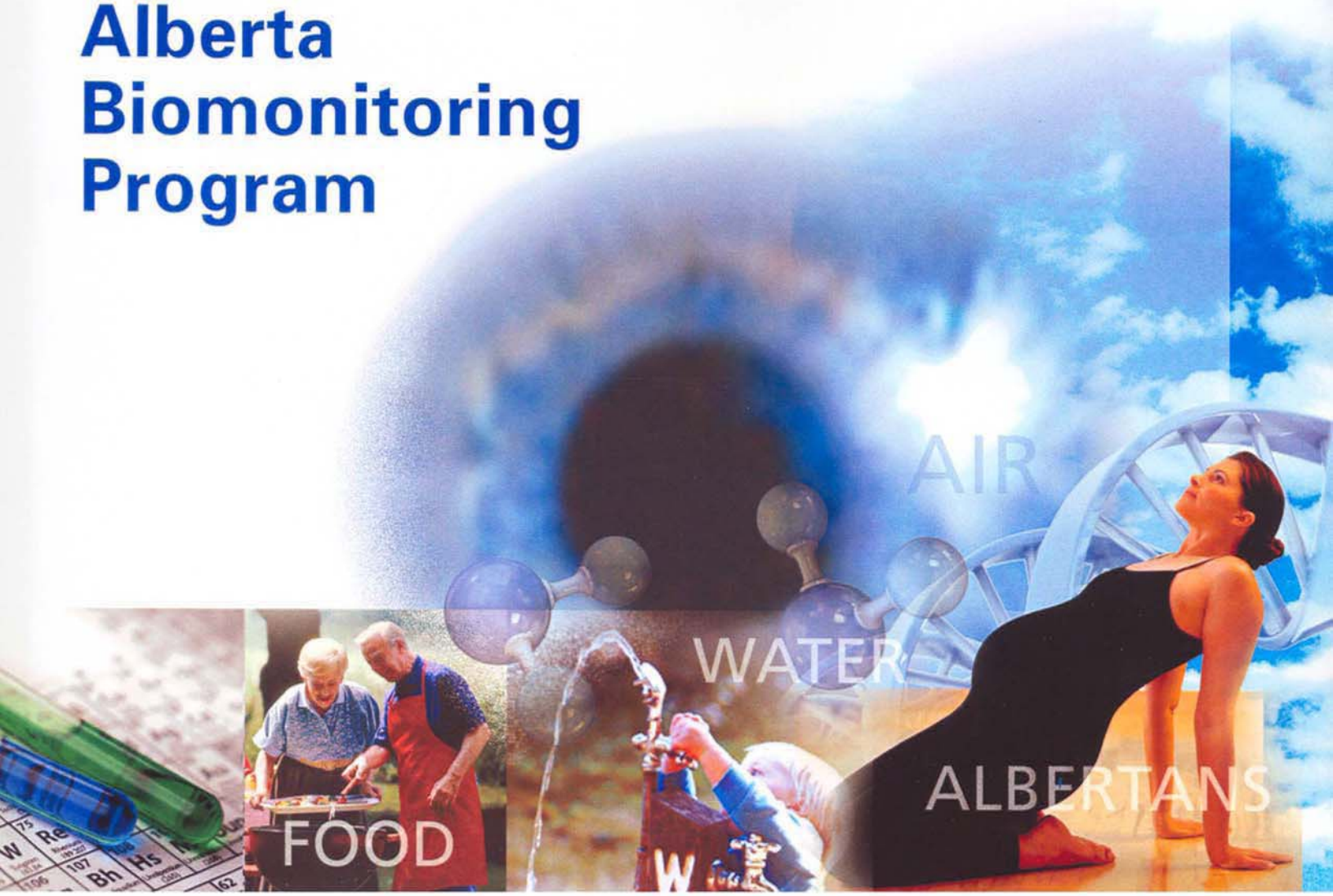
Alberta Biomonitoring Program



Chemicals in Serum of Children in Southern Alberta 2004–2006

Influence of Age and Comparison to Pregnant Women

March 2010

Government of Alberta

The
ALBERTA BIOMONITORING PROGRAM

Chemicals in Serum of Children in Southern Alberta (2004–2006) –
Influence of Age and Comparison to Pregnant Women

A Final Report
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Executive Summary

This biomonitoring study of children in Southern Alberta was conducted by a multi-disciplinary committee of academic and professional experts from the University of Alberta, Alberta Health and Wellness, the Alberta Centre for Toxicology at Calgary, the Alberta Children's Hospital, the Provincial Public Health Laboratory (Edmonton), and Alberta Environment. A comprehensive list of priority environmental contaminants were monitored in blood serum of healthy children with the objective to examine the influence of age (≤5, 6–13), and to compare these new data with concentrations in pregnant women that were reported previously for the same region (Biomonitoring of Priority Chemicals in Blood of Pregnant Women in Alberta, 2005; Influence of Age, Location and Seasonality).

Small volumes of children's serum (400 uL) were drawn anonymously from 1373 archived samples stored at the Alberta Children's Hospital. The children were all healthy, but had presented for an elective surgery between 2004 and 2006. Examples of such surgeries include hernia repairs, strabismus, tonsillectomy, adenoidectomy, and otoplasties. Individual blood serum samples were not analyzed, rather 196–240 small samples were pooled together within each age class, and three replicate pools were made for each age class.

The chemicals measured were both man-made or naturally occurring chemicals that may be absorbed from food, drinking water, air, soil, household dust, or commercial products. The following specific classes of chemical contaminants were monitored: tobacco smoke markers, phytoestrogens, polychlorinated biphenyls, chlorinated dioxins and furans, organochlorine pesticides, polybrominated diphenyl ethers, perfluorinated compounds, methylmercury, metals and mineral micronutrients, various pesticides and herbicides, and phenolic compounds, including bisphenol A. The laboratories tasked with analyzing the samples included the Alberta Centre for Toxicology (nicotine, cotinine, phytoestrogens, and most metals) and ALS Laboratory Group, Edmonton, AB Canada. Quality control samples were also analyzed with the children's serum samples to monitor for possible contamination by collection vessels and routine sample handling. Both analytical laboratories were blind to the nature of the samples.

In general, concentrations of detected contaminants were either lower or similar to concentrations reported in other studies of children in North America or around the world. Overall, the effect of children's age (≤5 or 6–13 years) was not a significant factor in our analysis of any chemical, except for small differences observed for perfluorononanoate and molybdenum. However, the 95 percent confidence intervals around the estimated mean blood serum concentrations were always rather wide. This is due, in part, to the minimal number of replicates (i.e., three) we were able to generate during pooling for each age class. However, many significant differences were observed when comparing children's serum concentrations to pooled serum concentrations of pregnant women collected from the same general region (Southern Alberta) during the same general time period (2005).

Among organic contaminants, the only chemical that was significantly lower in children than pregnant women was cotinine, a metabolite of nicotine commonly used as a biomarker of smoking and environmental tobacco smoke. The most notable examples of other organic contaminants that were higher in children than pregnant women of all age

classes were perfluorinated compounds (perfluorohexane sulfonate, perfluorooctane sulfonate, perfluorooctanoate, and perfluorononanoate), bisphenol A, the herbicide 2,4-D, and a metabolite of a common pyrethroid insecticide, trans-DCCA. A few congeners of chlorinated dioxins and furans, and certain polybrominated diphenyl ether flame retardants were also higher in some children than certain pregnant women (i.e., depending on age class).

Among metals and mineral micronutrients, some differences between children and pregnant women were also observed. Among metals, children had lower concentrations of chromium and silver than pregnant women of all ages, and some differences were also found for cesium, depending on age. Unfortunately, lead could not be detected in children's serum with confidence due to trace contamination of the tubes commonly used to store the children's blood samples. For mineral micronutrients, children had lower concentrations of cobalt, selenium, and zinc than pregnant women, however it is important to consider that most pregnant women take vitamins containing these elements during pregnancy. Children had higher concentrations of boron, molybdenum, and nickel than pregnant women of all ages, and some differences in copper concentrations, depending on age. For children under 6 years or age, methyl mercury was significantly lower than all pregnant women, and for children aged 6–13, methylmercury was significantly lower than pregnant women, ages 26 and older.

The health implications posed by most of the detected contaminants, at the concentrations observed, are difficult to measure at this time. However, the very low levels of serum cotinine measured in children is a positive finding due to the myriad of known adverse consequences associated with postnatal exposure to environmental tobacco smoke. Among the other organic chemicals that were higher in children than pregnant women, 2,4-D may be expected to decline in future years due to recent provincial restrictions on its application to lawns in the form of fertilizer/herbicide combination products. The perfluorinated chemicals have global sources, and although future exposure to all of these should slowly decline due to restrictions and regulations in developed countries on their manufacture or use (including Canada), PFOS continues to be manufactured in developing countries, thus future exposure is difficult to predict for the major perfluorinated substances in human serum. Although bisphenol A can no longer be used to manufacture baby bottles for sale in Canada, this does not address exposure to children or adults, and its exposure sources and health effects continue to be investigated by scientists. Continued biomonitoring will provide valuable information on the effectiveness of current and future chemical regulatory actions.

Preface

Purpose of Biomonitoring

Humans routinely come into contact with natural or synthetic chemical substances in the environment. Common routes of exposure include inhalation, ingestion, or dermal contact with environmental media such as air, water, soil, dust, food, and consumer products. The human health risks posed by a chemical are a function of the inherent chemical toxicity, how long we are exposed, and how much of the substance gets absorbed into our bodies; the internal dose. Any chemical has the potential to cause harm if the dose is high enough, and hence *the dose makes the poison*. The internal dose is difficult to predict because it is controlled by many environmental variables, and also because humans differ widely in physiology and behaviour. The most accurate way to assess the internal dose is to measure concentrations in relevant human samples such as blood, urine, hair, fat, or breast milk - this is known as *biomonitoring*.

Purpose of Biomonitoring in Children

Biomonitoring data from adults cannot necessarily be extrapolated to children. Children may have higher or lower exposure to contaminants due to differences in size and anatomy, behaviour, and diet. For example, children generally ingest more soil and house dust (and hence contaminants associated with these matrixes) due to play activities and have much more hand-to-mouth activity than adults. Furthermore, since children undergo developmental processes and growth, children may be more sensitive than adults to an equivalent exposure. The purpose of this biomonitoring study was to establish the magnitude of children's exposure to environmental contaminants in a representative population in Alberta. Neither Canada nor Alberta have previously monitored chemicals in the blood of children in a systematic fashion, and this is one of the most extensive biomonitoring surveys for a comprehensive set of established and emerging environmental chemicals in children's serum. The influence of age was examined for two age classes in Southern Alberta; ≤5 yrs and 6–13 yrs. Wherever possible, children's serum data was compared to the serum of pregnant women in Southern Alberta, which was reported previously. The range of exposure concentrations may serve as a starting point to assess health risks, as a benchmark to track future exposure, as an indicator of exposure source, and to prioritize future research in Alberta.

What Do These Data Mean for My Children?

In this study individual human samples were combined and analyzed as "pools", thus the concentrations reported in this report represent the average exposure in the population. With recent advancements in analytical methodologies and sophisticated analytical instrumentation, we are now able to measure very low concentrations of environmental chemicals in human samples. Therefore, it is important to keep in mind that the detection of

an environmental chemical in human blood does not mean this chemical is causing any adverse health effect. This is because, for most chemicals, there is a dose threshold below which no measurable health effects can be detected. This threshold is sometimes called the "No Observed Effect Level" or the "Safe Human Dose". The exception is for chemicals that may cause cancer in humans by a mechanism involving tumor initiation. Only carcinogens judged to be genotoxic are treated, for regulatory purposes, as if there is no level of exposure below which the risk of cancer is zero. Although the merits of this no-threshold approach for genotoxic carcinogens cannot be proven or disproven by scientific experiment, it is commonly used for precautionary public policy to establish tolerable limits of exposure representing negligible health risks.

Selection of Chemicals for Biomonitoring

The targeted chemicals monitored in this report are similar to the list that was monitored in a previous study in Alberta entitled: Chemical Biomonitoring in Serum of Pregnant Women in Alberta (2005) Influence of Age, Location and Seasonality. Therefore, data in the current report have been compared to that previous study as much as possible. In general, the chemicals reported in this study may be naturally occurring or man-made, current-use or phased-out, and either rapidly excreted or bioaccumulative.

Study Protocol

Selection of Sample Population

Children in this study came from within the general geographic area of the former Calgary Health Region; including Banff, Canmore, Didsbury, Cochrane, Airdrie, Black Diamond, Okotoks, Strathmore, High River, Nanton, Vulcan, Claresholm, and Carmangay. Participants in the study were healthy children (ages 2–13 years inclusive) presenting for elective surgeries (e.g., hernia repairs, strabismus, tonsillectomy, adenoidectomy, otoplasties). Only children with the ASA (American Society of Anesthetists) classification of I (normal, healthy patient) were eligible for the study. Excluded were children with chronic illnesses, autoimmune diseases, asthma, recurrent fractures, those undergoing diagnostic biopsies, various forms of endoscopy, lipid modifying treatments, or any child assigned an ASA score of II or more. The time frame in which the samples were collected was from 2004–2006.

Study Design for Pooling of Samples and Controls

All samples used in this study had been frozen in Nalgene cryogenic vials at -80 C before selection. Out of a total of 1845 serum samples available for pooling (1084 boys, 761 girls), 1373 met the criteria as outlined above and had enough volume available. These were subsequently pooled based on age. The two age classes examined were ≤5 years and 6–13 years, and pooling for each of these age classes was replicated three times, all with unique individual samples. From each individual sample, 400 µl was drawn and placed into one of three pools for each age class, resulting in a total of six pools:

Pool 1 (≤5):	240 samples x 400ul = 96ml
Pool 2 (≤5):	196 samples x 400ul = 87.4ml
Pool 3 (≤5):	239 samples x 400ul = 95.6ml
Pool 4 (6–13):	240 samples x 400ul = 96ml
Pool 5 (6–13) :	218 samples x 400ul = 87.2ml
Pool 6 (6–13) :	240 samples x 400ul = 96ml

For quality assurance purposes, seven control pools consisting of bovine serum or water were prepared in a similar manner. The purpose of the controls was to monitor chemical contamination introduced by the routine handling of the blood samples or during the pooling process. Only the staff of Alberta Children's Hospital had access to the demographic information of individual samples. Randomized study codes were assigned to each pool before the samples were tested so that the subsequent chemical analyses were performed "blind". The study codes were revealed for statistical analysis once the chemical analysis had been completed.

Statistical Analysis

Concentrations were blank subtracted, and means were calculated for the combined age class data, and for each of the two age classes individually. Where appropriate, concentrations below the analytical limit of detection (LOD), or limit of quantification (LOQ), were substituted by half the LOD/LOQ for statistical analysis. Therefore, in subsequent sections the reported mean concentrations may be below the LOD or LOQ.

The estimated concentrations can be analyzed by standard regression methods in which age is considered an independent variable. As discussed in the previous report, Chemical Biomonitoring in Serum of Pregnant Women in Alberta (2005), Influence of Age, Location and Seasonality, there are two complications to this analysis related to pooled sampling. First, the distribution of chemical contaminants within individual samples is generally assumed to be log normally distributed. According to the Central Limit Theorem, however, estimates derived from a sample created by pooling a large number of individual samples will be normally distributed. Consequently, no transformation of data is required prior to a standard analysis, and significance tests that assume normal distributions remain appropriate. The second complication is the parameters of the distribution of pooled estimates depend upon the number of individual samples that make up each pooled sample. Because pooled samples were constructed with differing numbers of samples, data were differentially weighted for accurate analysis.

Weighted regression analyses were conducted using SPSS (version 17). Graphs were generated using Sigmaplot (version 11). In what follows, graphs of estimated concentrations are presented and where relevant, the data for pregnant women from the previous report were also plotted for comparison purposes. Error bars in each subsequent figure represent the 95 percent confidence intervals, separately derived for each estimate. In these graphs, where the 95 percent confidence intervals do not overlap, the means differ significantly at the $\alpha = 0.05$ level. An overlap of up to 28 percent would also be significant at 0.05 levels in a single comparison; where this has occurred it is noted in the text.

List Of Chemicals Analyzed

The following are the lists of specific chemical contaminants that were analyzed in this study, also showing whether the particular chemical was detected and reported here. Also shown is whether the same chemical was previously detected and reported for maternal blood. If the chemical was reported for children and for maternal blood, a plot of the combined data will be shown in subsequent sections.

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
1. TOBACCO SMOKE BIOMARKERS			
Cotinine	0.5 ng/mL serum	Yes	Yes
Nicotine	0.5 ng/mL serum	No	No
2. PHYTOESTROGENS			
Daidzein	0.2 ng/mL serum	Yes	Yes
Genistein	0.2 ng/mL serum	Yes	No
3. POLYCHLORINATED DIBENZO-P-DIOXINS AND POLYCHLORINATED DIBENZOFURANS			
1,2,3,6,7,8-Hexachlorodibenzo-p-dioxin (HxCDD)	0.01 pg/g serum	Yes	Yes
1,2,3,4,6,7,8-Heptachlorodibenzo-p-dioxin (HpCDD)	0.01 pg/g serum	Yes	Yes
1,2,3,4,6,7,8,9-Octachlorodibenzo-p-dioxin (OCDD)	0.01 pg/g serum	Yes	Yes
1,2,3,7,8-Pentachlorodibenzofuran (PeCDF)	0.01 pg/g serum	No	Yes
2,3,4,7,8-Pentachlorodibenzofuran (PCDF)	0.01 pg/g serum	Yes	Yes

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
1,2,3,4,7,8-Hexachlorodibenzofuran (HxCDF)	0.01 pg/g serum	Yes	Yes
1,2,3,6,7,8-Hexachlorodibenzofuran (HxCDF)	0.01 pg/g serum	Yes	Yes
1,2,3,4,6,7,8-Heptachlorodibenzofuran (HpCDF)	0.01 pg/g serum	Yes	Yes
1,2,3,4,6,7,8,9-Octachlorodibenzofuran (OCDF)	0.01 pg/g serum	Yes	Yes
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)	0.01 pg/g serum	No	No
1,2,3,7,8-Pentachlorodibenzo-p-dioxin (PCDD)	0.01 pg/g serum	No	No
1,2,3,4,7,8-Hexachlorodibenzo-p-dioxin (HxCDD)	0.01 pg/g serum	No	No
1,2,3,7,8,9-Hexachlorodibenzo-p-dioxin (HxCDD)	0.01 pg/g serum	Yes	No
2,3,7,8-Tetrachlorodibenzofuran (TCDF)	0.01 pg/g serum	No	No
1,2,3,7,8,9-Hexachlorodibenzofuran (HxCDF)	0.01 pg/g serum	No	No
2,3,4,6,7,8-Hexachlorodibenzofuran (HxCDF)	0.01 pg/g serum	No	No
1,2,3,4,7,8,9-Heptachlorodibenzofuran (HpCDF)	0.01 pg/g serum	No	No
4. COPLANAR AND MONO-ORTHOSUBSTITUTED POLYCHLORINATED BIPHENYLS			
2,2′,3,4′,5,5′-Hexachlorobiphenyl (PCB 146)	5 pg/g serum	No	Yes
2,3,3′,4,4′,5-Hexachlorobiphenyl (PCB 156)	5 pg/g serum	No	Yes
2,3,3′,4,4′,6-Hexachlorobiphenyl (PCB 158)	5 pg/g serum	No	Yes
2,2′,3,3′,4,4′,5-Heptachlorobiphenyl (PCB 170)	5 pg/g serum	Yes	Yes
2,2′,3,4,4′,5,5′-Heptachlorobiphenyl (PCB 180)	5 pg/g serum	Yes	Yes
2,2′,3,4,4′,5′,6-Heptachlorobiphenyl (PCB 183)	5 pg/g serum	No	Yes
2,2′,3,4′,5,5′,6-Heptachlorobiphenyl (PCB 187)	5 pg/g serum	Yes	Yes
2,2′,3,3′,4,4′,5,5′-Octachlorobiphenyl (PCB 194)	5 pg/g serum	No	Yes
2,2′,3,3′,4,5,5′,6′-Octachlorobiphenyl (PCB 199)	5 pg/g serum	No	Yes

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
2,4,4′-Trichlorobiphenyl (PCB 28)	5 pg/g serum	No	No
2,2,5,5-Tetrachlorobiphenyl (PCB 43/52)	5 pg/g serum	No	No
2,3′,4,4′-Tetrachlorobiphenyl (PCB 66)	5 pg/g serum	No	No
2,4,4′,5-Tetrachlorobiphenyl (PCB 74)	5 pg/g serum	No	No
3,3′,4,4′-Tetrachlorobiphenyl (PCB 77)	5 pg/g serum	No	No
3,4,4′,5-Tetrachlorobiphenyl (PCB 81)	5 pg/g serum	No	No
2,2′,3,4,5′-Pentachlorobiphenyl (PCB 87)	5 pg/g serum	No	No
2,2′,4,4′,5-Pentachlorobiphenyl (PCB 99)	5 pg/g serum	No	No
2,2′,4,5,5′-Pentachlorobiphenyl (PCB 101)	5 pg/g serum	No	No
2,3,3′,4,4′-Pentachlorobiphenyl (PCB 105)	5 pg/g serum	No	No
2,3,3′,4′,6-Pentachlorobiphenyl (PCB 110)	5 pg/g serum	No	No
2,3′,4,4′,5-Pentachlorobiphenyl (PCB 118)	5 pg/g serum	No	No
3,3′,4,4′,5-Pentachlorobiphenyl (PCB 126)	5 pg/g serum	No	No
,2′,3,3′,4,4′-Hexachlorobiphenyl (PCB 128)	5 pg/g serum	No	No
2,2′,3,4,4′,5-Hexachlorobiphenyl (PCB 138)	5 pg/g serum	Yes	No
2,2′,3,4′,5′,6-Hexachlorobiphenyl (PCB 149)	5 pg/g serum	No	No
2,2′,3,5,5′,6-Hexachlorobiphenyl (PCB 151)	5 pg/g serum	No	No
2,2′,4,4′,5,5′-Hexachlorobiphenyl (PCB 153	5 pg/g serum	Yes	No
2,3,3′,4,4′,5′-Hexachlorobiphenyl (PCB 157)	5 pg/g serum	No	No
2,3′,4,4′,5,5′-Hexachlorobiphenyl (PCB 167)	5 pg/g serum	No	No
3,3′,4,4′,5,5′-Hexachlorobiphenyl (PCB 169)	5 pg/g serum	No	No
2,2′,3,3′,4,5,5′-Heptachlorobiphenyl (PCB 172)	5 pg/g serum	No	No
2,2′,3,3′,4,5′,6′-Heptachlorobiphenyl (PCB 177)	5 pg/g serum	No	No
2,2′,3,3′,5,5′,6-Heptachlorobiphenyl (PCB 178)	5 pg/g serum	No	No

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
2,3,3′,4,4′,5,5′-Heptachlorobiphenyl (PCB 189)	5 pg/g serum	No	No
2,2′,3,3′,4,4′,5,6-Octachlorobiphenyl (PCB 195)	5 pg/g serum	No	No
2,2′,3,3′,4,4′,5,6′-Octachlorobiphenyl (PCB 196)	5 pg/g serum	No	No
2,2′,3,4,4′,5,5′,6-Octachlorobiphenyl (PCB 203)	5 pg/g serum	No	No
2,2′,3,3′,4,4′,5,5′,6-Nonachlorobiphenyl (PCB 206)	5 pg/g serum	No	No
2,2′,3,3′,4,4′,5,5′,6,6′-Decachlorobiphenyl (PCB 209)	5 pg/g serum	No	No
5. ORGANOCHLORINE PESTICIDES			
Mirex	0.05 ng/g serum	No	Yes
4,4′-DDE	0.1 ng/g serum	Yes	Yes
Hexachlorobenzene	0.1 ng/g serum	No	Yes
alpha Hexachlorocyclohexane	0.1 ng/g serum	No	No
beta Hexachlorocyclohexane	0.05 ng/g serum	No	No
gamma Hexachlorocyclohexane	0.05 ng/g serum	No	No
delta Hexachlorocyclohexane	0.1 ng/g serum	No	No
4,4′-DDT	0.1 ng/g serum	No	No
2,4′-DDT	0.1 ng/g serum	No	No
Chlordane	0.05 ng/g serum	No	No
Oxychlordane	0.05 ng/g serum	No	No
***trans*-Nonachlor**	0.1 ng/g serum	No	No
Heptachlor	0.1 ng/g serum	No	No
Heptachlor Epoxide	0.1 ng/g serum	No	No
Aldrin	0.05 ng/g serum	No	No

