Health risks of heavy metals from long-range transboundary air pollution

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Joint WHO/Convention Task Force on the Health Aspects of Air Pollution

Abstract

The heavy metals cadmium, lead and mercury are common air pollutants, being emitted mainly as a result of various industrial activities. Although the atmospheric levels are low, they contribute to the deposition and build-up in soils. Heavy metals are persistent in the environment and are subject to bioaccumulation in food-chains.

Cadmium exposures are associated with kidney and bone damage. Cadmium has also been identified as a potential human carcinogen, causing lung cancer. Lead exposures have developmental and neurobehavioural effects on fetuses, infants and children, and elevate blood pressure in adults. Mercury is also toxic in the elemental and inorganic forms, but the main concern is associated with the organic compounds, especially methylmercury, that accumulate in the food-chain, i.e. in predatory fish in lakes and seas, as these are the main routes of human exposure.

Long-range transboundary air pollution is only one source of exposure to these metals but, because of their persistence and potential for global atmospheric transfer, atmospheric emissions affect even the most remote regions. This report, based on contributions from an international group of experts, reviews the available information on the sources, chemical properties and spatial distribution of environmental pollution with cadmium, lead and mercury caused by long-range transboundary air pollution, and evaluates the potential health risks in Europe.

Contents

Abbreviations

Organizations

ATSDR	Agency for Toxic Substances and Disease Registry
CDC	Centers for Disease Control and Prevention (http://www.cdc.gov).
ECEH	WHO European Centre for Environment and Health (www.euro.who.int)
EMEP	Co-operative Programme for Monitoring and Evaluation of the Long-range Transmission of Air Pollutants in Europe (http://www.emep.int)
FAO	Food and Agriculture Organization of the United Nations (http://www.fao.org)
IARC	International Agency for Research on Cancer (http://www.iarc.fr)
ILO	International Labour Organization (www.ilo.org)
IPCS	International Programme on Chemical Safety, a joint programme of ILO, UNEP and WHO (http://www.who.int/ipcs/en/)
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MSC-E	EMEP Meteorological Synthesizing Centre – East (http://www.msceast.org/)
MSC-HM	EMEP Meteorological Synthesizing Centre – Heavy Metal
NHANES	National Health and Nutritional Examination Surveys
TFMM	EMEP Task Force on Measurements and Modelling (http://www.nilu.no/projects/ccc/tfmm/index.html)
UNECE	United Nations Economic Commission for Europe (www.unece.org)
UNEP	United Nations Environment Programme (http://www.unep.org)
USEPA	United States Environmental Protection Agency (http://www.epa.gov)

Technical terms

ALAD	δ-aminolevulinic acid dehydratase (an indicator of lead poisoning)
B-Cd	blood cadmium
β_2-M	β_2-microglobulin (protein; an indicator of tubular damage)
BMDL	benchmark dose level
B-Pb	blood lead
bw	body weight
Cd	cadmium (metallic element; atomic number 48)
CdO, CdS, $CdCl_2$	cadmium oxide, cadmium sulfide, cadmium dichloride (inorganic cadmium compounds)
CI	confidence interval (a measure of statistical uncertainty in numerical estimates)
H-Hg	mercury level in hair
Hg	mercury (metallic element; atomic number 80)
IQ	intelligence quotient (a measure of personal mental capacities)
LOAEL	lowest observed adverse effect level
P-value	statistical parameter estimating the probability of a random association
Pb	lead (metallic element; atomic number 82)
PbO, $PbSO_4$, $PbCl_2$	lead oxide, lead sulfate, lead dichloride (inorganic lead compounds)
PTWI	provisional tolerable weekly intake
r	correlation coefficient
RGM	reactive gaseous mercury
U-Cd	urinary cadmium

Foreword

Long-range transport of air pollution has been recognized as an important factor affecting ecosystems and the human population. The United Nations Economic Commission for Europe (UNECE) Convention on Long-range Transboundary Air Pollution (LRTAP) is a powerful international instrument aimed at reducing and preventing air pollution. The effects of the Convention can be partly assessed by the reduction in emissions of pollution by the countries that are Parties to the Convention. However, more important than this is evaluation of the extent to which cuts in emissions achieved from implementation of the Convention and other actions (such as national legislation or regulations) translate into decreases in the burden of long-range transport of air pollution on the environment and human health.

The Protocol on Heavy Metals to the UNECE Convention on Long-range Transboundary Air Pollution was signed in 1998 and came into force in 2003. The objective of the Protocol was to introduce measures for the reduction of cadmium, lead and mercury emissions into the atmosphere, with a view to preventing adverse effects on human health and the environment. It describes the measures and best available techniques for controlling emissions, and indicates programmes, strategies and policies for achieving the heavy metal limit values specified in the Protocol.

UNECE, the Executive Body for the Convention, at its 17th Session held in Gothenburg (29 November to 3 December 1999), requested the Joint WHO/Convention Task Force on the Health Aspects of Air Pollution to assess the health effects of cadmium, lead and mercury from LRTAP and to document the supporting scientific information on the subject. The assessment should support quantification of the contribution of transboundary air pollution to human health risks and help in defining priorities that may serve as a guide for determining future monitoring and abatement strategies. The Task Force was invited to prepare a preliminary assessment in 2002 as a contribution to the Review and Assessment of Air Pollution Effects and their Recorded Trends. The current update is based on the work of the Task Force, carried out according to a Memorandum of Understanding between UNECE and the WHO Regional Office for Europe (ECE/ENHD/EOA/2006/001), and adopted by the Executive Body for the Convention.

The Task Force used existing reviews such as the Environmental Health Criteria documents published by the International Programme on Chemical Safety (IPCS), the WHO *Air quality guidelines for Europe* and other relevant publica-

tions as a basis for the identification of the health hazards caused by cadmium, lead and mercury, and for information on exposure–response relationships.

This report is based on contributions from an international group of experts delegated by their governments, and from experts of the Co-operative Programme for Monitoring and Evaluation of the Long-range Transmission of Air Pollutants in Europe (EMEP). The WHO European Centre for Environment and Health, Bonn acted as Secretariat to the Task Force. The Working Group on Effects of the Convention evaluated the drafts of the report and reviewed the conclusions of the assessment, allowing their presentation to the Executive Body of the Convention.

Joint WHO/Convention Task Force on the Health Aspects of Air Pollution

Executive summary

Heavy metals such as cadmium, lead and mercury are common air pollutants and are emitted (predominantly into the air) as a result of various industrial activities. This report reviews the available information on the sources, chemical properties and spatial distribution of pollution by cadmium, lead and mercury from LRTAP, and evaluates the potential health effects in Europe.

Cadmium

Kidney and bone are the critical target organs with regard to environmental exposure. The main critical effects include increased excretion of low-molecular-weight proteins in the urine (as a result of proximal tubular cell damage) and an increased risk of osteoporosis. An increased risk of lung cancer has also been reported following inhalation exposure in occupational settings.

The margin of safety between the present daily intake of cadmium in the diet and the intake that can result in effects is very narrow and, for highly exposed subpopulations, even non-existent. Population groups at risk include the elderly, people with diabetes, and smokers. Women may be at increased risk because they have lower iron stores than men and, consequently, absorb more cadmium at the same level of exposure.

Food is the main source of cadmium exposure in the general population (representing >90% of the total intake in non-smokers). In heavily contaminated areas, dust resuspension can constitute a substantial part of the crop contamination and exposures via inhalation and digestion.

Annual inputs from LRTAP and mineral and organic fertilizers to topsoil are roughly of the same magnitude. They all continue to contribute to the existing (relatively large) accumulation of cadmium in the topsoil.

In spite of the decrease in cadmium emissions, ambient air concentrations and deposition, recently published data do not show a decrease in the cadmium body burdens in non-smokers in the last decade. Studies on the cadmium balance in the top layers of arable soils indicate that the input of this heavy metal still exceeds its removal. Cadmium is accumulating in soils and catchments under certain environmental conditions, thus increasing the risk of future exposure through food. Therefore, in view of the narrow margin of safety, every effort should be made to make further reductions regarding cadmium emission into the atmosphere and other types of cadmium input into soil.

Lead

Lead is a well-known neurotoxin. Impairment of neurodevelopment in children is the most critical effect. Exposure in utero, during breastfeeding and in early childhood may all be responsible for the effects. Lead accumulates in the skeleton, and its mobilization from bones during pregnancy and lactation causes exposure to fetuses and breastfed infants. Hence, the lifetime exposure of woman before pregnancy is important.

Epidemiological studies consistently show that effects in children are associated with blood lead (B-Pb) levels of about 100–150 μg/l. There are indications that lead is harmful even at B-Pb concentrations considerably below 100 μg/l; there may be no threshold for these effects.

In many areas there have been major decreases in B-Pb levels in recent decades, mainly because of the phasing out of leaded petrol but also because of reductions in other sources of exposure. At present, the lowest average B-Pb level in several European countries is about 20 μg/l, but reliable B-Pb information from many parts of Europe is lacking.

The relative contributions of sources of pollution differ depending on local conditions. Food is the predominant source of lead uptake in the general population. Ingestion of contaminated soil, dust and old lead-based paint due to hand-to-mouth activities may also be important regarding lead intake in infants and young children. When tap-water systems with leaded pipes are used, lead intake via drinking-water can be an important source, especially in children. Inhalation exposure may be significant when lead levels in the air are high.

Lead levels in ambient air have decreased in recent decades: between 1990 and 2003, lead levels in air in Europe fell by 50–70%. Similar decreases have been observed for atmospheric deposition.

The annual lead inputs from LRTAP and from the addition of organic and inorganic fertilizers to topsoil are roughly similar in magnitude, depending on the country and the agricultural activity. Those inputs are relatively small in comparison with the existing accumulations, natural sources and resuspension. However, LRTAP may contribute significantly to the lead content of crops through direct deposition. Although uptake via plant roots is relatively small, rising lead levels in soils over the long term are a matter of concern and should be avoided because of the possible health risks of low-level exposure. Lead emissions to the atmosphere should therefore be kept as low as possible.

Mercury

Emissions of mercury to the air from both anthropogenic and natural sources are in inorganic forms that can be converted biologically to methylmercury in soil and water. Methylmercury bioaccumulates and enters the human body readily via the dietary route. Airborne concentrations of mercury in Europe, and also globally, are generally well below those known to cause adverse health effects from inhalation exposure. Concentrations of inorganic mercury species in surface water and groundwater are generally well below those known to cause adverse health effects from drinking water.

Methylmercury is a potent neurotoxic chemical. Unborn children (i.e. fetuses) are the most susceptible population group, the exposure being mainly from fish in the diet of the mother. Methylmercury is also excreted in mothers' milk. Human biomonitoring and diet-modelling data indicate that tolerable dietary intakes of methylmercury are exceeded among subpopulations that consume large amounts of fish, e.g. in Scandinavia, North America and France. For several species of (mainly large predatory) freshwater and marine fish and mammals, a mercury level of 0.5 mg/kg, the value used as a guideline in many countries, is often exceeded.

Historical data, e.g. from lake sediments in Scandinavia, show a two- to fivefold increase in mercury concentrations with respect to the pre-industrial era, reflecting anthropogenic emissions and long-range transport. Methylmercury in freshwater fish originates from inorganic mercury in the soil and direct atmospheric deposition. Anthropogenic emissions of mercury in Europe decreased by approximately 50% after 1990, and a similar decrease is predicted by modelling and limited monitoring data on the deposition of mercury in the region. However, a concomitant decrease in the concentration of methylmercury in freshwater fish has not been observed.

Little information is available on the provenance of methylmercury in marine fish and on the contribution of long-range transport to the process. Evidence exists showing increasing levels of mercury in marine fish and mammals in the Arctic, indicating the impact of long-range transport. In general, fish consumption has important beneficial effects on health. However, in some populations consuming large amounts of fish, or consuming contaminated fish, the intake of methylmercury may reach hazardous levels. Thus, reducing the concentrations in fish should be given a high priority. Reducing emissions to the atmosphere and long-range transport of pollution represents a means of achieving this aim.

1. Introduction

One of the consequences of the current stage of industrialization and the demand for improved quality of life has been increased exposure to air pollution coming from industrial activities, traffic and energy production. Several decades ago, convincing scientific data emerged that related specific air pollutants to health effects, and the results of such studies provided, inter alia, arguments for setting limit values for specific pollutants in ambient air. In response to the mounting evidence concerning the importance of long-range transboundary transport of air pollution, cooperation was established between the affected governments to develop international legal instruments for reducing the emissions of the most dangerous pollutants. As result of this, the Convention on Long-range Transboundary Air Pollution was signed in 1979, with activities initially focusing on reducing the effects of acid rain through control of sulfur and nitrogen emissions. The scope of the Convention was later widened to address the formation of ground-level ozone (Protocol to Abate Acidification, Eutrophication and Ground-level Ozone, 1999) and, more recently, persistent organic pollutants (Protocol on Persistent Organic Pollutants (POPs), 2001) and heavy metals (Protocol on Heavy Metals, 1998).

Factors associated with the possible health effects of exposure to cadmium, lead and mercury have been investigated over many years in occupational settings, using experimental animals and humans exposed to environmental pollution. The types of adverse health effect are known to a great extent but, because of the very strong influence of confounding factors, it is very difficult or almost impossible to find thresholds for some outcomes such as impairment of cognitive functions in children exposed to lead or mercury.

Results of studies on the adverse effects on human health have been summarized in numerous reports published by international organizations, e.g. the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), or governmental agencies such as the Centers for Disease Control and Prevention (CDC) in the United States.

In spite of the decreases in environmental exposure to these three metals due to technological improvements and the elimination of, or reduction in, some processes, products and materials, these metals are still present in the atmosphere and are carried to places remote from the sources of emission by means of long-range atmospheric transport. Anthropogenic sources generally outweigh natural emissions and, even with the current trend towards reductions in the former, releases into the environment continue to lead to slow increases

in soil contamination in large parts of the world, because of the persistence of the metals. These metals are bioaccumulative in ecosystems, and mercury levels can be biomagnified in predatory animals (e.g. fish) that are also used as human food.

This report evaluates the importance of the contribution of LRTAP to the potential for human health risks from environmental exposure to cadmium, lead and mercury. It summarizes the available information concerning the health effects from exposure to these metals, and estimates human exposures and health risks resulting from their long-range transport.

1.1. The process

The preliminary assessment of the health risks of heavy metals from LRTAP conducted in 2002 was revised using recent scientific evidence and updated estimates of emissions, levels in air, deposition and fate in the environment. The permanent members of the Joint WHO/Convention Task Force on the Health Aspects of Long-range Transboundary Air Pollution and representatives of the Parties to the Convention were asked to recommend experts. On the basis of the recommendations received, 11 experts were invited to participate in the working group to develop the background material for the update. Using the 2002 preliminary assessment as a basis, the WHO European Centre for Environment and Health (Bonn Office), acting as Secretariat, prepared draft 1 of the update that was sent to the working group members.

Updates for various sections of draft 1 were invited by early May 2006, to be combined into draft 2, which was delivered for review by the working group members, invited international reviewers and the Parties to the Convention.

To finalize the assessment, the ninth meeting of the Joint WHO/Convention Task Force on the Health Aspects of Air Pollution was convened in Berlin on 30–31 May 2006. The meeting reviewed the draft, taking into account the comments received from the reviewers. The meeting prepared and approved conclusions for each metal. These conclusions were approved by the Working Group on Effects at its 25th session in Geneva on 30 August – 1 September 2006.

On the basis of the conclusions formulated at the Berlin meeting, as well as the reviews received before and after the meeting, the staff of the WHO European Centre for Environment and Health in Bonn, in close collaboration with the main authors of the chapters, carried out the final editing of the background material presented in the individual chapters of this document.

1.2. Structure of the document

To assess the risk to human health in relation to long-range transport of cadmium, lead and mercury, the experts considered the ability of these metals to be transported over long distances after their release into the environment, their persistence and accumulation in different environmental compartments, the

pathways of human environmental exposure, and data concerning the hazardousness of these substances.

The report consists of one main chapter for each metal, each with the following sections:

- an introduction, summarizing sources, monitored and modelled levels for air and deposition, and the fate of the metal in the environment;
- pathways and levels of human exposure in relation to LRTAP;
- health hazard characterization, based on existing toxicological and epidemiological evidence; and
- human health implications of the LRTAP.

2. Cadmium

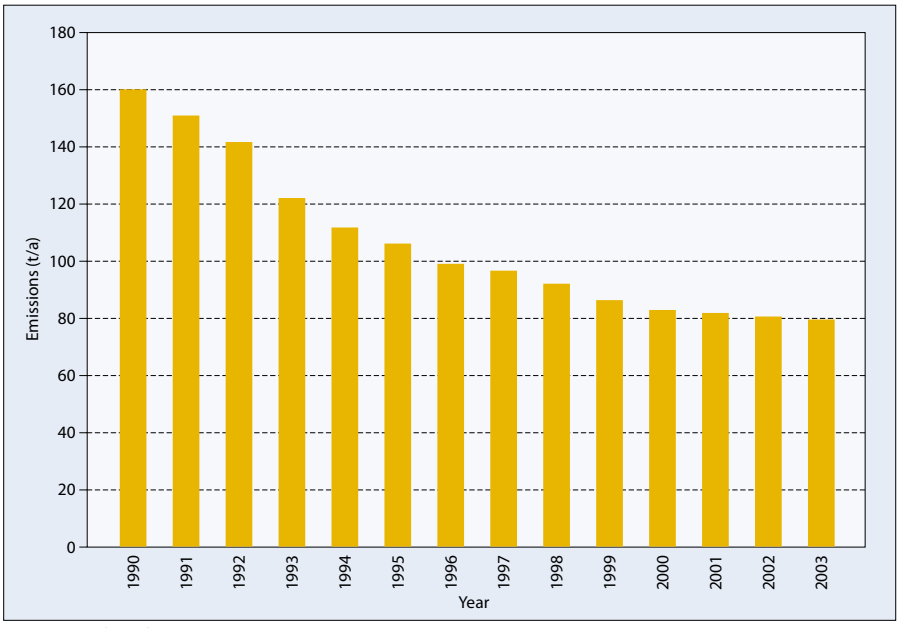
2.1. Introduction

2.1.1. Emissions

Cadmium is released into the atmosphere by natural and anthropogenic means. Volcanoes, windborne particles and biogenic emissions are considered the main natural sources of cadmium in the atmosphere (Nriagu, 1989). The anthropogenic sources of cadmium include non-ferrous metal production, stationary fossil fuel combustion, waste incineration, iron and steel production and cement production.

Cadmium emissions in Europe constituted 485 t in 1990 and 257 t in 2003. Besides the official reported data, estimations for countries that did not report their emission results are based on the expert estimation procedure presented by Berdowski et al. (1997, 1998) (Ilyin & Travnikov, 2005). More detailed trends for emissions can be estimated for 24 countries (involved in EMEP), using reported annual emission data for the period 1990–2003. Emissions from these countries have decreased by 50%, from 160 t/a to 80 t/a, and have levelled off in recent years (Fig. 2.1).

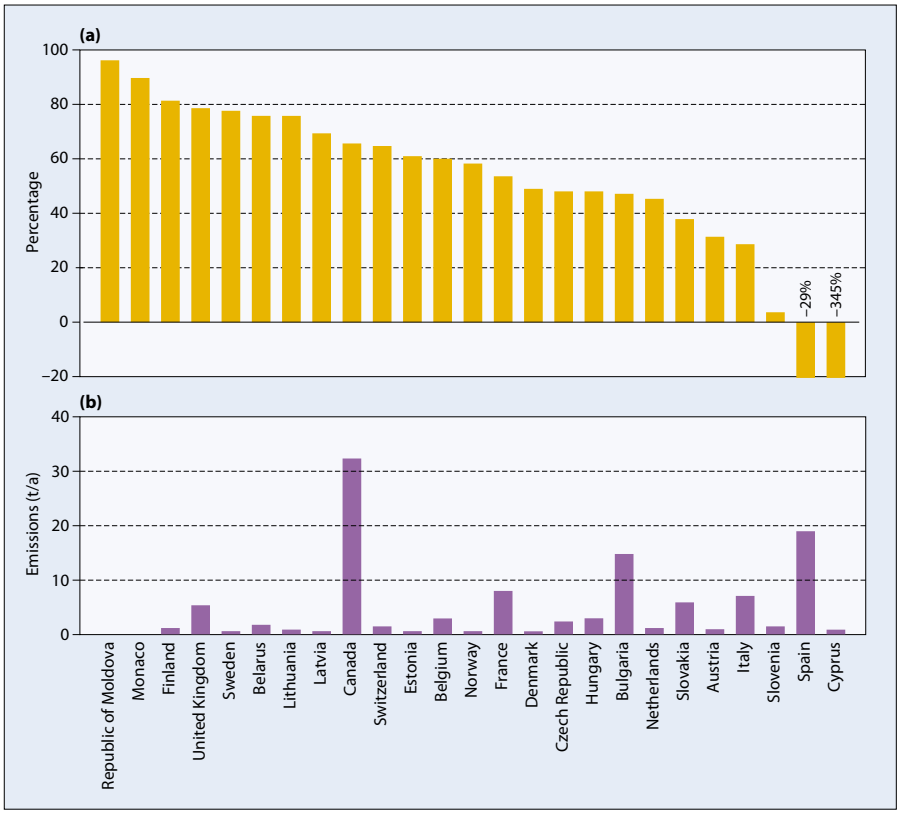
Fig. 2.1. Reported emissions of cadmium in the EMEP region (24 countries).



Source: UNECE (2006a).

The relative reduction in emissions officially reported between 1990 and 2003 was calculated as $((E_{1990} - E_{2003})/E_{1990}) \times 100\%$, where E_{1990} and E_{2003} are emission magnitudes in 1990 and 2003, respectively. Modest reductions in cadmium emissions relative to 1990 occurred, for example, in Slovenia (4%). The highest reduction obtained (by the Republic of Moldova; 96%) was 25 t/a, and contrasted with increased emissions in Spain and Cyprus (up by 29% and 345%, respectively; Fig. 2.2a). The emission levels achieved by the EMEP countries by 2003 (according to the official information) are presented in Fig. 2.2b.

Fig. 2.2. (a) Relative reductions in cadmium emissions in the 24 countries of the EMEP region and Canada for the period 1990–2003, based on official data. Negative values are shown for growths in emissions. (b) Official emissions, by country, in 2003.



Source: UNECE (2006a).

The main sectors involved in cadmium emission in Europe in 1990 and 2003 are identified on the basis of officially reported information from only eight countries (Fig. 2.3). Their contribution to the total emissions of these countries was 91%. In 1990, the maximum contribution to the total cadmium emission was from the "waste incineration" sector (about 20%), followed by "metal production" and "public electricity and heat production". In 2003, the "metal production" sec-

tor took the lead (about 26%). More detailed information about emission data officially reported for 1990–2003 is presented by Vestreng et al. (2005).

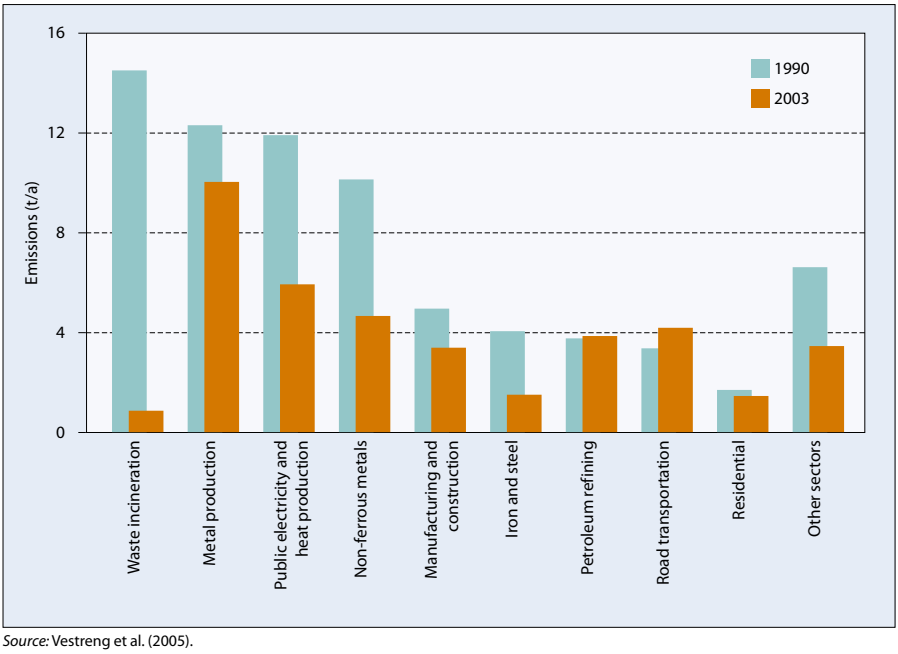
2.1.2. Physicochemical properties allowing atmospheric transport

In the atmosphere, cadmium occurs attached to particles, especially those in the submicron category (approximately 0.5–1 μm) (Milford & Davidson, 1985; Allen et al., 2001; Molnar et al., 1995; Pakkanen et al., 2001; Kuloglu & Tuncel, 2005; Dillner et al., 2005). Molnar et al. (1995) also identified a second, smaller maximum particle size of approximately 0.1 μm. The main cadmium species upon emission are oxides, chlorides, sulfides and the elemental form. Oxides (CdO) are emitted by most of the anthropogenic sources. Elemental cadmium is released during high-temperature processes such as organic fossil fuel combustion and waste incineration. Sulfides (CdS) are prominent in the emissions from non-ferrous metal production and coal combustion. Refuse incineration is a source of cadmium chloride ($CdCl_2$) (AMAP, 1998).

2.1.3. Behaviour in the environment, persistence and bioaccumulation

In order to characterize the residence time of a pollutant in the atmosphere and its ability to travel over long distances, the term "lifetime" is often used, defined as the time required for a species concentration to decrease to e-1 (i.e. approxi-

Fig. 2.3. Changes in cadmium emissions from anthropogenic sources (various sectors) between 1990 and 2003 in eight countries.

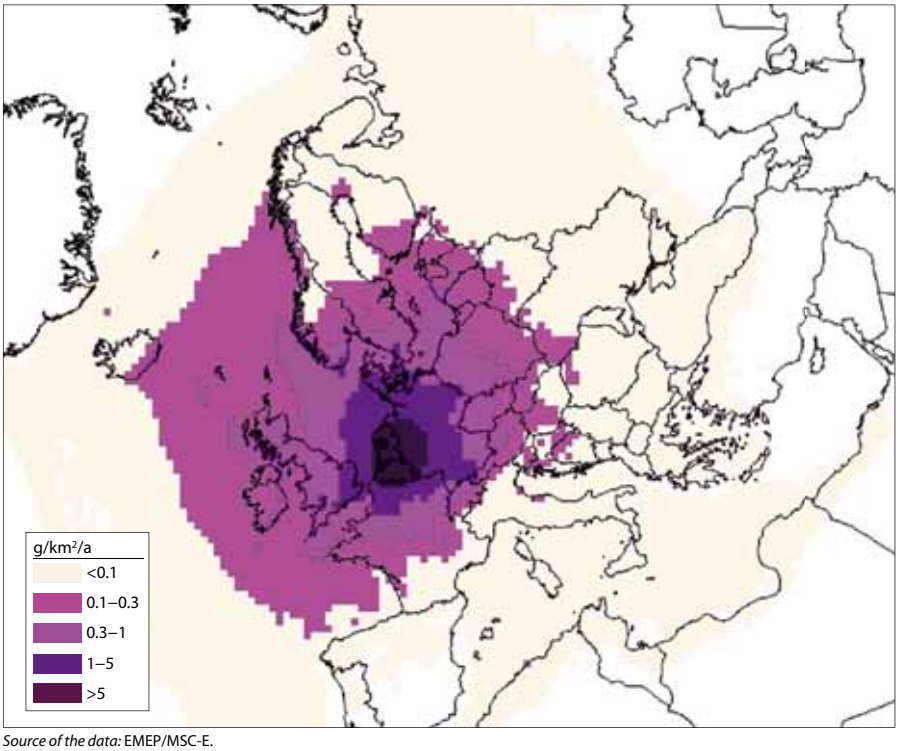


Source: Vestreng et al. (2005).

mately 37% of its original concentration). The atmospheric lifetime of a 1-μm particle is around a few days, being strongly dependent on particle density and meteorological parameters. For example, Gong & Barrie (2005) assume the lifetime of metal-bearing particles in the Arctic to be 3–7 days in summer and 3–7 weeks in winter, characterized by higher atmospheric stability and lower precipitation. A lifetime of a few days or longer implies significant potential for long-range transport: assuming a wind speed in the planetary boundary layer of 5 m/s, the air-mass travel distance would be ~1300 km within 3 days. Wet deposition and dry deposition are the processes responsible for the removal of cadmium from the atmosphere. The ability of cadmium to be transported over long distances is exemplified by Fig. 2.4, which shows modelled annual depositions of cadmium in 2003 from Belgian sources. The highest depositions occurring in Belgium and the neighbouring Netherlands (>5 g/km^2/a) are surrounded by elevated depositions (>1 g/km^2/a) predicted for almost the whole of Denmark and Germany and parts of France and the United Kingdom.

The transfer of cadmium from soil to the food-chain depends on a number of factors, such as the type of plant, the type and pH of the soil and the zinc and organic matter content in the soil. Soil cadmium is distributed between a number of pools or fractions, of which only the cadmium in soil solution is thought to be

Fig. 2.4. Modelled depositions of cadmium from Belgian sources in 2003.



Source of the data: EMEP/MSC-E.

directly available for uptake by plants. Soil pH is the principal factor governing the concentration of cadmium in the soil solution. Cadmium adsorption to soil particles is greater in neutral or alkaline soils than in acidic ones and this leads to increased cadmium levels in the solution. As a consequence, plant uptake of cadmium decreases as the soil pH increases.

The possible influences of pH, clay content and organic matter content on the critical cadmium contents in soil for which the food-quality criterion for lettuce was not exceeded are presented in Table 2.1. However, a relationship between metal content in plants and soil was found only for cadmium in wheat (de Vries et al., 2003). Moreover, the relationship varies substantially between different kinds of wheat.

Table 2.1. Calculated critical cadmium contents in soil in view of the food quality criterion for lettuce as a function of soil properties.

Clay content (%)	Organic matter content (%)	Critical content in soil (in mg/g)		
		pH 5	pH 6	pH 7
2	2	0.61	1.1	3.3
2	5	0.88	2.1	4.8
2	10	1.2	2.7	6.4
20	2	1.9	4.4	10
20	5	2.8	6.5	15
20	10	3.7	8.6	20

Source: de Vries et al. (2003).

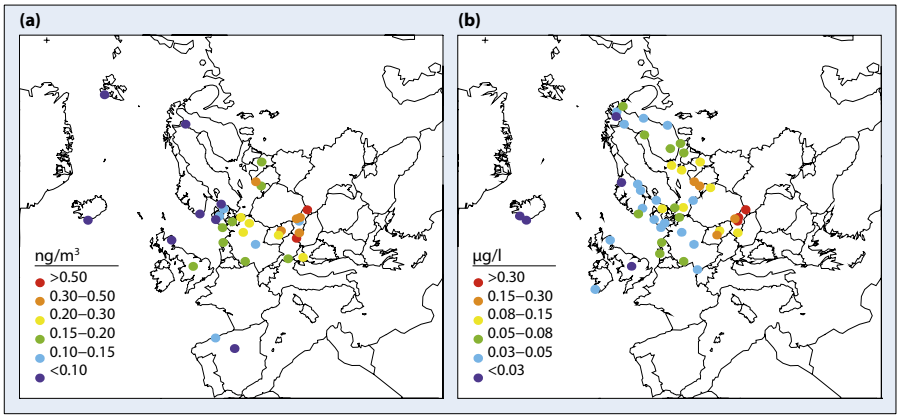
The metal burden of a crop depends on the uptake by the root system and the direct foliar fixation of atmospheric deposition of particulate matter. LRTAP does not cause vegetables grown on soils with low cadmium content to exceed the maximum tolerable concentrations for this metal. Deposition rates of 1 g/m²/a or more are needed to exceed such thresholds (Harmens et al., 2005).

In animals, cadmium accumulates largely in the liver and kidney, and not in the muscle tissue. Plant–animal bioconcentration factors (worst-case scenario) for cows and sheep reached 2.99–2.08, 0.554–1.85 and 3.3×10^{-3} to 2.9×10^{-3} in kidney, liver and meat, respectively (de Vries et al., 2003). There are large differences in the concentrations of cadmium in different kinds of food (milk, 1 µg/kg; meat, fish and fruit 1–50 µg/kg; wheat, rice, potatoes and leafy vegetables 10–300 µg/kg; kidney, liver and oysters 100–1000 µg/kg). These figures indicate that people in population groups consuming excessive amounts of specific food items (mussels, kidney, liver, leafy vegetables) have a higher risk of cadmium exposure.

2.1.4. Monitoring and modelling

The background concentrations of cadmium in air measured in Europe in 1990 ranged between 0.2 and 1 ng/m³ (Fig. 2.5a). In 2003, the typical ranges for

Fig. 2.5. Background concentrations of cadmium in air (a) and in precipitation (b) in 2003.



Source: Aas & Breivik (2005).

concentration in air were 0.05–0.2 ng/m^3 in Northern Europe, 0.2–0.5 ng/m^3 in central Europe and 0.06–0.12 ng/m^3 in southern Europe (Aas & Breivik, 2005).

