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Environmental exposure to metals of newborns, infants and young children

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Abstract

Anthropogenic emissions, such as those from combustion of fossil fuel, waste incineration and industrial use, contribute to higher levels of metal pollutants, including Cd, Pb and Sb, in the urban environment. These widespread and persistent environmental pollutants have the potential for developmental and reproductive toxicity. Health risks are particularly associated with exposure in utero and the early years of life, since the developing organism is at greater risk from permanent damage, and both absorption and retention can be considerably greater in infants than adults. In order to assess risk to humans, the information on environmental levels of pollutants (environmental monitoring) should be integrated with information on biomarkers of exposure, effect or susceptibility in biological fluids or tissues (biological monitoring). The analysis of tissue from the target organ obtained at autopsy provides a direct record of the accumulation of toxins and allows temporal and geographical trends to be studied. Few literature reports on tissue content of potentially toxic elements include data on newborns and young children since collections of autopsy samples in this age range are rare. Existing data are sometime questionable, because of inadequate sensitivity of the analytical techniques, insufficient control of contamination and lack of validation. Our recent work aimed to establish reliable reference values for the content of Cd, Pb and Sb in the liver of pediatric subjects. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Antimony; Cadmium; Child; Lead; Liver; Human milk

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1. Introduction

Toxic metal compounds are present in the human environment and have the potential for adverse health effects. Health risks are particularly associated with exposure in utero and the early years of life, since developmental and reproductive toxicity may occur even at low levels of exposure. Fetuses, newborns and infants are developing organisms undergoing rapid changes in the structure and function of major organs and are therefore more vulnerable to the toxic effects of chemicals. Risk assessment for the definition of acceptable or tolerable limits for chemicals in the environment must take into account the protection of the most vulnerable risk groups and consider the possibility of damage affecting the health of adults later in life and even future generations (e.g. damages to DNA or impairment of the reproductive function) [1,2]. Biomarkers are now recognized as essential tools for the evaluation of the extent and the effects of human exposure to chemicals [3,4]. Substantial differences exist between the physiology, metabolism and lifestyle of young children compared to adults, which modify the patterns of exposure and limit the applicability of data obtained from the adult population. However, both ethical, technical and conceptual difficulties limit the collection of samples from pediatric populations and therefore studies documenting concentrations of xenobiotics in biological fluids or tissues for this age range are scarce and sometimes questionable. This paper reviews information relevant to the risk assessment of environmental exposure to Cd, Pb and Sb, including the results of a recent study aiming to establish reference values for the concentrations of these metals in liver tissue from pediatric populations [5].

2. Biological specificity of young children affecting exposure to chemicals

According to the WHO [1], the term newborn applies from birth to 4 weeks, infant should be used from 1 month to 1 year and young child from 1 to 5 years. The use of different terms is

necessary, since the first years of life are characterized by major changes in growth and development. Children in these early stages of life have physiological characteristics, such as higher resting metabolic rate, which enhance their vulnerability to the noxious effects of chemicals. Exposure to environmental contaminants occurs, as for adults, through inhalation, ingestion and percutaneous absorption. Newborns, infants and young children have twice as high an intake of air per unit of body weight (bw) than adults, food consumption per unit bw is higher and surface area per unit bw is larger than in adults. Infants have a higher percentage of water in the body as a whole and in organs and tissues, which results in twice as large an extracellular water compartment compared to adults. The percentage water content decreases with age, according to the maturation of the different organs, whereas, because of rapid growth, weight gain occurs at a faster rate than in the rest of life. Expected weight gain in the first months of life is between 200 and 300 g/kg bw per month. Xenobiotics which can be stored in tissues may therefore accumulate to a greater extent than in adults. Variations in organ composition may also have implications for the absorption, distribution and accumulation of specific chemicals in target organs and tissues (e.g. Pb in bones).