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
Dieldrin	0.1 ng/g serum	No	No
Endrin	0.05 ng/g serum	No	No
4,4′-DDD	0.1 ng/g serum	No	No
Endosulfan	0.1 ng/g serum	No	No
Methoxychlor	0.1 ng/g serum	No	No
Octachlorostyrene	0.1 ng/g serum	No	No
Toxaphene	0.1 ng/g serum	No	No
6. POLYBROMINATED DIPHENYL ETHERS (BDEs)			
BDE 28	0.07 ng/g lipid	Yes	Yes
BDE 47	0.2 ng/g lipid	Yes	Yes
BDE 66	0.2 ng/g lipid	No	Yes
BDE 77	0.2 ng/g lipid	No	No
BDE 85	0.3 ng/g lipid	No	Yes
BDE 99	0.3 ng/g lipid	Yes	Yes
BDE 100	0.2 ng/g lipid	Yes	Yes
BDE 138	0.2 ng/g lipid	No	No
BDE 153	0.2 ng/g lipid	Yes	Yes
BDE 154	0.2 ng/g lipid	Yes	Yes
BDE 183	0.2 ng/g lipid	No	No
BDE 209	0.2 ng/g lipid	No	No

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
Perfluorohexane sulfonate (PFHxS)	0.5 ng/g serum	Yes	Yes
Perfluorooctane sulfonate (PFOS)	0.5 ng/g serum	Yes	Yes
Perfluorodecane sulfonate (PFDS)	0.5 ng/g serum	No	No
Perfluorooctanoate (PFOA)	0.5 ng/g serum	Yes	Yes
Perfluorononanoate (PFNA)	0.5 ng/g serum	Yes	Yes
Perfluorodecanoate (PFDA)	0.5 ng/g serum	No	Yes
Perfluoroundecanoate (PFUA)	0.5 ng/g serum	No	Yes
Perfluorododecanoate (PFDoA)	0.5 ng/g serum	No	Yes
Perfluorotetradecanoate (PFTA)	0.5 ng/g serum	No	Yes
8. METHYL MERCURY			
Methylmercury	0.03 ng/g serum	Yes	Yes
9. METALS AND MICRONUTRIENTS			
Aluminium	10 μg/L serum	No	Yes
Antimony	0.2 μg/L serum	No	Yes
Arsenic	0.5 μg/L serum	No	No
Barium	0.2 μg/L serum	No	Yes
Beryllium	0.2 μg/L serum	No	No
Boron	2 μg/L serum	Yes	Yes
Cadmium	0.2 μg/L serum	No	No
Chromium	0.2 μg/L serum	Yes	Yes

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
Cobalt	0.2 µg/L serum	Yes	Yes
Copper	0.2 µg/L serum	Yes	Yes
Iron	10 µg/L serum	Yes	Yes
Lead	0.2 µg/L serum	No	Yes
Zinc	5 µg/L serum	Yes	Yes
Mercury	0.2 µg/L serum	Yes	Yes
Manganese	0.2 µg/L serum	No	Yes
Molybdenum	0.2 µg/L serum	Yes	Yes
Nickel	0.2 µg/L serum	Yes	Yes
Selenium	0.5 µg/L serum	Yes	Yes
Silver	0.2 µg/L serum	Yes	Yes
Thallium	0.2 µg/L serum	No	No
Vanadium	0.2 µg/L serum	Yes	Yes
Cesium	0.2 µg/L serum	Yes	Yes
Platinum	0.2 µg/L serum	No	No
Tungsten	0.2 µg/L serum	No	No
Uranium	0.2 µg/L serum	No	No

CHEMICAL NAME	LOD/LOQ	Reported Here for Children's Blood?	Reported Previously for Maternal Blood?
10. HERBICIDES & PESTICIDES			
***cis*-DCCA**	30 pg/g serum	No	No
***trans*-DCCA**	30 pg/g serum	Yes	No
2,4-Dichlorophenoxyacetic acid	100 pg/g serum	Yes	No
2,4,5-Trichlorophenoxyacetic acid	60 pg/g serum	No	No
fluoro-3-phenoxybenzoic acid	25 pg/g serum	No	No
3-phenoxybenzoic acid	50 pg/g serum	No	No
11. PHENOLS			
Bisphenol A	10 pg/g serum	Yes	Yes
Nonylphenol	2000 pg/g serum	No	Yes
Pentachlorophenol	250 pg/g serum	Yes	No
2,4,5-Trichlorophenol	40 pg/g serum	No	No
2,4,6-Trichlorophenol	40 pg/g serum	No	No

Summary Of Analytical Methods

Select chemical analyses were done internally at the Alberta Centre for Toxicology (Calgary) including nicotine, cotinine, phytoestrogen and metals. The remaining chemicals were analyzed in a private laboratory (ALS Laboratory Group, Edmonton, AB Canada). This laboratory was selected in a competitive bid process based on evaluated fee as a fixed amount, timeline, processes and procedures, and experience as a blood analysis firm (years, number and type of projects).

Methylmercury

Isotopically labelled methylmercury was added to 2.5 mL of blood. The enriched sample was subjected to alkaline digestion followed by extraction of methylmercury into dichloromethane and back extraction into water. Methylmercury was converted to the volatile ethyl derivative, purged and trapped on a solid-phase collection medium, and then introduced into the gas chromatography – inductively coupled plasma mass spectrometry (GC-ICPMS) system. The GC-ICPMS system consisted of a Fisons Instruments (now Thermo Electron) 8000 Series gas chromatograph equipped with a 15-m capillary column (0.53 mm i.d., 1.5 μm BP-1, Supelco) and coupled to an ICP - sector field mass spectrometry instrument (Element2, Thermo Scientific, Bremen, Germany) operated in low resolution mode and with guard electrode in order to maximize sensitivity.

Polychlorinated Dioxins & Furans

Isotopically labelled dioxins and furans, and an equal amount of formic acid and HPLC grade water (1:1:1) were added to an aliquot (25 g) of serum. The mixture was vortexed, sonicated and subjected to solid-phase extraction using an EZ-Extract C_{18} (10 g / 75 mL) cartridge at 5 mL per minute. The cartridge was dried (via vacuum for 1h) and the analytes were eluted with hexane (50 mL). The extract was concentrated and cleaned up using a multi silica column. Further cleanup was performed using basic alumina and Florisil. Analyses were performed using high resolution gas chromatography/high resolution mass spectrometry (GC: Hewlett Packard 5890 Series II, HRMS: Kratos Concept 1S HRMS W/ SUN Sparc computer running Mach 3 Data system, Autosampler: LEAP Technologies CTC A200SE).

Polychlorinated Biphenyls

Isotopically labelled PCBs along with an equal amount of formic acid and HPLC grade water (1:1:1) were added to an aliquot (5 g) of serum. The mixture was vortexed, sonicated and subjected to solid phase extraction using an EZ-Extract C_{18} (10g/75 mL) cartridge at 5 mL per minute. The cartridge was dried (via vacuum for 1h) and the analytes were eluted with hexane. The extract was concentrated and cleaned up using a multi silica column, followed by basic alumina and Florisil. Analyses were performed using high resolution gas chromatography/high resolution mass spectrometry (GC: Hewlett Packard

5890 Series II, HRMS: Kratos Concept 1S HRMS W/ SUN Sparc computer running Mach 3 Data system, Autosampler: LEAP Technologies CTC A200SE).

Organochlorine Pesticides

Surrogates (tetrachloro-m-xylene and decachlorobiphenyl) were added to an aliquot (4 g) of serum. Following denaturation with 4 mL methanol, the sample was extracted with 8 mL hexane/diethyl ether (1:1) via vortex and sonication. Following removal of the solvent, the extraction was repeated twice more with hexane/diethyl ether. The resulting extracts were combined, dried over sodium sulphate and concentrated to 1 mL. Cleanup was performed using Florisil and the extract was concentrated to 75 μL. After addition of internal standard (25 μL pentachloronitrobenzene) the final extract was analyzed by gas chromatography/dual column electron capture detection (Agilent Model: 6890N, Towers/ Injectors: 7683B)

Polybrominated Diphenyl Ethers

Isotopically labelled PBDEs along with an equal amount of formic acid and HPLC grade water (1:1:1) were added to an aliquot (10 g) of serum. The mixture was vortexed, sonicated and subjected to solid-phase extraction using an EZ-Extract C18 cartridge at 5 mL per minute. The cartridge was dried (via vacuum for 1h) and the analytes were eluted with hexane. The extract was concentrated and cleaned up using a multi silica column, followed by basic alumina. Analyses were performed using high resolution gas chromatography/high resolution mass spectrometry (Mass spectrometer: Finnigan MAT 95 XP (Thermo) equipped with two GC Agilent Technologies 6890, Mass spectrometrer: DFS (Thermo), equipped with Trace GC Ultra).

Perfluorinated Compounds

Formic acid along with isotopically labelled PFOS, PFOA, PFNA and PFDA were added to 1 mL of serum. The mixture was vortexed, sonicated and subjected to solid phase extraction using an OASIS HLB cartridge. The perfluorinated compounds were then eluted with 1% ammonium hydroxide/acetonitrile. The extract was concentrated to 100 μL and recovery standard (fluoro-n-heptanoic acid) was added along with 200 μL of 90% 20 mM acetic acid/10% methanol. Analysis was performed by LC/MS/MS (API 3000 LC/MS/MS Sciex, Perkin-Elmer 200 Autosampler, Series 200 Micropump Perkin-Elmer) using multiple reaction monitoring (MRM).

Phenols

These included: 2,4,5-trichlorophenol, 2,4,6-trichlorophenol, bisphenol A, nonylphenol and octylphenol. A subset of samples were also analyzed for ortho-phenylphenol and 2,5-dichlorophenol. Isotopically labelled standards and an equal volume of formic acid and HPLC grade water (1:1:1) were added to an aliquot (5 g) of serum. The mixture was extracted using a 500 mg / 6 mL Strata x SPE cartridge. Following drying with a stream of nitrogen, the SPE cartridge was eluted with acetone and dichloromethane. The

resulting extract was concentrated, derivatized using acetic anhydride/pyridine and analyzed using high resolution gas chromatography/high resolution mass spectrometry (Micromass (Waters) Autospec M-Series with Agilent 5890 Series II GC and with CTC A200S Autosampler).

Herbicides

Isotopically labelled pesticides (2,4-D, Atrazine, Alachlor and Metolachlor) were added to an aliquot (10 g) of serum. Following the addition of trichloroacetic acid the mixture was extracted with methyl-t-butyl ether. The resulting extract was concentrated, methylated with diazomethane and analyzed using gas chromatography/selected ion-monitoring mass spectrometry (Micromass (Waters) Autospec M-Series with Agilent 5890 Series II GC and with CTC A200S Autosampler).

Pyrethroids

Isotopically labelled permethrin was added to an aliquot (10 g) of serum, and was then extracted with methyl-t-butyl ether. The resulting extract was concentrated, exchanged into toluene and analyzed using gas chromatography/mass spectrometry (Micromass (Waters) Autospec M-Series with Agilent 5890 Series II GC and with CTC A200S Autosampler).

Metals and Micronutrients

A solution of butanol, EDTA, ammonia hydroxide and Triton X-100 containing a mixture of internal standards is prepared for sample dilution. The serum sample is diluted ten times with this basic solution. The supernatatant is analyzed following three minutes of centrifugation. Due to high concentrations of some metals and micronutrients in the sample, a 100-fold dilution was also performed.

The determination of trace metals in serum was performed on an Agilent 7500c Inductively Coupled Plasma Mass Spectrometer (ICP-MS) with Octopole Reaction System (ORS). The diluted sample was directly introduced into the ICP-MS through a Babington nebulizer. The ICP-MS employed plasma as the ionization source. When ions from the sample entered the ORS, they interacted with the reaction gas (either hydrogen or helium), resulting in the reduction of the molecular interference. Then the ions were focused into a quadrupole mass analyzer, which separates the ions based on their mass/charge ratio.

Phytoestrogens

0.5 mL of serum per sample was used for the analysis of daidzein and genistein. Internal standards were added for quantification and to compensate for any loss during sample preparation. This method involved enzymatic hydrolysis using β-glucuronidase and sulphatase from Helix pomatia, followed by protein precipitation. Samples were then centrifuged and filtered before injecting on the LC/MS/MS.

10 µL of treated sample was injected onto a LC/MS/MS (Agilent 1100 HPLC/Sciex API 4000). The LC column was a Zorbax SB-C_{18} rapid resolution column (4.6 x 50 mm, 3.5 µm). The mobile phases were 5 mM ammonium formate in Type I water and 5 mM

ammonium formate in methanol. The flow rate was 800 μL/min and the run time was 10.5 minutes.

Daidzein and genistein were analyzed in MRM mode with daidzein-d3 and genistein-d4 as internal standards. Identification is based on retention time and MRM ratio. Quantification is based on area ratio and a six point calibration curve (0, 0.5, 1, 2,5, 10, 20 ng/mL). The MRM transitions monitored for daidzein, genistein, and internal standards are as follows: daidzein (253/91, 253/208), genistein (269/132.9, 269/159), daidzein-d3 (256.2/226.1), genistein-d4 (273.2/134.9).

Nicotine and Cotinine

200 μL of serum sample was used for the analysis of nicotine and cotinine. Deuterated internal standards were added for quantification and to compensate for any sample loss during preparation. The serum was diluted ten fold with a mixture of methanol: water (10:90, v:v) containing 20mM ammonium formate and 0.1% formic acid. The diluted samples were immersed in 100 C water and kept at approximately 100 C for ten minutes to facilitate precipitation of proteins from the serum. The samples were then centrifuged and filtered through a 0.45μm syringe filter followed by a 0.22μm syringe filter into the auto-sampler vials.

To avoid contamination, an initial screen of samples with an injection volume of 5 uL and a set of calibrators 0, 50, and 100 ng/mL was performed. After the initial screen, samples with concentrations greater than 100 ng/mL were re-prepared with an upfront dilution and 25 μL of the prepared sample was injected onto the Agilent 6410 Triple Quad (LC/MS/MS) with a set of calibrators. The LC column was a Zorbax SB-Phenyl 4.6 x 75 mm, 3.58 μm. The LC mobile phases were water with 20mM ammonium formate and 0.1% formic acid, and methanol with 20mM ammonium formate and 0.1% formic acid. The run was performed isocratically at 60%B with a flow rate of 0.4mL/min at 40ºC and the run time was 5 minutes.

Nicotine and cotinine were identified based on retention time and transitions from target ion to qualifier ions in MRM mode. They were quantified based on area ratios and a seven point calibration curve (0, 0.5, 2, 10, 25, 50, and 100ng/mL) for concentrations greater than 25 ng/mL, or based on a five point calibration curve (0, 0.5, 2, 10, and 25ng/mL) for concentrations less that 25 ng/mL. The MRM transitions monitored for nicotine, cotinine and the internal standards are as follows: nicotine (163.1/130.1, 163.1/117.1), nicotine-d3 (166.1/130.1), cotinine (177.1/98.1, 177.1/80.1), cotinine-d3 (180.1/101.1, 180.1/80.1).

ORGANIC CONTAMINANTS

Cotinine

GENERAL INFORMATION

Sources

Tobacco smoking can lead to disability, disease, and death. Childhood exposure to tobacco smoke is associated with increased health risks.[1,2] Strategies to reduce children's exposure to tobacco smoke have been proposed by the World Health Organization.[2] Tobacco smoke contains thousands of chemical components. Rather than attempting to determine exposure to all of these, nicotine and its metabolites are often used as markers of cigarette smoke exposure.

Nicotine is a naturally occurring component in all tobacco products. One cigarette contains approximately 6–12 mg of nicotine.[3] With each cigarette smoked, about 1 mg of nicotine is absorbed into the body of the smoker.[4] The remaining 75 percent, or more, of the nicotine from a cigarette is emitted to the air, and thus nicotine and its metabolites are also a marker of environmental tobacco smoke (ETS).[5,6]

Assessment of exposure to tobacco smoke can be done by measuring nicotine and its metabolites in different body fluids such as serum[7], saliva[8], urine[9], and cord blood.[10] One of the main human metabolites of nicotine is cotinine. The concentrations of cotinine in body fluids are proportional to the extent of exposure to tobacco smoke. Children of parents who are cigarette smokers are exposed to more tobacco smoke than children of non-smokers and demonstrate a larger concentration of cotinine in their saliva.[8] Thus, cotinine has been widely used as a biomarker for tobacco exposure, including second hand smoke[6,11], because it has a longer half-life in blood (16 hr), and has fewer analytical interferences.[12-14]

Smoking Rates and Regulations in Alberta

In Alberta, approximately one-fifth (22.8 percent) of the population smokes. Among smokers, 78 percent are daily smokers, and 22 percent are considered occasional smokers.[15] In 2004/2005, 18 percent of Alberta students in grades five to nine had ever tried smoking.[16] This rate is down from 39 percent in 1994.

In March 2002, the Alberta Government introduced the Alberta Tobacco Reduction Strategy (ATRS) to co-ordinate tobacco reduction efforts in Alberta. The ATRS aims to prevent youth from beginning to use tobacco products, thus reducing the rate of smoking to 9 percent among fifteen to seventeen year olds in Alberta by 2011/2012.[17]

On November 14, 2007, Alberta declared a new Tobacco Reduction Act and approved a province-wide smoking ban in all public places and workplaces. This took effect on January 1, 2008. Smoking from windows and near doorways of public places is also restricted to protect indoor air quality. However, there are no restrictions on smoking in private homes and cars, which is where the majority of children are exposed to tobacco smoke.[18]

Possible Health Effects

Tobacco smoke, both direct and second-hand smoke, has significant adverse effects on health. The main health risks from tobacco smoke are related to diseases of the cardiovascular system, diseases of the respiratory tract, and cancers; particularly lung, larynx,

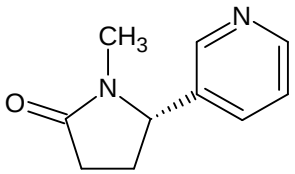
and mouth.[19,20] In addition to adverse effects of active smoking on the smoker, passive smoking has negative effects on non-smokers.[21-23] Prenatal and postnatal exposure to tobacco smoke has been associated with increased tremors in infants[24], sudden infant death syndrome[25,26], increased childhood cancer risk[26], decreased auditory response[24,27], increased respiratory disease[28,29], wheezing[30,31], middle ear disease[32], decreased pulmonary function[33] and asthma in infants and children.[26] Tobacco smoke exposure has also been associated with lower intelligence scores[34,35], behavioural problems in childhood[23,36,37], and a decrement in reading, math, and visuospatial skills.[23,38]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean cotinine concentrations in blood serum of children in Southern Alberta ranged from 0.28 to 0.59 ng/mL (Figure 1). On average, these cotinine concentrations are just below the limit of detection of 0.5 ng/mL for both age groups (0.44 ± 0.08 ng/mL in the <5 year group and 0.39 ± 0.07 ng/mL in the 6–13 year group). The concentrations are not significantly different between age groups in the children, but are approximately 30–80 times less than in pregnant women.

The concentrations of cotinine measured in pregnant women indicate that many pregnant Albertan women were smokers at the time of their blood sample collection. Non-smokers exposed to normal levels of tobacco smoke have serum cotinine levels less than 1 ng/mL. Heavy exposure to tobacco smoke results in serum cotinine concentrations in the range 1–10 ng/mL.[39] This suggests the children in this study were exposed to low to normal levels of tobacco smoke at the time of sample collection. Nonsmokers (three to eleven years) examined in the U.S. National Health and Nutrition Survey (NHANES, 2003-2004) (Fourth Report, CDC) had a geometric mean of 0.137 ng/mL serum cotinine.[40] In contrast, in a previous U.S. NHANES study (1988-1991), serum cotinine concentrations among smokers (males and females, >seventeen years old) ranged from 22 to 113 ng/mL.[41]



Cotinine

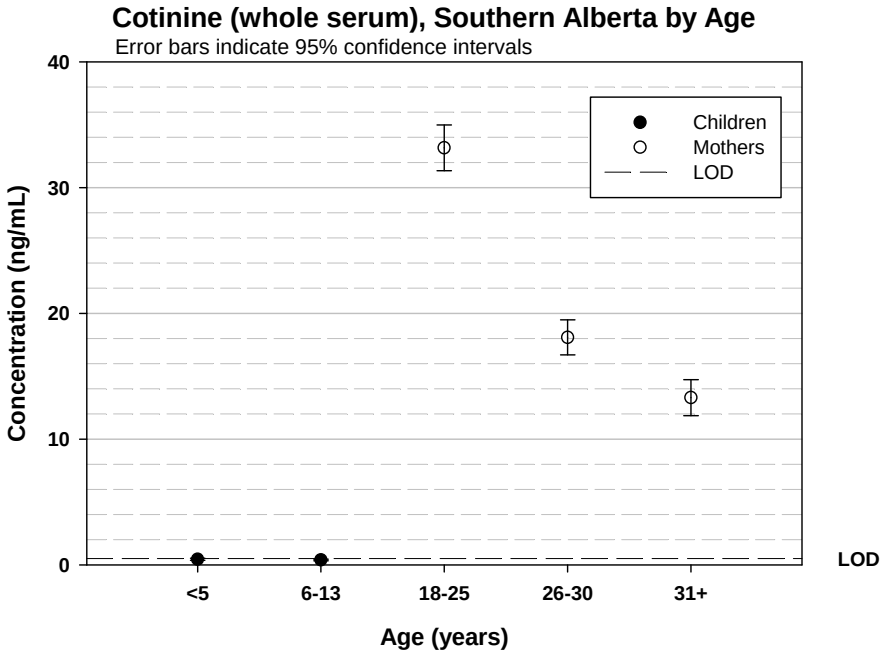


Figure 1

Phytoestrogens

GENERAL INFORMATION

Sources

Phytoestrogens are naturally occurring chemicals in plants, and have non-steroidal estrogen-like activities.[42,43] These compounds consist of three major groups: isoflavones (e.g., genistein, daidzein and glycitein), lignans and coumestans.[44,45] Dietary intake is the major source of phytoestrogens for humans, and the main sources include isoflavones in soy bean, soy bean products (e.g., tofu), and legumes; while lignans are found in flaxseed, citrus fruit, wheat, fennel, celery, and nuts.[46]

Normally the Asian and Latin American diets are relatively high in phytoestrogens because of the common use of soy products and legumes. Western diets (i.e., U.S. and Canada) generally contain a low or moderate amount of phytoestrogens due to lesser intake of soy products and legumes.[47-49] For example, 20–80 mg/day of isoflavones are present in the Japanese diet, whereas the typical Western diet contains less than 1 mg of isoflavones per day.[50] However, due to the health benefits of phytoestrogens, such as protection against various cancers, the use of soy products in foodstuffs, and the use of phytoestrogens as dietary supplements are gradually increasing in Canada.[50] Soy-based formula and human breast milk are the major sources of phytoestrogens to infants, and exposure through breast milk is related to the level of maternal dietary intake of soy products.[51,52]

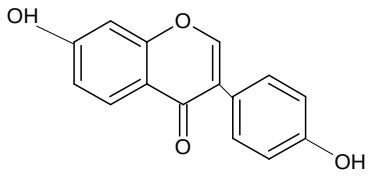
Possible Health Effects

Phytoestrogens do not accumulate in the human body. After being readily absorbed in the gut, they circulate in blood and are rapidly excreted in the urine.[53] Several studies have suggested that phytoestrogens have various health benefits, including protection against breast and colorectal cancer, cardiovascular disease, osteoporosis and menopausal symptoms.[54-56] Most of these studies have focused on the beneficial effects of phytoestrogens, but recently a few studies were conducted to investigate their potential adverse health effects. Since phytoestrogens have estrogen-like activities, it is possible that high consumption of these substances may result in effects similar to those associated with excess estrogen. However, no definitive conclusions have been reached, as some results are contradictory. For example, one report has shown that a high soy content vegetarian diet during pregnancy could be associated with an increased incidence of hypospadias[57], while other studies reported no observed hormonal effects in long-term soy-based formula fed infants.[58] Phytoestrogens have been associated with early breast development[59], delayed breast development in a study of nine year old girls[60], as well as having a preserving effect on breast tissue that develops early in infancy.[61] One long-term study reported an association between being fed soy-based formula as an infant and more painful and slightly longer duration menstrual cycles in adulthood.[62] Another report stated that after adjustment for body weight, infants fed exclusively soy-based formulas are exposed daily to as much as thirteen times the amount of isoflavones shown to affect the hormonal regulation of a woman's menstrual cycle.[63] More clinical and epidemiological studies are required in the area of phytoestrogen effects on young and older children.