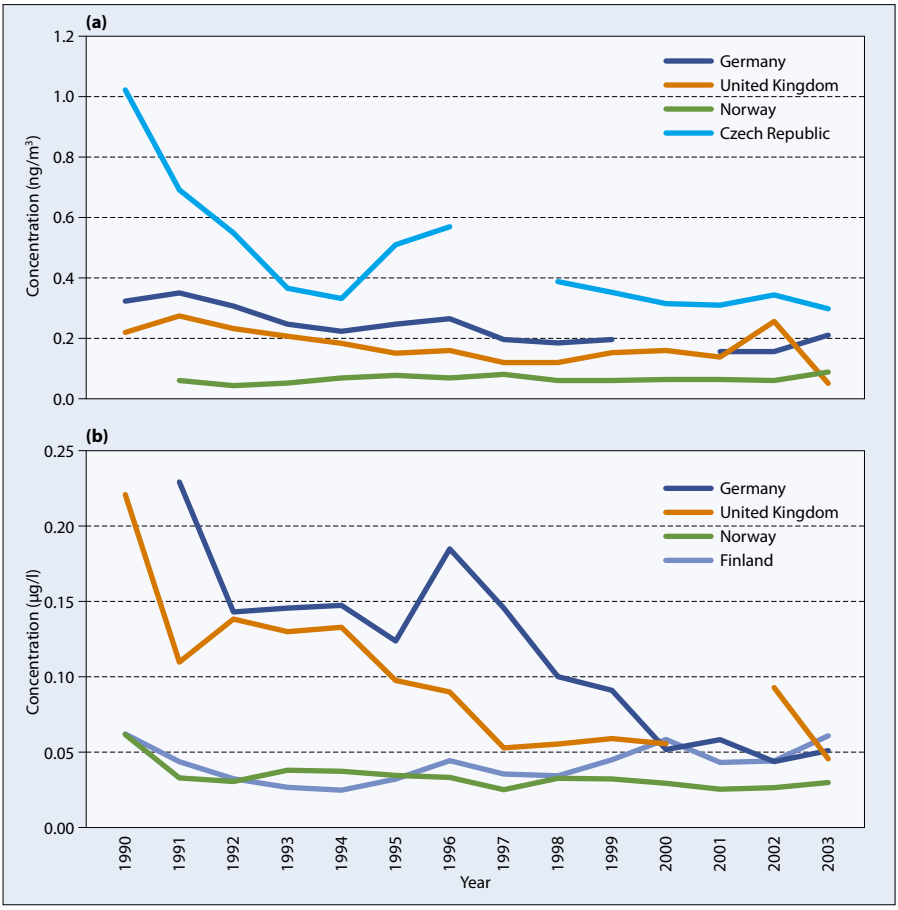
In urban areas, cadmium concentrations were in the range 1–10 ng/m^3; e.g. in Minsk, Belarus, the average annual concentration of atmospheric cadmium in 2004 was 3 ng/m^3. In industrialized regions, the levels are in the range 1–20 ng/m^3. The levels are even higher (100 ng/m^3) in the proximity of industrial sources of cadmium (WHO/IPCS, 1992): e.g. close to a non-ferrous plant in northern Belgium (Beerse), mean annual concentrations of 27 ng/m^3 (with daily peaks of 370 ng/m^3) have been reported. A WHO air quality guideline for cadmium of 5 ng/m^3 has been recommended in order to prevent any further increases in cadmium levels in agricultural soils (WHO, 2000).

The annual mean concentrations of cadmium in precipitation in Europe in 2003 ranged between 0.03 and 0.35 µg/l (Fig. 2.5b). By 2003, data on measured levels became available from central Europe and from stations in the Baltic Sea region. In northern Europe, the concentrations typically are 0.02–0.1 µg/l, and in central Europe they are 0.04–0.2 µg/l (Aas & Breivik, 2005).

From the early 1990s to 2003, the country-averaged concentrations of cadmium in air decreased around 2 times in central and north-western Europe (Fig. 2.6a). Measured concentrations in precipitation decreased 65–75% in central and north-western Europe (Fig. 2.6b). In the northern part of Europe, trends for concentrations in precipitation are not evident for this period (1990–2003) but the levels are much lower. Numerical information on observed cadmium background levels for 2003 is available in Aas & Breivik (2005) and at the Chemical Coordinating Centre web site (http://www.nilu.no/projects/ccc/emepdata.html).

Analysis of the observed cadmium wet depositions revealed significant inconsistencies between measured levels and total European anthropogenic emissions (Ilyin & Travnikov, 2005). Expert estimates (based on the procedure presented by

Fig. 2.6. Long-term variations in measured concentrations of cadmium in air (a) and in precipitation (b) in different parts of Europe.



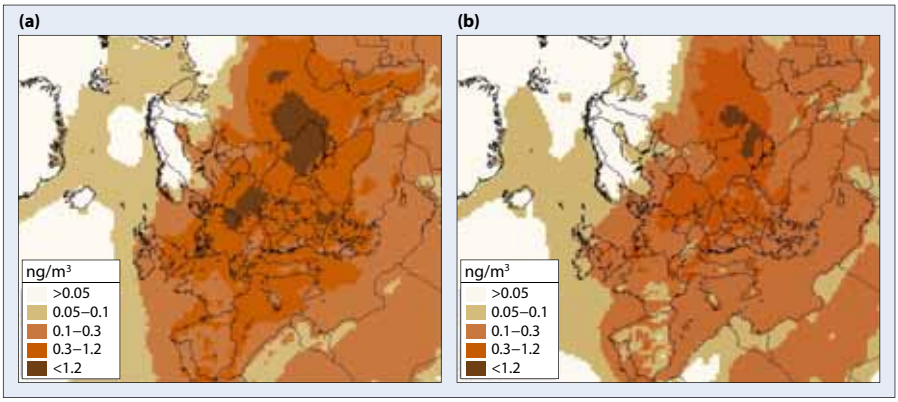
Source: UNECE (2006b).

Berdowski et al., 1997) were used in the case of missing data. These inconsistencies could be explained by underestimation of either the reported official data or the natural emissions or re-emissions of historical depositions with regard to total European emissions. These inconsistencies should be investigated further.

For the period 1990–2003, cadmium pollution levels were modelled using the EMEP Meteorological Synthesizing Centre Heavy Metal (MSC-HM) model (with a spatial resolution of 50×50 km^2) and expert estimates of emissions. These emission estimates comprise anthropogenic sources, preliminary estimates of natural emissions and re-emissions. For a detailed description of the approach, see Ilyin & Travnikov (2005). In 1990 over most of Europe, modelled concentrations exceeded 0.3 ng/m^3 (Fig. 2.7a). By the end of the period studied, concentrations over western and central parts of Europe declined, ranging from 0.1 to 0.3 ng/m^3 (Fig. 2.7b). Total modelled depositions of cadmium in 1990 typically

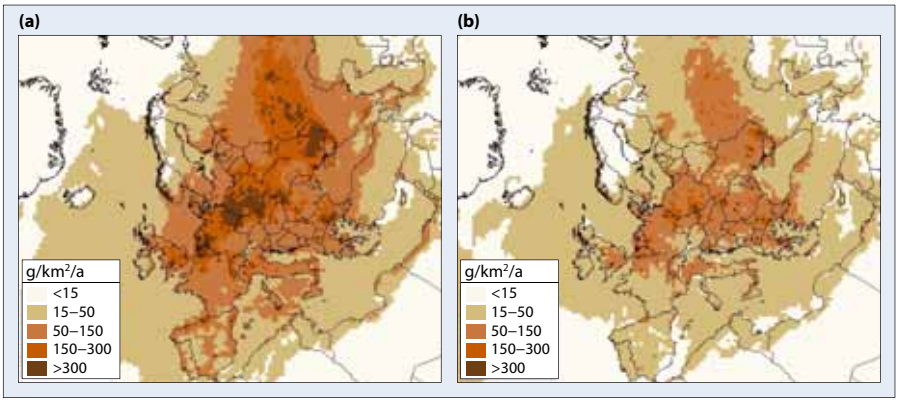
ranged from 50 to 300 g/km²/a (Fig. 2.8a). By 2003, deposition had decreased in most regions of Europe. A typical range for depositions then was 15–150 g/km²/a (Fig. 2.8b). In the Mediterranean region, which is not covered by EMEP monitoring stations, the concentrations in air are as high as those in central Europe, but deposition is somewhat lower. Depositions on individual land-cover categories are also evaluated. Deposition in forests is markedly higher than that on crops (Fig. 2.9a,b).

Fig. 2.7. Spatial distribution of modelled air concentrations of cadmium over the EMEP region in 1990 (a) and 2003 (b).



Source: UNECE (2006b).

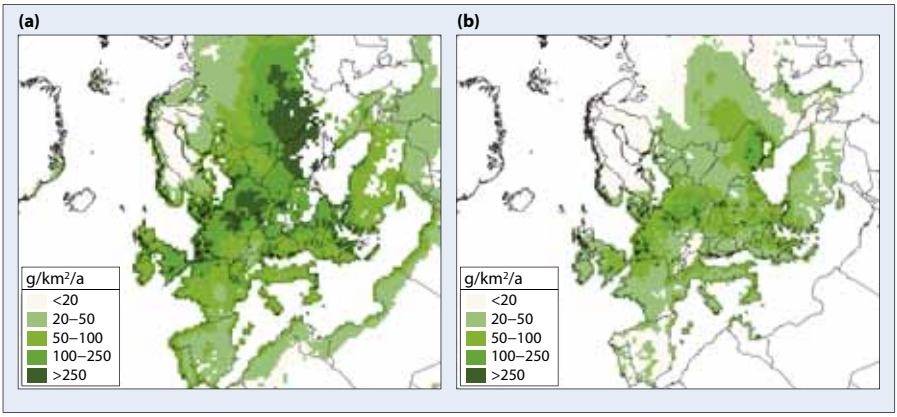
Fig. 2.8. Spatial distribution of modelled total deposition of cadmium over the EMEP region in 1990 (a) and 2003 (b).



Source: UNECE (2006b).

For Europe as whole, atmospheric concentrations of cadmium were characterized by about a twofold decrease. In individual countries, the highest estimated decline in concentrations took place in Monaco (3.4 times) and the Netherlands (3.3 times). In 13 countries, the decrease was 2.5 times or more. In 16 countries, the decrease ranged from 2 to 2.5 times.

Fig. 2.9. Spatial distribution of modelled total deposition of cadmium in coniferous forests (a) and crops (b) in the EMEP region.



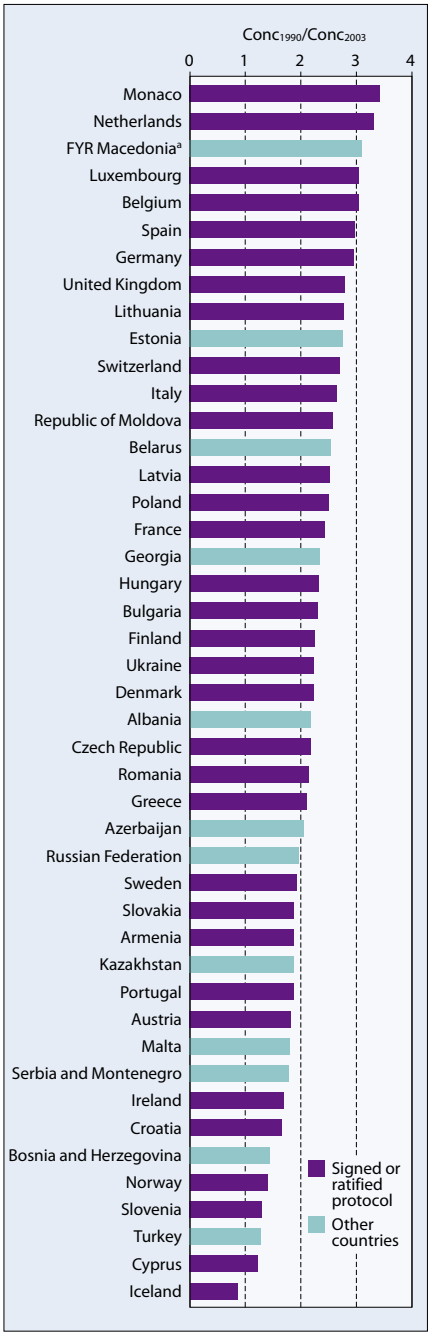
Similar magnitudes of estimated decrease were obtained for depositions in individual countries. For Europe as a whole, the decrease was 2.3 times and in individual countries (Monaco, the Netherlands) it reached 3.3 times. As many as 27 countries were characterized by at least a twofold decrease in deposition.

The contribution of transboundary transport from anthropogenic sources in Europe to the deposition of cadmium in European countries varies between 83% (Republic of Moldova) and 7% (Spain) (Fig. 2.11). In 16 countries, this estimated contribution exceeds 50% and in 27 countries it exceeds 30%. The contribution of external sources to deposition in individual countries shows similar variability.

Both monitoring and modelling have demonstrated a decrease in atmospheric cadmium levels in Europe. Cadmium pollution levels exhibit about a twofold decrease for Europe as a whole in the period 1990–2003. In some individual countries the estimated magnitude of the fall in cadmium pollution is as much as 3–4 times. The typical range for cadmium deposition in Europe in 1990 was 50–300 g/km² and in 2003 it was 15–150 g/km². Transboundary transport is responsible for 10–80% of cadmium deposition in the countries of Europe. Numerical information concerning modelling results is available from the EMEP Meteorological Synthesizing Centre – East (MSC-E) on request.

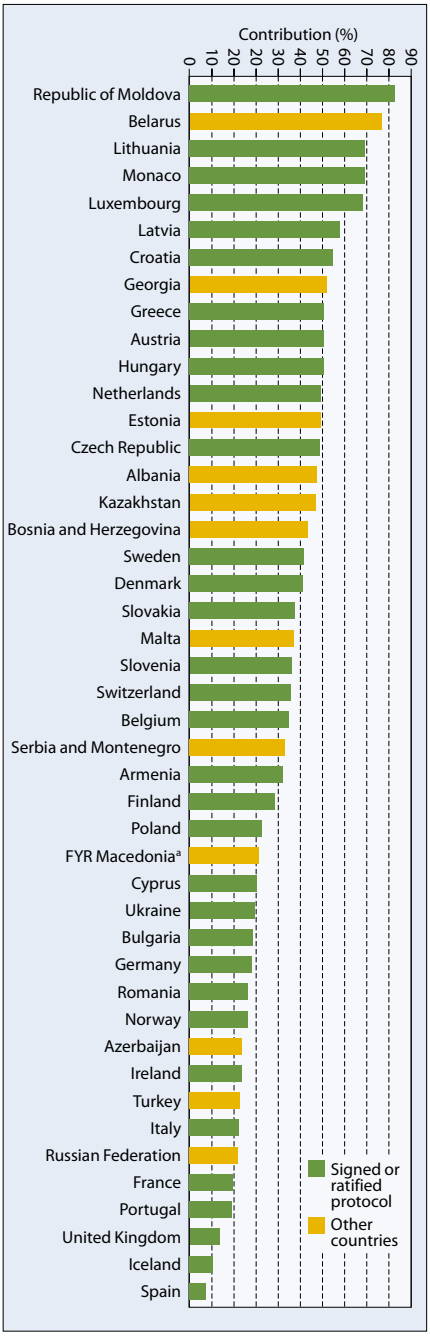
Verification of the modelling results for cadmium presented several problems; results were compared with observed data and with the results produced using other transport models. Analysis showed that the intrinsic model uncertainty (i.e. the uncertainty of the model without emission data) varies across Europe from 20 to 60% for concentrations in air, in precipitation and for total deposition (Travnikov & Ilyin, 2005). Intercomparison of atmospheric transport models for cadmium demonstrated that air concentrations and deposition levels produced using the MSCE-HM model agree well with the results obtained by the EMEP

Fig. 2.10. Ratio between modelled country average air concentrations for cadmium in 1990 and those in 2003 for the countries of Europe.



[a] The former Yugoslav Republic of Macedonia.
Source: UNECE (2006b).

Fig. 2.11. Contribution of anthropogenic sources outside Europe to deposition of cadmium in European countries in 2003.

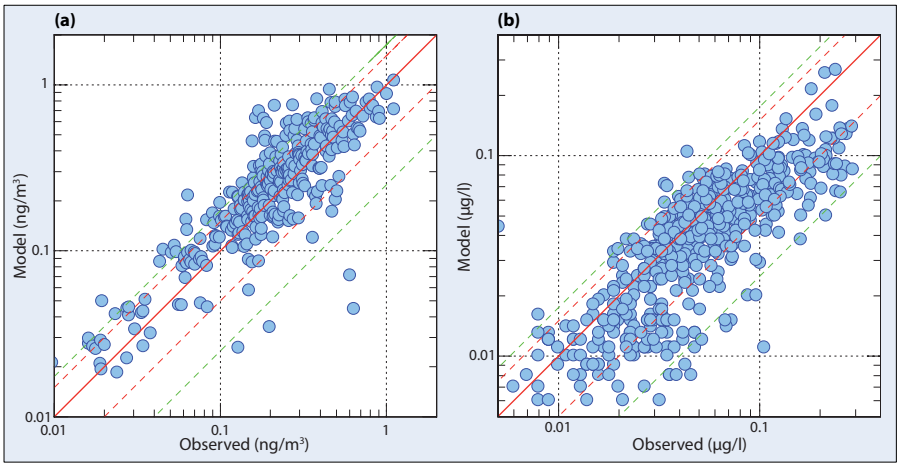


[a] The former Yugoslav Republic of Macedonia.
Source: UNECE (2006b).

Task Force on Measurements and Modelling (TFMM) using other transport models (UNECE, 2006c).

Cadmium concentrations in air predicted by the model for 1990–2003 based on expert estimates of emissions are in good agreement with the aggregated available monitoring data (Ilyin & Travnikov, 2005). The correlation is high (the coefficient is 0.8) and for more than 70% of compared values the difference between modelled and measured concentrations does not exceed ±50% (Fig. 2.12). The observed cadmium concentrations in precipitations are frequently underestimated by the model. However, the correlation between the modelled and measured values is high (the coefficient is almost 0.8) and almost 80% of the model/measurement pairs for concentrations in precipitations agree (within ±50% of the measured value). More details about verification of the modelling results are available in Ilyin & Travnikov (2005).

Fig. 2.12. Comparison of annual mean modelled and observed concentrations of cadmium in air (a) and in precipitations (b) for 1990–2003. Solid red line, 1:1 ratio; broken line, deviation ±50% (red) and ±75% (green).



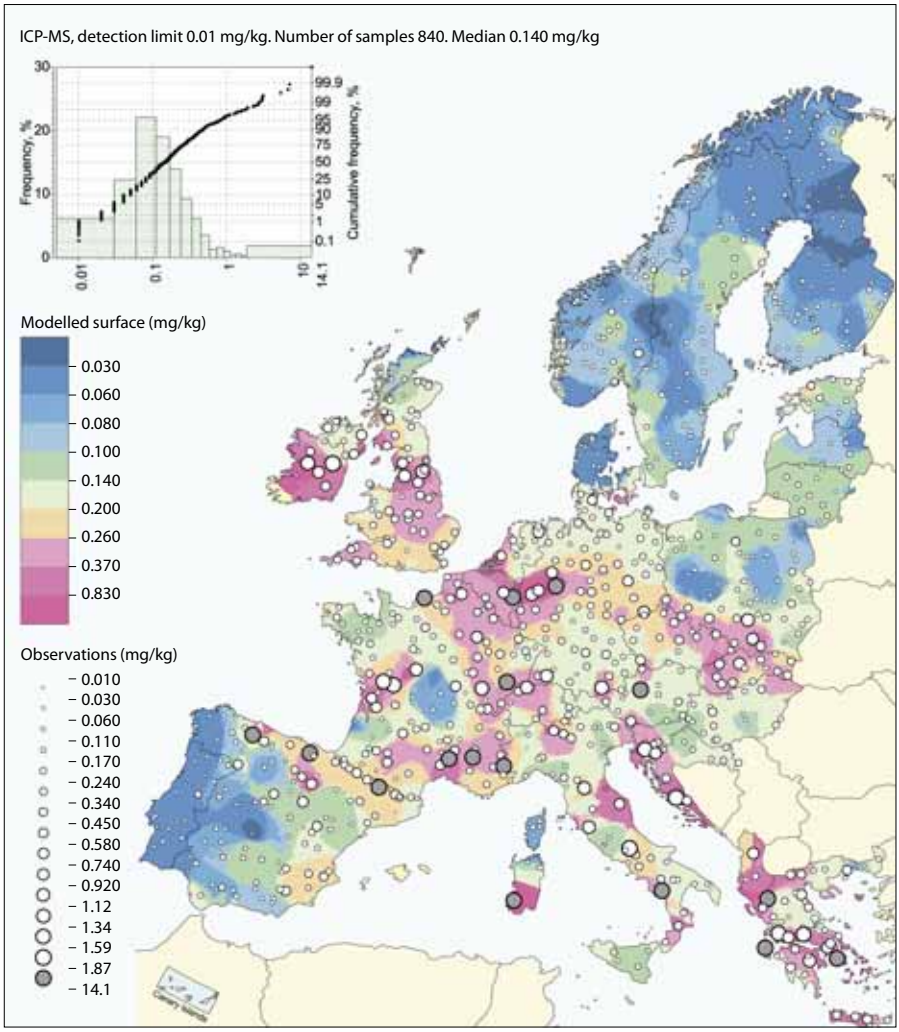
Source: Ilyin & Travnikov (2005).

In October 2005, a TFMM workshop devoted to the review of the MSC-E models was held in Moscow. The main conclusion of the workshop members was that the "MSC-E model is suitable for the evaluation of long range transboundary transport and depositions of heavy metals in Europe" (UNECE, 2006c).

2.1.5. Cadmium in soil and water

On the basis of the cadmium contents in surface soils from many parts of the world, the average value lies between 0.07 and 1.1 mg/kg; values above 0.5 mg/kg usually reflect anthropogenic inputs (Kabata-Pendias & Pendias, 1984). In soils derived from anomalous parent materials, the cadmium content can reach 30 mg/kg (Thornton et al., 1995). However, cadmium incorporated in minerals is not

Fig. 2.13. Concentrations of cadmium in topsoils; observations from field measurements and modelling.



Source: Salminen et al. (2005).

readily available for leaching and for uptake by vegetation. The mean cadmium level in unpolluted topsoils in the United States is approximately 0.25 mg/ kg (ATSDR, 1999), in urban garden and allotment soils in the United Kingdom the geometric mean was 0.53 mg/kg in 1987/1988, and in unpolluted paddy soils in Japan it amounted to 0.4 mg/kg (Thornton, 1992). Cadmium concentrations in the topsoils of Europe vary from <0.03 to >0.8 mg/kg, the median value being 0.14 mg/kg (Fig. 2.13).

There are three main anthropogenic sources of terrestrial cadmium: atmospheric deposition, agricultural application of phosphate fertilizers, and use of municipal sewage sludge as a fertilizer on agricultural soils. It has been reported

that 90% of the cadmium in soil remains in the top 15 cm (ATSDR, 1999). Accumulation of cadmium in the soil depends on the soil properties, with clay soils in general retaining more cadmium than sandy soils.

The most difficult flux to estimate in the balances is loss through leaching. Recently, some data have been produced that can be used to estimate leaching of cadmium from the plough layer (Table 2.2). Data on cadmium concentrations in suction lysimeters and saturation extracts from soils in southern Sweden, recalculated as amounts (assuming a precipitation excess of 200 mm/a), indicate a leaching value of 40 g/km². Saturation extracts from two clay-rich neutral soils from central Sweden had concentrations corresponding to 12–28 g/km²/a. These values are considerably lower than the reported range for near-neutral soils (90–380 g/km²/a) (Belgian Federal Department of the Environment, 1999). Those estimates are based on data from other European countries. However, it should be pointed out that the data presented are usually based on soil–liquid distribution coefficients obtained from studies with soil suspensions. Few studies based on in situ pore-water concentrations are available. One reason why cadmium concentrations in Swedish soils are probably lower than those in soils in many central European countries may be the predominance of clay-rich soil, as one third of the soils in Sweden contain more than 25% clay.

Table 2.2. Estimated cadmium leaching downwards in the soil profile.

Cadmium contents in drainage water at approx. 1 m depth
30–70 g/km²/a
(4 mineral soils: near-neutral pH; different textures and climatic conditions)
(Andersson et al., 1988)
Estimated leaching from plough layer
2 soils from central Sweden:
12–28 g Cd/km²/a (saturation extracts; Jansson et al., 2002)
1 soil from southern Sweden:
34–46 g Cd/km²/a (saturation extracts; Jansson et al., 2002)
3 soils from southern Sweden:
40 g Cd/km²/a (suction lysimeters; Stolt et al., 2006)

Table 2.3 shows a cadmium balance for a farm without livestock in the southernmost part of Sweden. This part of Sweden is similar to Denmark and northern Germany with regard to cadmium deposition and leaching. The balance for the plough layer shows that, with input via fertilizer reduced to a minimum, deposition from LRTAP accounts for most of the total cadmium input. The main outputs are from crop harvesting and leaching. Inputs are slightly higher than outputs. From the point of view of uptake in the crops, a balance for the rooting

Table 2.3. Cadmium balances for a farm without livestock in southern Sweden where phosphorus was applied as a "low-cadmium" fertilizer.[a]

	Plough layer	"Root zone"
Supply (g/km²/a)		
Phosphorus fertilizer	12	12
Manure	–	–
Deposition	70	70
Lime	2	2
Total	84	84
Removal (g/km²/a)		
Crops	23	23
Leaching	40	6
Total	63	29
Supply minus removal (g/km²/a)	21	55
Annual change in topsoil content (%)	0.03	–

[a] Crop rotation: barley, oats, rapeseed, winter wheat, oats, winter wheat; phosphate fertilizer 1000 kg P/km²/a; deposition calculated from moss data; Cd content in topsoil assumed to be 75 kg/km².

zone is probably more relevant than one just for the plough layer. The leaching from the subsoil is much smaller than that from the plough layer (Table 2.4). Some of the cadmium leaching out of the plough layer is obviously adsorbed in the subsoil, presumably in its upper part, where plant roots are also active. In the "root-zone" balance, the net accumulation is twice that in the plough layer balance (Table 2.5).

The balances presented in tables 2.3, 2.4 and 2.5 indicate that measures for reducing inputs via fertilizers at a national level have led to a situation in which further improvements can only be reached by lowering the deposition.

The near balance has been reached in Sweden by achieving reductions in both deposition rates and the use of phosphate fertilizers. In situations of higher deposition rates and phosphate fertilizers containing higher cadmium levels, each of these inputs is often larger than the outputs. This was the situation in Sweden about 10 years ago (Andersson, 1992), and may still be the situation in at least parts of central Europe.

The annual rate of cadmium input to arable land from phosphate fertilizers has been estimated for the countries of the EEC: the average is 0.5 kg/km²/a (WHO/IPCS, 1992).

The final report of the European Union (EU) Concerted Action AROMIS (Eckel et al., 2005) provides summary information on metal inputs to agricultural soils from mineral and organic fertilizers and other sources. Within the framework of AROMIS, 24 research institutions from 21 European countries contrib-

Table 2.4. Cadmium balances for a farm without livestock and a farm with pigs for slaughter, in central Sweden where phosphorus was applied as a "low-cadmium" fertilizer.[a]

	Farm without livestock		Slaughter-pig farm
	Plough layer	"Root zone"	Plough layer
Supply (g/km²/a)			
Phosphorus fertilizer	12	12	–
Feed	–	–	30
Deposition	45	45	45
Lime	4	4	4
Total	61	61	79
Removal (g/km²/a)			
Crops	20	20	19
Leaching	20	6	20
Total	40	26	39
Supply minus removal (g/km²/a)	21	35	38
Annual change in topsoil content (%)	0.03	–	0.05

[a] Crop rotation: barley, oats, rapeseed, winter wheat, oats, winter wheat; phosphate fertilizer 1000 kg P/km²/a; deposition calculated from moss data; Cd content in topsoil assumed to be 75 kg/km².

uted information on fertilizer use, nutrient and metal contents in fertilizers and other data needed to calculate metal balances. Because the data gathered were not homogenous, the metal fluxes from fertilizer use could be derived for only some of the countries. Furthermore, calculations are presented of metal inputs and outputs for a selected number of model farms, reflecting the most important production types in Europe.

Since the percentage of the land that is subject to the application of sewage sludges and composts is very low in most countries, these sources of cadmium are excluded from consideration here, though information is provided in the AROMIS database. However, at the individual field level, these inputs can be considerable.

The ratio of cadmium inputs to agricultural soils from different sources on a national scale (the total amount of metal divided by the total agricultural land area) for several European countries is provided in Table 2.6. The proportion contributed by atmospheric deposition was calculated using monitoring data, for which the methods for deposition monitoring differed from country to country.

The cadmium fluxes at farm or field scale show great variability. For 32 representative farm types (not using sludges and composts) in 12 European countries, the calculated range for cadmium input via mineral fertilizer was 0–1.4 kg/km²/a, and that for input via manure was 0–0.37 kg/km²/a. For farms with

Table 2.5. Cadmium balance for a farm without livestock in central Sweden where phosphorus was applied as a "high-cadmium" fertilizer or as sewage sludge.[a]

	Plough layer	
	100 mg Cd/kg P	Max-Cd sludge[b]
Supply (g/km²/a)		
Phosphorus fertilizer	100	75
Manure	–	–
Deposition	45	45
Lime	4	4
Total	149	124
Removal (g/km²/a)		
Crops	20	20
Leaching	20	20
Total	40	40
Supply minus removal (g/km²/a)	109	84
Annual change in topsoil content (%)	0.15	0.11

[a] Crop rotation: barley, oats, rapeseed, winter wheat, oats, winter wheat; phosphate fertilizer 1000 kg P/km²/a; deposition calculated from moss data; Cd content in topsoil assumed to be 75 kg/km². Cd concentration in soil 0.07–1.1 mg/kg; deposition 100 g/km2/a; contribution to concentration in top 10–15 cm 0.001 mg/kg; LRTAP contribution (annual) 0.1–1.6%.

[b] Max-Cd sludge: maximum allowable input, via sewage sludge, for Swedish agricultural soils (75 g Cd/km²/a).

complete datasets for input and output fluxes, cadmium balances could be calculated. All 13 animal farms (mainly involving cattle, pigs and poultry) that could be considered had positive cadmium balances, i.e. the inputs were higher than the outputs. Out of a total of 17 crop farms, 15 showed positive cadmium balances.

The application of municipal sewage sludge can also be a significant source of cadmium. In 1986, the European Commission established a limit value of 20–40 mg/kg for cadmium in sludges applied to agricultural land, and also established limits of 1 mg/kg (dry weight) (recommended) and 3 mg/kg (limit for cadmium in sludged land) (Thornton, 1992). The United States Environmental Protection Agency (USEPA) has set a limit of 85 mg/kg for the maximum permitted cadmium concentration in sewage sludge, and a maximum annual cadmium loading of 190 kg/km² (ATSDR, 1999).

In Sweden, the cadmium content in agricultural land was estimated to be increasing by about 0.2% per year, despite the falling input of cadmium from phosphate fertilizers (Järup et al, 1998).

Markedly elevated levels may occur in topsoils near industrial sources. For example, in the vicinity of a smelter in Helena in the United States the average soil values were 72 mg/kg within 1 km and 1.4 mg/kg between 18 and 60 km (ATSDR, 1999).

Table 2.6. Estimated cadmium inputs (percentage of total) to agricultural soils in Germany, the Netherlands, Switzerland and the United Kingdom.[a]

	Manure[b]	Mineral fertilizers (%)	Atmospheric deposition (%)	Average total input rate ($g/km^2/a$) (%)
Germany	17	29	51	500
Netherlands	29	47	22	450
Switzerland	6	22	64	180
United Kingdom	10	30	54	360

[a] Inputs from sludges, corrosion, dredgings and hunting were not considered.
[b] Solid manure and slurry from breeding cattle, pigs and poultry.

Sources: Alloway (1998); Candinas et al. (1999); Eckel et al. (2005); Lijzen & Ekelenkamp (1995); Lijzen & Franken (1994); Wilcke & Döhler (1995).

Drinking-water generally contains low cadmium levels, and a value of 1 µg/l or less is often assumed to be a representative content in most situations. Thus, cadmium exposure from drinking-water is relatively unimportant compared with the dietary contribution (WHO/IPCS, 1992). WHO (1993) has recommended a guideline value of 3 µg/l for drinking-water.

2.2. Pathways of human exposure and their relationships to LRTAP

2.2.1. Exposure via inhalation

Assuming a daily inhalation of 20 m^3, and on the basis of the highest concentration of cadmium found in rural, urban and industrialized areas, the amount of cadmium inhaled daily does not, on average, exceed 0.04, 0.2 and 0.4 µg/day, respectively. In the general population, exposure from inhalation is low, but house dust is potentially an important and persistent source of cadmium exposure in areas with contaminated soils, especially where driveways have been covered with residues from non-ferrous metal production (e.g. zinc ashes or sintels as oven sludge).

Cigarette smoking represents an additional source of cadmium, which may exceed that from food. One cigarette contains about 1–2 µg cadmium. An average of about 10% of this is inhaled during smoking. It can thus be estimated that a person smoking 20 cigarettes per day will absorb about 1 µg of cadmium (Järup et al., 1998). According to Erzen & Kragelj (2006), the median blood cadmium (B-Cd) concentration in Slovenia was 0.5 µg/l in non-smokers, 1.0 µg/l in light-to-moderate smokers (less than 20 cigarettes/day) and 1.5 µg/l in heavy smokers (more than 20 cigarettes/day).

2.2.2. Exposure via the gastrointestinal tract

For non-smokers, food constitutes the principal environmental source of cadmium. In recent years, the mean daily intake of cadmium from food amounted to 17.3 µg in Croatia (Sapunar-Postruznik et al., 1996), 11–19 µg in the Czech Republic (Puklova et al., 2005), 27 µg in France (Biego et al., 1998), 10–14 µg in Germany (Muller et al., 1998), 23.3 µg in Poland (in females) (Marzec et al.,

2004), 11–29 µg in Spain (Rubio et al., 2006) and 11–16 µg in Sweden (Berglund et al., 1994).

Dietary cadmium intake is log-normally distributed. Therefore, a small increase in the population's average daily intake of cadmium will result in a much larger increase in the fraction of the population having the highest intake. An increase in the median daily intake by a factor of 2 (i.e. from 15 to 30 µg/day) would correspond to an increase in the 95th percentile from about 20 to 60 µg/day (Järup et al., 1998). The provisional tolerable weekly intake (PTWI) set by WHO and the Food and Agriculture Organization of the United Nations (FAO) (WHO/FAO, 1993) for cadmium is 500 µg (a weekly intake of 7 µg/kg body weight (kg_{bw}), corresponding to a daily intake of 70 µg or 1 µg/kg_{bw}/day. The USEPA Reference Dose amounts to 1 µg/kg_{bw}/day in food and 0.5 g/kg_{bw}/day in drinking-water (USEPA, 1999). These values are based on the chronic effects of cadmium on kidney function. However, it has been suggested that the PTWI should be lowered (Nordberg, 1999; Järup et al., 1998).

Drinking-water contains very low concentrations of cadmium, usually between 0.01 and 1 µg/l. The average daily intake of water is about 2 l per person.

2.2.3. Relevance of various routes of exposure

A comparison of cadmium intake and uptake via respiratory and dietary routes in China and Japan was presented by Zhang et al. (1997). On average, the cadmium concentration in air was 7.3 ng/m^3 in China, the daily exposure via the respiratory tract was calculated to be 0.11 µg and the uptake (50% absorption) was 0.05 µg. The daily intake via food was reported to be 9.9 µg and the uptake (7.5% absorption) was 0.74 µg/day. In Japan, uptakes via the respiratory and food routes were calculated to be 0.07 and 2.41 µg/day, respectively. The uptake via food was estimated to amount to 93.7% in China and 97.2% in Japan.