In the human child, the development of most organs, physiological systems and metabolic pathways continues long after birth and in some cases only reach full maturity in adolescence. During intrauterine life, the interactions between maternal and fetal circulations provide for the exchange of respiratory gases, provision of nutrients and removal of degradation products. The respiratory, gastrointestinal, endocrine, immune and reproductive systems and the renal function are all immature at birth and evolve toward maturity at different rates. Accordingly, several metabolic pathways must change dramatically after the transition to independent existence, e.g. the hepatic handling of essential metals, such as copper, iron and zinc [6]. These differences affect both the extent of exposure and the kinetics of xenobiotics entering the body and may cause more serious effects than those expected in adults. Gastroin-

testinal absorption of several chemicals, including some metals, is higher in the young compared to the mature animal, because of the characteristics of both intestinal function and structure at this age, as well as the type of diet and the higher food intake per unit bw. Binding of toxins to plasma proteins is less, because of the lower concentrations of albumin found in the plasma of newborns and competition for binding sites with endogenous substances. This, however, may not result in faster elimination, because of the immaturity of the kidneys. The renal function in newborns and infants is tailored for their special needs, thus they have higher retention of nitrogen and minerals than adults and older children. Glomerular filtration at birth is only 30–40% of that found in adults and tubular secretion and reabsorption are also less efficient. The presence of unbound toxins in plasma may enhance their retention in tissues, at a faster rate because of rapid growth. Organ maturation and relative organ weight may favor higher uptake of certain classes of xenobiotics, for example the brain may be at greater risk because the blood–brain barrier is not fully developed until approximately 6 months after birth.

3. Patterns of exposure during infancy and early childhood

Exposure to toxic chemicals (e.g. ethanol, narcotics, volatile Hg compounds and Pb) occur even before birth by the placental circulation. After birth, the routes of exposure are the same as adults, but with characteristics specific for these age groups. Exposure of the general population occurs through food, beverages and drinking water, from the general environment and from lifestyle habits, such as tobacco usage and alcohol consumption. Diet, the environmental surroundings, behavior and activities differ substantially when newborns, infants and young children are considered.

Exposure to atmospheric pollutants through inhalation is substantially the same as for adults, but the volume of inhaled air per unit bw is larger in young children. Exposure may be enhanced if

the concentration of pollutants increases closer to the ground, as from car exhausts.

During the first months of life, diet consists mainly of breast or cow milk or formulas. Milk, as a secretion from the mammary gland, can be an additional route of excretion for unwanted substances, possibly through the same routes as other milk components. The extent and rate of transfer from blood to milk depends on several factors such as solubility in lipids, molecular mass and strength of binding to plasma proteins. Several studies have provided evidence of the transport of xenobiotics from the mother to suckling animals and breast-fed infants [7–10], but data are not available for other potential environmental pollutants. For children given formula feeds, the water used to make it up can also be a source of exposure. Compared with adults or older children using the same water supply, infants need a larger intake of fluids per unit bw, equivalent to one-seventh of their own weight, to replace water lost through larger surface area, higher metabolic rate and inability of kidneys to concentrate urine.

Oral exploration constitutes an important part of a normal development between 6 and 36 months of age. Ingestion of soil, house and street dust through hand-to-mouth activities (typically 100 mg/day) [11] is recognized as an important source of exposure in children below 5 years of age.

4. Sources of exposure to Cd, Pb and Sb for children in urban environments

Air pollution, food and beverages, smoking habits and alcohol consumption are the main sources of exposure of adult general population to Cd, Pb or Sb. For newborns and infants, differences in diet (breast or formula milk, weaning food) and the additional contribution of contaminants present in dust and soil must be taken into account. Parental smoking habits contribute directly to higher exposure during pregnancy and breastfeeding and indirectly through passive smoking.

Anthropogenic activities, such as fuel combus-

tion for both heating and transport, waste incineration and other traffic emissions (e.g. vehicle and vehicle parts wear) account for most of environmental pollution in urban sites. Information on sources and levels of environmental exposure to Cd [12] or inorganic Pb [13] for the general population have been comprehensively reviewed in recent WHO reports. Emissions of Sb in the environment result from both natural events, such as rock weathering and soil erosion, and human activities, especially mining, smelting and traffic emissions [14]. The presence of Sb in domestic environments has been thoroughly investigated by the UK Expert Group on Sb and cot death [15]. Besides Sb uses in industry and, in medicine, for the therapy of visceral leishmaniasis, Sb compounds are present as fire retardants in materials in common use (e.g. textiles, carpet backings, plastics and synthetic fibers) and in the production of polyesters, ceramics, glass and rubber, e.g. for vehicle tyres. Accordingly, much higher levels of Sb are measured in urban dust than would be expected from its natural occurrence in the earth crust [16].