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

In the present study, two isoflavones (daidzein and genistein) were measured in blood serum samples of children. Overall, the concentration range for daidzein was 0.46 to 3.02 ng/mL and 1.4 to 8.71 ng/mL for genistein. Figure 2 shows no significant difference in daidzein concentration between the children's age groups or between the children and the pregnant women aged 18–25 and 26–30. The daidzein concentration in the pregnant women aged 31 and up is significantly higher than that measured in the children and the younger pregnant women. Values are more highly variable in the children as compared to the pregnant women, possibly because of the smaller number of children's samples. Genistein is only reported here for children because poor method performance precluded reporting of the pregnant women's data. From Figure 2 it can be seen there is no significant difference in genistein concentrations between the children's age groups and the measured concentrations are quite variable for both groups. The estimated 50th centile among individuals was 0.18 ng/mL for daidzein and 0.50 ng/mL for genistein. In a study of 268 children (aged eight to fifteen) in the Czech Republic, the median daidzein concentration in serum was 0.11 ng/mL and the median genistein concentration was 0.10 ng/mL.[64]



Daidzein

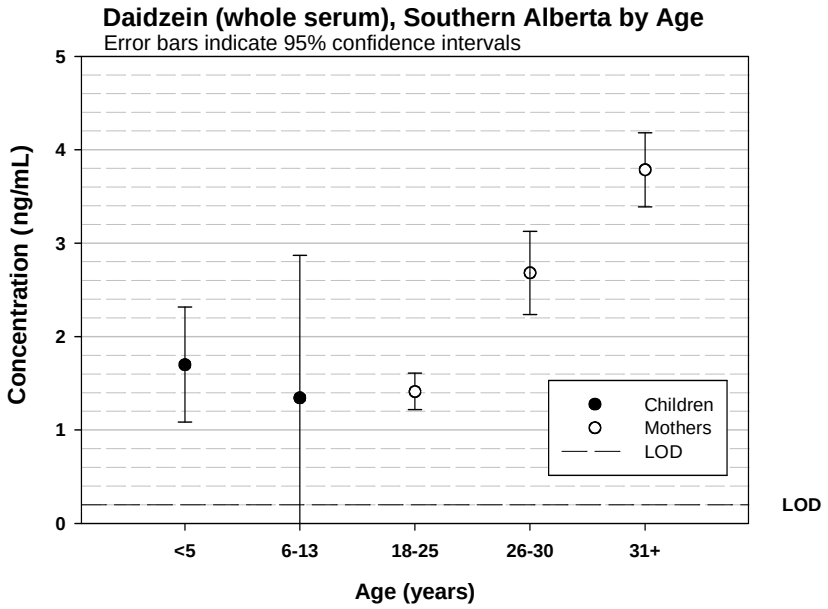
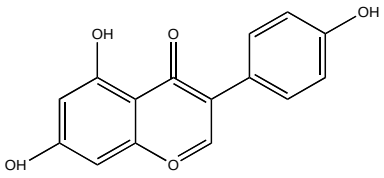


Figure 2



Genistein

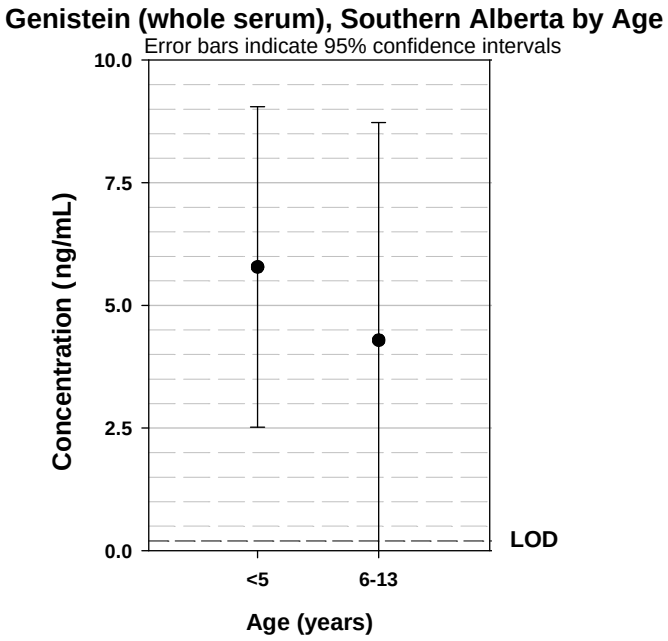


Figure 3

Polychlorinated Biphenyls

GENERAL INFORMATION

Sources

Polychlorinated biphenyls (PCBs) do not occur naturally and were historically produced commercially in large quantities as mixtures of 209 possible chlorinated congeners. They were used for many decades in a wide variety of industrial and commercial materials such as coolants and lubricants in transformers, capacitors and other electrical equipment, in sealing and caulking compounds, cutting oils, inks and paint additives.[65,66] PCBs were released to the environment (air, water and soil) during their manufacture, use, and disposal. Although PCB manufacturing no longer occurs, PCBs can still be detected in the environment because they are resistant to degradation and can persist in the environment for long periods of time. PCBs can also travel long distances in air and water, and so are detectable all over the world, including in remote regions far from their points of use.

People may be exposed to PCBs in old homes or buildings constructed with PCB-laden materials, or where old electrical devices and PCB containing transformers may be found. However, the most important source of PCB exposure in the general population is through the diet. The main dietary sources of PCBs include animal fats from fish, meat and dairy products.[67] This is because PCBs are present at low concentrations in the oceans, freshwater, and most pasture and agricultural soils around the world. Due to their lipophilic nature, PCBs can accumulate in fatty tissues of animals, and also in human breast milk.[68] In fact, human milk is a major source of PCBs to infants[68,69] and although there are reports of subtle effects as the infants age[70-72], the benefits of breastfeeding[73] are still considered to outweigh known risks.

Regulations in Canada

Since 1977, the Canadian Government has adopted several regulations to minimize exposure and environmental releases of PCBs.[74] PCBs were never manufactured in Canada, but they were widely used here. In 1977, the production, processing, import and sale of PCBs, and equipment containing a liquid with a PCB concentration greater than 50 mg/kg, were restricted in Canada. The storage, export and import of equipment and other products containing a PCB concentration of 50 mg/kg or more were also controlled by several other regulations as they were adopted in 1988, 1996, 2005, and 2008.[74,75] In November 2006, the Canadian Federal Government set a specific deadline of December 2009 for ending the use and storage of equipment and other materials containing PCBs in concentrations at or above 50 mg/kg.[75] The continued use of certain equipment containing PCBs is still allowed in Canada, but according to the Stockholm Convention on Persistent Organic Pollutants (POPs), Canada is required to phase out the remaining uses of PCBs by 2025, and to dispose of these PCBs properly by 2028.[75]

Possible Health Effects

The human health effects of PCBs depend on the dose, the length and timing of exposure, and other factors. It has long been recognized that background human populations are exposed to very low concentrations of PCBs in foods and the environment. At these low levels, PCBs are not known to cause any adverse health effect. At high doses, such as in the case of accidental releases, unusual occupational exposures, or accidental consumption of highly contaminated food, PCBs may cause adverse health effects such as chloracne (a severe form of acne) and skin rashes, fatigue, headache, cough, unusual skin sores and problems related to nervous systems.[67,76-79] The health effects of PCBs in children of pregnant women who were exposed to relatively high levels of PCBs through fish[80-82], were examined in a number of studies. These studies concluded the fetus/infants of pregnant women eating large amounts of PCB-contaminated fish were at higher risk of some health effects. These effects may include low birth-weight, immune system abnormalities, depressed motor skills, and a decrease in short-term memory.[77,80-82]

Pre and postnatal PCB exposure has been associated with developmental enamel defects (for children in PCB contaminated regions[83] or from exposure to PCBs through a diet rich in seafood and whale blubber[84]), lower respiratory tract infections in Inuit children[85], and recurrent middle ear disease.[86] PCB exposure has had mixed results for being associated with altered thyroid hormone status.[87,88] A Dutch study of mothers living in a highly industrialized city showed an association between prenatal exposure to PCBs and poorer cognitive functioning in children[89], as did a study of the general population in North Carolina.[90] However, other studies have shown no evidence for an association between PCB exposure and poorer cognitive functioning.[91,92] These inconsistencies may be a result of variations in PCB exposure intensity.[93]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

The following polychlorinated biphenyls (PCBs) were measured in the blood serum samples of children in Alberta:

1. 2,4,4′-Trichlorobiphenyl (PCB 28)
2. 2,2,5,5-Tetrachlorobiphenyl (PCB 43/52)
3. 2,3′,4,4′-Tetrachlorobiphenyl (PCB 66)
4. 2,4,4′,5-Tetrachlorobiphenyl (PCB 74)
5. 3,3′,4,4′-Tetrachlorobiphenyl (PCB 77)
6. 3,4,4′,5-Tetrachlorobiphenyl (PCB 81)
7. 2,2′,3,4,5′-Pentachlorobiphenyl (PCB 87)
8. 2,2′,4,4′,5-Pentachlorobiphenyl (PCB 99)
9. 2,2′,4,5,5′-Pentachlorobiphenyl (PCB 101)
10. 2,3,3′,4,4′-Pentachlorobiphenyl (PCB 105)
11. 2,3,3′,4′,6-Pentachlorobiphenyl (PCB 110)
12. 2,3′,4,4′,5-Pentachlorobiphenyl (PCB 118)
13. 3,3′,4,4′,5-Pentachlorobiphenyl (PCB 126)
14. 2,2′,3,3′,4,4′-Hexachlorobiphenyl (PCB 128)

15. 2,2′,3,4,4′,5-Hexachlorobiphenyl (PCB 138)
16. 2,2′,3,4′,5,5′-Hexachlorobiphenyl (PCB 146)
17. 2,2′,3,4′,5′,6-Hexachlorobiphenyl (PCB 149)
18. 2,2′,3,5,5′,6-Hexachlorobiphenyl (PCB 151)
19. 2,2′,4,4′,5,5′-Hexachlorobiphenyl (PCB 153)
20. 2,3,3′,4,4′,5-Hexachlorobiphenyl (PCB 156)
21. 2,3,3′,4,4′,5′-Hexachlorobiphenyl (PCB 157)
22. 2,3,3′,4,4′,6-Hexachlorobiphenyl (PCB 158)
23. 2,3′,4,4′,5,5′-Hexachlorobiphenyl (PCB 167)
24. 3,3′,4,4′,5,5′-Hexachlorobiphenyl (PCB 169)
25. 2,2′,3,3′,4,4′,5-Heptachlorobiphenyl (PCB 170)
26. 2,2′,3,3′,4,5,5′-Heptachlorobiphenyl (PCB 172)
27. 2,2′,3,3′,4,5′,6′-Heptachlorobiphenyl (PCB 177)
28. 2,2′,3,3′,5,5′,6-Heptachlorobiphenyl (PCB 178)
29. 2,2′,3,4,4′,5,5′-Heptachlorobiphenyl (PCB 180)
30. 2,2′,3,4,4′,5′,6-Heptachlorobiphenyl (PCB 183)
31. 2,2′,3,4′,5,5′,6-Heptachlorobiphenyl (PCB 187)
32. 2,3,3′,4,4′,5,5′-Heptachlorobiphenyl (PCB 189)
33. 2,2′,3,3′,4,4′,5,5′-Octachlorobiphenyl (PCB 194)
34. 2,2′,3,3′,4,4′,5,6-Octachlorobiphenyl (PCB 195)
35. 2,2′,3,3′,4,4′,5,6′-Octachlorobiphenyl (PCB 196)
36. 2,2′,3,3′,4,5,5′,6′-Octachlorobiphenyl (PCB 199)
37. 2,2′,3,4,4′,5,5′,6-Octachlorobiphenyl (PCB 203)
38. 2,2′,3,3′,4,4′,5,5′,6-Nonachlorobiphenyl (PCB 206)
39. 2,2′,3,3′,4,4′,5,5′,6,6′-Decachlorobiphenyl (PCB 209)

However, only the following congeners were detected, and concentration ranges among pools are shown based on wet weight and lipid weight:

PCBs	**Whole weight (pg/g serum)**	**Lipid weight (ng/g lipid)**
2,2′,3,4,4′,5-Hexachlorobiphenyl (PCB 138)	16 to 25	3.8 to 7.9
2,2′,4,4′,5,5′-Hexachlorobiphenyl (PCB 153)/(PCB 168)	25 to 42	5.6 to 13
2,2′,3,3′,4,4′,5-Heptachlorobiphenyl (PCB 170)	2.5 to 6.9	0.56 to 2.2
2,2′,3,4,4′,5,5′-Heptachlorobiphenyl (PCB 180)	12 to 21	2.7 to 6.6
2,2′,3,4′,5,5′,6-Heptachlorobiphenyl (PCB 187)	2.5 to 6.6	0.56 to 2.1

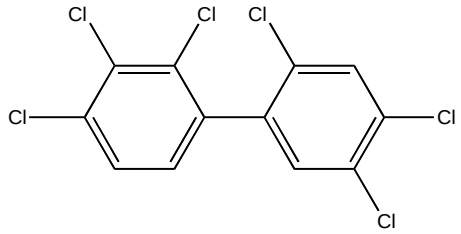
It should be noted that the PCB profiles of children, and previously of pregnant women, are not always consistent with other published literature and a comparison of children and pregnant women was not possible for many of the congeners in this study.

This is due to our use of stored serum samples previously obtained from various sources, and the resulting contamination that may have occurred during original sample processing, storage, or sample aliquotting and pooling. Due to our extensive quality control program, many congeners that are easily detectable in other studies could not always be reported in this work, though as many comparisons as possible were made.

Figures 4 through 13 show the concentrations of each of the detected PCBs in children's whole serum (and lipid adjusted) as well as in the pregnant women (where applicable). For PCB 138 (lipid adjusted, Figure 4) there is no significant difference in concentration between the children's age groups. The difference between age groups is not statistically significant for PCB 153/168 (lipid adjusted, Figure 6). Problems with the pooling blanks precluded reporting of PCB 138 and 153/168 in the pregnant women.

For PCB 170 (lipid adjusted, Figure 8), PCB 180 (Figure 10, lipid adjusted), and PCB 187 (Figure 12, lipid adjusted) the concentrations are not significantly different between children's age groups, but the data in the 6–13 year group was always more variable than that of the <5 year group. The concentrations in the children are not significantly different than those of the pregnant women in the 18–25 and 26–30 year age groups, but are lower than the concentrations in the 31+ age group. Overall the pregnant women's data shows an increase in concentration of PCBs with age. PCBs are highly bioaccumulative, which likely explains the increasing trend with age observed in Figures 4–13.

In a study of mothers and seven year old children in the Faroe Islands, PCB 138, 153, 170, 180 and 187 were measured in serum. In children the median concentrations measured were 250 (PCB 138), 310 (PCB 153), 58 (PCB 170), 140 (PCB 180) and 77 ng/g lipid (PCB 187). Concentrations of all these congeners were higher in the mothers.[94] In a study of twelve year old Slovakian children from Bratislava, which is an urban center with low levels of environmental PCB contamination, total serum concentrations of 15 PCB congeners were measured to be 147.2 ng/g lipid in boys and 117.9 ng/g lipid in girls (median values).[95] A study of eight to nine year old Russian boys measured co-planar PCBs in serum to be 181 pg/g lipid and mono-ortho PCBs to be 52 pg/g lipid (median values).[96] All of the values from the other reports above are higher than those in the present study.



PCB 138

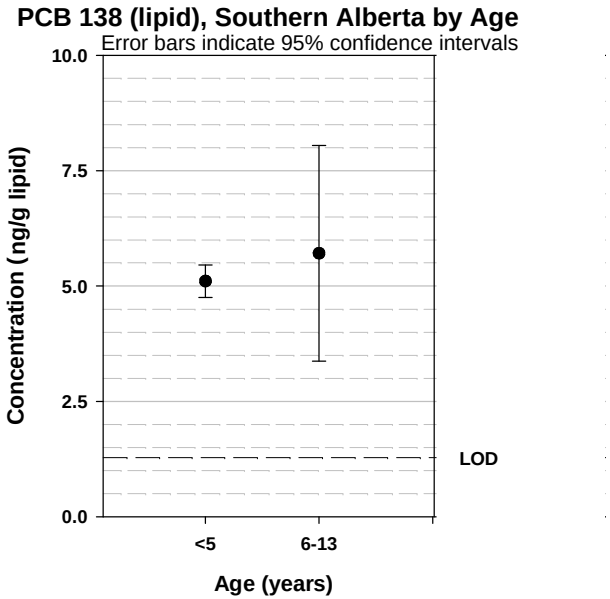


Figure 4

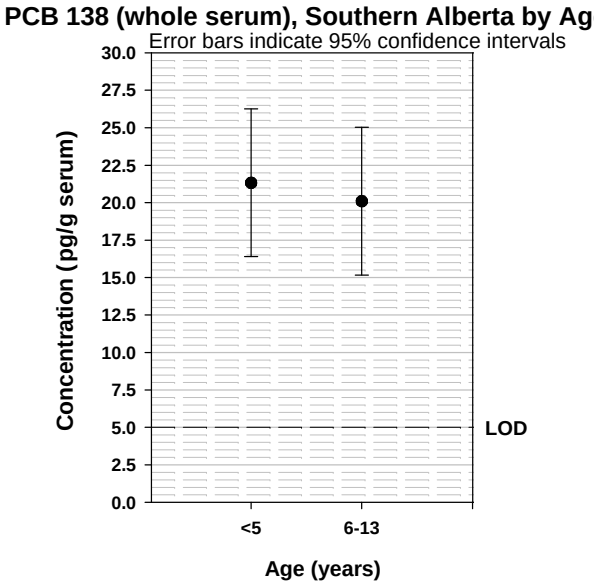
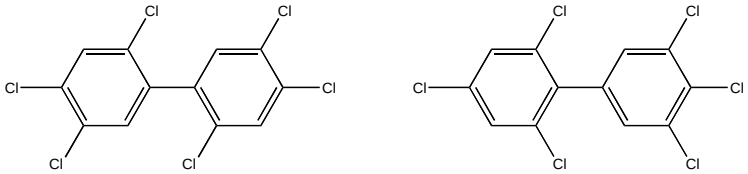


Figure 5



PCB 153 / PCB 168

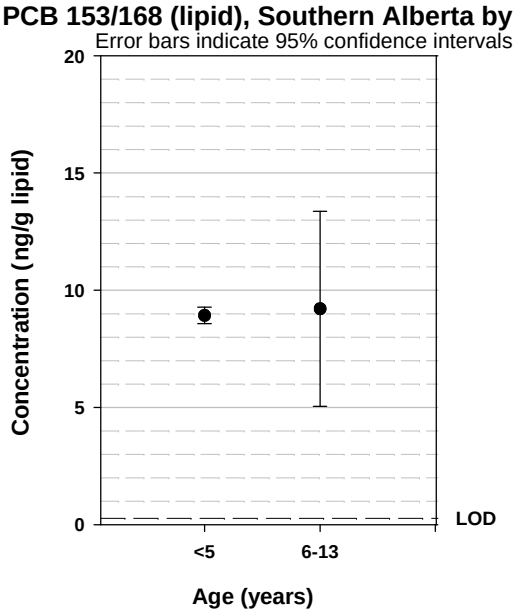


Figure 6

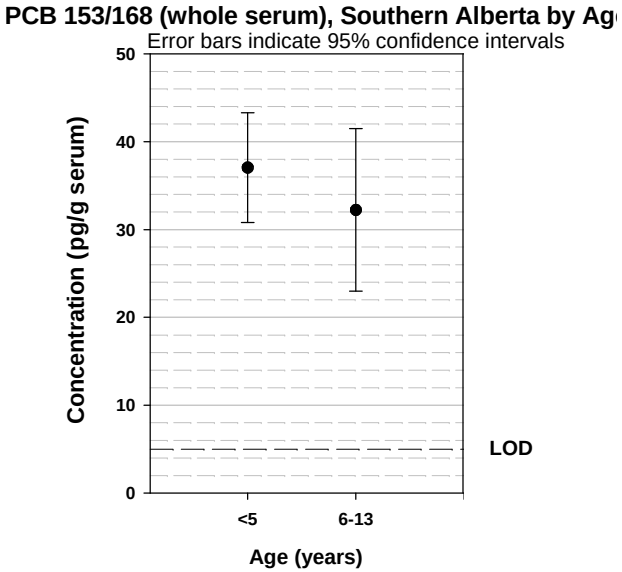
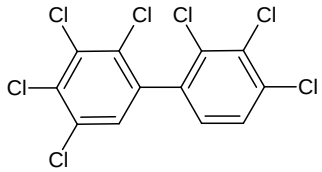


Figure 7



PCB 170

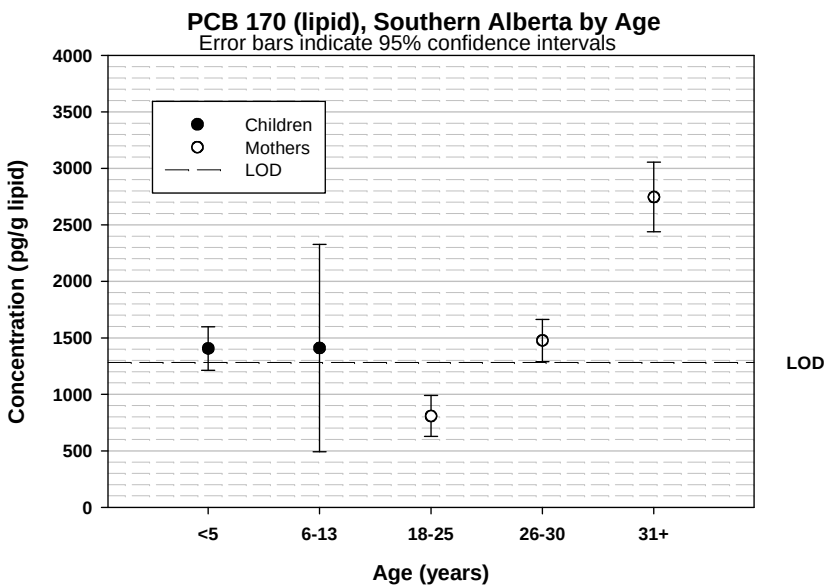


Figure 8

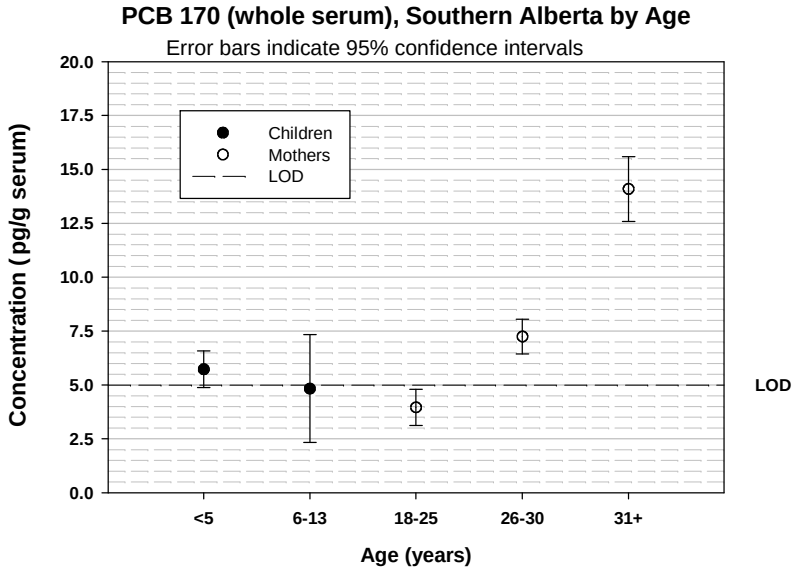
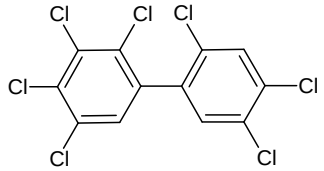


