

Environmental health in the Baltic region — toxic metals

by Staffan Skerfving, MD,¹ Vladimir Bencko, MD,² Marie Vahter, PhD,³ Andrejs Schütz, PhD,¹
Lars Gerhardsson, MD¹

Skerfving S, Bencko V, Vahter M, Schütz A, Gerhardsson L. Environmental health in the Baltic region — toxic metals. *Scand J Work Environ Health* 1999;25 suppl 3:40–64.

Recent reports on concentrations of lead, cadmium, methylmercury, arsenic and nickel in some biological media in populations in the Baltic region are reviewed. In particular, children in parts of Poland, the Czech Republic, and Germany have uptakes of lead sufficient to cause adverse effects on the central nervous system and kidneys. Cadmium exposure is also high in Poland. Slight cadmium-induced effects on the kidneys have been reported from Germany and Sweden. Methylmercury uptake is dependent upon the intake of fish, in particular from contaminated lakes and rivers in Sweden and Finland, as well as the eastern coast of the Baltic Sea. There are some indications of immunotoxic effects associated with the intake of such fish. However, fish also contain other immunomodulating agents. Exposure to arsenic seems to be low everywhere in the Baltic region. There is high nickel exposure in northern Russia.

Key terms arsenic, effects, exposure, cadmium, lead, mercury, nickel, toxic.

Introduction

Exposure to toxic metals results in health problems in many areas of the world. The exposure can be due to the natural occurrence of metals, for example, to arsenic in bedrock, which contaminates drinking water and, mostly, anthropogenic sources.

The aim of the present paper is to summarize and evaluate the information on exposure to, and toxic effects of, some toxic metals in the Baltic region. This region includes countries within the watershed of the Baltic Sea (ie, parts of Russia, Estonia, Latvia, Lithuania, Poland, the Czech Republic, Germany, Denmark, Sweden, and Finland). For reasons of comparison, some nearby areas have been included. Countries in the Eastern part of the Baltic region are particularly focused upon.

Selection of data for review

In this review, only information relevant for the exposure in the general environment is discussed. Thus, data from occupationally exposed workers have not been included. However, in some cases, the interpretation of the environmental exposure information is dependent upon

knowledge obtained from workers; then, of course, such information is included.

There have been great changes in the exposure to some metals over time. For example, the exposures to lead, cadmium, and mercury have changed fairly rapidly in many areas. Hence it is of little value to include historical information. Therefore, this review is restricted primarily to the situation from the mid-1980s on. However, in some cases, when there are no recent data for a particular geographic area, or when the time sequence is particularly interesting, older information is also discussed.

People can be exposed to many toxic metals. However, all are not relevant to health. Thus this review focuses on lead, cadmium, mercury, and arsenic. In addition, some data on nickel and beryllium are presented. The 4 first-mentioned elements are of interest because they have often been associated with health effects, and there is a wealth of information available, which makes geographic comparisons meaningful. Furthermore, the information available allows interpretation of the data in terms of health. For each of the 4 elements, a brief general description of the toxicology is presented. In particular, dose-response relationships are discussed. Thereaf-

¹ Department of Occupational and Environmental Medicine, University Hospital, Lund, Sweden.

² Institute of Hygiene & Epidemiology, First Faculty of Medicine, Charles University of Prague, Czech Republic.

³ Institute of Environmental Medicine, Karolinska Institute, Solna, Sweden.

Reprint requests to: Dr. Staffan Skerfving, Department of Occupational and Environmental Medicine, University Hospital, S-221 85 Lund, Sweden. E-mail: staffan.skerfving@ymed.lu.se

ter, information on the exposure and adverse health effects in populations in the Baltic region is given.

Biological monitoring of exposure and risk

Traditionally, exposure monitoring has been concerned primarily with concentrations in environmental media, for example, air, drinking water, food, and soil. Such source-oriented monitoring is essential for identifying major sources and routes of exposure. However, it provides little information on the amount of the pollutant that actually comes in contact with people, and even less on the dose taken up into the body. In combination with information on the intake from the various media and information on bioavailability, crude estimates of the absorbed dose can be obtained. In particular, determining various metals in duplicate in diets, or prepared diets, has been employed. Such data are of interest for many metals, as dietary intake is often the main source of exposure. In some cases, concentrations in feces have been used to estimate the dietary intake of metals with low absorption in the gastrointestinal tract. However, such information is not considered in this review.

Instead, for estimates of the total exposure to metals, as well as for assessments of the risk for health effects, it is often useful to rely upon determinations of the elements in biological indicator media, such as blood, organs (eg, teeth, bone, and kidney), hair, and urine. (For reviews on this topic, see references 1 and 2.)

Measuring the concentrations in biological indicator media has several advantages. Generally, exposure occurs from several sources simultaneously (eg, air, drinking water, food, soil, and tobacco), and the absorption into the body takes place both through the lungs and the gastrointestinal tract. (Skin absorption is not relevant in the present context.) For many metals, the concentration in biological matrices provides information on the total dose absorbed. In some cases it is possible to determine the concentration in organs. Of particular interest is the critical organ, the one most sensitive to adverse effects. For example, the concentration of cadmium in kidney cortex is relevant for the assessment of health risk. In other cases, one has to rely upon information on levels in matrices which are not damaged at exposure, but which can serve as an index of uptake and risks, if information on the toxicokinetics is available. Concentrations in blood are good examples.

Often, long-term exposure determines the health effects. Then, the concentrations of elements in tissues with a slow turnover can be particularly informative. For example, the concentrations of cadmium in the kidney and lead in certain bones reflect the uptake over decades. Other tissues can have more complex kinetic patterns, with several components. Compartments with short half-times can provide information on recent exposure, and such information can be crucial for studies of changes in

uptake. Concentrations of lead and cadmium in the blood are examples of such indicators.

In this review, the selection of data to be discussed was mainly based on a combination of considerations of the usefulness of biological indices to reflect short- and long-term exposure to the elements lead, cadmium, mercury, and arsenic, and the amount of information available for populations in the Baltic region. It must be stressed that the compilation of the published data may not give a representative picture of the exposure situation of the general population, since sampling was often made at particularly contaminated sites, for example, in the vicinity of smelters. This possibility must be taken into consideration when the information from different areas is compared.

Quality of information

For the interpretation of information on the concentrations of elements, it is crucial to take into consideration the quality of the analytic data. During the last few decades, there has been a gradually increasing awareness of the quality aspects, and the reporting of quality control data in the scientific papers has increased. However, there is still a large variation in the extensiveness of such information. In principle, sufficient information requires data on the full analytic procedure, including work-up steps, and final determinations (3). Furthermore, the report should contain data on detection limit, imprecision, and accuracy. The latter should be supported by information on results of internal and external quality control materials, analyzed together with the collected samples, or results of interlaboratory comparison programs, using samples with concentrations unknown to the participating laboratories (4).

In this review, information on the quality of the reported analytic quality control procedure is graded on a scale of 0 to 3 (from none at all to very good). This grading helps point out the type of information that is really useful in the evaluation. However, it must be emphasized that, in some cases, the information is not given in the quoted paper, but reference is given to other publications containing such information. No systematic back-tracking of such references has been done, as the information should always be given in context with the data on the actual samples reported. Otherwise it is often not known whether the quality control information given in other papers is really relevant for the current samples; the analytic performance often varies over time. Furthermore, it has not been possible to judge the analytic quality on the basis of a firm set of criteria, and therefore the scoring is partly subjective.

For the sake of completeness and overview, all available information has been included in the tables. However, conclusions are based on data with documented high analytic quality.

For the analytic methods used to determine elements in biological material, individual results have been truncated to 2 digits (means to 3).

Lead

General toxicology

There are several recent reviews on the toxicology of lead (1, 5–9), as well as on environmental aspects (10).

In blood, lead (B-Pb) appears mainly in the erythrocytes, and to a limited extent in plasma (11–14). In the erythrocytes, lead is mainly bound to the enzyme delta-aminolevulinic dehydratase (15–17). The concentrations of lead in whole blood show a nonlinear relationship with uptake, concentrations in plasma, and toxic effects (18).

Lead accumulates in calcified tissues (5, 9). Hence high levels occur in the teeth. Bone also contains high concentrations. The biological half-time of B-Pb is about 1 month, and in bone it is more than a decade (19).

Inorganic lead can cause toxic effects in several organs (5, 9). If the B-Pb concentration is in excess of about 100 µg/l, neurobehavioral and neurophysiological effects have been claimed to occur in the child. In the same range, effects on erythropoietic functions have been recorded. Furthermore, lead is toxic to the kidney. The part of the kidney first affected is the proximal tubuli.

Exposure

Information on B-Pb in different areas has been compiled in table 1. Much recent information is available on B-Pb levels in Poland, Germany, Denmark, and Sweden. For Finland, Russia, Latvia, and the Czech Republic, there are only scattered data, while no information at all is available for Estonia and Lithuania.

Several factors with no relation to the geographic areas are of importance for the B-Pb concentration. Thus gender is frequently a determinant, males having higher concentrations than females (table 1), partly due to the fact that adult men have higher packed-cell volumes than women and that B-Pb is mainly present in the erythrocytes. In children, the influence is less evident (58).

Furthermore, B-Pb often varies with age (table 1). The highest B-Pb levels are found in young children, 1–4 years of age, mainly as a result of their frequent hand-to-mouth activities. This factor will be of special importance in areas with high lead contamination of soil and dust (59). Thus, for young children, blood samples taken in the fall show higher levels than those taken during the winter.

There is, in some studies, an age effect for adults as well, with higher levels in old people than in young ones. This finding may, at least partly, reflect higher exposure earlier. The lead accumulated in the skeleton over many

years will cause endogenous exposure that will increase the B-Pb, especially in subjects with marked demineralization of the skeleton (18).

Several studies show that smokers have somewhat higher B-Pb levels than nonsmokers (table 1). Often, even children exposed to environmental tobacco smoke have higher B-Pb levels than others (60, 61). The reason is not known. Lead exposure from the smoke is hardly sufficiently high to explain the effect. Furthermore, alcohol consumption, especially wine, is associated with a slight increase in B-Pb. The intake of canned food can cause exposure from lead in solder (62).

Parental occupational lead exposure can be associated with increased B-Pb in children (table 1). The main reason is contamination of the home with workplace dust from the worker's clothes. A low socioeconomic status is also associated with a high B-Pb, probably partly because of the more frequent occupational lead exposure among the children. Gun shooting, rifle activities and hunting have, in some studies, also increased the exposure of adults (63, 64). Immigrants from non-European countries sometimes have increased B-Pb levels, probably because of food habits different from the European populations, use of lead-containing cosmetics, and exposure to leaded gasoline.

In several studies, living close to lead-emitting industries, such as primary and secondary smelters, was associated with increased B-Pb, and children living in city centers often have higher levels than those staying in rural areas (table 1). Sometimes elevated B-Pb levels are caused by lead pipes in the drinking water system. Such effects were noted in the eastern part of Germany. Elevated B-Pb levels, especially in children, can also be associated with the use of lead paint in buildings. However, the general impression is that such exposure is relatively uncommon in the Baltic region. Instead, the urban effect noted in many studies (table 1) is mainly caused by the exposure to lead in automobile exhaust. The use of lead in gasoline has decreased in many countries during the last few decades. In Sweden, the use stopped almost entirely in 1994 (figure 1). In some other Baltic countries, leaded gasoline is still in use. The decreased emission of lead in automobile exhaust is paralleled by a dramatic decrease in B-Pb in Swedish children (figure 1), as well as in adults. Similar decreases have been noted in some other areas in the Baltic region. While the main effect is related to the elimination of gasoline lead, other preventive measures may also be important, such as restrictions on the emissions from industries and replacement of soldered cans by welded ones.

There are some obvious differences in B-Pb levels between the Baltic countries (table 1). The most extensive information is available from Sweden. Extremely low B-Pb levels have been recorded in several studies of children and adults in this country, with average levels

Table 1. Lead levels in blood (B-Pb) in populations in the Baltic region. (QC = quality control, N = number of samples, M = median)

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	B-Pb (µg/l) ^{b, c}			Determinants	Comment
								Mean ^d	M	Range		
Finland												
Pönkä et al, 1993 (20)	South	-	1988	0	Male, female	<7	35	30	-	21—83	Time	-
Russia												
Smith-Sivertsen et al, 1997 (194) Schütz et al, to be published	North	Smelter	1994—1995	2	Male	Adult	37	50	-	-	Gender	-
				2	Female	Adult	12	14	-	-	Gender	-
	West	-	1995	3	Male	15—17	36	42	40	19—120	Gender	-
				3	Female	15—17	48	25	23	8—54	Gender	-
Latvia												
Schütz & Leja, 1991 (65)	West	Smelter	1990	3	Male, female	5—13	49	48	-	21—100	Gender	-
			1990	3	Male, female	4—12	25	63	-	31—110	Gender	-
			1990	3	Male, female	6—10	33	54	-	24—90	-	-
Poland												
Zielonka & Wodzien, 1993 (21)	South	Smelter	1987—1989	1	Male, female	12	220	200	200	27—720	Season (?)	-
			1987—1989	1	Male, female	12	211	300	250	52—920	Closeness to smelter	-
			1987—1989	1	Male, female	12	152	230	220	4—570	Closeness to smelter	-
Laudanski et al, 1991 (22)	East	-	≤1990	0	Female	17—75	89	68	-	-	-	-
					Male, female		175	62	-	-	-	-
Osman et al, 1992 (23)	South	Smelter	1991	3	Male, female	7—8	10	-	163	77—260	Distance to smelter	-
					Female	22—39	8	-	38	24—64	-	Pregnant
Kaniewski et al, to be published	South	Smelter	1991	3	Male, female	8—9	42	121	106	64—260	-	-
			1991	3	Male, female	8—9	40	71	64	40—130	-	-
			1991	3	Male, female	8—9	39	67	60	30—200	-	-
	West	Factory	1991	3	Male, female	8—9	45	66	68	32—110	-	-
			1991	3	Male, female	8—9	40	61	55	32—140	-	-
			1991	3	Male, female	8—9	40	57	54	26—120	-	-
Fagher et al, 1993 (87)	East	-	≤1992	3	Female	?	24	38	-	-	-	Pregnant
Pietrzyk et al, 1996 (24)	South	Industrial	1992—1994	0	Female	Adult	336	42	-	11—140	-	Pregnant
Zareba & Rudkowski (25)	South	Smelter	1992—1994	1	Male, female	7—15	3,030	93—114	-	-	Time	-
Jakubowski et al, 1996 (26)	South	Smelter	1992—1994	3	Male, female	<10	707	(74—110)	-	-	Closeness to smelter	-
					Adult	539	(49—150)	-	-	Smoking, gender	-	
					<10	555	(30—62)	-	-	-	-	
	Urban		1992—1994	3	Male, female	Adult	567	(24—77)	-	-	Smoking, gender	-
Dutkiewicz et al, 1993 (27)	South	Smelter	≤1993	1	Male, female	7—8	575	168	-	44—500	-	-
						14—15	453	133	-	39—500	-	-
Andrzejak et al, 1993 (28)	South-west	Smelter	1993	1	Male, female	2—18	28	310	-	-	Time	-
					Adult	32	470—490	-	-	Time	-	
Zejda et al, 1995 (29)	South	Industrial	1993	1	Male, female	7	431	(79)	-	<40—250	Family size, housing, traffic, holidays away	-
Zejda & Grabecki, 1994 (30)	South	Industrial	1993—1994	0	Male, female	3—5	2,675	73	-	-	-	-
Zejda et al, 1996 (31)	South	Industrial	1993—1996	0	Male, female	3—5	6,969	56—67	-	-570	Age, town, floor, home quality, carpets, vegetable intake, trips away, number of siblings, traffic	-
Janousek et al, 1994 (32)	South	Industrial	≤1994	1	Male, female	0	13	-	39	24—72	-	Cord blood
Osman et al, 1994 (33)	South	Industrial	≤1994	3	Male, female	8—9	140	79	-	35—350	Parents' education, holidays away, fathers' smoking	-
Nowak & Czerwionka-Szarflaska, 1996 (34)	Central	Industrial	≤1996	0	Male, female	3—15	64	154	-	61—520	Age	-
			≤1996	0	Male, female	3—15	253	132	-	52—460	Age	-
			≤1996	0	Male, female	3—15	169	105	-	36—360	Age	-
Osman et al, 1998 (58)	South	Industrial	1995	3	Male, female	9	211	62	55	19—400	Siblings, holidays away, housing, mothers' smoking, outdoor playing	-
Osman et al, 1998 (35)	South	Industrial	1996	3	Male, female	4—14	157	82	70	19—260	Income	-