Annual average levels of Cd in air, as measured in several countries in the late-1970s, ranged from 1 to 150 ng/m³ in urban areas, compared with concentrations between 1 and 5 ng/m³ in rural areas [12,17]. Lead levels in air were higher even in rural areas (0.1–0.3 µg/m³) and between 0.5 and 3 µg/m³ in urban areas [13], but are now decreasing, following restrictions to the use of leaded gasoline. Current values in most European cities are between 0.15 and 0.5 µg/m³, in agreement with the recommended WHO guidelines aimed to ensure that concentrations of Pb in blood do not exceed 100 µg/l for at least 98% of the population including pre-school children [18]. Similarly it is recommended that the Cd concentrations in air should not exceed 5 ng/m³ in rural areas and 10 ng/m³ in urban or industrial areas [18]. Antimony concentrations in air are low even at urban sites (< 0.03 ng/m³) [19]. Daily intakes of inhaled Cd, Pb or Sb from ambient air are therefore negligible in adults (typically approximately 0.2 µg Cd, 50 µg Pb and 0.6 ng Sb, assuming 20 m³ of air to be inhaled daily on average and indoor concentrations similar to out-

door concentrations). Absorption from the lungs ranges from an average 15%, for Cd and Sb, to 50% for Pb, but it also depends on the size of the inhaled atmospheric particles and the solubility of the element compounds. Children below 5 years of age have a higher air intake per unit bw and may absorb a higher percentage of inhaled metals. Metals, especially Cd, are present in tobacco and are released in both inhaled smoke and the environment. Airborne Cd, a marker of environmental tobacco smoke, is significantly higher (up to 30 times in extreme cases) in public places and houses where smokers live [20]. In these environments, higher Sb concentrations have also been reported (0.5–1.9 ng m³) [19].

Metals in ambient air are transferred by wet or dry deposition to soil and water where they can enter the food chain. The rate of transfer from soil to plants depends on several factors, such as the type of soil, plant, pH, use of fertilizers and meteorological conditions. Food processing, storage and preparation add to the levels of contaminants. Provisional tolerable weekly intakes (PTWI) of 6.4 µg Cd/kg bw [21] and 25 µg Pb/kg bw [22] have been proposed by a joint WHO/FAO Expert Group taking into account adults, children and infants. For a 2 year-old child, weighing 10 kg, these limits correspond to daily intakes of 9 µg Cd and 36 µg Pb. Daily intakes of approximately 10–25 µg Cd/day have been reported for adults in European countries and in North America [12]. Surveys carried out between 1980 and 1991 in several countries have shown wide variations of Pb intake from food (from 15 to 316 µg Pb/day), with those from the USA at the lower end, following interventions to reduce the use of lead-soldered cans and of leaded gasoline [13]. For example, median intakes of Cd and Pb reported in a recent survey carried out in the Great Lakes Region as part of the US National Human Exposure Assessment Survey were 0.19 µg Cd/kg bw/day and 0.10 µg Pb/kg bw/day (approx. 14 and 7 µg/day), respectively [23]. Daily dietary intake of Sb was estimated as 29 µg/day and 3 µg/day in two separate studies in the UK [15].

Gastrointestinal absorption in adults is estimated as approximately 5% for Cd, 5–15% for Sb

and 40% for Pb. These figures may be substantially higher in children and in adults under certain conditions, e.g. Cd absorption increases up to 20% in women with severe iron deficiency. Trace elements consumed via food or inhaled can be transferred to the developing fetus and contribute to the child's body burden. This has been demonstrated in the case of Pb by the comparison of maternal and cord blood Pb levels at birth [24,25]. The placental barrier is more effective in protecting the fetus from Cd, and concentrations in blood and tissues of newborns are very low [12]. Antimony concentrations ranging from < 1 to

200 ng/g (median 9 ng/g) were reported for cord blood [26].