In the Czech Republic, the daily intakes via the respiratory route, water and food were estimated to be 0.01 µg/day, 0.17 µg/day and 18.2 µg/day (0.05%, 0.92% and 99.3%), respectively (Kliment, 1996).

In Canada, the estimated daily cadmium intakes in adults over 20 years (assumed to weigh 70 kg, to breath 23 m^3 of air, drink 0.4 litres of water and ingest 20 mg of soil daily, and to smoke 20 cigarettes/day) were as follows: from air the intake was 0.33–1.3 ng/kg_{bw}/day; from drinking-water it was <0.057–0.51 ng/kg_{bw}/day; from food it was 210 ng/kg_{bw}/day; from soil it was 0.16–0.33 ng/kg_{bw}/day; and from cigarettes it was 53 ng/kg_{bw}/day (Newhook et al., 1994).

At a cadmium concentration of 1 mg/kg soil, the intake of cadmium from ingestion of soil would be approximately 0.05–0.2 µg/day, assuming a soil-ingestion rate of 0.05–0.2 g/day for adults (Choudhury et al., 2001).

The data presented above indicate that food is the main source of cadmium exposure in the general population, being responsible for more than 90% of the total intake in non-smokers.

2.2.4. Trends in cadmium exposure

Some studies have reported a decreasing trend in human B-Cd in Europe and some other areas. In Belgium, in a group of men not occupationally exposed to cadmium and who were examined annually between 1984 and 1988, the mean B-Cd concentration decreased from 2.25 µg/l to 0.79 µg/l (14% annual decrease). A similar decline (about 10%) was suggested from the data reported in Germany, where the fall was from 1.19 µg/l in 1979 to 0.39 µg/l in 1986 (Ducoffre et al., 1992).

In the following years, however, the geometric mean for B-Cd in Germany did not continue to decrease in the general population aged 25–9 years (0.45 µg/l in 1985–1986, 0.37 µg/l in 1990–1992 and 0.44 µg/l in 1998; Becker et al., 2002). The geometric mean concentration for B-Cd decreased in Japan between 1980 and 1990 from 3.8 µg/l to 1.79 µg/l in men and from 3.57 µg/l to 1.84 µg/l in women (Watanabe et al., 1993).

Friis et al. (1998) reported that over the period from 1976 to 1995/1996 there was a reduction in cadmium concentrations in renal cortices in Sweden, especially in people younger than 50 years of age. In non-smokers aged 40–49 years, the cadmium level in the kidney decreased from 17.4 mg/kg wet weight to 6.82 mg/kg wet weight, and in the whole population it fell from 21.7 mg/kg wet weight to 13.2 mg/kg wet weight. In the 1990s, the highest individual concentration of cadmium in renal cortices from 171 autopsies was 41 mg/kg wet weight, which is still below the critical level associated with environmental exposure.

Recently, time trends for cadmium, mercury and lead were evaluated in Sweden in the population-based MONICA (Multinational monitoring of trends and determinants in cardiovascular disease) study. Concentrations in erythrocytes were determined for 600 men and women aged 25–74 years in surveys carried out in 1990, 1994 and 1999 (Stegmayer et al., 2003). Annual decreases of 5–6% were seen for lead and mercury levels in erythrocytes. For cadmium levels in erythrocytes, the decline was seen only among smokers, indicating that exposure to this metal from tobacco had decreased but that other environmental sources had not changed significantly (Wennberg et al., 2006).

2.3. Health hazard characterization

2.3.1. Toxicokinetics

Pulmonary absorption of inhaled cadmium ranges from 10% to 50% (WHO/IPCS, 1992). The average normal gastrointestinal absorption of ingested cadmium in humans ranges from 3% to 7%. Cadmium in the tissues is mainly bound to metallothionein. The synthesis of this protein probably represents the body's defence mechanism against the toxic cadmium ion.

Liver and kidney tissues are the two main sites of cadmium storage. The newborn infant is virtually free of cadmium but, over a lifetime, these organs accumulate considerable amounts of cadmium (about 40–80% of the body burden).

In low-level environmental exposures, about 30–50% of the cadmium body burden is stored in the kidneys.

Cadmium elimination from blood has been described, in an open two-compartment model, as having a fast-decay half-time of 15–120 days and a slow-decay half-time of 7.4–16 years (Järup et al., 1983).

Cadmium is eliminated in urine and faeces: daily faecal and urinary excretion is estimated to constitute 0.007% and 0.009% of the body burden, respectively (ATSDR, 1999).

2.3.2. Health effects in humans

Important health endpoints include kidney and bone damage and cancer. The kidney is the critical organ with regard to long-term occupational and environmental exposure to cadmium, and all health-based recommendations relate to the early disturbance of renal function.

Indices of tubular and glomerular damage in the kidney

Several highly sensitive indicators of tubular damage, particularly the urinary excretion of β2-microglobulin (β2-M), have been developed and used in epidemiological studies of cadmium-exposed groups. The concentration of β2-M in plasma is usually around 2 mg/l. β2-M is normally freely filtered through the glomerulus into primary urine. The normal urinary excretion of β2-M is less than 0.3 mg in 24 h and comprises less than 0.1% of the filtered load. A relatively small drop in the tubular reabsorptive capacity, from 99.9% to 99.0%, will bring about a 10-fold increase in β2-M excretion in urine (Järup et al., 1998). There are several other sensitive indicators of tubular damage, e.g. retinol-binding protein, α1-microglobulin (protein HC) and Clara cell protein. They are all plasma proteins that are filtered through the glomerulus. Other urinary markers that have been used to detect early kidney dysfunction are, for example, intracellular enzymes (proteins indicative of subtle tubulotoxic effects), N-acetyl-β-d-glucosaminidase, an enzyme localized in the lysosomes of tubular cells, and human intestinal alkaline phosphatase. In particular, the urinary excretion of this enzyme is a very sensitive marker.

Following occupational exposure, three main effect thresholds have been identified (Lauwerys et al., 1993): 2 μg/g creatinine for the increased excretion of 6-keto-PGF1a and sialic acid; 4 μg/g creatinine for the increased excretion of renal brush-border antigen, N-acetyl-β-d-glucosaminidase, intestinal alkaline phosphatase and the high-molecular-weight proteins albumin and transferrin; and 10 μg/g creatinine for the increased excretion of tissue-non-specific alkaline phosphatase, brush-border antigen HF5, and the low-molecular-weight proteins β2-M and retinol-binding protein. The average cadmium concentrations in renal cortex, corresponding to urinary cadmium (U-Cd) thresholds of 2, 4 and 10 μg/g creatinine, were 110, 139 and 182 mg/kg, respectively.

The effects associated with the cadmium threshold of 10 μg/g creatinine, such as a decrease in glomerular filtration rate or a reduction in the filtration reserve capacity, are known as predictors of a more rapid decline in renal function and should therefore be regarded as adverse effects. Increased urinary excretion of low-molecular-weight proteins may lead to an exacerbation of the age-related decline in the glomerular filtration rate (Järup et al., 1993; Roels et al., 1989). Tubular proteinuria has long been considered to be irreversible. Roels et al. (1997) found that when the microproteinuria was mild (urinary β2-M >300 and <1500 μg/g creatinine) and historical U-Cd values never exceeded 20 μg/g creatinine there were indications of a reversible tubulotoxic effect of cadmium. When severe microproteinuria (urinary β2-M >1500 μg/g creatinine) was diagnosed along with U-Cd values exceeding 20 μg/g creatinine, cadmium-induced tubular dysfunction was progressive in spite of any reduction in, or cessation of, exposure. Also, in a group of workers exposed to cadmium in a cadmium-battery factory, Trzcinka-Ochocka et al. (2002) found that tubular proteinuria and a decline in glomerular filtration rate may be reversible, even in cases of relatively high levels of past exposure.

A study of the general population suggested that the threshold effect levels of cadmium may be lower than those found in adult male workers. The survey of populations environmentally exposed to cadmium, conducted in 1985–1989 in Belgium (the CadmiBel Study), showed an association between cadmium exposure and increased prevalence of abnormal results in kidney-function tests (above the 95th percentile in the control group). In particular, the urinary excretion of calcium, β2-M, retinol-binding protein and N-acetyl-β-d-glucosaminidase were significantly associated with the cadmium body burden as assessed from urinary excretion of cadmium. There was a 10% probability of values being higher than normal when cadmium excretion exceeded 2–4 μg per 24 h (Buchet et al., 1990).

During a 5-year follow-up of a subcohort from the CadmiBel Study (Hotz et al., 1999), the U-Cd and B-Cd levels decreased, respectively, by 16% and 35% in men and by 14% and 28% in women. No indication of progressive renal damage was found. Overall, the results suggest that the effects on the kidney from low levels of environmental exposure to cadmium are weak, stable or even reversible after the introduction of measures to reduce exposure, and that tubular effects are not necessarily associated with a subsequent deterioration in glomerular function.

It has been suggested that, for the general population, the U-Cd levels should be below 2 μg/g creatinine (Buchet et al., 1990) or below 2.5 μg/g creatinine (Järup et al., 1998). Such excretion occurs when the average cadmium concentration in the renal cortex is approximately 50 mg/kg. However Järup et al. (2000) used a different indicator of tubular damage (α1-microglobulin in urine, HC) and suggested that renal tubular damage may develop at lower concentrations.

They observed a 10% increase in the prevalence of tubular proteinuria at a U-Cd concentration of 1 μg/g creatinine in a population living close to a nickel–cadmium battery plant.

The results obtained by Noonan et al. (2002) and Trzcinka-Ochocka et al. (2004) revealed that the urinary excretion of early biomarkers of kidney dysfunction can be increased at urine cadmium levels of approximately 2.0 μg/g creatinine. In a cross-sectional European survey of approximately 800 children, the urinary excretion of retinol-binding protein and Clara cell protein were positively correlated with B-Cd with no threshold or a low threshold (0.31 μg/l) (de Burbure et al., 2006).

The relationship between cadmium exposure and tubular and glomerular function was investigated in Sweden in 820 women aged 53–64 years. B-Cd and U-Cd levels of 0.38 μg/l (median) and 0.52 μg/l (0.67 μg/g creatinine), respectively, were associated with effects on renal tubules, as indicated by increased levels of human complex-forming protein and N-acetyl-β-d-glucosaminidase in urine. The associations remained significant even at the low levels of exposure in women who had never smoked. Associations with markers of glomerular filtration rate and creatinine clearance were also found at a mean U-Cd level of 0.6 μg/l (0.8 μg/g creatinine).

According to Järup et al. (1998), adverse health effects (in the form of tubular damage) from environmental cadmium exposure – indicated by the increased excretion of β2-M – may develop in 1% of the adult general population at daily cadmium intake levels of 30 μg/day over the lifespan. With a lifelong average exposure to cadmium of 70 μg/day from food (current PTWI), 7% of the adult general population would be expected to develop cadmium-induced tubular damage.

Diamond & Thayer (2003) conducted an analysis of epidemiological studies of associations between exposure to cadmium and kidney effects. Dose–response functions relating low-molecular-weight proteinuria to various indices of the cadmium dose were obtained from 15 studies of diverse exposures (occupational, general environmental and environmental contamination). Estimates of the dose corresponding to the probabilities of low-mocular-weight proteinuria of 0.1, 0.15 or 0.2 were transformed from the reported dose units into corresponding estimates of target organ dose (μg Cd/g renal cortex, RC) by simulation using a pharmacokinetic model. The median RC associated with 0.1 probability (RC10M) of low-mocular-weight proteinuria was predicted to be 153 μg Cd/g cortex (95% confidence interval 84–263). The lower confidence limit on the RC10M (RC10L, 84 μg/g cortex) was predicted to be attained with a constant chronic intake of 1.0 μg/kg/day in females and 2.3 μg/kg/day in males. The RC10L was 2.5–5 times higher than the median RCs predicted to result from dietary cadmium intake in non-smokers in the United States (μg Cd/g cortex: 33 females; 17 males) and 1.6–3 times higher than the corresponding 95th percentile RCs (53 females; 27

males). Additional exposure from smoking cigarettes (20/day) was predicted to increase the median RC by approximately 45–70%.

Bones and calcium metabolism

The available data show that cadmium can affect calcium and phosphorus metabolism generally, both in industrial workers and in people exposed in the general environment. Painful bone disorders, including osteomalacia, osteoporosis and spontaneous bone fracture, have been observed in humans chronically exposed to cadmium in food. In Japan, in the Jinzu river basin, exposure to cadmium was caused by contamination of river water. Osteomalacia most often affects women with several risk factors such as poor nutrition and multiparity (WHO/IPCS, 1992).

The regression coefficients obtained as a result of the CadmiBel Study (average excretion of cadmium in urine: 1.04 μg per 24 h for men, 0.8 μg per 24 h for women) indicated that when the U-Cd level increased twofold, serum alkaline phosphatase and urinary calcium rose by 3–4% and 0.25 mmol per 24 h, respectively; in men, serum calcium levels fell by 6 μmol/l (Staessen et al., 1991).

Alfven et al. (2000) measured bone mineral density in the forearm in 520 men and 544 women aged 16–81 years and environmentally and occupationally exposed to cadmium, using a dual energy X-ray absorptiometry technique. There was a dose–response relationship between the cadmium dose and the presence of osteoporosis. The odds ratio for men was 2.2 (95% CI, 1.0–4.8) in the dose group 0.5–3 μg Cd/g creatinine and 5.3 (2.0–14) in the highest-dose category (3 μg Cd/g creatinine) compared with the lowest-dose group (<0.5 μg Cd/g creatinine). For women, the odds ratio was 1.8 (0.65–5.3) in the dose group 0.5–3 μg Cd/g creatinine. The authors concluded that exposure to low levels of cadmium is associated with an increased risk of osteoporosis.

In postmenopausal women, a twofold increase in the U-Cd level correlated with a 0.01 g/cm^2 decrease in bone density (P<0.02). The relative risks associated with a doubled U-Cd level were 1.73 (95% CI, 1.16–2.57; P = 0.007) for fractures in women and 1.60 (0.94–2.72; P = 0.08) for height loss in men. The mean cadmium excretion at baseline was 8.7 nmol daily (Staessen et al., 1999). Other studies have shown that there is an increased risk of forearm fractures with increasing cadmium dose. In people aged 50 and above, the hazard ratio reached 3.5 (90% CI, 1.1–11) in the group of subjects with a U-Cd level between 2 and 4 μg/g creatinine, compared to the reference group (Alfven et al., 2004).

During a 6.6-year follow-up of a subcohort of the CadmiBel Study in postmenopausal women, a twofold increase in the U-Cd level correlated with a 0.01 g/cm^2 decrease in bone density. The relative risks associated with a doubled U-Cd level were 1.73 (95% CI, 1.16–2.57) for fractures in women and 1.60 (0.94–2.72) for height loss in men. The fracture rates were 16.0 and 10.3 cases per 1000 person-years for the districts near to the smelters and for a reference area, respectively,

and the population-attributable risk was 35% (Staessen et al., 1999). Similar results were observed in a number of European and Chinese studies (Nordberg et al., 2002; Jin et al., 2004).

The results of an investigation performed in Japan on 1380 female farmers did not confirm the European studies showing that low-dose cadmium exposure increases the risk of osteoporosis. The investigated population was first divided into four groups, using three cut-off values for the U-Cd (2.5, 3.5 and 5.0 μg/g creatinine). Because age and menstrual status can affect bone metabolism, each subgroup was further divided into four classes accordingly: premenopausal (aged 41–48 years), perimenopausal (49–55), younger postmenopausal (56–65) and older postmenopausal (66–75). Although bone mineral density showed a clear negative correlation with the U-Cd levels when subjects of all ages were considered together, this correlation disappeared when the premenopausal and perimenopausal groups were considered individually. The authors performed multivariate analyses for body mass index and U-Cd levels, using possible confounding factors as well as cadmium exposure as independent variables. In every model for bone mineral density, age and body mass index were the first and second significant factors. Cadmium exposure at a level insufficient to induce renal dysfunction had no effect on bone mineral density or U-Cd excretion (Horiguchi et al., 2005).

Studies conducted in Simferopol, Ukraine showed associations between internal dose of cadmium and heart function at different physical load levels in 15- and 18–19-year-old children (Slusarenko et al., 2004; Glivenko 2005). Similar association was found with heart rate variability as an indicator of the autonomous nervous system tone in 12–13-year-olds (Tymchenko et al., 2005). Slusarenko (2003) investigated children aged 7–11 years in urban areas and found negative correlations between parameters of cellular and humoral immunity (including B-lymphocytes and O-lymphocytes) and cadmium content in hair. Evstafyeva et al. (2006) investigated the brain function of 33 young men aged 18–19 years in Simferopol, Ukraine and revealed an increase in amplitude of the conditional negative wave of the event-related potentials in both hemispheres with increasing cadmium concentration in hair (up to 0.17 μg/g).

On the basis of the studies conducted in Europe (Buchet et al., 1990; Hotz et al., 1999; Järup et al., 2000), it appears that renal effects can be detected in the general population (mainly exposed by the oral route) for cadmium body burdens below 5 μg/g creatinine (2 μg/g creatinine (Buchet et al., 1990), 0.5 μg/g, 1.2 μg/g or 2.6 μg/g creatinine (Järup et al., 2000) depending on the calculation method). It is very difficult to define values such as the lowest observed adverse effect level (LOAEL) on the basis of data from these types of study, because of the complexities of the relationship examined. Aggregating all these data, a LOAEL of 2 μg Cd/g creatinine is proposed. In a later evaluation of the risk-assessment document, the EC Scientific Committee on Toxicity, Ecotoxicity and the Environment concluded that the LOAEL was not based on strong scientific evidence, in that

effects may occur even at lower levels (as low as 0.5 μg/g creatinine) (Scientific Committee on Toxicity, Ecotoxicity and the Environment, 2004).

Two main mechanisms for the influence of cadmium on bone have been proposed. Initially, it was thought that bone lesions were a secondary response to kidney damage. A possible mechanism for the development of osteomalacia is that cadmium accumulates in the proximal tubular cells, depressing cellular functions, which may result in reduced conversion of 25-hydroxy-vitamin D_3 to 1,25-dihydroxy-vitamin D_3. This is likely to lead to decreased calcium absorption and decreased bone mineralization, which in turn may produce osteomalacia (WHO/IPCS, 1992).

The second likely mechanism is direct action by cadmium on bone cells by enhancing bone resorption (Miyahara et al., 2001; Regunathan et al., 2003) and reduced bone formation (Blumenthal et al., 1995; Dohi et al., 1993; Long, 1997; Miyahara et al., 1988). Several investigators have demonstrated skeletal injury due to cadmium at exposure levels that do not impair kidney function (Honda et al., 2003; Sacco-Gibson et al., 1992; Wang & Bhattacharyya, 1993), providing evidence that the metal acts directly (rather than indirectly) on bone. However, the exact mechanism of action has not been fully elaborated, particularly in relation to low levels of lifetime exposure to cadmium. Results obtained recently by Brzóska & Moniuszko-Jakoniuk (2005) in rats indicate that even a relatively low exposure to cadmium during the intensive period of skeletal development that occurs in the first few months of life disturbs the accumulation of bone mass, leading to exposure-level-dependent osteopenia or more serious disorders of bone-mineral status; continuation of the exposure up to the stage of skeletal maturity intensifies this effect. Cadmium leads to low levels of bone turnover at the stage of intensive skeletal development and induces high levels of bone turnover, due to enhanced resorption, at the stage of consolidation of bone mass at skeletal maturity.

2.3.3. Cancer

In its latest evaluation of the carcinogenic risk from cadmium exposure, IARC (1993) concluded that there was sufficient evidence to classify cadmium and cadmium compounds as human carcinogens (Group I). This assessment was, to a great extent, dependent on the significant relationship between the risk of lung cancer and estimated cumulative exposure to cadmium reported by Thun et al. (1985) and Stayner et al. (1992) in their analyses of mortality in a cohort of workers from a single cadmium recovery plant in the United States. On the basis of this analysis, the lifetime excess of lung cancer at 100 μg/m³ of cadmium fume would be approximately 50–111 lung cancer deaths per 1000 workers.

Sorohan & Lancashire (1997) performed a re-analysis of this cohort, with the inclusion of data on arsenic exposure. The results of this re-evaluation indicate that cadmium is carcinogenic only under conditions of a concomitant exposure to arsenic.

In a study of cadmium-exposed workers in the United Kingdom, a non-significant negative trend was noted between cumulative cadmium exposure and the risk of mortality from lung cancer. These findings do not support the hypothesis that an exposure to cadmium oxide fume increases the risk of mortality from lung cancer (Sorohan et al., 1995).

The evidence for cadmium as a human carcinogen is rather weak. EU has classified cadmium to carcinogen category 2, USEPA (1999) to category B1, and ACGIH (2005) to category A2.

2.3.4. Other effects

Data from animal experiments have indicated that, under certain exposure conditions, cadmium induces hypertension in animals. However, human data concerning oral exposure to cadmium have been weak and inconclusive. Case–control and cohort epidemiological studies that were adequately controlled for smoking have typically found no association between body cadmium levels and hypertension (ATSDR, 1999). In a large population study performed in Belgium, a possible association was investigated between cadmium exposure and blood pressure elevation or increased prevalence of cadiovascular diseases. The results were negative (Staessen et al., 1991). Moreover, inhalation exposure to cadmium does not appear to have a significant effect upon the cardiovascular system (Järup et al, 1998).

The existing evidence is inadequate for evaluating an association between inhalation exposure to cadmium and reproductive effects. Gennart et al. (1992) studied the effects of cadmium exposure on male reproductive functions. The mean U-Cd level in 83 workers exposed to cadmium (mean duration of 24 years) was 6.9 μg/g creatinine; 25% of these workers had signs of kidney dysfunction. The fertility of exposed workers and controls was assessed from the childbirth experiences of their wives; no effects were observed. Men occupationally exposed to cadmium at the levels that produce renal damage showed no abnormalities in testicular endocrine function, as measured using serum levels of testosterone, luteinizing hormone and follicle-stimulating hormone (Mason, 1990). No significant correlation was found between seminal cadmium concentrations and conventional semen parameters or between cadmium concentrations and fertility status (Keck et al., 1995).

As there are currently no convincing observations, the reproductive and developmental effects of cadmium cannot be considered critical in humans (WHO/IPCS, 1992; Järup et al, 1998).

Several hypotheses have been proposed to explain the nephrotoxicity of cadmium. There is evidence for a protective role for intracellular metallothionein, and one hypothesis attributes the nephrotoxicity to the fraction of intracellular cadmium that is not bound to metallothionein. Another hypothesis is that extracellular cadmium bound to metallothionein is toxic. Cadmium–metallothionein is filtered by the renal glomeruli and reabsorbed by the proximal tubular lining

cells, where it is catabolized, releasing cadmium ions that cause renal damage. Yet another hypothesis is that intracellular cadmium interacts with the cell membrane, resulting in lipid peroxidation (WHO/IPCS, 1992; ATSDR, 1999).

2.3.5. Sensitive subgroups

The population groups at highest risk are smokers, women with low iron stores, people having a cadmium-rich diet, and people living in the vicinity of industrial emitters of cadmium (e.g. non-ferrous mills).

People with kidney damage from causes unrelated to cadmium exposure, including those with diabetes, those exposed to certain drugs and chemicals and those experiencing the natural age-related decline in kidney function, could be expected to exhibit nephrotoxicity at low levels of cadmium exposure. People with depleted stores of calcium, iron or other dietary components, as a consequence of multiple pregnancies and/or dietary deficiencies, could be expected to have increased cadmium absorption from the gastrointestinal tract.

People with diabetes have also been showed to have an increased risk (Åkesson et al., 2005).

2.3.6. Biological indicators of exposure

The B-Cd represents two major aspects of cadmium exposure: one mainly reflects recent exposure, with a half-life of 2–3 months; the other is related to the body burden, with an approximate half-life of about a decade (Järup et al., 1983). For populations with relatively low continuous environmental exposure to cadmium, B-Cd is a good marker of long-term exposure. The geometric mean B-Cd concentration in non-smokers has been reported to be 0.2 μg/l in Sweden (Bensryd et al., 1994), 0.36 μg/l in Italy (Alessio, 1993), 0.5–0.65 μg/l in Poland (Jakubowski, 1995), 0.7 μg/l in Croatia (Blanusa et al., 1991) and 0.28 μg/l in Germany (Becker et al., 2002).

The U-Cd level is mainly influenced by the body burden, and is proportional to the concentration in healthy kidney. The half-life of U-Cd is approximately 10–15 years. In general, the geometric mean concentrations for U-Cd in non-smokers in Europe amounted to 0.15–0.20 μg/g creatinine in Sweden (Berglund et al., 1994; Järup et al., 1995) 0.19 μg/l in Spain (Gomez-Catalan et al., 1996), 0.69 μg/g creatinine in Belgium (Roels et al., 1993), 0.5–0.6 μg/g creatinine in Poland (Jakubowski, 1995) and 0.15 μg/g creatinine in Germany (Becker et al., 2003). U-Cd concentrations increase with age. According to the data obtained as a result of the National Health and Nutrition Examination Surveys (NHANES) in the United States, the mean U-Cd concentrations in males in the age categories 12–16, 20–39, 40–59 and >60 years amounted to 0.14, 0.18, 0.28 and 0.38 μg/g creatinine, respectively. In females, the U-Cd concentrations were higher, being (in the same respective age groups) 0.19, 0.30, 0.66 and 0.81 μg/g creatinine (Choudhury et al., 2001).

The cadmium level in the kidney increases with age up to about 50–60 years, after which it decreases. In Europe, the mean cadmium concentrations in the renal cortex in the age group 40–60 years (non-smokers) was reported to be 6.8–8 μg/g in Sweden (Friis et al., 1998; Nilsson et al., 1995), 15.8 μg/g in Germany (Drasch et al., 1997), 12 μg/g in the United Kingdom (Scott et al., 1987) and 13 μg/g in the United States (Morgan et al., 1990). These concentrations are usually higher, by 50–100%, in current or former smokers than in non-smokers.

The average daily dietary intake that would give rise to an average cadmium concentration of 200 mg/kg wet weight in the renal cortex at the age of 50 would be 260–480 μg/day, assuming 5% gastrointestinal absorption, and 140–260 μg/day assuming a 10% absorption rate (WHO/IPCS, 1992).

A model developed by Choudhury et al. (2001) predicts, at an assumed daily intake of cadmium of about 21.5 μg/day for the United States population, a mean peak kidney-cortex cadmium concentration of 15 μg/g wet cortex (5th to 95th percentile range, 10–22 μg/g) in males and 29 (range 19–43 μg/g) in females. Females may absorb a larger fraction of ingested dietary cadmium than males, and this difference may be the result of lower iron stores in females compared with males. This would suggest that females may be at greater risk of developing cadmium-induced health effects than males.

2.4. Human health implications in relation to LRTAP

Kidney and bone are the critical target organs following chronic environmental exposure. The main effects include an increased excretion of low-molecular-weight proteins in the urine (as a result of proximal tubular cell damage) and increased risk of osteoporosis. An increased risk of lung cancer has also been reported following inhalation exposure in occupational settings.

The margin of safety between the current daily intake of cadmium in diet and the intake that can result in deleterious health effects is very narrow, and might be non-existent for people in subpopulations with high levels of exposure.

Population groups at risk include elderly people, those suffering from diabetes and smokers. In addition, women may be at increased risk because, at the same level of exposure, they absorb more cadmium than do men, because of their lower iron stores.

Food is the main source of cadmium exposure in the general population (representing >90% of the total intake in non-smokers). In heavily contaminated areas, dust resuspension can constitute a substantial part of the exposure for the local population. In Europe, the annual inputs from transboundary air pollution and from the use of mineral and organic fertilizers are of roughly the same magnitude. They all continue to contribute to the existing relatively large accumulations of cadmium in the topsoil.

In spite of the decreasing cadmium emissions, ambient air concentrations and deposition, the recently published data do not show decreases in cadmium body

burdens in non-smokers over the last decade. The studies on cadmium balance in the top layers of arable soils indicate that the supply of this metal still exceeds its removal. The available information indicates that cadmium is accumulating in soils and catchments under certain environmental conditions, thus increasing the risk of future exposure through food. Therefore, in view of the narrow margin of safety involved, sufficient effort should be made to achieve further reductions in cadmium emissions and in the direct input of cadmium to the soil.

2.5. References

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3. Lead

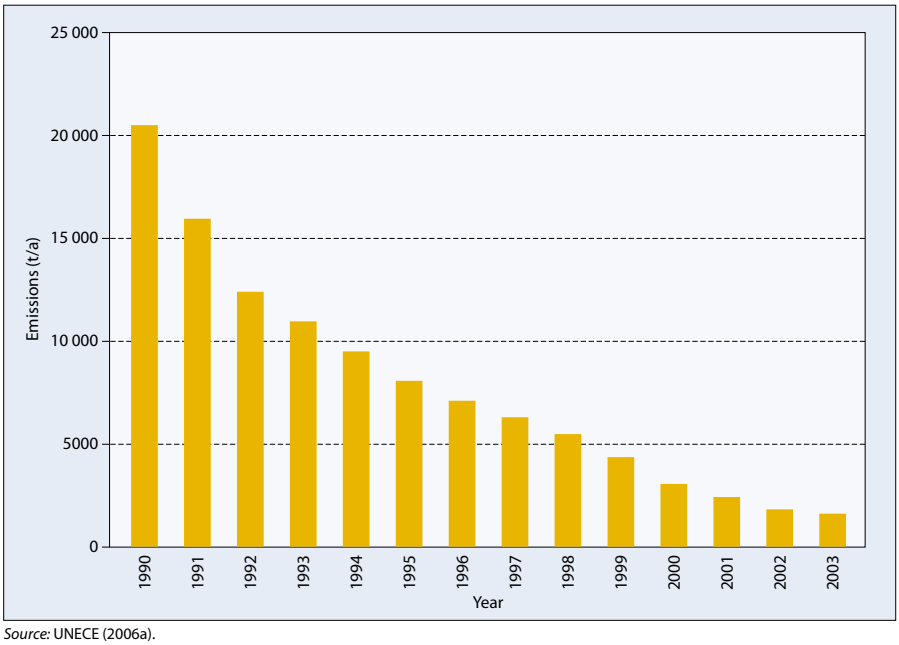
3.1. Introduction

3.1.1. Emissions

Lead is released into the atmosphere from natural and anthropogenic sources. Natural emissions are from wind resuspension and from sea salt, volcanoes, forest fires and biogenic sources (Nriagu, 1989). According to Nriagu (1989), these emissions are not entirely natural but contain some contributions from historical depositions of anthropogenic lead. Major anthropogenic emission sources of lead on a global scale include the combustion of fossil fuels from, for example, traffic, non-ferrous metal production and iron and steel production. Some contributions are also made by cement production and waste disposal (Pacyna & Pacyna, 2001).

The magnitude of anthropogenic emissions in Europe can be obtained from the officially reported data or from expert estimates. The total emissions in Europe, based on a combination of officially reported emissions and expert estimates obtained using the procedure presented by Berdowski et al. (1997, 1998), were about 35 kt/a and 8.6 kt/a in 1990 and 2003, respectively. Expert estimates

Fig. 3.1. Reported emissions of lead in the EMEP region (24 countries).



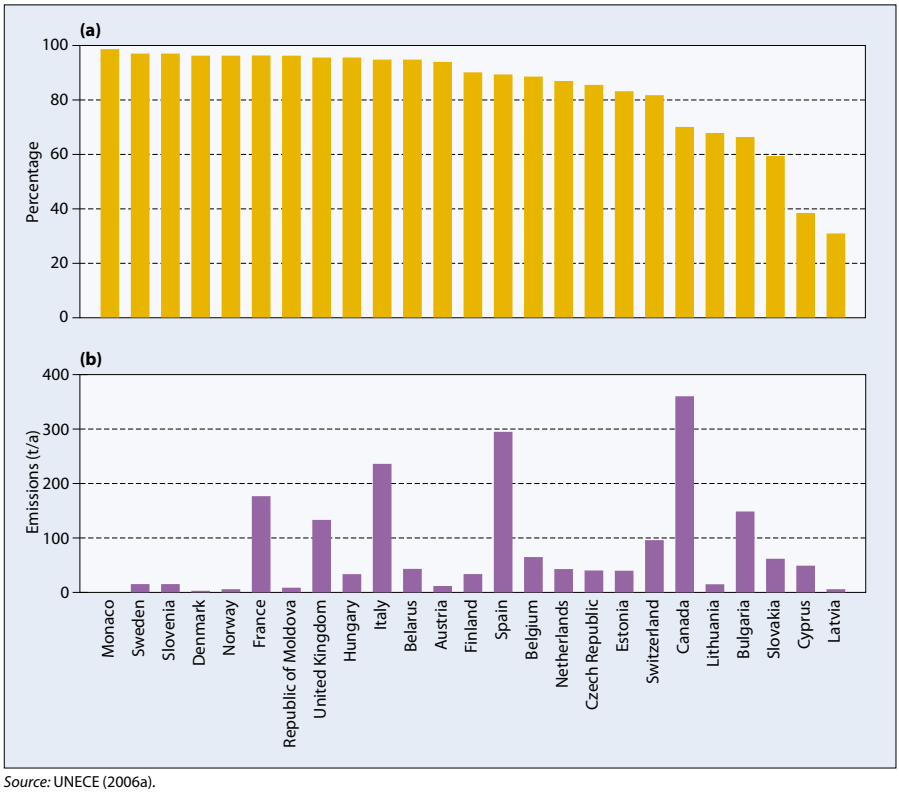
Source: UNECE (2006a).

were used for countries that did not produce official reports regarding their emission data. More details about the combining of official and expert emission data are available in Ilyin & Travnikov (2005). Emission trends can be analysed for 24 out of 50 Parties to the Convention. According to these official data, the total emissions of lead in these countries decreased by more than 90% between 1990 and 2003 (Fig. 3.1) because of restrictions on the use of leaded petrol.

The relative reduction in reported emissions between 1990 and 2003 was calculated as $((E_{1990} - E_{2003})/E_{1990}) \times 100\%$, where E_{1990} and E_{2003} are the emission magnitudes for 1990 and 2003, respectively. Fig. 3.2a shows the relative reductions in lead emissions for the period 1990–2003 in the 24 countries of the EMEP region and Canada, based on reported data. Emissions of lead have decreased in all of the countries, by amounts varying from about 31% (Latvia) to 99% (Monaco), relative to the 1990 levels. Fig. 3.2b demonstrates the official emission levels achieved by these countries by 2003.

