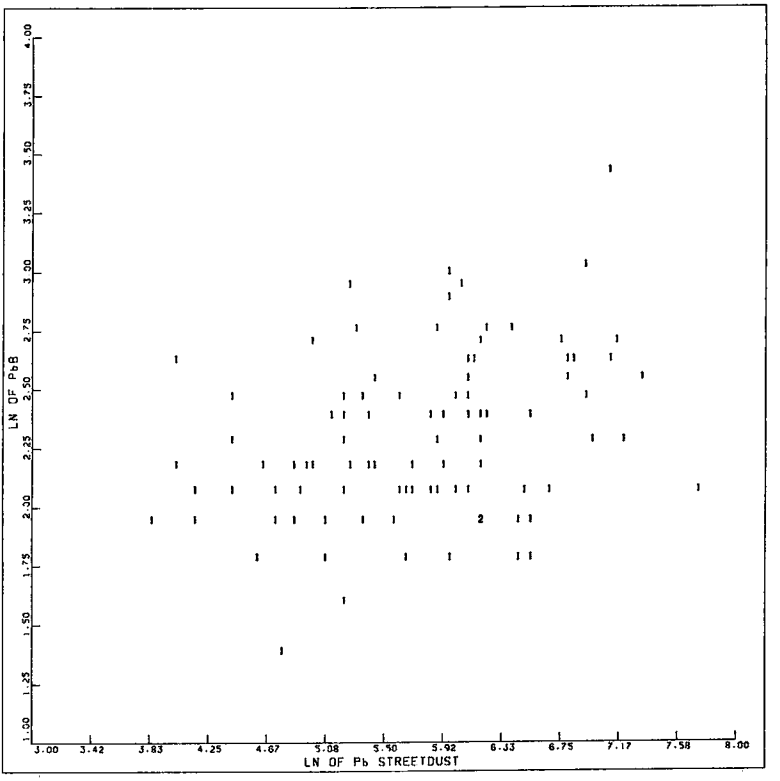
Plots of PbB versus various exposure variables

The upper plot of each of the following 8 pages shows the residual of Ln PbB versus the residual of Ln (exposure variable); the lower plot shows Ln PbB versus Ln (exposure variable), unadjusted for adjustment variables.


RES OF PbB
RES OF Pb DEP OUTDOORS


LN OF PbB
LN OF Pb DEP OUTDOORS


RES OF PbB
1.00
.83
.67
.50
.33
.17
.00
-.17
-.33
-.50
-.67
-.83
-1.00
-3.00 -2.50 -2.00 -1.50 -1.00 -.50 .00 .50 1.00 1.50 2.00 2.50 3.00
RES OF Pb STREETDUST