Lead and other trace elements are secreted in milk and concentrations of Cd and Pb in human milk can be correlated with concentrations in maternal blood [27–29]. The trace element content of human milk has been the subject of an extensive collaborative WHO/IAEA study, involving subjects from six different countries [30]. Method validation and quality assurance were documented in detail and constituted a large part of the study procedures. In their concluding remarks, the authors suggest values of < 1 µg/l,

Table 1
Concentrations of Cd, Pb and Sb measured in human milk (median, range or mean ± S.D.)

Area	Cd (µg/kg)	Pb (µg/kg)	Sb (µg/kg)	Year
India	0.09 ± 2.8 ^b	1.9 ± 2.0 ^b		1999 [31]
Canada		0–4		1999 [32]
Austria	< 0.2–0.8	< 0.1–9.9	< 0.4–1.6	1998 [33]
Australia		0.09–3.1		1998 [34]
Egypt		0–158 ^a		1996 [35]
Polonia	0.6 ± 0.28 ^a			1996 [36]
Sweden	0.06 ± 0.04 ^a	0.7 ± 0.4 ^a		1995 [37]
Austria		35.8 ± 15 ^a		1993 [38]
Mexico		24.7 ^{a,b}		1993 [39]
Italy	2, 1–65	16, 2–77		1990 [40]
Guatemala	< 1 ^a	3 ^a	1.0 ^a	1989 [30]
Hungary	< 1	15 ^a	1.6 ^a	1989 [30]
Nigeria	3.67 ^a	5 ^a	4.1 ^a	1989 [30]
Philippines	2.67 ^a	17 ^a	11 ^a	1989 [30]
Sweden	< 1	17 ^a	3 ^a	1989 [30]
Zaire	< 1 ^a	5 ^a	3.6 ^a	1989 [30]
Czechoslovakia	< 0.05–1.08 ^a	0.10–6.75 ^a		1989 [41]
Bavaria		2.5		1988 [28]
Germany (non smokers)	0.07			1987 [42]
Germany (smokers > 20 cig.)	0.16			1987 [42]
Italy		< 4–132 ^a		1986 [43]
Canada	< 0.002–4.05	< 0.05–15.8		1986 [44]
Kuala Lumpur		48		1985 [29]
Germany (rural)		9		1985 [45]
Germany (urban)		13		1985 [45]
UK (urban)	0.4 ^a	2 ^a		1984 [46]
Yugoslavia			0.06–0.43 ^a	1983 [47]
Finland	1.2–3.1			1983 [48]
Italy			< 0.05–12.9	1982 [49]
Scotland (urban)		21		1982 [27]
Sweden	< 0.4–3.8	0.5–9.0		1981 [50]

^aIn µg/l.

^bGeometric mean and geometric S.D.

2–5 $\mu\text{g}/\text{l}$ and 1–4 $\mu\text{g}/\text{l}$ as the range of concentrations to be expected for Cd, Pb and Sb, respectively, in human milk under ‘usual’ conditions, i.e. after exclusion of areas where exceptionally low or high values were reported. Table 1 summarizes these and other available literature data on the concentrations of Cd, Pb and Sb in human milk. Concentrations of Cd in milk are largely compatible with the PTWI of 6.4 $\mu\text{g}/\text{kg}$ bw, assuming an average 800 ml daily intake in a 6-kg infant. Lead levels are more widely variable and may lead to dietary intakes by breast-fed infants exceeding the PTWI of 25 μg Pb/kg bw. Other components of newborn and infant diet, such as cow milk and formulas, were reported to contain less than 1 ng/g Cd and Sb, and slightly higher concentrations of Pb (approx. 2 ng/g) [51,52].