(continued)

Table 1. Continued

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	B-Pb (μg/l) ^{b, c}			Determinants	Comment
								Mean ^d	M	Range		
Czech Republic												
World Health Organization, 1995 (83)	Central	Smelter	1992—1994	1	Male, female	1—14	338	(47—114)	-	<4—290	Distance to smelter, lead in soil, home-production of fruits or vegetables, local drinking-water well, family's smoking, siblings, mother's education	-
Bernard et al, 1995 (82)	East	Smelter	≤1995	2	Male, female	12—15	144	94—149	-	32—350	Gender	-
	South- east	Rural	≤1995	2	Male, female	12—15	51	84—87	-	42—290	Gender	-
Kučera et al, 1995 (36)	Central	-	≤1995	0	Male	Adult	138	71	-	22—250	Gender	-
					Female	Adult	128	42	-	4—97	Gender	-
					Male	7—14	20		-	50—120	-	-
Janousek et al, 1994 (32)	Central	Rural	≤1994	1	Male, female	0	8	-	38	9—52	-	Cord blood
Germany												
Krause et al, 1989 (81)	-	-	1985—1986	2	Male, female	25—69	2,346	75	69	<10—550	Gender, smoking, age, community size	-
Brockhaus et al, 1998 (37)	North- west	Smelter	1986	2	Male, female	7—9 13—15	109 41	(74) (56)	71 54	42—180 24—110	-	-
		Urban/ industrial	1986	2	Male, female	6—7	1,188	(62—66)	62—67	25—210	-	-
		Rural	1986	2	Male, female	6—7	263	(55—60)	55—61	23—200	-	-
Ewers et al, 1990 (38)	North- west	Smelter	1988	2	Female	55—66	13	(64—73)	-	34—140	Smoking	-
		Urban	1987—1988	2	Female	55—66	1,094	(55—80)	-	23—210	Smoking	-
		Rural	1987—1988	2	Female	55—66	412	(52—69)	-	13—180	Smoking	-
Hofstetter et al, 1990 (39)	North- west	Smelter	1989	1	Male, female	6—7	299	(63)	-	26—160	Immigrant, parent lead worker, traffic	-
Englert & Höring, 1994 (40)	South- east	Lead pipes	1990—1991	1	Male, female	9—12	113	-	83	33—340	Water lead	-
Begerow et al, 1994 (41)	North- west	Urban	1991	2	Male, female	6	1,028	(44)	-	13—150	Turkish immigrants	-
	South- east	Urban	1991	2	Male, female	6	1,283	(53)	-	15—170	-	-
Hense et al, 1992 (42)	South	-	1987—1988	3	Male	28—67	1,703	90	-	-	Gender, smoking	-
					Female	28—67	1,661	65	-	-	Alcohol, hematocrit	-
Winneke et al, 1994 (84)	North- west	Smelter	1991	1	Male, female	6	107	(49)	-	14—120	-	-
	East	Urban	1991	1	Male, female	6	174	(69)	-	27—160	Lead pipes	-
	"Rural"	Urban	1991	1	Male, female	6	68	(48)	-	14—130	-	-
Denmark												
Lynby et al, 1990 (43)	West	Urban	1982—1983	3	Male, female	9—10	146	-	-	17—140	Gender, siblings, parents' smoking, canned food	Selected because of high or low tooth lead
Møller & Kristensen, 1993 (44)	East	Urban	1987	0	Male	51	439	83	-	2—62	Hematocrit	-
Molin Christensen & Holst, 1988 (45)	East	Urban	1987	3	Male	51	151	-	71	44—110	Time	-
Grandjean et al, 1992 (46)	Central	-	≤1991	2	Male	20—69	100	56	52	40—180	Alcohol, smoking	-
					Female	20—69	100	45	37	10—170	-	-
Sweden												
Granvik et al, 1988 (47)	Central	Industrial	≤1987	2	Male	Children	418	33	27	<10—270	-	-
					Female	Children		19	18	<10—61	-	-
Andrén et al, 1988 (185)	South	Rural	1985	3	Male, female	8—13	127	(35)	-	10—89	Parents' smoking	-
Willers et al, 1992 (60)	South	Urban	1987	3	Male, female	26—52 7—10	107 77	(28—66) (31—34)	-	16—220 2—68	Smoking, lead work Parents' lead work	-
Vahter et al, 1991 (48)	Central	Urban	≥1986	3	Female	27—46	15	30	-	15—44	-	Non-smokers

(continued)

Table 1. Continued

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	B-Pb (μg/l) ^{b, c}			Determinants	Comment
								Mean ^d	M	Range		
Sweden continued												
Svensson et al, 1987 (104)	South	Rural	1987	3	Male, female	20—66	286	-	60	20—410	Smoking	-
Gustafson et al, 1989 (49)	South	Urban	1987	3	Male	37	40	52	-	-	-	-
Bensryd et al, 1994 (63)	South	Rural	1989—1990	3	Male	17—77	237	-	39	10—210	Smoking, hunting, rifle activity	-
Jakobsson	North	Smelter	1989—1991	1	Female	Adult	209	29	-	<10-?	-	Pregnant
Lagerkvist et al, 1993 (113)		Rural	1989—1991	1	Female	Adult	149	25	-	<10-?	-	
Bjerre et al, 1993 (50)	Central	Industrial	1991	3	Male, female	1—7	49	31	30	13—79	Season, parental smoking	-
Berglund et al, 1994 (51)	Central	Urban	1991	3	Male, female	Adult	35	29	27	7—74	-	-
						1—2	41	27	27	9—73	-	-
Kaniewski et al, to be published	South	Smelter	1991	3	Male, female	8—9	48	37	-	14—63	Parental smoking	-
		Urban	1991	3	Male, female	8—9	94	32	-	15—58	Parental smoking	-
		Rural	1991	3	Male, female	8—9	78	30	-	11—75	Parental smoking	-
Bæcklund, 1996 (52)	-	-	1992—1994	3	Male, female	<55->90	424	-	27	6—150	Gender, smoking	-
Berglund et al, 1994 (59)	Central	Urban	1993	3	Male, female	1—3	90	30	28	9—77	Season	-
Berglund et al, 1994 (53)	Central	Industrial	1993	3	Male, female	1—4	71	28	27	7—56	Direction to industry	-
Strömberg et al, 1995 (66)	South	Smelter	1994	3	Male, female	7—8	49	(29)	-	13—97	Gender	-
		Urban	1994	3	Male, female	7—8	44	(24)	-	12—49	Gender	-
		Rural	1994	3	Male, female	7—8	42	(22)	-	12—120	Gender	-
Berglund et al, 1995 (54)	Central	Industrial	1994	3	Male, female	1—5	72	-	19	11—48	-	-
Hanberg & Ahlborg, 1995 (55)	Central	Industrial	1994	1	Female	18—50	136	22	-	6—77	-	-
Skerfving et al, 1997 (56)	South	Urban	1995—1996	3	Male, female	7—8	85	22	-	9—49	-	-
		Rural	1995—1996	3	Male, female	7—8	145	24	-	9—68	-	-
Nordberg et al, 1996 (57)	Central	Urban	≤1995	1	Male, female	>75	177	-	31—37	-	-	-

^a 0=no, 3=very good. ^b All determinations were made by atomic absorption spectrometry (flame or electrothermal), except for Hanberg & Ahlberg (55) (who used inductively coupled plasma-mass spectrometry). ^c 100 µg/l=0.48 µmol/l. ^d Arithmetic mean except when in parentheses; values in parentheses are geometric means.

in the range of 20—30 µg/l in recent years. Even in mining and smelter areas, the concentrations are low.

The scarce information available indicates that the levels may be as low in Finland as in Sweden (table 1). For Russia and Latvia, there are also limited data. Direct comparison between children in 2 areas in those countries and Sweden is possible, because sampling was made in close cooperation, and the analyses were made in the same laboratory with the same method (65, 66 and Schütz et al, to be published). It seems as if the B-Pb levels of the Russian and Latvian children are only slightly higher than in Swedish ones.

The rather extensive information available from Germany and Denmark indicates that the populations in these countries have somewhat higher B-Pb levels than in Sweden (table 1). Possibly, although the information is limited, the B-Pb values in the Czech Republic are similar. However, for both Germany and the Czech Republic, there is a considerable variation in B-Pb concentrations. In areas affected by emissions from smelters or lead pipes in the drinking-water system and bad housing, average

levels in the range of 80—120 µg/l have been recorded. Such concentrations have been associated with toxic effects. (See also the section on the toxic effects of lead.)

In Poland, the lead contamination seems generally to be more severe than in Germany and the Czech Republic (table 1). Direct comparisons with southern Sweden are again possible (58 and Kaniewski et al, to be published). The general levels seem to be at least twice as high in Poland as in Sweden. In the vicinity of lead emitting industries, in particular smelters in the south, the average levels are high. Mean values well above 100 µg/l have been reported, with individual values above 200 µg/l. These are concentrations which are definitely associated with toxic effects. However, also in Poland, there is a trend towards decreasing lead exposure (58).

As to the concentration of lead in tooth (T-Pb) (table 2) and bone (Bone-Pb) (table 3), which reflect accumulation over many years, the information is less extensive. Hence far-reaching conclusions are not possible. However, the general picture is the same as for B-Pb. There are very large variations, however, if the uncertainties in

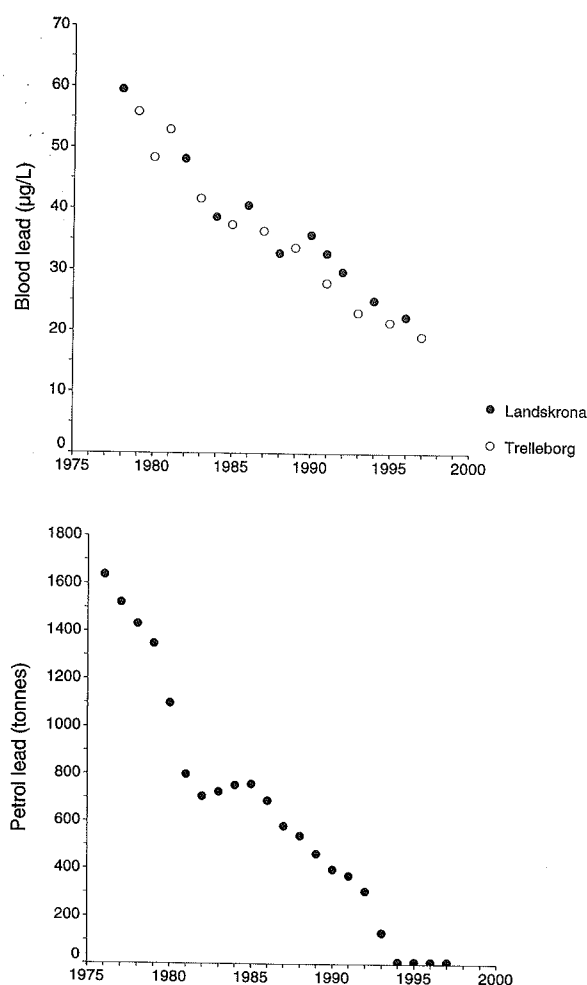


Figure 1. Yearly estimates of lead quantity in gasoline sold in Sweden in 1976–1997 and blood lead concentrations (geometric means) in 1978–1997 for 2771 children in southern Sweden, living in the towns Landskrona (closed symbols), a secondary lead smelter is situated there, and Trelleborg (open symbols) and their surroundings (56, 66).

analyses and the differences between different parts of the tooth and skeleton are taken into consideration. In the Czech Republic, T-Pb in children living close to a smelter was clearly elevated. Furthermore, for Bone-Pb, much higher concentrations were recorded in eastern as compared with western Germany, possibly due to earlier exposure.

In a study of the 427 schoolchildren in Lithuania, the mean lead level in hair was 5.3 (range 0.1–260) µg/g (80). This is a fairly high concentration. In 1360 adult Germans, the mean level was 2.6 (range <0.4–290) µg/g (81). There is no information from Lithuania on lead levels in other media.

Toxic effects

While there are numerous studies on exposure to lead, few have addressed the issue of the toxic effects of lead.

In a study of children (12–15 years of age) in schools situated in the vicinity of a lead smelter in the Czech Republic, there was increased urinary excretion of proteins, as compared with that of children from a rural school (82) (table 1). In particular, there was a relation between the excretion of retinol-binding protein and B-Pb; this relation indicates a slight effect on the proximal tubuli. This effect was statistically significant in the highest tertile of B-Pb, which had a mean of 120 (range up to 290) µg/l. There was no significant effect on heme synthesis, as indicated by blood levels of zinc protoporphyrin.

In another study of preschool children living around a smelter in the Czech Republic, there was an association between a summary score of psychomotor development and B-Pb (83) (table 1). However, the authors acknowledged that the study was small and the control of potential confounders insufficient. No significant associations between the results of neurobehavioral tests and B-Pb was found for schoolchildren.

In a study of neurobehavioral and neurophysiological effects of lead in 6-year-old children in East and West Germany, living in a small city, a large one with lead pipes in the drinking-water system and a large one with contaminated air, there were significant associations between tapping, pattern recognition, and Benton's test (but not for a series of other tests, including visual evoked potentials), on one hand, and B-Pb (but not T-Pb), on the other, after adjustment for confounders or covariates (84). The median for B-Pb was 50 (95% below 100, range up to 190) µg/l (table 1), and for T-Pb it was 2 (range 0.2–14) µg/g (table 2). The results may indicate that even B-Pb levels below 100 µg/l are associated with subtle neurobehavioral impairment. It should be stressed, however, that, in this type of study, it is difficult to control for confounding (5) and that the B-Pb levels measured at the age of 6 years may not be representative of exposure in utero and during early childhood, and such exposure may have been higher and may have been more relevant for the induction of the effects.

In a study of 157 children (age 4–14 years) in southern Poland, the renal glomerular filtration rate decreased with an increasing B-Pb concentration [median 70 (range 19–260) µg/l] (85) (table 1), and the urinary excretion of α_1 -microglobulin increased. This finding indicates a slight effect on the kidney. There was also an association between increased hearing thresholds and B-Pb (86).

In a Polish-Swedish study of pregnant women, there were no associations between preterm labor on one hand and lead levels in blood, myometrium, and placenta on the other (87) (table 1).

Concluding remarks

There is a large amount of information on lead concentrations in blood and some on levels in teeth and bone.