Figure 9



PCB 180

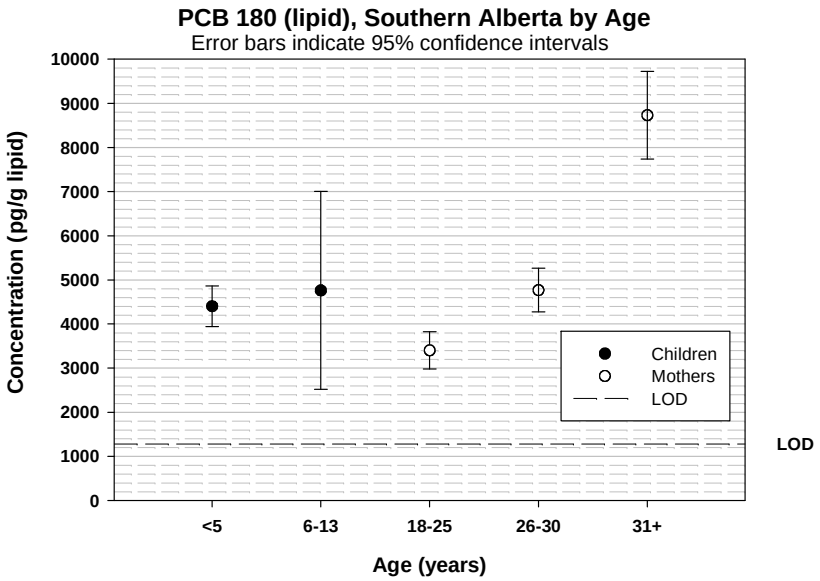


Figure 10

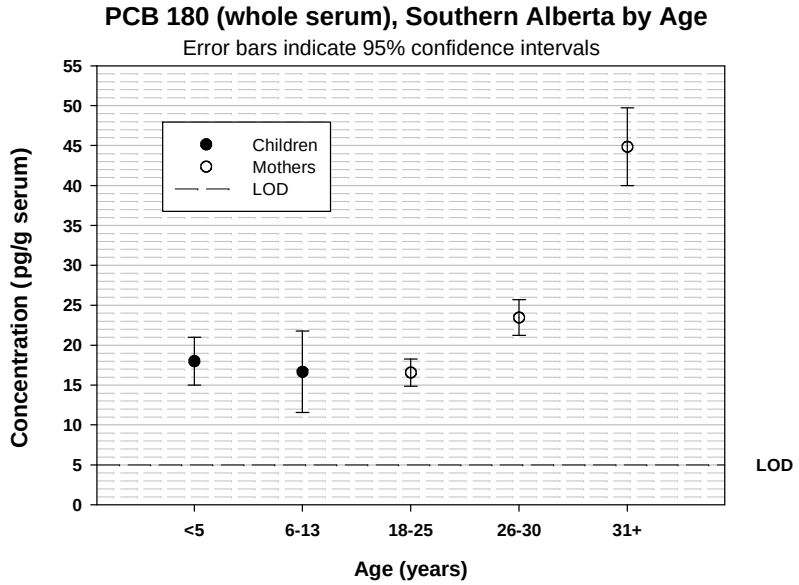
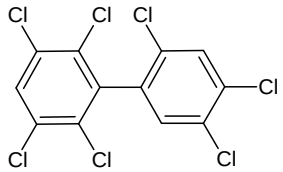


Figure 11



PCB 187

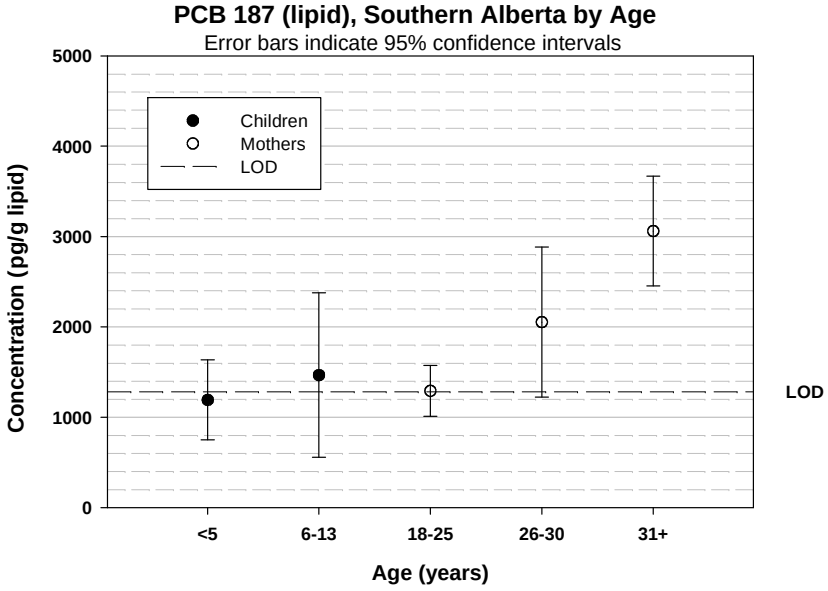


Figure 12

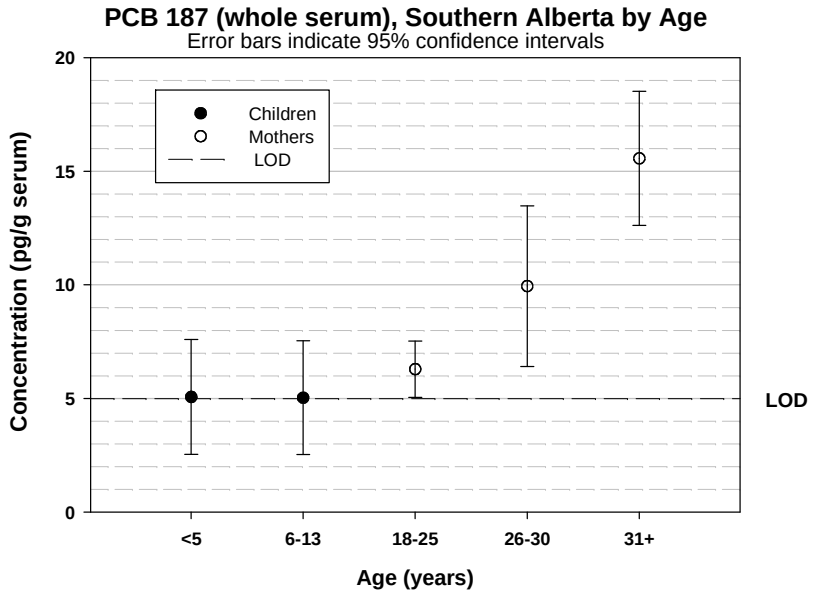


Figure 13

Perfluorochemicals

GENERAL INFORMATION

Sources

Perfluorochemicals (PFCs) are a group of man-made fluorinated organic compounds that have been widely used for decades in industrial processes and various consumer and commercial products. These highly fluorinated molecules are unique in their ability to resist high temperatures and to repel oil, grease and water. A major use of PFCs has been as active ingredients in stain repellent polymer formulations for paper, textiles, food packaging, carpets, and leather, while other uses include their application as surfactants, fire-fighting foams, and fluoropolymer processing aids.[97,98]

PFCs do not occur naturally, and can be released into our homes and into the environment (air and water) from these various consumer products, industrial or manufacturing processes, and accidental spills.[99] The general population is exposed to some extent to PFC in our homes and in the workplace via dust.[100] Another potential route of exposure is through the diet, mainly from fish and food products of animal origin, which are exposed to PFC-containing air, water and feed.[101-103] The use of PFCs in grease and water repellent coatings for food packaging is also known to be a source of exposure.[104,105] In the environment PFCs can travel long-distances such that they are detectable all over the world, including in remote regions far from their sources of production or use.

Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are the two most abundant PFCs in humans and in the environment, but many related PFCs are also known to co-occur. These are highly stable in the environment and in our bodies. The half-lives in humans are 5.4 years for PFOS and 3.8 years for PFOA.[106] PFCs are widely found in wildlife, adult and children's blood[107-111], and PFCs are known to cross the placental barrier.[112,113]

Regulations in Canada

PFCs used in Canada are imported from other countries and are not manufactured in Canada.[114] In 2002, the predominant global manufacturer, and the only manufacturer of PFOS in the U.S., voluntarily phased out the production of PFOS and other related chemicals. As a result its uses decreased significantly in Canada after 2002.[114] In December 2006, the Canadian Government proposed a regulation to prohibit the manufacture, use, sale, offer for sale, and import of PFOS and its salts with certain minor exemptions including for use in semiconductors, photographic films, or for use in laboratories for scientific research.[114] In April 2008, the *Perfluorooctone Sulfonate Virtual Elimination Act* became law and PFOS was added to the *Virtual Elimination List* under Schedule 1 of the Canadian Environmental Protection Act (CEPA).[115] The Canadian Government has also taken actions on fluorotelomers, which are PFCs that can degrade to PFOA in the atmosphere and in organisms. In June 2006, the Canadian Federal Government proposed a regulation to prohibit the introduction of four new fluorotelomer-based substances into Canada, and also recommended the addition of these substances to the List of Toxic Substances under Schedule 1 of CEPA.[116]

Possible Health Effects

Human studies relating to possible health effects of PFC exposure are limited. A few studies suggested negative associations between PFOS or PFOA concentrations in pregnant women or cord blood and the infant's birth weight or size.[117,118] There are comparably more data from animal studies at higher concentration. Adverse health effects in animals include developmental and reproductive effects, general systemic toxicity, effects on the liver and the thyroid hormone system.[119-122]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

The following PFCs were measured in the blood serum samples of children in Alberta:

Perfluoroalkyl sulfonates

1. Perfluorohexane sulfonate (PFHxS)
2. Perfluorooctane sulfonate (PFOS)
3. Perfluorodecane sulfonate (PFDS)

Perfluoroalkyl carboxylates

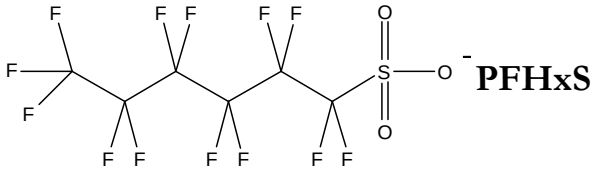
1. Perfluorooctanoate (PFOA)
2. Perfluorononanoate (PFNA)
3. Perfluorodecanoate (PFDA)
4. Perfluoroundecanoate (PFUA)
5. Perfluorododecanoate (PFDoA)
6. Perfluorotetradecanoate (PFTA)

The detection limits in this study are higher than in the previous study for maternal blood, thus only PFHxS, PFOS, PFOA and PFNA were detected here. Ranges of mean concentrations are shown based on wet weight in blood serum samples:

PFCs	Wet weight (ng/mL serum)
PFHxS	5.3 to 16
PFOS	7.0 to 13
PFOA	3.8 to 5.2
PFNA	0.90 to 1.1

PFHxS concentrations (Figure 14) did not differ significantly between the <5 and 6–13 year age groups. However, concentrations in children were higher than in all age ranges of pregnant women. Likewise, PFOS concentrations (Figure 15) were not significantly different between the <5 and the 6–13 year age groups but concentrations in the children's groups were significantly higher than those in the pregnant women. PFOA (Figure 16) shows a similar trend in which concentrations in the children are not significantly different between age groups, but concentrations in both groups of children are higher than in pregnant women. For PFNA (Figure 17) concentrations in the <5 year age group are slightly lower than the concentrations in the 6–13 year group, and concentrations in the children's groups are approximately double the concentrations in all age ranges of pregnant women.

In the pooled serum samples from the children who participated in the U.S. National Health and Nutrition Survey (NHANES, 2001–2002), the mean concentrations of PFHxS in the serum of non-Hispanic white females and males aged three to five were 18.7 and 13.1 ng/mL, respectively. PFHxS in non-Hispanic white females and males aged six to eleven were 12 and 13.15 ng/mL in serum, respectively. However, for PFHxS data in previous reports it is possible that concentrations are overestimated due to endogenous steroid sulfate interferences.[123] PFOS concentrations in non-Hispanic white females and males aged three to five were 41.9 and 39.1 ng/mL in serum, respectively, and 44.35 and 40.55 ng/mL in female and male children aged six to eleven, respectively. PFOA concentrations in non-Hispanic white females and males aged three to five were 7.4 and 7.75 ng/mL, and 7.55 and 7.6 ng/mL in female and male children aged six to eleven years, respectively. PFNA concentrations in non-Hispanic white females and males aged three to five were 1.05 and 0.75 ng/mL, and 0.95 and 0.85 ng/mL in female and male children aged six to eleven years, respectively.[124] These results for American children show higher exposure than in the present study, but the current study used samples collected at a later time (2005) and it is likely that human exposure in North America has declined since 2001 due to manufacturing phase-outs in the US, as has been shown for infants in New York State.[125]



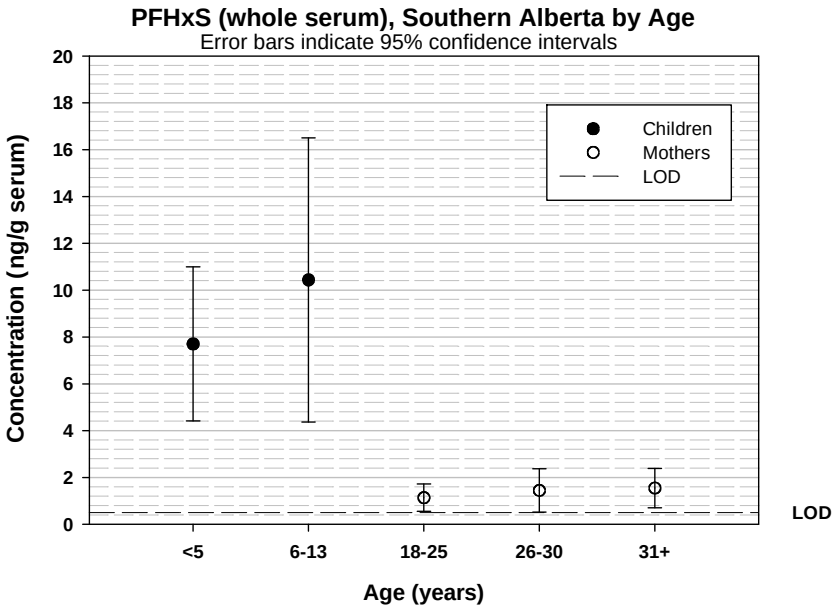
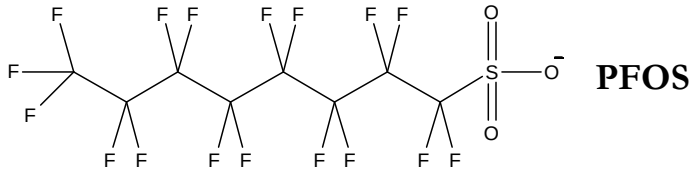


Figure 14



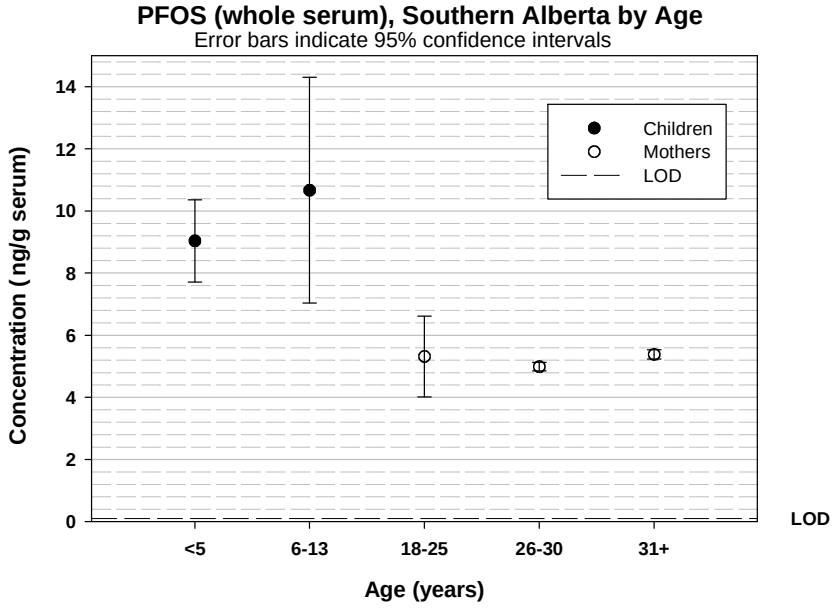
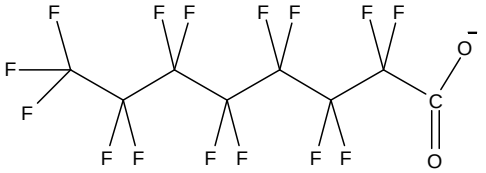


Figure 15



PFOA

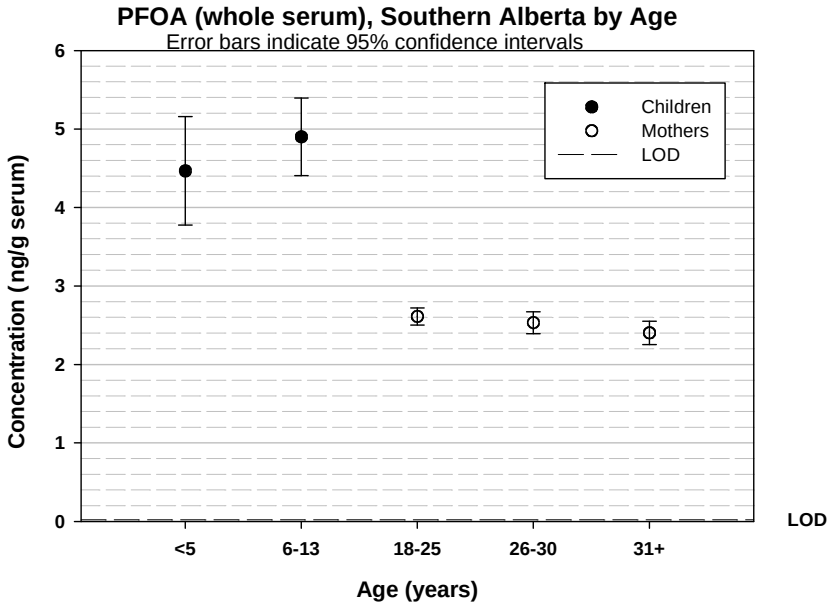
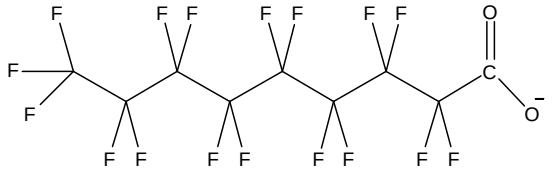


Figure 16



PFNA

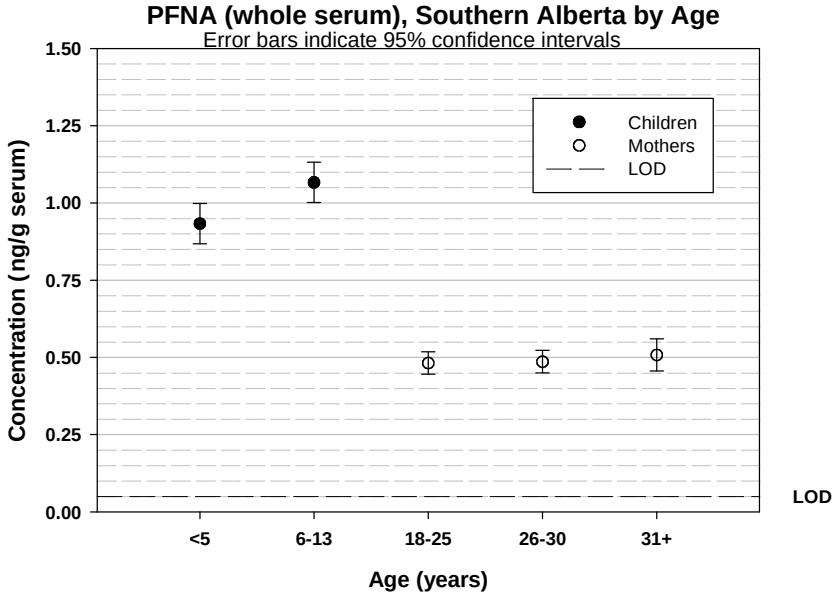


Figure 17

Dioxins and Furans

GENERAL INFORMATION

Sources

Polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), more commonly known as dioxins and furans, are relatively toxic and persistent environmental contaminants. Depending on the pattern of chlorine atoms on these molecules, dioxin and furan molecules can vary widely in their toxic potency.[126,127] They are not directly produced for any purpose, but are by-products of several industrial processes (e.g., incineration, pulp bleaching, pesticide production), burning of municipal and medical waste, backyard burning of household waste, wood burning and electrical power generation. Dioxins and furans can also be produced naturally such as during forest fires and volcanic eruptions. After their release to the environment they can travel long distances including to remote regions far from their sources.

The predominant source of dioxin and furan exposure in the general human population is through the diet. Due to their lipophilic (literally 'fat-loving') nature, they accumulate in fatty tissues of fish and animals after being deposited to soil or water. Dietary intake through food products of animal origin is estimated to account for 90 percent of total human exposure.[128-130] Children are exposed to more dioxins from food than adults based on body weight.[131] However, children also eliminate dioxins at a faster rate than adults.[132] In general, however, these compounds accumulate in our bodies and take a long time to be excreted. Some of the maternal body burden can be transferred to the fetus or infant during pregnancy or lactation, respectively.[133,134]

Regulations in Canada

Dioxins and furans are designated to be virtually eliminated in Canada.[135] Since July 1st, 1992, the releases of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and 2,3,7,8-tetrachlorodibenzofuran (TCDF), which are the most toxic forms of dioxin and furan, have been prohibited in pulp and paper mill effluent in Canada.[135] By 1995, the emissions from this source reached non-detectable concentrations.[135] Canada signed the United Nations Economic Commission for Europe's (UNECE) protocol (Dec 1998) and the Stockholm convention on persistent organic pollutants (POPs) (May 2001), respectively, to protect human health and the environment from chemicals such as dioxins and furans.[135]

Possible Health Effects

Dioxins and furans can cause several adverse health effects in humans. These depend on the dose, the length of exposure, and the timing of exposure. Due to their ubiquity in the environment and our food, all people have a certain concentration of dioxins and furans in their body. Such background concentrations of dioxins and furans usually do not affect human health. At higher doses, such as which may occur through occupational exposures (e.g., past workers in the pulp and paper industry, in incineration plants, and at hazardous waste sites) or by accidental consumption of highly contaminated food, dioxins and furans may cause skin disorders (e.g., chloracne), liver problems, impairment of the immune system and the endocrine system, including diabetes, reproductive dysfunctions, and there have

been contradictory results about whether they are associated with certain types of cancers in cohorts that experienced high level, long-term industrial exposure or with extreme exposure from major accidental releases.[136-142] Pre- and postnatal exposure to environmental levels of dioxins may be associated with negative effects on the thyroid hormone system in infants[143], while perinatal exposure to background environmental levels has been associated with decreased lung function[144] as well as immunologic disturbances in children.[145]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

The following polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) were measured in the blood serum samples of children in Alberta:

1. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)
2. 1,2,3,7,8-pentachlorodibenzo-p-dioxin (PCDD)
3. 1,2,3,4,7,8-hexachlorodibenzo-p-dioxin (HxCDD)
4. 1,2.3,6,7,8-hexachlorodibenzo-p-dioxin (HxCDD)
5. 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (HxCDD)
6. 1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin (HpCDD)
7. 1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin (OCDD)
8. 2,3,7,8-tetrachlorodibenzofuran (TCDF)
9. 1,2,3,7,8-pentachlorodibenzofuran (PCDF)
10. 2,3,4,7,8-pentachlorodibenzofuran (PCDF)
11. 1,2,3,4,7,8-hexachlorodibenzofuran (HxCDF)
12. 1,2,3,6,7,8-hexachlorodibenzofuran (HxCDF)
13. 1,2,3,7,8,9-hexachlorodibenzofuran (HxCDF)
14. 2,3,4,6,7,8-hexachlorodibenzofuran (HxCDF)
15. 1,2,3,4,6,7,8-heptachlorodibenzofuran (HpCDF)
16. 1,2,3,4,7,8,9-heptachlorodibenzofuran (HpCDF)
17. 1,2,3,4,6,7,8,9-octachlorodibenzofuran (OCDF)

However, only the following congeners were detected, and concentration ranges among pools are shown based on wet weight and lipid weight:

PCDDs and PCDFs	Wet weight (pg/g serum)	Lipid weight (pg/g lipid)
1,2,3,6,7,8-hexachlorodibenzo-p-dioxin (HxCDD)	0.080 to 0.18	19 to 57
1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin (HpCDD)	0.10 to 0.16	23 to 50
1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin (OCDD)	0.73 to 0.95	170 to 280
1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (HxCDD)	0.005 to 0.05	1.1 to 16
1,2,3,7,8-pentachlorodibenzofuran (PCDF)	0.005 to 0.09	1.1 to 28
2,3,4,7,8-pentachlorodibenzofuran (PCDF)	0.005 to 0.1	1.1 to 31
1,2,3,4,7,8-hexachlorodibenzofuran (HxCDF)	0.020 to 0.060	4.3 to 19
1,2,3,6,7,8-hexachlorodibenzofuran (HxCDF)	0.02 to 0.04	4.3 to 13
1,2,3,4,6,7,8-heptachlorodibenzofuran (HpCDF)	0.070 to 0.11	18 to 35

Figures 18 through 35 show the concentrations of the measured dioxins and furans versus age of the children and pregnant women.

