
Chapter 19

LEAD EXPOSURE

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SUMMARY

Exposure to lead causes a number of diseases, including mild mental retardation resulting from loss of IQ points, as well as increased blood pressure, anaemia, and gastrointestinal effects. Several other disease outcomes have been associated with exposure to lead, but evidence is considered insufficient at this time for a quantitative assessment of their impact on health to be made here.

The exposure variable used was the population distribution of blood-lead concentrations. We compiled data on concentrations of lead in blood from general population samples in countries around the world, as reported in more than 700 published studies. Only recent studies (published in or after 1995) were considered, because of changes in lead exposure that have taken place since the 1970s, mainly as a result of the implementation of lead reduction programmes (e.g. the phasing out of leaded petrol). Where current data were not available, we applied an adjustment of 39% reduction in blood-lead concentrations to allow for the effects of implementation of five-year lead reduction programmes. For countries for which data were not available, exposure reduction due to existing lead reduction programmes was accounted for by extrapolation.

Blood-lead concentrations of about 0.016 µg/dl have been measured in pre-industrial humans, indicating that the contribution of natural sources of lead to human exposure is minimal. Estimates published recently suggest that the theoretical-minimum-risk of health effects may occur at blood-lead concentrations as low as 0–1 µg/dl.

The association of increased blood-lead concentrations with loss of IQ points has been described in a meta-analysis by Schwartz (1994). Hazards for blood lead and blood pressure were from a meta-analysis by Schwartz (1994) and a published analysis of data from the second National Health and Nutrition Examination Survey (NHANES II).

Hazards for anaemia and gastrointestinal effects were based on a large review of toxicological and epidemiological data (ATSDR 1999). Based on the results of a study by Schwartz et al. (1990), as a consequence of individual variation we considered that only 20% of the people with blood-lead concentrations above those indicated by the Agency for Toxic Substances and Disease Registry (ATSDR) would actually develop symptoms.

The number of people with mild mental retardation as a result of IQ loss was determined on the basis of a standardized intelligence curve. To account for the higher prevalence of other mild mental retardation risk factors (e.g. malnutrition) in some subregions,¹ the prevalence of lead-induced mild mental retardation was adjusted for the known ratio of mental retardation caused by other factors. A number of health outcomes and social consequences of lead exposure (e.g. increased risk of violence and drug abuse) could not be quantified owing to insufficient evidence on hazard size.

In 2000, an estimated 120 million people around the world had blood-lead concentrations of between 5 and 10 µg/dl, and about the same number had concentrations of >10 µg/dl. Forty per cent of all children had blood-lead concentrations of >5 µg/dl and half of these children had blood-lead concentrations of >10 µg/dl; of these children, 97% were living in developing countries. The burden of disease caused by mild mental retardation attributable to exposure to lead resulted in 9.8 million disability-adjusted life years (DALYs), and the burden from cardiovascular diseases caused by elevated blood pressure resulted in 229 000 premature deaths and 3.1 million DALYs. In total, these two outcomes alone account for about 0.9% of the global burden of disease. Several health outcomes resulting from exposure to lead could not be quantified in this analysis, in particular, increased delinquent behaviour and its impact on injuries. Health impacts from anaemia and gastrointestinal effects caused by exposure to lead were relatively small. People affected by exposure to lead were concentrated mainly in developing countries. The burden of disease associated with exposure to lead could be virtually eliminated through interventions that have proven successful in developed countries, most importantly, the removal of lead from petrol.

1. INTRODUCTION

The toxic nature of lead has been recognized for millennia, with the earliest published reports dating back to 2000 BC (Needleman 1999). However, the range of health effects that exposure to lead can cause and the low concentrations of lead in blood at which these effects can occur is only now being fully appreciated. It is now understood that lead is toxic, especially to children, at levels that were previously thought to be safe.

Lead, due to its multiplicity of uses (e.g. leaded petrol, lead in paints, ceramics, food cans, make-up, traditional remedies, batteries), is present

in air, dust, soil and water to varying degrees. Each of these media can act as a route of human exposure, through ingestion or inhalation and, to a small degree for organic lead compounds, dermal absorption. Human exposure can be assessed directly, through body burden measurements (lead in blood, teeth or bone) or indirectly, by measuring levels of lead in the environment (air, dust, food or water).

Multiple health effects have been associated with lead exposure, including systemic effects (e.g. gastrointestinal effects, anaemia, hypertension and hearing loss), effects on the nervous system (e.g. on behaviour and cognition), on development, and on the reproductive system, as well as genotoxicity, carcinogenicity and social effects (ATSDR 1999). The strength of evidence supporting the association of these health effects with exposure to lead varies, and not all of these effects have been investigated sufficiently to permit quantification of their consequences in terms of disease burden.

1.1 RISK FACTOR DEFINITION

In this analysis, exposure was characterized by the population mean and the population distribution of blood-lead concentrations. Occupational exposures or "hot spots" (i.e. areas of local relevance where lead levels are unusually high, such as around smelters) were excluded, unless they were assessed within general population samples.

1.2 THEORETICAL-MINIMUM-RISK EXPOSURE DISTRIBUTION

The definition of an elevated concentration of lead in the blood according to the Centers for Disease Control and Prevention (CDC 1991) is 10 µg/dl. However, evidence indicating that some health effects can occur below this threshold is accumulating. Recent analyses suggest that health effects may become apparent at concentrations of <5 µg/dl (Lanphear 2000) and, indeed, that no evidence exists for a threshold, even at 1 µg/dl (Schwartz 1994). For the purpose of this analysis, the concentration of blood-lead incurring the lowest population risk was considered to be 0–1 µg/dl, in the absence of scientific consensus and pending further investigation. The measurement of blood-lead concentrations in pre-industrial humans has shown that the contribution of natural sources of lead to human exposure is small; Flegal and Smith (1992) have estimated that pre-industrial humans had blood-lead concentrations of only 0.016 µg/dl.

2. ESTIMATING RISK FACTOR LEVELS

2.1 CHOICE OF EXPOSURE VARIABLE

The concentration of lead in blood was chosen as the measure of exposure of the population because:

- it is an objective physiological measure, which can be measured accurately;
- it is directly related to health outcome and can be expected to reflect exposure more closely than estimates derived from measurement of the concentration of lead in air, soil, dust or food; and
- it is the only parameter for which measurements are available from many parts of the world, thus making it preferable to other physiological measures, such as the concentration of lead in bone.

Blood-lead concentrations are indicative of recent lead exposure (within the preceding few weeks) rather than of cumulative long-term exposure. However, as exposure to lead varies relatively little over a time span of a year (WHO 1998), this measure can also be a sign of longer-term exposure.

2.2 DATA ON BLOOD-LEAD CONCENTRATIONS

DATA SOURCES

Exposure data were obtained from studies identified principally through Medline searches. The primary database used was compiled by the CDC (1999) and contained exposure data from over 700 articles published between 1965 and 1998. The search strategy used was the term “lead” paired with any of the following keywords: newborn, cord, adult, pregnancy, occupation, blood, tooth, hair, milk, placenta, urine, smelter, ceramics, pottery, petrol, cosmetics, kohl, surma, medicine, neurological deficit, cognitive function, pregnancy outcome, fertility and birth defect. Initial queries were followed up using the “related-articles” option of Medline and further searches on the basis of author. The reference list of each relevant article was also examined. Additionally, the authors conducted searches of the databases LILACS (Latin American and Caribbean Information System of Health Sciences), IMEMR (Index Medicus of the World Health Organization’s [WHO] Regional Office for the Eastern Mediterranean—EMRO) and African Index Medicus, using the same keywords. Medline was also re-consulted to ensure coverage of the most recent publications (up to the end of 2000).

COMPILATION AND PRESENTATION OF DATA

Blood-lead concentrations in the population generally have a log-normal distribution, as reported in numerous countries and populations (Al-Saleh et al. 1999; Baghurst et al. 1995; Brody et al. 1994; CDC 2001; Harlan et al. 1985; Hense et al. 1992; Molla et al. 1997; Pocock et al. 1988; Schwartz 1991; Tong et al. 1998). Geometric means with standard deviations were therefore compiled to represent population exposures.

A few studies reported small differences (typically <10%) between blood-lead concentrations in males and females (e.g. CDC 2001; Nielsen et al. 1998; Omokhodion 1994; Paoliello et al. 1997). We therefore com-

bined exposure data for men and women in this analysis. Exposure data were compiled separately for children and adults where this information was available.

2.3 COUNTRY ESTIMATES AND SUBREGIONAL AGGREGATION

ADJUSTMENTS FOR DATA FROM COUNTRIES CURRENTLY PHASING OUT LEAD IN PETROL

Blood-lead concentrations can change dramatically over a few years in response to programmes to eliminate the use of lead in petrol. Therefore, data which were more than one year old from countries that had reduced exposure to lead required downward correction to avoid overestimating exposure.

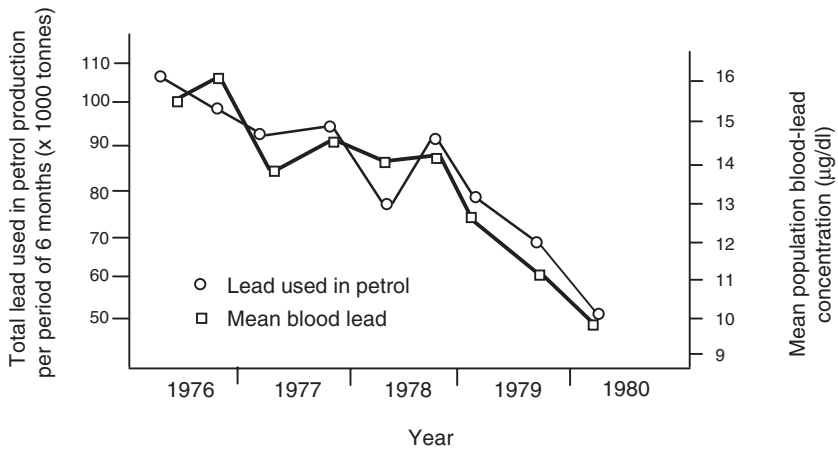
Decreases in blood-lead concentrations correlate well with the removal of lead from petrol (Thomas et al. 1999). Therefore, progress in phasing out lead was used to adjust exposure levels. Although leaded petrol is not the only source of lead in the environment, it is a good indicator of reduction in exposure to lead (Landrigan et al. 2000). Multiple studies have shown reductions in blood-lead concentrations in parallel with decreases in levels of lead in petrol (Thomas et al. 1999). Full implementation of lead reduction programmes has produced decreases in blood-lead concentrations in children of $\geq 90\%$ over 25 years (CDC 1997, 2000).