Table 2. Tooth lead levels (T-Pb) in populations in the Baltic region. (QC = quality control, N = number of samples, M = median, AAS = atomic absorption spectrometry, PIXE = particle-induced X-ray emission)

Country	Area	Pollution	Year	Method	QC ^a	Gender	Age (years)	N	T-Pb (μg/g)			Determinants	Comment
									Mean ^b	M	Range		
Finland													
Haavikko et al, 1984 (67)	South	Urban	1978	PIXE	1	Male, female	6+9	53	-	2.0—2.5	0.2—14?	-	Dentine
	Central	Urban	1978	PIXE	1	Male, female	6+9	52	-	2.7—2.9	0.6—12	-	Dentine
	South	-	1984—1985	PIXE	1	Male, female	6—7	18—31	8.8	-	-	-	Dentine
	-	-	≤1983	PIXE	2	Male, female	Children	120	3.2	-	-	-	Whole teeth
Czech Republic													
Bencko & Cikrt, 1990 (2)	Central	Industrial	<1990	AAS	0	Male, female	Children	25	3.8	-	-	-	-
Bencko, 1992 (70)	Central	Smelter	≤1992	AAS	0	Male, female	Children	24	12	-	-	-	-
	Urban	≤1992	AAS	0	Male, female	Children	25	3.9	-	-	-	-	
	Rural	≤1992	AAS	0	Male, female	Children	19	4.9	-	-	-	-	
World Health Organization, 1995 (83)	Central	Smelter	1992—1994	AAS	1	Male, female	6—14	159	(1.4—4.0)	-	<1—23	-	-
Germany													
Brockhaus et al, 1988 (37)	North-west	Smelter	1986	AAS	2	Male, female	Children	41	(3.5)	3.1	1.2—7.3	-	Whole teeth
	Urban	1986	AAS	2	Male, female	Children	909	(2.3—2.4)	2.2—2.5	0.6—36	-	Whole teeth	
	Rural	1986	AAS	2	Male, female	Children	288	(1.8—2.0)	1.8—2.0	0.5—9.7	-	Whole teeth	
Winneke et al, 1994 (84)	North-west	Smelter	1991	AAS	1	Male, female	6	55	(1.6)	-	0.4—6.9	-	-
	East	Urban	1991	AAS	1	Male, female	6	93	(2.6)	-	0.6—9.3	-	-
	"Rural"	1991	AAS	1	Male, female	6	36	(1.5)	-	0.2—4.1	-	-	
Denmark													
Grandjean et al, 1986 (71)	West	Urban	1982—1983	AAS	2	Male, female	7	14	-	-	≈1—≈40	-	Circumpulpal dentine
Lyngbye, 1991 (72)	West	Urban	1983	AAS	3	Male, female	7	914	(8.4)	-	-	-	Circumpulpal dentine
Sweden													
Möller et al, 1982 (73)	Central, south	-	≤1982	PIXE	1	Male, female	10—18	165	2.9	-	<8	-	Whole teeth

^a 0=no; 3=very good.^b Arithmetic mean except when in parentheses; values in parentheses are geometric means.**Table 3.** Bone lead levels (Bone-Pb) in populations in the Baltic region. (QC = quality control, N = number of samples, M = median, AAS = atomic absorption spectrometry, ICP-MS = inductively coupled plasma/mass spectrometry)

Country	Area	Pollution	Year	Method	QC ^a	Gender	Age (years)	N	Bone-Pb (µg/g)			Determinants	Comment
									Mean ^b	M	Range		
Finland													
Keinonen, 1992 (74)	South	Urban	1976—1979	ICP-MS	1	?	Adults	7	-	3.6	1.8—3.7	-	Bone not defined
Poland													
Baranowska et al, 1995 (75)	South	Industrial	1993	AAS	1	Male, female	26—55	35	58	45	2.9—200	-	Sternum
Germany													
Drasch et al, 1987 (76)	South	-	1983—1985	AAS	1	Male, female		240	(1.6)	1.7	0.3—10	Gender, age	Pelvis
								240	(3.7)	3.9	0.8—20	Gender, age	Femur
Drasch et al, 1994 (77)	East	Urban	1990—1991	AAS	1	Male, female	>19	50	48	-	-	-	Femur
								50	30	-	-	-	Ileum
Sweden													
Lindh, 1980 (78)	North	Rural	≤1980	AAS	0	Male, female	Adults	5	-	2.8	2.4—4.9	-	Femur
Gerhardsson et al, 1992 (79)	North	Rural	≤1992	AAS	1	Male	Adults	5	-	12	-	-	Femur
										15	-	-	Sternum

^a 0=no; 3=very good.^b Arithmetic mean except when in parentheses; values in parentheses are geometric means.

However, the data for Russia and the Baltic States are very limited. There were great geographic differences. In some areas, the uptake was extremely low, in others very high, especially in people living close to smelters. Lead-contaminated drinking water is a problem in some areas of eastern Germany. In particular, children in the southern part of Poland and in the Czech Republic had high uptakes, sufficient to cause adverse effects on the central nervous system (CNS), hearing and kidneys. However, CNS effects may also occur in Germany. The reduction of lead in gasoline has caused a major decrease in B-Pb levels.

Cadmium

General toxicology

There are recent extensive reviews on the toxicology (88) and environmental aspects (89) of cadmium. Tobacco smoking is the most important source of exposure (88). For nonsmokers, diet is the most important source. In particular, shellfish (90) and liver and kidney (91) have high levels. Furthermore, grains and vegetables contain cadmium, as a result of the uptake of cadmium from the soil (92, 93).

The cadmium level in blood (B-Cd) is often used as an index of recent exposure. However, B-Cd is influenced by the body burden of cadmium (94, 95). The elimination of cadmium from the blood has at least 2 components, the shortest having a half-time of 1–2 months (94).

Cadmium is distributed to the liver and the kidneys (88). The level in kidney (K-Cd) can be determined by *in vivo* X-ray fluorescence (96, 97). The biological half-time in the kidney is on the order of decades. In general, the cadmium concentration in urine (U-Cd) is an indicator of the concentration in the kidney (96, 97).

The kidney is the critical organ for the toxic effects of cadmium (88). The earliest effect is proximal tubular damage, which can lead to an increase in the excretion of low-molecular-weight proteins and tubular enzymes. A study of the general population in Belgium indicates that the critical K-Cd concentration is about 50 µg/g (98). A recent evaluation of all available data points in the same direction (99). The corresponding U-Cd excretion is 2 µg/day [about 1 µg/l (or 1 µg/g creatinine)] for men and about 1.3 µg/l (or 2 µg/g creatinine) for women and corresponds to about 2 µg/l in blood (94). Occupational exposure to cadmium is associated with lung cancer (100).

Exposure

Naturally high levels of cadmium in soil are present in some areas of Sweden (101). Cadmium in soil can also

be present naturally or originate from contamination from fertilizers or industries. The cadmium concentrations in agricultural soil in Sweden (102) and Denmark (103) have increased continuously for many years. Acid precipitation is a problem since a low pH of the soil increases this absorption (92, 93, 101). A low pH of water is also associated with an elevated cadmium concentration (63, 104).

Data on cadmium exposure over time indicate that levels in grain (105, 106), liver from herring in the Baltic Sea (107), pig kidney (91), and total human diet (99, 108, 109) have increased in Sweden.

There are several studies on the concentrations of cadmium in blood (B-Cd) in populations in the Baltic region (table 4). Smoking has a strong effect on B-Cd. Thus heavy smokers have levels about 5 times higher than those of nonsmokers. This effect masks any other environmental factors. It is therefore only meaningful to make comparisons for nonsmoking populations. On the other hand, the B-Cd in nonsmokers is low. Thus there is an analytic challenge.

In principle, there are few known determinants for B-Cd, much fewer than for B-Pb. This situation may partly be due to analytic problems, but also to the fact that fewer studies have been devoted to cadmium than to lead. However, age seems to be of importance for B-Cd (table 4). Thus adults have about twice the levels found in children. Furthermore, low iron stores are associated with an increase in B-Cd (90, 95). As low iron stores are more common in women than in men, one could expect women to have higher B-Cd levels than men, and it is often the case. However, men are exposed to cadmium occupationally or via smoking more often than women. The intake of dietary fibers (95) and shellfish (90) was related to a slight increase in B-Cd, probably because of a higher content of cadmium in the fiber-associated part of the grain and in shellfish.

Living close to smelters has rarely been associated with an increase of B-Cd (table 4). However, studies in Germany (112) and Poland (Kaniewski et al, to be published) seem to indicate such an effect, and one in northern Sweden can be interpreted to give some indication in the same direction (113). Living in a city center does not seem to affect B-Cd significantly.

The most extensive information on cadmium exposure is available from Sweden and Germany (table 4). In Sweden, the B-Cd is generally low, 0.1–0.2 µg/l for children and 0.2–0.3 µg/l for adults. Little information is available as regards Finland. In its northern regions, the level may be dependent upon the nearness to Russian smelters. There is no information on the conditions in Russia, nor in the Baltic countries. In Poland, a comparison using the same sampling technique and analysis indicates that B-Cd may be about twice the levels of those in Sweden (58, 87 and Kaniewski et al, to be published).

In particular, the levels are increased in southern Poland, where a relationship to the distance of habitation from a smelter was found. The levels in southern Poland are sufficiently high to be assumed to be associated with slight kidney effects in part of the population, in particular among smokers. Low B-Cd levels have been reported from the Czech Republic (in fact, the lowest ever reported), Germany and Denmark.

In the absence of kidney damage, U-Cd is a better index of the body burden than B-Cd is. However, the available information as regards populations in the Baltic region is far more scarce than for B-Cd. There are also analytical problems due to the low concentrations. Thus comparative data have not been included in this paper. Studies on nonsmoking Swedish women 20–50 years of age have shown average values of about 0.15 µg/g creatinine (90, 95). Among 62 nonsmoking women and men, those who lived ≤0.5 km from a closed nickel cadmium battery in southern Sweden had a median U-Cd of about 1 µg/g creatinine, and for those in the range of 0.5–1 km had values of about 0.4 µg/g, while 24 men from the region had values of about 0.2 µg/g (114).

Data on concentrations of K-Cd are available for some areas (table 5). The quality control has not been sufficient in most studies. However, the effect of smoking is again clear. Other determinants have not been studied. There are no pronounced differences between geographic areas. However, it seems that subjects from southern Poland have higher levels than the other areas, in accordance with the B-Cd concentrations discussed earlier. For other areas, there are no clear differences. The average level in southern Poland is so high that, theoretically, slight kidney effects in part of the population, particularly among smokers, should be expected when a probable skewed distribution towards high levels is taken into consideration. There are indications that K-Cd concentrations have increased during this century in southern Germany (128). In Sweden data indicate both an increase (99, 129) and a later decrease (130, 131).

In a study of 427 schoolchildren in Lithuania, the mean cadmium concentration in hair was 0.22 (range 0.20–0.26) µg/g (80). For 1341 adult Germans, the mean level was 0.15 (range <0.02–4.1) µg/g (81). No information from Lithuania on cadmium levels in other media is available.

Toxic effects

A study of the nephrotoxic effects of cadmium exposure was made among 65-to-66-year-old women (smokers and nonsmokers) in 2 areas in northwestern Germany contaminated with cadmium from smelters and in an uncontaminated area (table 4) (111). The geometric mean B-Cd values for the 2 contaminated areas were 0.86 and 0.58 (range up to 5.5) µg/l. In the unpolluted area, the mean B-Cd was 0.53 µg/l. There was no significant dif-

ference between the areas regarding the urinary excretion of high- or low-molecular-weight proteins.

On the other hand, another study in Germany indicates that cadmium may have a nephrotoxic effect. Hence subjects who worked 1.5 km from a battery factory (median B-Cd 8.2 µg/l, U-Cd 5.1 µg/g creatinine) (112) had clearly higher urinary excretions of the tubular brush-border (alanine aminopeptidase and alkaline phosphatase) and lysosomal (N-acetyl-β-glucosaminidase = NAG) enzymes (but lower of albumin) than subjects without known cadmium exposure (B-Cd 1.0 µg/l, U-Cd 0.8 µg/g creatinine). Both groups included smokers and nonsmokers in approximately the same proportions. The health significance of the enzymuria is not clear.

Similarly, among 64 women and men who lived ≤1 km from a closed nickel-cadmium battery plant in southern Sweden, there were associations between distance to the plant and U-Cd (see the preceding discussion) on one hand and the excretion of NAG in urine and U-Cd (range about 0.1–3 µg/g creatinine) on the other (114).

In the study of children from schools close to a smelter in the Czech Republic, there was no effect of the cadmium exposure on kidney function, which, however, was low (table 4) (82).

Pregnant Polish women had higher cadmium levels in blood, myometrium, and placenta than Swedish women, even among nonsmokers (table 4) (87). The B-Cd level was significantly higher in women who delivered preterm than in those who went full term.

Concluding remarks

There is a wealth of information on cadmium exposure in Sweden, Germany and Poland, much less for the rest of the region, and none for Russia and the Baltic states. Limited data indicate that living close to cadmium-emitting industries causes an increase in uptake. The cadmium concentrations in blood and kidney differed much geographically. The highest levels were found in southern Poland, where the levels are so high that they, on the basis of other information on the relation between levels in biological media and response, may cause proximal tubular damage in a fraction of the population. Slight kidney effects have been found in populations living in the vicinity of cadmium-emitting industries in Germany and Sweden.

Mercury

General toxicology

Mercury occurs in several different chemical forms. From an environmental and toxicologic point of view, inorganic mercury in the form of elemental mercury and methylmercury are of particular importance. Thus this review focuses on these agents.

Table 4. Cadmium levels in blood (B-Cd) in populations in the Baltic region. (QC = quality control, N = number of samples, M = median, ND = none detected)

Country	Area	Pollution	Year	QC*	Gender	Age (years)	N	B-Cd (µg/l) ^{b, c}			Determinants	Comment
								Mean ^d	M	Range		
Finland												
Luoma et al, 1995 (110)	North	-	≤1991	1	Male	20—82	152	0.3—0.7	-	ND-35	Closeness to Russia	Nonsmoker
							78	1.2—3.5	-	-	Closeness to Russia	Smoker
Poland												
Zielonka & Wodzien, 1993 (21)	South	Smelter	1987—1991	1	Male, female	12	220	3.3	3.3	0.1—17	-	-
		Urban	1987—1991	1	Male, female	12	211	2.9	2.7	0.2—7.6	-	-
		Rural	1987—1991	1	Male, female	12	152	3.9	3.9	0.1—15	-	-
Laudanski et al, 1991 (22)	North-east	-	≤1990	0	Female	17—75	89	2.9	-	-	-	-
							175	2.5	-	-	-	Nonsmoker, smoker
Osman et al, 1992 (23)	South	Industrial	1991	3	Female	22—39	8	-	0.7	0.4—1.3	-	Nonsmoker, smoker
Kaniewski et al, to be published	South-west	Industrial Urban	1991	3	Male, female	7—8	10	-	0.5	0.3—0.8	-	-
			1991	3	Male, female	8—9	45	0.19	-	0.08—0.41	-	-
			1991	3	Male, female	8—9	40	0.18	-	0.06—0.38	-	-
	South	Smelter Urban	1991	3	Male, female	8—9	40	0.16	-	0.06—0.28	-	-
			1991	3	Male, female	8—9	42	0.38	-	0.14—0.88	-	-
			1991	3	Male, female	8—9	40	0.28	-	0.14—0.56	-	-
	Rural	1991	3	Male, female	8—9	39	0.30	-	0.10—0.66	-	-	
		1991	3	Male, female	8—9	39	0.30	-	0.10—0.66	-	-	
Fagher et al, 1993 (87)	North-east	Industrial	≤1992	3	Female	27	9	1.8	-	-	Smoking	Nonsmoker, smoker
Andrzejak et al, 1993 (28)	South-west	Smelter	≤1993	1	Male, female	2—18	28	19	-	-	Time	Correct level?
						Adults	32	35—38	-	-	Time	Correct level?, nonsmoker, smoker?
Osman et al, 1992 (23)	South	Industrial	≤1994	3	Male, female	8—9	140	-	0.4	0.2—2.4	Time	-
Osman et al, 1998 (58)	South	Industrial	1995	3	Male, female	9	211	0.4	0.4	0.1—4.6	Siblings, body weight	-
Janousek et al, 1994 (32)	South	Industrial	≤1994	1	Male, female	0	13	-	2.2	1.2—9.4	-	Cord blood
Osman et al, 1998 (35)	South-Central	Industrial Urban	1996	3	Male, female	4—14	157	0.4	0.3	0.1—3.2	-	Cord blood
			≤1994	1	Male, female	0	8	-	2.0	0.9—3.0	-	Cord blood
Czech Republic												
Bernard et al, 1995 (82)	East-South-east	Smelter	≤1995	2	Male, female	12—15	144	0.05—0.1	-	0.01—0.37	-	-
		Rural	≤1995	2	Male, female	12—15	51	0.06—0.07	-	0.02—0.32	-	-
Kuřera et al, 1995 (36)	Central	Urban	≤1995	1	Male, female	Adults	406	0.4	-	<0.02—0.96	Smoking	Nonsmoker
							55	2.5	-	0.02—1.1	Smoking	Heavy smokers
Germany												
Ewers et al, 1985 (111)	North-west	Smelter	1983	2	Female	65—66	200	(0.58—0.86)	-	0.2—5.5	Smoking husband	-
		Urban	1983	2	Female	65—66	86	(0.53)	-	0.2—3.8	Smelter worker, residence area	-
Krause et al, 1989 (81)	-	-	1985—1986	2	Male, female	25—69	2,331	0.95	0.40	<0.1—12	-	Nonsmoker, smoker
Brockhaus et al, 1988 (37)	North-west	Urban/industrial Rural	1986	2	Male, female	6—7	987	-	0.30	-	-	Nonsmoker
			1986	2	Male, female	6—7	363	-	1.4	-	-	Nonsmoker
			1986	2	Male, female	6—7	363	-	0.13—0.15	<0.1—4.8	-	Smoker
			1986	2	Male, female	6—7	363	-	0.14—0.19	<0.1—0.6	-	-
Ewers et al, 1990 (38)	North-west	Smelter	1988	2	Female	55—66	11	(0.4)	-	0.2—1.4	-	Nonsmoker
		Urban	1986	2	Female	55—66	662	(1.8)	-	1.3—2.4	-	Smoker
		Urban	1986	2	Female	55—66	158	(0.4)	-	0.1—3.7	-	Nonsmoker
		Rural	1986	2	Female	55—66	221	(1.8)	-	0.3—8.3	-	Smoker
						31	(1—6)	-	0.1—1.4	-	Nonsmoker	
								-	0.3—4.2	-	Smoker	