For 1,2,3,6,7,8-HxCDD (both lipid adjusted and whole serum, Figures 18 and 19) the concentrations in the children's age groups are not significantly different from each other. However, for the lipid adjusted data (Figure 18) the concentrations in the <5 year age group are significantly higher than the concentrations in any of the pregnant women. For the whole serum data (Figure 19) the concentration of 1,2,3,6,7,8-HxCDD in the <5 year group is significantly higher than the concentrations in the 18–25 and 26–30 year old pregnant women, but not significantly different from the concentration in the 31+ pregnant women. The concentrations in the 6–13 year group are not significantly different from the pregnant women in either the serum or lipid adjusted data.

For 1,2,3,4,6,7,8-HpCDD (both lipid adjusted and whole serum, Figures 20 and 21) the concentrations in the <5 year age group and 6–13 year age group are not significantly different. For the lipid adjusted data (Figure 20) the concentrations in the 6–13 year group are significantly higher than the concentrations in the 26–30 year old pregnant women, but not significantly different from the 18–15 or 31+ year old pregnant women. The concentrations in the <5 year group are not significantly different from those in the pregnant women. For the whole serum data (Figure 21) the concentrations in both children's groups are not significantly different from those in any of the pregnant women.

For OCDD (only for lipid adjusted, Figure 22) the concentrations in the <5 year and 6–13 year age groups are not significantly different from each other. The concentrations in the <5 year group are not significantly different from the concentrations in the pregnant women, but the concentration in the in the 6–13 year group is higher than the concentration in the 18–25 and the 26–30 year old pregnant women. For the whole serum OCDD data (Figure 23), the concentrations in the children's groups are not significantly different from each other. The concentrations in the <5 year age group are not statistically different from the concentrations in the pregnant women. However, the concentration in the 6–13 year group is higher than in the 18–25 year old pregnant women. Overall, the OCDD

concentrations are much higher than those for any other congener, consistent with other studies.

For 1,2,3,7,8,9-HxCDD (both lipid adjusted and whole serum, Figure 24 and 25) concentrations are not significantly different between the <5 and 6–13 year age groups and concentrations in the children are not significantly different from those in the pregnant women.

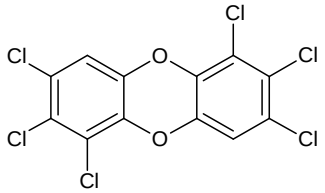
1,2,3,7,8-PCDF (both lipid adjusted and whole serum, Figure 26 and 27) was only detected in one sample in the 6–13 year group and the other samples were below the detection limit. All samples in the <5 year age group were below the detection limit. The maternal data is shown for comparison, but no statistical tests were conducted.

For 2,3,4,7,8-PCDF (both lipid adjusted and whole serum, Figure 28 and 29) concentrations in the children's age groups are not significantly different from each other or from the concentrations in the pregnant women.

For 1,2,3,4,7,8-HxCDF (both lipid adjusted and whole serum, Figure 30 and 31) concentrations in the <5 year and 6–13 year groups are not significantly different. In the lipid adjusted data (Figure 31) the concentration in the <5 year age group is higher than that in all of the pregnant women. However, in the whole serum data (Figure 31) the <5 year concentrations are higher than the pregnant women in the 18–25 and 26–30 year age groups, but not statistically different from the concentrations in the 31+ year group.

1,2,3,6,7,8-HxCDF (both lipid adjusted and whole serum, Figure 32 and 33) concentrations are not statistically different between the <5 year and 6–13 year age groups. In the lipid adjusted data (Figure 32) the concentrations in the <5 year group are higher than those in the 26–30 and 31+ year old pregnant women, but are not significantly different from the 18–25 year old pregnant women. The whole serum (Figure 33) <5 year concentrations are higher than the concentrations in the 26-30 year old pregnant women, but not significantly different from the 18–25 and 31+ year old pregnant women.

Concentrations of 1,2,3,4,6,7,8-HpCDF (both lipid adjusted and whole serum, Figure 34 and 35) are essentially the same in the <5 year and 6–13 year age groups. Concentrations in the children's age groups are higher than the concentrations in all of the pregnant women.



1,2,3,6,7,8 HxCDD

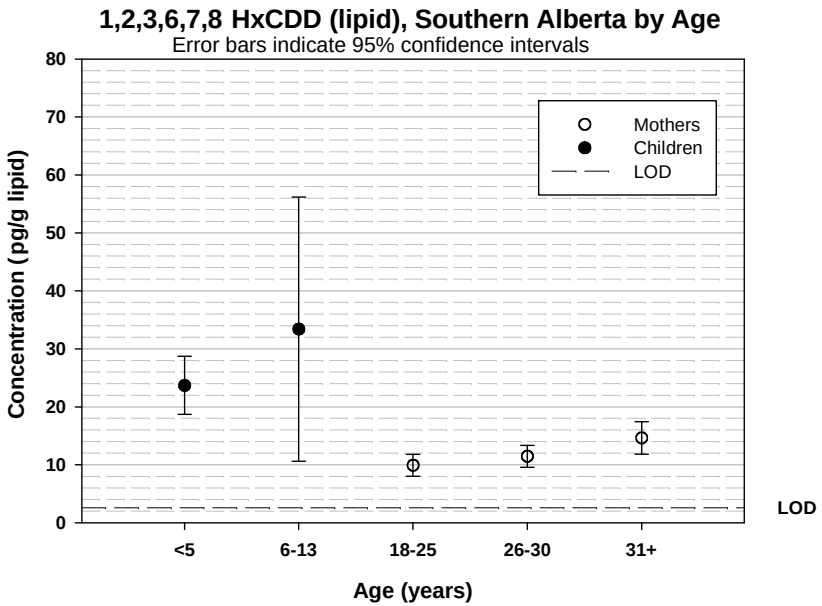


Figure 18

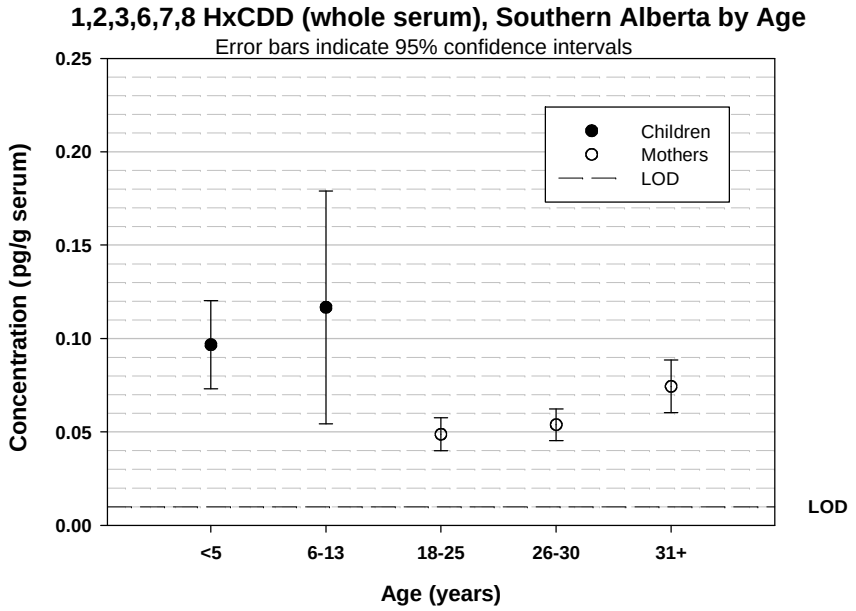
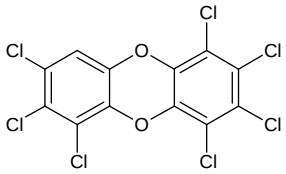


Figure 19



1,2,3,4,6,7,8 HpCDD

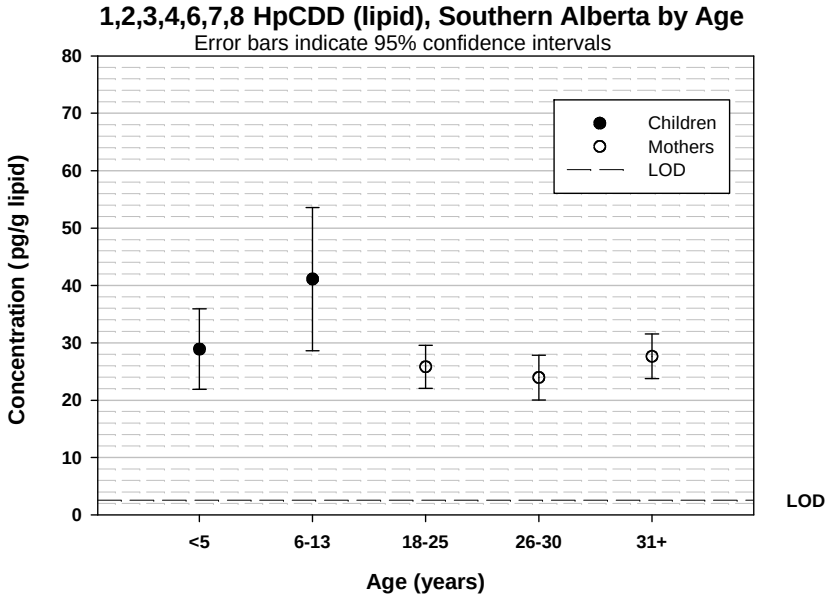
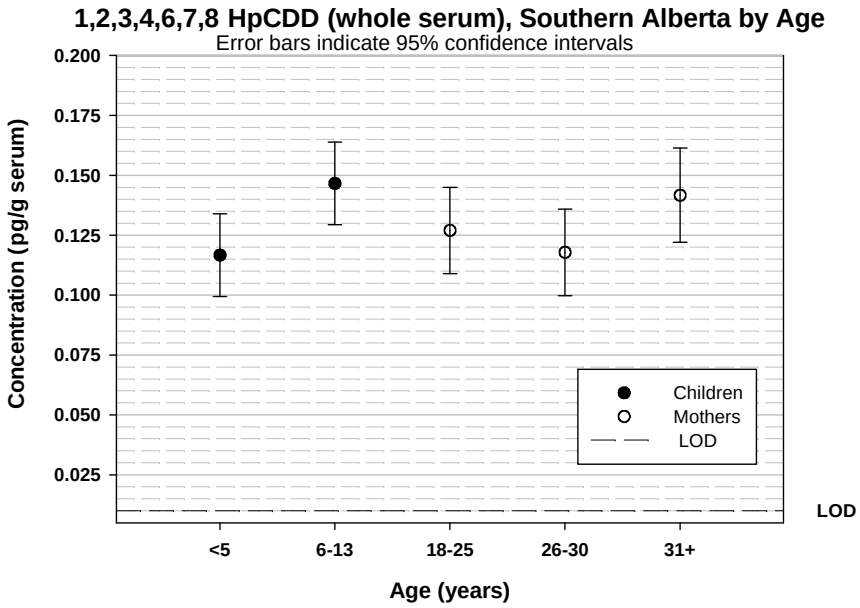


Figure 20



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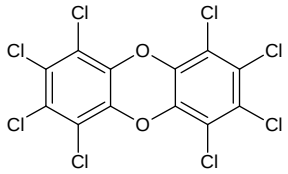
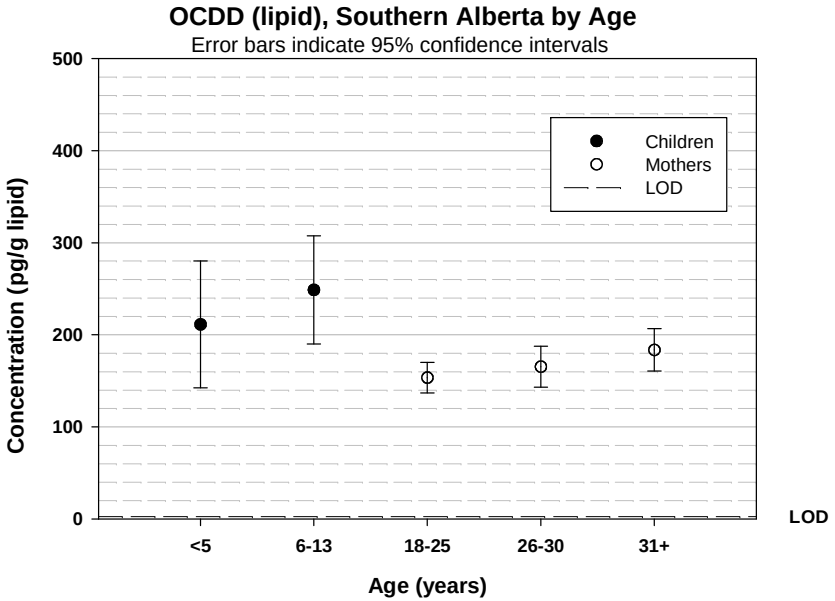


OCDD



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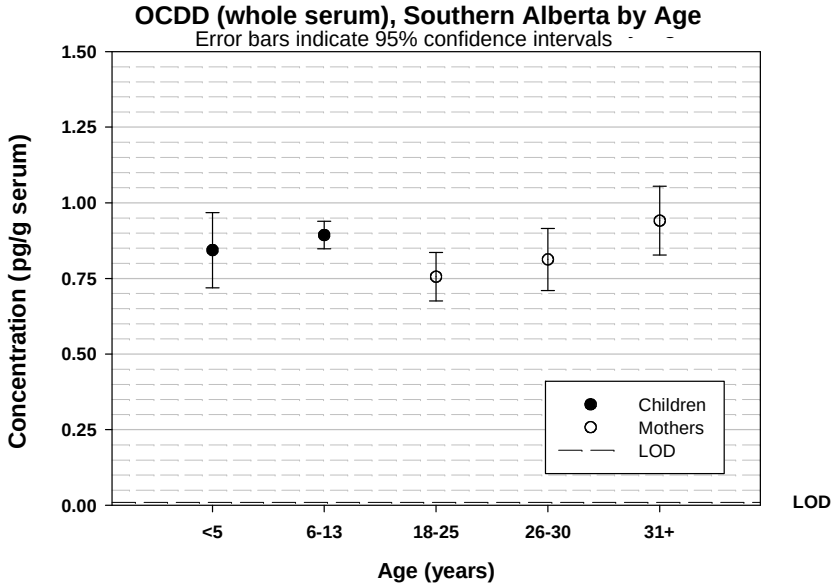

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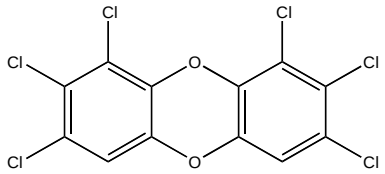
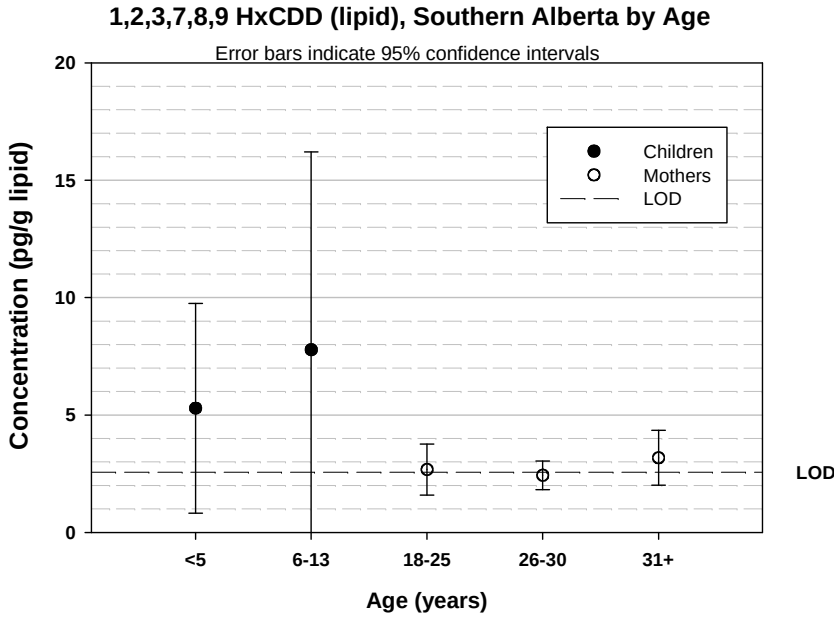


1,2,3,7,8,9 HxCDD



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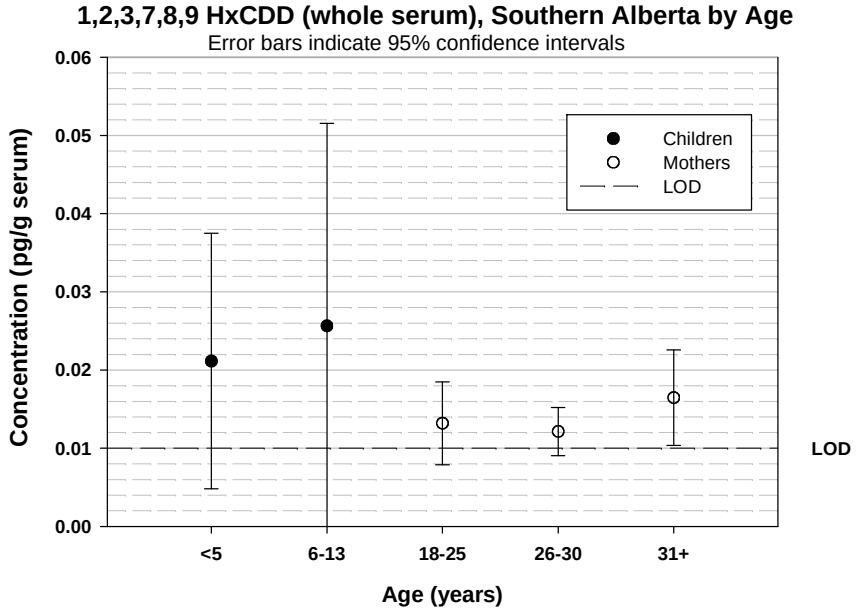
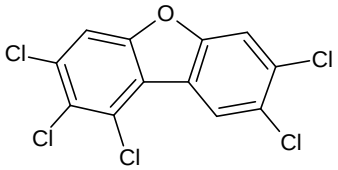
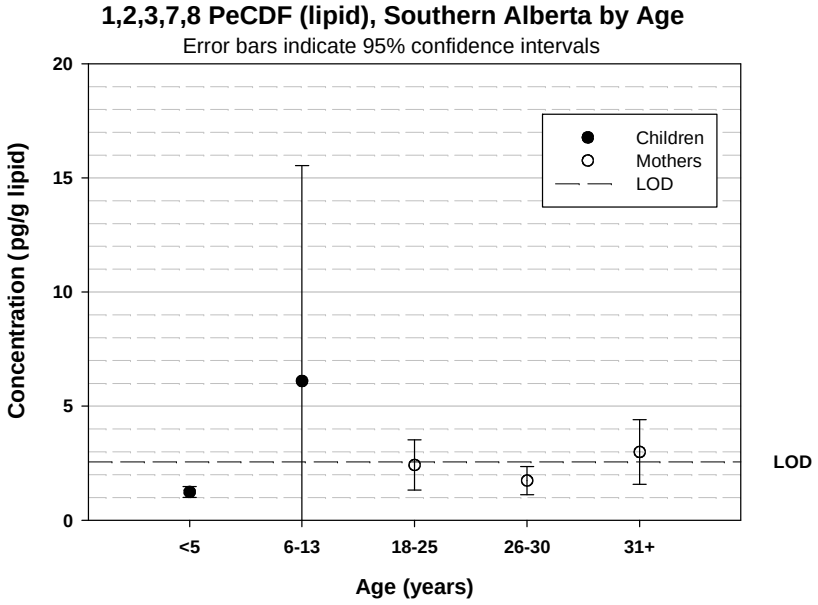


Figure 25



1,2,3,7,8 PeCDF



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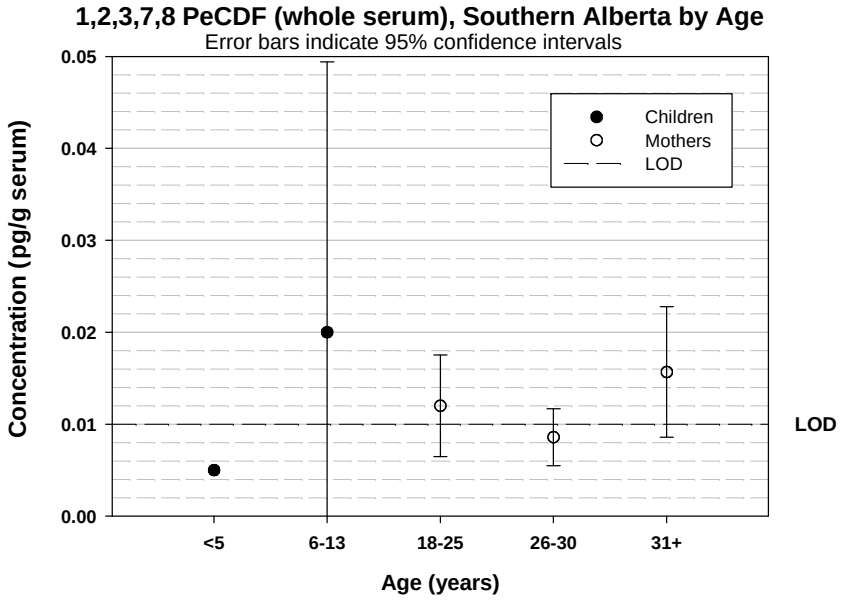
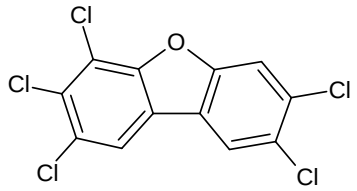