Figure 19.1 shows changes in population blood-lead concentrations in the United States of America over a five-year period, during the early stages of a lead reduction programme (Annest 1983; Annest et al. 1983). During this period, the mean blood-lead concentration dropped by 37%. Other studies conducted in various countries have shown very similar results (Elinder et al. 1986; Schuhmacher et al. 1996; Wietlisbach et al. 1995), with decreases ranging from 30–48% over a five-year period. We chose the midpoint of 39% as a reduction factor for data that had been collected 5 years before the initiation of a leaded petrol phasing-out process or, for shorter periods, 7.8% decrease per year. Data which were >6 years old were not used. Only the most recent data were selected, provided that they were consistent with trends observed in older data.

Use of leaded petrol and the timing of any changes in the concentration of lead in petrol were assessed using data derived from the World Resources Institute (WRI 1998), the Earth Summit Watch (UNEP 2000), Car Lines (Walsh 2001) and M.P. Walsh (personal communication, 2002). A summary of the global situation with regard to reducing exposures to lead in petrol is provided in Figure 19.2 and below.

- *AFR-D and AFR-E*: With the exception of South Africa, countries in these subregions have not implemented lead reduction programmes.
- *AMR-A*: Blood-lead concentrations are likely to be significantly higher in Cuba than in Canada or the United States, as Cuba started lead reduction programmes more recently.

Figure 19.1 Decrease in mean population blood-lead concentrations in relation to reduction of lead in petrol,^a in the United States



^a The lead reduction programme started in 1974–1975.

Source: Annett (1983).

Figure 19.2 Sales of leaded petrol as a percentage of total petrol sales, by country, end of 2001



Source: Map based on data provided by M.P. Walsh.

- *AMR-B and AMR-D*: Most countries have now phased out leaded petrol. However, other sources, such as battery recycling and lead-glazed ceramics, are of importance in these subregions. Some countries, including Mexico and Peru, are major producers of lead.
- *EMR-B and EMR-D*: Some countries have now started a lead reduction programme. Egypt and Saudi Arabia are almost lead-free with regard to petrol.
- *EUR-A*: Most countries have phased out lead in petrol, and lead reduction programmes have been in place for a considerable period of time.
- *EUR-B and EUR-C*: While lead reduction programmes in some countries are relatively advanced, the great majority of countries have made little progress. EUR-C is less advanced than EUR-B in terms of phasing out leaded petrol.
- *SEAR-B and SEAR-D*: While Thailand has phased out lead in petrol, significant amounts of leaded petrol are still used in other countries. Sources other than leaded petrol (especially lead-containing cosmetics and local medications) greatly contribute to exposure in certain parts of these subregions.
- *WPR-A*: All countries have undertaken lead reduction programmes, most of which have been fully implemented. Japan began implementing lead reduction programmes at a very early stage.
- *WPR-B*: Some countries in this subregion, such as China and the Philippines, have made considerable efforts to phase out leaded petrol. Other countries have made little or no progress.

EXPOSURE IN RURAL POPULATIONS

Where leaded petrol is still in use, blood-lead concentrations in rural populations are generally lower than those in urban populations (Nriagu et al. 1997a; Piomelli et al. 1980; Rhainds and Levallois 1993; Vasilios et al. 1997).

Thomas et al. (1999) showed that soon after the elimination of leaded petrol, population blood-lead concentrations tend to converge on an average of 3.1 µg/dl (SD 2.3 µg/dl). This value is similar to the mean, 3.0 µg/dl, of the data from rural areas available from countries in which lead has not been totally or partially phased out (3.4 µg/dl, Grobler et al. 1985; 2.3 µg/dl, Khwaja 2002; 3.8 µg/dl, Nriagu et al. 1997a; 3.4 µg/dl, Piomelli et al. 1980; 2.1 µg/dl, Vasilios et al. 1997). We therefore selected 3.1 µg/dl as the mean blood-lead concentration for rural populations in countries where concentrations of blood-lead in urban areas were higher than this value. In Latin America and the Caribbean, however, it was assumed that rural populations would have higher concentrations of blood-lead as other sources, such as ceramics and recy-

cling of batteries, contribute significantly to lead exposure in these areas (Romieu 2001a). The mean of the most recently-reported blood-lead concentrations in urban Latin American countries that have phased out lead is 4.3 µg/dl (Garcia and Mercer 2001; Sepulveda 2000), and we also used this value to represent rural blood-lead concentrations in this subregion.

After the complete phasing-out of leaded petrol, blood-lead concentrations continue to decrease, mainly as a result of additional efforts to reduce other sources of lead in the environment. Recent assessments from the United States have reported mean blood-lead concentrations of 1.6 µg/dl for the total population and 2.0 µg/dl for children aged <5 years (CDC 2001). In such cases, the same values were used to characterize urban and rural populations, as assuming higher exposures in urban environments did not seem justifiable.

CALCULATING SUBREGIONAL MEANS

For each country with more than one source of data for blood-lead concentrations, geometric means were calculated (weighted by sample size) after the above adjustments. Means for urban and rural populations were estimated separately. Subregional means were calculated by weighting the mean for each country by the size of its urban population. For subregions with countries at different stages of lead phase-out (all subregions except EUR-A and AFR-D), urban means were estimated separately for countries which had made different degrees of progress in eliminating lead. In summary, we superimposed two or three log-normal distributions for each subregion to characterize the distribution of blood-lead concentrations in the population, each of which was weighted by the size of the population they represent. The urban/rural breakdown was based on data from UNDP (2000).

Fewer data on standard deviations were available than on mean blood-lead concentrations. In order to estimate standard deviations for areas for which data were sparse, we grouped subregions according to economic and lead-use patterns and calculated the average standard deviation for each grouping (AMR-A; EUR-A and WPR-A; AMR-B and D; remaining B and C subregions; remaining D and E subregions). Country averages (weighted by sample size) were estimated, and then averaged into the subregional standard deviations by weighting for the size of the urban population. For the grouping of D and E subregions, we did not weight by population size because the large countries contained within these two groupings were not representative of other countries. Table 19.1 shows the urban means for children and adults, the standard deviations, and the distribution of the population into categories of blood-lead concentration. As mentioned above, mean blood-lead concentrations in rural populations are assumed to be 3.1 µg/dl, or equal to blood-lead concentrations for urban populations in which levels have declined after lead reduction programmes.

Table 19.1 Blood-lead concentrations in children and adults, by subregion

Subregion	AFR-D ^{c,c}	AFR-E ^{c,c}	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
Mean blood-lead concentration, urban children ($\mu\text{g}/\text{dl}$) ^b	11.1	9.8	2.2	7.0	9.0	6.8	15.4	3.5	5.8	6.7	7.4	7.4	2.7	6.6
Mean blood-lead concentration, urban adults ($\mu\text{g}/\text{dl}$) ^c	11.6	10.4	1.7	8.5	10.8	6.8	15.4	3.7	9.2	6.7	7.4	9.8	2.7	3.6
Standard deviation ($\mu\text{g}/\text{dl}$) ^c	5.6	5.6	2.9	3.9	3.9	3.9	5.6	1.9	3.0	3.0	3.0	5.6	1.9	3.0
Percentage of urban population	36	25	77	74	58	67	37	78	62	72	31	26	80	32
Countries with recent data	Nigeria ¹	South Africa ²	Canada, ³ USA ⁴	Argentina, ⁵ Brazil, ⁶ Chile, ⁷ Jamaica ⁸	Ecuador, ¹² Nicaragua, ¹³ Peru ¹⁴	Saudi Arabia ¹⁵	Egypt, ¹⁶ Morocco, ¹⁷ Pakistan ¹⁸	Denmark, ¹⁹ France, ²⁰ Germany, ²¹ Greece, ²² Israel, ²³ Sweden ²⁴	Poland, ²⁵ Turkey, ²⁶ Former Yugoslavia ²⁷	Hungary, ²⁸ Russian Federation ²⁹	Indonesia, ³⁰ Thailand ³¹	Bangladesh, ³² India ³³	Australia, ³⁴ Japan, ³⁵ New Zealand, ³⁶ Singapore ³⁷	China, ³⁸ Micronesia, ³⁹ Philippines, ⁴⁰ Republic of Korea ⁴¹
Percentage of children with 5–10 $\mu\text{g}/\text{dl}$	18.6	19.1	12.4	21.2	23.2	23.3	18.1	22.7	22.7	23.6	21.8	19.2	14.1	21.8
Percentage of children with 10–20 $\mu\text{g}/\text{dl}$	10.0	8.9	4.7	16.3	16.4	15.7	10.1	5.1	13.8	16.3	11.2	8.8	2.9	10.9
Percentage of children with >20 $\mu\text{g}/\text{dl}$	13.9	9.5	1.9	16.7	17.2	11.4	17.2	0.5	8.9	11.9	6.5	8.3	0.3	5.8

continued

Table 19.1 Blood-lead concentrations in children and adults, by subregion (continued)

Countries with recent data	Nigeria ¹	South Africa ²	Canada ³	USA ⁴	Venezuela ¹¹	Peru ¹⁴	Ecuador, ¹² Nicaragua, ¹³ Uruguay, ¹⁰ Mexico, ⁹ Jamaica, ⁶ Chile, ⁷ Brazil, ⁶ Argentina, ⁵	Poland, ¹⁵ Turkey, ²⁶ Former Yugoslavia ²⁷	Hungary, ²⁸ Russian Federation ²⁹	Indonesia, ³⁰ Thailand ³¹	Bangladesh, ³² India ³³	Australia, ³⁴ Japan, ³⁵ New Zealand, ³⁶ Singapore ³⁷	China, ³⁸ Micronesia, ³⁹ Philippines ⁴⁰	Republic of Korea ⁴¹
Percentage of adults with 5–10 µg/dl	18.5	19.1	9.1	22.1	22.6	23.3	18.1	24.3	22.5	23.6	21.8	19.1	14.1	20.6
Percentage of adults with 10–20 µg/dl	10.0	8.9	3.2	17.2	16.6	15.7	10.1	5.7	16.7	16.3	11.2	9.0	2.1	8.4
Percentage of adults with >20 µg/dl	14.3	9.8	1.1	19.9	20.1	11.4	17.2	0.6	15.5	11.9	6.5	9.7	0.1	2.8

^a Exposure data for these subregions were combined for this analysis.