LN OF PbB
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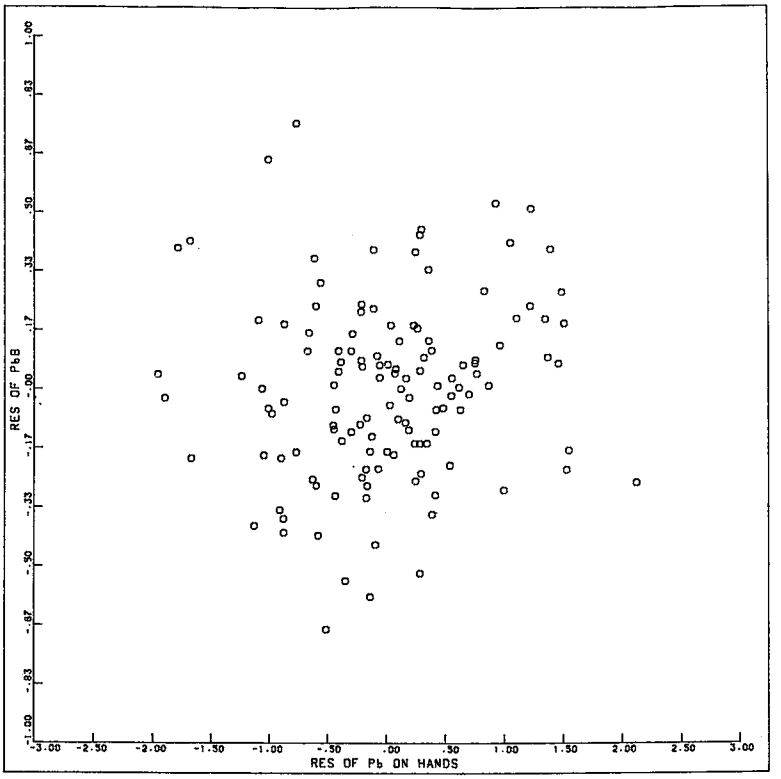
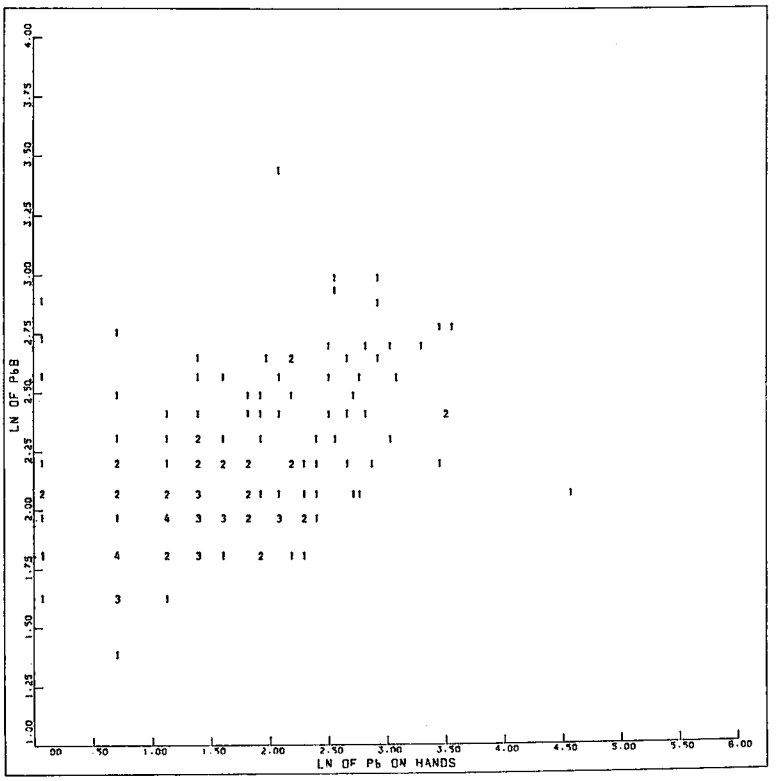
3.75
3.50
3.25
3.00
2.75
2.50
2.25
2.00
1.75
1.50
1.25
1.00
3.00 3.42 3.83 4.25 4.67 5.08 5.50 5.92 6.33 6.75 7.17 7.58 8.00
LN OF Pb STREETDUST


RES OF PbB
1.00
.83
.67
.50
.33
.17
.00
-.17
-.33
-.50
-.67
-.83
-1.00
-3.00 -2.50 -2.00 -1.50 -1.00 -.50 .00 .50 1.00 1.50 2.00 2.50 3.00
RES OF Pb ON HANDS


LN OF PbB
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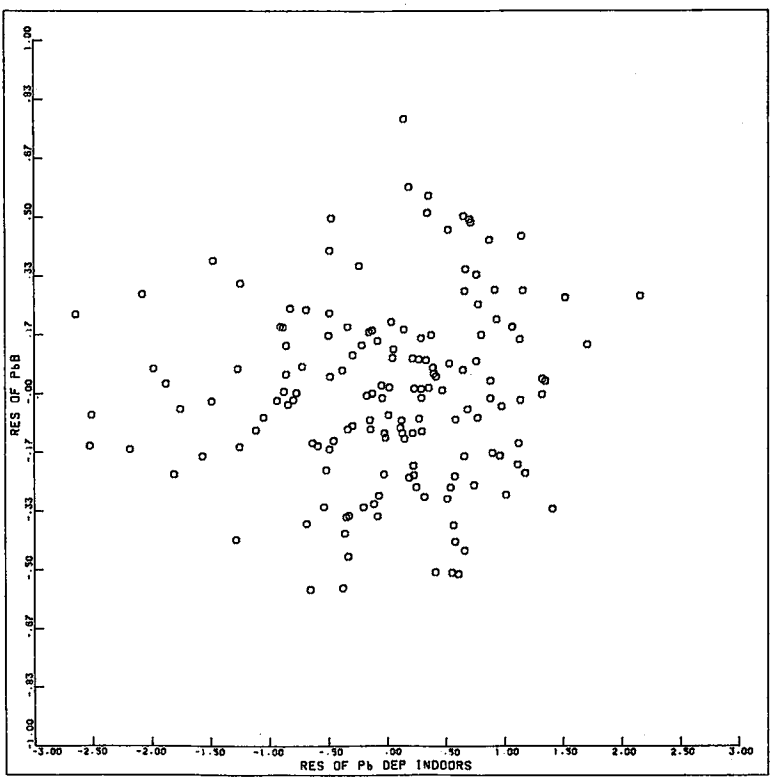
3.75
3.50
3.25
3.00
2.75
2.50
2.25
2.00
1.75
1.50
1.25
1.00
.00 .50 1.00 1.50 2.00 2.50 3.00 3.50 4.00 4.50 5.00 5.50 6.00
LN OF Pb ON HANDS