Figure 27



2,3,4,7,8 PeCDF

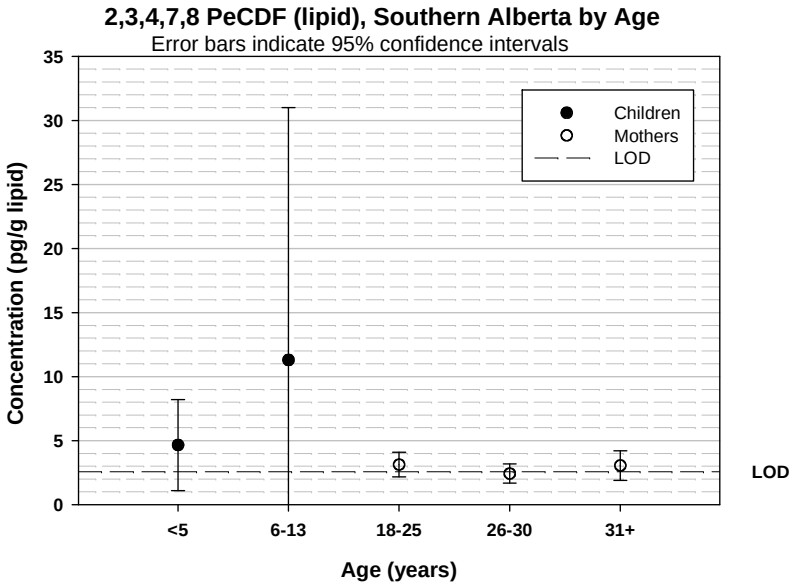
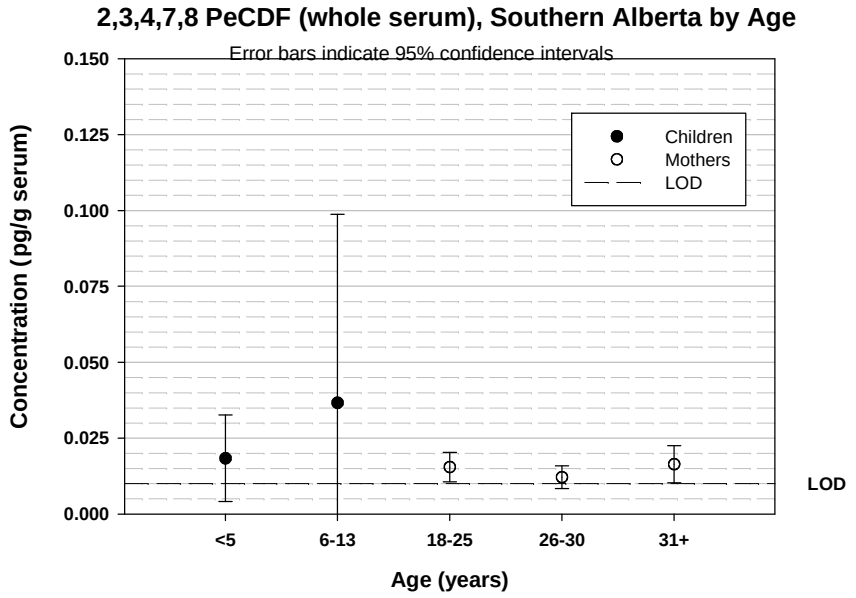


Figure 28



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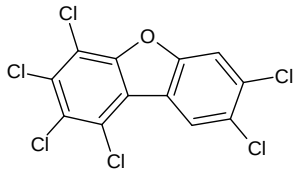


1,2,3,4,7,8 HxCDF

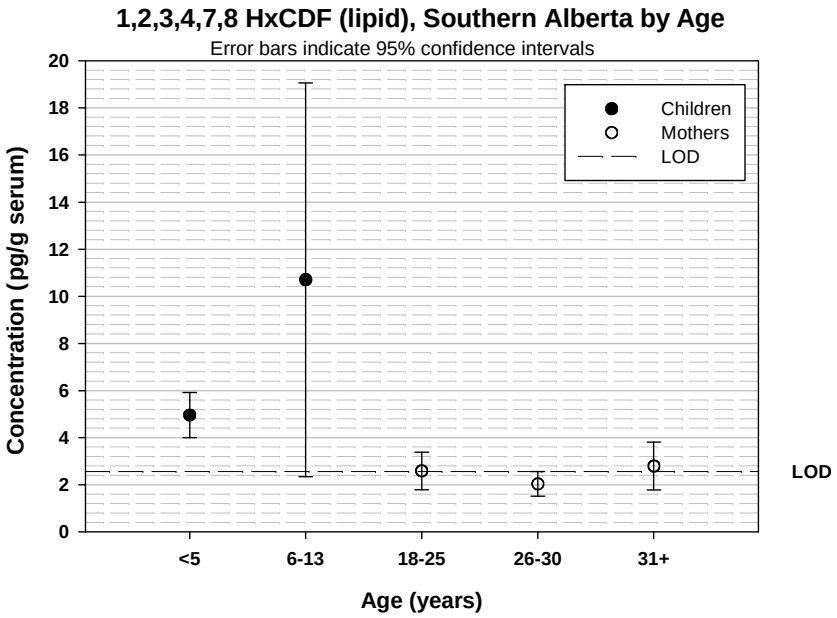
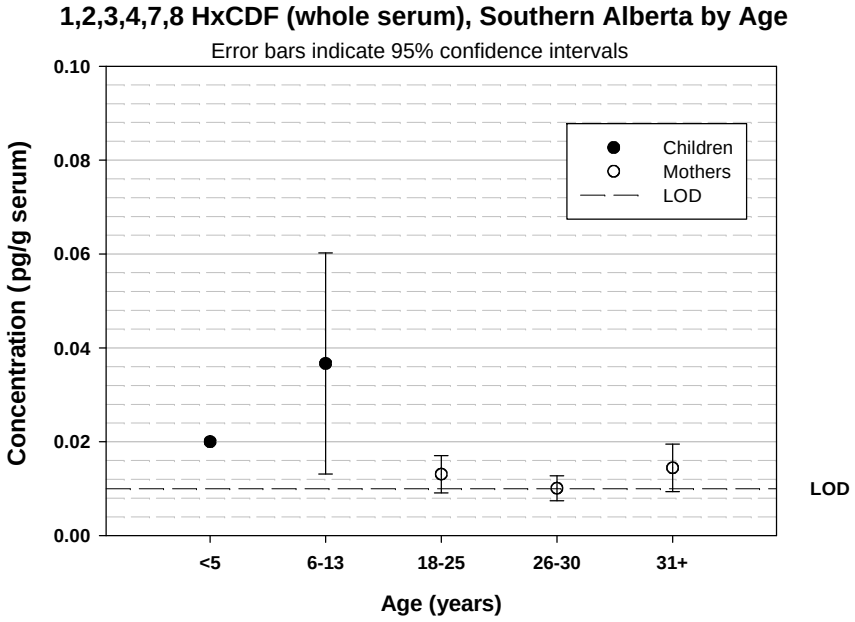


Figure 30



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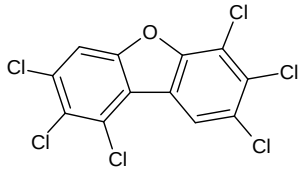


1,2,3,6,7,8 HxCDF

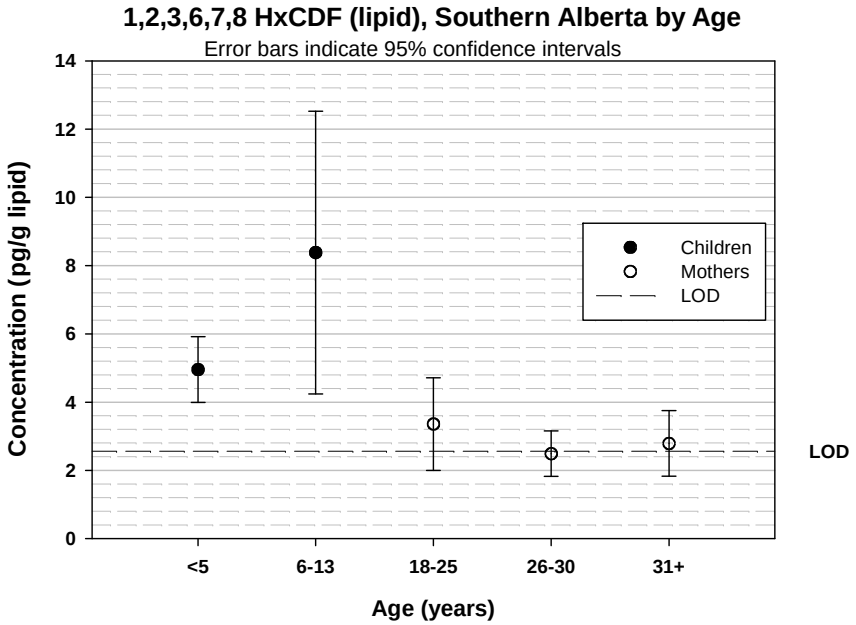


Figure 32

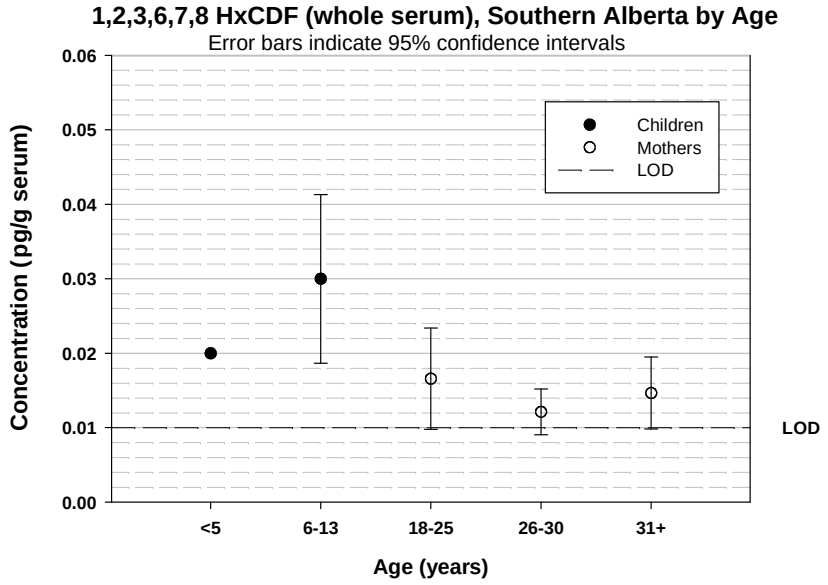
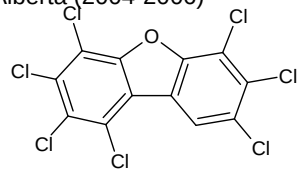


Figure 33



1,2,3,4,6,7,8 HpCDF

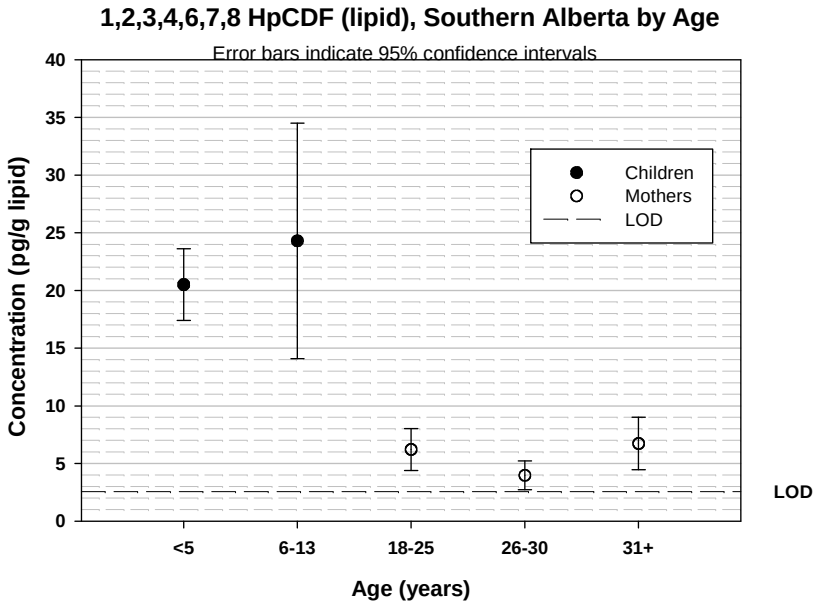


Figure 34

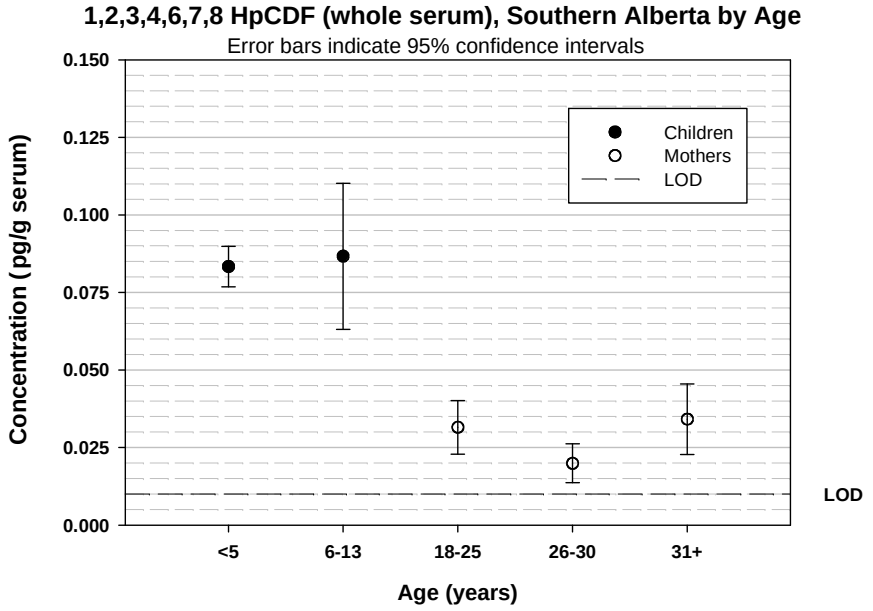


Figure 35

Methylmercury

GENERAL INFORMATION

Sources and Guidelines

Mercury is widely distributed around the earth in its elemental, inorganic and organic forms. Elemental and inorganic mercury are released to air and water from the combustion of fossil fuels (mainly coal), mining, smelting, and other industrial processes. Inorganic mercury in the atmosphere (mercury vapour), is ultimately redeposited to the earth in precipitation. If incorporated into aquatic sediments, it may be transformed by microorganisms to methylmercury (CH_3Hg^+), an organic form of mercury that can accumulate in organisms. For example, plant and sedimentary materials containing methylmercury are consumed by small fish that are, in turn, consumed by progressively larger fish and finally by humans. At each stage in this food-chain, methylmercury concentrations can increase through the process of biomagnification, resulting in higher concentrations of methylmercury in our food sources.[146,147]

The major source of methylmercury exposure in the general population is through the consumption of certain fish and seafood.[148] Large predatory fish at the top of aquatic food-chains generally have higher mercury concentration than small fish lower in the food-chain. Shark, large tuna, sword fish, marlin, and king mackerel contain 10–20 times higher concentrations of methylmercury than fish such as herring, cod, pollack, and shellfish such as shrimp or scallops.[149] Canned light tuna generally has lower methylmercury concentrations than canned albacore (white) tuna or fresh tuna steaks, and thus is a good alternative for limiting mercury intake while maintaining fish consumption.

In 2007, Health Canada updated the guidelines on fish consumption to limit mercury exposure, and has advised Canadians to limit their consumption to 150 grams per week of fresh and frozen tuna, shark, swordfish, escolar, and marlin. The new guidelines suggest a limit of 150 grams per month of these fish for pregnant women, breastfeeding pregnant women and women who might become pregnant. According to these guidelines, the recommended amount of these fish for children aged five to eleven is 125 grams per month, and for children aged one through four is 75 grams per month.

Behaviour in the Body

Methylmercury is rapidly absorbed into our blood from the gastrointestinal tract. Blood-borne methylmercury is present primarily in red blood cells and the blood can deliver methylmercury to the brain where it may accumulate while slowly being converted back to inorganic mercury.[150] Human pharmacokinetic studies indicate that the amount of time it takes to remove half of the body's methylmercury stores is approximately 70 days.[148,151] It is removed slowly through urine, feces, and breast milk. The half-life of ethyl mercury in infants is between two to seven days[152,153], but no studies could be found discussing the half-life of methylmercury in children.

Possible Health Effects

The human health effects of mercury are diverse and can depend on the dose, the form of mercury present in our bodies, the length of exposure, and the timing of the exposure. Methylmercury is more toxic than inorganic or elemental mercury.[154] At high doses, such as in the case of accidental poisonings, methylmercury is well documented to be a human neurotoxin, and may cause adverse effects on the motor and sensory systems.[155,156] At lower doses during pregnancy, development of the fetus' central nervous system can be sensitive to methylmercury exposure.[156] High maternal fish consumption has been associated with better infant cognition, but high mercury levels were associated with lower cognition. Consumption of varieties of fish with lower mercury levels is suggested during pregnancy.[157] Health Canada's guidelines for methylmercury in whole blood are as follows: (i) concentrations between 20 to 100 ng/g are considered a " level of concern" or "increasing risk", and (ii) concentrations greater than 100 ng/g are considered "at risk" or a "level of action".[158]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentration and Trends

Overall, mean methylmercury concentrations in blood serum of children in Alberta ranged from 0.041 ng/g to 0.065 ng/g. Concentrations of methylmercury (Figure 36) are essentially the same in the <5 year and 6–13 year groups. Concentrations in the <5 year age group are lower than in all of the pregnant women. Methylmercury concentrations are not significantly different between the 6–13 year children's group and the 18–25 year old pregnant women. However, concentrations in the 6–13 year children are lower than those in the 26–30 and 31+ year old pregnant women. The general increase with age is most likely related to the bioaccumulative nature of methylmercury.

Discussion and Interpretation

Although Health Canada has set guidelines for methylmercury in whole blood, it is difficult to interpret the present results in this context because serum is known to contain only a small fraction (5 percent) of total methylmercury[159] – red blood cells were excluded from the analysis here due to limitations in our study design. If we assume our study design excluded 95 percent of methylmercury in red blood cells, the current data can be multiplied by 20 to arrive at an estimated whole blood concentration. Using data from the <5 and 6–13 year old age groups, mean whole blood concentrations are estimated to be approximately 1 ng/g, which is well below Health Canada's prescribed "level of concern" of 20 ng/g.

Although these cannot be directly compared, a study of seven year old children in the Faroe Islands found mean concentrations of methylmercury in whole blood to be 5.27 ng/mL.[160] In general, higher values are reported for people who have geographic proximity to a steady supply of fresh fish than more inland populations.[161,162] The whole blood mercury concentration in non-Hispanic white children aged one to five who participated in the U.S. National Health and Nutrition Survey (NHANES) in 1999 and 2000 was 0.27 ng/mL. Concentrations ranged from non-detectable (5^{th} percentile) to 1.58 ng/mL (95^{th} percentile).[163] Total blood mercury is a reasonable measurement of methylmercury concentrations in people who eat fish and are not exposed to significant amounts of

inorganic or elemental mercury.[164] Data from the NHANES 1999–2000 survey found mean mercury concentrations in whole blood to be three times higher in mothers than in children.[163] Serum methylmercury concentrations in the 31+ year old pregnant women were approximately three times those in the children's age groups here.

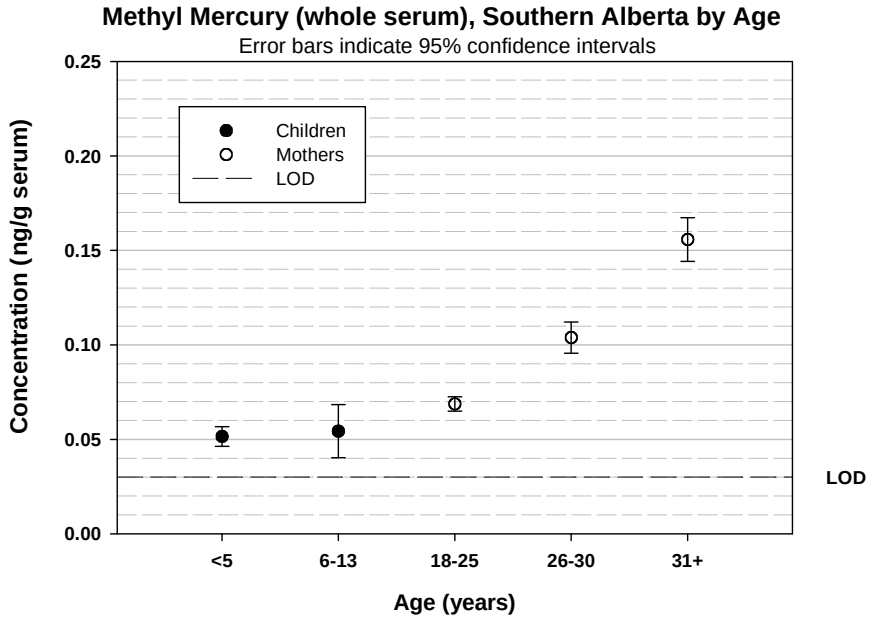


Figure 36

Dichlorodiphenyldichloroethylene

GENERAL INFORMATION

Organochlorine (OC) pesticides are synthetic chlorinated hydrocarbon compounds once widely used as insecticides and fungicides before their extreme environmental persistence, long-range transport, and high bioaccumulation potential were recognized. While these chemicals were generally quite effective for their intended purpose, eventual awareness of these chemicals at high concentration in humans and wildlife, and eventual recognition of their potential to cause adverse health effects, led to much public awareness in the 1960s. The growing environmental and human heath-related concerns caused many countries to regulate these chemicals in an effort to minimize future environmental and human exposure. While most of these chemicals are also tightly controlled by the international agreement on persistent organic pollutants (POPs, The Stockholm Convention), they persist in the global environment such that they are now referred to as "legacy pollutants". Examples of such chemicals include methoxychlor, DDT, hexachlorobenzene, mirex, heptachlor, chlordane, aldrin, dieldrin and endrin.

In general these chemicals were released into the local environment (air, water and soil) during their manufacture, use and disposal. These chemicals are considered semi-volatile, meaning that these chemicals can partition into the atmosphere and travel long distances on wind currents across international boundaries and into remote regions of the globe. The major source of OC pesticide exposure in the general human population today is through the diet. They enter the human food-chain because the largest fraction of OCs are now stored in the world's soils, and due to their lipophilic (literally 'fat-loving') nature, OCs may accumulate in plants and in the fatty tissues of livestock or other wildlife. Other minor sources of exposure are through absorption, ingestion and inhalation of contaminated water and air. In our bodies OC pesticides may accumulate in human breast milk and can also cross the placenta.[165-167] In these ways some level of OC pesticides can be passed to the fetus or to infants during pregnancy and lactation, respectively.[167] However, breastfeeding is encouraged due to the many associated health-benefits.[73]

In the present study, the following OC pesticides were measured in blood serum samples of children in Alberta: alpha-, beta-, gamma- and delta- hexachlorocyclohexane (HCH), heptachlor, aldrin, heptachlor epoxide, endosulfan, dieldrin, 4,4′-DDT, 4,4′-DDE, 4,4′-DDD, endrin, methoxychlor, chlordanes, hexachlorobenzene, trans-nonachlor, mirex and octachlorostyrene. However, only 4,4′-DDE was detected in the blood serum samples. Detailed information about DDE can be found in the following section.

Sources of DDE

In the 1940s dichlorodiphenyltrichloroethane (DDT) was widely applied as an agricultural insecticide and for control of mosquitoes to prevent diseases such as malaria. Due to eventual environmental and human health-related concerns the uses of DDT were phased out in Canada and the U.S. by the mid-1970s. However, DDT still persists in the environment as a result of long half-lives in soil, water and animal tissues, and also due to its continuing use in some countries, primarily for malaria control.