^b High and low means of urban blood-lead concentrations were used for subregions where countries were at different stages of the phasing-out of leaded petrol. The distribution is therefore a superposition of two or three log-normal distributions, and the mean and standard deviation do not necessarily reflect the distributions; therefore only one mean and standard deviation, as well as the distribution of people in exposure categories 5–10 µg/dl, 10–15 µg/dl and 15–20 µg/dl are displayed.

^c Only data from South Africa, 1999, were used to represent countries with efforts in lead reduction in African subregions; older data were used to represent countries without such efforts.

Table references

- Nriagu et al. (1997b); Omokhodion (1994).
- Deveaux et al. (1986); Grobler et al. (1992); Karimi et al. (1999); Maresky and Grobler (1993); Nriagu et al. (1997a); von Schimming et al. (2001); White et al. (1982).
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- Nielsen et al. (1998).
- Flurin et al. (1998).
- Jacob et al. (2000).
- Vasilios et al. (1997).
- Teplerberg and Almog (1999).
- Bergdahl et al. (1997); Osterberg et al. (1997).
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- Bianusa et al. (1991); Factor-Litvak et al. (1996, 1998); Kostal et al. (1991).
- Bitco et al. (1997).
- Teplerberg and Almog (1999).
- Heinze et al. (1998).
- Wananukul et al. (1998).
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- Australian Institute of Health and Welfare (1996).
- Watanabe et al. (1996); Zhang et al. (1997).
- Fawcett et al. (1996).
- Chia et al. (1996, 1997); Neo et al. (2000).
- Gao et al. (2001); Murata et al. (1995); Shen et al. (1996, 2001); Wan et al. (1996); Yan et al. (1999); Zhang et al. (1997).
- Zhang et al. (1998).
- Moon et al. (1995); Yang et al. (1996).

Based on these methods, we estimated that globally 120 million people had blood-lead concentrations of between 5 and 10 µg/dl in the year 2000, and about the same number of people had blood-lead concentrations of >10 µg/dl. Forty per cent of all children had blood-lead concentrations of >5 µg/dl, and 20% had concentrations of >10 µg/dl, and 97% of the latter were living in developing countries. Nine per cent of children had blood-lead concentrations of >20 µg/dl, and 99% of these children were living in developing countries.

3. ESTIMATING RISK FACTOR–DISEASE RELATIONSHIPS

3.1 HEALTH OUTCOMES

Exposure to lead affects multiple health outcomes and physiological systems (ATSDR 1999), including the following: hypertension, the gastrointestinal system, anaemia, nephropathy, vitamin D metabolism, decreased growth, the immune system, the nervous system, behavioural/cognitive/IQ effects (and as a result, multiple social effects, including increased risk of violence and drug abuse), nerve conductive effects, hearing loss, effects on reproduction and development and death from encephalopathy.

Evidence relating exposure to lead and various health effects has been reviewed extensively (ATSDR 1988, 1993, 1999; International Programme on Chemical Safety 1977, 1995; National Research Council 1993; Pocock et al. 1994; Schwartz 1994). The most recent comprehensive review of the evidence on the risk factor–disease relationship was conducted by ATSDR in the United States (1999). Health effects considered in this review included systemic effects (e.g. raised blood pressure, gastrointestinal effects and anaemia) and nervous system effects (IQ reduction). Nephropathy and encephalopathy were not included as they rarely occur after environmental exposures but rather as a result of high-level exposure, such as ingestion of lead or lead salts, e.g. from local medication (Woolf 1990) or occupational exposure. A number of suggested health outcomes (e.g. developmental, reproductive and social effects) were not considered because of difficulties in quantifying the level of exposure at which a health outcome occurs, inadequate evidence of causality, or lack of information regarding baseline disease levels.

3.2 EVIDENCE AND EXPOSURE–RISK RELATIONSHIPS

GENERAL NERVOUS SYSTEM EFFECTS

The central and peripheral nervous systems are considered to be the principal targets affected by toxicity caused by the absorption of lead (Tsuchiya 1986; WHO 1996). Proposed mechanisms of toxicity (reviewed in ATSDR 1999) are based on the ability of lead to inhibit or mimic the action of calcium, and to interact with proteins. In terms of

general effects on the nervous system, the key mechanism is likely to be the substitution of lead for calcium as a “second messenger” in neurons. Lead blocks voltage-regulated calcium channels, inhibiting the influx of calcium and release of neurotransmitters and thus inhibiting synaptic transmission.

The most severe neurological effect of exposure to lead is encephalopathy. However, neurotoxic effects are apparent at much lower blood-lead concentrations than those that cause encephalopathy (i.e. $\leq 90 \mu\text{g}/\text{dl}$ for children, $\leq 140 \mu\text{g}/\text{dl}$ for adults, depending on the individual). Studies investigating occupational exposure to lead have reported symptoms such as loss of appetite, malaise, lethargy, headache, fatigue, forgetfulness and dizziness in workers with blood-lead concentrations of $40\text{--}120 \mu\text{g}/\text{dl}$.

In the 1940s, Byers and Lord (1943) reported that children who had previously suffered from lead poisoning made poor progress at school, had a shorter attention span and exhibited behavioural disorders. Such observations were followed by epidemiological studies to determine the effects of low-level exposure to lead on children’s intellectual abilities and behaviour. Low-level exposure to lead has been associated with failure to complete schooling, reading disability, longer reaction times, delinquent activity and other signs indicating effects on the central nervous system (Needleman et al. 1990, 1996). A large cohort study (Burns et al. 1999) showed that children exposed to relatively low levels of lead experienced an array of emotional and behavioural problems. Similarly, children who had experienced prenatal and postnatal exposure to lead were found to have an increased risk of cognitive deficit (Bellinger et al. 1990), problem behaviour and other dysfunctions, such as inappropriate approaches to tasks, or difficulty with simple directions and sequences of directions (Bellinger et al. 1994; Leviton et al. 1993). Nevin (2000) reported that long-term trends in population exposure to lead (indexed through use of leaded petrol and paint) were remarkably consistent with changes in violent crime; these findings are consistent with the reported link between IQ and social behaviour. Although it has been suggested that neurophysiological changes may be reversible (Ruff et al. 1993), the results of numerous studies indicate that this is unlikely (Schwartz et al. 2000b; Stokes 1998; Tong et al. 1998).

Effects on the nervous system other than loss of IQ and consequent mental retardation could not be quantified at the population level. This was either because of insufficient evidence linking effects to blood-lead concentrations, or because the outcome was not, in the strict sense, a quantifiable health effect (e.g. behavioural problems).

LOSS OF IQ POINTS

Analyses of the body of evidence regarding the link between exposure to lead in early childhood and decrease in IQ score suggest that the relationship is causal (International Programme on Chemical Safety 1995;

Pocock et al. 1994; Schwartz 1994). In a meta-analysis, Schwartz (1994) estimated that a mean loss of 2.6 IQ points was associated with an increase in blood-lead concentration from 10 to 20 µg/dl. This result was robust to the inclusion or exclusion of the results of the strongest individual studies. This meta-analysis included eight cross-sectional and longitudinal studies, the largest longitudinal study being the Port Pirie cohort study in Australia (Baghurst et al. 1992) with about 500 participants and a follow-up of several years. Other meta-analyses report similar findings (International Programme on Chemical Safety 1995; Pocock et al. 1994). We selected the analysis by Schwartz (1994) to define the outcome as this study quantified the loss of IQ points and provided a point estimate with a confidence interval. At blood-lead concentrations of >20 µg/dl, we assumed a loss of 2–5 IQ points (midpoint of 3.5 IQ points) on the basis of the conclusions of the ATSDR report, which were derived from evidence from two studies (de la Burde and Choate 1972; Rummo et al. 1979).

Schwartz (1994) also reported that loss of IQ points is likely to be found between 5 and 10 µg/dl, with an even steeper relationship than in higher concentrations. For comparison, CDC currently defines blood-lead concentrations in excess of 10 µg/dl as elevated, although acknowledging Schwartz' analysis as evidence for subtle effects at lower concentrations (CDC 2000). The existence of such effects has recently been confirmed by Lanphear et al. (2000), whose analysis of data from about 5000 children showed that children with blood-lead concentrations of between 5 and 10 µg/dl had poorer cognitive skills.

In summary, to quantify IQ loss in the population, we assumed a linear relationship of 1.3 IQ points lost per 5 µg/dl increase in blood lead, for blood-lead concentrations of between 5 and 20 µg/dl (according to the analysis of Schwartz 1994, which showed a loss of 2.6 IQ points for an interval of 10 µg/dl). This linear relationship was divided into three segments, or increments, of 5 µg/dl, and the mean loss of IQ points in each increment was assigned to its mean blood-lead concentration—that is, 0.65 points for the increment 5–10 µg/dl with a mean of 7.5 µg/dl; 1.95 points for the increment 10–15 µg/dl with a mean of 12.5 µg/dl; and 3.25 points for the increment 15–20 µg/dl. The mean loss of IQ points is 0.65 (1.3/2) for the first increment, 1.95 (0.65+1.3) for the second, and 3.25 (1.95+1.3) for the third. This is illustrated in Figure 19.3. A loss of 3.5 IQ points was assumed for blood-lead concentrations of >20 µg/dl.