The major sources of lead emission in Europe, according to the information reported for eight countries for 1990 and 2003, are shown in Fig. 3.3. In 1990,

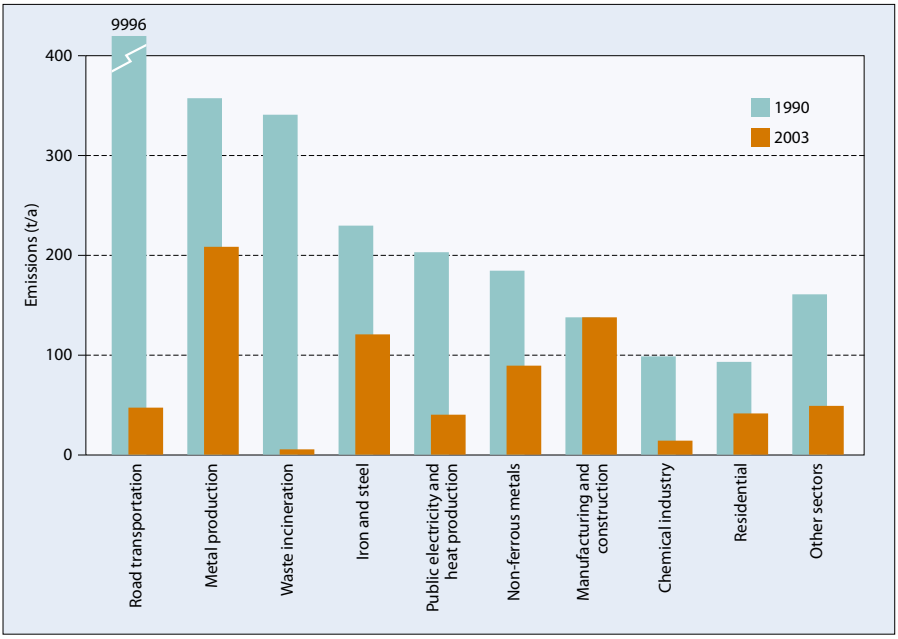
Fig. 3.2. (a) Relative reductions in lead emissions in 24 countries of the EMEP region and Canada for the period 1990–2003, based on official data. (b) Official emission values in 2003.



Source: UNECE (2006a).

the maximum contribution (about 85%) to the total lead emission was from the "road transportation" sector. In 2003, its contribution to total emissions dropped to about 6%. In 2003, the "metal production" sector became the largest source (about 28%). More detailed information about the emission data reported for 1990–2003 is available in Vestreng et al. (2005).

Fig. 3.3. Anthropogenic lead emission sources in eight countries of the EMEP region in 1990 and 2003.



Source: Vestreng et al. (2005).

In China, the current environmental trends for lead are increasing, despite the switch to unleaded petrol in 1997. The emission sources remain unidentified, but may include metal production processes (Zhu et al., 2003; Sun et al., 2006).

3.1.2. Atmospheric levels of lead

Atmospheric lead is bound to particulate matter. It tends to be associated with particles 0.2–1.0 μm in size (aerodynamic diameter). A super-micron mode exists, too, but is less significant (Milford & Davidson, 1985; Allen et al., 2001; Molnar et al., 1995; Horvath et al., 1996; Pakkanen et al., 2001; Salma et al., 2005; Singh et al., 2002; Smolik et al., 2003; Dillner et al., 2005). The main species upon emission are chlorides, oxides and sulfates. In particular, oil combustion releases lead as lead oxide (PbO), whereas non-ferrous metal production releases lead sulfate ($PbSO_4$) and PbO. Lead dichloride ($PbCl_2$) is emitted during coal combustion and refuse incineration (AMAP, 1998). Removal of lead from the atmosphere occurs via wet scavenging and dry deposition. Similarly to cadmium,

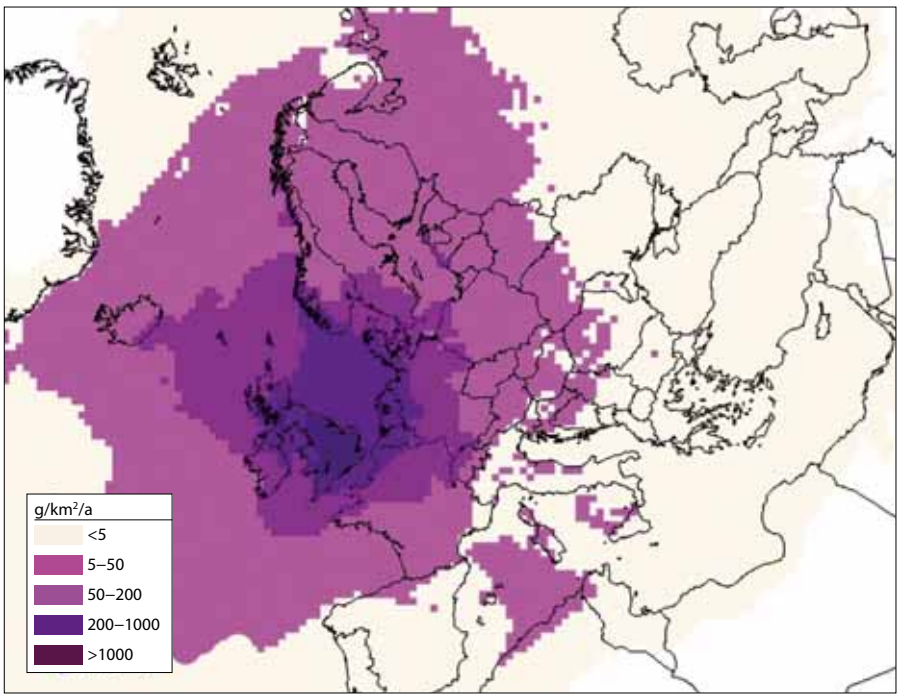
atmospheric lead has the potential for long-range transportation (over hundreds, or even thousands, of kilometres). This is most convincingly demonstrated by the presence of lead in the polar regions, which have obviously been dominated by anthropogenic mobilization for many centuries (Boutron et al., 1994; Heidam et al., 2004; Shotyk et al., 2005). An example of the ability of lead to participate in long-range transport at a regional level is given in Fig. 3.4, which shows that the predicted deposition of lead over the central part of the United Kingdom exceeds 1.0 kg/km²/a. However, the depositions in rather remote regions (e.g. Denmark, northern Germany and south-western Norway) are quite comparable with those in the United Kingdom, and range from 0.2 to 1.0 kg/km²/a.

In Europe in 1990, the background concentrations of lead in air were mainly within the 10–30 ng/m³ range. In 2003, the concentrations mainly ranged between 5 and 15 ng/m³ (Aas & Breivik, 2005) (Fig. 3.5a).

In Minsk, Belarus, the average annual concentration of lead in 2004 was 83 ng/m³. In cities and in the vicinities of industrial sources (i.e. at a distance of 1–10 km), higher concentrations prevail (up to an order of magnitude higher; e.g. Herpin et al., 2004; Wenzel et al., 2006; Landesumweltamt, 2005).

The background concentrations in precipitation in central Europe in 1990 were around 2–5 µg/l. In 2003, these concentrations were typically in the range 1–3 µg/l (Aas & Breivik, 2005) (Fig. 3.5b).

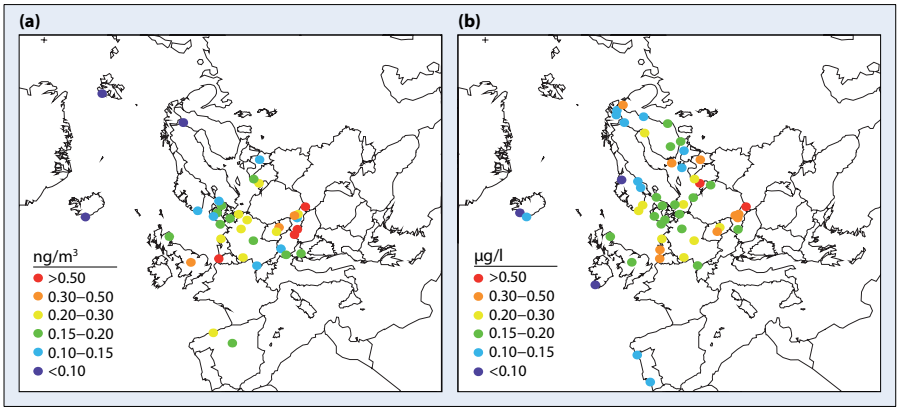
Fig. 3.4. Modelled depositions of lead from British sources in 2003.



Source of the data: EMEP/MSC-E.

Trends towards decreasing levels have also been observed in vegetation, e.g. in mosses and spruce needles in Austria and Germany in the 1990s (Umweltprobenbank, 1999; Herman et al., 2001; Herpin et al., 2004). Lead monitoring within EMEP does not cover the Mediterranean region. As other emission-reduction measures are less efficient than the use of fuel additives, lead in the European environment is expected to level off at a concentration that is still high

Fig. 3.5. Background concentrations of lead in air (a) and in precipitation (b) in 2003.



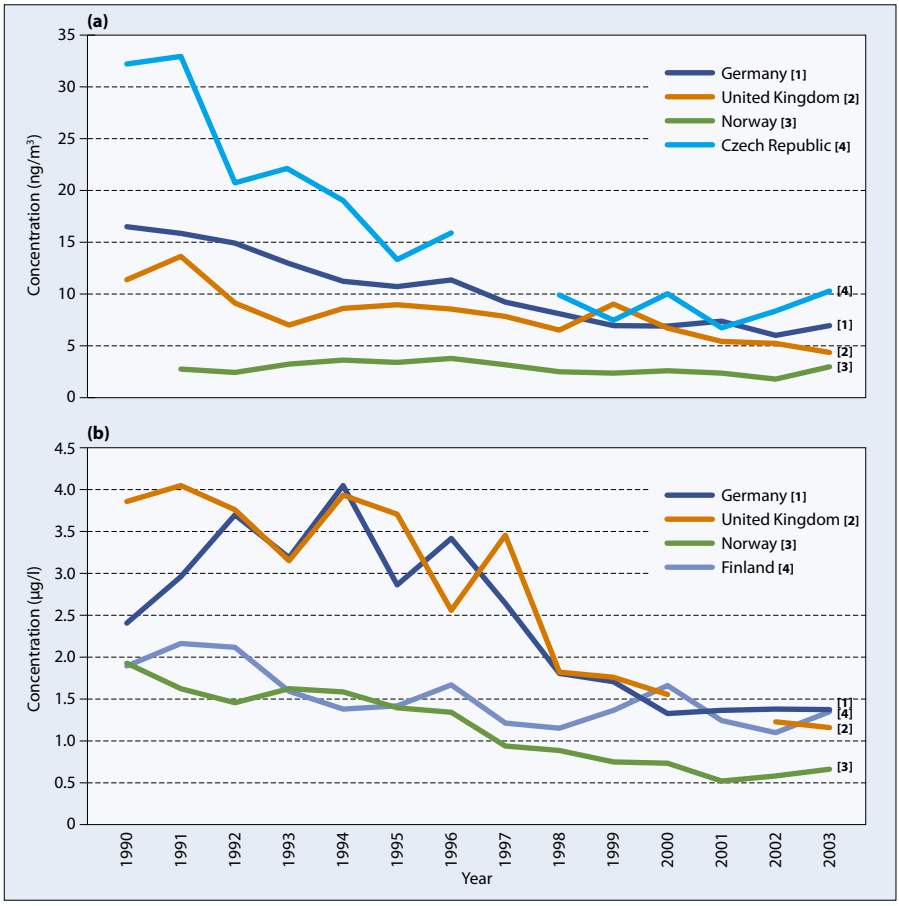
Source: Aas & Breivik (2005).

in comparison with naturally mobilized lead. The long-term changes in the lead concentrations in air and precipitation vary considerably across Europe. In central and north-western Europe, the decrease was about 2–3 times from 1990 to 2003, according to data from these (Fig. 3.6a,b) and other studies (Lammel et al., 2002; von Storch et al., 2003). In northern Europe, the decrease in the concentrations in precipitation was 1.5–3 times. In general, the observed trends can be reproduced by modelling, at least for the years until 1995 (von Storch et al., 2003), which suggests that the reported emissions and our understanding of the environmental fate of lead species correspond with each other.

Long-term changes in European emissions should be reflected in the environment. However, as the pollutant is regionally distributed, trends in lead levels in the environment are not expected to reflect the domestic situation but rather the regional one. In fact, in some countries the reduction in emissions for 1990–2003 was more than 10 times, but the decline in observed lead levels in air and in precipitation was only 2–3 times (Ilyin & Travnikov, 2005). Lead pollution levels in the United Kingdom are mainly affected by national emission sources, while in Norway, long-range transport dominates, and the observed trend reflects emission trends in France and the United Kingdom, i.e. in the countries that are the major sources of emissions in the region (Fig. 3.7a,b).

Both monitoring and modelling data indicate a two- to threefold decrease in lead levels for Europe as a whole for 1990–2003. In some individual countries,

Fig. 3.6. Long-term variations in concentrations of lead in air (a) and in precipitation (b) in different parts of Europe.

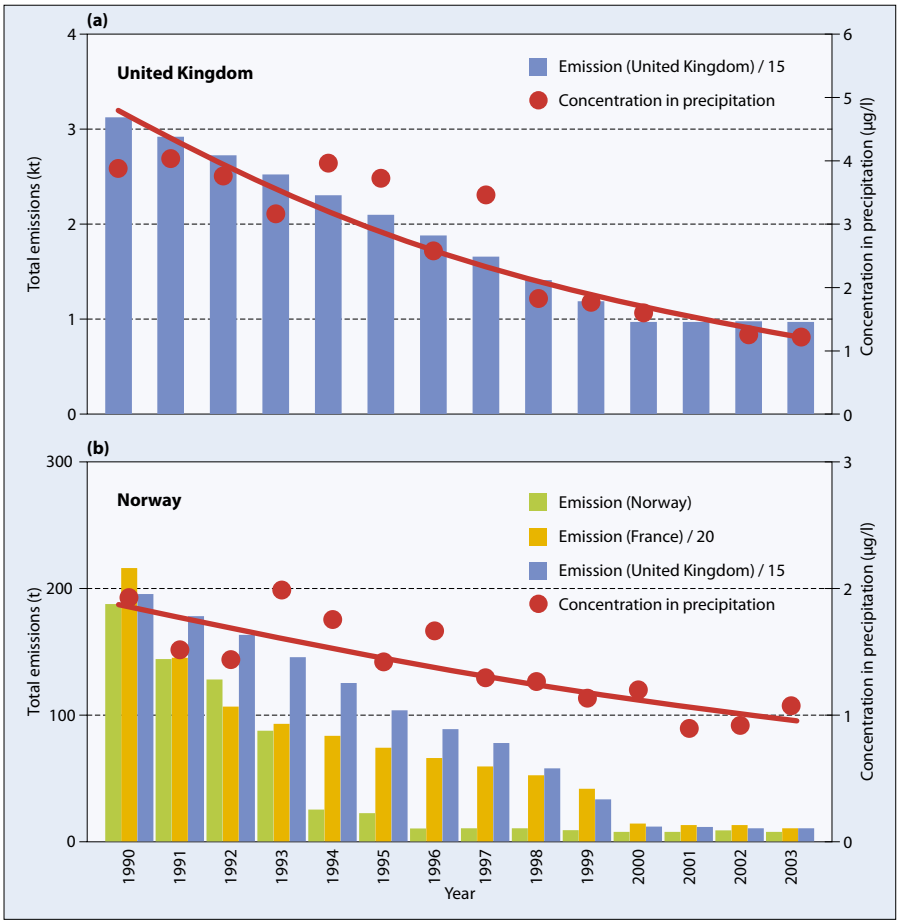


Source: UNECE (2006b).

the magnitude of the lead pollution decrease is as much as 6–7 times. Both for Europe as a whole and for some individual countries, inconsistencies between lead emissions and measured lead atmospheric levels are revealed. The contribution of non-domestic European anthropogenic sources to depositions of lead in European countries varied from about 10% to 90%. For countries that are leading the way in implementing mitigation measures for lead, the regional distribution of this pollutant implies that transboundary sources are becoming more prominent; this notion is supported by recent observations (Lammel et al., 2002).

Inconsistencies between observed environmental levels of lead and estimated total European emissions is evident for both individual countries and for Europe as a whole (Ilyin & Travnikov, 2005). These inconsistencies may be due either to the underestimation of emissions or to a significant unconsidered influence from natural emissions and the resuspension of historical depositions, or both.

Fig. 3.7. Long-term trends for total anthropogenic emissions of lead in some countries, and mean concentrations in precipitation in the United Kingdom (a) and Norway (b). Red circles show annual measurements (red line = exponential approximation).



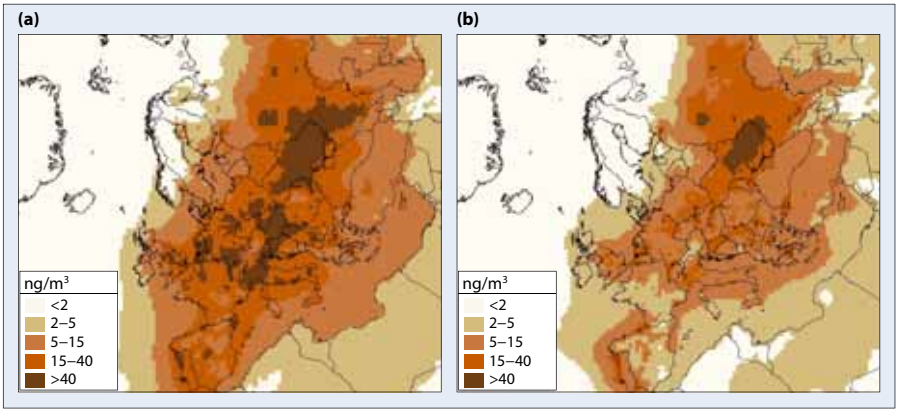
Source: Ilyin & Travnikov (2005).

An evaluation of transboundary transport of lead for the period 1990–2003 was performed on the basis of expert emission estimates prepared by MSC-E (Ilyin & Travnikov, 2005). These expert estimates include anthropogenic emissions, and preliminary estimates of natural emissions and re-emissions. Fig. 3.8a shows the spatial distribution of the annual mean concentrations of lead in air in 1990 and 2003, produced using the MSCE-HM model (Ilyin & Travnikov, 2005). Overall, the model results agree well with the observations from monitoring. In 1990 over significant parts of Europe, concentrations varied between 15 and 40 ng/m^3, and in some areas exceeded 40 ng/m^3. By 2003, the concentrations in air had decreased markedly and were within 2–15 ng/m^3 over most of Europe (Fig. 3.8b). The spatial distribution of the depositions is similar to that of the concentrations. In 1990 over most parts of Europe, the modelled deposi-

tions were in the range 2–8 kg/km^2/a (Fig. 3.9a). By 2003, the depositions had decreased and their values were mainly within the range 0.5–4 kg/km^2/a (Fig. 3.9b). In the Mediterranean region, which is not covered by EMEP monitoring stations, the levels are in general higher than those in northern Europe, but they are lower than those in central Europe. Examples of modelled depositions of lead on unit areas of coniferous forests and crops are given in Fig. 3.10. Modelled depositions for forests are normally significantly larger than those for crops, which is similar to the situation for cadmium deposition.

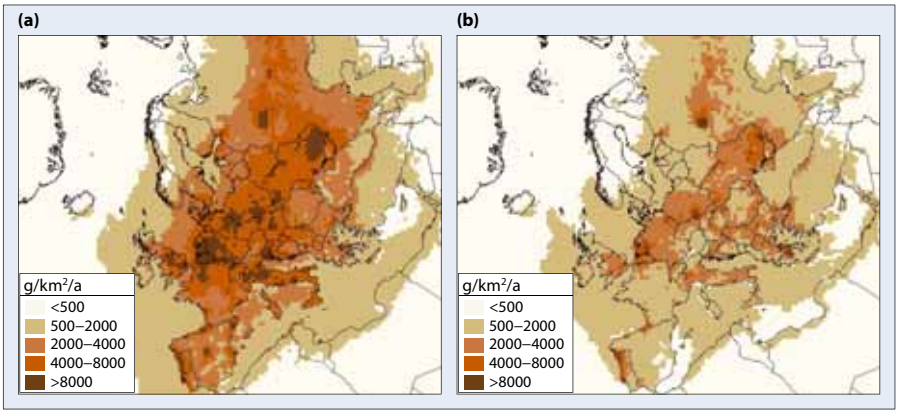
The largest decrease in air concentrations, averaged over the country's territory (Fig. 3.11) took place in Slovenia (7 times). In 18 countries the concentrations decreased at least 3 times, and in 16 countries the concentrations decreased between 2 and 3 times.

Fig. 3.8. Spatial distribution of modelled air concentrations of lead in the EMEP region in 1990 (a) and 2003 (b).



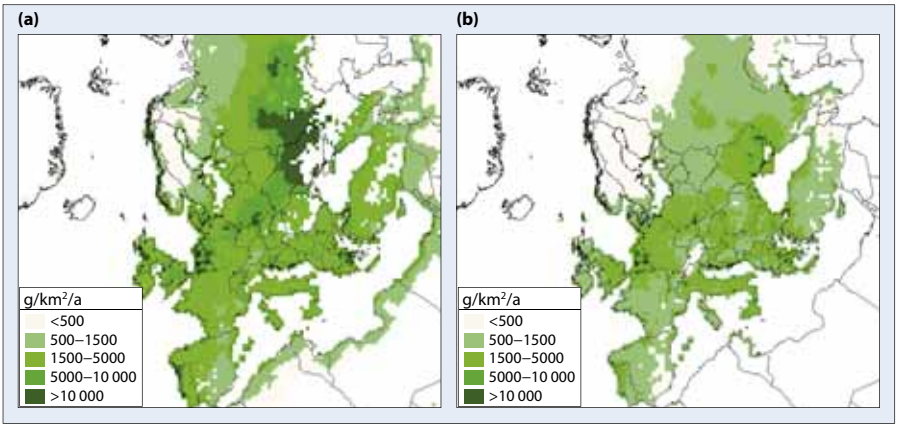
Source: UNECE (2006b).

Fig. 3.9. Spatial distribution of modelled total depositions of lead in the EMEP region in 1990 (a) and 2003 (b).



Source: UNECE (2006b).

Fig. 3.10. Spatial distribution of modelled total depositions of lead over the EMEP region to coniferous forests (a) and crops (b).



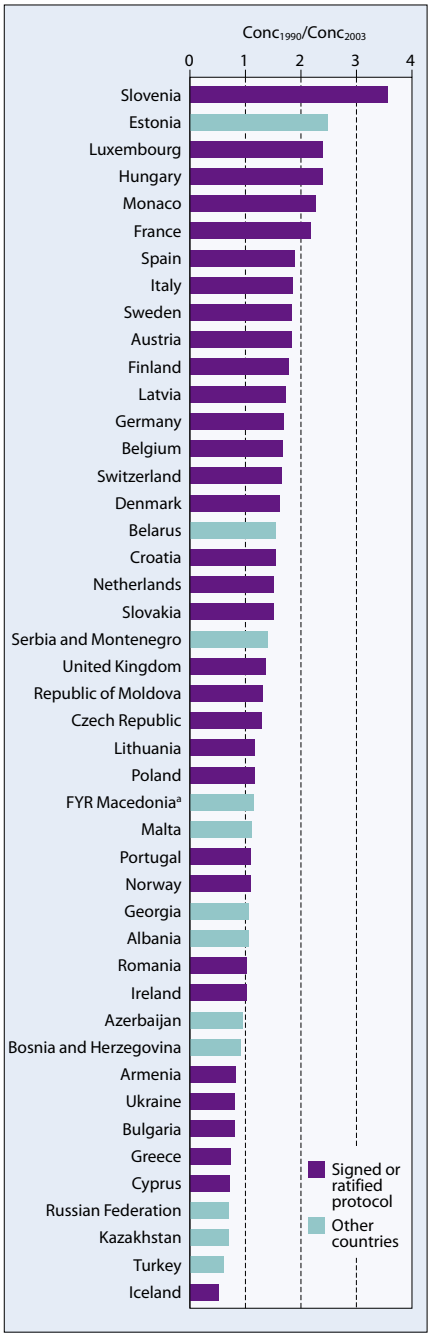
Similar decreases took place for air depositions: from 6 times in Slovenia to minor changes (<10%) in Iceland and Greece. In 16 countries, the decrease exceeded 3 times. In 17 countries the decrease ranges from 2 to 3 times. For the period under consideration, lead depositions on Europe as a whole decreased from about 40 000 t to 17 500 t (2.3 times).

According to the model simulation, the contribution of transboundary transport to lead depositions in different countries varies significantly (10–90%) (Fig. 3.12). The highest contributions occurred in the Republic of Moldova, Luxembourg, Monaco and Belarus. In 20 countries, the contribution exceeded 50% and in 36 countries it exceeded 30%. The contribution of transboundary transport to depositions over different territories of individual countries is characterized by similar variability. Numerical information concerning the modelling results is available from EMEP/MSC-E on request.

The results from the MSCE-HM model were evaluated by analysing the model uncertainties and comparing the modelled data with observations and with data computed using other models. Analysis of the model uncertainties demonstrated that the intrinsic model uncertainty (i.e. the uncertainty of the model without emission data) varies across Europe from 20% to 60% for concentrations in air, concentrations in precipitation and total depositions (Travnikov & Ilyin, 2005). Intercomparison of atmospheric transport models for lead showed that the air concentrations and depositions estimated using the MSCE-HM model are in good agreement with the data from other transport models (UNECE, 2005, 2006c).

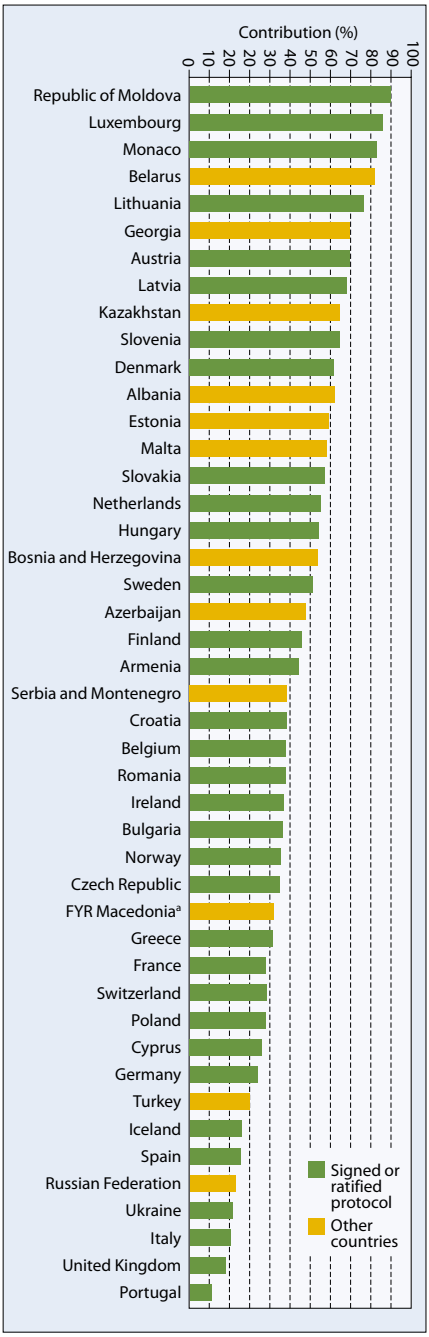
Modelling results, based on emission expert estimates, for 1990–2003 (Ilyin & Travnikov, 2005) demonstrated that the modelled concentrations of lead in air and in precipitation agree well with the measurements (Fig. 3.13). The correlation coefficient for annual lead concentrations in air is almost 0.9, and for concentrations in precipitation it is –0.7. About 90% of the modelled lead

Fig. 3.11. Ratio of the modelled country average air concentrations of lead in 1990 to those in 2003 in countries of Europe.



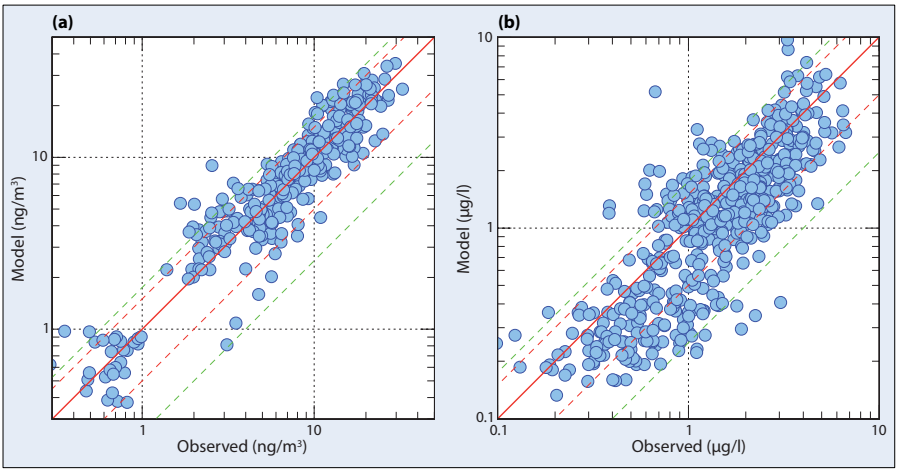
[a] The former Yugoslav Republic of Macedonia.
Source: UNECE (2006b).

Fig. 3.12. Contribution of anthropogenic sources outside Europe to depositions of lead in European countries in 2003.



[a] The former Yugoslav Republic of Macedonia.
Source: UNECE (2006b).

Fig. 3.13. Comparison of annual mean modelled and observed concentrations of lead in air (a) and in precipitation (b) for 1990–2003. Solid red line depicts 1:1 ratio; dashed lines: deviation ±50% (red) and ±75% (green).



Source: Ilyin & Travnikov (2005).

concentrations in air and 70% of the concentrations in precipitation agree with measured data, with an accuracy better than ±50% of the measured value. More detailed information about model verification is available in Ilyin & Travnikov (2005).

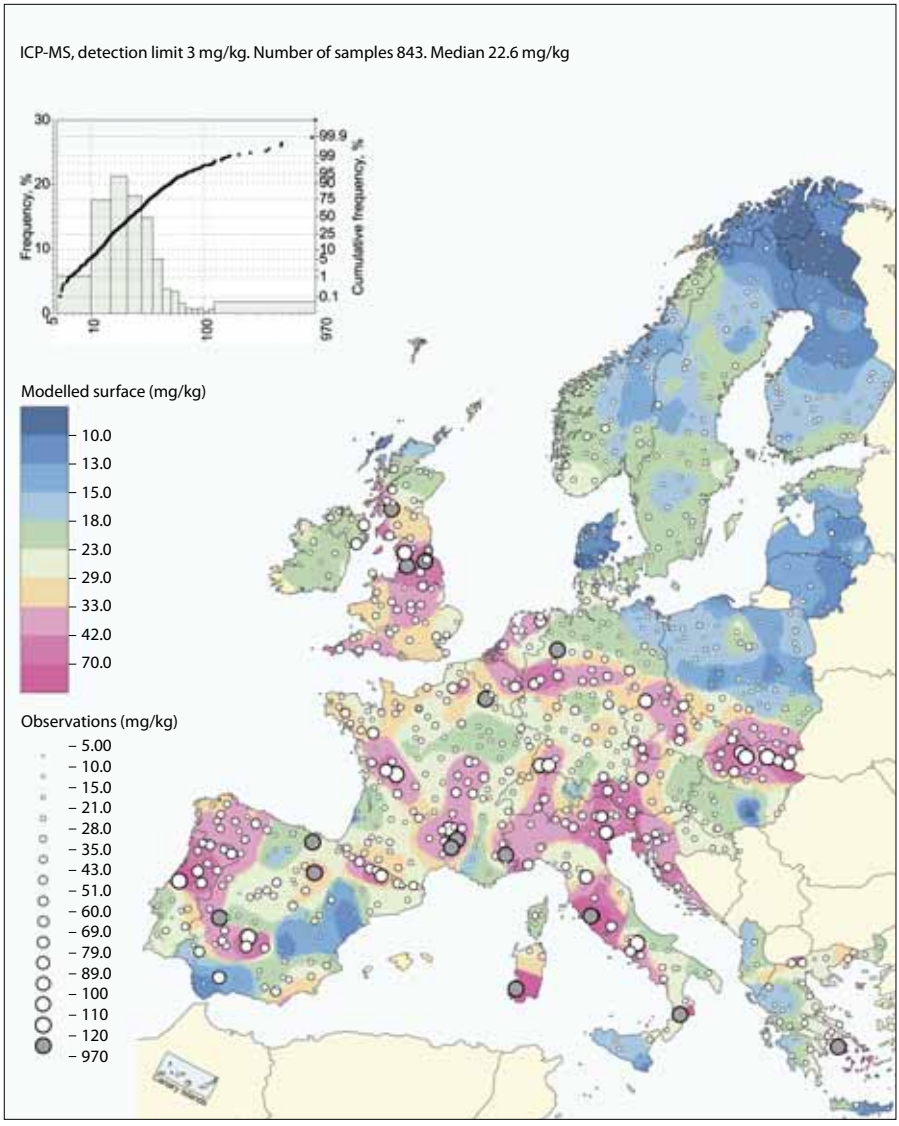
In October 2005, a TFMM workshop devoted to the review of the MSCE-HM model was held in Moscow (UNECE, 2005). The workshop concluded that the "MSC-E model is suitable for the evaluation of long range transboundary transport and depositions of heavy metals in Europe" (UNECE, 2006c).

3.1.3. Lead in soils

Because lead is immobilized by the organic component of soil, lead deposited from the air is generally retained in the upper 2–5 cm of undisturbed soil (CDC, 1991). The natural lead content in soil typically ranges from below 10 mg/kg soil up to 30 mg/kg soil. In the Minsk region of Belarus, the maximum concentration of lead in soil is 19 mg/kg. The concentration of lead in the top layer of soils varies considerably because of the deposition, and accumulation, of atmospheric particulates from anthropogenic sources. In Europe, lead concentrations in topsoils are spatially heterogeneous and vary from below 10 mg/kg up to >70 mg/kg (Fig. 3.14). The median value is estimated to be 22.6 mg/kg.

The lead concentration in soil generally decreases as the distance from the contaminating source increases. Soil levels within 25 m of roads were typically 30–2000 mg/kg higher than the natural levels, although these levels drop exponentially over a distance of up to 25 m from the road. Lead levels in soils adjacent to non-ferrous smelters range from several thousand mg/kg to 60 000 mg/kg. Soils adjacent to houses painted with exterior lead paints had lead levels of

Fig. 3.14. Concentrations of lead in topsoil; observations from field measurements and modelling.



Source: Salminen et al. (2005).