In the environment DDT rapidly transforms to a very stable, highly persistent and lipophilic (literally 'fat-loving') chemical form, dichlorodiphenyldichloroethylene (DDE).[168] There are not, and never have been, any commercial uses for DDE, but it is now widely detected in soil, sediments, water and in the food chain throughout the world.[169] Diet is the main source of exposure to DDE in the general human population, and the human fetus and infants are exposed though the placenta and breastfeeding, respectively.[165,166,168] Absorption, ingestion and inhalation of water and air containing trace concentrations of DDE are other sources of minor exposure.[168]

Regulations in Canada for DDT

DDT was not manufactured in Canada, but in 1946 was registered for insecticide use to control agricultural insects, and also for household and industrial uses.[170] Most uses of DDT were banned in Canada by the mid-1970s, and the remaining uses were phased out by 1985.[170] According to the Pest Control Products Act in Canada, all storage of DDT was supposed to be sold or disposed of by December 31, 1990, and any uses of DDT after that time would be considered violations under this Act.[170]

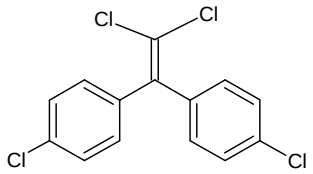
Possible Health Effects

The human health effects of DDE depend on the dose, the length and timing of exposure, and other factors. Background concentrations of DDE in humans usually are not known to cause any adverse health effect. However, at high doses, such as in the case of accidental releases, unusual occupational exposures, or accidental consumption of highly contaminated food, DDE may cause adverse health effects including respiratory problems, impairment of the immune system, neurotoxicity, birth defects and reproductive toxicity in infants and children.[169,171-174]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall mean DDE concentrations in blood serum of children in Alberta was relatively variable, ranging from 0.12 to 1.4 ng/g of serum or, expressed on a serum lipid basis, from 36 to 440 pg/g lipid. Concentrations of DDE (lipid adjusted and whole serum, Figure 37 and 38) were not significantly different between the <5 year and 6–13 year age groups, nor were they different from the concentrations in the pregnant women. DDE was measured in the serum of four year old children from two different environmental conditions: Menorca Island and Ribera d'Ebre – an inland industrial area of Catalonia, Spain. Mean concentrations of DDE in four year old children on Menorca Island were 1.6 ng/mL and 1.7 ng/mL in children from Ribera d'Ebre.[175] Mean serum DDE was measured in children aged six to eleven from Alaska to be 11 ng/mL.[176] These values are substantially greater than those observed in the present study.



DDE

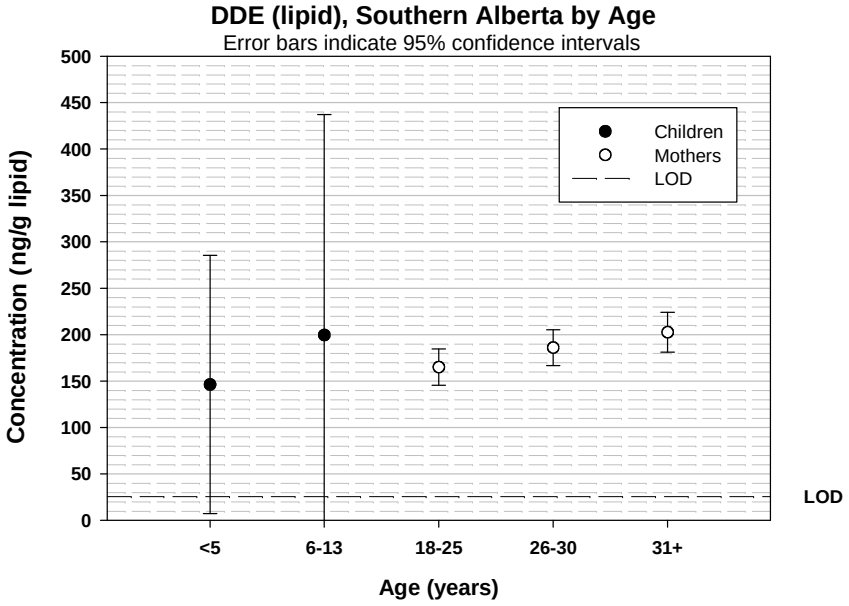


Figure 37

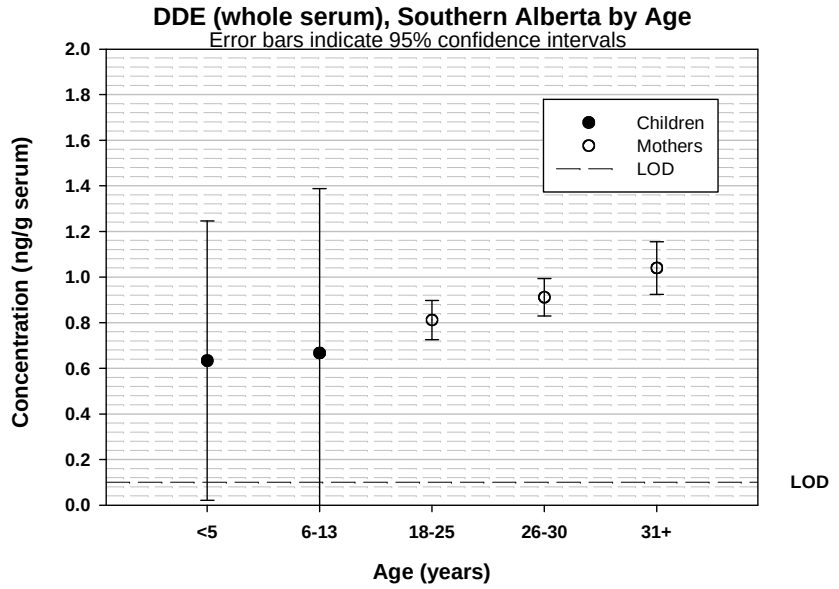


Figure 38

Polybrominated Diphenyl Ethers

GENERAL INFORMATION

Sources

Polybrominated diphenyl ethers (PBDEs) are additive (i.e., not bound into the material) brominated flame retardants, which have been used for many decades in commercial products including computers, televisions, foam furniture, carpet underlay, and electrical appliances.[177,178] They are incorporated into these products to minimize the risk of fires, and hence save lives. PBDEs are manufactured as commercial mixtures, and three main types have been used historically: penta-BDE, octa-BDE and deca-BDE, so named based on the average bromine content. Penta-BDE was used mainly in foam products for stuffing (such as household furniture and seat cushions), octa-BDE for high-impact plastic products (such as telephone, FAX machines and computers), and deca-BDE is used primarily in plastics for electric components (such as wire and cable insulation).[177,179] PBDEs can be released from these products into our homes or into the environment. PBDEs are rather persistent in the environment and can travel long-distances such that they are detectable all over the world, including in remote regions far from their source.

Owing to their use in commercial products, people are exposed through PBDE-containing products in their houses and workplaces via dust.[180-182] Another potential source of exposure is through dietary intake, primarily from meat, dairy, fish and eggs.[183,184] Human milk is a major source of PBDEs to infants.[185] The indoor environment is suggested to be the greatest contributor to the exposure of everyone from young children up to adults.[181] As the PBDEs are lipophilic (literally "fat-loving") compounds, they can build up in our body over time, including in fatty tissues and human breast milk. PBDEs can also cross the placenta.[186] In these ways PBDEs can be passed to the fetus or to infants during pregnancy and lactation, respectively.[187] Recent human breast milk studies show Canadians contain the second-highest concentrations of PBDEs in the world, which is five to ten times higher than in Europeans and Japanese.[188] Growing environmental and human heath-related concerns have caused many countries to begin regulating these chemicals in an effort to minimize future environmental and human exposure.

Regulations in Canada

PBDEs used in Canada are imported from other countries and are not manufactured in Canada. In July 2006, the Federal Government proposed the addition of PBDEs to the List of Toxic Substances in Schedule 1 of the Canadian Environmental Protection Act (CEPA).[189] In December 2006, penta-, tetra- and hexa-BDE congeners were identified as "toxic", as defined by CEPA, and thus these PBDEs were added to the "List of Toxic Substances".[189] Also by the end of 2006, the Canadian Government announced regulations to ban the manufacturing, use, sale, and import of commercial PBDE mixtures of penta-BDE and octa-BDE.[189] The use of deca-BDE is not currently regulated in Canada.

Some other countries also have regulations controlling PBDEs. In August 2004, the European Union (EU) banned the use of penta- and octa-BDEs. Deca-BDE was also banned in the EU for use in electronic products as of July 1st, 2006, and a complete ban for deca-BDE is now in place in the EU as of April 1, 2008.[190] Japan has also voluntarily phased

out the use of penta-BDE.[191] Several U.S. states adopted bans on the manufacture and use of penta- and octa-BDEs since 2005.[189] The main U.S. manufacturer of penta- and octa-BDE mixtures voluntarily stopped production of these two PBDEs at the end of 2004. Otherwise, the use of deca-BDE is not restricted in the U.S. except in Washington and Maine.[189]

Possible Health Effects

There are 209 varieties of PBDEs (also known as "congeners"), varying in the number and relative position of bromine atom substitution.[184] In general, smaller PBDE congeners (with lower numbers of bromine atoms, one to five atoms) are better absorbed into our bodies than larger PBDEs, and are also more toxic.[192] The larger congeners, such as deca-BDE, eliminate rapidly from the human body (half-life, 6.8 days), whereas smaller congeners such as hepta-BDE are more slowly eliminated (long half-life, 86 days).[192,193] PBDE concentrations in children's serum have been shown to be higher than in infants or adults.[194] Deca-BDE is known to be less toxic than penta- and octa-BDEs, however recent studies indicate that it breaks down to lower brominated PBDEs in the environment, which may be an indirect exposure source for humans.[178,195] Currently there are few studies examining the effects of PBDEs in infants and young children.

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

The following PBDEs were measured in the blood serum samples of children in Alberta:

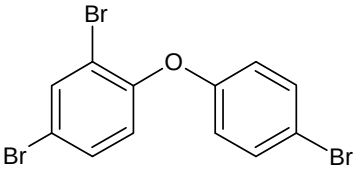
1. 2,4,4'-tribromodiphenyl ether (BDE 28)
2. 2,2',4,4'-tetrabromodiphenyl ether (BDE 47)
3. 2,3',4,4'-tetrabromodiphenyl ether (BDE 66)
4. 3,3',4,4'-tetrabromodiphenyl ether (BDE 77)
5. 2,2',3,4,4'-pentabromodiphenyl ether (BDE 85)
6. 2,2',4,4',5-pentabromodiphenyl ether (BDE 99)
7. 2,2',4,4',6-pentabromodiphenyl ether (BDE 100)
8. 2,3,3′,4,4′,5′-hexabromodiphenyl ether (BDE 138)
9. 2,2',4,4',5,5'-hexabromodiphenyl ether (BDE 153)
10. 2,2',4,4',5,6'-hexabromodiphenyl ether (BDE 154)
11. 2,2',3,4,4',5′,6-heptabromodiphenyl ether (BDE 183)
12. Decabromodiphenyl ether (BDE 209)

However, except for BDE 66, 77, 85, 138, 183 and 209, all other PBDE congeners were detected, and concentration ranges among pools are shown based on lipid weight in blood serum samples:

PBDEs	Lipid weight (ng/g lipid)
BDE 28	0.15 to 2.5
BDE 47	38 to 91
BDE 99	11 to 24
BDE 100	9.4 to 24
BDE 153	16 to 26
BDE 154	0.74 to 2.4

For the BDE congeners 28, 99, and 154, (Figures 39, 41, and 44) there were no differences in concentration apparent between the children's age groups or between the children and the pregnant women's groups. For BDE 47 and BDE 100 (Figures 40 and 42) the concentrations in the <5 year group were higher than concentrations in the 31+ year pregnant women. For BDE 153 (Figure 43) concentrations in the <5 and 6–13 year age groups are higher than those in the 18–25 and 31+ year old pregnant women.

In a study of pollution in Canadian families, 5 PBDE congeners were measured in seven children aged ten to fifteen. The median concentrations of all PBDEs in children's plasma was 0.118 ng/mL and the range of concentrations was 0.01–0.13 ng/mL.[196] PBDE congeners 47, 99, 100 and 153 were measured in the serum of Australian children in 2006–2007. Mean concentrations of the sum of the four congeners were 31 ng/g lipid in children aged zero to two, 41 ng/g lipid in children aged two to six and 26 ng/g lipid in children aged seven to twelve.[194] PBDE concentrations in children aged zero to four years were found to be four to five times higher than in adults aged sixteen and older.[197] This difference in concentration between children and adults is higher than in the present study. Concentrations of PBDE in the serum of Norwegian children aged zero to four years 0.26 ng/g lipid (BDE-28), 6.2 ng/g lipid (BDE-47), 1.6 ng/g lipid (BDE-99), 1.7 ng/g lipid (BDE-100), 1.5 ng/g lipid (BDE-153) and 0.45 ng/g lipid (BDE-154). Concentrations in children aged four to fourteen years were 0.20 ng/g lipid (BDE-28), 2.0 ng/g lipid (BDE-47), 0.37 ng/g lipid (BDE-99), 0.66 ng/g lipid (BDE-100), 0.86 ng/g lipid (BDE-153), and 0.39 ng/g lipid (BDE-154)[198], which are generally lower than the values in the present study.



BDE 28

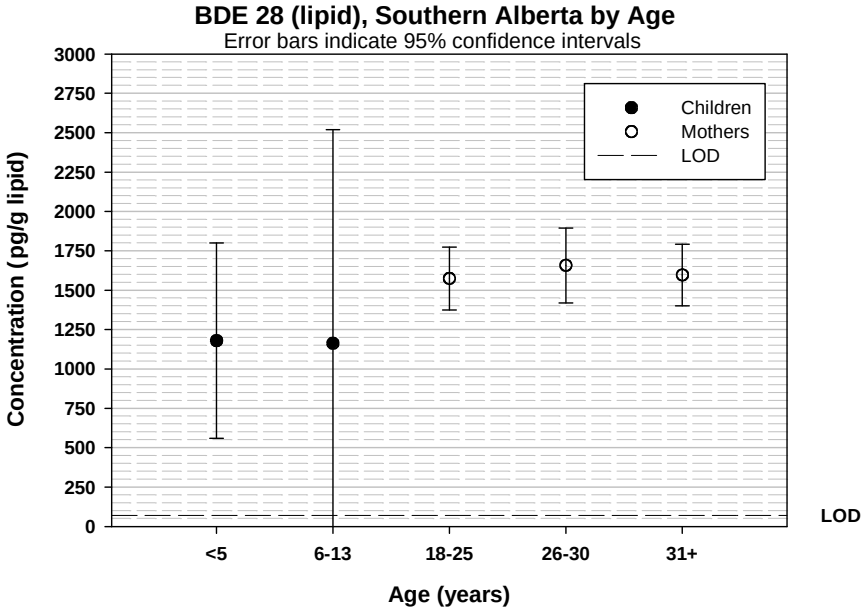
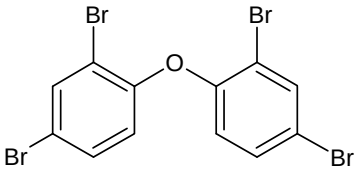


Figure 39



BDE 47

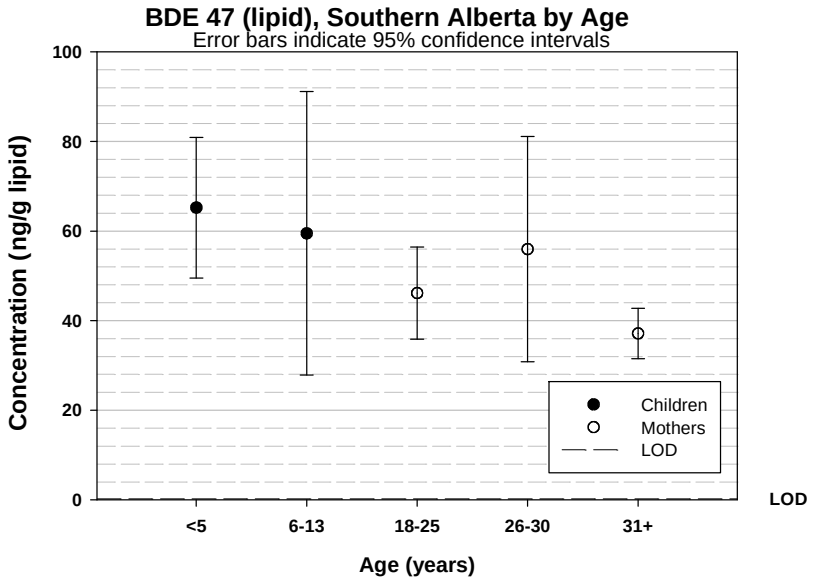
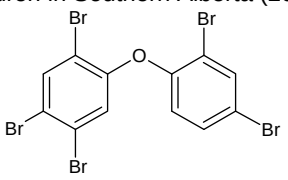


Figure 40



BDE 99

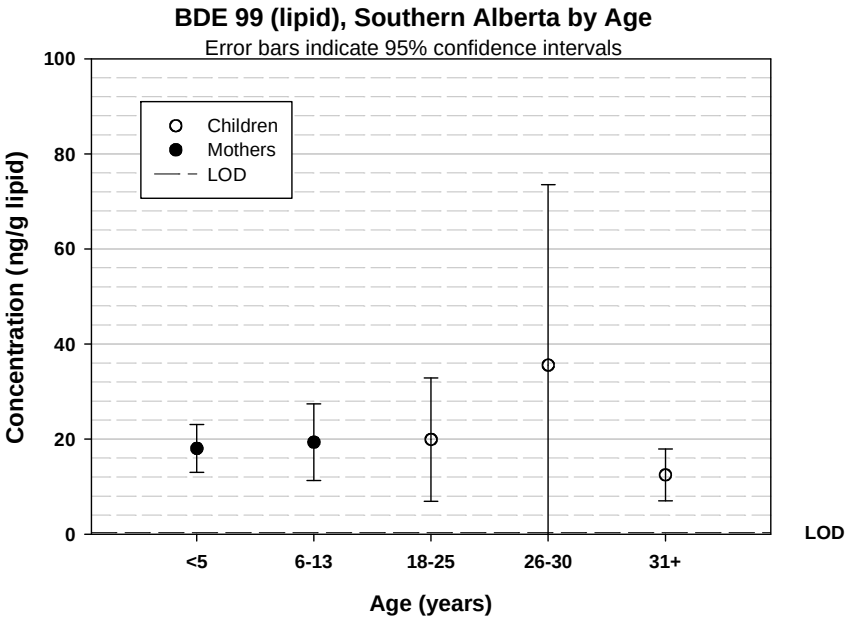
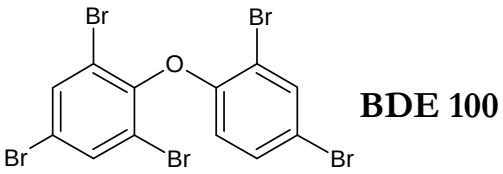


Figure 41



BDE 100

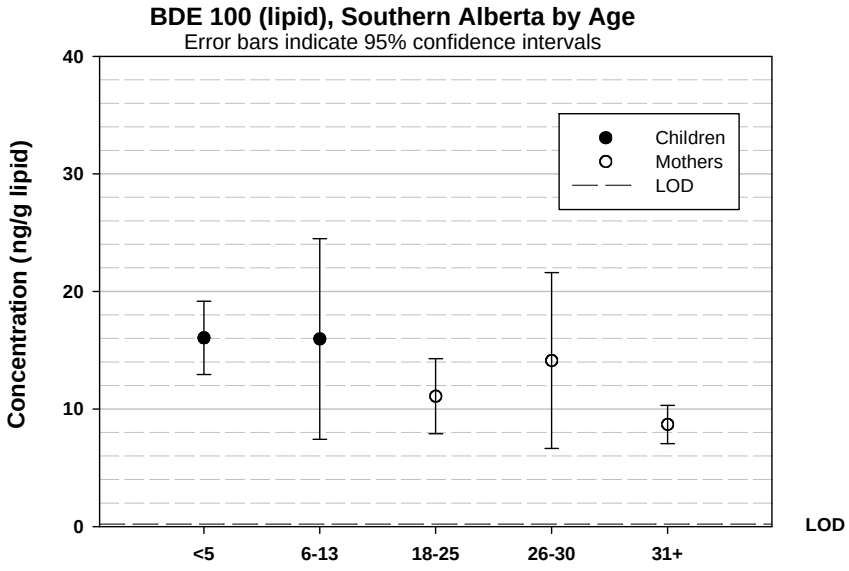
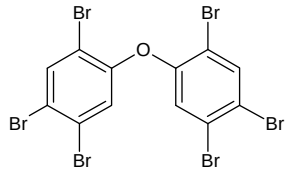


Figure 42



BDE 153

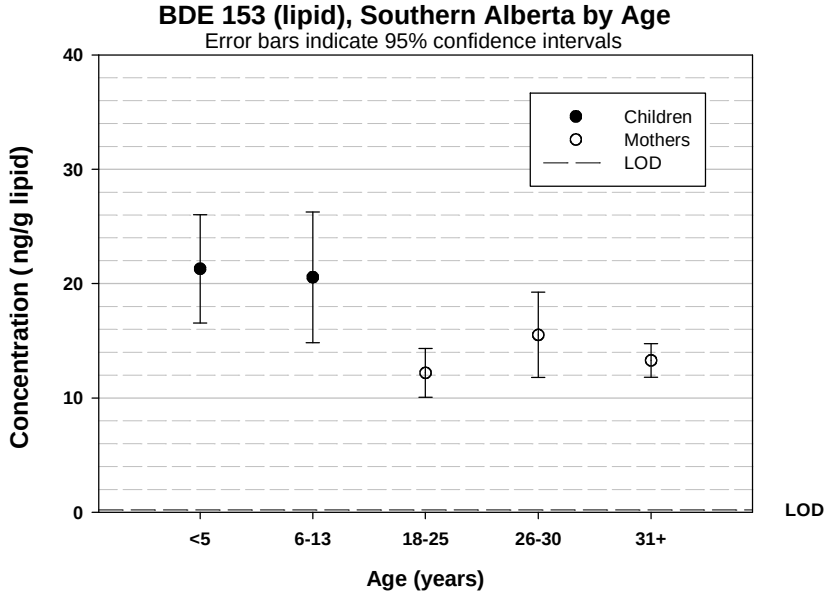
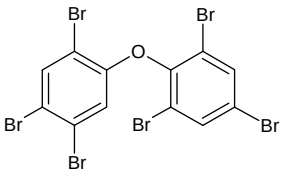


Figure 43



BDE 154

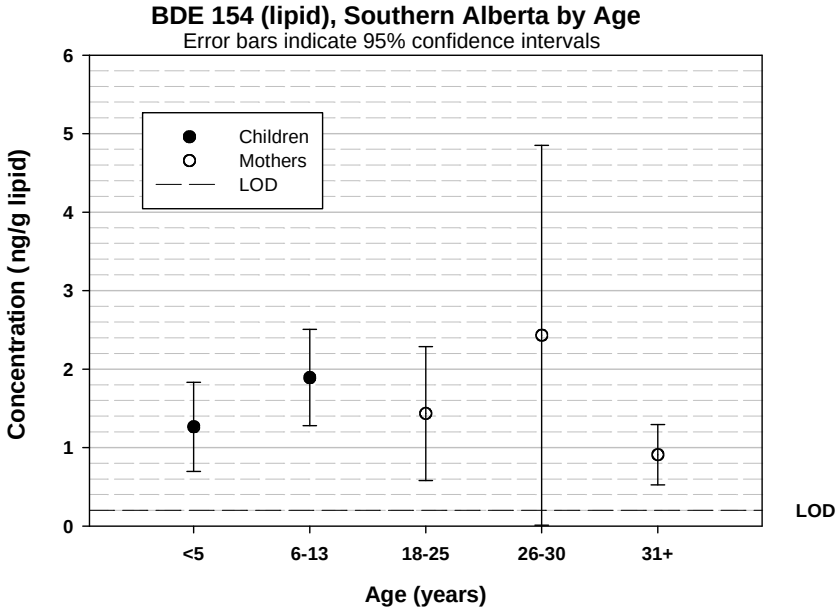


Figure 44

trans-DCCA

GENERAL INFORMATION

Sources

trans-DCCA (trans-3-(2,2-(dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid) is a metabolite of the pyrethroid insecticides permethrin, cypermethrin, and cyfluthrin.[199] Pyrethroids are man-made chemicals, but are based on chemical structures of naturally occurring pyrethrins. More than one thousand pyrethroids have been synthesized, but fewer than twelve are currently in use in the United States.[200] However, the use of pyrethroids in the U.S. has increased in the last decade as a result of the declining use of organochlorine pesticides.[201]

Pyrethroids are typically found in the air as a result of their use as insecticides. Most pyrethroids are degraded by sunlight within one or two days of being released to the environment. They also bind strongly to soil and are therefore unlikely to contaminate drinking water supplies. However, some of the recently developed pyrethroids can persist in the environment for a number of months.[200]

Pyrethroids are quickly metabolized by mammals and their toxicity depends on the route of exposure.[202] trans-DCCA does not have any commercial uses, but is found in the blood and urine of people exposed to permethrin, cypermethrin and/or cyfluthrin.[203-205] The most likely route of exposure to pyrethroids is through the diet but exposure can also occur through inhalation or dermal contact. Children may be more likely to be exposed to pyrethroids as a result of greater ingestion of soil and dust, and may also be more susceptible to pyrethroids than adults.[200]

Regulations in Canada for Pyrethroids

Maximum residue limits (MRL) for permethrin were established under the *Food and Drugs Act* ranging from 0.1 ppm in fat, meat, and meat by-products to 20 ppm in lettuce and spinach.[206] Maximum residue limits for cyfluthrin in the *Food and Drugs Act* range from 0.01 ppm in eggs to 15 ppm in milk fat.[207] Maximum residue limits are not specifically stated for cypermethrin in the *Food and Drugs Act* and it is therefore given an MRL of 0.1 ppm.[208]

Possible Health Effects

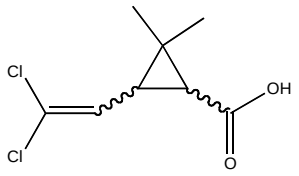
Background concentrations of pyrethroids such as those in the environment or resulting from normal use of pyrethroid-containing substances are not likely to cause any adverse health effects in humans.[200] At high doses, such as in the case of accidental poisonings and occupational exposure, health effects such as facial itching and dermatitis can occur in milder cases while severe poisoning may cause convulsive attacks, coma, or pulmonary edema.[209]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

trans-DCCA was detected in all pooled children's serum samples. Concentrations ranged from 164 pg/g to 815 pg/g of serum. Concentrations of trans-DCCA (Figure 45) are not significantly different between the <5 and 6–13 year age groups. Using the same analytical method, trans-DCCA was only detected in 8 percent of pooled serum samples of pregnant women in Southern Alberta (age 26–30), with a maximum concentration of 83 pg/g. Thus, although a statistical analysis is not possible it is clear children have higher blood concentrations of trans-DCCA than pregnant women in the same region.