MILD MENTAL RETARDATION AS A CONSEQUENCE OF LOSS OF IQ POINTS

As loss of IQ points *per se* is not considered to be a disease by the international classification of disease (ICD) system, we converted IQ loss into mild mental retardation. Although loss of IQ potentially increases the risk for other diseases, injuries and adverse outcomes, such as violence (Needleman et al. 1996; Nevin 2000), no quantification could be made

Figure 19.3 Decrease in IQ points per increment increase in blood-lead concentration (“best estimate”)

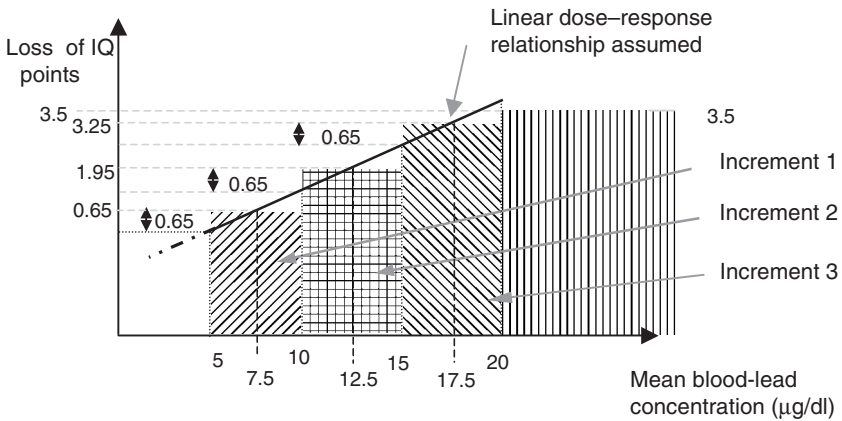
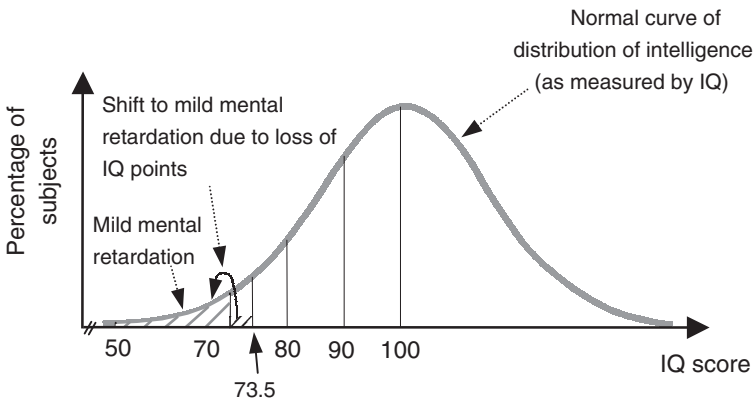


Figure 19.4 Loss of IQ points resulting in mild mental retardation



owing to the very heterogeneous nature of these relationships in different populations. For the purpose of this study, a reduction in IQ points was considered to be a disease burden when resulting in mild intellectual impairment, which was defined as having an IQ score of 50–69 points (see Figure 19.4). Intelligence in human populations approximates a normal distribution (Lezak 1995), except for an excess below IQ 50 (representing brain damage and disorder). To estimate the incidence of mild mental retardation resulting from IQ reduction attributable to lead exposure, we first estimated the proportion of children who would have

Table 19.2 Proportion of the population having an IQ score of between 70 and 73.50, assuming a normal distribution^a

IQ (points)	% of the population (assuming a normal IQ distribution)
70–70.65	0.24
70–71.95	0.80
70–73.25	1.45
70–73.50	1.59

^a Mean IQ score of 100, standard deviation of 15.

Source: Lezak (1995).

IQ scores close to the threshold defined and for whom the loss of a few IQ points would result in a total score of <70 points. This included the fractions of the child population with IQ scores of between 70 and 70.65, 71.95, 73.25 and 73.50 points (i.e. the intervals of interest defined by the loss of IQ points as specified above, representing increments of 0.65, 1.95, 3.25 and 3.5 points), assuming a normal distribution for IQ according to Lezak (mean IQ score of 100, standard deviation of 15; see Table 19.2).

The proportion of mild mental retardation attributable to exposure to lead was estimated as the proportion of children losing a number of IQ points (i.e. ratio of children with blood-lead concentrations within intervals 5–10 µg/dl, 10–15 µg/dl or 15–20 µg/dl; see Table 19.1), multiplied by the fraction of children within the interval 70+x IQ points (Table 19.2), for whom a loss of x points results in a final IQ score of <70 points (Figure 19.4). This is similar to the method used by INSERM (1999).

This standard IQ distribution does not include additional risk factors for IQ loss, which may be more common than exposure to lead. Several diseases that occur more frequently in developing countries result in cognitive impairment or mental retardation. The detailed estimates of the global burden of disease listed in the *World health report 2001* (WHO 2001) provide prevalences of cognitive impairment and mental retardation as a consequence of anaemia, meningitis and pertussis, Japanese encephalitis, ascariis, trichuriasis and infection with hookworm, as well as prevalences of cretinoidism and cretinism caused by iodine deficiency, for the 14 subregions studied here (Murray and Lopez 1996; WHO/EIP, unpublished data, 2001). The literature confirms that there are differences in the prevalence rates of mild mental retardation in developed countries compared to developing countries (Roeleveld et al. 1997), most of these differences being explained by noncongenital causes.

As the normal distributions of IQ scores were established on the basis of data from developed countries, the number of additional cases of mild

mental retardation that are likely to be observed in developing countries because of the additional risks mentioned above had to be estimated. This adjustment was based on the assumption that congenital causes of impaired cognitive function were separable and additive as compared to other risk factors. We thus assumed that the increase in the incidence of mild mental retardation (defined as an IQ score of 50–69 points) caused by factors other than exposure to lead was proportional to the increase in frequency of the IQ scores of slightly more than 70 points (i.e. between 70 and 73.5 points).

The prevalence of mild mental retardation and cognitive impairment resulting from known, noncongenital causes (see above) was estimated, values from developed and developing countries were compared, and an “adjustment ratio” to account for the increased risk of mental retardation in developing countries was estimated:

$$AR = \frac{P_R - P_{\text{baseline}} + P_{\text{MR standard}}}{P_{\text{MR standard}}}$$

AR	Adjustment ratio
MR	Mild mental retardation
P_R	Region-specific prevalence of MR from known causes from the Global Burden of Disease (GBD) database (WHO/EIP, unpublished data, 2001)
P_{baseline}	Prevalence of MR from known, noncongenital causes in developed countries
$P_{\text{MR standard}}$	Prevalence of MR according to the standard distribution of IQ score

The baseline prevalence of mild mental retardation caused by known, noncongenital factors of 420 per 100 000 population (typical in developed countries), and the total rate of mental retardation of 2270 per 100 000 population, as taken from the standard distribution, were used. The resulting subregion-specific adjustment ratios are summarized in Table 19.3. We assumed that the same adjustment ratio applied for the

Table 19.3 Adjustment ratios to account for excess prevalence rates of mild mental retardation caused by communicable diseases and iodine deficiency as compared to standardized rates

Subregion	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
Adjustment ratio	2.05	2.01	1.00	2.71	2.64	1.90	1.90	1.00	1.53	1.19	3.25	2.06	1.00	3.03

considered ranges of IQ (i.e. 70–73.5) in an attempt to take into account additional risks prevailing in certain developing subregions. It should be noted, however, that protein–energy malnutrition, potentially the most important risk factor for mild mental retardation, could not be taken into account here. The estimated prevalence rates per 1000 people affected by lead-induced mild mental retardation were multiplied by the subregion-specific adjustment ratios given in Table 19.3.

Lower mental ability has been associated with lower life expectancy. For example, a longitudinal cohort study of childhood IQ score and survival (Whalley and Deary 2000) found lower survival probabilities at age 76 for people who had a 15-point disadvantage in IQ score at age 11 years (RR = 0.76, 95% CI 0.75–0.84). Various mechanisms to explain this association were proposed, including childhood IQ as a record of bodily insult (e.g. antenatal care), as an indicator of “system integrity” (the availability of a cerebral reserve capacity to deal with other risks of cognitive decline), as a predictor of healthy behaviour and of entry into safer environments. All but the first mechanism would be relevant in relating the lead-induced loss of IQ points to additional adverse health effects or to reduced life expectancy, rather than considering mild mental retardation in isolation. Additional evidence, however, is needed to quantify this association.

INCREASED BLOOD PRESSURE

Schwartz (1995) conducted a meta-analysis examining the relationship between blood-lead concentration and systolic blood pressure in adult males (see Table 19.4). This analysis showed a significant association, with a reduction in blood-lead concentration from 10 µg/dl to 5 µg/dl being correlated with a decrease in blood pressure of 1.25 mmHg (95% CI 0.87–1.63). It has been suggested that lead exerts an influence on calcium metabolism, which is linked to modulation of blood pressure through vascular tone. *In vitro* studies have reported increased blood pressure in isolated tail arteries and increased responsiveness to alpha-adrenergic stimulation in response to exposure to lead. Raised blood pressure has been associated with increases in risk of cardiovascular and cerebrovascular disease.

A more recent meta-analysis by Nawrot et al. (2002) of data from 32 000 men estimated that a two-fold increase in blood-lead concentration was associated with a 1.2 mmHg increase in systolic blood pressure. While this analysis considered a two-fold increase in blood-lead concentration as the measure of exposure, most of the studies in the meta-analysis fell within the interval of 5–10 µg/dl considered by Schwartz (1995). The analysis of data from the second National Health and Nutrition Examination Survey (NHANES II) revealed decreases in blood pressure of 2 mmHg associated with a reduction in blood-lead from 20 µg/dl to 15 µg/dl and also from 15 µg/dl to 10 µg/dl (Pirkle et al. 1998; Schwartz 1988).