200–800 mg/kg but may have had levels exceeding 10 000 mg/kg (ATSDR, 2005). The concentrations of lead in household dust vary greatly in different dwellings and in different areas of the world.

In addition to atmospheric deposition, agricultural practices are a source of lead input to soils. The final report of the EU Concerted Action AROMIS (Assessment and reduction of heavy-metal input into agro-ecosystems) (Eckel et al., 2005) provides summary information on metal inputs to agricultural soils from

mineral and organic fertilizers and other sources. Within the framework of the AROMIS 24 research, institutions from 21 European countries contributed information on fertilizer use, nutrient and metal contents in fertilizers, and other data necessary to determine metal balances. Because the data gathered were not homogeneous, only a part of the countries' metal fluxes from fertilizer use could be determined. Furthermore, calculations of metal inputs and outputs for only a selection of model farms, reflecting the most important production types in Europe, are presented.

Because the percentage of land to which sewage sludges and composts are applied is very low in most countries, these two sources of lead are excluded from consideration here, although information on this is available in the AROMIS database. At field scale, however, these inputs can be considerable.

The ratio of lead inputs to agricultural soils from different sources on a national scale (total amount of metal divided by the total agricultural land area) for several European countries is provided in Table 3.1. The proportion represented by atmospheric deposition was calculated using monitoring data, but the methods for monitoring deposition differed from country to country.

The lead fluxes on the farm or field scale vary greatly according to the management practices used. For 32 representative farm types (not using sludges and

Table 3.1. Estimated lead inputs (percentage of total) to agricultural soils in Germany, the Netherlands, Switzerland and the United Kingdom.[a]

	Manure[b] (%)	Mineral fertilizers (%)	Atmospheric deposition (%)	Average total input rate (kg/km²/a)
Germany	15	12	66	8.6
Netherlands	21	12	54	8.0
Switzerland	12	3	66	6.0
United Kingdom	6	2	78	7.0

[a] Inputs from sludges, corrosion, dredgings and hunting were not considered.
[b] Solid manure and slurry from breeding cattle, pigs and poultry.

Sources: Alloway (1998); Candinas et al. (1999); Eckel et al. (2005); Lijzen & Ekelenkamp (1995); Lijzen & Franken (1994); Wilcke & Döhler (1995).

composts) in 12 European countries, the calculated range for lead input from mineral fertilizer was 0–2.0 kg/km²/a, while that for input from manure was 0–2.7 kg/km²/a. For farms with complete datasets for input and output fluxes, lead balances could be calculated: 12 of 13 animal farms (mainly comprising cattle, pigs and poultry) had a positive lead balance, i.e. the inputs were higher than the outputs; and all 17 crop farms that could be considered showed a positive balance.

3.2. Pathways of human exposure and their relationships to LRTAP

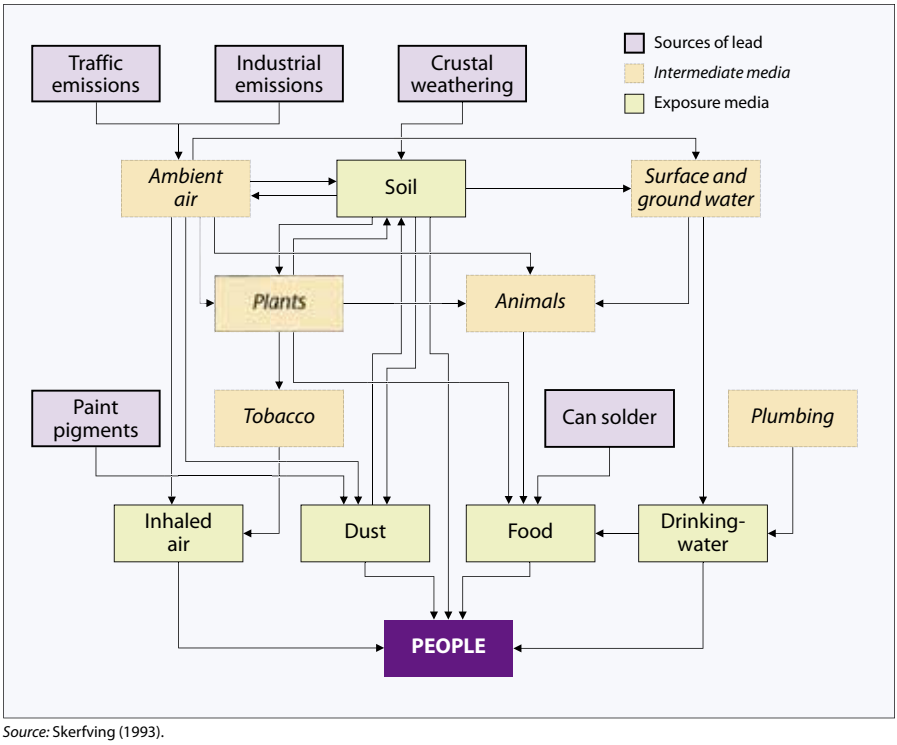
Lead is a multimedia pollutant, i.e. several sources and media contribute to the exposure. Any attempt to picture all major sources and exposure routes for lead ends up in a complex pattern (Fig. 3.15).

3.2.1. Sources and exposure by inhalation

For the general population, airborne lead is a minor exposure pathway. However, in areas where the air levels of lead are high they represent a significant, or even dominating, source of lead exposure. Ikeda et al. (2000a,b) studied the contribution of lead in air at levels of the order of 75 ng/m^3 and estimated that air then contributed about half of the absorbed lead in women living in Tokyo and Kyoto.

A large-scale source of exposure was the organolead added to petrol. During combustion in vehicle engines, the organic lead was transformed into inorganic lead oxide, and emitted almost entirely in that form. This caused exposure to inorganic lead, in particular in people living in areas with heavy traffic. In cities where leaded petrol is still in use or has only recently been phased out, mean air-lead levels of the order of 200–400 ng/m^3 are common in residential areas (Lu et al., 2003; He et al., 2004). Kaul et al. (2003) reported 2000–3900 ng/m^3 in traffic

Fig. 3.15. Sources and routes of lead exposure in the general population.



Source: Skerfving (1993).

areas in the city of Lucknow in India, and Hashisho & El-Fadel (2004) reported an average of 2860 ng/m^3 in urban Beirut. Similar levels were observed in the Valley of Mexico in 1987, when lead was still being added to petrol in relatively high concentrations (Schnaas et al., 2004). By 1997, lead in petrol had been reduced by over 98.5%, and in 2002 the annual mean air lead concentration had dropped to 70 ng/m^3.

Industrial emissions as well as recycling activities can cause exposure in neighbourhood populations. Moreover, environmental contamination from previous industrial emissions affects exposures via resuspension of contaminated soils. Hence, lead exposure through inhalation and, perhaps more importantly, through ingestion (due to hand-to-mouth activities of children) is increased near industrial sources of lead emission, whether current or historical. For example, Wilhelm et al. (2005a) investigated exposure in people living in the vicinity of metal refining plants in Germany, and found increased B-Pb levels in children but not in their mothers; the ambient air-lead levels were in the range 50–730 ng/m^3. The variation in air-lead levels is large: for example, air-lead concentrations near lead–acid battery recycling plants in Brazil has been found to vary from 70 ng/m^3 to 18 300 ng/m^3 (Paoliello & De Capitani, 2005). Near an Australian lead smelting plant in Port Pirie, a mean lead level of 2150 ng/m^3 was obtained about 600 m from the blast furnace (Esterman & Maynard, 1998), and in British Columbia a mean level of 300 ng/m^3 was found at two stations within 2 km of the smelter, in contrast to the level of 1100 ng/m^3 obtained during a previous period when an older lead smelter was in use (Hilts, 2003).

Some additional inhalation exposure occurs through cigarette smoking, although the association between smoking and B-Pb may, to some extent, be confounded by alcohol intake (Grandjean et al., 1981). Also, there is an association between children's lead exposure and environmental tobacco smoke (Baghurst et al., 1992; Willers et al., 1992).

The pattern of deposition of inhaled lead aerosol in the respiratory tract is dependent upon the particle size (cf. Skerfving, 2005). Particles with an aerodynamic diameter >5 μm are mainly deposited in the upper and middle-sized airways, cleared by the mucociliary mechanism and swallowed. Some of this lead is then absorbed from the gastrointestinal tract (see below). For particles inhaled via the mouth, and with a size in the range 0.01–5 μm, 10–60% are deposited in the alveolar tract; for particles inhaled via the nose, the fraction is lower. Most of the lead deposited in the alveolar part of the lung is absorbed. The rate of absorption is dependent upon the solubility of the chemical species of lead.

3.2.2. Ingestion of lead

In general, ingestion of lead through food and water is the major exposure pathway for lead in adults. For infants and young children in particular, dust/soil and in some cases old lead-containing paints may constitute a major source of inges-

tion, because of their tendency to put things into their mouths (Gustavsson & Gerhardsson, 2005).

Lead carbonate hydroxide has been used widely as a pigment in house paint in some countries, and weathering, chalking and peeling paint releases lead-containing particles into the environment. In particular, dust in homes painted with paint containing lead pigment, and soil around lead-emitting industries, can contain very high lead levels (WHO/IPCS, 1995; CDC, 2002, 2005c). Young children, because of their tendency to put things into their mouths, can be exposed to lead from contaminated soils in residential areas. The maximum uptake in infants seems to occur at around 2 years of age, and is higher in the summer than in the winter (Baghurst et al., 1992; Yiin et al., 2000). The hand-to-mouth behaviour of children is important for lead intake (Lanphear et al., 1998) and even small babies unable to grasp objects receive much of their lead exposure from sucking their own fingers (Kranz et al., 2004). If a soil contains lead at 100 mg/kg, the average child could be exposed to 5 µg lead per day from this source alone.

With regard to drinking-water, lead contamination of the water reservoir may be of importance. Such contamination can occur from, for example, industrial discharges or highway run-offs. Furthermore, drinking-water can be contaminated with lead from lead pipes, lead-soldered copper pipes, lead-containing brass joints in plastic pipes, or from other parts of the water system. In particular, soft water has the potential for dissolving lead. The level of contamination is therefore dependent upon the time during which the water sat in the pipe.

The lead content of drinking-water can vary considerably. Hence, intakes of about 1 µg/day or less have been reported from Sweden (Svensson et al., 1987), whereas a study in Hamburg, Germany, in an area where lead pipes are common in old plumbing systems, showed a large variation in the lead concentration in tap water (<5–330 µg/l; mean 15 µg/l (Fertmann et al., 2004). High concentrations of lead in drinking-water are of concern for children, especially for bottle-fed babies if the formula feed is prepared from tap water (Hilbig et al., 2002).

The limit value for lead in drinking-water in the EU is currently 25 µg/l and will be reduced to 10 µg/l by 2013 (EU, 1998). The value of 10 µg/l is derived from a health-based guideline value for bottle-fed infants (PTWI 25 $\mu g/kg_{bw}$ = 3.5 $\mu g/kg_{bw}$/day (bw 5 kg; 50% allocation to water); rounded figure 0.75 l/day; JECFA, 2000).

Lead is incorporated into several crops through absorption, by the roots, from soil and through direct deposition on plant surfaces. The lead levels in various food crops amounted to 2–136 mg/kg for grains and cereals, 5–649 mg/kg for vegetables and 6–73 mg/kg for fats and oils (WHO/IPCS, 1995). The uptake of soil-borne lead by vegetables is very low. This explains the very low lead concentrations in root vegetables, tubers, seeds and fruit. In leafy vegetables, the accumulation of airborne lead largely exceeds the soil-borne part taken up via the roots. Airborne lead is mainly accumulated at the leaf surface and can be

removed, to a large extent, by thorough washing of the crop. There is, however, a relationship between the lead content of the soil and the lead content of the atmospheric deposition, as part of it consists of resuspended soil particles originating from short- and mid-range transport. At a deposition rate of about 13 kg Pb/km²/a, more than half of the lead accumulated by leafy vegetables is of airborne origin (de Temmerman & Hoenig, 2004).

The current lead levels of Swedish cereal crops are as follows: winter wheat contains <0.04 mg/kg (dry weight) in more than 90% of the harvest; spring barley contains <0.04 mg/kg (dry weight) in approximately 85% of the harvest; and oats have a median value of 0.044 mg/kg (Eriksson et al., 2000). Hence, almost half of the harvest contained lead concentrations of <0.04 mg/kg (dry weight) (95th percentile 0.098 mg/kg (dry weight)). The low values indicate that lead is generally strongly bound in agricultural soils and thus not very available to plants. Higher levels of lead in plants could be expected only if soils have very high lead concentrations naturally or due to pollution, or if the current level of lead deposition is high. There is direct deposition on leafy vegetables such as lettuce and spinach, and particularly for those with a long growing season such as kale, which can contain high levels of lead.

Fruits and vegetables, cereal and bakery items, and beverages are major sources of lead, together supplying most of the intake in the diet (EU, 2004). Lead levels amounted to 3–83 mg/kg in dairy products and 2–159 mg/kg in meat, fish and poultry (WHO/IPCS, 1995). Within the EU, the maximum permissible level of lead in foods ranges from 0.02 mg/kg wet weight for milk and milk supplements for infants up to 1 mg/kg for mussels (EU, 2001). In France, the major sources of lead in the diet, contributing to 5–11% of the exposure in the population, are cereal and bakery items, soups, vegetables, fruits, drinking-water, non-alcoholic and alcoholic drinks and sugar. The other vectors contribute less than 5% to the total dietary exposure (Leblanc, 2004). In a German duplicate study on children living in an industrialized area, cereal and bakery items and fish were the only significant determinants of the total dietary intake of lead (Wilhelm et al., 2005b). Additionally, consumption of home-grown products did not increase the dietary intake of lead.

Lead intake from foodstuffs varies greatly between countries. For example, in the United States, an average intake in adults of 3 μg/day has been reported (JECFA, 2000), while higher values have been given for Denmark (18 μg/day) and the United Kingdom (27 μg/day; EU, 2004). Children have a considerably higher dietary intake of lead in relation to body weight than do adults (JECFA, 2000; EU, 2004). The dietary intake in Denmark decreased between 1983 and 1997 to an estimated level of <2 $\mu g/kg_{bw}$/week for adults and <5 $\mu g/kg_{bw}$/week for children (Larsen et al., 2002). However, duplicate studies with children from Germany showed that the dietary lead intake remained fairly stable between 1988/1989 and 1998 (Wilhelm et al., 2005b). The most recent data (1998) point

to a geometric mean intake of 5.3 μg/kg_{bw}/week, which corresponds to 21% of the PTWI (Wilhelm et al., 2005b). Leblanc (2004) evaluated the dietary lead intake in France as 12.8 μg/day for children aged 3–14 years and 18 μg/day for adults. The dietary lead intake from United States total diet studies is also <2 μg/kg_{bw}/week for adults and <6 μg/kg_{bw}/week for children (Egan et al., 2002).

Because of the dramatic change in the levels of lead pollution, the concentrations in foods (and in dietary intakes) should decrease over time. A PTWI of 25 μg/kg_{bw}/week has been established for all age groups by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2000). The value was calculated for populations exposed to lead mainly from food and drinking-water, but is used as a reference to assess the dose from all sources of exposure.

Nursing infants are exposed to lead from breast milk. This route of exposure is affected both by the mother's current exposure as well as from her accumulated reserves from long-term exposure due to the redistribution of cumulative maternal lead stores in the bone. Ettinger et al. (2004) found that lead in breast milk accounted for 12% of the variance of the infant B-Pb. Because lead in the bone has a long half-life, infants will continue to be at risk for exposure long after any environmental sources have abated.

Alcoholic beverages can cause lead exposure (Grandjean et al., 1981). In particular, wines can contain considerable lead concentrations, partly because of the use of lead arsenate as a fungicide in vineyards and partly through contamination from containers (Graziano & Blum, 1991). Intake of some (ayurvedic) herbal medicines can cause lead exposure (Saper et al., 2004).

Lead-glazed or lead-painted pottery can be a significant source of lead; in particular, storage of acidic foods/beverages, such as fruit juice, in lead-glazed ceramics can cause high levels of lead intake (Téllez-Rojo et al., 2004; Hellström-Lindberg et al., 2006).

From studies of the uptake of stable lead in adults, an average absorption level of 15–20% can be estimated (cf. Skerfving, 1993, 2005). There are indications of a higher level of gastrointestinal absorption in children. Nutritional status affects the fractional uptake of lead: for example, a low iron intake (Cheng et al., 1998) and a deficient iron status (Berglund et al., 1994; Osman et al., 1998; Bárány et al., 2005) has been shown to be associated with increased B-Pb, though the causality is not clear (CDC, 2002). The oral bioavailability of lead from soil may be less than that from food, but the former varies considerably depending on the soil properties and lead mineralogy (Marschner et al., 2006).

3.2.3. Dermal lead exposures

There is some uptake of lead through the skin. However, the major influence of skin exposure appears to be the fact that lead contamination of the hands contributes to the oral intake (Askin and Volkmann, 1997; Kranz et al., 2004). Exposure can occur from cosmetics (Al-Ashban et al., 2004).

3.2.4. Biomarkers of exposure

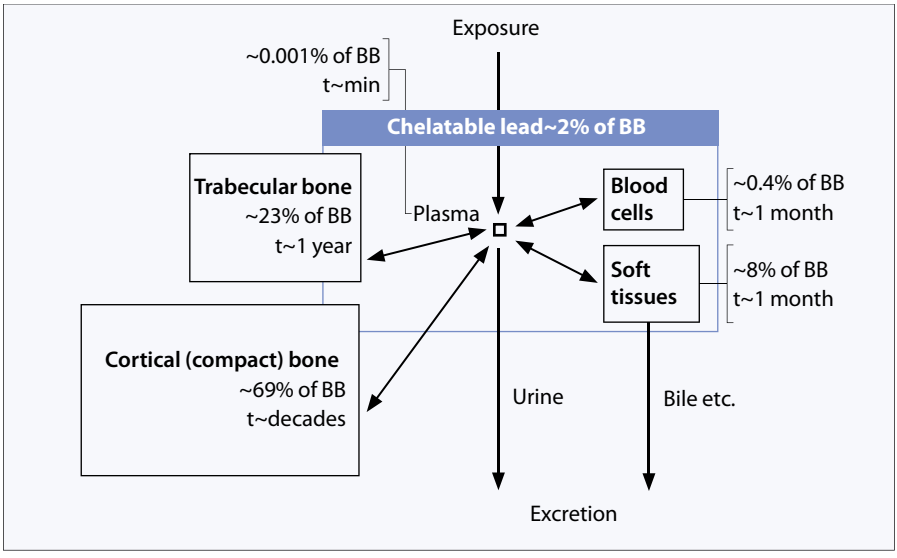
Most of the information on human exposure to, and the health effects of, lead is based on B-Pb data. Lead in the blood has two main pools: one has a half-life of about a month and the other a half-life of decade(s). Thus, the B-Pb level reflects a combination of recent lead exposure (during recent months) and that that occurred several years previously. The short-half-life pool is in the blood and soft tissues, while the long-half-life pool is in the skeleton (Fig. 3.16).

The B-Pb is usually determined from an analysis of venous blood. Most of the lead in the blood is present in the cells, being bound to the enzyme δ-aminolevulinic acid dehydratase (ALAD, also known as porphobilinogen synthetase; Bergdahl et al., 1997a). A long series of experimental and epidemiological studies have been devoted to examining the relationship between B-Pb and the exposure, intake or uptake of lead.

The relationship between lead uptake and B-Pb is curvilinear. Thus, at low lead uptakes there is a steady increase in B-Pb with increasing uptake, while at high lead uptakes, the curve flattens out and the B-Pb then changes only marginally with an increase in uptake, probably because of saturation of lead-binding sites in the erythrocytes (Bergdahl et al., 1997b).

It has been assumed that a 1 μg/m^3 increase in the lead concentration in ambient air results in a B-Pb increase of about 16 μg/l in adults and 19 μg/l in children (CDC, 1991). WHO/IPCS (1995) concluded that there was a 20 μg/l increase in the B-Pb for every 1000 mg/kg increase in the lead concentration in soil or dust

Fig. 3.16. Metabolic compartment model for lead in an adult man.[a]



[a] The figures shown for the percentages of the body burden (BB) that are present in different compartments are those corresponding to approximately steady-state conditions. The sizes of the boxes are not proportional. "Chelatable lead" denotes the amount available for binding to a chelating agent in a mobilization test. t, Biological half-life.

Source: Skerfving et al. (1993).

in the residential area. According to Carlisle & Wade (1992), the B-Pb in children would rise by 0.7 μg/l when the dietary lead content increased by 1 mg/kg. A 1 μg/day increase in lead intake from drinking results in a 1.6 μg/l rise in the B-Pb in children and a 0.4 μg/l rise in adults (Carlisle & Wade, 1992). In all these cases, the changes were supposed to occur in the low range of exposure, where the saturation of B-Pb had a limited influence.

A physiologically based pharmacokinetic model of the kinetics of lead through drinking-water (which is far more complicated than the simple compartmental model shown in Fig. 3.16) has been developed and validated by USEPA (1994) for children below 7 years of age. White et al. (1998) estimated B-Pb levels as a geometric mean of 36 μg/l (geometric standard deviation 16 μg/l) by using a model with the following default values: dietary intake 0.6 μg/day; outdoor air-lead concentration 0.1 μg/m3; and lead concentration in soil and dust 200 mg/kg. The probability of exceeding 100 μg/l was estimated to be 1.5%.

The model developed by O'Flaherty (1993) estimates lifetime lead exposures, uptake and disposition from birth to adulthood. It has been supplemented with a probabilistic module (Beck et al., 2001) and tested for B-Pb in people working with lead (Fleming et al., 1999) and in children (O'Flaherty, 1995), as well as for bone-lead levels in people working with lead (Fleming et al., 1999). Both B-Pb and bone lead are very labile in early childhood: they respond rapidly to increases in exposure, and decrease almost as rapidly to near-pre-exposure concentrations when exposure returns to background levels. From the peak in adolescence and into early adulthood, the rate of bone turnover drops dramatically and, hence, the ability to reverse bone-lead accumulation rapidly decreases.

Lead is present in blood plasma, generally making up less than 1% of the total B-Pb concentration (Schütz et al., 1996; Bergdahl et al., 1997b; Smith et al., 2002). Plasma is readily transported to target organs and has a very rapid turnover. This should make the lead concentration in plasma or serum a good measure of lead uptake and health risk but, because of the low concentrations, the determination of lead levels in plasma or serum has long been difficult and of doubtful accuracy. However, the use of inductively coupled plasma mass spectrometry (ICP-MS) has made these analyses much simpler (Bergdahl et al., 2006).

Lead accumulates in bone, and the lead concentration in bone can be determined in vivo by non-invasive methods based on X-ray fluorescence. With its slow turnover, bone lead reflects long-term lead exposure. It also reflects the total body burden, since the dominant fraction (>90%) of the body burden of lead is in the skeleton. Lead determinations have been carried out on different bones, mainly in people exposed to lead occupationally, including finger bone (Nilsson & Skerfving, 1993; Schütz et al., 2005), patella (Watanabe et al., 1994; Hu et al., 1998), tibia and calcaneus (Erkkilä et al., 1992; Todd & Chettle, 1994). Lead from the maternal skeleton, mobilized during gestation, is transferred across the

placenta to the fetus and is later passed, during lactation, to the nursing infant (Gulson et al., 2003).

Several studies have been carried out on bone lead in the general population. Determinations are possible for the tibia, the calcaneus and the patella, at least in populations with relatively high levels of exposure. However, the sensitivity of determinations in finger bone has not been sufficient. Because bone-lead levels reflect the long-term exposure to lead, they are attractive measures in epidemiological studies where assessments of retrospective exposure are required, such as in studies of the long-term effects on the developing brain (Hu et al., 1998). Indeed, stronger associations with neurological outcomes have been shown for bone lead, as compared with B-Pb, in a study from Kosovo (Wasserman et al., 2003).

Bone-lead concentrations are associated with the lead concentration in both whole blood and plasma (Christoffersson et al., 1984; Erkkilä et al., 1992; Börjesson et al., 1997). Lead is incorporated into the teeth during their formation (cf. Skerfving, 1993). The turnover of lead in the teeth is slow. Tooth lead has been widely used in epidemiological studies as an index of exposure in children. The urinary lead level has been used in the biological monitoring of lead, but only to a limited extent.

Haem synthesis is inhibited by lead. Hence, biomarkers of such effects (ALA in urine or serum, zinc protoporphyrin in blood cells) have been used to monitor exposure and risk (cf. Skerfving, 1993, 2005). Hair has sometimes been used for the biomonitoring of lead exposure (cf. Skerfving, 2005). However, because of external contamination, it is not a useful index of uptake into the body (Wilhelm & Idel, 1996).

3.2.5. Geographical differences and time patterns

There are large variations in lead exposure on both a global and a local scale. Because leaded petrol has long been a significant source of environmental lead, living close to a road with heavy traffic may be a determinant of exposure level (Strömberg et al., 2003), as well as living close to a lead-emitting industrial plant or in an area with lead-painted houses. People living in city centres have higher B-Pb levels than people living in rural areas.

On a global scale, the highest B-Pb levels occur in South and Central America, the Middle East, parts of eastern Europe and the countries of the former USSR. Using data from published studies, Fewtrell et al. (2004) assessed mean B-Pb concentrations in different parts of the world (Table 3.2) and estimated that about 25% or more of the children in these areas have B-Pb levels above 100 μg/l. In Australia, North America and western Europe, the corresponding proportion of children was less than 10%.

The lead body burden of the general population in the 1990s was estimated to be three orders of magnitude higher than that of prehistoric humans (Patterson

et al., 1991). Historically, lead emissions peaked during the 1970s, with annual emissions estimated at 400 000 t/a (Nriagu, 1996).

There has been a significant, and well-documented, decrease in B-Pb in the developed world during recent decades. For example, the mean B-Pb in a sample of adults living in the United States dropped 78% (from 128 μg/l to 28 μg/l) between 1976 and 1991, and a similar decline was seen among children (Pirkle et al., 1994). By 1999–2002, the overall percentage of B-Pb levels exceeding 100 μg/l was down to 0.7%. In the 1970s, as many as 80% of children in the United States had B-Pb levels greater than 100 μg/l. Between 1999 and 2002, 1.6% of children aged 1–5 years had B-Pb levels exceeding 100 μg/l – the highest percentage of any age group (CDC, 2003, 2005a,b; USEPA, 2005).

In Turin, Italy, the mean B-Pb in adults dropped by 58% (from 153 μg/l to 64 μg/l) between 1985/1986 and 1993/1994 (Bono et al., 1995), and in Swedish

Table 3.2. Mean B-Pb concentrations in urban children and adults in different areas.

WHO Region	Surveyed countries	B-Pb (μg/l)	
		Children	Adults
African	Nigeria	111	116
	South Africa	98	104
American	Canada, United States	22	17
	Argentina, Brazil, Chile, Jamaica, Mexico, Uruguay, Venezuela Ecuador, Nicaragua, Peru	70	85
Eastern Mediterranean	Saudi Arabia	68	68
	Egypt, Morocco, Pakistan	154	154
European	Denmark, France, Germany, Greece, Israel, Sweden	35	37
	Turkey, Yugoslavia	58	92
	Hungary, Russian Federation	67	67
South-East Asian	Indonesia, Thailand	74	74
	Bangladesh, India	74	98
Western Pacific	Australia, Japan, New Zealand, Singapore	27	27
	China, Philippines, Republic of Korea	66	36

Source: Fewtrell et al. (2004).

children a dramatic decline was observed between 1978 and 2005 (Strömberg et al., 2003; Fig. 3.17). In German adults, the geometric mean B-Pb levels decreased from 62 μg/l in 1985/1986, to 46 μg/l in 1990/1992, and to 31 μg/l in 1998 (Becker et al., 2002). For German schoolchildren (n = 3964) in the period 1979–2000, the geometric mean B-Pb levels decreased from 190 μg/l to 31 μg/l in an industrialized area and from 120 μg/l to 21 μg/l in a rural area (Wilhelm et al.,

2005b, 2006). Erythrocyte samples from adults indicated that there was decrease in Swedes throughout the 1990s (about a 4% annual decrease; Wennberg et al., 2006). In all these cases, the decrease in or removal of lead in petrol was certainly the main reason for the declining B-Pb levels, though the removal of lead from soldered cans probably also played a role.

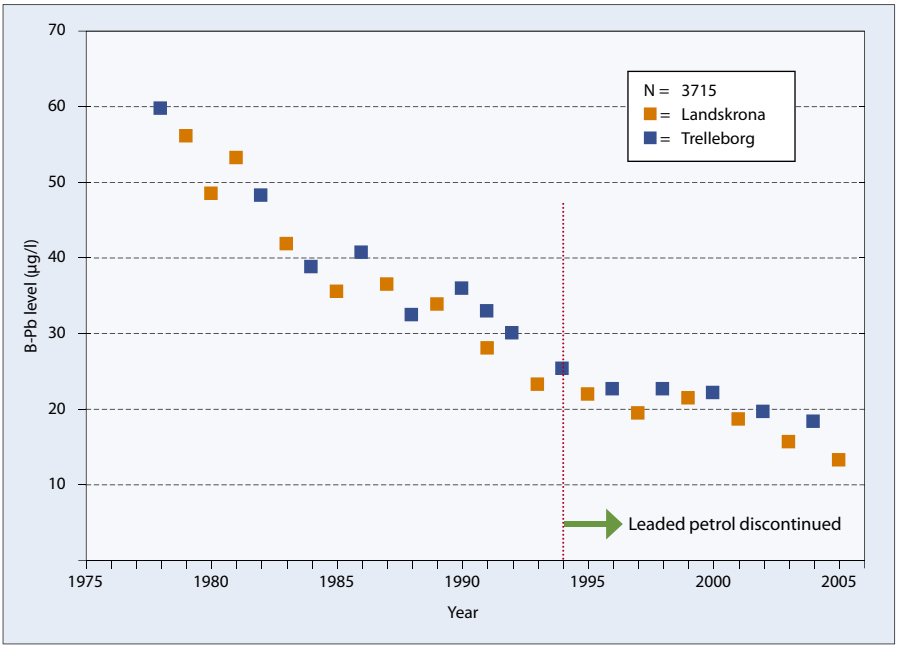
The phasing-out of leaded petrol is not yet complete. As of 1 January 2004, leaded petrol was still being used in most African countries, parts of eastern Europe and the former USSR (though not in the Russian Federation), as well as a number of other countries, i.e. Cuba, Indonesia, Iraq, Lebanon, Paraguay, Peru, the Syrian Arab Republic, Turkey and Uruguay (EIA, 2004). However, it was subsequently reported that several of the nations in sub-Saharan Africa are now phasing out leaded petrol (Burke, 2004).

In addition to the exposure from the general environment, many work environments imply exposure to lead. Hence, between 100 and 200 different lead-exposing occupations have been identified (cf. Skerfving, 2005).

3.3. Health hazard characterization

Lead is by far the most well-studied toxic metal, and a wide range of biological effects dependent upon the level and duration of the exposure are known (see extensive reviews, e.g. from the Agency for Toxic Substances and Disease Registry (ATSDR) in the United States (ATSDR, 2005).

Fig. 3.17. B-Pb levels (geometric means) in 3715 Swedish children for 1978–2005.



Source: Strömberg et al. (2003); Strömberg et al., unpublished data.

The main health effects of lead exposure are summarized, together with routes of exposure, affected population groups and critical lead levels (B-Pb), in Table 3.3. Mortality in workers exposed to high levels of lead is increased, and adults who were poisened by lead during childhood have increased blood presure, which is a significant risk factor for cardiovascular diseases and mortality. Non-fatal mechanisms include renal effects; anaemia owing to the inhibition of several enzymes involved in haem synthesis; acceleration of skeletal maturation; alteration of hormone levels and immunity parameters; and encephalopathy (at high exposure) and various other diseases of the nervous system, among which cognitive and neurobehavioural deficits in children at low levels of exposure are of great concern.

Table 3.3. Main routes of lead exposure and critical effects identified with associated B-Pb levels for various population groups.

Routes of intake	Population group(s)	Effects	Critical B-Pb (µg/l)
Placenta	Fetuses	Delays in neurological development	Probably no threshold
Mother's milk, inhaled air	Neonates and young children	Inhibition of ALAD	30–300
		Physical development	<70
Inhaled air, hand–mouth behaviour, ingestion	Children	Decreased nerve-conduction velocity	200–300
		Cognitive development and intellectual performance	<100
		Hearing loss	<100
		Jaundice	350
		Anaemia	>200
Inhaled air, food ingestion	Adults	Decreased ALAD activity	30–340
		Blood pressure	<20
		Damage to renal function (decrease in glomerular filtration rate)	20–100
		Sperm count	400–500

Sources: ATSDR (2005); Scientific Committee on Toxicity, Ecotoxicity and the Environment (2000).

3.3.1. Dose–response relationship

There are extensive data, from epidemiological studies, on the association between B-Pb levels and lead-related health effects (Table 3.4).

3.3.2. Susceptible population groups

Certain population subgroups are more susceptible to exposure to lead. Groups at risk include infants, children and women of reproductive age (in terms of the lead exposure of the fetus and of the nursing infant during lactation). Per kilogram of body weight, children drink more fluids, eat more food and breathe more air than adults. Children's behaviour and lifestyle (e.g. more hand-to-mouth ac-

Table 3.4. Lead-related health effects in children and adults in relation to B-Pb concentrations (i.e. concentration range associated with each effect).

Effect	B-Pb (µg/l)	
	Children	Adults
Depressed ALAD	<50	<50
Neurobehavioural		>40 (in the elderly)
Neurodevelopmental	<100	
Sexual maturation	<100	
Depressed glomerular filtration rate		<100
Elevated blood pressure		<100
Depressed vitamin D levels	>150	
Elevated erythrocyte protoporphyrin	>150	>200 (in females)
Depressed nerve-conduction velocity	>300	
Enzymuria/proteinuria		>300
Depressed haemoglobin	>400	>500
Neurobehavioural, altered thyroid function, reduced fertility, peripheral neuropathy		>400
Colic	>600	
Death	>1 000	>1 500

Source: ATSDR (2005).

tivities, being physically closer to ground level, and more time spent outdoors) may result in additional lead exposures compared with adults. Gastrointestinal absorption of lead is much higher in children. The neurodevelopmental effects have been observed in children exposed to lead both in utero and postnatally at rather low levels. Thus, in addition to the existence of interindividual variations in relation to exposure, absorption and retention, there are population strata comprising people that are particularly susceptible to the toxicodynamics of lead. The developing brain of the fetus, for example, is sensitive to maternal exposure to lead (cf. Skerfving, 2005). Also, there is mobilization of lead from the maternal skeleton (accumulated from childhood onwards) during lactation, and there is also excretion of lead in the breast milk. Hence, the breastfed infant can be exposed, and its sensitive brain affected.