(continued)

Table 4. Continued

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	B-Cd (µg/l) ^{b, c}			Determinants	Comment
								Mean ^d	M	Range		
Germany continued												
Hofstetter et al, 1990 (39)	North-west	Smelter	1989	2	Male, female	6—7	229	(0.14)	-	<0.1—0.54	Immigrant-ship	-
Begerow et al, 1994 (41)	North-west	Urban	1991	2	Male, female	6	1,028	(0.13)	-	<0.05—10	-	-
	South-east	Urban	1991	2	Male, female	6	1,283	(0.13)	-	<0.05—0.63	-	-
Denmark												
Grandjean et al, 1992 (46)	Central	-	≤1991	2	Male, female	20—69	96	0.26	<0.3	<0.3—2.6	-	Nonsmoker
							23	2.7	2.6	0.1—6.4	-	Heavy smokers
Sweden												
Svensson et al, 1987 (104)	South	Rural	1987	3	Male, female	20—66	145	0.25	-	<0.2-?	Smoking	Nonsmoker
Willers et al, 1992 (60)	South	Urban	1987	3	Male, female	26—52	62	(0.19—0.24)	-	0.07—1.3	Smoking	Nonsmoker
						7—10	45	(1.3—2.0)	-	0.19—3.7	-	Smoker
							77	(0.08—0.09)	-	0.04—0.20	-	-
Willers et al, 1988 (61)	South	Smelter	1988	3	Male, female	4—11	13	(0.16)	-	0.09—0.42	-	-
	Urban		1988	3	Male, female	4—11	53	(0.13)	-	0.05—0.61	-	-
	Rural		1988	3	Male, female	4—11	39	(0.14)	-	0.06—0.34	-	-
Vahter et al, 1991 (48)	Central	Urban	1988	3	Female	27—46	15	0.32	0.30—0.33	0.11—0.86	-	Nonsmoker
Bensryd et al, 1994 (63)	South	Rural	1989—1990	3	Male	17—77	144	0.18	-	0.08—0.58	-	Nonsmoker
							40	1.3	-	0.18—4.0	-	Smoker
Jakobsson	North	Smelter	1989—1991	1	Female	Adults	135	0.65	-	-	Smoking, closeness to smelter??	Nonsmoker
Lagerkvist et al, 1993 (113)	Rural		1989—1991	1	Female	Adults	96	0.54	-	-		Nonsmoker
		Smelter	1989—1991	1	Female	Adults	74	1.3	-	-		Smoker
		Rural	1989—1991	1	Female	Adults	53	1.4	-	-		Smoker
Berglund et al, 1995 (54)	Central	Industrial	1991	3	Male, female	1—4	71	0.26	0.24	0.09—1.0	-	-
Vahter et al, 1996 (90)	West	Urban	≤1994	3	Female	20—50	51	0.24—0.28	0.23—0.25	<0.09—0.68	Iron status, shellfish	Nonsmoker
Bæcklund, 1996 (52)	-	-	1992—1994	3	Male, female	<55	330	-	0.3	0.05—2.2	Smoking, age, occupational exposure	Nonsmoker
						>90	67	-	1.3	0.1—6.8		Smoker
Kaniewski et al, to be published	South	Smelter	1991	3	Male, female	8—9	48	0.09	-	0.03—0.20	-	-
	Urban		1991	3	Male, female	8—9	94	0.10	-	0.03—0.28	-	-
	Rural		1991	3	Male, female	8—9	78	0.09	-	0.04—0.20	-	-
Berglund et al, 1994 (95)	West	Urban	≤1994	3	Female	20—50	57	0.24—0.32	0.23—0.25	≤0.09—0.96	Iron status, age, fiber intake	Nonsmoker
Berglund et al, 1994 (53)	Central	Industrial	1994	3	Male, female	1—5	72	-	0.04	≤0.03—0.25	-	-
Hanberg & Ahlborg, 1995 (55)	Central	Industrial	1994	1	Female	18—50	53	0.2	-	0.05—0.7	Smoking	Nonsmoker
							21	1.0	-	0.4—2.7	Smoking	Smoker
Nordberg et al, 1996 (57)	Central	Urban	≤1996	1	Male, female	>75	124	-	0.2	-	Smoking	Nonsmoker
							21	-	4.0	-	Smoking	Smoker

^a 0=no; 3=very good. ^b All determinations were made by atomic absorption spectrometry (flame or electrothermal). ^c 1.0 µg/l = 9.2 nmol/l.

^d Arithmetic mean except when in parentheses; values in parentheses are geometric means.

The environmental aspects of mercury have been reviewed recently (132). The toxicology of inorganic mercury has been reviewed (133). The mercury level in blood (B-Hg) is often used as an index of recent uptake. The elimination of mercury from the blood has at least 2 components, one with a half-time of about 1 month and the other a half-time several times longer (134). Mercury in the kidney of the fetus is influenced by maternal amalgams (135), as is the mercury level in milk (136).

B-Hg values of 20 µg/l and urinary mercury (U-Hg) values of about 50 µg/l (about 50 µg/g creatinine) or higher have been associated with effects on the CNS and kidneys (133).

There is a recent review on the toxicology of methylmercury (137). In the blood of subjects exposed to methylmercury, mercury is mainly bound to the erythrocytes. The total (and sometimes organic) mercury level in whole blood (B-Hg), erythrocytes (Ery-Hg) and

Table 5. Cadmium levels in kidney (K-Cd) in populations in the Baltic region. (QC = quality control, N = number of samples, AAS = atomic absorption spectrometry, NAA = neutron activation analysis, XRF = X-ray fluorescence, ICP-MS = inductively coupled plasma/mass spectrometry)

Country	Area	Pollution	Year	Method	QC ^a	Gender	Age (years)	N	K-Cd (μg/g)			Deter- minants	Comment
									Mean ^b	Median	Range		
Finland													
Ala-Opas & Tahvonen, 1995 (115)	Central	-	1992	AAS	2	Male, female Male	40—75	8	16	-	3.4—21	Smoking	Nonsmoker
								5	28	-	22—39	Smoking	Smoker, kidney cancer
Poland													
Bem et al, 1993 (116)	South	Urban	1985—1989	AAS	2	Male, female	60	27	35	25	-	Smoking	Nonsmoker
							50	46	48	40	-	Smoking	Smoker
Bem et al, 1993 (117)	Central	Urban	1985—1989	AAS	2	Male, female	48	13	26	20	-	Smoking	Nonsmoker
							52	35	62	57	-	Age	Smoker
Bem et al, 1993 (118)	North-east	Industrial	1991	AAS	1	Male, female	51	35	20	-	-	Smoking	Nonsmoker
							50	43	38	-	-	Smoking	Smoker
							[41—60] ^c	[7] ^c	[42] ^c	-	-	-	Nonsmoker, smoker
Germany													
Thürauf von et al, 1981 (119)	South	-	1980	AAS	1	Male, female	17—92	39	-	7.9	0.6—25	-	Nonsmoker, smoker, whole kidney
Drasch, 1982 (120)	South	Urban	1980—1981	AAS	1	Male, female	51	33	24	-	-	Smoking	Nonsmoker
							49	21	73	-	-	Smoking	Heavy smokers
Summer et al, 1986 (121)	South	?	≤1986	AAS	1	Male, female	43—56	14	≈18	-	5—99	Smoking	Nonsmoker
							39—60	21	33	-	≈8—≈55	Smoking	Heavy smokers
Hahn et al, 1987 (122)	North-west	Urban	≤1986	AAS	2	Male, female	0—90	89	(13)	-	-	Smoking	Nonsmoker
							66	(27)	-	-	Smoking	Heavy smokers	
							[41—50] ^c	[10] ^c	[17—23] ^c	-	-	Smoking	Nonsmoker
Drasch et al, 1994 (77)	East	Urban	1990—1991	AAS	1	Male, female	≥19	50	17	-	-	-	Nonsmoker, smoker
Denmark													
Hansen et al, 1989 (123)	All	-	1981—1987	AAS	1	Male, female	0—85	129	12	-	0.4—46	-	Nonsmoker, smoker
							[41—45] ^c	[8] ^c	[24] ^c	-	[2.3—40] ^c	-	Nonsmoker, smoker
Sweden													
Elinder et al, 1976 (130)	Central	Urban	1973—1974	AAS	1	Male, female	3—94	52	9.9	-	-	Smoking, gender	Nonsmoker
								75	20	-	7-150	Smoking, gender	Smoker
Svartengren et al, 1986 (124)	Central	Urban	1983	AAS	3	Male, female	30—59	20	18 14	17 14	3—39 -	-	Whole kidney Cortex
Lindqvist et al, 1989 (125)	North	-	≤1989	NAA	1	Male, female	16—69	22	8.7	8.6	2.9—22	-	Nonsmoker, smoker?
Bensryd, 1993 (126)	South	Rural	1989—1990	In vivo XRF	1	Male	17—77	40	18	-	2—210	-	Nonsmoker
Nilsson et al, 1995 (96)	South	Urban	1992—1993	In vivo XRF	1	Male	47	11	-	10	3—28	Smoking	Nonsmoker, smoker
Lutz et al, 1996 (135)	Central	Urban	1992—1994	AAS	3	Male, female	Fetuses	14	2.6	2.2	0.7—7.8	-	ng/g
Nilsson et al, 1995 (96)	South	Urban	≤1995	In vivo XRF	1	Male, female	26—60	10	10	8	3—80	Smoking	Nonsmoker
							27—65	10	26	28	4—33	Smoking	Smoker
Friis et al, 1998 (131)	Central	-	1995—1996	AAS	2	Male, female	4—95	58	(2.5—6.9)-	-	-	Smoking	Nonsmoker
							60	(5.1—19)	-	-	Smoking	Smoker	
Barregård et al, 1997 (127)	West	-	≤1997	ICP—	3	Male, female	27—71	38	19	-	2.5—46	-	Biopsies
			MS										

^a 0=No; 3=very good. ^b Arithmetic mean except when in parentheses; values in parentheses are geometric means. ^c The fraction of middle-aged subjects is shown in brackets (to facilitate comparisons).

sometimes plasma or serum (138) is used as an index of exposure, body burden, and the risk of toxicity of methylmercury. The elimination of methylmercury from the blood follows a 1-compartment pattern with a half-time of about 1 month.

Methylmercury passes the blood-brain barrier and reaches the CNS (137). It also passes through the placenta into the fetus. The mercury concentration in hair (H-Hg) is often used as an index of exposure, body burden, and risk of toxic effects. The critical H-Hg in preg-

nant women for effects on the CNS of the fetus has been estimated to be 10–20 µg/g or even lower. There is some experimental evidence of carcinogenicity for methylmercury (137).

Exposure

Data on B-Hg have been compiled in table 6. Amalgam fillings affect the B-Hg level to some extent. Fish intake is a major determinant of B-Hg. In subjects who do not eat fish, B-Hg is about 1 µg/l. In particular, a high intake of fish from contaminated waters can cause substantially increased B-Hg levels. The concentrations of methylmercury in fish are clearly elevated in many lakes, rivers, and coastal waters, especially in Sweden and Finland, mainly as a result of mercury emissions from the chlorine alkali industry and earlier use of mercury as a preservative in the pulp and paper industry. B-Hg values of up to about 50 µg/l in erythrocytes, a level which corresponds to about 25 µg/l in whole blood, have been reported in fishermen and their wives in Sweden and Latvia (Gulf of Riga). In populations with a lower intake of contaminated fish, and in other areas, the B-Hg values were lower.

In earlier studies in populations with a high consumption of contaminated fish in Sweden and Finland, much higher exposure levels have been reported (Ery-Hg values up to about 1200 µg/l) (152). However, such extreme concentrations are not encountered nowadays, since restrictions on the emissions of mercury have been enforced, the waters with the highest levels in fish have been black-listed, and warnings from the authorities to the population against the consumption of such fish have been issued.

Table 7 contains information on H-Hg. Again, fish intake is a major determinant. Levels up to 10–15 µg/g were found in subjects with a high intake of fish. A decreasing time trend was found in 1 study (158), in accordance with the observed decreasing B-Hg level (159, 152).

The B-Hg and H-Hg values reported during the last decade are rather low, as compared with the ones associated with reported effects by methylmercury on the adult CNS. However, the highest levels are in the range where effects on the developing CNS have been observed. In Sweden, this finding has resulted in recommendations for restrictions on fish consumption, especially for women of child-bearing age. However, the present information is incomplete. Thus there is no information at all from Russia, where the environmental contamination with mercury is known to be extensive in some areas. Furthermore, the distribution of levels in populations living in areas with contaminated fish is skewed; thus, a few people who still consume such fish may well have much higher levels.

For U-Hg, fish intake is not important, but dental amalgam is a major determinant (table 8). Thus subjects without amalgam have <1 µg/l, while those with many fillings may have a few micrograms per liter or more. In particular, subjects with many fillings, who frequently use chewing gum, especially nicotine gum, have increased levels. In such cases, U-Hg values of up to 50 µg/l have been reported (165, 166). This level corresponds to the lowest reported to be associated with subtle effects on the CNS and kidney in workers exposed to elemental mercury vapor (133). After the removal of amalgam fillings, there was a decrease (167). In some studies, women had higher levels than men, and older subjects had higher values than younger ones. U-Hg shows no obvious geographic differences.

Toxic effects

In an immunotoxicologic study of Latvian fishermen, there was a statistically significant correlation between B-cell counts and the CD4+/CD8+ ratio on one hand and Ery-Hg on the other (168). However, the association may not be causal since a high fish diet includes several other potentially immunomodulating agents. Furthermore, a similar study of Swedish fishermen did not reveal a pattern consistent with an effect of methylmercury (169).

In a study in Finland, there were associations between acute myocardial infarction and total mortality on one hand and fish intake and H-Hg on the other (158). In the highest H-Hg tertile (>2 µg/g), there was a 2.9-fold [95% confidence interval (95% CI) 1.2–6.6] increase in cardiovascular deaths. Furthermore, there was an association between acute myocardial infarction and U-Hg. The results are interesting, but the high average H-Hg found in the study population is confusing. In a similar study in Sweden, high Ery-Hg counts were associated with low risk (Hällgren, et al to be published).

Exposure to methylmercury among subjects consuming large amounts of contaminated fish was associated with an increased frequency of chromosomal aberrations (170), which is a risk indicator of later cancer (171). However, due to control measures, such high exposure is now uncommon.