Table 19.4 The reduction in systolic blood pressure caused by a reduction in blood-lead concentration of 10 µg/dl in adult males

Reference	Reduction in systolic blood pressure (mmHg)	Standard error	Age range (years)	Study type
Orssaud et al. (1985)	1.74	0.73	24–55	Cross-sectional
Schwartz and Pitcher (1988)	2.24	0.86	20–74	Cross-sectional
Pocock et al. (1988)	1.45	0.49	40–59	Cross-sectional
Kromhout (1988)	3.15	1.20	57–76	Cross-sectional
Elwood et al. (1988, Wales)	0.25	0.49	18–64	Cross-sectional
Elwood et al. (1988, Caerphilly)	0.39	0.63	49–65	Cross-sectional
Neri et al. (1988)	1.05	0.70	NA	Cross-sectional and longitudinal
Moreau et al. (1988)	1.50	0.76	23–57	Cross-sectional
de Kort and Zwennis (1988)	0.90	0.39	25–60	Cross-sectional
Sharp et al. (1988))	0.80	1.25	28–64	Cross-sectional
Morris et al. (1990)	3.17	1.59	NA	Longitudinal
Egeland et al. (1992)	1.26	0.62	NA	Cross-sectional
Møller and Kristensen (1992)	1.86	0.63	40–51	Cross-sectional
Møller and Kristensen (1992)	0.90	0.74	40–51	Longitudinal
Hense et al. (1993)	1.45	0.51	28–67	Longitudinal

NA Not applicable.

Source: Adapted from Schwartz (1995).

As a conservative estimate, we used the same change of 1.25 mmHg in systolic blood pressure for all three intervals in blood-lead concentration. The relationship was assumed to be linear between 5 and 20 µg/dl, with a 1.25 mmHg rise in blood pressure for each incremental increase of 5 µg/dl. As with loss of IQ points, we converted the linear increase into three equal increments, using the midpoints of the increments with the corresponding increase in blood pressure.

In women, the association between systolic blood pressure and blood-lead concentrations is weaker and less well documented. The most recent and comprehensive estimate, using data from 24 000 women suggests that an increase of 0.8 mmHg in systolic blood pressure is associated with a doubling in blood-lead concentration (Nawrot et al. 2002). The association was not different from that of men in a statistically significant manner. We used an increase of 0.8 mmHg in systolic blood pressure for each 5 µg/dl increase in blood-lead concentration for women, for the interval between 5 and 20 µg/dl.

The disease burden caused by exposure to lead and mediated through increased blood pressure was based on the method used in chapter 6.

ANAEMIA

Absorbed lead inhibits the activity of a number of enzymes involved in haem biosynthesis. Several studies have shown that the activity of ALAD (δ -aminolevulinic acid dehydratase) is affected at very low blood-lead levels, with no apparent threshold (International Programme on Chemical Safety 1995). Typically, lead-induced anaemia arises from a combination of reduced haemoglobin formation (caused either by impaired haem synthesis or globin chain formation) and reduction in erythrocyte survival because of haemolysis (National Research Council 1993).

Adverse effects start to appear following decreases in concentrations of haemoglobin, which occurs at blood-lead concentrations of approximately 50 $\mu\text{g}/\text{dl}$ in adults and 40 $\mu\text{g}/\text{dl}$ in children, although there is increasing evidence that effects in children may occur at lower concentrations. Schwartz et al. (1990) studied the relationship between various levels of exposure to lead and anaemia in 579 children aged between 1 and 5 years living close to a primary lead smelter. The analysis related blood lead and hematocrit concentrations, and observed an increase in anaemia in children with blood-lead concentrations of $>20 \mu\text{g}/\text{dl}$. However, ATSDR (1999) defines children with blood-lead concentrations of $\geq 70 \mu\text{g}/\text{dl}$ and adults with $\geq 80 \mu\text{g}/\text{dl}$ to be at risk of anaemia, and we chose these thresholds for estimating disease burden. The number of studies looking at more severe health effects and issues of individual variability is relatively limited; however, results suggest that only a proportion of those exposed become ill. In the study conducted by Schwartz et al. (1990), 20% of children with a blood-lead concentration of $\geq 60 \mu\text{g}/\text{dl}$ exhibited signs of anaemia. This value was used in the present analysis to estimate the proportion of those exposed who became ill.

GASTROINTESTINAL EFFECTS

Abdominal pain, constipation, cramps, nausea, vomiting, anorexia and weight loss, collectively known as colic, are early symptoms of lead poisoning in both adults and children. In adults, such symptoms occur at blood-lead concentrations of $>80 \mu\text{g}/\text{dl}$ (International Programme on Chemical Safety 1995) and typically at concentrations of 100–200 $\mu\text{g}/\text{dl}$, while concentrations of 60–100 $\mu\text{g}/\text{dl}$ are more typical for children (ATSDR 1999). No dose–response relationship for blood-lead and gastrointestinal effects has been published, so the same correction factor (20%) as that assumed for anaemia was used.

OTHER HEALTH EFFECTS

A number of health effects, such as nephropathy and encephalopathy, are associated with higher exposures to lead. These effects were not quantified as they occur in extreme cases for which population-based data from assumed distributions are highly uncertain.

Other health effects associated with lead exposure, such as hearing loss, cognitive deficits and reproductive effects, were not included in this

estimate. Exclusion was based on a number of factors, including difficulty in determining the threshold at which an effect could be expected to occur, inadequate causal evidence, or an outcome that fell outside of those for which the disease burden had been estimated in the GBD project.

SUMMARY

Table 19.5 summarizes blood-lead concentrations at which the population is considered to be at risk of the health outcomes discussed here and the quantitative relationship between exposure and outcome. The values given in this table do not necessarily indicate the lowest levels at which lead exerts an effect.

USE OF ABSOLUTE VERSUS RELATIVE RISK RATIOS

The majority of studies investigating the relationship between lead exposure and disease have assessed incidence rates of disease for exposed and unexposed individuals in developed countries. These two rates are then generally combined into a relative risk. The exposure–risk relationships could therefore be applied to the populations of developing countries by transferring either the relative risks of disease, or the absolute disease

Table 19.5 Summary of health risks associated with blood-lead concentrations considered in this analysis

Outcome	Blood-lead concentration threshold ($\mu\text{g}/\text{dl}$)		Description of relationship
	Children	Adults	
IQ reduction ^a	5	NA	Linear relationship between 5 and 20 $\mu\text{g}/\text{dl}$ (loss of 1.3 IQ points per 5 $\mu\text{g}/\text{dl}$ BPb ^c); loss of 3.5 IQ points above 20 $\mu\text{g}/\text{dl}$
Increased systolic blood pressure ^b	NA	5	Linear relationship assumed between 5 and 20 $\mu\text{g}/\text{dl}$ (increase of 1.25 mmHg per increase of 5 $\mu\text{g}/\text{dl}$ BPb for males, and 0.8 mmHg for females), and increase of 3.75 mmHg above 20 $\mu\text{g}/\text{dl}$ for males, and 2.4 for females
Gastrointestinal effects	60	NA	20% of people are assumed to be affected above these concentrations
Anaemia	70	80	20% of people are affected above these concentrations

NA Not applicable.

^a Children aged 0–4 years.

^b Applied to adults aged 20–79 years.

^c BPb: blood-lead concentration.

rates for those exposed at equivalent levels. A transfer of relative risk rates to a country with higher baseline rates of the considered disease would result in a higher burden of disease for lead-induced illness than if absolute rates were transferred.

In the case of lead-induced outcomes occurring at high concentrations of blood-lead, including gastrointestinal symptoms and anaemia, it may be argued that lead poisoning acts independently of the baseline rates of disease and the presence of other risk factors in the population. We therefore determined incidences for gastrointestinal symptoms and anaemia on the basis of absolute risks rather than of relative risks. However, the risk of anaemia from exposure to lead may be magnified by other risk factors, and therefore a relative risk approach may be envisaged when more solid exposure–risk relationships become available.

With regard to the effects of lead on cognitive functions, data reported in the literature mainly provide mean decreases in IQ points, rather than relative risks for selected decreases. However, exposure to lead may interact with other risk factors, resulting in a magnifying effect, as previously mentioned.

As the exposure distribution relies on a database containing limited information concerning very high concentrations of blood-lead, the estimation of the percentage of the population that experiences extreme levels of exposure becomes very uncertain. Although the number of individuals with lead-induced nephropathy and encephalopathy could, in principle, be estimated, calculating disease burden would be misleading.

3.3 ESTIMATION OF THE NUMBER OF PEOPLE AFFECTED BY EXPOSURE TO LEAD

To estimate the number of people whose health was affected by exposure to lead, the exposure–risk relationships described in section 3.2 were applied to the fraction of the population having the blood-lead concentrations at which these health effects occur. Figure 19.5 shows schematically how this was applied to the distribution of blood-lead concentrations in a population.

4. SOURCES OF UNCERTAINTY

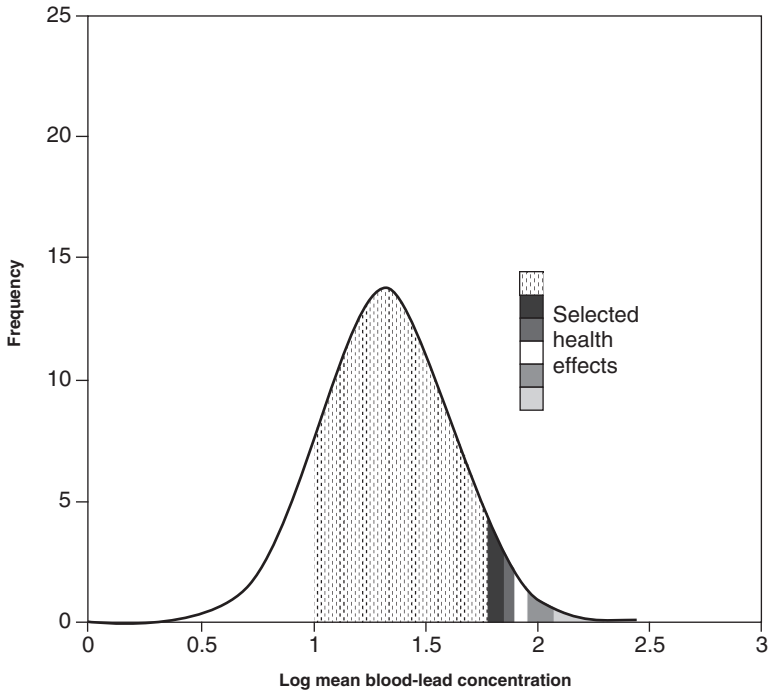
We estimated upper and lower uncertainty bounds for the best estimates by selecting upper and lower values for those parameters which were most likely to contribute significantly to uncertainty and which could be quantified.