Other groups at risk include individuals with iron and calcium deficiencies (i.e. mainly women of childbearing age), who show increased gastrointestinal absorption of lead. Also, the *ALAD* genotype seems to modify the toxicity of lead for several organs (cf. Skerfving, 2005). There is a polymorphism in the gene encoding *ALAD*, which may affect lead metabolism. Several studies have shown higher B-Pb levels in $ALAD^2$ subjects than in $ALAD^1$ subjects (Wetmur et al., 1991; Alexander et al., 1998; Fleming et al., 1998; Schwartz et al., 2000), although the support for these data remains weak (Bergdahl et al., 1997c). Other gene–environment interactions have also been reported, but less extensively studied (cf. Skerfving, 2005).

In addition, people with diseases of organs that are affected by lead toxicity are particularly sensitive, e.g. patients with hypertension, anaemia or kidney and nervous-system disorders (whether of genetic origin or not) (cf. Skerfving, 2005), and diabetes (Tsaih et al., 2004).

3.3.3. Effects of low exposure levels

To determine the influence of LRTAP on human health, the effects produced at lower dose levels of environmental lead exposure should be discussed. The most sensitive end-points of lead toxicity are neurodevelopmental and other neurological effects, cardiovascular effects and renal effects. Prenatal exposure from lead in maternal blood crossing the placenta is especially important because the fetus lacks a functioning blood–brain barrier. Young children remain vulnerable because of the developmental status of their brains and nervous systems, as well as because of the incompletely developed blood–brain barrier. Recent scientific evidence has not been able to confirm the existence of a safe threshold level for some of the adverse neurological effects; these effects have been documented at exposure levels once thought to be harmless (<100 μg/l) (ATSDR, 2005). Children and pregnant women can absorb up to 70% of ingested lead, whereas adults typically absorb up to 20%. Adults may ultimately retain only 1% of the absorbed lead, but children tend to retain more than adults. In infants from birth to 2 years of age, approximately 30% of the total amount of lead is absorbed.

Both cross-sectional and prospective studies on lead and neuropsychological development in children have confirmed that children represent a group that is particularly at risk. Indicators used by different researchers have included tests of fine motor skills, language, memory and learning, attention, and executive functioning (Bellinger et al., 1994; Schnaas et al., 2006; Schwartz, 1994; Winneke & Kramer, 1997; Chiodo et al., 2004).

Meta-analyses (summary in ATSDR, 2005) conducted on cross-sectional studies and prospective studies suggest that a doubling of B-Pb from 100 μg/l is associated with an average loss in intelligence quotient (IQ) of 1–5 points. An examination of NHANES III data showed cognitive effects (arithmetic, reading, block design and digit span), in children aged 6–16 years, that were associated with B-Pb levels below 50 μg/l (Lanphear et al., 2000). Canfield et al. (2003) reported that a B-Pb increase of 10 μg/l was associated with an IQ decrease of 1.4 points. In this study, the effect was even more pronounced at lower B-Pb levels, suggesting a non-linear dose–response curve. However, the existence of a U-shaped dose–response curve is still a matter of scientific debate.

An association between neurodevelopmental effects and B-Pb has been reported recently for levels as low as 30 μg/l (Chiodo et al., 2004). An international pooled analysis showed a 6-point IQ reduction for the B-Pb range 10–100 μg/l (Lanphear et al., 2005). Even a small deficit in IQ may have large effects in popu-

lation strata in the upper and lower ends of the IQ distribution, thus potentially posing a substantial public health risk (Winneke & Krämer, 1997).

Effects on the nervous system also include a constellation of other effects, such as poor school performance, problems with impulse control, and attention deficits (Schwartz, 1994; Winneke & Krämer, 1997). Bellinger & Dietrich (1994) previously reported that social and emotional dysfunctions and academic performance deficits are correlated with increased lead exposure. The neurotoxicity of lead is of particular concern, because evidence from prospective longitudinal studies has shown that neurobehavioural effects, such as impaired academic performance and deficits in motor skills, may persist even after B-Pb levels have returned to normal (Needleman et al., 1990). Prospective studies support the hypothesis that the changes are irreversible, or at least long-lasting (up to adulthood) (Needleman, 1991; Bellinger et al., 1992; Shen, 2001). The extent to which prenatal, perinatal and postnatal lead exposures contribute to these neurotoxic effects remains to be clarified. However, the results reported by Schnaas et al. (2006) indicate that the period at about 28 weeks gestation may be the critical time at which fetal lead exposure can affect the subsequent intellectual development of the child.

Several studies of associations between lead exposure and hearing thresholds in children have been reported, but the results are inconsistent. A study of 49 children aged 6–12 years revealed an increase in the latencies of waves III and V of the brainstem auditory evoked potentials associated with B-Pb measurements obtained 5 years prior to the tests (mean 280 μg/l) (Otto & Fox, 1993). Osman et al. (1999) investigated children in the Katowice region of Poland and reported increased latency for wave I of the brainstem auditory evoked potentials in children with B-Pb above 100 μg/l compared to children with values below 46 μg/l. Rothenberg et al. (2000) found that I–V and III–V interpeak intervals decreased as the B-Pb increased from 10 μg/l to 80 μg/l and then increased as the B-Pb rose from 80 μg/l to 310 μg/l. Increased brainstem auditory evoked potential interpeak latencies were also described in a study of Chinese children with a mean B-Pb of 88 μg/l (range 32–380 μg/l) after controlling for age and gender as confounding factors (Zou et al., 2003; cf. ATSDR, 2005). These findings suggest that lead (even at low levels) impairs both the peripheral and central portions of the auditory system. Other studies failed to confirm the effects of low-level lead exposure of children on the hearing threshold (ATSDR, 2005): Counter et al. (1997) found no difference in hearing thresholds between groups of children who had experienced relatively low or higher exposures to lead (mainly from local ceramics glazing and car-battery disposal; B-Pb 60 μg/l; range 40–120 μg/l, n = 14; B-Pb 530 μg/l; range 100–1100 μg/l, n = 62), respectively).

The effects of lead on blood pressure are evident at high levels in occupational settings and in animal studies (Hu et al., 1996; Glenn et al., 2003). There is no general agreement as to whether lead exposure at lower levels increases

blood pressure. Several recent epidemiological studies have compared the associations of B-Pb levels and lead levels in bone with blood pressure and hypertension (Martin et al., 2006). For example, Rothenberg et al. (2002) found that in normotensive pregnant women a 10 mg/kg increase in calcaneus bone lead was associated with a 0.70 mmHg increase in third-trimester systolic blood pressure and a 0.54 mmHg increase in diastolic blood pressure. The evaluation of the NHANES III study dataset did not show a consistent relationship between blood pressure and B-Pb levels (den Hond et al., 2002). The study of Martin et al. (2006) with elderly participants showed that a 10 μg/l increase in B-Pb was associated with a 0.99 mmHg increase in systolic blood pressure, while lead in the tibia bone was associated with hypertension. The B-Pb levels and the lead levels in the tibia were considered to represent average values for the United States population.

There are indications from several studies that lead exposure at environmental levels may be associated with renal effects. By analysing data from NHANES III, Muntner et al. (2003) found an association between B-Pb and chronic kidney disease in persons with hypertension. A weak association between lead exposure and a longitudinal decline in renal function among middle-aged and elderly individuals with diabetes and hypertension was observed by Tsaih et al. (2004). A recent study with children from various European countries reported a negative association between B-Pb and serum concentrations of creatinine, cystatin C and β_2-M, suggesting that environmental lead exposure induces early renal hyperfiltration (de Burbure et al., 2006; Muntner et al., 2003).

Recently, the variability in the susceptibility to lead exposure as well as variability in health outcomes is thought to be the result of genetic polymorphism of the *ALAD* gene, the gene for the vitamin D receptor and the haemochromatosis gene. The roles of the latter two genes are not clear. However, there are now many data suggesting that polymorphisms of the *ALAD* gene are associated with the accumulation and distribution of lead in the blood, bone and other internal organs of the body, and susceptibility to lead (Hu et al., 2001; Bellinger et al., 1994; Bergdahl et al., 1997a; Sakai, 2000); further research is needed.

3.3.4. National and international guidelines

A critical B-Pb limit of 100 μg/l for children and women of reproductive age has been recommended by several organizations (WHO, CDC, United States Food and Drug Administration, German Human Biomonitoring Commission) (ATSDR, 2005; WHO, 2000; Ewers et al., 1999). In the United States in 1991, CDC identified a goal to reduce children's B-Pb below 100 μg/l (CDC, 2005c); intervention for individual children was recommended at levels of 150 μg/l and above. The EU has no separate regulation. The reference values of the German Human Biomonitoring Commission for B-Pb are 70 μg/l for women, 90 μg/l for men and 50 μg/l for children (Wilhelm et al., 2004, 2006).

Because of the consistent findings on developmental effects at lower B-Pb levels, regulatory bodies should consider the revision of the allowable blood level in children. Hence, 100 μg/l should not be interpreted as a safe level for the general population, but in the treatment of individual patients it can be used to identify raised levels of lead exposure.

In the United States, the ambient air quality standard is 1.5 $\mu g/m^3$ (quarterly average; USEPA, 2003). The EU (1999) ambient air quality guideline for lead is 0.5 $\mu g/m^3$, to be met in 2005. In the immediate vicinity of specific industrial sources, the value is 1 $\mu g/m^3$ until 2010.

3.4. Human health implications in relation to LRTAP

Lead is a well-known neurotoxic metal. Impairment of neurodevelopment in children is the most critical lead effect. Exposure in utero, during breastfeeding, and/or in early childhood may all be responsible for the effects. Lead accumulates in the skeleton, and its mobilization from the bones during pregnancy and lactation causes exposure of the fetus and the breastfed infant. Hence, the lifetime exposure of a woman before pregnancy is important.

Epidemiological studies consistently show that cognitive effects in children are associated with B-Pb levels (in the pregnant woman, in the cord blood or in the child) of about 100–150 μg/l. There are indications that lead is harmful even at blood concentrations considerably below 100 μg/l and that there may be no threshold for these effects.

In many areas there has been a major decrease in B-Pb levels over the last few decades, mainly because of the phasing out of leaded petrol, but also because of reductions in other sources of lead. The current lowest average B-Pb in several European countries is about 20 μg/l, but reliable information on B-Pb levels in some parts of Europe is lacking.

The relative contributions of different lead sources differ depending on local conditions. Most often, food is the predominant source of lead uptake in the general population. However, these exposures are generally well below the PTWI. Higher levels of exposure occur in some people, such as infants and young children who have ingested contaminated soil, dust and old (lead-based) paint because of their tendency towards hand-to-mouth activities. Where tap-water systems involve lead pipes, lead intake via drinking-water can be an important source, especially for children. Inhalation exposure may be significant when lead levels in the air are high. Elevated exposures are generally due to local sources rather than being the result of LRTAP.

Lead levels in ambient air have decreased during the last few decades. Between 1990 and 2003, there was a two- to threefold decrease in the lead levels in air in Europe. Similar decreases took place for atmospheric deposition.

The annual lead inputs due to transboundary air pollution and the application of mineral and organic fertilizers to topsoils are of roughly the same magnitude.

Those inputs are relatively small in comparison to lead stores that have already accumulated and those that are from natural sources. However, LRTAP may contribute significantly to the lead content of crops, through direct deposition. Although uptake via plant roots is relatively small, rising lead levels in soils over the long term is a matter for concern and should be avoided because of the possible health risks of low-level exposure to lead.

3.5. References

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4. Mercury

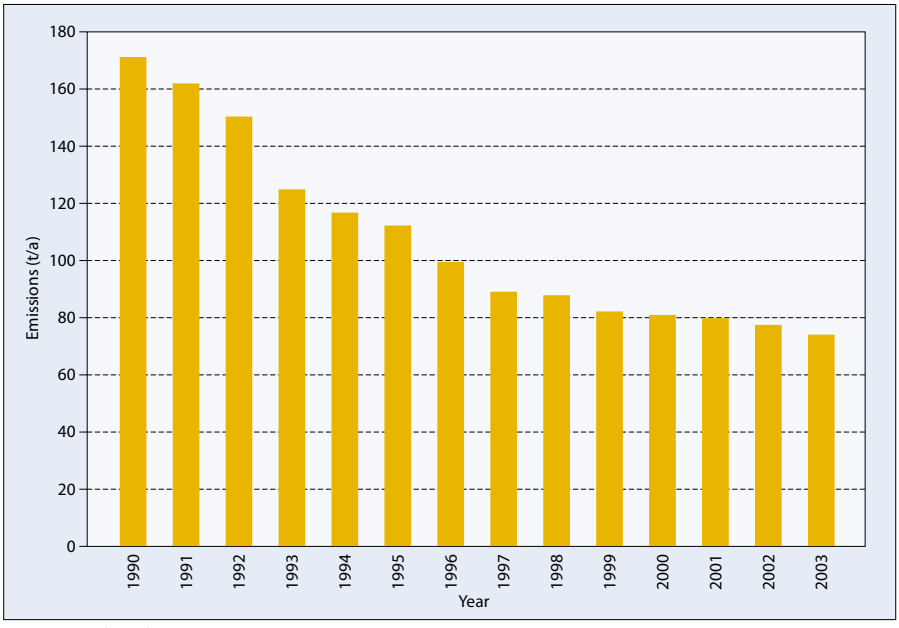
4.1. Introduction

4.1.1. Emissions

Mercury is an element that occurs naturally in the environment. However, human activity has significantly changed its cycling in recent centuries. The main natural sources of mercury are diffusion from the Earth's mantle though the lithosphere, evaporation from the sea surface, and geothermal activity (Lindqvist & Rhode, 1985; Pirrone et al., 1996; Jackson, 1997; Pirrone et al., 2001a, 2003). The largest anthropogenic source of mercury on a global scale is the combustion of coal and other fossil fuels. Others sources include metal production, cement production, waste disposal and cremation. In addition, a significant contribution to global emissions of mercury comes from gold production (Pirrone et al., 1996; Pacyna & Pacyna, 2001; Pirrone et al., 2001a,b). On a global scale, the estimated natural emission of mercury represents about one-third of the total, and anthropogenic emissions represent about two-thirds (Lamborg et al., 2002).

The emissions of mercury in Europe can be characterized by data officially reported to UNECE by the Parties to the Convention on Long-range Transbound-

Fig. 4.1. Reported emissions of mercury in the EMEP region (24 countries).

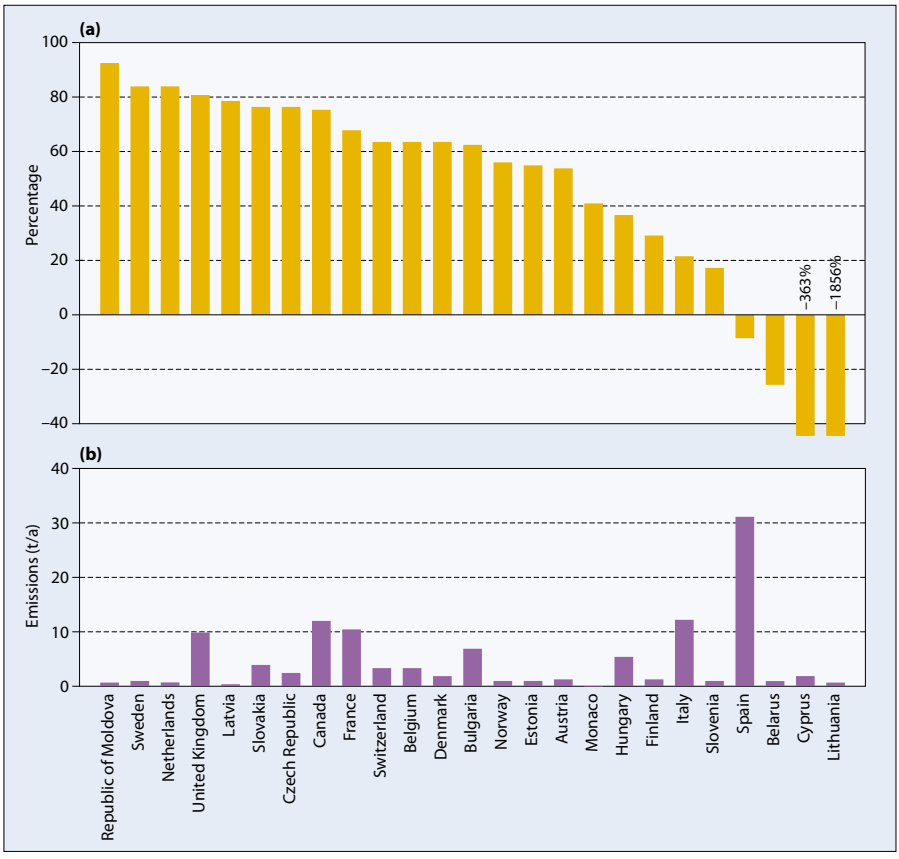


Source: UNECE (2006a).

ary Air Pollution, and by expert estimates. According to official emission data, supplemented with the expert estimates of Berdowski et al. (1997, 1998), the total for anthropogenic emissions in Europe was 413 t/a in 1990 and 195 t/a in 2003. The expert estimates of Berdowski et al. (1997, 1998) were used for countries that did not report their data. Long-term trends for mercury emissions in Europe can be evaluated for 24 countries that reported emission data to UNECE for both 1990 and 2003. The emissions in these countries decreased by about 57% and have levelled off since the end of the 1990s (Fig. 4.1).

The relative reduction in reported emissions between 1990 and 2003 was calculated as $((E_{1990} - E_{2003})/E_{1990}) \times 100\%$, where E_{1990} and E_{2003} represent emission magnitudes in 1990 and 2003, respectively. The reported reductions in mercury emissions for 1990–2003 vary between 17% (Slovenia) and 92% (Republic of Moldova) (Fig. 4.2a). In Spain and Belarus, mercury emissions increased by

Fig. 4.2. (a) Reductions in mercury emissions in the 24 countries of the EMEP region and Canada for the period 1990–2003, based on official data reported for both 1990 and 2003. Increasing emissions are shown as negative reductions. (b) Official emission values in 2003.



Source: UNECE (2006a).

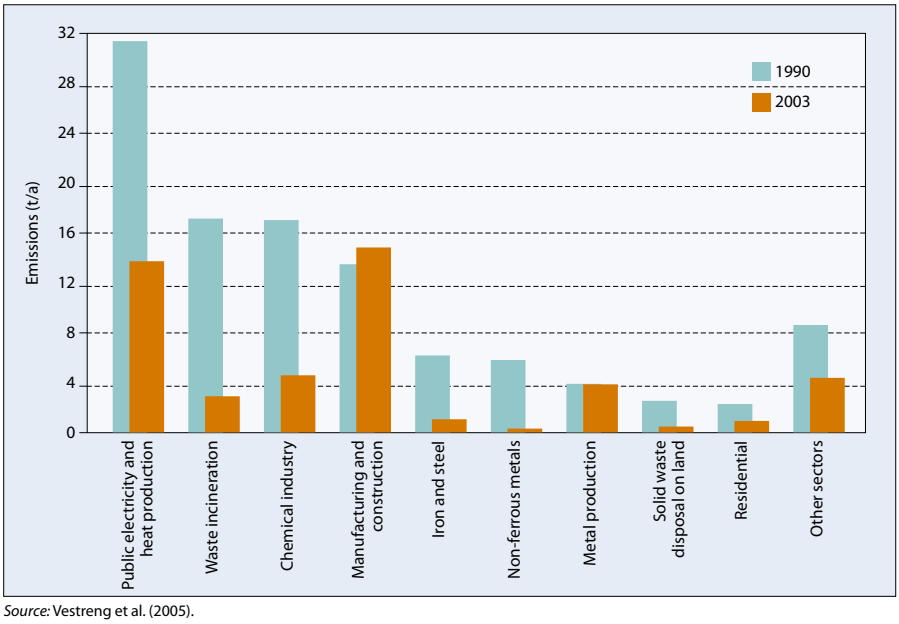
about 9% and 26%, respectively. In Cyprus, emissions of mercury increased almost 5 times, and in Lithuania the emissions increased almost 20 times according to the data reported. Fig. 4.2b shows the official levels of mercury emission in 2003.

Fig. 4.3 shows estimates of mercury emissions in the nine sectors that were the largest sources in 1990 and 2003. Their contribution to the total level of emissions in the eight countries was about 92% in 1990 and 91% in 2003. In 1990, the maximum contribution to the total for mercury emissions was from the sector "Public electricity and heat production" (about 29%). In 2003, the sector "Other manufacturing industries and construction" became the largest source of emissions (about 31%). The sector "Public electricity and heat production" became the second largest source (about 29%). More detailed information about emission data officially reported for 1990–2003 is available from Vestreng et al. (2005).

4.1.2. Atmospheric mercury

Atmospheric mercury is characterized by the variety of its chemical and physical forms. The most abundant mercury species is elemental mercury (Hg^0). It exists in the gaseous phase, and its contribution to the total atmospheric mercury burden is more than 90%. Gaseous inorganic mercury (or so-called reactive gaseous mercury (RGM)) exists in the atmosphere in much smaller amounts. Measurements show that the concentrations of RGM constitute about 1–5% of total

Fig. 4.3. Anthropogenic sources of mercury emission in 1990 and 2003 (for eight countries).



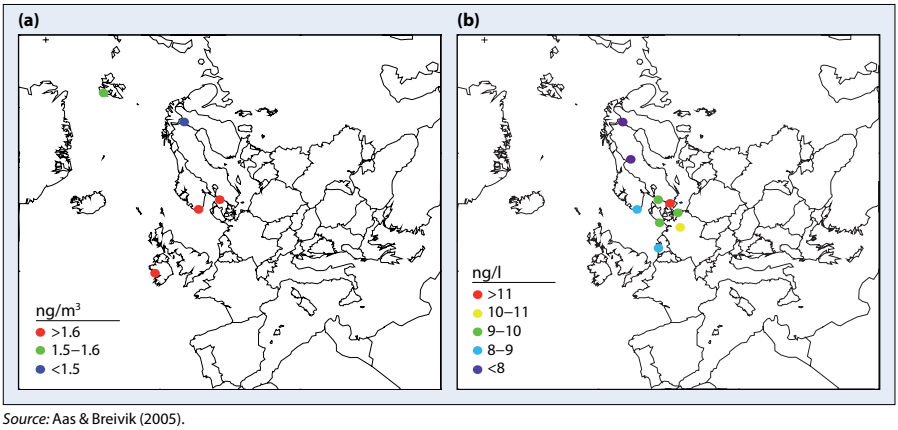
Source: Vestreng et al. (2005).

mercury concentrations (Ebinghaus et al., 1999a; Lindberg & Stratton, 1998). Nevertheless, the RGM contribution to atmospheric deposition is considerable, especially in the vicinity of emission sources. It is believed that RGM is present in the form of mercuric chloride ($HgCl_2$) and mercuric hydroxide ($Hg(OH)_2$). However, the composition of gaseous inorganic mercury compounds has not been adequately investigated (Ebinghaus et al., 1999b). The speciation of mercury bound to particles is not known, but it is most likely that divalent mercury compounds are present on the particle surface or integrated into the particle (Schroeder et al., 1991). The fraction of particle-bound mercury in background atmosphere ranges from less than 1% to 6% (e.g. Ebinghaus et al., 1999a; Lamborg et al., 1999; Slemr, 1996) but its contribution to deposition from the atmosphere is significant. It is worth noting that the contribution of RGM and aerosol mercury (in comparison with gaseous elemental mercury) to total atmospheric mercury can vary greatly at both regional and local level (Wängberg et al., 2003).

Elemental mercury is characterized by a long atmospheric lifetime and so it can be transported globally (Schroeder & Munthe, 1998). The low water solubility of elemental gaseous mercury (depending on the meteorological conditions and ambient concentrations of the major atmospheric oxidants) means that it has an atmospheric lifetime that can range from a few weeks to several months (Hedgecock & Pirrone, 2004). This contrasts with oxidized gaseous mercury, which is soluble in water and has an atmospheric lifetime that can range from a few days to a few weeks. Particulate-bound mercury is efficiently scavenged by precipitation events and therefore has a short residence time in the atmosphere (Hedgecock & Pirrone, 2004).

The spatial and temporal variability of atmospheric concentrations at a regional level is relatively low. According to the measurements from EMEP stations and from several EU-funded projects, collected for the period 1990–2003, the air

Fig. 4.4. Background concentrations of mercury in air (a) and in precipitation (b) in 2003.



Source: Aas & Breivik (2005).

concentrations of mercury ranged from 1.3 ng/m^3 to 2 ng/m^3 (Wängberg et al., 2001; Pirrone et al., 2001b, 2003; Aas & Breivik, 2005) (Fig. 4.4a).

In 1990, measurements of background concentrations in precipitation in Europe were too scarce to draw any conclusions about spatial patterns. The mercury concentration, averaged over a few stations, was around 15 ng/l. In 2003, the concentrations were typically 5–10 ng/l in northern and central Europe (Aas & Breivik, 2005) (Fig. 4.4b). However, mercury monitoring within EMEP covers only northern and central Europe. In the Mediterranean region, ambient concentrations were measured at coastal background sites and over the sea during an oceanographic cruise. The elemental mercury concentrations were in the range 1.2–2.4 ng/m^3, whereas the RGM and the particulate-bound mercury were, respectively, 5–35 pg/m^3 and 5–25 pg/m^3) (Pirrone et al., 2003; Sprovieri et al., 2003). Very few data from eastern Europe are available.

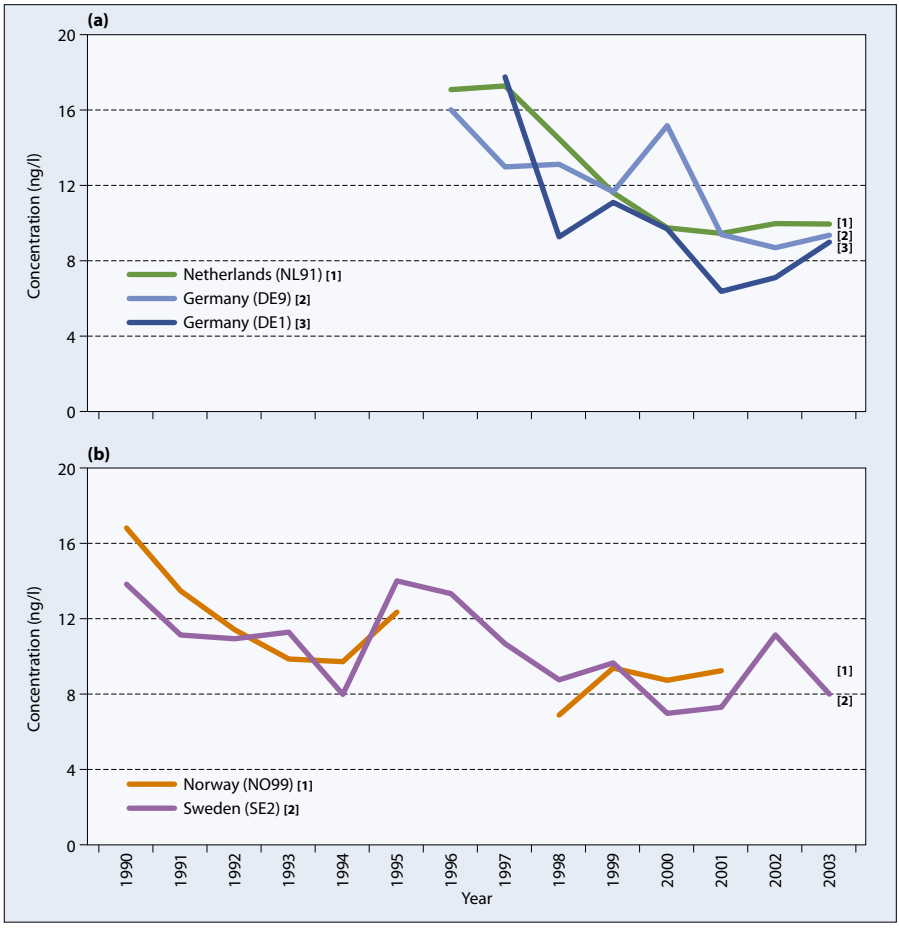
There are only a few stations in Europe providing long-term measurements of mercury. The concentrations of mercury in air do not demonstrate any noticeable long-term trend. The concentrations in precipitation, based on these limited data, have decreased about twice in central and northern Europe (Fig. 4.5a,b). Numerical information on the observed mercury background levels for 2003 is available from the Chemical Coordinating Centre web site (www.nilu.no/projects/ccc/emepdata.html).

Air concentrations of mercury measured at the Arctic stations, rather like those for Europe, do not demonstrate any long-term trends. For example, the annual mean concentrations of mercury at Station Alert (Canada) varied between 1.52 ng/m^3 and 1.62 ng/m^3 for the period 1995–2002 (Steffen et al., 2005). Measurements taken at the Norwegian Arctic station (Zeppelin) vary between 1.2 ng/m^3 and 1.7 ng/m^3 for 1994–2003. Nevertheless, seasonal variability of mercury concentrations is high because of so-called "mercury depletion events" (e.g. Schroeder et al., 1998; Sprovieri et al., 2005a,b; Steffen et al., 2005). During these events, the near-surface concentrations of elemental mercury in surface air drop almost to zero and then rapidly rise to their typical values (around 1.5–1.7 ng/m^3). Normally, this phenomenon is observed in the Arctic and the Antarctic and lasts from the beginning of spring to early summer. Significant re-emission of mercury from the snowpack and during the snowmelt period also occurs, thus returning some of the deposited mercury to the atmosphere.

4.1.3. Modelled transport and deposition

Modelling of mercury pollution levels in the atmosphere has been performed using the EMEP MSCE-HM model with the official reported emission data. For countries for which official emission data were not available, expert estimates from Berdowski et al. (1997) were used. The modelled concentrations of mercury in precipitation in 1990 lie mainly within the range 12–40 ng/l over central and eastern parts of Europe, and are 6–12 ng/l in the northern and south-western

Fig. 4.5. Observed concentrations of mercury in precipitation at stations in central (a) and northern (b) parts of Europe.

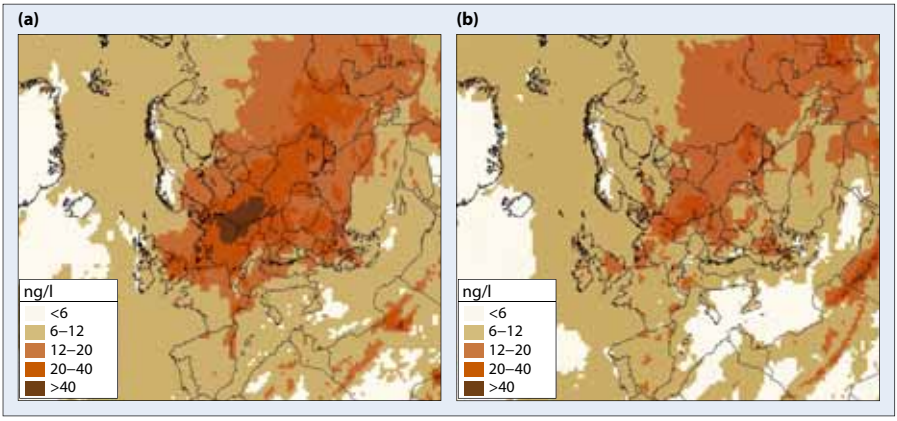


Source of the data: EMEP/MSC-E.

parts (Fig. 4.6a). In 2003, the concentrations were lower than those in 1990 (Fig. 4.6b). They ranged from 6 ng/l to 12 ng/l over most of Europe, and from 12 ng/l to 20 ng/l in the eastern part of Europe. Mercury concentrations and depositions are calculated using a spatial resolution of 50 × 50 km^2; within each 50-km grid cell, depositions on individual land types are also computed. The deposition fluxes of mercury with respect to forests are, as a rule, larger than those on low vegetation such as crops (Fig. 4.7), which is similar to the situation for cadmium and lead.

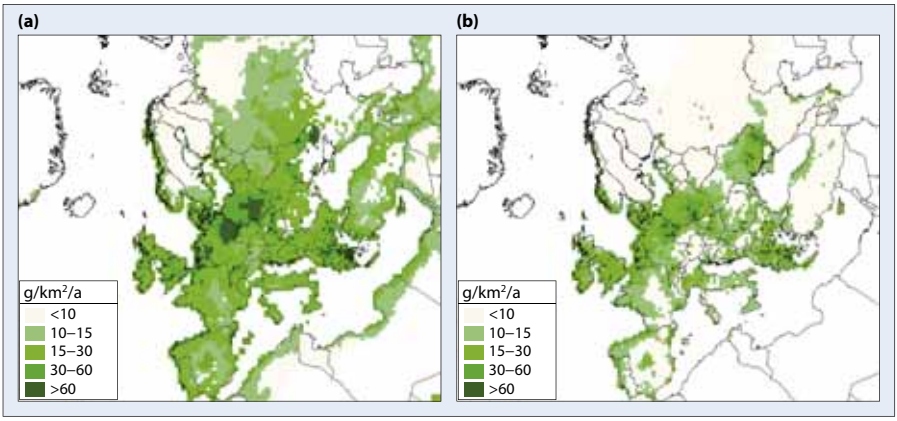
For Europe as a whole, the depositions for 1990–2003 were estimated to have decreased by a factor of 1.6. In individual countries, the decrease differs, reaching about three times in Germany, the Czech Republic, the Republic of Moldova and Slovakia (Fig. 4.8). In 11 countries, a twofold decrease was estimated to have taken place. In 12 countries, the depositions decreased by about 1.5–2 times.

Fig. 4.6. Modelled concentrations of mercury in precipitation over the EMEP region in 1990 (a) and 2003 (b).



Source: UNECE (2006b).

Fig. 4.7. Spatial distribution of modelled total deposition of mercury (across the EMEP region) on coniferous forests (a) and crops (b).