Ingestion of dust is a significant source of exposure to potentially toxic elements for children below 5 years of age. Lead in dust is estimated as the major source of Pb exposure in children [53], accounting for 75% of the total Pb intake in 2-year-old infants in the USA (1990) [13]. Similar findings (65%) were reported from a comprehensive study, including environmental, biological, behavioral and dietary aspects, carried out on 2-year-old children living in Birmingham (UK) [54]. The Pb content of dust and soil vary widely from 100 to over 2000 $\mu\text{g}/\text{g}$ [55]. An extensive survey involving over 4500 samples of house dust or garden soil in the UK found an average level of 6.4 μg Cd/g, compared with an average concentration of less than 0.1 $\mu\text{g}/\text{g}$ in the earth’s crust [12]. A downward trend in the street dust content of Pb is expected, following the restrictions imposed on the use of leaded gasoline in Europe and other countries. However, gasoline emissions are not the only important sources of Pb or other elements in dust. Antimony, which is present at low concentrations in rocks and soil (< 0.5 $\mu\text{g}/\text{g}$), was measured in dust samples from 100 homes, selected at random from four locations in the UK, and produced a median value of 13 $\mu\text{g}/\text{g}$ with extreme values in excess of 1500 $\mu\text{g}/\text{g}$ [16]. According to these average values, the daily intake of Cd, Sb and Pb for a child ingesting approximately 100 mg of dust would add approximately 0.6 μg Cd, 1.3 μg Sb and from 10 to 200

μg Pb, largely exceeding average Pb intake from the diet and the FAO/WHO PTWI. Differences in the composition of soils, either natural or from earlier metal extraction and refining, result in higher levels of metals in ‘geochemical hotspots’ such as certain areas of Belgium (Cd) and England (Cd, Pb).

5. Analysis of Cd, Pb and Sb in autopsy tissues: ethical and technical issues

The collection of data for the concentrations of potentially toxic elements in biological fluids and tissues provides objective indices of their absorption and retention within the body and in specific target organs. Most Cd absorbed from the lungs or the intestine is first deposited in the liver and then slowly transferred to the kidneys where it is stored bound to metallothionein. Estimates of the biological half-life of Cd are approximately 10 years in the liver and slightly longer in the kidneys. Lead absorbed into the body is distributed in three compartments (blood, soft tissue and bone) with half-lives of 36 days, 40 days and 27 years, respectively. Antimony distribution within the body depends on the oxidation state. Trivalent Sb binds to erythrocytes and is deposited in soft tissues, mainly liver, whereas Sb(V) is more rapidly cleared from blood plasma and excreted in urine [14].

Information on the amount of a toxin stored within the body over a period of time is important for the risk assessment to humans in general and especially for susceptible populations. Because of physiological and behavioral differences, data available from adult populations do not adequately represent children below 5 years of age and therefore do not provide adequate reference intervals for comparison. Setting age-specific reference values for biochemical indices in pediatric subjects is a task with inherent difficulties [56]. Newborns and infants are not a homogeneous population, since development and maturation occur rapidly and is influenced by gestational age at birth. Ethical considerations may limit the systematic collection of autopsy samples in this range of age and attention should be given to pathologi-

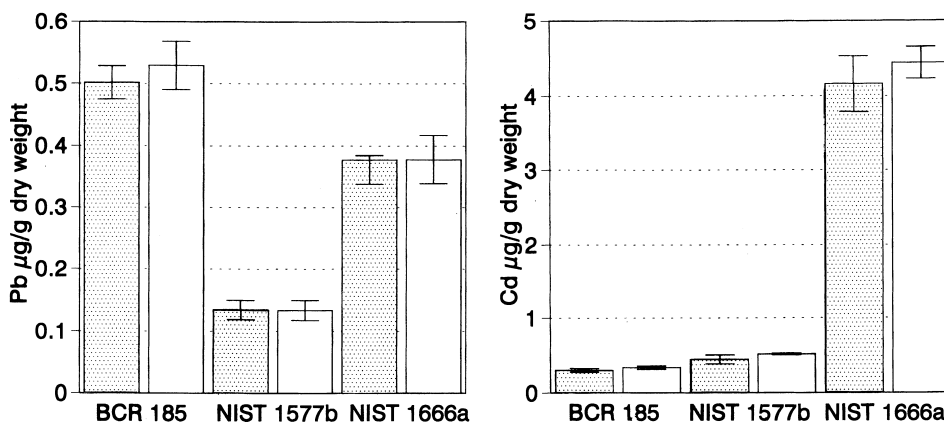


Fig. 1. Comparison between target (stippled bars) and measured (open bars) values of Pb and Cd in certified reference materials (BCR 185 Bovine liver, NIST 1577b Bovine liver, NIST 1666a Oyster tissue).