4.1 UNCERTAINTY IN EXPOSURE ASSESSMENT

STANDARD DEVIATION OF BLOOD-LEAD CONCENTRATIONS

Fewer data are available for standard deviations of population blood-lead distributions than for mean blood-lead concentrations. We selected

Figure 19.5 Schematic diagram of the distribution of blood-lead concentrations in the population and the number of individuals who are at risk of selected health effects



upper and lower values for the standard deviation by recalculating subregional values after eliminating the upper and lower 20% of the reported standard deviations. The calculated values varied by approximately 13%.

TEMPORAL CHANGE IN BLOOD-LEAD CONCENTRATIONS

Population blood-lead concentrations drop rapidly in countries that make substantial efforts to reduce exposure to lead, including the phasing-out of leaded petrol. Although we examined comprehensive sources documenting such efforts, and adjusted blood-lead concentrations to account for changes in exposure since the most recent assessment, uncertainty remained due to differences in the period of time needed to reduce the use of lead and the lack of data on timing of lead reduction programmes for some countries. In addition, lead reduction programmes other than the phasing-out of leaded petrol may have influenced blood-lead concentrations in the population since the year in

which the data were collected. The exposure level may therefore not always exactly correspond to the year 2000, but to a short time span around that year. To account for uncertainty in the timing of lead reduction, mean blood-lead concentrations were varied by $\pm 16\%$, reflecting a two-year difference in progress in lead reduction programmes, assuming that blood-lead concentrations would change by 39% over a five-year period. Although not strictly applicable to the subregions in which leaded petrol has already been phased out for some time, we maintained this variation around the mean blood-lead concentration in these subregions to account for other factors that may have contributed to uncertainty.

EXTRAPOLATION TO DATA-POOR COUNTRIES

Recent exposure information representative of parts of the general population was available for 41 countries. Many countries (or age groups) were, however, not represented. Exposure to lead in these countries was assumed to be similar to that in countries within the same subregion and which shared socioeconomic characteristics and similar implementation of lead reduction programmes.

MEASUREMENTS OF CONCENTRATIONS OF BLOOD LEAD

Uncertainty in the accuracy of measurement of blood-lead concentrations can be due to a deviation of the measured sample from the study population (i.e. bias), or to contamination problems during sampling or laboratory analysis. Also, the use of blood-lead measurements taken at a single point in time does not capture temporal variation in exposure to lead. Many sources of exposure, however, are likely to occur virtually continuously (e.g. lead in air, in drinking water, in certain foods or through use of leaded ceramics), limiting temporal variation other than that already accounted for.

4.2 UNCERTAINTY IN THE EXPOSURE–RISK RELATIONSHIPS

BODY BURDEN OF LEAD AND ASSOCIATED HEALTH EFFECTS

Measurements of the concentration of lead in bone, which reflects long-term exposure, may be a better predictor of health effects than concentrations of lead in blood (Cheng et al. 2001; González-Cossío et al. 1997; Hu et al. 1996), but there are relatively few studies on which to base a global estimate. Also, the evidence on exposure–response relationships has not yet been quantified.

HEALTH EFFECTS THRESHOLDS AND INDIVIDUAL VARIABILITY

Health effects are likely to occur at lower concentrations of blood-lead than have been considered in this study. There may be no threshold for IQ/cognitive effects, and both renal and cardiac effects have recently been

reported to occur at low concentrations of blood-lead (Cheng et al. 1998; Payton et al. 1994). Health-effect thresholds are linked to individual variability, for which a number of factors are known to be important, including dietary factors (such as calcium; Harlan et al. 1985), general level of health, and genetic differences (e.g. Glen et al. 2001; Kelada et al. 2001; Schwartz et al. 2000a). Current knowledge does not allow the influence of such factors to be assessed precisely.

THE RELATIONSHIP BETWEEN EXPOSURE AND EFFECT FOR BLOOD-LEAD CONCENTRATIONS AND BLOOD PRESSURE

To quantify uncertainty regarding the effects of exposure to lead on blood pressure, the confidence interval around the risks of 30% reported by the meta-analysis (Schwartz 1995) was used.

POPULATION-SPECIFIC BACKGROUND MILD MENTAL RETARDATION

A limitation of the approach used to estimate the risk of mild mental retardation attributable to lead exposure was the lack of studies examining the distribution of IQ scores in different populations. Additionally, population distributions have been found to change over time. In our estimate, the same normal distribution was applied worldwide. For estimating the uncertainty in mild mental retardation rates, we varied the mean IQ score (98 and 102, instead of 100). The lower bound for mild mental retardation was estimated by assuming that health effects occurred at $>10\mu\text{g}/\text{dl}$ instead of at $>5\mu\text{g}/\text{dl}$ as used in the best estimate.

4.3 ESTIMATION OF UPPER AND LOWER UNCERTAINTY BOUNDS

To derive an upper estimate for the proportion of people affected by lead exposure, the upper estimates for exposure assessment (i.e. upper estimates for standard deviation and mean of blood-lead concentrations) were multiplied by the upper rates in the risk estimates. A similar approach was used to obtain the lower estimates.

5. RESULTS

5.1 LOSS OF IQ POINTS AND MILD MENTAL RETARDATION

The incidence rates of mild mental retardation in children aged <5 years are summarized in Table 19.6. We assumed that loss of IQ and resulting mild mental retardation occurred only once, during the first year of life. Older age groups were assumed to have already experienced this health impact in previous years. Values presented in Table 19.6 are those estimated for the age group 0–1 year, but are divided by a factor of 5 (as the age group 0–4 years includes five 1-year cohorts of children).

The highest rates of mild mental retardation caused by exposure to lead occurred in developing countries, where the mean blood-lead concentrations were estimated to be many times higher than those in

Table 19.6 Proportion of children aged 0–1 year^a affected by loss of IQ points caused by exposure to lead, and incidence rates of mild mental retardation caused by exposure to lead in children aged 0–1^a year, in the year 2000

IQ loss category	Proportion (number per 1000 children)													
	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
0.65 IQ points	186	191	124	222	232	233	181	227	227	236	218	192	141	218
1.95 IQ points	66	61	33	104	105	102	66	41	92	106	76	61	23	75
3.25 IQ points	34	28	14	59	58	54	35	10	46	57	36	28	6	34
3.5 IQ points	139	95	21	167	172	114	172	5	89	119	65	83	3	58
Total	425	375	192	552	567	503	454	283	454	518	395	364	173	385
<i>Mean incidence rate (number per 1000 children)</i>														
Mild mental retardation														
Best estimate	7.5	5.8	1.1	13.2	10.2	7.6	8.0	1.1	5.2	4.9	8.7	5.5	0.7	7.7
Lower estimate	4.2	3.0	0.5	7.0	5.3	3.6	4.6	0.3	2.4	2.3	3.9	2.8	0.2	3.4
Upper estimate	12.5	10.0	2.1	22.0	17.2	13.3	13.0	2.7	9.3	8.6	16.3	9.7	1.7	14.6

^a GBD results were reported for children aged 0–4 years. As the effect is mostly irreversible, the entire cohort will remain affected.

developed countries. Latin American regions had relatively high incidence rates despite recent efforts to phase out lead.

5.2 INCREASED BLOOD PRESSURE

The proportion of adult men and women affected by increased blood pressure in age groups ranging from 20 to 79 years, are displayed in Table 19.7. To calculate the burden of disease for ischaemic heart disease, cerebrovascular disease, hypertensive disease and other cardiac diseases, these rates were converted into disease-specific relative risks, according to the methods used for the risk factor in chapter 6.

5.3 ANAEMIA AND GASTROINTESTINAL SYMPTOMS

Tables 19.8 and 19.9 summarize the proportion of people affected by anaemia and gastrointestinal symptoms, assuming that these people are not removed from the source of lead or treated in order to reduce their blood-lead concentrations.

As anaemia and gastrointestinal effects were not included in the list of diseases for which baseline global data were available, they could not be quantified in terms of the attributable fraction of total disease or DALYs.

6. DISCUSSION

This estimate of the global burden of disease caused by exposure to lead suggests that lead had a significant impact on health in the year 2000, mainly in developing countries where lead reduction programmes have not yet been fully implemented or, in some cases, initiated. In many sub-regions, relatively large fractions of the population had significantly elevated blood-lead concentrations. In particular, blood-lead concentrations in many developing countries in 2000 were comparable to, or even higher than, concentrations reported in the United States and Europe in the 1970s. The main disease end-points considered in this analysis included mild mental retardation caused by cognitive impairment and reduction of IQ, ischaemic heart disease, cerebrovascular disease, hypertensive disease and other cardiac diseases induced by increased blood pressure. Several additional disease outcomes associated with exposure to lead could not be considered in this analysis, either because the evidence was considered insufficient for a quantitative assessment at this point in time, or because baseline global data were not available. We estimated that 120 million people around the world had blood-lead concentrations of between 5 and 10 µg/dl in the year 2000, and about the same number had concentrations of >10 µg/dl. Forty per cent of all children had blood-lead concentrations of >5 µg/dl and 20% had concentrations of >10 µg/dl; 97% of these children were living in developing countries. These exposures resulted in a burden of disease of 9.8 million DALYs caused by mild mental retardation and 229 000

Table 19.7 Number of adult men and women^a (per 1000) affected by increased systolic blood pressure with increased blood-lead concentrations caused by exposure to lead in the year 2000

Incremental increase in blood-lead concentration	Number of adults (per 1000)													
	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	AMR-B	EMR-B	EMR-D	EMR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A
0.625 mmHg in males, 0.4 mmHg in females	185	191	91	221	226	233	181	243	225	236	218	62	141	206
1.875 mmHg in males, 1.2 mmHg in females	66	61	23	108	106	102	66	46	106	106	76	29	17	61
3.125 mmHg in males, 2.0 mmHg in females	34	28	9	63	60	54	35	11	61	57	36	97	3	24
3.75 mmHg in males, 2.4 mmHg in females	143	98	11	199	201	114	172	6	155	119	65	97	1	28
Total	428	378	134	591	593	503	454	306	547	518	395	285	162	319

^a Aged 20–79 years.