RES OF Pb8
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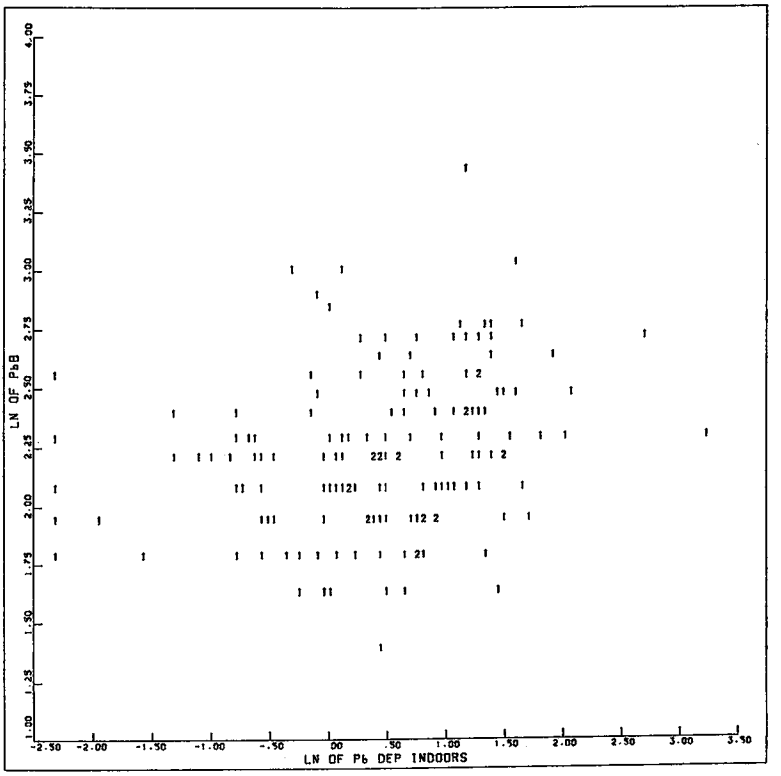
.83
.67
.50
.33
.17
.00
-.17
-.33
-.50
-.67
-.83
-1.00
-3.00 -2.50 -2.00 -1.50 -1.00 -.50 .00 .50 1.00 1.50 2.00 2.50 3.00
RES OF Pb DEP INDOORS