cal alterations affecting the comparability of such tissues with those of similar organs in a 'healthy' pediatric population. Samples from a pediatric population are more difficult to analyze because of their smaller size and since the expected concentrations may be close to the detection limits of most techniques. Several factors can influence the accuracy of measurements and the comparability of data obtained on samples handled and analyzed in different ways. Inadequate procedures of sampling, storage, sample manipulation and analysis as well as poor sensitivity, inadequate validation of methods and lack of suitable reference materials (RMs) may compromise the reliability of results. For tissue samples, the pre-analytical phase involves several steps and strict contamination control is an essential requisite. For some elements, neutron activation analysis and, more recently, inductively coupled plasma mass spectrometry (ICP-MS) are the only techniques providing adequate sensitivity and the ability for simultaneous multi-element determinations. However, absence of interferences and method characteristics should be thoroughly validated for each element, especially in complex matrices and when the concentrations to be analyzed are close to the detection limits. The analysis of matrix-specific RMs is recommended, but may provide little information on the reliability of data, when the measured concentrations are much lower than in the RMs.

In a recent study [5], we have described the analytical difficulties encountered in the determination of several trace elements including Cd, Pb and Sb, in pediatric liver samples collected at autopsy between 1991 and 1996 in the UK. Liver samples were stored frozen at -80°C without addition of any preservative. Freeze-dried aliquots were digested in a microwave oven with ultrapure nitric acid and the digests diluted with ultrapure water and analyzed by ICP-MS. All glass and plasticware was acid washed before use and sample manipulation was carried out in a laminar flow clean air cabinet. Nevertheless, erratic blank fluctuations were occasionally observed when analyzing replicate digest blanks for Cd or Sb, resulting in higher method detection limits – i.e. 0.6, 4.3 and 1.5 ng/g wet weight (ww) for Cd, Pb and Sb, respectively – than could be expected from the analysis of the diluted nitric acid reagent (0.14, 3.8 and 0.38 ng/g ww, respectively). Standard solutions at three different concentrations were used for calibration, which was repeated at least every twenty samples. Observed values for Cd and Pb in certified RMs (Fig. 1) and for Sb in NIST SRM 1666a Oyster tissue (the only available RM with at least an indicative value for Sb) were in good agreement with target values. However, because these materials are designed for food analysis, they give little information on the performance of the method at much lower concentrations. This problem was partly overcome by

performing isotope dilution (ID) analysis on a subset of samples. The results of the comparison between ID and external standardization (Ext) are summarized by the equations:

$$[\text{Cd}]_{\text{Ext}} = 1.01 [\text{Cd}]_{\text{ID}} - 0.8 \text{ ng/g},$$

$$r = 0.999, \quad N = 23$$

and

$$[\text{Sb}]_{\text{Ext}} = 0.97 [\text{Sb}]_{\text{ID}} + 0.2 \text{ ng/g},$$

$$r = 0.997, \quad N = 9.$$

6. Reference values for concentrations of Cd, Pb and Sb in human liver

Several studies have investigated elemental concentrations in human tissues from various geographical areas. Reference intervals for selected elements in clinical samples, including liver tis-

sue, have been reviewed [57–59], but few results are available for subjects below 5 years of age. The concentrations of either Cd, Pb or Sb in liver tissue of 141 subjects below 1 year of age, from our work on a total of 157 subjects between 0 and 6 years [5], are shown in Table 2 and compared with those found from an extensive search of the published biomedical literature since 1975 onward, for fetuses, newborns and infants. For comparison, the average Cd liver content in adult populations was estimated as approximately 2 $\mu\text{g/g}$ from values reported before 1985 [57] and reference values of 0.79 $\mu\text{g/g}$ (range 0.28–1.16) and 2.62 $\mu\text{g/g}$ (range 0.51–6.13) were proposed in two more recent studies [76,77]. Lead concentrations in adult liver range from 0.250 to 2.30 $\mu\text{g/g}$ [58,59] and Sb concentrations from 7 to 13 ng/g have been reported [78–80]. The differences among results reported for Cd and Pb over a period of 25 years are mainly due to dramatic improvement of analytical techniques and contamination control, rather than temporal trends.