Table 19.8 Number of people (per 1000) affected by anaemia caused by exposure to lead in the year 2000

	Number of people (per 1000)													
	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	AMR-B	EMR-D	EMR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
<i>Children</i>														
Best estimate	10	6	0	6	7	2	14	0	2	2	1	5	0	1
Lower estimate	4	3	0	2	2	0	6	0	0	0	0	2	0	0
Upper estimate	20	13	1	16	18	8	27	0	6	9	5	10	0	4
<i>Adults</i>														
Best estimate	9	6	0	7	8	2	13	0	3	2	1	6	0	0
Lower estimate	4	2	0	2	2	0	5	0	0	0	0	2	0	0
Upper estimate	18	12	0	18	21	7	25	0	12	7	4	12	0	1

Table 19.9 Number of children (per 1000 children) affected by gastrointestinal effects^a caused by exposure to lead in the year 2000

	Number of children (per 1000 children)													
	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
Children														
Best estimate	12	7	0	8	9	3	16	0	2	3	2	6	0	1
Lower estimate	5	3	0	2	3	0	7	0	0	0	0	2	0	0
Upper estimate	22	14	1	20	22	11	30	0	8	11	6	11	0	5

^a The basis for lower and upper estimates is outlined in section 4.

premature deaths and 3.1 million DALYs caused by cardiovascular disease. These two health outcomes alone account for about 0.9% of the global burden of disease.²

Assuming that each cohort of children aged 0–1 year is exposed to the same amount of lead year after year, the resulting prevalence of mild mental retardation attributable to lead exposure would be the following (obtained from Table 19.6):

- approximately 1–1.2% in AMR-B and AMR-D;
- approximately 0.5–0.8% for AFR, EMR, SEAR, WPR-B, EUR-B and EUR-C; and
- <0.1% in developed countries.

Prevalences of mild mental retardation reported for developed countries are generally about 1–3% (meta-analysis by Andersen et al. 1990; Baird and Sadovnick 1985; Murphy et al. 1995; Roeleveld et al. 1997; WHO 1985). Although it is commonly acknowledged that prevalence rates are higher in developing countries than in developed countries, data are scarce. Reported ranges vary greatly (0.4–9.5%, Roeleveld et al. 1997), and the median of available rates gives a prevalence of mild mental retardation of 6.5% (Durkin et al. 1998; Roeleveld et al. 1997). While the contribution of lead to the total incidence of mild mental retardation in developed countries is small, in developing countries as much as 15–20% of mild mental retardation could be caused by exposure to lead. A study from Australia (Wellesley et al. 1991) estimated that 40% of mental retardation was of genetic origin, 20% was caused by environmental factors and 40% was of unknown etiology. Also, the meta-analysis by Roeleveld et al. (1997) concluded that the high prevalence of mild mental retardation observed in developing countries points towards a role for partly avoidable exogenous influences.

An alternative approach for considering the effects of IQ loss was offered by the Dutch Burden of Disease study (Stouthard et al. 1997). This study used a severity weighting of 0.06 for any loss of IQ of between 1 and 4 points, whether this resulted in mental retardation or remained within the normal IQ range. Such an approach would magnify the effects of exposure to lead, but was not employed in this analysis, since incremental IQ loss is not considered to be a disease in the strict sense. At the same time, although in most instances a loss of IQ points does not lead to a recognizable health condition, it can affect physical functioning and life achievement (e.g. survival and earning potential). The Dutch approach is also supported by recent studies relating reduced mental ability to survival and to reduced lifetime earning capacity (Grosse et al. 2002; Korten et al. 1999; Whalley and Deary 2000).

The burden of ischaemic heart disease, cerebrovascular disease, hypertensive disease and other cardiac disorders caused by exposure to lead amounts globally to 3.1 million DALYs, which is about 2% of the total burden of cardiovascular disease. Worldwide, exposure to lead causes 229 000 deaths from these diseases. Ischaemic heart disease and cerebrovascular diseases are the two main contributors to the burden of disease in this group. Again, the burden is borne mainly by developing countries, owing to the higher exposures to lead in these areas. Together with mild mental retardation caused by exposure to lead, this brings the estimated total burden of disease in this analysis to 0.9%, in terms of DALYs. With quantification of additional outcomes discussed in this chapter, in particular, increased delinquent behaviour and its impact on injuries, the burden would most probably exceed 1% of the global total.

Lead did not contribute significantly to the global burden of anaemia, because other causes, such as iron deficiency, accounted for much higher prevalences of anaemia. The burden of gastrointestinal symptoms caused by lead was also relatively small as compared to that provoked by major risk factors such as unclean water, poor sanitation and hygiene, or unsafe food.

To improve the accuracy of these estimates, more population-representative blood-lead surveys from subregions for which little information has been published so far would be required. Also, additional information on the health impact of low lead levels would be needed in order to make estimates of the burden of disease caused by low doses of lead. The lack of quantitative information on health effects occurring at low exposure levels, the exclusion of data concerning exposure occurring around hot spots or at the workplace, combined with a number of conservative choices made throughout this study, all contribute to a probable underestimation of the burden of disease caused by lead. One particular health effect that could not be quantified but which has been associated in children with low levels of exposure to lead, and which may cause a significant disease burden, although indirectly, is violence.

Intentional injuries represent an important part of the burden of disease, a proportion of which may be attributable to low blood-lead concentrations encountered at high prevalences in many parts of the world.

In addition to the burden of disease, lead exposure may also contribute to socioeconomic burdens. Glotzer et al. (1995) estimated, for example, that in the United States, 45 000 cases of reading disability could be prevented by lead reduction programmes, saving more than US\$900 million per year in overall costs of remedial education. This also has implications for inequalities in health, as exposure to lead tends to be higher in the lower socioeconomic groups of the population (Needleman 1994). These people often live in areas which are more exposed to industrial pollution or in degraded housing. Grosse et al. (2002) estimated that each IQ point raises worker productivity by 1.76–2.38%, resulting in an economic benefit of US\$110–319 billion for each year's cohort of children.

All of the lead-induced disease burden is, in principle, preventable by phasing out the use of leaded petrol, reducing industrial emissions, removing lead from products such as ceramics, paint, “folk remedies” (traditional medicines) and food and drink cans, and replacing leaded pipes used for drinking-water. The phasing-out of leaded petrol is a particularly effective intervention, having the advantage of being a single action which permanently removes or reduces a health risk to current and future generations.

Although lead is one of the best-studied environmental pollutants, its full impact on population health is only now coming to light. The impacts of many other potentially harmful substances, such as heavy metals, pesticides or solvents, some of which are steadily accumulating in the environment, are as yet largely unknown.

7. PROJECTIONS

Although exposure to lead can occur via a number of routes and from a range of sources, the level of lead in petrol is a key predictor of blood-lead concentrations at a country level. It has been shown that decreases in the use of leaded petrol are closely followed by parallel decreases in blood-lead concentrations (Annest 1983; Annest et al. 1983; Elinder et al. 1986; Schuhmacher et al. 1996; Thomas et al. 1999; Wietlisbach et al. 1995). We based the projected exposure estimates on predicted changes in transportation energy use by subregion (EIA 2001) and estimated completion dates of leaded petrol phase-out programmes (Walsh 2001). For countries that had not embarked upon lead reduction programmes, it was assumed that urban blood-lead concentrations would rise as a consequence of increases in transportation energy use, shown in Table 19.10. Where a lead reduction programme had been initiated, it was assumed that policy would not change and that the programme would be seen through to completion.

Table 19.10 Transportation energy use by subregion, 1990–2020

Subregion of analysis	Energy Information Administration regional equivalent	Transportation energy consumption (million barrels of oil equivalent/day)				Average annual % change
		1990	1999	2010	2020	1999–2020
AMR-A	North America	13	15	19	23	2.0
EUR-A	Western Europe	6	7	8	9	1.0
WPR-A	Industrialized Asia	3	3	3	3	1.0
EUR-B, EUR-C	Eastern Europe/ Former Soviet Union	3	2	3	4	2.8
SEAR-B, SEAR-D, WPR-B	Asia	3	6	10	16	5.1
EMR-B, EMR-D	Middle East	1	2	3	5	4.8
AFR-D, AFR-E	Africa	1	1	2	2	3.0
AMR-B, AMR-D	Central and South America	2	2	4	6	4.6

Source: Adapted from EIA (2001).

The starting point for the projection was the estimated mean blood-lead concentration for each subregion in the year 2000. In cases where a national lead reduction programme was due to be completed prior to 2010, urban blood-lead concentrations were assumed to converge at 3.1 µg/dl, according to the calculations of Thomas et al. (1999). The exceptions to this assumption were AMR-B and AMR-D. As countries in these subregions possess other important sources of lead, such as lead-glazed pottery, blood-lead concentrations were assumed to drop to 4.3 µg/dl, based on the mean of the most recently reported urban blood-lead concentrations in Latin American countries that have phased out leaded petrol (Garcia and Mercer 2001; Sepulveda et al. 2000). Energy use projections were available only until the year 2020; however, in the absence of other data, trends in 2000–2020 were assumed to continue until 2030. As urbanization is expected to increase steadily in most subregions (UN 1997), we also included a predicted change in urbanization in our projections of changes in blood-lead concentrations.