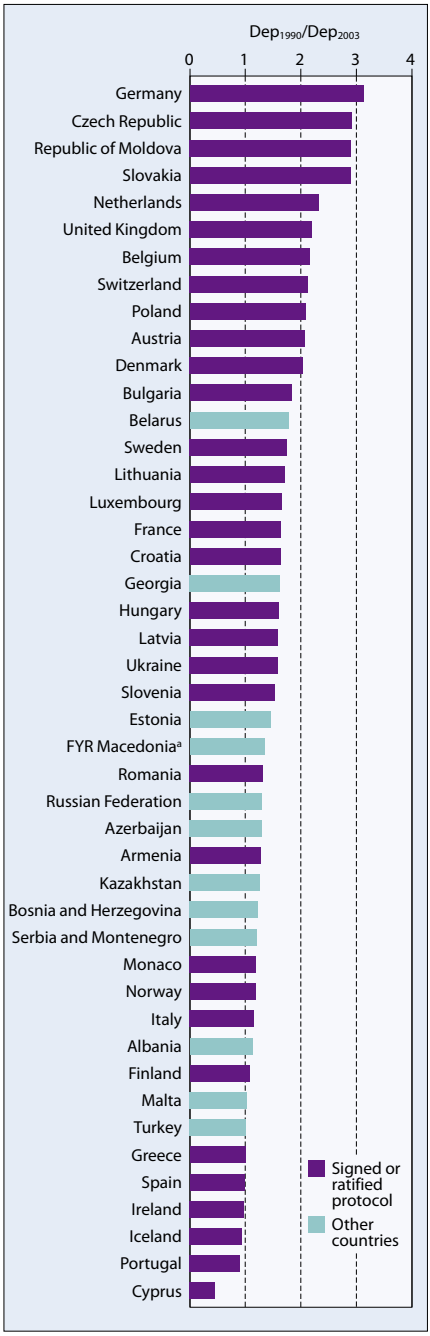


Source: UNECE (2006b).

The contributions that anthropogenic European LRTAP sources make to mercury depositions in different countries vary from 2% to 55% (Fig. 4.9). In 11 countries this contribution is greater than 30%. The contributions of natural and global sources outside Europe, and re-emissions, are higher than for cadmium and lead, ranging from 20% in Poland to 98% in Iceland.

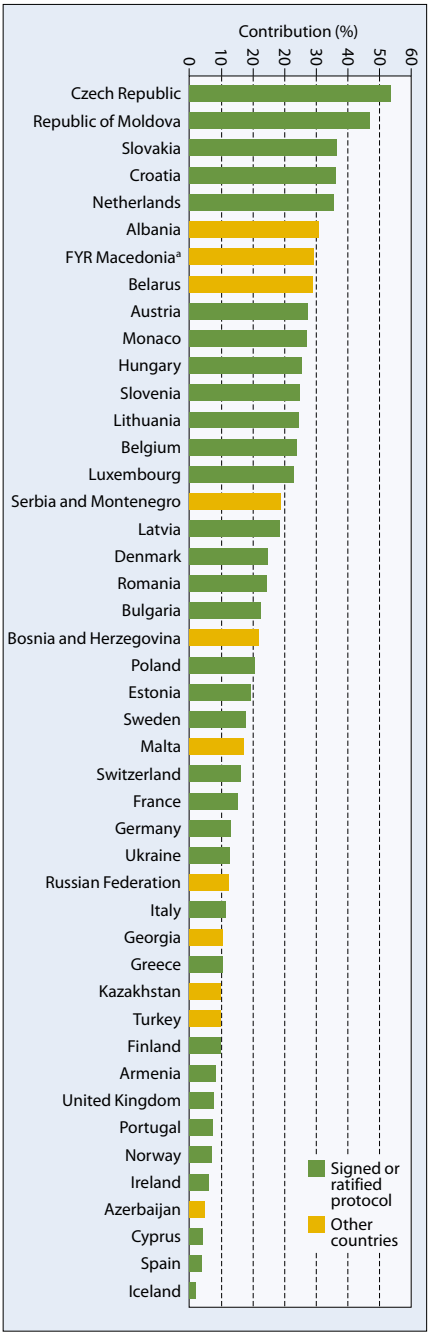
Only about one third of the mercury deposition in Europe originates from European emissions, whereas the remaining two thirds is transported from outside (Travnikov & Ryaboshapko, 2002). A map of the depositions of mercury from European sources is shown in Fig. 4.10: it shows that the depositions within the EMEP region vary from 5 g/km^2/a to 35 g/km^2/a. However, even in remote regions such as North America or the Russian Artic, depositions can range from 1.2 g/km^2/a to 5 g/km^2/a.

Fig. 4.8. Ratio between modelled total depositions of mercury in 1990 and those in 2003 in European countries.



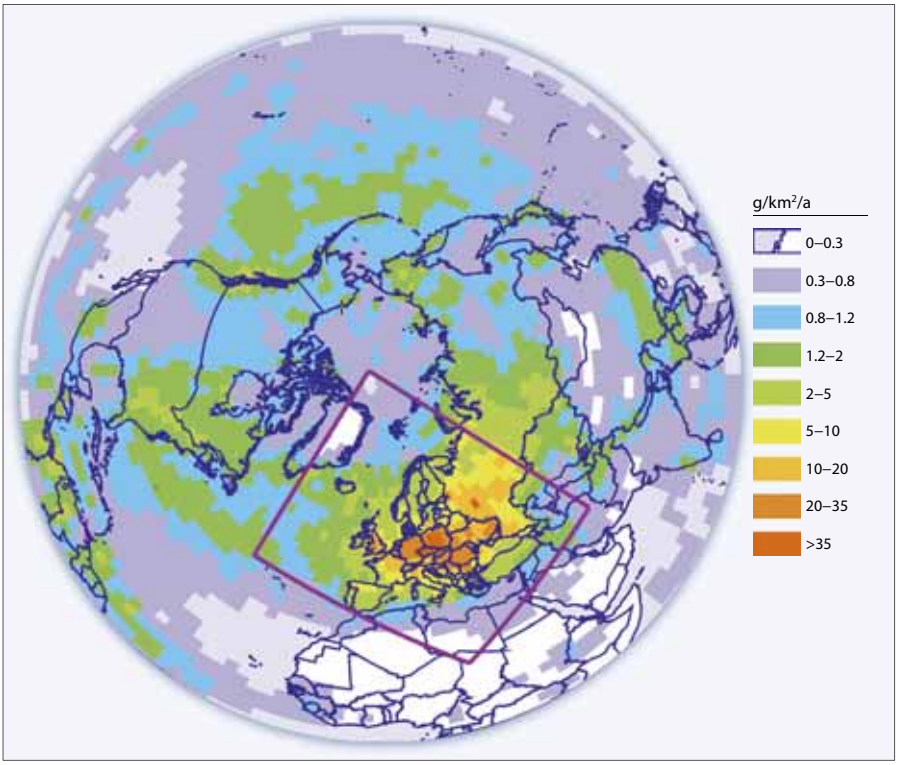
[a] The former Yugoslav Republic of Macedonia.
Source: UNECE (2006b).

Fig. 4.9. Contribution of transboundary transport from anthropogenic sources outside Europe to depositions of mercury in European countries.



[a] The former Yugoslav Republic of Macedonia.
Source: UNECE (2006b).

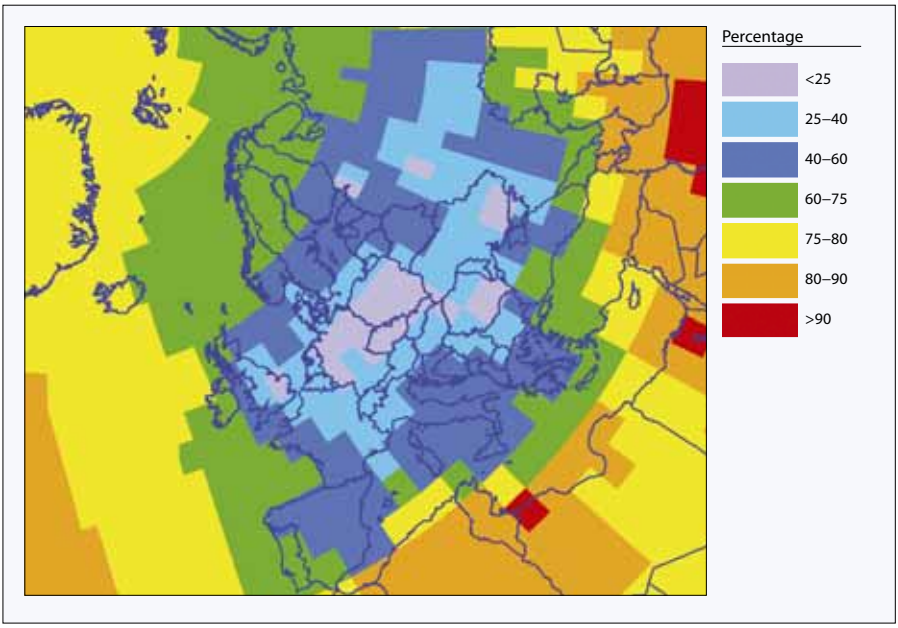
Fig. 4.10. Annual deposition field of mercury from European anthropogenic sources. The red rectangle indicates the EMEP domain.



Sources located outside Europe also influence mercury levels within Europe by about 25% in the central area, while on the periphery of the region the influence exceeds 60% (Fig. 4.11) (Ilyin & Travnikov, 2003). The high contribution of global sources is similar to that in the United States, where it has been estimated that more than 80% of the total deposition is attributable to sources outside the United States. Numerical values for modelled mercury concentrations, depositions and transboundary and intercontinental transport of mercury are available from EMEP/MSC-E by request.

Elemental and divalent gaseous mercury, as well as mercury bound to particles, are emitted as a result of anthropogenic activities, as described above. Because of the chemical stability of elemental mercury, it can be distributed on a global or hemispherical scale before it is eventually oxidized in the atmosphere and deposited (in wet or dry form) on land or water surfaces. Long-range transport of mercury in Europe was first observed in Sweden in the late 1970s. Since then, long-term monitoring activities carried out in Scandinavia have shown a clear gradient for wet deposition of mercury, with elevated fluxes occurring in the south-western part of the region, i.e. closer to the main emission sources in central Europe (Iverfeldt, 1991; Munthe et al., 2001). Similar patterns have been

Fig. 4.11. Relative contribution of non-European sources to mercury deposition in Europe in 1996.



Source: Ilyin & Travnikov (2005).

shown in North America. The Scandinavian studies have also revealed a significant decrease in wet deposition after a reduction in mercury emissions around 1990 (Iverfeldt et al., 1995; Munthe et al., 2001). This means that the situation in northern Europe has improved, although a gradient showing higher levels of mercury deposition in the south is still discernable in Scandinavia. However, at the same time as emissions in Europe have been decreasing, a new trend of increasing mercury emissions in Asia has been observed (Jaffe et al., 2005).

Mercury emissions are due to combustion of coal for power production, and have primarily regional effects. On the other hand, sustained or increasing emissions of mercury also have global consequences. Because of anthropogenic emissions, the atmospheric pool of elemental mercury is probably 2–3 times higher today than it was before industrialization (Lamborg et al., 1999). As a result, mercury deposition has also increased by about the same factor. Mercury deposition is dependent upon geographical precipitation patterns and other meteorological parameters, but is otherwise evenly distributed. Consequently, even remote areas such as the polar regions are affected. The increased deposition has resulted in an increased influx of mercury into lakes. In Europe, this has been documented mainly in Scandinavia, where lakes unaffected by local sources are abundant. Analysis of mercury in lake sediments has clearly shown a regional pattern, with enhanced concentrations in the top layers of the sediments in the southern parts of Finland, Norway and Sweden and gradually decreasing values towards the

north (Verta, 1990; Johansson, 1985; Rognerud & Fjeld, 2001). Compared to the pre-industrial background concentrations (found in the deep layers of the sediments), the concentrations in the surface sediments have increased by a factor of about 5 in southern Scandinavia and by about a factor of 2 or less in the northernmost part of the region.

Methylmercury is known to form in aquatic ecosystems via bacterial methylation of inorganic mercury. It enters the food-chain via organisms living in the sediments, and then undergoes biomagnification though consumption by higher organisms. The processes eventually leading to elevated concentrations of methylmercury in fish are complex and dependent upon the particular characteristics and dynamics of the local ecosystem. Thus, predicting how changes in atmospheric deposition will affect methylmercury levels in fish is not straightforward. For freshwater systems, a model for calculating critical loads of mercury has been developed within the framework of the UNECE Convention on Long-range Transboundary Air Pollution (UNECE, 2004).

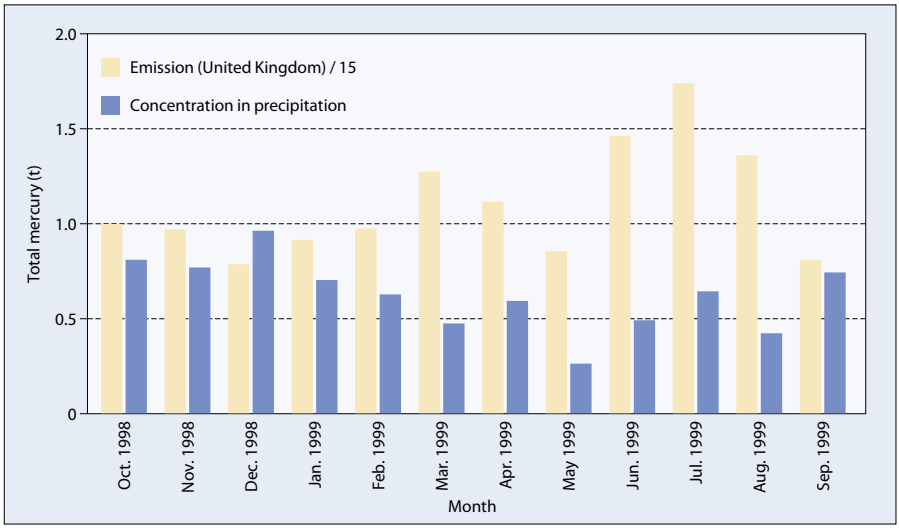
Both monitoring and modelling results indicate decreases in mercury levels in Europe. Mercury levels have decreased by a factor of approximately 1.5–2.0 for Europe as whole. In individual countries, the magnitude of the decrease is estimated to be as high as 3 times. In 1990, modelled mercury concentrations in precipitation across Europe ranged from 6 ng/l to 40 ng/l. In 2003, they were between 6 ng/l and 20 ng/l. The contribution of external anthropogenic sources to depositions of mercury in European countries ranged from about 2% to about 55%; about 25–60% of depositions are caused by sources located outside Europe.

Recent estimates of atmospheric deposition fluxes of mercury into the Mediterranean Sea have shown that dry deposition is the major diffuse source of mercury entering marine ecosystems (Fig. 4.12) compared to wet deposition fluxes (which show a sharp increase during the summer months) (Hedgecock et al., 2006).

Meanwhile, recent findings by Hedgecock et al. (2006) show that the Mediterranean Sea may represent an important source of elemental gaseous mercury released to the atmosphere. The annual emission of gaseous mercury from the Mediterranean Sea estimated with the Integrated Mercury Cycling, Transport and Air–Water Exchange (MECAWEx) model (Hedgecock et al., 2006) was found to be 90 t/a; the value for mercury entering through deposition processes is nearly 20 t/a (Fig. 4.13). These findings suggest that, on the basis of our current knowledge of mercury cycling in the Mediterranean basin, mercury emissions contributed about 70 t/a to the regional and global atmospheric mercury burden.

The MSCE-HM model for mercury was evaluated via uncertainty analysis and comparison of its results with observed data and with the results of other mercury transport models. Analysis of the MSCE-HM model uncertainties for mercury demonstrates that the intrinsic uncertainty of the model (i.e. the uncertainty

Fig. 4.12. Total mercury deposition (dry and wet) across the Mediterranean basin, estimated with the MECAWEx model.



Source: Hedgecock et al. (2006).

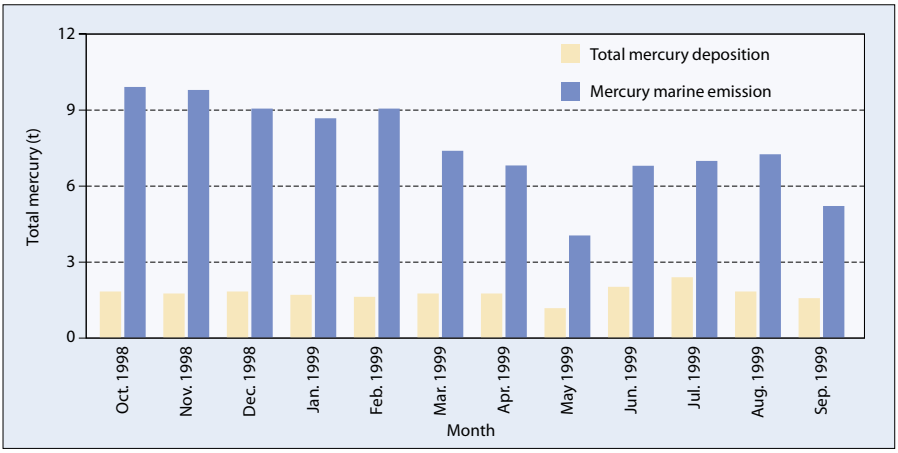
of the model without emission data) varies across Europe from 15% to 20% for concentrations in air, from 30% to 70% for concentrations in precipitation, and from 20% to 60% for total depositions (Travnikov & Ilyin, 2005).

A multi-stage mercury intercomparison study has shown that the models investigated could be used to predict the observed concentrations of elemental mercury with an accuracy of ±20%. The accuracy for wet deposition was within a factor of 2, whereas discrepancies between the models did not exceed 40%. A detailed description of the mercury intercomparison results is available from Ryaboshapko et al. (2002) and from MSC-E reports (Ryaboshapko et al., 2003, 2005).

Concentration levels for mercury in air and in precipitation are reproduced well by the MSCE-HM model using available official emission data and expert estimates. Only a few of the modelled mean annual values for total gaseous mercury concentrations differed from the observed values by more than 30% (Fig. 4.14a). The correlation coefficient is not high; this is explained by the fact that mercury concentrations in air exhibit very low spatial and temporal variability at a regional level. This degree of variability is comparable with the uncertainties of the model. As much as 80% of the modelled values for mercury concentrations in precipitation agreed with actual measurements (i.e. were ±50% with respect to the measured value) (Fig. 4.14b). However, the model tends to somewhat overestimate mercury concentrations in precipitation. A more detailed analysis of the comparison of modelled and measured mercury concentrations is presented by Ilyin & Travnikov (2005).

The results of the model verification were discussed in detail in the TFMM workshop (Moscow, October 2005). The workshop was devoted to the review

Fig. 4.13. Total mercury deposition to, and mercury emission from, the Mediterranean basin, estimated with the MECAWEx model.



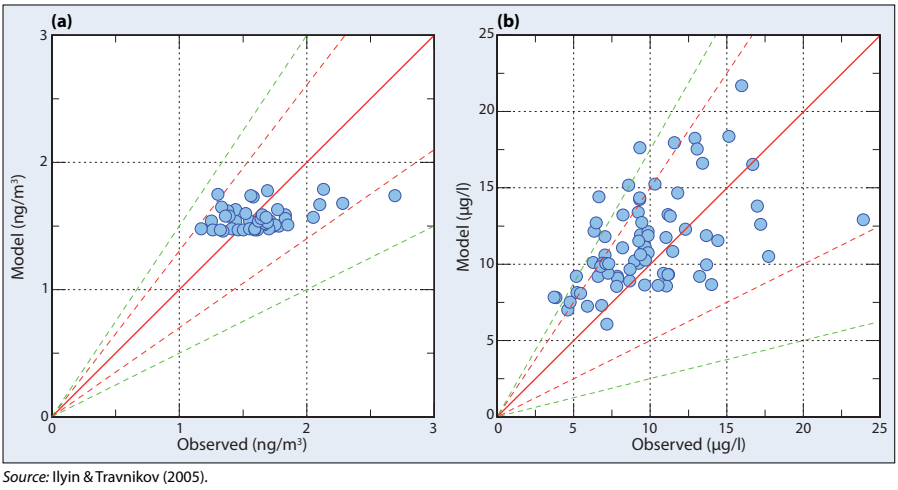
Source: Hedgecock et al. (2006).

of the EMEP/MSCE-HM model, and concluded that the "MSC-E model is suitable for the evaluation of long-range transboundary transport and depositions of heavy metals in Europe" (UNECE, 2006c).

4.1.4. Mercury in soils

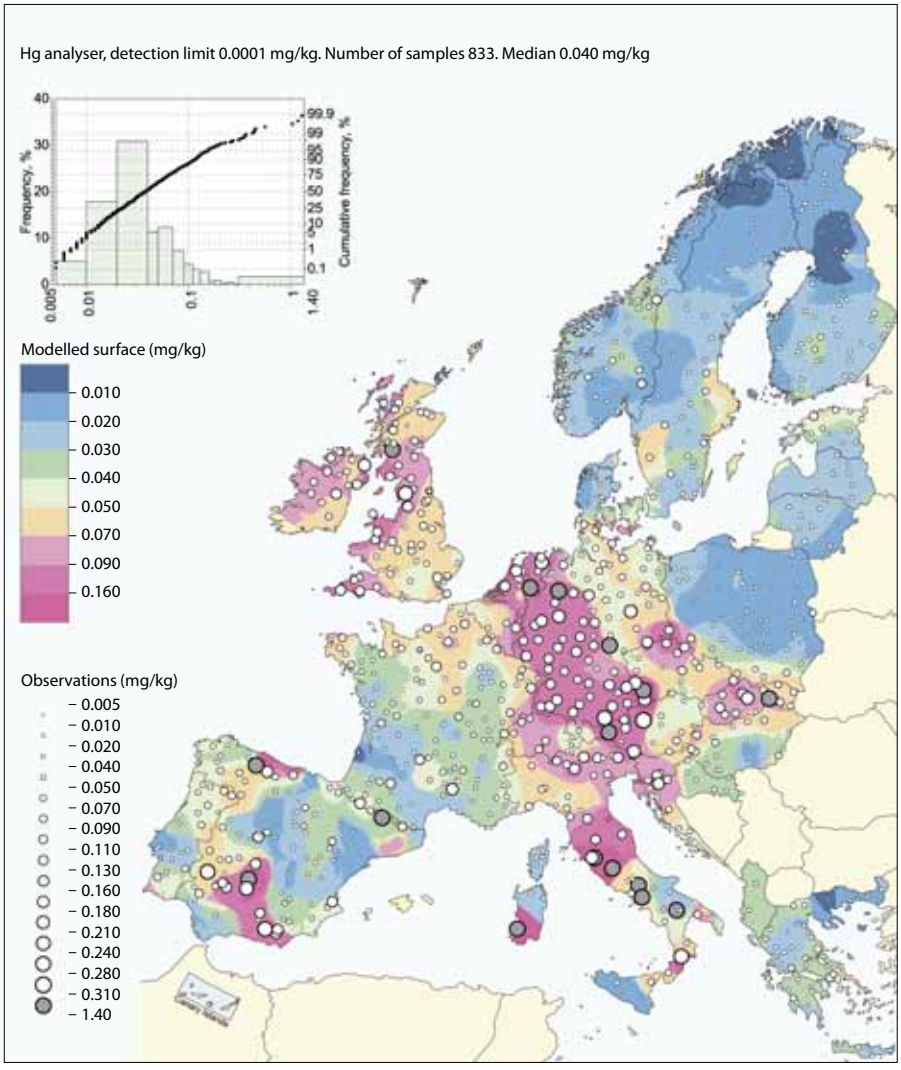
The average mercury content of surface soils from a number of countries ranged from 20 µg/kg to 625 µg/kg. The highest concentrations were found in soils from urban locations. The mercury content of most soils varies with depth, the highest

Fig. 4.14. Comparison of annual mean modelled and observed total gaseous mercury concentrations in air (a) and total mercury concentrations in precipitation (b) for 1990–2003. Solid lines, 1:1 ratio; broken lines: (a) deviation ±30% (red) and ±50% (green), (b) deviation ±50% (red) and ±75% (green).



Source: Ilyin & Travnikov (2005).

Fig. 4.15. Concentrations of mercury in topsoil; observations from field measurements and modelling.



Source: Salminen et al. (2005).

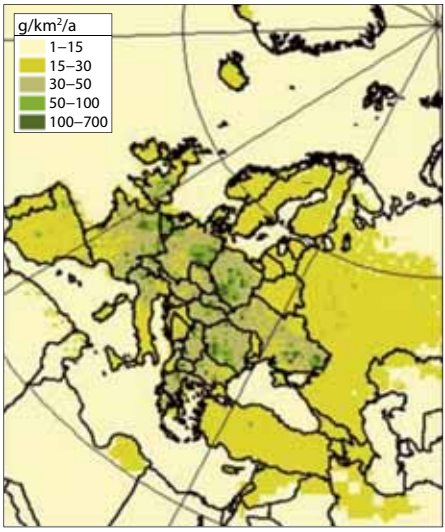
mercury concentrations generally being found in the surface layers (ATSDR, 1999). In the topsoils of Europe, mercury concentrations range from 10 μg/kg to 160 μg/kg, reaching a median value of 40 μg/kg (Fig. 4.15).

Mercury is deposited on the soil mainly in the form of inorganic compounds, which are readily bound to organic matter (Fig. 4.16). The important processes involving mercury in the soil are revolatilization, methylation and mobilization to the aquatic environment. Revolatilization occurs after reduction of the mercury to the elemental form, and is dependent on environmental parameters such as sunlight, temperature and humidity (e.g. Xiao et al., 1991; Zhang & Lindberg,

1999; Lindberg et al., 2002). Volatilization occurs at a higher rate in soils with naturally high mercury content (Gustin et al., 2003).

A very small fraction of the mercury in soils can also be methylated to form monomethylmercury. Methylation mainly occurs under anaerobic conditions via sulfate-reducing bacteria. Thus, methylation in soils occurs mainly in wetlands or other water-rich soils. The mobility of mercury bound to organic matter in soils is very low, which has led to an accumulation in, for example, forest soils in northern Europe. The release of mercury from soils into the aquatic environment is only a fraction of the atmospheric input to the soil but may still constitute an important source to lake ecosystems, for example.

Fig. 4.16. Total mercury deposition in 1998.



Source: Ilyin et al. (2000).

4.1.5. Mercury in water

The total concentrations of mercury in natural waters are low. Representative values for dissolved total mercury are: open ocean 0.5–3 ng/l; coastal seawater 2–15 ng/l; freshwater lakes and rivers 1–3 ng/l. The concentration range for mercury in drinking-water is, on average, about 25 ng/l (WHO/IPCS, 1990). The WHO guideline value is 1 µg/l (WHO, 2004).

Mercury is transported to freshwater mostly bound to dissolved and particulate organic matter. In lakes, a proportion of the mercury can be transformed to the methylated form. This, together with input from catchment soils, constitutes the main source of methylmercury, which can accumulate in aquatic food-chains. The major fraction of the inorganic mercury remains bound to organic matter and may be buried in sediments. The fraction of the mercury that is methylated, and the subsequent uptake and bioaccumulation in the food-chain, varies greatly and, to a large extent, depends on ecosystem characteristics in addition to the mercury load.

Balance between influx and outflux of mercury in soil and lake systems

Atmospheric deposition is considered as the predominant source of mercury input to most soils and lakes in the boreal forest zone (Lindqvist et al., 1991). Such deposition has increased from 2-fold to more than 20-fold over the last few centuries because of anthropogenic emissions and subsequent dispersal at local,

regional and global levels. For example, in Sweden, attention has focused on the alarmingly high mercury levels found in lake fish, as the values exceed the advisory health guidelines in tens of thousands of lakes (Håkanson et al., 1988, 1990; Lindqvist et al., 1991; Andersson & Lundberg, 1995). The future situation regarding mercury loading in lakes in boreal regions of Europe will depend on both future deposition and changes in the leaching of mercury and methylmercury from catchment soils. Atmospheric inputs are far greater than the stream-based outputs from most catchments, and mercury is efficiently accumulated in soils. Future loading is thus dependent on the long-term stability of this soil-bound mercury.

In connection with the development of concepts for critical load calculations for mercury, a model relating the concentrations in precipitation to the methylmercury concentrations in fish has been developed (Meili et al., 2003a,b; UNECE, 2004). The aim of the modelling is to estimate the mercury concentration in precipitation that is allowable in order to limit the methylmercury concentration in fish to <0.5 mg/kg (i.e. the EU recommended general limit value for fish). The model data indicate that the maximum tolerable concentration in precipitation is about 2 ng/l, which is about half the current level found in remote areas. More recent evaluations of health impacts indicate that a lower limit value of 0.3 mg/kg (JECFA, 2003; USEPA, 2001) is more appropriate, which would suggest that the lower tolerable concentration in precipitation should be lower.

4.2. Pathways of human exposure and their relationships to LRTAP

Methylmercury and dimethylmercury are among the most toxic chemical species of mercury and are generally of the greatest concern from a human perspective. Human exposure to methylmercury occurs mainly through the diet, more specifically from the consumption of fish. Humans are also exposed to elemental mercury vapour and other inorganic mercury species. The major route of non-occupational exposure to inorganic mercury is via dental amalgam fillings; the contributions from breathing ambient air and consuming drinking-water are insignificant. The use of skin-lightening creams and soaps containing mercury compounds also constitute a source of exposure in some countries. This may occur through penetration of the skin and also via inhalation of mercury vapour (Al-Saleh & Al-Doush, 1997).

The mercury concentration in air is, in most areas, close to the mean global background value, which is 1.5–2.0 ng/m^3 (Slemr et al., 2003). In Europe, the highest background concentration of total gaseous mercury is found in central Europe. No regular measurements, such as those performed within the EMEP network, are performed in these counties. Hence, information on atmospheric mercury is limited. However, measurements in a remote area in southern Poland showed that the concentration of total gaseous mercury was 2–10 ng/m^3, with

the highest concentrations occurring during the wintertime. The elevated total gaseous mercury levels are due to coal combustion used for domestic heating (Zielonka et al., 2005). Emission from coal-fired power plants in the area also contributes to the elevated mercury concentrations. The mercury concentrations close to anthropogenic emission sources in many western European urban areas can also reach 10 ng/m^3 or more. However, in this case also, very few data are available. Nevertheless, except for occupationally exposed individuals, exposure due to inhalation for the vast majority of the population is likely to be negligible. This means that, in general, mercury in the air does not represent an important source of human exposure.

Dental amalgam fillings release mercury vapour into the oral cavity (Clarkson et al., 1988a,b; Skerfving, 1991). The resulting concentrations in the intra-oral air substantially exceed those found in the ambient atmosphere. Dental amalgam constitutes the most significant route of exposure from elemental mercury. It has been estimated that the average daily amount of mercury entering the pulmonary system ranges from 3 μg to 17 μg (WHO/IPCS, 1991; Risher, 2003; Berglund, 1990; Lorscheider et al. 1995; Sandborgh-Englund, 1998), although higher levels of uptake sometimes occur (Barregård et al., 1995; Sallsten et al., 1996).

The concentration of mercury in drinking-water is normally very low (below 1 ng/l). Values of up to 25 ng/l are reported (WHO/IPCS, 1990). On the basis of the assumption that an adult consumes about 2 litres of water per day, the daily intake of mercury from drinking-water is less than 50 ng/day. The WHO guidelines and much national legislation set the limit at 1000 ng/l (WHO, 2004).

The average mercury concentration in surface soil is reported to be 20–625 μg/kg (Reimann & de Caritat, 1998). Higher concentrations are reported in soils from urban locations and from those close to sources of mercury pollution (smelting, mining or coal-burning facilities, the chloralkali industry, etc.). In Europe, very little knowledge is available concerning the direct exposure of humans to mercury in soils.

In most foodstuffs, the mercury concentration is below 0.02 mg/kg. Cattle are able to demethylate mercury in the rumen and, consequently, beef and milk contain very low concentrations of mercury. Fish is different, however, as mercury bioconcentrates in aquatic organisms and is biomagnified in aquatic food-chains. For example, the concentration of mercury in small fish (such as anchovies) that are low down in the food-chain have levels below 0.085 mg/kg, while in swordfish, shark and tuna, values above 1.2 mg/kg are frequently reported (WHO/IPCS, 1990). Up to 100% of the mercury in swordfish and tuna can be in the form of methylmercury (Storelli et al., 2003). Total mercury concentrations in the range 0.38–6.5 mg/kg have been found in tuna and shark from the Mediterranean Sea (Storelli et al., 2001). In Scandinavian predatory freshwater fish (perch and pike), the average mercury levels are about 0.5 mg/kg. Elevated mercury levels are also found in fish from the Arctic region. Higher methylmercury concentrations in

marine mammals can cause high levels of exposure in some human population groups. The mean concentrations for total mercury in the livers of ringed seals are in the range 1–20 mg/kg wet weight (AMAP, 2002).

Exposure to methylmercury among pregnant women in Sweden (measured within the national environmental health monitoring programme) indicated an intake well below the USEPA reference dose of 0.1 g/kg_{bw}/day (Berglund et al., 2001; Rödström et al., 2004; Gerhardsson et al., 2005). Between 1% and 5% of the pregnant women had a higher level of exposure (hair mercury (H-Hg), >1 μg/g; Barregård, 2006). Moreover, in Northern Europe in populations consuming freshwater fish frequently, a much higher intake of methylmercury is common, resulting in higher blood mercury levels and H-Hg levels (Björnberg et al., 2005; Johnsson et al., 2004, 2005). In Mediterranean coastal areas, the average intake is also higher (Evens et al., 2001), and in certain subpopulations with high levels of fish consumption it is much higher still (Murata et al., 1999; Carta et al., 2003).

To safeguard public health, limits on total mercury levels in seafood have been established in various countries. The United States Food and Drug Administration has set a maximum total mercury limit of 1 mg/kg wet weight for fish. In Europe, a value of 0.5 mg/kg was set by the European Commission in 1993, although exemptions have been made for some commercially important species (for which the limit has been set at 1 mg/kg). In Japan, fish with total mercury concentrations higher than 0.4 mg/kg are considered unfit for human consumption.

The estimated daily intake of mercury in the general population is shown in Table 4.1 (WHO/IPCS, 1990). Fish and fish products are the predominant sources of human exposure to methylmercury. This is also the case when low levels of fish consumption are assumed, as in Table 4.1. The uptake of elemental mercury from amalgam fillings appears to be significant (Bellinger et al., 2006; de Rouen et al., 2006) but exposure to mercury from air (via breathing) is not. The numbers given in Table 4.1 were calculated on the assumption that the total concentration of mercury is 2 ng/m^3, which is valid for the northern hemisphere. The uptakes of inorganic mercury and methylmercury were estimated on the assumption that the contributions from these two species to the total mercury concentration are 5% and 20%, respectively; however, subsequent measurements have indicated that the ambient concentrations of methylmercury and inorganic mercury are at least a factor of 10 lower than these values.