Concluding remarks

Methylmercury uptake is dependent upon the intake of fish, in particular from contaminated lakes and rivers, which occur in Sweden and Finland, as well as the eastern coast of the Baltic Sea. Consumers of such fish may attain rather high mercury concentrations in blood and hair. There are some indications of immunotoxic effects in association with the intake of such fish. However, these effects may not be caused by methylmercury since fish contain other immunomodulating agents. The exposure to inorganic mercury is mainly from amalgam fillings, without much geographic variation.

Table 6. Blood mercury levels (B-Hg) in populations in the Baltic region. (N = number of samples, M = median)

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	B-Hg (μg/l) ^{b, c, d}			Deter- minants	Comment
								Mean ^e	M	Range		
Finland												
Aitio et al, 1983 (139)	?	Chlorine alkali plant	≤1983	2	Male	40	10	4.0	-	-	-	-
Piikivi & Hänninen (140)	North-west	-	≤1989	2	Male	28—55	60	3.8	-	1.0—10	-	-
Luoma et al, 1992 (141)	North	-	≤1992	0	Male	41	101	6.0	-	-	Fish intake	-
Latvia												
Leja et al, 1993 (142)	West	-	1992	3	Male	?	13	[19] [8.9]	- -	[4.7—48] [2.2—25]	Fish intake Fish intake	Fishermen Fish processing industry
Hagmar et al, 1995 (168)	West	-	≤1995	3	Male, female	25—79	19	-	[1.5]	[0.8—4.2] [0.08—8.6]	Fish intake Fish intake	Low fish Organic mercury, low fish
						24—64	24	-	[7.2]	[0.9—44]	Fish intake	Intermediate fish
						27—64	25	-	[18]	[8.8—37]	Fish intake	High fish
Czech Republic												
Kučera et al, 1995 (36)	Central	-	≤1995	1	Male, female	Adults	611	0.7—1.2	-	-	-	-
Poland												
Osman et al, 1992 (23)	South	Industrial	1991	3	Female	22—39	8	<4	-	<4	-	Pregnant
Osman et al, 1998 (35)	South	Industrial	1995	3	Male, female	7—8	10	<4	-	<4	-	-
						4—14	211	0.6	0.6	0.1—2.2	-	-
Germany												
Schaller et al, 1983 (143)	South	Urban	1981	1	Male, female	3-?	181	-	0.6	0.1—7.2	-	-
		Rural	1981	1	Male, female	3-?	65	-	0.8	0.1—4.9	-	-
Krause et al, 1989 (81)	-	-	1985—1986	2	Male, female	25—69	2,294	0.5	0.7	<0.2—11	Fish intake	-
Trepka et al, 1997 (144)	East	Industrial	1992—1993	3	Male, female	5—14	803	(0.2)	-	0.1—2.8	Fish intake, - amalgam	-
Denmark												
Grandjean et al, 1992 (46)	Central	-	≤1991	2	Male	20—69	100	1.2	1.3	<1.0—4.1	Fish intake, -	-
					Female	20—69	99	1.6	1.6	<1.0—6.2	dental amalgam	-
Sweden												
Langworth et al, 1991 (145)	-	-	1985—1986	3	Male	44	75	3.0	-	0.2—13	Fish intake	-
Skerfving, 1988 (146)	East	-	≤1986	1	Female	18—38	10	[24]	-	[6—46]	Fish intake	Pregnant
Åkesson et al, 1991 (147)	South-east	-	≤1987	3	Male, female	37	81	3.4	-	1.2—12	Fish intake, dental amalgam	-
Svensson et al, 1992 (159)	South-east	-	≤1987	3	Male, female	15—79	96	5.1—6.7	-	1.8—26	Fish intake	Fish ≥3/week
						25—57	13	1.8	-	1.2—2.4	-	No fish Partly same as (150)
Schütz et al, to be published	South	-	1989	3	Male, female	7—9	161	1.5	-	0.6—3.7	Fish intake, dental amalgam	-
Bensryd et al, 1994 (63)	South	Rural	1989—1990	3	Male	17—77	237	-	2.6	0.7—19	Fish intake	-
Erfurth et al, 1990 (148)	South	-	≤1990	3	Male	24—62	21	[3.8]	-	[1.3—6.9]	-	-
Molin et al, 1990 (149)	North	-	≤1990	3	Male, female	25—44	5	[4.7]	-	-	-	-
Molin et al, 1991 (150)	North	-	≤1991	3	Male, female	25—63	18	[4.4]	-	[1.4—8.9]	Dental amalgam	Amalgam free
						29—41	5	[4.0]	-	[2.2—6.5]	Fish intake	Lactating
Oskarsson et al, 1996 (136)	North	-	≤1995	3	Female	30	30	2.3	-	0.9—4.6	-	-
Herrström et al, 1997 (151)	South-west	Urban	≤1997	3	Male, female	19	77	-	0.3	-	Dental amalgam	-

^a 0=No; 3=very good. ^b All determinations were made by cold vapor atomic absorption spectrometry. ^c 1 µg/l = 4.9 mmol/l.
^d Erythrocyte levels within brackets. ^e Arithmetic mean except when in parentheses; values in parentheses are geometric means.

Table 7. Hair mercury levels (H-Hg) in populations in the Baltic region. (QC = quality control, N = number of samples)

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	H-Hg (µg/l) ^b		Determinants	Comment
								Mean	Range		
Finland											
Mussalo-Rauhamaa et al, 1996 (153)	South	Urban	1982—1984	1	Male, female	?	29	0.6	0.02—2.7	-	-
	North	-	1991	1	Male, female	45	25	1.6—2.2	0.2—6.2	-	-
Salonen et al, 1995 (158)	East	-	1984—1989	1	Male	42—60	1833	1.9	0—16	Fish intake, time	-
Germany											
Airey et al, 1983 (154)	North	Urban	≤1983	1	Male, female	?	28	0.5	0.2—3.0	Fish intake	-
Sweden											
Forhammar et al, 1984 (155)	North	-	1983	1	Female	Adults	70	0.62	0.2—2.5	Fish intake	Pregnant
Oskarsson et al, 1994 (156)	North	Smelter	1989—1991	2	Female	28	124	0.26	-	Fish intake	Pregnant
	North	"Rural"	1989—1991	2	Female	27	79	0.32	-	Fish intake	Pregnant
Oskarsson et al, 1996 (136)	North	-	≤1996	3	Female	30	30	0.28	0.07—0.7	Fish intake	Lactating
Oskarsson et al, 1990 (157)	Central	-	1985	2	Male, female	21—81	50	3.2	0.3—11	Gender, fish intake	Fish from contaminated lakes

^a 0=no; 3=very good. ^b All determinations were made by cold vapor atomic absorption spectrometry.

Table 8. Urinary mercury levels (U-Hg) in populations in the Baltic region. (QC = quality control, N = number of samples, M = median)

Country	Area	Pollution	Year	QC ^a	Gender	Age (years)	N	U-Hg (µg/l) ^{b, c}			Determinants	Comment
								Mean ^d	M	Range		
Finland												
Salonen et al, 1995 (158)	East	-	1984—1989	2	Male	42—60	207	1.2	-	0—5.0	Fish intake	Half sample myocardial infarction
Piikivi & Hänninen, 1989 (140)	North-west	-	≤1989	1	Male	28—55	60	2.1	-	1.0—6.7	-	-
Germany												
Schaller et al, 1983 (143)	South	Urban	1981	1	Male, female	3-?	165	-	0.6	0.1—1.9	-	-
Krause et al, 1989 (81)	-	Rural	1981	1	Male, female	3-?	58	-	1.3	0.3—3.2	-	-
Dolgnier et al, 1988 (160)	-	-	1985—1986	2	Male, female	25—69	2,519	0.9	0.25	<0.5—54	Gender, age	-
Zander et al, 1990 (161)	North-west	Urban	1986	1	Male, female	5—6	144	0.45 ^e	-	0.1—6.5 ^e	-	-
Zander et al, 1990 (162)	West	Industrial	≤1990	2	Male, female	1—79	703	0.75 ^e	0.80	<0.1—19 ^e	Gender, age	-
Zander et al, 1992 (163)	?	-	≤1990	1	Male, female	18—63	21	0.18	-	<0.1—1.1	Dental amalgam	No fillings
Trepka et al, 1997 (144)	-	-	≤1990	1	Male, female	18—63	72	0.57	-	<0.1—7.7	Dental amalgam	Fillings
Zander et al, 1992 (163)	West	-	≤1992	2	Male, female	22—63	29	0.5	-	0.1—4.1	Dental amalgam	-
Trepka et al, 1997 (144)	East	Industrial	1992—1993	3	Male, female	5—14	803	(0.3) ^e	-	0.03—14 ^e	Dental amalgam	-
Sweden												
Langworth et al, 1991 (145)	-	-	1985—1986	3	Male	44	75	1.9 ^e	-	0—7.5 ^e	Dental amalgam	-
Langworth et al, 1993 (164)	-	-	<1992	1	Male, female	20—70	39	2.2 ^e	-	0.6—10 ^e	-	-
Svensson et al, 1987 (104)	South-east	-	≤1987	3	Male, female	15—79	125	1.3—2.8	-	0.2—18	Dental amalgam, gender	-
Åkesson et al, 1991 (147)	South-east	-	≤1987	3	Male, female	37	81	1.9 ^e	-	0.2—10 ^e	Dental amalgam	Part of (59)
Molin et al, 1990 (149)	North	-	≤1990	3	Male, female	25—44	10	3.1 ^e	-	-	-	-
Molin et al, 1990 (167)	North	-	≤1990	3	Male, female	20—32	8	0.5—0.6 ^e	-	-	-	-
Erfurth et al, 1990 (148)	South-east	-	≤1990	3	Male	24—62	21	0.7—1.0 ^e	-	0.2—2.3 ^e	-	-
Molin et al, 1991 (150)	North	-	≤1991	3	Male	25—63	18	1.4	-	0.4—37	Dental amalgam	-
Sällsten et al, 1996 (166)	South-west	-	≤1996	3	Male, female	29—41 42—61	5 19	0.5 ^e 2.6 ^e	- 2.1	0.4—0.9 ^e 0.7—6.7 ^e	- Dental amalgam	Amalgam free

^a 0 = no; 3 = very good. ^b All determinations were made by cold vapor atomic absorption spectrometry. ^c 1 µg/l = 4.9 mmol/l.

^d Arithmetic mean except when in parentheses; values in parentheses are geometric means. ^e µg/g creatinine (1 µg/g creatinine ≈ 1 µg/l).

Arsenic

General toxicology

The toxicology of inorganic arsenic has been reviewed (172, 173). Arsenic occurs in several different chemical forms. From a toxicologic point of view, the inorganic arsenic compounds are the most important, especially arsenite (trivalent) and arsenate (pentavalent). In the marine food web, arsenate is methylated and transformed into arsenobetaine and various arsenosugars, which accumulate in algae, fish, and shellfish. These forms of arsenic are considerably less toxic than inorganic arsenic.

Trivalent arsenic is methylated, mainly in the liver, to methylarsonic acid and dimethylarsinic acid, which are rapidly excreted in the urine (173). Arsenic in urine is often used as an index of exposure to inorganic arsenic. However, it is largely influenced by the rapid excretion of the organic arsenic compounds in seafood (174, 175). The elimination pattern of inorganic arsenic has several components; in general, half the dose is excreted within 3–4 days. Inorganic arsenic is also excreted in hair, which may be used as a biological index of exposure (176).

There are scant data on the relation between toxic effects and urinary arsenic (U-As) levels (172). However, a concentration of 50 µg As/l in drinking water has been associated with a lifetime risk for cancer of the skin, bladder, lung, and kidney of 1–13/1000 of the population (177, 178). This concentration in water has been found to correspond to a U-As of 25–65 µg/l (179). In smelters, where the workers are affected by lung cancer and slight vascular and neurological effects, the U-As has been in the range of 40–200 µg/g creatinine (180).

Exposure

Information on U-As is reviewed in table 9. When the data are examined, the chemical forms of arsenic determined must be kept in mind. One study indicates an influence of exposure to environmental tobacco smoke on U-As in children (185). As expected, fish intake has a significant effect on the concentrations of total and organic arsenic (175, 186). One study also shows a slight effect of fish intake on the concentrations of metabolites of inorganic arsenic.

No clear difference between areas within the Baltic region have been noted.

Toxic effects

In general, the reported average concentrations of inorganic arsenic and its metabolites correspond to a low cancer risk. However, there are only few studies on the toxic effects of arsenic. Bencko et al (187, 188) reported a significant hearing loss in children living close to a power plant burning local coal with high arsenic content (table 9). In the same area, there was a high incidence of

skin basalomas in the local populations (189). In Sweden, men living in the vicinity of a copper smelter, which, in the past, had emitted large quantities of arsenic, had an increased risk of dying of lung cancer (190).

Other metals

There are 2 recent reviews on the toxicology of nickel (191, 192). The nickel level in urine (U-Ni) is often used as an index of recent uptake.

Nickel is a well-known skin-sensitizer (191, 192). Moreover, inhalation exposure to nickel causes mucosal irritation and asthma (possibly allergic), as well as nasal and lung cancer.

In northern Russia, on the Kola Peninsula, nickel smelters and refineries emit massive amounts of nickel (as well as other pollutants, especially sulfur dioxide). A series of studies has been made comparing Russian areas with nearby Norwegian ones. High air concentrations have been reported in Russia, much higher than in Norway, but the analytical accuracy for the former samples has been challenged (193). The concentration seemed to increase with decreasing distance to the nickel industry (194). Furthermore, the Russian drinking-water samples had a much higher nickel concentration than Norwegian samples. In addition, large surveys showed a higher U-Ni concentration in Russian populations (medians 1.9–3.4 µg/l) than in Norwegian ones (medians 0.6–1.2 µg/l), although without any clear gradient reflecting the distance to the metal industries, which confused the authors (195). Only a 4th of the Russians were occupationally exposed; these people had even higher U-Ni levels (medians 1.6–5.6 µg/l).

The Norwegian population had a higher prevalence of skin patch-test positivity to nickel than the Russians (194). Both prevalences were high, and the difference was particularly pronounced for the women. Serum levels of total and respiratory disease-specific immunoglobulin E were higher in Russia. Nevertheless, the reporting of atopic respiratory and skin disease was more prevalent among Norwegians than among Russians. There were no differences in reported asthma. However, the Russians had a higher prevalence of chronic obstructive lung disease, which was partly due to frequent smoking among the men; it could not be ascribed to the sulfur dioxide levels. However, there was no corresponding difference in lung-function parameters. Neither were there any differences in pregnancy outcomes. In summary, in spite of the high nickel exposure among the Russians, the authors did not find any health effects judged to be associated with nickel exposure.