The effect of changes in energy use on blood-lead levels was calculated using the approach employed to adjust for the phasing-out of lead. Thus, as a 50% change in lead use (generally equivalent to the completion of a five-year leaded petrol reduction programme) is equal to a 39% change in blood-lead concentrations (see section 2.3), a 1% change in emissions would result in a 0.78% change in blood-lead concentrations. It was assumed that mean blood-lead concentrations would not increase beyond 30 µg/dl, as means exceeding this have rarely been reported.

Standard deviations were assumed to remain the same as in the year 2000. Projected blood-lead concentrations are presented in Table 19.11 for children and in Table 19.12 for adults. In subregions where many countries have not yet started to phase out lead (i.e. AFR, EMR, and EUR-B and C), it was estimated that blood-lead concentrations would increase steadily owing to the current widespread use of leaded petrol and lack of actions to reduce lead emissions. In most other subregions, lead emissions were predicted to decline gradually, with subsequent reductions in lead in the environment and in food. A large drop in blood-lead concentrations was projected to occur in many subregions between 2000 and 2010, as existing lead reduction programmes begin to take effect. After this period, rises in blood-lead concentrations would be observed due to continuing increases in the number of persons with elevated blood-lead concentrations living in countries and subregions which have not phased out lead.

Table 19.13 shows the projected incidence of mild mental retardation caused by exposure to lead for the years 2010, 2020 and 2030, using the methods described above and assuming constant prevalences of other diseases with cognitive impairment sequelae. As the proportion of people with elevated blood-lead concentrations will decrease in subregions where lead reduction programmes have recently been initiated (see Table 19.12), the incidence of mild mental retardation caused by exposure to lead is predicted to decline. Where no efforts to reduce exposure to lead are made, urbanization and increases in vehicle emissions are predicted to cause an increased incidence in lead-induced mild mental retardation. In the worst cases, in the African and Eastern Mediterranean subregions, exposure to lead could cause nearly 1.5% of cases of mild mental retardation.

The estimates for the incidence of anaemia and gastrointestinal symptoms caused by exposure to lead probably already carry the highest uncertainties, owing to the fact that these conditions appear at higher blood-lead concentrations, at which the distribution model is less accurate. Therefore projections for these outcomes have not been presented. In addition to the sources of uncertainty inherent in data collection and in the analysis for 2000, a number of additional uncertainties have been introduced into the projections we have made for future exposures, which are dominated by assumptions about policy and technology changes for lead reduction. Although it may well seem unacceptable that leaded petrol could still be in use in 10, 20 or 30 years' time, it must be remembered that lead has not been removed from the petrol supply of any country except by vigorous and concerted efforts by institutions concerned for the health of the public and especially of children.

For certain countries or subregions with significant additional sources of exposure to lead, the projections made here may be too optimistic. In general, however, we expect that appropriate lead-reduction measures will have been taken at a global level towards the end of the next decade.

Table 19.11 Projections of blood-lead concentrations in children for the years 2010, 2020 and 2030, by subregion

Year	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B	
Subregional mean of urban blood-lead concentrations ($\mu\text{g}/\text{dl}$)	2010	14.1	9.7	2.2	4.7	4.3	7.7	17.0	3.1	6.3	8.3	3.2	3.7	3.1	
	2020	18.1	12.8	2.2	4.9	4.3	10.5	20.9	3.1	7.7	10.5	3.3	3.8	3.2	
	2030	23.5	17.4	2.2	5.1	4.3	14.7	20.6	3.1	9.2	13.1	3.5	3.7	3.1	
Subregional mean of rural blood-lead concentrations ($\mu\text{g}/\text{dl}$)	2010–2030	3.1	3.1	2.2	4.3	4.3	3.1	3.1	3.1	3.1	3.1	3.1	3.1	3.1	
Standard deviation ($\mu\text{g}/\text{dl}$)	2010–2030	5.6	5.6	2.9	3.8	3.8	3.0	5.6	1.9	3.0	3.0	3.0	5.6	1.9	3.0
Percentage of children with 5–10 $\mu\text{g}/\text{dl}$	2010	17.9	18.3	12.5	20.8	22.1	21.5	16.7	19.6	22.0	23.5	19.8	18.2	11.2	19.7
	2020	16.9	17.7	12.5	20.3	21.7	19.1	15.7	19.6	21.5	22.5	19.6	17.9	11.3	19.6
	2030	15.7	16.8	12.5	19.8	21.4	15.6	15.3	19.6	20.2	20.7	19.3	17.8	11.3	19.5
Percentage of children with 10–20 $\mu\text{g}/\text{dl}$	2010	10.8	9.5	4.8	13.9	13.3	16.5	10.3	3.8	14.9	18.5	8.1	8.2	1.2	8.1
	2020	11.4	10.1	4.8	13.9	13.4	17.4	10.6	3.8	16.5	20.5	8.5	8.5	1.2	8.3
	2030	11.8	10.4	4.8	13.9	13.4	16.2	11.0	3.8	17.1	21.6	8.7	8.5	1.2	8.5
Percentage of children with >20 $\mu\text{g}/\text{dl}$	2010	19.2	13.1	1.6	12.1	9.2	16.3	22.9	0.4	11.7	16.5	2.8	6.9	0.0	2.7
	2020	25.4	17.7	1.6	13.6	9.5	25.1	28.7	0.4	16.3	22.7	3.6	7.7	0.0	3.0
	2030	32.2	23.1	1.6	14.5	9.9	36.0	31.2	0.4	21.0	29.8	4.6	7.8	0.0	3.3

Table 19.12 Projections of blood-lead concentrations in adults for the years 2010, 2020 and 2030, by subregion

Year	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
Subregional mean of urban blood-lead concentrations ($\mu\text{g}/\text{dl}$)	2010 14.8	10.1	1.7	4.8	4.3	7.7	17.0	3.1	8.6	8.3	3.2	3.8	2.4	2.7
	2020 19.0	13.3	1.7	5.0	4.3	10.5	20.9	3.1	10.7	10.5	3.3	3.8	2.4	2.7
	2030 24.6	18.1	1.7	5.1	4.3	14.7	20.6	3.1	12.7	13.1	3.5	3.7	2.4	2.7
Subregional mean of rural blood-lead concentrations ($\mu\text{g}/\text{dl}$)	2010–2030 3.1	3.1	2.2	4.3	4.3	3.1	3.1	3.1	3.1	3.1	3.1	3.1	2.7	3.1
Standard deviation ($\mu\text{g}/\text{dl}$)	2010–2030 5.6	5.6	3.0	3.8	3.8	3.0	5.6	1.9	3.0	3.0	3.0	5.6	1.9	3.0
Percentage of adults with 5–10 $\mu\text{g}/\text{dl}$	2010 17.8	18.3	9.3	20.8	22.1	21.5	16.7	19.6	20.4	23.5	19.8	18.2	12.4	19.8
	2020 16.8	17.6	9.3	20.2	21.7	19.1	15.7	19.6	18.9	22.5	19.6	17.8	12.4	19.6
	2030 15.6	16.7	9.3	19.8	21.4	15.6	15.3	19.6	17.1	20.7	19.3	17.8	12.4	19.5
Percentage of adults with 10–20 $\mu\text{g}/\text{dl}$	2010 10.8	9.5	3.2	13.9	13.3	16.5	10.3	3.8	16.0	18.5	8.1	8.2	1.4	8.0
	2020 11.4	10.0	3.2	13.9	13.4	17.4	10.6	3.8	16.6	20.5	8.5	8.5	1.4	8.3
	2030 11.7	10.4	3.2	13.9	13.4	16.2	11.0	3.8	16.1	21.6	8.7	8.5	1.4	8.5
Percentage of adults with >20 $\mu\text{g}/\text{dl}$	2010 19.7	13.3	0.9	12.3	9.2	16.3	22.9	0.4	18.3	16.5	2.8	6.9	0.1	2.6
	2020 26.0	18.0	0.9	13.8	9.5	25.1	28.7	0.4	24.3	22.7	3.6	7.8	0.1	2.9
	2030 32.8	23.5	0.9	14.5	9.9	36.0	31.2	0.4	29.6	29.8	4.6	7.8	0.1	3.2

Table 19.13 Projected incidence rates of mild mental retardation in children (aged 0–1 years) caused by exposure to lead in the years 2010, 2020 and 2030^a

	Incidence rate (number per 1000)													
	AFR-D	AFR-E	AMR-A	AMR-B	AMR-D	EMR-B	EMR-D	EUR-A	EUR-B	EUR-C	SEAR-B	SEAR-D	WPR-A	WPR-B
2010	9.4	7.0	1.0	10.4	6.9	9.2	9.7	0.9	6.0	6.1	5.6	4.9	0.4	5.2
2020	11.6	8.6	1.0	11.1	7.0	12.0	11.5	0.9	7.4	7.5	6.1	5.2	0.4	5.4
2030	13.8	10.4	1.0	11.4	7.1	14.9	12.3	0.9	8.6	9.0	6.7	5.2	0.4	5.6

^a GBD results reported for the 0–4 year age group.

In countries where mean population blood-lead concentrations are currently low, it is expected that health effects caused by lead will no longer be a concern for most people. However, exposure to lead is likely to remain a hazard for a minority of people, in particular, the children of the socially disadvantaged, including those living in houses containing leaded paint, or lead piping, or in areas affected by industrial contamination containing lead. Control of these sources will require continuing efforts.

NOTE

- 1 See preface for an explanation of this term.
- 2 Editorial note: The GBD mortality database includes a small number of deaths (approximately 5000) due to lead-induced mild mental retardation (MMR). These deaths are in fact deaths where MMR, regardless of being caused by lead or otherwise, has been specified as the underlying cause of death in the death registration data from some developed countries. The GBD has not attempted to make consistent estimates of MMR deaths for other regions, or to attribute some of these to lead. Because of the current GBD cause-of-death classification, these deaths are included in the Annex Tables (see the CD-ROM accompanying this book) and summary results in chapters 26 and 27. These deaths are however excluded from the results reported and discussed in this chapter.

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