Table 2
Concentrations of Cd, Pb and Sb observed in liver tissue from pediatric subjects (median, range or mean \pm S.D.)^a

Country	N	Age	Cd ($\mu\text{g/g}$ ww)	Pb ($\mu\text{g/g}$ ww)	Sb (ng/g ww)	Year
UK	141	0–1 years	0.0025 (0.0006–0.0097)	0.065 (0.008–0.407)	1.8 (0.2–102)	1999 [5]
Canada	4	7–10 years	0.34 ^b			1999 [60]
Canada	21	Fetuses, 16–22 weeks	0.016 \pm 0.011	0.061 \pm 0.023	5 \pm 2	1997 [61]
UK	21	11 days–23 months			2.1 (0.7–37)	1997 [62]
UK	20	16 days–14 months			2.7 (0.5–58)	1997 [62]
Canada	5	2 months–5 years		0.01–0.23		1997 [63]
Venezuela	20	Stillborns, 36–40 weeks		0.28 \pm 0.12		1996 [64]
Austria	7	Fetuses, 17–36 weeks	0–0.02			1995 [65]
Austria	17	2 days–30 months	0–0.15			1995 [65]
Denmark	4	0–5 years	0.10–0.20			1989 [66]
USA	23	4–26 weeks	0.006 \pm 0.003	0.19 \pm 0.16		1983 [67]
New Zealand	6	0–10 years	0.2–0.4	0.5–1.3		1983 [68]
Germany	9	Fetuses, 23–38 weeks	< 0.1–0.4	0.3–6.2		1979 [69]
Canada	4	Stillborn	< 0.005–3.5	0.30–0.77		1978 [70,71]
Canada	7	0–1 years	< 0.005–0.2	< 0.1–0.91		1978 [70,71]
New Zealand	39	Fetuses, 22–43 weeks	< 0.002–0.07	< 0.025–0.60		1978 [72]
USA	19	Fetuses, 19–34 weeks	0.01–0.02			1976 [73]
USA	21	0–3 years	0.01–0.27			1976 [73]
Sweden	7	3–9 years	0.26 \pm 1.66 ^b			1976 [74]
UK	18	0–9 years		0.08–1.37		1975 [75]

^aData originally expressed on a dry weight basis converted to wet weight by multiplying by 0.25.

^bGeometric mean and geometric S.D.

Substantial overlapping of the concentration ranges can be seen for data collected after 1989. Our study demonstrates the feasibility of accurate determinations of trace elements in tissues down to less than 1 ng/g and provides a reliable estimate of current levels of exposure to Cd, Pb and Sb in a pediatric population [5]. The median concentrations are consistently lower than in adult liver and not associated with known risks to human development. Lead levels approximately 30 times higher than either Cd or Sb concentrations were attributed to persistent and ubiquitous Pb pollution. Although restrictions on the use of leaded gasoline in developed countries, Pb pollution may still be a threat in other areas of the world [81,82]. Also evidence is being found of fetal and neonatal exposure to Pb unrelated to current environmental levels. Lead mobilization from maternal bones, following physiological changes of Ca metabolism during pregnancy and lactation [83], smoking habits and alcohol consumption [84] have been suggested as sources of such exposure. Several studies are now addressing the possibility of neurobehavioral effects occurring even at levels of Pb exposure currently considered safe for children [85,86]. In addition low level Pb exposure has been associated with increased risk of preterm delivery or of low birth weight, the latter being strong predictor of survival and developmental outcomes [87,88].

7. Conclusions

The presence of toxic chemicals in the environment is a potential threat to health and quality of life. Urban environments are characterized by higher concentrations of pollutants arising from anthropogenic activities. Nowadays, concern is growing for the cumulative effects of life-long exposure to concentrations of pollutants which have been up to now considered safe. The systematic collection and analysis, under strict quality assurance procedures, of body fluids and tissues from selected population groups, including children, could improve our understanding of exposure to potentially toxic elements in urban envi-

ronments and allow trends in exposure to selected toxins to be monitored.

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