LN OF Pb8
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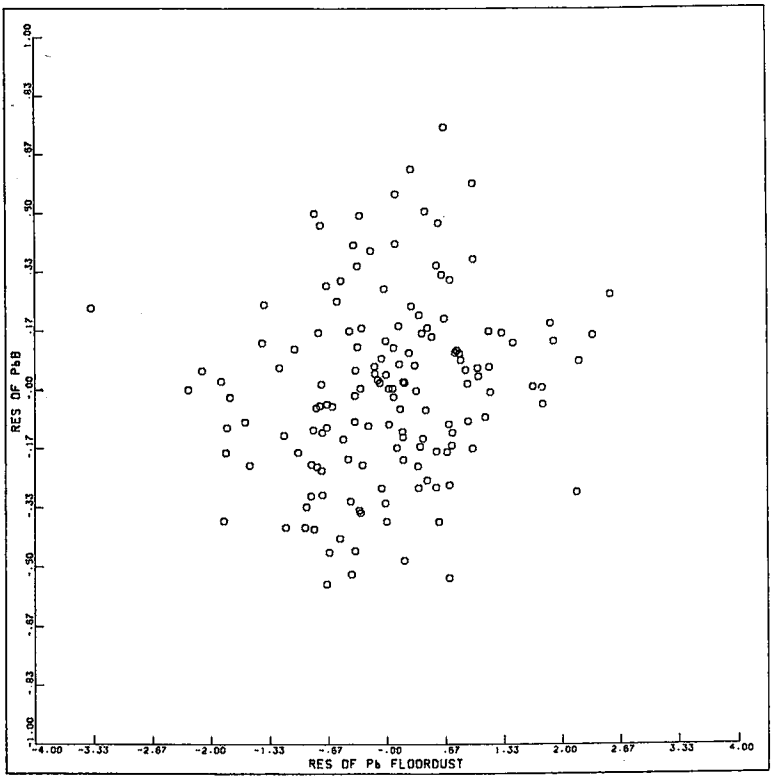
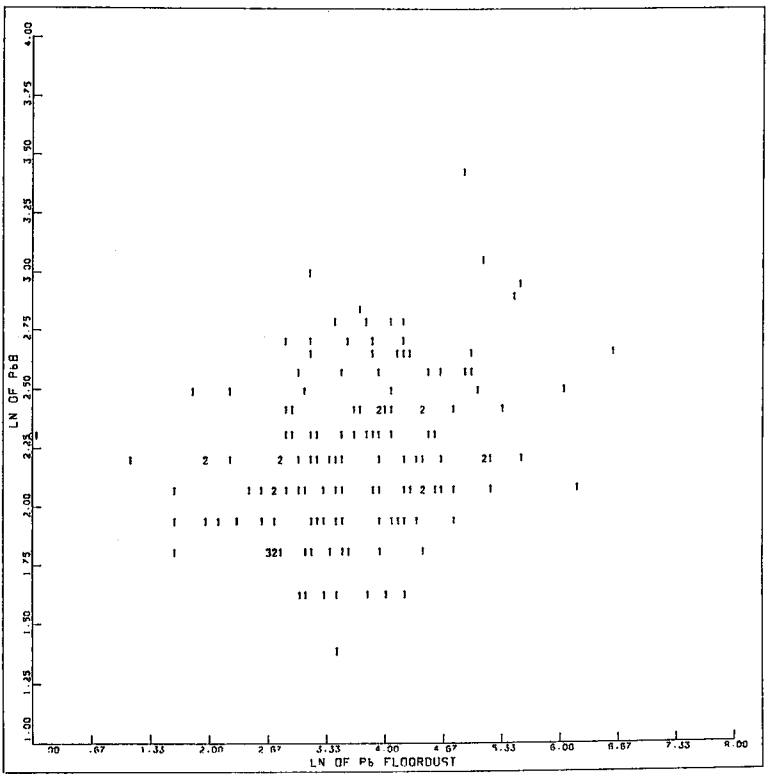
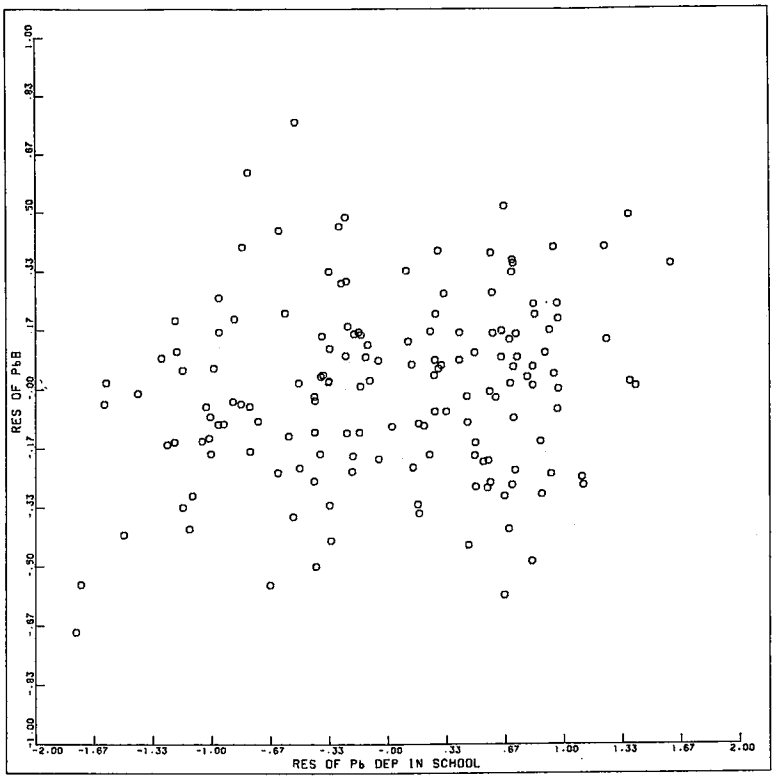
3.75
3.50
3.25
3.00
2.75
2.50
2.25
2.00
1.75
1.50
1.25
1.00
-2.50 -2.00 -1.50 -1.00 -.50 .00 .50 1.00 1.50 2.00 2.50 3.00 3.50
LN OF Pb DEP INDOORS