In another study, female nickel workers (mean U-Ni 10–16 µg/l) were suspected to have increased

Table 9. Urinary arsenic levels (U-As) in populations in the Baltic region. (QC = quality control, N = number of samples, M = median, AAS = atomic absorption spectrometry)

Country	Area	Pollution	Year	Method	QC ^a	Gender	Age (years)	N	U-As (μg/g)			Determinants	Comment
									Mean ^b	M	Range		
Finland													
Valkonen et al, 1983 (181)	-	-	≤1983	AAS	3	Male, female	?	300	31.8	-	-	Geography Geography	Total arsenic
Czech Republic													
Bencko, 1995 (176)	South	Power plant	≤1977	Colorimetric	1	Male	10	25	25	-	<0.1—100	Closeness to plant	Total arsenic
Kučera et al, 1995 (36)	South	Power plant	≤1977	Colorimetric	1	Male	10	20	19	-	<0.01—51	-	Total arsenic
Bencko & Symon, 1977 (182)	Central	Urban	≤1977	Colorimetric	1	Male	10	24	11	-	0.1—44	-	Total arsenic
Germany													
Dolgnier et al, 1988 (160)	North-west	Industrial	1983	AAS	1	Male, female	7—11	69	(2.6)	3.6	<0.1—20	-	Inorganic arsenic
								70	(14)	12	3—250	-	Total arsenic
		Rural	1983	AAS	1	Male, female	7—11	70	(2.0)	2.8	<0.1—19	-	Inorganic arsenic
Krause et al, 1989 (81)	-	-	1985—1986	AAS	2	Male, female	20	71	(12)	10	1—160	-	Total arsenic
								2553	8.6—69	4.5	<0.6—290	Gender, age, smoking, community size	Total arsenic
Lombeck et al, 1987 (183)	North-west	Urban	≤1987	AAS	1	Male, female	5	24	-	3.2 ^c	1.4—22 ^c	-	Total arsenic
							10	28	-	4.7 ^c	1.5—11 ^c	-	Total arsenic
						Female	Adults	22	-	9.0 ^c	2.3—34 ^c	-	Total arsenic
						Male	Adults	18	-	12 ^c	6.8—36 ^c	-	Total arsenic
Trepka et al, 1996 (186)	East	Industrial	1992—1994	AAS	1	Male, female	5—14	760	(4.3—5.1)	4.6—5.3	3.7—5.5	Fish intake, local	Total arsenic
		Smelter	1992—1994	AAS	1	Male, female	5—14	591	(5.1)	5.3	4.8—5.5	Vegetables, housing	Total arsenic
		Industrial	1992—1994	AAS	1	Male, female	5—14	169	(4.3)	4.6	3.7—4.9	Vegetables, housing	Total arsenic
		Rural	1992—1994	AAS	1	Male, female	5—14	190	(4.0)	4.1	3.5—4.5	Vegetables, housing	Total arsenic
Denmark													
Jensen et al, 1991 (184)	-	-	≤1991	AAS	1	Male, female	20—60	95	6.6—8.4 ^d	6.1—6.5 ^d	2.5—42 ^d	Age	Inorganic arsenic and metabolites
							3—10	21	15—18 ^d	12—13 ^d	5—38 ^d	Age	Inorganic arsenic and metabolites
Sweden													
Andrén et al, 1988 (185)	South	Rural	≤1985	AAS	3	Male, female	8—10	35	(5.1)	-	1.6—16	Gender, age, parents' smoking	Inorganic arsenic and metabolites
Vahter & Lind 1986 (175)	Central	Urban	≤1986	AAS	3	Male, female	21—72	49	(9.7—12)	7.4—7.9	1.7—53	Fish intake	Inorganic arsenic and metabolites
								50	31—60	14—18	<1—520	Fish intake	Organic arsenic
Jakobsson Lagerkvist et al, 1993 (113)	North	Smelter	1989—1991	AAS	3	Female	27	209	8.2	-	-	-	Pregnant, inorganic arsenic and metabolites
		Rural	1989—1991	AAS	3	Female	28	149	8.2	-	-	-	Inorganic arsenic and metabolites
Willers et al, 1992 (60)	South	Urban	1987	AAS	3	Male, female	26—52	107	(3.7—10)	-	1.6—82	-	Inorganic arsenic and metabolites
							7—10	77	(4.4—5.3)	-	2.0—21	-	Inorganic arsenic and metabolites

^a 0=no; 3=very good. ^b Arithmetic mean except when in parentheses; values in parentheses are geometric means.^c µg/24 hours. ^d µg/g creatinine.

prevalences of spontaneous abortions and malformations (196). Furthermore, the incidences of deaths, total as well as cardiovascular disease and cancer, were claimed to be higher in the population close to the nickel industries (193).

The toxicology of beryllium was recently reviewed (197). Occupational beryllium exposure may cause immunologically-induced granulomatous lung fibrosis (earlier often referred to as "berylliosis") and lung cancer.

Subjects in the general population of the Czech Republic, exposed to beryllium ($0.39\text{--}1.68\text{ }\mu\text{g}/\text{m}^3$) from a coal-burning power plant, displayed elevated levels of immunoglobulins A and G, autoantibodies against various organs, as well as antinuclear and antimitochondrial antibodies, as compared with supposedly less exposed referents (workers, sportsmen, and blood donors) (198, 199).

Acknowledgments

Valuable data were supplied by Drs Marika Berglund, DMedSci, and Ulf Strömberg, PhD.

Some of the work summarized in this report have been supported by the Swedish Work Environment Fund, the National Swedish Environment Protection Agency, the Medical Faculty, Lund University, and the county councils of Malmöhus, Malmö, Kristianstad, Blekinge, Kronoberg, and Halland.

References

1. Skerfving S. Biological monitoring of exposure to inorganic lead, I. In: Clarkson TW, Friberg L, Nordberg GF, Sager PR, editors. *Biological monitoring of toxic metals*. Plenum Publishing Corporation, 1988.
2. Bencko V, Cíkr M. Biological monitoring of human exposure to metals. *J Hyg Epidemiol (Praha)* 1990;34:233–41.
3. Cornelis R, Heinzow B, Herber RFM, Molin Christensen J, Paulsen OM, Sabbioni E, et al. Sample collection guidelines for trace elements in blood and urine. *Pure Appl Chem* 1995;67:1575–608.
4. Friberg L, Vahter M. Assessment of exposure to lead and cadmium through biological monitoring: results of a UNEP/WHO global study. *Environ Res* 1983;30:95–128.
5. Skerfving S. Inorganic lead: criteria documents from the Nordic expert group. Stockholm: Arbetarskyddsverket, 1993. *Arbete och Hälsa* 1993;1.
6. National Research Council (NRC). *Measuring lead exposure in infants, children, and other sensitive populations*. Washington (DC): NRC, National Academy Press, 1993:337 p.
7. Blaha K, Bencko V, Cíkr M. Exposure to lead and human health in the Czech republic. *Cent J Health* 1995;4:233–41.
8. Blaha K, Bencko V, Cíkr M. Exposure to lead and human exposure in the Czech Republic. *Cent Eur J Public Health* 1996;4:233–41.
9. World Health Organization (WHO). *Inorganic lead*. Geneva: International Programme on Chemical Safety, WHO, 1995:300 p. *Environmental health criteria*, no 165.
10. World Health Organization (WHO). *Lead — environmental aspects*. Geneva: International Programme on Chemical Safety, World Health Organization, 1989:106 p. *Environmental health criteria*, no 85.
11. Schütz A, Bergdahl IA, Ekholm A, Skerfving S. Measurement by ICP-MS of lead in plasma and whole blood of lead workers and controls. *Occup Environ Med* 1996;53:736–40.
12. Bergdahl IA, Schütz A, Gerhardsson L, Jensen A, Skerfving S. Lead concentrations in human plasma, urine, and whole blood. *Scand J Work Environ Health* 1997;23:359–63.
13. Bergdahl IA, Strömberg U, Gerhardsson L, Schütz A, Chettle DR, Skerfving S. Lead concentrations in tibial and calcaneal bone in relation to the history of occupational lead. *Scand J Work Environ Health*. 1998;24:38–45.
14. Bergdahl IA, Vahter M, Counter SA, Schütz A, Buchanan L, Ortega F, et al. Lead in plasma and whole blood from lead-exposed children. *Environ Res* 1999;80:25–33.
15. Bergdahl IA, Schütz A, Grubb A. Application of liquid chromatography-inductively coupled plasma mass spectrometry to the study of protein-bound lead in human erythrocytes. *J Anal Atom Spectrom* 1996;11:735–8.
16. Bergdahl IA, Gerhardsson L, Schütz A, Desnick RJ, Wetmur JG, Skerfving S. Delta-aminolevulinic acid dehydratase polymorphism: influence on lead levels and kidney function in humans. *Arch Environ Health* 1997;52:91–6.
17. Bergdahl IA, Grubb A, Schütz A, Desnick RJ, Wetmur JG, Sassa S, et al. Lead binding to δ -aminolevulinic acid dehydratase (ALAD) in human erythrocytes. *Pharmacol Toxicol* 1997;81:153–8.
18. Skerfving S, Nilsson U, Schütz A, Gerhardsson L. Biological monitoring of inorganic lead. *Scand J Work Environ Health* 1993;19 suppl 1:59–64.
19. Nilsson U, Attewell R, Christofferson J-O, Schütz A, Ahlgren L, Skerfving S, et al. Kinetics of lead in bone and blood after end of occupational exposure. *Pharmacol Toxicol* 1991;68:477–84.
20. Pönkä A, Salminen E, Ahonen S. Lead in the ambient air and blood specimens of children in Helsinki. *Sci Total Environ* 1993;138:301–8.
21. Zielonka E, Wodzien M. Blood cadmium and lead levels among school children in Cracow. *Folia Medica Cracoviensia* 1993;34:1–4.
22. Laudanski T, Sipowicz M, Modzelewski P, Bolinski J, Szamatowicz, Razniewska G, et al. Influence of high lead and cadmium soil content on human reproductive outcome. *Int J Gynecol Obstet* 1991;36:309–15.
23. Osman K, Björkman L, Lind B, Nordberg M. Biological monitoring of metals in children and pregnant women in Poland. *Int J Environ Health Res* 1992;2:212–22.
24. Pietrzyk JJ, Nowak A, Mitkowska Z, Zachwieja Z, Chłopicka J, Krosniak M, et al. Prenatal lead exposure and the pregnancy outcome: a case-control study in southern Poland. *Przegl Lek* 1996;53:342–7.
25. Zareba A, Rudkowski Z. Lead exposure of children from copper industry pollution. *Arch Environ health* 1996;51:480–1.
26. Jakubowski M, Trzcińska-Ochocka M, Razniewska G, Christensen JM, Starek A. Blood lead in the general population of Poland. *Int Arch Occup Environ Health* 1996;68:193–8.
27. Dutkiewicz T, Sokolowska D, Kulka E. Health risk assess-

- ment in children exposed to lead compounds in the vicinity of mine-smelter plant "Orzel Bialy". *Pol J Occup Med Environ Health* 1993;6:71—8.
28. Andrzejak R, Antonowicz J, Tomczyk J, Lepetow T, Smolik R. Lead and cadmium concentrations in blood of people living near a copper smelter in Legnica, Poland. *Sci Total Environ* 1993;suppl:233—6.
 29. Zejda JE, Sokal A, Grabecki J, Panasiuk Z, Jarkowski M, Skiba M. Blood lead concentrations in school children of upper Silesian industrial zone, Poland. *Cent Eur J Public Health* 1995;3:92—6.
 30. Zejda JE, Grabecki J. Environmental exposure to lead in children of upper Silesia, Poland. *Acta Biol Debr Oecol Hung* 1994;5:365—74.
 31. Zejda JE, Grabecki J, Krol B, Pansiuik Z, Jedrzejczak A, Jarkowski M. Blood lead levels in urban children of Katowice voivodship, Poland: results from the population-based biomonitoring and surveillance program [abstract]. In: International conference: environmental pollution and child health: critical needs and issues for Central and Eastern Europe, Sosnowiek, May 8—10, 1996.
 32. Janousek V, Krijt J, Malbohan M, Cibula D, Lukas W, Zejda JE, et al. Cord blood levels of potentially neurotoxic pollutants (polychlorinated biphenyls, lead and cadmium) in the areas of Prague (Czech Republic) and Katowice (Poland): comparison with reference values in the Netherlands. *Cent Eur J Public Health* 1994;2:73—6.
 33. Osman K, Björkman L, Milezyska D, Lind B, Sundstedt K, Palm B, et al. Blood levels of lead, cadmium and selenium in children from Bytom, Poland. *Int J Environ Health Res* 1994;4:223—35.
 34. Nowak A, Czerwionka-Szaflarska M. Blood lead levels in children from the district of Bydgoszcz. *Med Sci Monit* 1996;2:215—21.
 35. Osman K, Schütz A, Åkesson B, Maciag A, Vahter M. Interaction between essential and toxic elements in lead exposed children in Katowice, Poland. *Clin Biochem* 1998;31:657—65.
 36. Kučera J, Bencko V, Sabbioni E, Van der Venne MT. Review of trace elements in blood, serum and urine for the Czech and Slovak populations and critical evaluation of their possible use as reference values. *Sci Total Environ* 1995;166:211—34.
 37. Brockhaus A, Collet W, Dolgner R, Engelke R, Ewers U, Freier I, et al. Exposure to lead and cadmium of children living in different areas of North-West Germany: results of biological monitoring studies 1982—1986. *Int Arch Occup Environ Health* 1988;60:211—22.
 38. Ewers U, Brockhaus A, Dolgner R, Freier I, Turfeld M, Roswitha Engelke R, et al. Blutblei- und Blutcadmiumkonzentrationen bei 55—66 jährigen Frauen aus verschiedenen Gebieten Nordrhein-Westfalens — Entwicklungstrends 1982—1988 [Blood lead and cadmium concentrations in 55—66 year old women in various areas in Nordrhein-Westfalen — time trends 1982—1988.] *Zentralbl Hyg* 1990;189:405—18.
 39. Hofstetter I, Ewers U, Turfeld M, Freier I, Westerweller S, Brockhaus A. Untersuchungen zur Blei und Cadmiumbelastung von Kindern aus Stolberg. [Investigations on lead and cadmium loads in children in Stolberg, Germany]. *Öff Gesundheitswes* 1990;52:232—7.
 40. Englert N, Höring H. Lead concentration in tap-water and in blood of selected schoolchildren in Southern Saxonia. *Toxicol Lett* 1994;72:325—31.
 41. Begerow J, Freier I, Turfeld M, Krämer U, Dunemann L. Internal lead and cadmium exposure in 6-year-old children from western and eastern Germany. *Int Arch Occup Environ Health* 1994;66:243—8.
 42. Hense H-W, Filipiak B, Novak L, Stoeppeler M. Nonoccupational determinants of blood lead concentrations in a general population. *Int J Epidemiol* 1992;21:753—62.
 43. Lyngbye T, Jørgensen PJ, Grandjean P, Hansen ON. Validity and interpretation of blood lead levels: a study of Danish school children. *Scand J Clin Lab Invest* 1990;50:441—9.
 44. Møller LF, Kristensen TS. Bly — en mulig risikofaktor for forhøjet blodtryk og hjerte-kar-sygdom [Lead — a possible risk factor for blood pressure increase and coronary heart disease]. *Ugeskr Læger* 1993;155/40:3203—7.
 45. Molin Christensen J, Holst E. Evaluation of blood lead levels in Danes for the period 1976—1987. *Fresenius' Z Anal Chem* 1988;332:710—3.
 46. Grandjean P, Nielsen GD, Jørgensen PJ, Hørder M. Reference intervals for trace elements in blood: significance of risk factors. *Scand J Clin Lab Invest* 1992;52:321—37.
 47. Granvik M, Sandberg B-M, Friberg L, Lind B, Nilsson B. Låga halter av bly och kadmium i blod hos skolbarn i Dalarna [Low levels of lead and cadmium in blood in school children in Dalecarlia, Sweden]. *Läkartidningen* 1988;85:320—2.
 48. Vahter M, Berglund M, Slorach S, Friberg L, Saric M, Xingquan Z, et al. Methods for integrated exposure monitoring of lead and cadmium. *Environ Res* 1991;56:78—89.
 49. Gustafson Å, Hedner P, Schütz A, Skerfving S. Occupational lead exposure and pituitary function. *Int Arch Occup Environ Health* 1989;61:277—81.
 50. Bjerre B, Berglund M, Harsbo K, Hellman B. Blood lead concentrations of Swedish preschool children in a community with high lead levels from mine waste in soil and dust. *Scand J Work Environ Health* 1993;19:154—61.
 51. Berglund M, Lind B, Lannerö E, Vahter M. A pilot study of lead and cadmium exposure in young children in Stockholm, Sweden: methodological considerations using capillary blood microsampling. *Arch Environ Contam Toxicol* 1994;27:281—7.
 52. Bäcklund M. Environmental and genetic factors determining the concentration of cadmium and lead in blood from middle aged and elderly people. Solna: Institute of Environmental Medicine, Karolinska Institute: 1996:20 p.
 53. Berglund M, Bjerre B, Vahter M. Undersökning av bly- och kadmiumexponering hos barn i Smedjebacken. [Investigation of lead and cadmium exposures in children in Smedjebacken, Sweden]. Stockholm: Institute of Environmental Medicine, Karolinska Institute, 1994:7 p.
 54. Berglund M, Sörensen S, Vahter M. Undersökning av bly- och kadmiumexponering hos barn i Sala [Investigation of lead and cadmium exposure in children in Sala, Sweden]. Stockholm: Institute of Environmental Medicine, Karolinska Institute, 1995:9 p.
 55. Hanberg A, Ahlberg UG. PCB och tungmetaller hos kvinnor i Örebro län [PCB and heavy metals in women in Örebro county, Sweden]. Örebro: County Council of Örebro, 1995:16 p. Publication no 2.
 56. Skerfving S, Strömberg U, Schütz A. Blyexponeringens långsiktiga trend inom den nationella miljöövervakningen. Slutrapport för Statens Naturvårdsverks projekt 215 507B. [The long-term trend of lead exposure in the national monitoring of the environment in Sweden]. Lund: Yrkes- och miljömedicinska kliniken, Universitetssjukhuset i Lund, 1997. Report 1997—12—22.
 57. Nordberg M, Basun H, Palm B, Lind B, Winblad B. Metals in blood in normal ageing and in subjects with cognitive decline