4.2.1. Contributions of LRTAP to methylmercury concentrations in fish

As a result of increased transport of mercury to lakes, concentrations in fish increased during the last century. In the southern parts of Finland, Norway and Sweden, the mercury content in a 1-kg pike (*Esox lucius*) is about 0.5–1.0 mg/kg; the natural background value is estimated at about 0.2 mg/kg (Verta, 1990;

Table 4.1. Estimated average daily intake (retention is shown in parentheses) of total mercury (ng/day) in the general population not occupationally exposed to mercury.

Exposure	Elemental Hg vapour	Inorganic Hg compounds	Methylmercury	References
Air	30 (24)	2 (1)	n/a[a]	WHO/IPCS (1990)
Dental amalgam	1 200–27 000 (1 000–22 000)	0	0	ATSDR (1999)
Food				
Fish	0	600 (42)	2 400[b] (2 300)	WHO/IPCS (1990)
Non-fish	0	3 600 (250)	0	WHO/IPCS (1990)
Drinking-water	0	50 (35)	0	WHO/IPCS (1990)
Total retained	(1 000–22 000)	(330)	(2 300)	

[a] Not applicable.
[b] 2 400 ng/day is based on an example of a moderate level of consumption of uncontaminated fish (e.g. a 150-g fish meal per week, with a methylmercury concentration of 0.11 µg/g). The figure will, of course, vary with fish consumption and with the level of contamination (typically 500–20 000 ng/day).

Source: WHO/IPCS (1990).

Johansson et al., 2001; Rognerud et al., 1996). The recommended limit of 0.5 mg/kg is exceeded for 1-kg pike in about 50% of the lakes in Sweden and in 85% of the lakes in southern and central Finland (Lindqvist et al., 1991; Verta, 1990).

4.2.2. European and global trends in exposure

In recent years, emissions of mercury into the air in Europe have been declining. The decrease in mercury emissions in 1990–1996 in 39 countries ranged from 0% to - 56%. In contrast, emissions increased by up to 3% in only five countries: for example, the emission rate in the Russian Federation decreased from 15.6 t/a in 1990 to 10.1 t/a in 1996, and in Bulgaria, emissions decreased from 13.2 t/a to 4.7 t/a over the same period (Ryaboshapko et al., 1999).

The possibility of adverse effects on neurological development due to fetal methylmercury exposure has great significance for aboriginal communities. From the early 1970s to 1996, Health Canada was involved in a sampling programme for detecting methylmercury in blood and hair in First Nations and Inuit communities across Canada. Blood levels below 20 µg/l (6 µg/g in hair) were classified as within the acceptable range, and levels greater than 100 µg/l in blood (30 µg/g in hair) as "at risk" (Wheatley et al., 1979). A blood mercury concentration of 200 µg/l is the level at which the most sensitive 5% of a population might begin to show early signs of methylmercury toxicity, such as paraesthesia (WHO/IPCS, 1976).

The percentage of results at or above the "at risk" level of 100 µg/l has been steadily falling. Up to 1978, 2.54% of results were in the "at risk" category. Between 1979 and 1982, only 0.4% were in this category, and between 1983 and 1996, this figure dropped further to 0.3%. Between 1983 and 1996, 28 individuals had levels of 100 µg/l or more, but no such levels have been reported since 1989.

Concern about fetal exposure to methylmercury led to a focus of attention on the levels in maternal blood and fetal cord blood in populations living in areas in which elevated levels in adults were reported. From 1983 to 1996, the percentages for cord-blood levels (i.e. fetal blood) fell almost 10-fold, from 21.5% to 2.6% (Health Canada, 1999). Of the Northwest Territories women who participated, 30% had levels higher than 10 μg/l (Wheatley & Paradis, 1996). Recent survey results show that the levels of total mercury in maternal hair in most northern populations is declining (Van Oostdam et al., 2005).

4.3. Health hazard characterization

Globally, it is recognized that mercury and its compounds are highly toxic substances, but there is ongoing debate as to the degree of toxicity, especially with regard to methylmercury. New epidemiological findings from the past decade suggest that toxic effects may be taking place at lower concentrations than previously considered, such that a larger proportion of the global population is potentially being affected. Consequently, the determination of a safe level of exposure is a very complex matter, as demonstrated in the global mercury report of the United Nations Environment Programme (UNEP, 2002).

4.3.1. Elemental and inorganic mercury

Elemental mercury is poorly absorbed by the skin and from the intestines. Intestinal absorption varies greatly depending on the form of mercury involved, with the elemental form being the least well-absorbed form (0.01%) (Risher, 2003). Approximately 80% of the inhaled Hg^0 vapour is absorbed through the lungs and is rapidly transported to other parts of the body, including the brain and the kidneys. It readily crosses the blood–brain and placental barriers. Elemental mercury vapours in the blood of pregnant women can be passed on to the developing fetus, where it can be concentrated. Once in the body, most of the Hg^0 will accumulate in the kidneys and, to a lesser extent, the brain, where it is readily converted to an inorganic form. More mercury is deposited in the brain after exposure to Hg^0 than after exposure to inorganic mercury compounds. The estimated half-life of Hg^0 in the body is approximately 60 days (WHO, 2003).

When inorganic mercury compounds (salts) are ingested, generally less than 10% is absorbed through the intestinal tract, but the gastrointestinal absorption rate varies substantially depending on the chemical compound in question. Under certain rare conditions, such as in the presence of bleeding ulcers, up to 40% of the inorganic mercury can be absorbed into the body through the lesions in the stomach and/or intestines. Smaller amounts of inorganic mercury can be absorbed through the skin, but ingestion is the main pathway into the body. Absorbed inorganic mercury accumulates in the kidneys but does not cross placental or blood–brain barriers as easily as Hg^0 or methylmercury. However, inorganic mercury does accumulate in placental tissues. In a nursing mother, some of the

inorganic mercury from her body will be passed to the child through the breast milk (Risher, 2003).

The majority of inorganic and elemental mercury is excreted in urine and faeces over a period of several weeks to months. Smaller amounts of absorbed Hg^0 vapours exit the body more rapidly, via exhaled breath and through perspiration. The half-life in the whole body is within the range 29–60 days, with an average of 42 days for inorganic mercury. Concentrations in urine and blood have been extensively used in the biological monitoring of exposure to inorganic forms. Mercury levels in hair do not reliably reflect exposure to Hg^0 or inorganic mercury compounds (Risher, 2003).

4.3.2. Methylmercury

Methylmercury is easily and efficiently absorbed through the gastrointestinal tract into the blood stream, where it is rapidly transported to other parts of the body. About 95% of the methylmercury ingested through fish consumption is absorbed in the gastrointestinal tract (Clarkson, 2002). In the bloodstream, more than 90% of the methylmercury accumulates in red blood cells and plasma, where it is mainly bound to the plasma proteins (Kershaw et al., 1980). Approximately 5% of the body burden is found in the blood compartment and about 10% settles in the brain (National Research Council, 2000).

Methylmercury can be metabolized to inorganic mercury, which accumulates primarily in the kidneys. Kidney levels of inorganic mercury tend to build up after long-term exposure to methylmercury. Methylmercury is also converted to inorganic mercury in the brain. Elevated concentrations of inorganic mercury have been found in autopsy brain samples from people who died many years after an acute exposure to methylmercury (Davis et al., 1994). The inorganic mercury is believed to be in an inert, insoluble form that can remain in brain tissues for many years, perhaps for the lifetime of the individual (WHO/IPCS, 1990). The toxicological role of the inert, insoluble form remains a matter of some debate (Clarkson, 2002).

Methylmercury is excreted slowly over a period of several months, mostly as inorganic mercury in the faeces. It may take 45–70 days for the methylmercury concentrations to fall by a half in a person's blood, and 70–80 days in the entire body, but substantial variations in time-scale can occur (Nielsen & Grandjean, 2000). The kidneys retain the highest tissue concentrations of mercury, though the total amount deposited in muscles can be higher. Methylmercury also accumulates in hair. The brain–blood concentration ratio ranges from 3:1 to 6:1, and the hair–blood concentration ratio is approximately 250:1 in humans at the time of incorporation of the mercury into the hair (WHO/IPCS, 1990; Nielsen & Grandjean, 2000).

The mean total mercury level in blood in the general population is approximately 1–8 μg/l (ATSDR, 1999; CDC, 2005). The International Commission on

Occupational Health and the Commission on Toxicology of the International Union of Pure and Applied Chemistry determined, using a meta-analysis of published studies, that the the background blood level (mean value) in persons who do not eat fish was 2 μg/l (Nordberg et al., 1992). This background value represents the average level in blood in the general population. However, in populations of people without dental amalgam and who do not consume fish, the blood mercury levels are even lower. Nevertheless, in communities with high fish consumption, individuals have been estimated to have blood levels of 200 μg/l associated with a daily mercury intake of 200 μg/day (WHO/IPCS, 1990).

Hair is a biomarker of long-term exposure to methylmercury. Once mercury is incorporated into the hair, it remains unchanged. The H-Hg level is dependent on the amount of fish consumed. The background level of H-Hg associated with little or no fish consumption or with the consumption of fish with low methylmercury concentrations is approximately 0.25 μg/g in Germany (Drasch et al., 1997), 0.28 μg/g in the north of Sweden (Oskarsson et al., 1996) and 0.38 μg/g in Hong Kong (Dickman & Leung, 1998). Much higher H-Hg levels can result from the consumption of large amounts of fish or sea mammals. In the population of the Faroe Islands, the mean H-Hg level ranges from 1.6 μg/g (based on one fish meal per week) to 5.2 μg/g (based on four fish meals per week) (Grandjean et al., 1992). In fishermen from Madeira and their families, levels of 38.9 μg/g (men) and 10.4 μg/g (women) were found (Renzoni et al. 1998).

4.3.3. Health effects caused by mercury exposures

Elemental and inorganic mercury

The majority of the extensive literature on the health effects of mercury in humans and animals focuses on inhalation exposure to metallic Hg vapours (Hg^0). There is limited information on adverse effects from dermal exposure from ointments and creams that contain inorganic mercury compounds (ATSDR, 1999). The effects of exposure to Hg^0 in the occupational setting have been assessed, both for acute and long-term exposures. Data are available on accidental exposure in the general population and on low-level exposure from dental amalgams. The available information on Hg^0 and inorganic mercury is primarily based on Risher (2003) and UNEP (2002).

Acute poisoning following exposure to mercury vapour at high levels (more than 1000 $\mu g/m^3$) for a short period can cause severe irritation of the airways, pneumonitis, pulmonary oedema and other symptoms of lung damage. It can damage the brain, nerves, kidneys and lungs and, in extreme cases, can cause coma and/or death. Workers exposed to mercury vapour for 4–8 hours because of an accident experienced chest pains, dyspnoea, coughing, haemoptysis and impairment of pulmonary function (McFarland & Reigel, 1978).

Following chronic exposure to low levels of mercury vapour (50–100 $\mu g/m^3$), it can take some time for adverse effects on the central nervous system, kidneys

and thyroid to develop, and the effects can be subtle. It is difficult to distinguish mercury toxicity symptoms from those of some other common ailments. The symptoms include tremors, muscular weakness, depression, personality changes and short-term memory loss in adults, and skin rashes, particularly redness and peeling of the hands and feet, in children. Acute poisoning from inorganic mercury compounds or mercury salts is rare, except in cases of accidental ingestion. Chronic occupational exposure to mercury salts has been associated with effects on the central nervous system that are similar to those associated with exposure to Hg^0 vapour (ATSDR, 1999; Clarkson, 2002; UNEP, 2002). Table 4.2 summarizes the major effects of Hg^0 and inorganic mercury (i.e. mercury salts).

Neurotoxic effects have been reported among chloralkali workers exposed to mercury for many years. These people scored lower on verbal and memory tests than the members of a control group, but advanced statistical analyses were not done (Piikivi et al., 1984). Reports on accidental exposures to high concentrations of mercury vapour, as well as studies on populations chronically exposed to potentially high concentrations, have shown effects on a wide variety of cognitive, sensory, personality and motor functions (USEPA, 1997). Symptoms have been observed to subside after of the cessation of exposure. However, persistent effects (tremors, cognitive deficits) have been observed in occupationally exposed subjects 10–30 years after cessation of exposure (UNEP, 2002). In an assessment of studies on inhaled mercury-vapour exposure, Risher (2003) concluded that subtle effects on the central nervous system occur in people with long-term occupational exposure to mercury vapour at levels of approximately 20 $\mu g/m^3$ or more. A review of 18 epidemiological studies dealing with occupational exposure to inorganic mercury in workers with mean levels of internal exposures in the range 3–192 μg/g creatinine showed associations between attention, memory and motor performance and exposure (Meyer-Baron et al., 2004). However, quantitative dose–response relationships could not be established.

Evstafyeva (2003) investigated 72 teenagers (aged 15 years) in Simferopol, Ukraine, and revealed statistically significant changes in brain function (wave latencies, amplitudes) with increasing mercury concentration in hair (0.06–0.3 μg/g). Spectral analysis of brain activity revealed a negative correlation between low- and mean- frequency electroencephalogram rhythms and mercury content in the air (Pavlenko et al., 2000).

On the basis of the neurobehavioural effects observed in subjects in occupational settings, time-weighted average concentrations ranging from 23 $\mu g/m^3$ to 33 $\mu g/m^3$ were designated as the LOAELs for workers in an industrial exposure setting. Neurobehavioural effects have also been reported at levels as low as 14 $\mu g/m^3$ in dentists (Ngim et al., 1992). Conversion to general environmental conditions (24 h/day, 365 d/year, 70-year lifespan) results in LOAELs ranging from 6 $\mu g/m^3$ to 12 $\mu g/m^3$ (mean 9 $\mu g/m^3$). Increasing hostility ($r = 0.41$, $P<0.05$) and anxiety levels ($r = 0.37$, $P<0.05$) and decreasing mental stability ($r = -0.41$,

Table 4.2. The major effects of different forms of mercury.

	Form of mercury			
	Elemental	**Inorganic**	**Methylmercury**	**Ethylmercury**
Route of exposure	Inhalation	Oral	Oral (from fish consumption)	Parenteral (through vaccines)
Target organ	Central nervous system, peripheral nervous system, kidney	Kidney	Central nervous system	Central nervous system, kidney
Local clinical signs				
Lungs	Bronchial irritation, pneumonitis[b]	–	–	–
Gastrointestinal tract	Metallic taste, stomatitis, gingivitis, increased salivation[a]	Metallic taste, stomatitis, gasteroenteritis	–	–
Skin	–	Urticaria, vesication	–	–
Systemic clinical signs				
Kidney	Proteinuria	Proteinuria, tubular necrosis, acrodynia	–	Tubular necrosis
Peripheral nervous system	Peripheral neuropathy[c]		–	Acrodynia
Central nervous system	Erethism,[b] tremors	–	Paraesthesia, ataxia, visual and hearing loss[c]	Paraesthesia, ataxia, visual and hearing loss
Approximate half-life in whole body	60 days	40 days	70 days	20 days in adults; 7 days in infants

[a] Toxicology of mercury at >1000 μg/m^3 of air.
[b] Toxicology of mercury at >500 μg/m^3 of air.
[c] Toxicology of mercury at >200 μg/l blood.

Source: Clarkson et al. (2003).

P<0.05) and inferiority complex (r = – 0.38, P<0.05) were observed in 72 teenagers aged 15 years (Pavlenko et al., 2000; Evstafyeva, 2003).

Although several studies have reported that some mercury from dental amalgam fillings is absorbed into the body, no relationship was observed between the mercury release from amalgam fillings and the mercury concentration in the

brain (Saxe et al., 1999; Maas et al., 1996; Bellinger et al., 2006; de Rouen et al., 2006). Current evidence does not indicate that mercury exposure from dental amalgam is causing illness in the general public (Brownawell et al., 2005; Health Canada, 2004; Risher, 2003).

With regard to renal effects, the primary result of long-term oral exposure to low amounts of inorganic mercury compounds is renal damage. The kidney is also a critical organ with regard to exposure to mercury vapour. Elemental mercury can be oxidized in bodily tissues to the inorganic divalent form, which accumulates in the kidney. Occupational exposure at high levels can cause glomerulonephritis with proteinuria and nephritic syndrome, but there are relatively few reported cases of this (UNEP, 2002), and proteinuria is more common.

The possible long-term implications of tubular proteinuria are still unclear (Järup et al., 1998). Increased mortality from nephritis and nephrosis was reported in European male mercury miners (Boffetta et al., 2001), whereas no association was found in chloralkali workers (Barregård et al., 1990; Ellingsen et al., 1993). Recently, a WHO review concluded, on the basis of existing studies, that adverse effects on the kidney usually occur at exposures higher than those that induce neurophysiological effects (Risher, 2003). The data from humans do not allow identification of the lowest harmful or non-adverse exposure levels, especially for long-term exposure.

Exposures of longer duration, due to spills or occupational exposure, have been reported to result in increased blood pressure and increased heart rate (Risher, 2003). European mercury miners experienced increased mortality from hypertension (standardized mortality rate 1.46; 95% CI 1.08–1.93) and from heart disease (other than ischaemic disease) (1.36; 95% CI 1.20–1.53). These effects increased with increasing employment period and with estimated cumulative mercury exposure. However, such findings are not consistent among countries. No increases were reported for ischaemic heart disease or cerebrovascular diseases (Boffetta et al., 2001). An investigation with 25 teenagers (aged 15 years) showed no associations (at rest) between haemodynamic parameters and a mercury level in the hair (Evstafyeva, 2001) varying from 0.06 μg/g to 0.3 μg/g. However, at physical load, a correlation was found between mean blood pressure and the amplitudes of change in total peripheral resistance ($r = -0.49$, $P<0.02$; $r = 0.47$, $P<0.05$, respectively).

No association was found between mortality from respiratory failure and mercury exposure among workers exposed in the chloralkali industry (Barregård et al., 1990; Ellingsen et al., 1993), although the strength of the studies was low (UNEP, 2002). Merler et al. (1994) reported no excess mortality from respiratory disease in workers exposed to mercury in the fur hat industry. This was also true for European mercury miners, except for pneumoconiosis (Boffetta et al., 2001).

Elemental mercury crosses the placental barrier. From a toxicological point of view, effects on reproduction as well as on fetal brain development would not be

surprising. To date, however, studies have not provided support for the existence of such effects (WHO/IPCS, 1990; Risher, 2003).

There is no sound evidence from epidemiological studies indicating that inhalation of elemental mercury is associated with cancer in humans. Pirrone et al. (2001b) found lung cancer to be the only cancer that was consistently more frequent among various groups of workers exposed to metallic and inorganic mercury. However, possible co-exposure to other lung carcinogens, in particular arsenic (in the fur industry), radon and silica (among miners), and universal lack of data on tobacco smoking in workers are the principal limitations in the interpretation of these data. An increased number of brain cancers was observed in Swedish dentists and dental nurses (Ahlbom et al., 1986; McLaughlin et al., 1987), but no increased risk of overall cancer mortality or of brain cancer was observed among veterans in the dental profession of the United States Armed Forces (Hrubec et al., 1992). A Norwegian study on chloralkali workers exposed to levels of mercury that were orders of magnitude higher did not find an association between mercury levels and brain cancer (Ellingsen et al., 1993).

IARC (1993) reported that there was inadequate evidence in experimental animals with regard to the carcinogenicity of metallic mercury and that there was limited evidence in experimental animals for the carcinogenicity of mercuric chloride. IARC concluded that metallic mercury and inorganic mercury compounds are not classifiable (Group 3) with respect to their carcinogenicity in humans (IARC, 1993). USEPA has reviewed the carcinogenicity of mercury and has designated it as a Group D (non-classifiable) chemical.

The thyroid can accumulate mercury from chronic exposure to the elemental form (WHO/IPCS, 1991; Barregård et al, 1994; Falnoga et al., 2000; Ellingsen et al, 2000). However, no significant effects on the overall function of the thyroid have been reported. Some studies in workers occupationally exposed to medium levels of elemental mercury reported changes in the biochemistry of the immune response system (Pirrone et al., 2001b).

In the early 1950s, acrodynia or "pink disease" (causing pink cheeks, severe joint pains and photophobia) was reported in children exposed to calomel (mercurous chloride in teething powder) and/or metallic mercury vapour (Warkany & Hubbard, 1953). Mercurous chloride is no longer used in teething powder. Children are seldom exposed to high levels of mercury vapour except by accident.

Toxicity of methylmercury

The scientific evidence indicates that exposure to methylmercury is more dangerous for young children than for adults. This is because of the lower thresholds for neurological effects from methylmercury and the higher levels of distribution of methylmercury to the developing brains of young children, which can result in interference with the development of motor and cognitive skills (UNEP, 2002).

The most accurate overall dose–response curves for methylmercury originate from tragic incidents that involved the deaths of hundreds of people in Iraq in the 1970s (WHO/IPCS, 1976, 1990).

Methylmercury was implicated in the severe neurological impairment of individuals in the vicinity of Minamata Bay, Japan, during the 1950s, 1960s and 1970s. Since then, a considerable body of evidence from both human poisonings and experimental animal studies has accrued. The action of methylmercury on adults is characterized by a latent period between exposure and the onset of symptoms. The latency period can vary from several weeks to months depending on the dose and exposure period (Clarkson, 2002). In adults, the earliest effects are non-specific symptoms such as paraesthesia, malaise and blurred vision; with increasing exposure, there are signs such as constriction of the visual field, deafness, dysarthria and ataxia, ultimately leading to coma and death (Harada, 1995).

The symptoms of Minamata disease include the following: sensory disorders in the extremities (loss of sensation in the hands and feet); ataxia (difficulty in coordinating the movements of hands and feet); narrowing of the field of vision; hearing impairment; difficulty in maintaining balance; and speech impediments. In very severe cases, victims fall into a state of disorientation and confusion, lose consciousness and may die. In relatively mild cases, the condition is barely distinguishable from other ailments such as headaches, chronic fatigue and a generalized inability to distinguish tastes and smells.

In infants exposed to high levels of methylmercury during pregnancy, the clinical picture can be indistinguishable from cerebral palsy caused by other factors, the main pattern being microcephaly, hyperreflexia and gross motor and mental impairment, and, in rare cases, blindness or deafness (Harada, 1995; Takeuchi & Eto, 2000). In milder cases, the effects may only become apparent at a later stage, taking the form of psychomotor and mental impairment and persistent pathological reflexes (IPCS, 1990; National Research Council, 2000).

From methylmercury-associated poisonings in Iraq and Japan, it is known that the most severe effects take place in the development of the brain and nervous system of the unborn fetus. A series of large epidemiological studies have provided evidence that methylmercury from the consumption of fish by pregnant women, even at low mercury concentrations (i.e. about 1/10th to 1/5th of the observed effect levels in adults), may have subtle, persistent effects on the children's mental development (National Research Council, 2000).

Investigations on the risks from prenatal exposure have been carried out in Canada (McKeown-Eyssen et al., 1983), Peru (Marsh et al., 1995), New Zealand (Kjellström et al., 1986), the Faeroe Islands (Grandjean et al., 1997) and the Seychelles (Davidson et al., 1998; Myers et al., 1995, 1997, 2003). Table 4.3 shows methylmercury concentrations in the hair of pregnant mothers whose children showed some neurological deficit in these studies. In the Canadian study,

although there was a suggested link between "abnormal reflexes" and mercury exposure, the authors acknowledged that the results were of doubtful clinical significance. A further analysis of the dataset suggested that there were no prenatal effects (Marsh et al., 1995). A maternal H-Hg level above 6 μg/g was associated with lower IQs (from 93 to 90) in children in the New Zealand study (Kjellström et al., 1989).

The most comprehensive investigations performed so far are the studies that were conducted in the Seychelles (Davidson et al., 1998; Myers et al., 1995, 1997, 2003) and the Faeroe Islands (Grandjean et al., 1997). Using multiple regression analyses, the results of clinical examinations and neuropsychological testing were compared with methylmercury exposure in the mothers. No clear-cut mercury-related clinical abnormalities were found in either study.

In the Seychelles prospective study, the study population was a cohort of 779 children born to mothers exposed to methylmercury from a diet high in fish

Table 4.3. Lowest observed effect levels (LOELs) in hair from prenatal exposure to methylmercury.

Population	*n*	LOEL (μg/g)	Medium/reference
Crees	247	13–24[a]	Freshwater fish; McKeown-Eyssen et al. (1983)
Iraq	83	7–180[a]	Bread; Cox et al. (1989)
New Zealand	248	25[a]	Pelagic fish; Kjellström et al. (1989)
Peru	131	>8.3[a]	Pelagic fish; Marsh et al. (1995)
Faeroe Islands	1022	<10[b]	Pilot whales; Grandjean et al. (1997)
Seychelles	750	13–15[b,c]	Pelagic fish; Davidson et al. (1998)

[a] Peak level during pregnancy.
[b] Average hair level in pregnancy.
[c] LOEL established by Health Canada (1999).

Source: Health Canada (1999).

(typically 10–15 meals per week). Prenatal exposure to mercury was assessed in the maternal hair. Subsequently, maternal and children's hair samples were used as markers of methylmercury exposure. The neurological and developmental effects in the children were evaluated at 6.5, 19, 29, 66 and 107 months of age (Myers et al., 1995, 1997, 2003). No definite adverse neurodevelopmental effects were observed in infants up to 29 months of age at maternal hair levels of up to 12 μg/g (the overall H-Hg levels of the mothers in the study were 0.5–26.7 μg/g). At hair levels greater than 12 μg/g, the percentage of infants with normal Revised Denver 25 Developmental Screening Test scores decreased from 93% to 87% (Myers et al., 1995) but there was no effect on the developmental milestones of walking and talking (Myers et al., 1997). No consistent adverse association between prenatal methylmercury exposure at maternal hair levels of up to 12 μg/g (from fish consumption) and child development was identified in 643 children aged up to 9 years in this study (Myers et al., 2003; Huang et al., 2005). Twenty-one neurodevelopmental end-points were assessed.

In the Faeroe Islands prospective study, the population was exposed to methylmercury primarily from pilot-whale meat with methylmercury concentrations ranging from <1 mg/kg to more than 3 mg/kg (Grandjean et al., 1997). The original birth cohort of 1022 started between 1986 and 1987. Mercury levels were determined in maternal hair samples and in infants' umbilical cord blood at delivery, and in children's hair samples at age 12 months. According to Grandjean et al. (1997), the mercury concentration in cord blood appeared to be the best indicator for adverse neurodevelopmental effects. At 7 years of age, 917 children were tested for neurological (with the emphasis on motor coordination and motor performance), neurophysiological and neurodevelopmental effects. In 900 children from the Faeroe Islands, prenatal exposure to methylmercury was associated with a neurological deficit at 7 years of age. Neurological deficits were found in the areas of language, attention and memory, and were found to be related to increasing mercury exposure (Grandjean et al., 1997). Developmental delays were significantly associated with the methylmercury exposures, even when children whose mothers had H-Hg levels above 10 μg/g were excluded. Within the low-exposure range, each doubling of the prenatal exposure concentration was associated with a developmental delay of 1–2 months. There is some suggestion that the neurological deficit may be due to an interaction between methylmercury and polychlorinated biphenyl present in the diet (in whale blubber) of these mothers (Stewart et al., 2003). The results were approximately the same, however, when polychlorinated biphenyl levels were taken into account, and increased prenatal exposure to methylmercury appeared to enhance the toxicity of these hydrocarbons (Grandjean et al., 2001). The effects at these dose levels may not seem severe on an individual basis, but they may have serious implications for populations (UNEP, 2002).

The information generated from both of these studies were evaluated along with other available epidemiological data by the US National Research Council (2000), the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2003) and Health Canada (Gupta et al., 2005) (Table 4.4). To put the methylmercury exposure levels in perspective, for the neurodevelopmental effects, the benchmark dose level (BMDL) for a 5% effect (BMDL 05) from the Faeroe Islands study was approximately 58 ppb (μg/l) for mercury in cord blood. This was based on the neurobehavioural end-points in infants. On the basis of a BMDL 05 of 58 ppb (58 μg/l) for cord-blood mercury and with the application of a conversion (cord blood to maternal hair) factor of 200 (Grandjean et al., 1992), this BMDL 05 would be equivalent to a 12 ppm (12 μg/g) maternal H-Hg level, or 48 μg/l in terms of the maternal blood mercury level.

The normal dose of ethylmercury in children's vaccines is approximately 12.5–25 μg per 0.5 ml (American Academy of Pediatrics, 1999). Local hypersensitivity reactions have been observed in some cases (American Academy of Pediatrics, 1999; Ball et al., 2001). Ball et al. (2001) reviewed the literature and

Table 4.4. Estimated exposure limits for methylmercury.

	US NRC (2000)	JECFA (2003)	Health Canada (2004)
Number of studies	One	Two	One
Exposure biomarker	Cord blood (hair)	Hair	Cord blood (hair)
BMDL selected	58 µg/l cord blood	14 µg/g hair	58 µg/l cord blood
Uncertainty factor	10	6	5
Exposure limit	0.1 $\mu g/kg_{bw}$/day	1.6 $\mu g/kg_{bw}$/week	0.2 $\mu g/kg_{bw}$/day

concluded that there was no evidence of adverse effects caused by thiomersal in vaccines, except for the hypersensitivity response in children.

Renal toxicity in humans is not common following exposure to methylmercury. However, some evidence of renal toxicity exists from the Minamata poisoning incident following the consumption of mercury-contaminated fish (Tamashiro et al., 1986). Between 1970 and 1981, the number of deaths attributed to kidney disease was higher than expected among the female residents of a small area of Minamata city (standardized mortality rate 2.77; 95% CI 1.02–6.02) that had the highest prevalence of Minamata disease compared to age-specific rates for the entire city as standard. However, the death rate for men was in the expected range (standardized mortality rate 0.80; 95% CI 0.17–2.36).

Studies from one population exposed to methylmercury from fish suggest an association with increased incidence of cardiovascular diseases (Salonen et al., 1995; Rissanen et al., 2000). A statistically significant correlation was found between mercury levels and cardiovascular disease, even after correction for numerous cardiovascular risk factors, in an extensive study on the relationship between fish consumption, levels of mercury in urine and scalp hair, and risk of cardiovascular disease in a cohort of 1833 Finnish men (Salonen et al., 1995). In a subsequent study by the same researchers, a correlation between mercury accumulation and accelerated progression of carotid atherosclerosis was reported (Rissanen et al., 2000). In a recent study in the Faeroe Islands, an association between prenatal exposure to methylmercury and cardiovascular function in children aged 7 years was reported (Sorensen et al., 1999). Diastolic and systolic blood pressures increased by 13.9 mmHg and 14.6 mmHg, respectively, as the mercury level in cord blood increased from 1 µg/l to 10 µg/l. In boys, heart-rate variability (a cardiac autonomic control) decreased by 47% with an increase in cord-blood mercury concentration from 1 µg/l to 10 µg/l. These studies suggest that increases in methylmercury exposure can cause adverse effects on the cardiovascular system.

Epidemiological studies have found no associations between mercury exposure and overall cancer rates. Two studies found an association between exposure to mercury and acute leukaemia (National Research Council, 2000). In several animal studies, methylmercury chloride caused renal tumours in male mice ex-

posed through the diet, but not in female mice or rats of either sex. On the basis of the information available from animal studies, IARC (1993) concluded that there is sufficient evidence for the carcinogenicity of methylmercury chloride in experimental animals; however, on the basis of the limited existing scientific evidence on human population, the agency classified methylmercury compounds as "possibly carcinogenic to humans" (Group 2B).

Although other effects of methylmercury in humans, such as damage to chromosomes (Skerfving et al., 1974), have been suggested, other tissues seem to be unaffected, even when the exposure is severe (Health Canada, 1999). Some animal studies have led to the suggestion that methylmercury might be a weak mutagen (Ramal, 1972). Animal studies indicate effects on the immune system and the reproductive system.

4.4. Human health implications in relation to LRTAP

Emissions of mercury into the air from both anthropogenic and natural sources are in inorganic forms that can be converted biologically to methylmercury in soil and water. Methylmercury bioaccumulates and enters the human body readily via the dietary route.

Airborne concentrations of mercury in Europe, and also globally, are generally well below the levels known to cause adverse health effects from inhalation exposure. Concentrations of inorganic mercury species in surface water and groundwater are generally well below the levels known to cause adverse health effects from water consumption.

Methylmercury is a potent neurotoxin. Unborn children are the most susceptible population group, the exposure being mainly through fish in the diet of the mother. Methylmercury is also excreted in mothers' milk.

Human biomonitoring and diet modelling data indicate that tolerable dietary intakes of methylmercury are exceeded among subpopulations who consume large amounts of fish, e.g. in Scandinavia, North America and France. For several species of (mainly large predatory) freshwater and marine fish and mammals, a mercury level of 0.5 mg/kg, the value used as a guideline in many countries, is often exceeded.

Historical data, e.g. from lake sediments in Scandinavia, show a two- to five-fold increase relative to the pre-industrial era, reflecting anthropogenic emissions and long-range transport. Methylmercury in freshwater fish originates from inorganic mercury in the soil and direct atmospheric deposition. Anthropogenic emissions of mercury in Europe decreased by approximately 50% after 1990, and a similar decrease is predicted from modelling and limited monitoring data for the deposition of mercury in Europe. However, a concomitant decrease in the concentration of methylmercury in freshwater fish has not been observed.

Little information is available on the provenance of methylmercury in marine fish, and on the contribution of long-range transport in the process. Evidence

exists for increasing levels in marine fish and mammals in the Arctic, indicating the impact of long-range transport.

In general, fish consumption has important beneficial effects on human health. However, in some populations consuming large amounts of fish, or contaminated fish, the intake of methylmercury can reach hazardous levels. Thus, a high priority should be given to lowering the concentrations of methylmercury in fish. Reducing the emissions into the atmosphere and the long-range transport of pollution will be of great importance in the achievement of these goals.

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The heavy metals cadmium, lead and mercury are common air pollutants, being emitted mainly as a result of various industrial activities. Although the atmospheric levels are low, they contribute to the deposition and build-up in soils. Heavy metals are persistent in the environment and are subject to bioaccumulation in food-chains.

Cadmium exposures are associated with kidney and bone damage. Cadmium has also been identified as a potential human carcinogen, causing lung cancer. Lead exposures have developmental and neurobehavioural effects on fetuses, infants and children, and elevate blood pressure in adults. Mercury is also toxic in the elemental and inorganic forms, but the main concern is associated with the organic compounds, especially methylmercury, that accumulate in the food-chain, i.e. in predatory fish in lakes and seas, as these are the main routes of human exposure.

Long-range transboundary air pollution is only one source of exposure to these metals but, because of their persistence and potential for global atmospheric transfer, atmospheric emissions affect even the most remote regions. This report, based on contributions from an international group of experts, reviews the available information on the sources, chemical properties and spatial distribution of environmental pollution with cadmium, lead and mercury caused by long-range transboundary air pollution, and evaluates the potential health risks in Europe.

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