RES OF PbB
RES OF Pb FLOORDUST


LN OF PbB
LN OF Pb FLOORDUST


RES OF PbB
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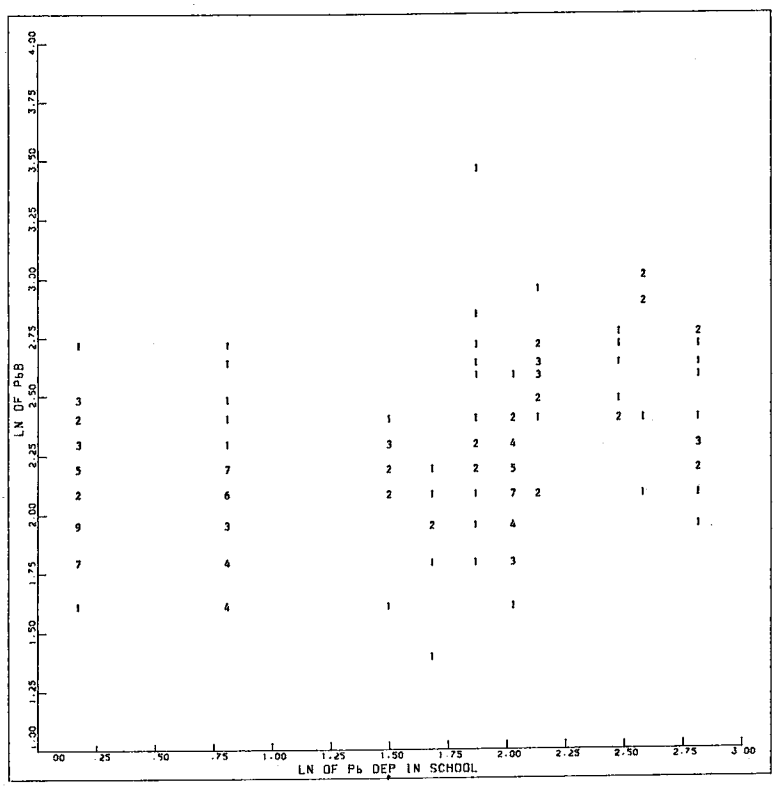
.83
.67
.50
.33
.17
.00
-.17
-.33
-.50
-.67
-.83
-1.00
-2.00
-1.67
-1.33
-1.00
-.67
-.33
-.00
.33
.67
1.00
1.33
1.67
2.00
RES OF Pb DEP IN SCHOOL