- [abstract]. In: 25th International Congress on Occupational Health, Stockholm, September 15—20, 1996.
58. Osman K, Zejda JE, Schütz A, Mielzynska D, Elinder CG, Vahter M. Assessment of exposure to lead and other metals in children from Katowice district, Poland. *Int Arch Occup Environ Health* 1998;71:180—6.
 59. Berglund M, Fahlgren L, Freland M, Vahter M. Metaller i mark i Stockholms innerstad och kranskommuner — förekomst och hälsorisker för små barn [Metals in soil in Central Stockholm and suburbs — occurrence and health risks for children]. Stockholm: Institute of Environmental Medicine, Karolinska Institute, 1994:48 p. Report 2/94.
 60. Willers S, Attewell R, Bensryd I, Schütz A, Skarping G, Vahter M. Exposure to environmental tobacco smoke in the household and urinary cotinine excretion, heavy metals retention and lung function. *Arch Environ Health* 1992;47:357—63.
 61. Willers S, Schütz A, Attewell R, Skerfving S. Relation between lead and cadmium in blood and the involuntary smoking of children. *Scand J Work Environ Health* 1988;14:385—9.
 62. Vahter M, Berglund M, Lind B, Jorhem L, Slorach S, Friberg L. Personal monitoring of lead and cadmium exposure — a Swedish study with special reference to methodological aspects. *Scand J Work Environ Health* 1991;17:65—74.
 63. Bensryd I, Rylander L, Högstedt B, Aprea P, Bratt I, Fähræus C, et al. Effect of acid precipitation on retention and excretion of elements in man. *Sci Total Environ* 1994;145:81—102.
 64. Svensson B, Schütz A, Nilsson A, Skerfving S. Lead exposure in indoor firing ranges. *Int Arch Occup Environ Health* 1992;64:219—21.
 65. Schütz A, Leja M. Lead levels in blood in children from different regions of Latvia. Presented at the Conference on Environmental Toxicology and Health, Stockholm, May 13—15, 1991.
 66. Strömberg U, Schütz A, Skerfving S. Substantial decrease of blood lead in Swedish children 1978—94, associated with petrol lead. *Occup Environ Med* 1995;52:764—9.
 67. Haavikko K, Anttila A, Helle A, Vuori E. Lead concentrations of enamel and dentine of deciduous teeth of children from two Finnish towns. *Arch Environ Health* 1984;39:79—84.
 68. Anttila A. Lead content of deciduous tooth enamel from a high-radon area. *Acta Odont Scand* 1987;45:283—8.
 69. Järvinen V, Anttila A, Lappalainen R, Rytömaa I. Lead content of deciduous molar enamel in Finland, as measured by proton-induced X-ray emission. *Scand J Work Environ Health* 1984;10:103—7.
 70. Bencko V. Occupational and environmental lead exposure and toxicity. In: Human exposure to lead: report on the human exposure assessment location (HEAL) programme meeting held in Bangkok, Thailand 16—19 November 1992. Chapter 13.
 71. Grandjean P, Lyngbye T, Nørby Hansen O. Lead concentration in deciduous teeth: variation related to tooth type and analytical technique. *J Toxicol Environ Health* 1986;19:437—45.
 72. Lyngbye T. Bly og børn: en undersøgelse af børns blyretention og dennes muligt sundhedsskadelige effekter samt faktorer der indebærer en risiko for absorption og retention [A study of children's lead retention and its possible health damaging effects and factors involving a risk of absorption and retention] [dissertation]. Egtved Kursus Center/Edition Egtved, 1991.
 73. Möller B, Carlsson L-E, Johansson GI, Malmqvist KG, Hammarström L, Berlin M. Lead levels determined in Swedish permanent teeth by particle-induced X-ray emission. *Scand J Work Environ Health* 1982;8:267—72.
 74. Keinonen M. The isotopic composition of lead in man and the environment in Finland 1966—1987: isotope ratios of lead as indicators of pollutant source. *Sci Total Environ* 1992;113:251—68.
 75. Baranowska I, Krzysztof Czernicki K, Aleksandrowicz R. The analysis of lead, cadmium, zinc, copper and nickel content in human bones from the Upper Silesian industrial district. *Sci Total Environ* 1995;159:155—62.
 76. Drasch GA, Böhm J, Baur C. Lead in human bones. Investigations on an occupationally non-exposed population in southern Bavaria (F.R.G.), I: adults. *Sci Total Environ* 1987;64:303—15.
 77. Drasch G, Müller RK, Grasemann F, Adang M, Roider G, Wowra D. Vergleich der belastung der Bevölkerung im Leipziger und Münchner Raum mit der Schwermetallen Kadmium, Blei und Quecksilber — eine Untersuchung an menschlichen Organmaterial [Comparison of the cadmium, lead and mercury loads of the population in Leipzig and Munich, Germany — a study of human organs]. *Gesundheits-Wesen* 1994;56:263—267.
 78. Lindh U. Levels of antimony, arsenic, cadmium, copper, lead, mercury, selenium, silver, tin and zinc in bone tissue of industrially exposed workers. *Sci Total Environ* 1980;16:109—16.
 79. Gerhardsson L, Akantis A, Nordberg G, Schütz A, Skerfving S. Blyhalter i kortikalt och trabekulärt ben hos blyarbetare och kontroller [Lead levels in cortical and trabecular bone in lead workers and controls] [abstract]. *Hygiea* 1992;101:115—6.
 80. Vesaite B. Lithuania: research on human health effects of exposure to lead and cadmium. In: Human exposure to lead. Report on the human exposure assessment location (HEAL) programme meeting held in Bangkok, Thailand 16—19 November 1992. Chapter 20.
 81. Krause C, Chutsch M, Henke M, Huber M, Kleim C, Schulz C, et al. Umwelt-Survey, Band I: Studienbeschreibung und Humanbiologisches Monitoring: Deskription der Spurenelementgehalte in Blut, Urin und Haar der Bevölkerung in der Bundesrepublik Deutschland 1985/86. [Description of trace element levels in blood, urine and hair in the population of German Federal Republic 1985/86.] Berlin: Institut für Wasser-, Boden-, und Lufthygiene des Bundesgesundheitsamtes, 1989:285 p. WaBoLu Hefte 5/1989.
 82. Bernard AM, Vyskočil A, Roels H, Kriz J, Kodl M, Lauwers R. Renal effects in children living in the vicinity of a lead smelter. *Environ Res* 1995;68:91—95.
 83. World Health Organization (WHO). National integrated programme on environment and health in the Czech Republic: final report on the programme to reduce environmental lead exposure in children living in contaminated areas. Geneva: WHO, Regional Office for Europe, European Center for Environment and Health, Bilthoven Division, 1995.
 84. Winneke G, Altmann L, Krämer U, Turfeld M, Behler R, Gutsmuths FJ, et al. Neurobehavioural and neuropsychological observations in six year old children with low lead levels in East and West Germany. *Neurotoxicology* 1994;15:705—14.
 85. Osman K, Elinder CG, Schütz A, Grubb A. Evidence of nephrotoxicity in children environmentally exposed to lead in Poland. In: Osman K. Health effects in children environmentally exposed to lead in Poland. Stockholm: Karolinska institute, 1998.
 86. Osman K, Pawlas K, Schütz A, Gazdzik M, Sokal JA, Vahter M. Poland: Lead exposure and hearing effects in children in

- Katowice. Environ Res 1999;80:1—8.
87. Fagher U, Laudanski T, Schütz A, Sipowicz M, Åkerlund M. The relationship between cadmium and lead burdens and pre-term labor. Int J Gynecol 1993;40:109—14.
88. World Health Organization (WHO). Cadmium. Geneva: International Programme on Chemical Safety, WHO, 1992:280 p. Environmental health criteria, no 134.
89. World Health Organization (WHO). Cadmium — environmental aspects. Geneva: International Programme on Chemical Safety, WHO, 1992:156 p. Environmental health criteria, no 135.
90. Vahter M, Berglund M, Nermell B, Åkesson A. Bioavailability of cadmium from shellfish and mixed diet in women. Toxicol Appl Pharmacol 1996;136:332—41.
91. Pettersson-Grawé K, Thierfelder T, Jorhem L, Oskarsson A. Cadmium levels in kidneys from Swedish pigs in relation to environmental factors — temporal and spatial trends. Sci Total Environ 1997;208:111—22.
92. Öborn I, Jansson G, Johnsson L. A field study on the influence of soil pH on trace element levels in spring wheat (*Triticum aestivum*), potatoes (*Solanum tuberosum*) and carrots (*Daucus carota*). Water Air Soil Pollut 1995;85:835—40.
93. Oskarsson A, Nordberg G, Block M, Rasmussen F, Pettersson R, Skerfving S, et al. Adverse health effects due to soil and water acidification: a Swedish research program. Ambio 1996;25:527—31.
94. Welinder H, Skerfving S, Henriksen O. Cadmium metabolism in man. Br J Ind Med 1977;34:221—8.
95. Berglund M, Åkesson A, Nermell B, Vahter M. Intestinal absorption of dietary cadmium in women depends on body iron stores and fiber intake. Environ Health Perspect 1994;102:1058—66.
96. Nilsson U, Schütz A, Skerfving S, Mattsson S. Cadmium in kidneys in Swedes measured in vivo using X-ray fluorescence analysis. Int Arch Occup Environ Health 1995;67:405—11.
97. Börjesson J, Gerhardsson L, Schütz A, Perfekt R, Mattsson S, Skerfving S. Kidney cadmium as compared to other markers of cadmium exposure in workers at a secondary metal smelter. Am J Ind Med. In press.
98. Lauwerys RR, Bernard AM, Buchet JP, Roels HA, Bruaux P, Claeys F, et al. Does environmental exposure to cadmium represent a health risk?: conclusions from the Cadmibel study. Acta Clin Belg 1991;46:219—25.
99. Järup L, Berglund M, Elinder CG, Nordberg G, Vahter M. Health effects of cadmium exposure — a review of the literature and a risk estimate. Scand J Work Environ Health 1998;24 suppl 1:52 p.
100. International Agency for Research on Cancer (IARC). Beryllium, cadmium, mercury, and exposures in the glass manufacturing industry. Lyon: IARC, 1993:444 p. IARC monographs on the evaluation of carcinogenic risks to humans, vol 58.
101. Eriksson J, Öborn I, Jansson G, Andersson A. Factors influencing Cd-content in crops — results from Swedish field investigations. Swed J Agric Res 1996;26:1—8.
102. Andersson A. Trace elements in agricultural soils — fluxes, balances and background values. Swedish Environmental Protection Agency, 1992. Report 4077.
103. Tjell JC, Hansen JA, Christensen TH, Hovmand MF. Prediction of cadmium concentrations in Danish soils. In: L'Hermite P, Ott H, editors. Characterization, treatment and use of sewage sludge. Dordrecht: Reidel Publishing Co, 1981:625—64.
104. Svensson BG, Björnham Å, Schütz A, Lettewall U, Nilsson A, Skerfving S. Acidic deposition and human exposure to toxic metals. Sci Total Environ 1987;67:101—15.
105. Kjellström T, Lind B, Linnman L, Elinder CG. Variations in Swedish wheat and barley: an indicator of changes in daily cadmium intake during the 20th century. Arch Environ Health 1975;30:321—8.
106. Andersson A, Borgefors S. Trends and annual variations in cadmium concentrations in grain of winter wheat. Acta Agric Scand 1985;35:339—44.
107. Bigner A. Comments concerning the national Swedish contaminant monitoring programme in marine biota. Stockholm: Swedish Museum of Natural History, 1996.
108. Schütz A. Cadmium and lead. Gastroenterology 1979; 14:223—350.
109. Abdulla M, Bebehani A, Dashti H. Dietary intake and bioavailability of trace elements. Biol Trace Elem Res 1989;21:173—8.
110. Luoma PV, Näyhä S, Pyy L, Hassi J. Association of blood cadmium to the area of residence and hypertensive disease in Arctic Finland. Sci Total Environ 1995;160/161:571—5.
111. Ewers U, Brockhaus A, Dolgner R, Freier I, Jerman E, Bernard A, et al. Environmental exposure to cadmium and renal function of elderly women living in cadmium-polluted areas of the Federal Republic of Germany. Int Arch Occup Environ Health 1985;55:217—39.
112. Jung K, Pergande M, Graubaus HJ, Fels LM, Endl U, Stolte H. Urinary proteins and enzymes as early indicators of renal dysfunction in chronic exposure to cadmium. Clin Chem 1993;39:757—65.
113. Jakobsson Lagerkvist B, Söderberg H-Å, Nordberg GF, Ekesrydh S, Englyst V. Biological monitoring of arsenic, lead and cadmium in occupationally and environmentally exposed pregnant women. Scand J Work Environ Health 1993;19 suppl 1:50—3.
114. Järup L, Carlsson MD, Elinder CG, Hellström L, Persson B, Schütz A. Enzymuria in a population living near a cadmium battery plant. Occup Environ Med 1995;52:770—2.
115. Ala-Opas M, Tahvonen R. Concentrations of cadmium and lead in renal cell cancer. J Trace Elem Med Biol 1995;9:176—80.
116. Bem EM, Jerzy K, Piotrowski K, Turzynska E. Cadmium, zinc and copper levels in the kidneys and liver of the inhabitants of North-eastern Poland. Pol J Occup Med Environ Health 1993;6:133—41.
117. Bem EM, Orlowski C, Piotrowski JK, Januszewski K, Pajak J. Cadmium, zinc, copper, and metallothionein levels in the kidney and liver of inhabitants of Upper Silesia (Poland). Int Arch Occup Environ Health 1993;65:57—63.
118. Bem EM, Kaszper BW, Orlowski C, Piotrowski JK, Wojcik G, Zolnowska E. Cadmium, zinc, copper and metallothionein levels in the kidney and liver of humans from central Poland. Environ Monit Assess 1993;25:1—13.
119. Thürauf von JRE, Schaller K-H, Valentin H, Weltle D. Zur gegenwärtigen Belastung der Bevölkerung mit Kadmium. Vergleich der Kadmium Konzentrationen im Nierengewebe von Autopsiefällen aus den Jahren 1969—1980 [On the load of the population with cadmium. Comparison of the cadmium concentrations in kidney tissue in autopsy cases in the years 1969—1980]. Fortschr Med 1981;99:1312—7.
120. Drasch G. Kadmium-Belastung in südbayerischen Raum [Cadmium load in the southern Bavarian area]. Münch Med Wschr 1982;124:1129—32.
121. Summer KH, Drasch GA, Heilmaier HE. Metallothionein and cadmium in human kidney cortex: influence of smoking. Hum Toxicol 1986;5:27—33.
122. Hahn R, Ewers U, Jeremann U, Jeremann E, Freier I, Brockhaus