LN OF PbB
4.00
3.75
3.50
3.25
3.00
2.75
2.50
2.25
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1.75
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1.00
.00
.25
.50
.75
1.00
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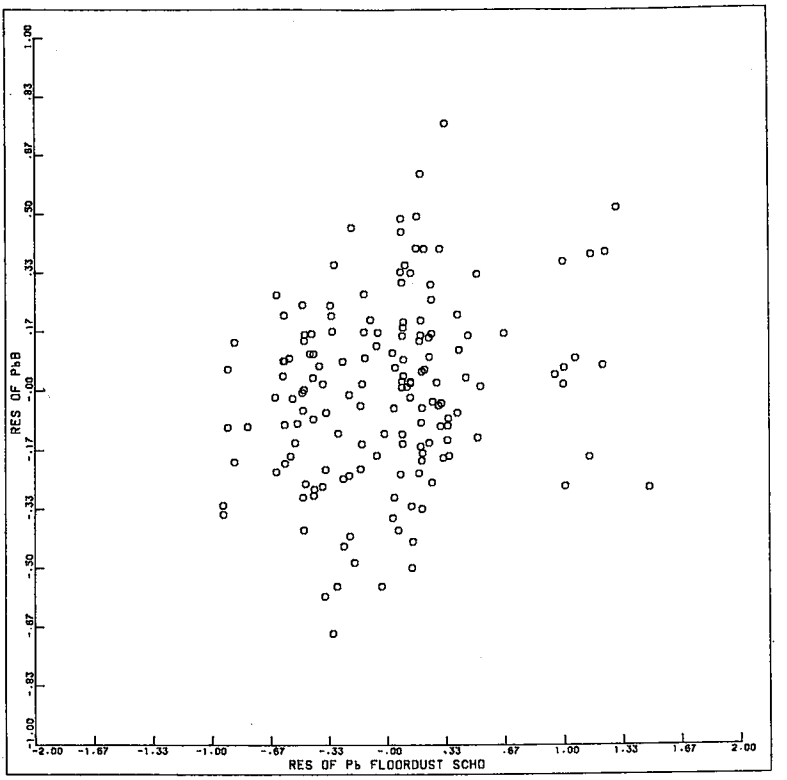
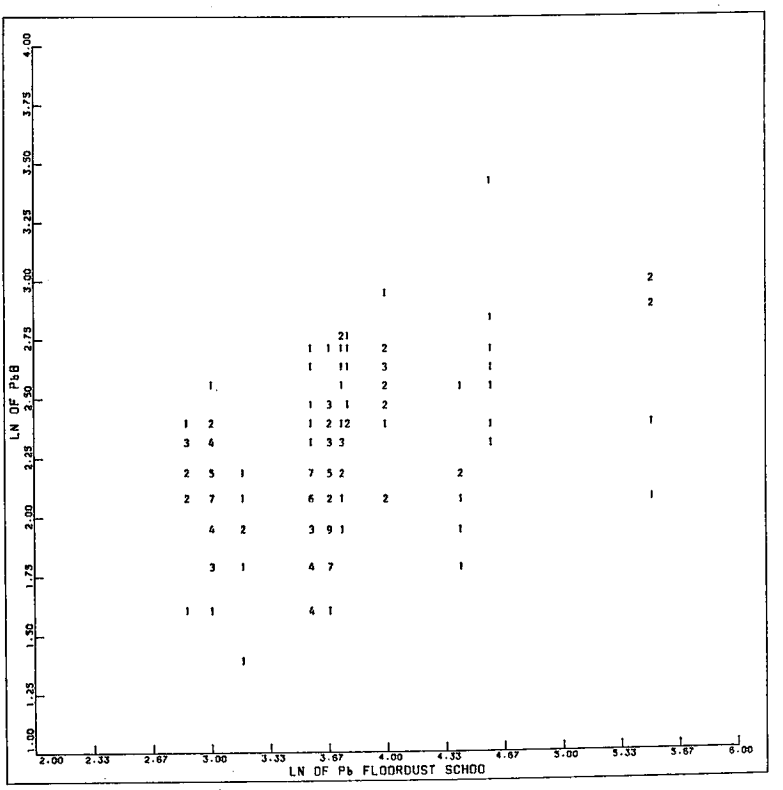
1.50
1.75
2.00
2.25
2.50
2.75
3.00
LN OF Pb DEP IN SCHOOL


RES OF PbB
1.00
.83
.67
.50
.33
.17
.00
-.17
-.33
-.50
-.67
-.83
-1.00
-2.00
-1.67
-1.33
-1.00
-.67
-.33
-.00
.33
.67
1.00
1.33
1.67
2.00
RES OF Pb FLOORDUST SCHO


LN OF PbB
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3.75
3.50
3.25
3.00
2.75
2.50
2.25
2.00
1.75
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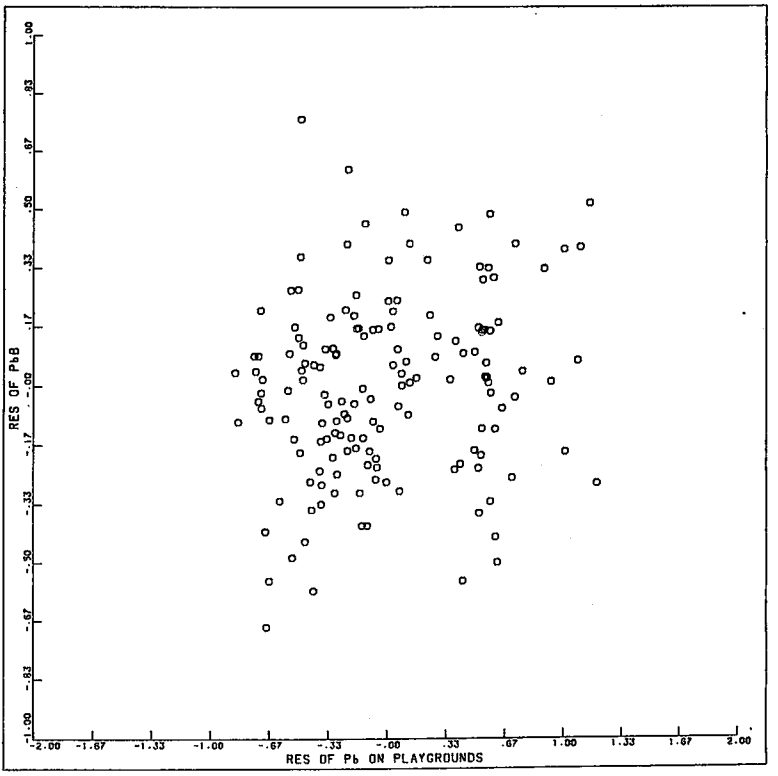
1.25
1.00
2.00
2.33
2.67
3.00
3.33
3.67
4.00
4.33
4.67
5.00
5.33
5.67
6.00
LN OF Pb FLOORDUST SCHOO


RES OF PbB
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.83
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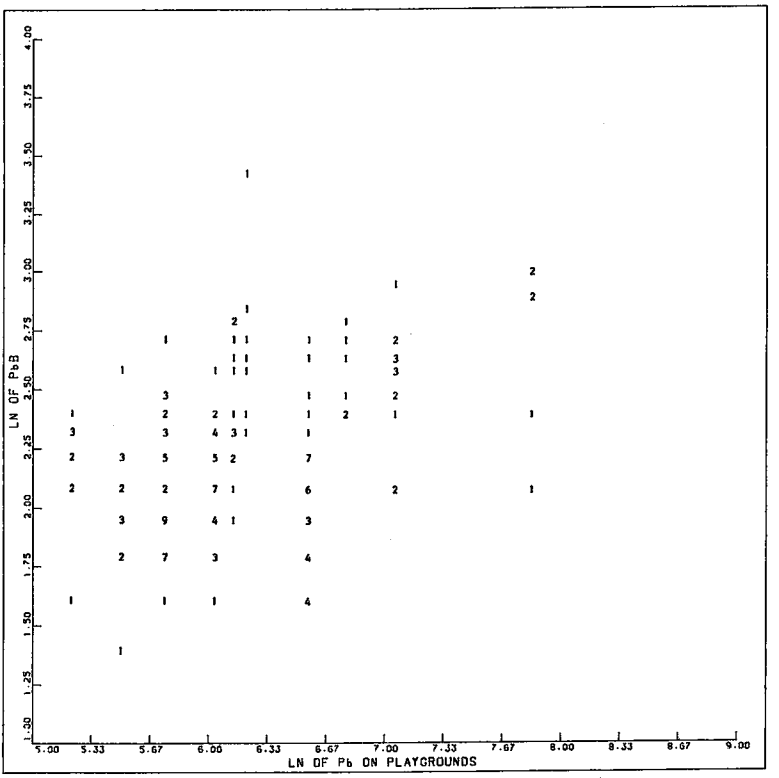
.50
.33
.17
.00
-.17
-.33
-.50
-.67
-.83
-1.00
-2.00
-1.67
-1.33
-1.00
-.67
-.33
-.00
.33
.67
1.00
1.33
1.67
2.00
RES OF Pb ON PLAYGROUNDS


LN OF PbB
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3.75
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3.00
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1.00
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5.33
5.67
6.00
6.33
6.67
7.00
7.33
7.67
8.00
8.33
8.67
9.00
LN OF Pb ON PLAYGROUNDS

APPENDIX 4.