- A, et al. Cadmium in kidney cortex of inhabitants of North-West Germany: its relationship to age, sex, smoking and environmental pollution by cadmium. *Int Arch Occup Environ Health* 1987;59:165—76.
123. Hansen JC, Grøn P, Abild Jespersen BA, Voigt J, Simonsen J, Dalgaard JB, et al. Cadmium exposure in Denmark: based on analyses of liver and kidney tissues. *Dan Med Bull* 1989;36:499—502.
124. Svartengren M, Elinder CG, Friberg L, Lind B. Distribution and concentration of cadmium in human kidney. *Environ Res* 1986;39:1—7.
125. Lindqvist B, Nyström K, Stegmayr B, Wirell M, Eriksson A. Cadmium concentration in human kidney biopsies. *Scand J Urol Nephrol* 1989;23:213—7.
126. Bensryd I. Mätning av kadmium-halten i njure hos lantbrukare [Determination of the cadmium level in kidneys in farmers]. *Bulletin från Yrkes- och miljömedicinska kliniken vid Lasarettet i Lund* 1993;3:6.
127. Barregård L, Schütz A, Svalander C, Westberg G, Attman PO, Sällsten G, et al. Kadmium och kvicksilver i njurbiopsier [Cadmium and mercury in kidney biopsies][abstract]. *Hygiea* 1997;106:122.
128. Drasch GA. An increase of cadmium body burden for this century — an investigation on human tissues. *Sci Total Environ* 1983;26:111—9.
129. Elinder CG, Kjellström T. Cadmium concentrations in samples of human kidney cortex from the 19th century. *Ambio* 1977;6:270—72.
130. Elinder C-G, Kjellström T, Friberg L. Cadmium in kidney cortex, liver, and pancreas from Swedish autopsies. *Arch Environ Health* 1976;31:292—302.
131. Friis L, Petersson L, Edling C. Reduced cadmium levels in human kidney cortex in Sweden. *Environ Health Perspect* 1998;106:175—8.
132. World Health Organization (WHO). Mercury — environmental aspects. Geneva: International Programme on Chemical Safety, WHO, 1989:115 p. Environmental health criteria, no 86.
133. World Health Organization (WHO). Inorganic mercury. Geneva: International Programme on Chemical Safety, WHO, 1991:168 p. Environmental health criteria, no 118.
134. Barregård L, Sällsten G, Schütz A, Attewell R, Skerfving S, Järholm B. Kinetics of mercury in blood and urine after brief occupational exposure. *Arch Environ Health* 1992;47:176—84.
135. Lutz E, Lind B, Herin P, Krakau I, Bui TH, Vahter M. Concentrations of mercury, cadmium and lead in brain and kidney of second trimester foetuses and infants. *J Trace Elem Med Biol* 1996;10:61—7.
136. Oskarsson A, Schütz A, Skerfving S, Palminger Hallén I, Ohlin B, et al. Total and inorganic mercury in breast milk and blood in relation to fish consumption and amalgam fillings in lactating women. *Arch Environ Health* 1996;51:234—41.
137. World Health Organization (WHO). Methylmercury. Geneva: International Programme on Chemical Safety, WHO, 1990:144 p. Environmental health criteria, no 101.
138. Bergdahl I, Schütz A, Ahlqvist M, Bengtsson C, Lapidus L, Lissner I, et al. Methylmercury and inorganic mercury in serum — correlation to fish consumption and dental amalgam in a cohort of women born in 1922. *Environ Res* 1998;77:20—4.
139. Aitio A, Valkonen S, Kivistö H, Yrjänheikki E. Effect of occupational mercury exposure on plasma lysosomal hydrolases. *Int Arch Occup Environ Health* 1983;53:139—47.
140. Piikivi L, Hänninen H. Subjective symptoms and psychological performance of chlorine-alkali workers. *Scand J Work Environ Health* 1989;15:69—74.
141. Luoma PV, Näyhä S, Pyy L, Korpela H, Hassi J. Blood mercury and serum selenium concentrations in reindeer herders in the arctic area of northern Finland. *Med Toxicol* 1992;15:172—5.
142. Leja M, Schütz A, Skerfving S. Mercury in erythrocytes in coastal fishermen around the gulf of Riga [abstract]. Arnold O Beckman/FCC. European conference on environmental toxicology, Munich, Germany, 16—18 June 1993.
143. Schaller KH, Breininger M, Schiele R, Schierling P. Der Quecksilberspiegel für Blut und Urin bei Normalpersonen [Mercury in blood and urine in normal subjects]. *Ärztl Lab* 1983;29:325—34.
144. Treпка MJ, Heinrich J, Krause C, Schulz C, Wjst M, Popescu M, et al. Factors affecting internal mercury burden among eastern German children. *Arch Environ Health* 1997;52:134—8.
145. Langworth S, Elinder CG, Göthe CJ, Vesterberg O. Biological monitoring of environmental and occupational exposure to mercury. *Int Arch Occup Environ Health* 1991;63:161—7.
146. Skerfving S. Mercury in women exposed to methylmercury through fish consumption, and in their newborn babies and breast milk. *Bull Environ Contam Toxicol* 1988;41:475—82.
147. Åkesson I, Schütz A, Attewell R, Skerfving S, Glantz P-O. Status of mercury and selenium in dental personnel: Impact of amalgam work and own fillings. *Arch Environ Health* 1991;46:102—9.
148. Erfurth EM, Schütz A, Nilsson A, Barregård L, Skerfving S. Normal pituitary hormone response to thyrotrophin and gonadotrophin releasing hormones in subjects exposed to elemental mercury vapour. *Br J Ind Med* 1990;47:639—44.
149. Molin M, Bergman B, Marklund S, Schütz A, Skerfving S. The influence of dental amalgam placement on mercury selenium, and glutathione peroxidase in man. *Acta Odont Scand* 1990;48:287—95.
150. Molin M, Schütz A, Skerfving S, Sällsten G. Mobilized mercury in subjects with varying exposure to elemental mercury vapour. *Int Arch Occup Environ Health* 1991;63:187—92.
151. Herrström P, Högstäd B, Holthuis N, Schütz A, Råstam L. Allergic disease, immunoglobulins, exposure to mercury and dental amalgam in Swedish adolescents. *Int Arch Occup Environ Health* 1997;69:339—42.
152. Skerfving S. Methylmercury exposure, mercury levels in blood and hair, and health status in Swedes consuming contaminated fish. *Toxicology* 1974;2:3—23.
153. Mussalo-Rauhamaa H, Kantola M, Seppänen K, Soininen L, Koivusalo M. Trends in the concentrations of mercury, copper, zinc and selenium in inhabitants of north-eastern Finnish Lapland in 1982—1991: a pilot study. *Arct Med Res* 1996;5:83—91.
154. Airey D. Total mercury concentrations in human hair from 13 countries in relation to fish consumption and location. *Sci Total Environ* 1983;157—80.
155. Forhammar M, Albanus L, Bruce Å, Mattsson P, Ohlin B. Fiskkonsumtion och kvicksilverhalt i hår hos gravida kvinnor [Fish consumption and mercury levels in hair in pregnant women]. *Vår Föda* 1984;36:2—13.
156. Oskarsson A, Jön Lagerkvist B, Ohlin B, Lundberg K. Mercury levels in the hair of pregnant women in a polluted area in Sweden. *Sci Total Environ* 1994;151:29—35.
157. Oskarsson A, Ohlin B, Ohlander EM, Albanus L. Mercury levels in hair from people eating large quantities of Swedish

- freshwater fish. *Food Add Contam* 1990;7:555—62.
158. Salonen JT, Seppänen K, Nyyssönen K, Korpela H, Kahvanen J, Kantola M, et al. Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in eastern Finnish men. *Circulation* 1995;91:645—55.
 159. Svensson B-G, Schütz A, Nilsson A, Åkesson I, Åkesson B, Skerfving S. Fish as a source of exposure to mercury and selenium. *Sci Total Environ* 1992;126:61—74.
 160. Dolgner R, Brockhaus A, Ewers U, Freier I, Jermenn E, Engelke R, et al. Untersuchungen zur Schwermetallbelastung von Kindern im Ruhrgebiet [Investigations on the heavy metals load in children in the Ruhr area, Germany]. *Öff Gesundheitswes* 1988;50:189—96.
 161. Zander D, Ewers E, Freier I, Jermann E, Westerweller S, Brockhaus A. Untersuchungen zur Quecksilberbelastung der Bevölkerung, I: Quecksilberkonzentrationen im Urin bei Normalpersonen [Investigations on the mercury load of the population, I: mercury in urine in the normal population]. *Zentralbl Hyg* 1990;190:315—24.
 162. Zander D, Ewers E, Freier I, Westerweller S, Jermann E, Brockhaus A. Untersuchungen zur Quecksilberbelastung der Bevölkerung, II: Quecksilberfreisetzung aus Amalgamfüllungen [Investigations on the mercury load of the population, II: mercury release from dental fillings]. *Zentralbl Hyg* 1990;190:325—34.
 163. Zander D, Ewers U, Freier I, Brockhaus A. Untersuchungen zur Quecksilberbelastung der Bevölkerung, IV: Quecksilberbelastung von Zahnärzten, Zahnärztinnen und Zahnarzthelferinnen [Investigations on the mercury load of the population, IV: mercury load in male and female dentists and dental assistants]. *Zentralbl Hyg* 1992;193:318—28.
 164. Langworth S, Elinder C-G, Sundqvist KG. Minor effects of low exposure to inorganic mercury on the human immune system. *Scand J Work Environ Health* 1993;19:405—13.
 165. Barregård L, Sällsten G, Järholm B. People with high mercury uptake from their own dental amalgam fillings. *Occup Environ Med* 1995;52:124—8.
 166. Sällsten G, Thorén J, Barregård L, Schütz A, Skarping G. Long-term use of nicotine chewing gum and mercury exposure from dental amalgam fillings. *J Dent Res* 1996;75:594—8.
 167. Molin M, Bergman B, Marklund SL, Schütz A, Skerfving S. Mercury, selenium and glutathione peroxidase before and after amalgam removal in man. *Acta Odont Scand* 1990;48:189—202.
 168. Hagmar L, Hallberg T, Leja M, Nilsson A, Schütz A. High consumption of fatty fish from the Baltic Sea is associated with changes in human lymphocyte subset levels. *Toxicol Lett* 1995;77:335—42.
 169. Svensson B-G, Hallberg T, Nilsson A, Schütz A, Hagmar L. Parameters of immunological competence in subjects with high consumption of fish contaminated with persistent organochlorine compounds. *Int Arch Occup Environ Health* 1994;65:351—8.
 170. Skerfving S, Hansson K, Mangs C, Lindsten I and Ryman N. Methylmercury induced chromosome damage in man. *Environ Res* 1974;7:83—98.
 171. Hagmar L, Brøgger A, Hansteen I-L, Heim S, Högstedt B, Knudsen L, et al. Cancer risk in humans predicted by increased levels of chromosomal aberrations in lymphocytes: Nordic Study Group on the Health Risk of Chromosome Damage. *Cancer Res* 1994;54:2919—22.
 172. Pershagen G, Vahter M. Criteria documents from the Nordic expert group: inorganic arsenic. Stockholm: Arbetsarskyddsvetket, 1991:193—234. *Arbete och Hälsa* 1991;50.
 173. Vahter M. Arsenic. In: Clarkson TW, Friberg L, Nordberg GF, Sager PR, editors. *Biological monitoring of toxic metals*. New York (NY): Plenum Press, 1988:303—21.
 174. Vahter M. What are the chemical forms of arsenic in urine, and what can they tell us about exposure? *Clin Chem* 1994;40:679—80.
 175. Vahter M, Lind B. Concentrations of arsenic in urine of the general population in Sweden. *Sci Total Environ* 1986;54:1—2.
 176. Bencko V. Use of human hair as a biomarker in the assessment of exposure to pollutants in occupational and environmental settings. *Toxicology* 1995;101:29—39.
 177. Environmental Protection Agency (EPA). *Skin cancer: nutritional essentiality*. Washington (DC): Risk Assessment Forum, EPA, 1988. Special report on ingested inorganic arsenic.
 178. Smith AH, Hopenhayn-Rich C, Bates MN, Goeden HM, Hertz-Picciotto I, Duggan HM, et al. Cancer risks from arsenic in drinking water. *Environ Health Perspect* 1992;97:259—67.
 179. Vahter M, Concha G, Nermell B, Nilsson R, Dulout F, Natarajan N. A unique metabolism of inorganic arsenic in native Andean women. *Eur J Pharmacol Environ Toxicol Pharmacol Section* 1995;293:455—62.
 180. Vahter M, Friberg L, Rahnster B, Nygren Å, Norlinder Å. Airborne arsenic and urinary excretion of metabolites of inorganic arsenic among smelter workers. *Int Arch Occup Environ Health* 1986;57:79—91.
 181. Valkonen S, Järvisalo J, Aitio A. Urinary arsenic in a Finnish population without occupational exposure to arsenic. In: Brätter P, Schramel P, editors. *Trace element — analytical chemistry in medicine and biology; vol 2*. Berlin: Walter de Gruyter & Co, 1983:611—21.
 182. Bencko V, Symon K. Health aspects of burning coal with a high arsenic content, I: arsenic in hair, urine, and blood in children residing in a polluted area. *Environ Res* 1977;13:378—85.
 183. Lombeck I, Altenhienne R, Bremer HJ. Urinary excretion of arsenic in children in relationship to age and diet. *Trace Elem Med* 1987;4:134—7.
 184. Jensen GE, Christensen JM, Poulsen O. Occupational and environmental exposure to arsenic — increased urinary arsenic level in children. *Sci Tot Environ* 1991;107:169—77.
 185. Andrén P, Schütz A, Vahter M, Attewell R, Johansson L, Willers S, et al. Environmental exposure to lead and arsenic among children living near a glassworks. *Sci Total Environ* 1988;77:25—34.
 186. Trepka MJ, Heinrich J, Schulz C, Krause C, Popescu M, Wjst M, Wichmann H-E. Arsenic burden among children in industrial areas of eastern Germany. *Sci Total Environ* 1996;180:95—105.
 187. Bencko V, Symon K, Chladek V, Pihrt J. Health aspects of burning coal with a high arsenic content, II: hearing changes in exposed children. *Environ Res* 1977;13:386—95.
 188. Bencko V. Health aspects of burning coal with a high arsenic content: the central Slovakia experience. In: Abernathy CO, Caldron RL, Chappell WR, editors. *Arsenic: exposure and health effects*. London: Chapman and Hall, 1997:84—92.
 189. Bencko V, Götzl M. Exposure assessment and arsenic related skin basalioma cancer epidemiology. In: *Proceedings of the 14th Asian Conference on Occupational Health*. October 1994, Beijing, China, p. 152.
 190. Pershagen G. Lung cancer mortality among men living near

- an arsenic-emitting smelter. *Am J Epidemiol* 1985;122:684—94.
191. International Agency for Research on Cancer (IARC). Chromium, nickel and welding. Lyon: IARC, 1990:648 p. IARC monographs on the evaluation of carcinogenic risks to humans, vol 49.
192. World Health Organization (WHO). Nickel. Geneva: International Programme on Chemical Safety, WHO, 1991: 383 p. Environmental health criteria, no 108.
193. Norseth T. Environmental pollution around nickel smelters in the Kola Peninsula (Russia). *Sci Total Environ* 1994;148:103—8.
194. Smith-Sivertsen T, Tchachtchine V, Lund E, Norseth T, Bykov V. A cross-section study of pollution and health in the border area. Tromsø (Norway): University of Tromsø, 1997:56 p (plus tables, figures and appendices). The Norwegian-Russian health study 1994/95. ISM skriftserie, no 42.
195. Smith-Sivertsen T, Tchachtchine V, Lund E, Bykov V, Thomassen Y, Norseth T. Urinary nickel excretion in populations living in the proximity of two Russian nickel refineries: a Norwegian-Russian population-based study. *Environ Health Perspect* 1998;106:503—11.
196. Cashschin VP, Artunina GP, Norseth T. Congenital defects, abortion, and other health effects in nickel refinery workers. *Sci Total Environ* 1994;148:287—91.
197. World Health Organization (WHO). Beryllium. Geneva: International Programme on Chemical Safety, WHO, 1990:210 p. Environmental health criteria, no 108.
198. Bencko V, Vasielieva EV, Symon K. Immunological aspects of exposure to emissions from burning coal of high beryllium content. *Environ Res* 1980;22:439—49.
199. Bencko V, Wagner V. Metals, metalloids and immunity. Methodological approaches and group diagnostics. *Cent Eur J Occup Environ Med* 1995;1:327—37.