Correlation matrices of variables concerning the origin of lead in the environment

Matrix 1. Ln Lead on streets and its potential determinants (Table 4.19) n=78

	1	2	3	4	5	6
1 Ln lead on streets	1.000					
2 Ln lead deposition outdoors	.535	1.000				
3 Years since repavement	-.064	.089	1.000			
4 Lead emitting neighbourhood facility[1]	.202	.394	.072	1.000		
5 Residential Precinct[2]	-.477	-.533	-.058	-.156	1.000	
6 Cracking and/or flaking outdoor paint[3]	.341	.707	.062	.278	-.426	1.000

1 0=no, 1=yes

2 Residential Precinct with restricted rights for wheeled traffic 0=no, 1=yes

3 0=no, 1=cracking and/or flaking paint visible on outside of home

Matrix 2. Ln lead on home floors and its potential determinants (Table 4.20) n=80

	1	2	3	4	5	6	7	8
1 Ln lead on home floors	1.000							
2 Ln lead deposition outdoors	.406	1.000						
3 Lead hobbies[1]	.069	.000	1.000					
4 Presence of pets[1]	.183	.246	.082	1.000				
5 Cracking and/or flaking paint indoors[1]	.100	.206	.158	.091	1.000			
6 Parental occupational exposure to lead[1]	.088	.265	.331	.132	.194	1.000		
7 Ln lead on sidewalks	.456	.581	-.175	.031	.113	.217	1.000	
8 Construction year of home[2]	.406	-.765	-.164	-.263	-.219	-.241	-.368	1.000

[1] 0=no, 1=yes
[2] minus 1000

Matrix 3. Ln lead deposition in homes and its potential determinants (Table 4.21) n=86

	1	2	3	4	5	6	7	8
1 Ln lead deposition in homes	1.000							
2 Ln lead deposition outdoors	.345	1.000						
3 Lead hobbies[1]	-.003	.005	1.000					
4 Presence of pets[1]	.371	.249	.034	1.000				
5 Cracking and/or flaking paint indoors[1]	.138	.232	.102	.132	1.000			
6 Parental occupational exposure to lead[1]	.183	.348	.199	.223	.105	1.000		
7 Ln lead on sidewalks	-.002	.583	-.110	.021	.152	.205	1.000	
8 construction year of the home[2]	-.452	-.763	.005	-.265	-.208	-.244	-.384	1.000

[1] 0=no, 1=yes
[2] minus 1000

Bibliography

Since 1978, a number of research projects concerning exposure of children to lead in the environment have been performed by the Department of Environmental and Tropical Health of the Agricultural University of Wageningen in cooperation with the Departments of Toxicology, Air Pollution and Soil Pollution, with the Coronel Laboratory of the University of Amsterdam, with the National Institute of Public Health in Bilthoven and with the National Institute for Water Supply in Voorburg.
Other papers and reports concerning these investigations were:

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Hij bezocht het gymnasium in Utrecht en studeerde van 1971 tot 1979 aan de Landbouwhogeschool te Wageningen (studierichting Milieuhygïne). Het afstudeerpakket bestond uit de vakken Gezondheidsleer, Luchtverontreiniging en Milieurecht. Na zijn studie trad hij in dienst bij de vakgroep Gezondheidsleer van de Landbouwhogeschool, waar hij het hier beschreven onderzoek uitvoerde. In de afgelopen jaren hield hij zich daarnaast uitgebreid bezig met luchtverontreiniging in woningen en de mogelijke gevolgen daarvan voor de volksgezondheid. In verband daarmee maakte hij o.a. deel uit van de Commissie Binnenhuisklimaat van de Gezondheidsraad.