In the U.S. National Health and Nutrition Survey (NHANES, 2001–2002) (Fourth Report, CDC), trans-DCCA was measured in the urine of children aged six to eleven. However, mean concentrations were not calculated as urinary trans-DCCA concentrations were mostly below the limit of detection of 0.4 ng/mL.[40] The German Environmental Survey on Children (2003–2006) measured urinary trans-DCCA in children aged three to fourteen. The 50th percentile was 0.25 ng/mL and the 95th percentile was 2.46 ng/mL.[199] However, urinary values cannot be directly compared to the blood serum.



DCCA

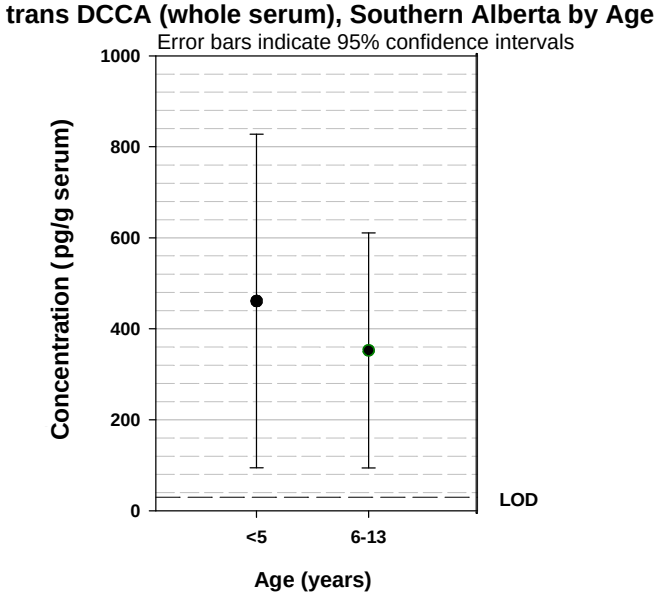


Figure 45

2,4-Dichlorophenoxyacetic acid

GENERAL INFORMATION

Sources

2,4-dichlorophenoxyacetic acid (2,4-D) is a member of the chlorophenoxy family of herbicides. It was introduced as a herbicide in 1946 and is the most widely used herbicide in the world.[210] 2,4-D is present in the environment in air, water, and soil as a result of crop spraying, application to ponds or streams, accidental drift, direct application to agricultural soil, and leaching from soil.[211] Exposure to 2,4-D can occur through food and water, although concentrations are below levels of concern in the US. Adults and children can also be exposed if treating lawns and other grassy areas with 2,4-D or by playing or swimming in these treated areas.[212] Inhalation, ingestion, and dermal contact are all routes of human exposure to 2,4-D.[213]

Regulations in Canada

2,4-D is registered as an herbicide under the *Pest Control Products Act*. Maximum residue limits for 2,4-D range from 0.5 ppm for cranberries to 5 ppm for asparagus.[207] As of January 1, 2010, combination fertilizer/herbicide products containing 2,4-D are banned for sale and use in Alberta.[214]

Possible Health Effects

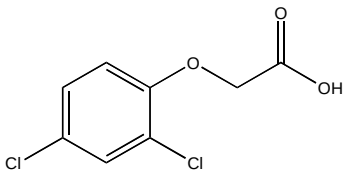
Health effects of 2,4-D at low environmental levels are not known.[40] Animal and human studies have demonstrated a low chronic toxicity for 2,4-D.[215] Higher doses in animals have identified potential target organs as the kidney, thyroid liver, testes, and eyes. The risk of 2,4-D as a carcinogen is negligible.[216]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentration and Trends

2,4-D was detected in all pooled children serum samples and concentrations ranged from 166 pg/g to 486 pg/g serum. Concentrations of 2,4-D (Figure 46) were not significantly different between the <5 and the 6–13 year age groups. Using the same analytical method 2,4-D was only detected in 21 percent of pooled serum samples of pregnant women in Southern Alberta (age 26–30) with a maximum concentration of 453 pg/g. Thus, although a statistical analysis is not possible it is clear that, on average, children have higher blood concentrations of 2,4-D than pregnant women in the same region.

In the U.S. National Health and Nutrition Survey (NHANES, 2001–2002) (Fourth Report, CDC) 2,4-D was measured in the urine of children aged six to eleven. However, mean concentrations were not calculated as urinary 2,4-D concentrations were mostly below the limit of detection of 0.2 ng/mL.[40]



2,4-D

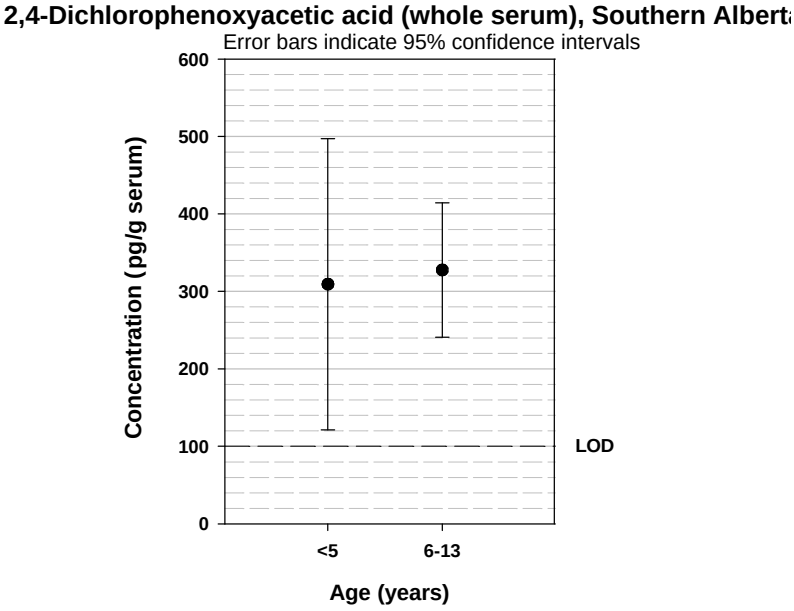


Figure 46

Bisphenol A

GENERAL INFORMATION

Sources

Bisphenol A (BPA) is a synthetic chemical used to manufacture polycarbonate plastics and epoxy resins. BPA is an endocrine disruptor with estrogen-like activities[217,218] and its production volumes are among the highest of all chemicals worldwide.[219] These plastics and resins are used in various consumer products such as toys, food and beverage bottles and cans, plastic baby bottles, bottle tops, eyeglass lenses, medical equipment, dental sealants, and water pipes.[220] The leaching of BPA from plastic bottles, food cans and dental sealants are confirmed by several studies.[221-224] This has led to wide-spread human exposure to BPA.[219]

Due to the extensive use of BPA in plastics and resins, the predominant source of BPA exposure in the general population is through the use of everyday plastic products, and consumption of contaminated canned and bottled foods and beverages.[219,225] Some studies have also shown that BPA leaches from municipal waste landfills into the surrounding ecosystem.[226,227] The leaching of BPA from baby bottles and infant formula cans into baby food is a source of BPA exposure for infants.[228-230] Due to the semi-lipophilic (literally "fat-loving") nature of BPA, it can accumulate in human breast milk.[231] BPA can also cross the placenta.[232] In these ways BPA can be passed to the fetus or to infants during pregnancy and lactation, respectively.

Regulations in Canada

In 2006, the Canadian Federal Government, as a part of the Chemicals Management Plan, selected BPA for a detailed safety review to assess the potential human and environmental effects. This process started in May 2007 and was recently completed. Canada is the first country to complete a risk assessment of BPA. The draft Assessment Report was published in the Canada Gazette on April 19, 2008, for a 60-day public comment period in an effort to decide whether to ban the import, sale, and use of baby bottles containing BPA. Based on the Assessment Report the Canadian Federal Government added BPA to the List of Toxic Substances in Schedule 1 of the Canadian Environmental Protection Act (CEPA) in June 2009.[233]

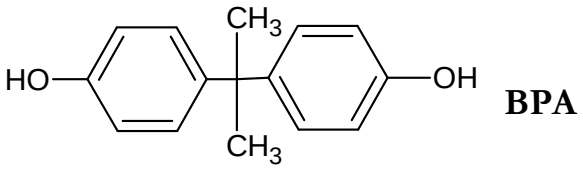
Possible Health Effects

Due to the high-volume production and wide-spread use of BPA, there is an increasing interest in investigating the effects of BPA exposure on human health. However, human studies are currently very limited, and most available data are from animal studies. As a hormone or endocrine disruptor, a high enough dose of BPA is associated with a number of adverse health effects in animals related to hormonal imbalance such as developmental and reproductive toxicity, neurotoxicity, ovarian dysfunction and recurrent miscarriages.[224,234-236]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

BPA concentrations (Figure 47) are essentially the same in the <5 and 6–13 year old age groups. However, the concentrations are approximately fourteen times higher than those measured in the 26–30 year old pregnant women. In the U.S. National Health and Nutrition Survey (NHANES 2003–2004) the geometric mean urinary concentration of BPA in children aged six to eleven was 3.55 ng/mL. This value is statistically greater than the mean concentration in adults aged 20 and older (2.41 ng/mL).[40] However, it is not possible to compare urinary concentrations to blood serum concentrations. As far as we know this is the first instance of measurement of blood serum concentrations of BPA in children.



BPA

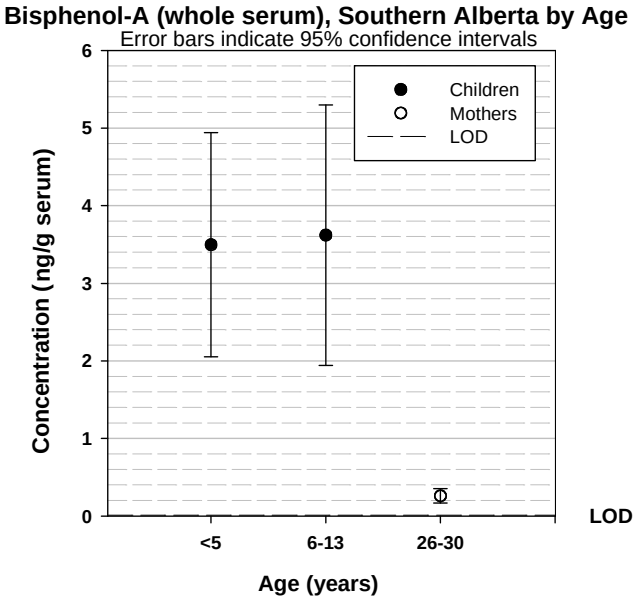


Figure 46

Pentachlorophenol

GENERAL INFORMATION

Sources

Pentachlorophenol (PCP) is a synthetic chemical that was widely used as a biocide and wood preservative before its use was restricted in the U.S. in the 1980s.[237] 80 percent of the U.S. consumption of pentachlorophenol now results from treating wood for making utility poles. It is also used as a biocide, which accounts for no more than 2 percent of U.S. consumption.[238]

As a result of its widespread use pentachlorophenol is found in the air (evaporation from treated wood and factory waste), surface and groundwater (factories, wood-treatment facilities, and hazardous waste sites), and soil (spills, hazardous waste sites, pesticide use).[238] The general population can be exposed to PCP through inhalation exposure, ingestion of contaminated drinking water or food, and dermal contact with contaminated soil or PCP treated wood products. Children are exposed to PCP through the same routes as adults, but are more likely than adults to have more contact with soil and be less concerned with hygiene thus increasing the likelihood of ingestion of PCP.[238] The half-life of PCP in humans varies from several days to two weeks depending on the exposure route.[239]

Regulations in Canada

Carex Canada ranks PCP as Group A (immediate high priority) for occupational and environmental settings.[240] Health Canada has listed PCP as a substance with a high health priority for action[241] and the Government of Canada has listed PCP as a Tier II substance (i.e., a substance identified as having the potential for causing widespread impact or having already had adverse local effects on the Great Lakes environment).[242] The use of PCP as a wood preservative in Canada is currently under re-evaluation by the Pest Management Regulatory Agency.[243]

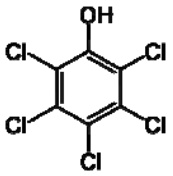
Possible Health Effects

Acute exposure to PCP can cause effects on the skin (eg, chloracne), metabolism (eg, fever), haematopoietic tissue, respiratory system, nervous system, kidneys, and gastrointestinal tract in humans.[244] Children accidentally exposed to PCP in concentrations much higher than observed in this study exhibited symptoms of hypothermia. [245] One study suggests young children may be more sensitive to the toxicity of PCP than adults.[246] Children aged eight to eighteen years living in log homes treated with PCP exhibited more alterations in immunological parameters.[247]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations of pentachlorophenol in blood serum of children in Alberta ranged from 0.90 ng/g to 1.4 ng/g serum. Concentrations of PCP (Figure 48) did not differ significantly between the <5 and 6–13 year age groups. PCP concentrations in the blood plasma of children living in an urban area of Germany were 3.67±4.58 ng/mL (zero to under six years old) and 2.64±1.70 ng/mL (six to under twelve years old).[239] Concentrations of PCP in four year old children living in Spain near a factory producing solvents had serum PCP concentrations of 6.4±6.0 ng/mL. Four year old children living in a more rural area of Spain had a serum PCP concentration of 0.61±0.69 ng/mL[248], which is a lower but similar concentration to that found in Albertan children in this study.



PCP

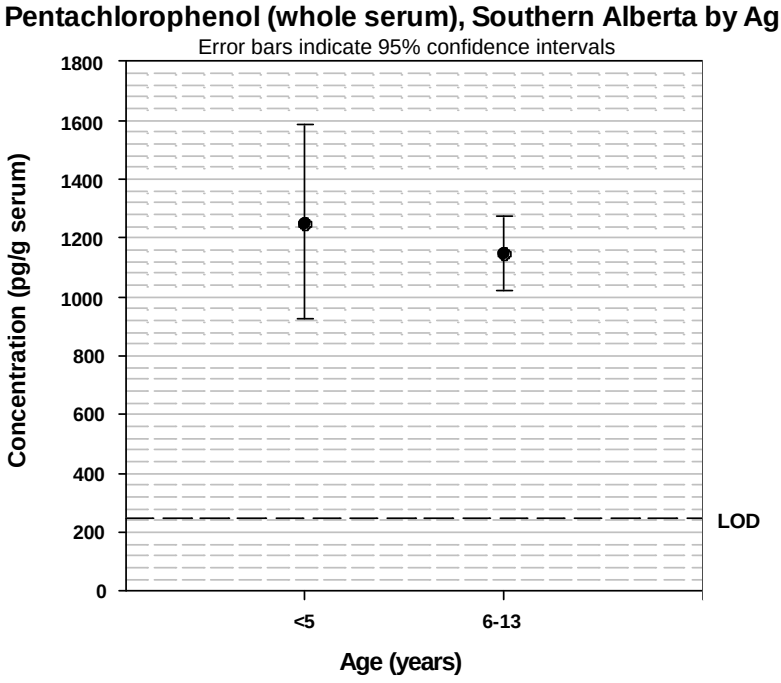


Figure 47

METALS AND MINERAL MICRONUTRIENTS

In the present study, the following metals were measured in blood serum samples of children in Alberta:

Mineral Micronutrients	Metals (Non-Micronutrients)
boron	aluminum
cobalt	antimony
copper	arsenic
iron	barium
manganese	beryllium
molybdenum	cadmium
nickel	cesium
selenium	chromium
zinc	lead
	mercury
	platinum
	silver
	thallium
	tungsten
	uranium
	vanadium

All analytes except for aluminum, antimony, arsenic, barium, beryllium, cadmium, lead, manganese, platinum, thallium, uranium, and tungsten were detected. Detailed analytical results for all detected metals are found in the subsequent sections, with an emphasis on discussion of exposure sources and possible health effects of the "non-micronutrient" metals.

METALS (NON-MICRONUTRIENTS)

Cesium (Cs)

GENERAL INFORMATION

Sources

Cesium (Cs) is a minor naturally occurring chemical element that enters the environment from natural processes such as weathering of rocks and minerals.[249] In the environment natural cesium exists as a stable isotope (^{133}Cs) and as various naturally occurring compounds including hydroxides, carbonates, iodides and bromides. Such cesium compounds are used in a wide variety of products including alkaline storage batteries, photoelectric cells, optical instruments and glasses, and atomic clocks.[249] Cesium can be released into the environment (air, water and soil) through use or disposal of such products, and also through mining and various industrial processes. After release to the environment, it can travel long distances in air including to remote regions far from the source. Absorption, ingestion and inhalation of food, water, soil, and air containing trace concentrations of cesium are the background sources of cesium exposure for the general population. People may be exposed to higher amounts of cesium in occupational settings where cesium-containing products are made.

Possible Health Effects

The human health effects of cesium depend on the dose, the length and timing of exposure, and other physiological factors. Background concentrations of ^{133}Cs in humans are not known to cause any adverse health effects.[249] Human studies addressing possible health effects from long term exposure to higher concentrations of cesium are very limited.[249]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations of cesium ranged from 0.48 ng/mL to 0.64 ng/mL. Concentrations of cesium (Figure 49) are not significantly different between the <5 year and 6–13 year age groups. However, concentrations in both of the children's age groups were higher than the concentrations in the 18–25 year old pregnant women. Concentrations in the 6–13 year olds were lower than in the 31+ year old pregnant women. In the U.S. National Health and Nutrition Survey (NHANES, 2003–2004) (Fourth Report, CDC) the geometric mean of cesium concentration in urine samples of children was 5.21 ng/mL[40], but that result cannot be compared to the present results from serum samples.

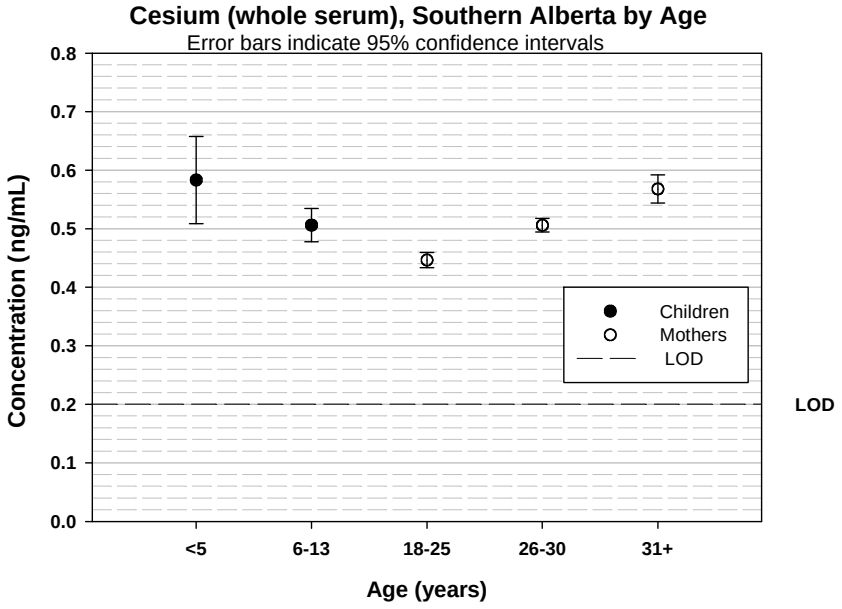


Figure 49

Chromium (Cr)

GENERAL INFORMATION

Sources

Chromium (Cr) is a naturally occurring chemical element that enters the environment from natural processes and sources such as weathering of rocks and minerals and volcanic eruptions. In the environment it may exist in several chemical forms such as metallic chromium Cr(0), Cr(III) or Cr(VI). These are used in, or found in, a wide variety of products including steel products, dyes and paints, chrome plating and magnetic tape.[250] Chromium can be released into the environment (air, water and soil) through use or disposal of such products and also through mining and various other industrial processes. Absorption, ingestion, and inhalation of food, water, soil, and air containing trace concentrations of chromium are the background sources of exposure to the general population. People may be exposed to higher chromium concentrations in occupational settings where chromium-containing products are manufactured or used.[250]

Possible Health Effects

The human health effects of chromium depend on the dose, the form of chromium present in the environment, the length and timing of exposure, and other physiological factors. Chromium (III) is an essential micro-nutrient, whereas chromium (VI) is considerably more toxic. Under a high dose long-term exposure scenario, such as in the case of accidental releases and unusual occupational exposures, chromium (VI) may cause adverse health effects such as irritations to eyes, skin, mucous membranes and nose, and problems with the digestive system. It is likely that children would have the same health effects as adults.[250]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations for total chromium ranged from 0.79 ng/mL to 1.20 ng/mL. Chromium concentrations (Figure 50) are essentially the same between the <5 and 6–13 year old groups. Concentrations in both of the children's age groups are lower than those in all of the pregnant women. The Alberta results are low compared with other studies. Serum chromium measured in healthy Iranian children with a mean age of twelve years was 77 ng/mL.[251] Mean serum chromium in Taiwanese preschool children aged three to six living in Taichung city was measured to be 295 (± 233) ng/mL. Those living in ten urban townships had mean serum chromium concentrations of 324 (± 160) ng/mL.[252] A Swedish study measured serum chromium concentrations in children aged four to sixty five months to be 0.73 (±0.72) ng/mL.[253] Serum chromium was measured in a Chinese study to be 48.4 ng/mL (newborns), 24.3 ng/mL (one year olds), 22.1 ng/mL (three year olds), 18.2 ng/mL (seven year olds) and 18.7 ng/mL (twelve year olds).[254]

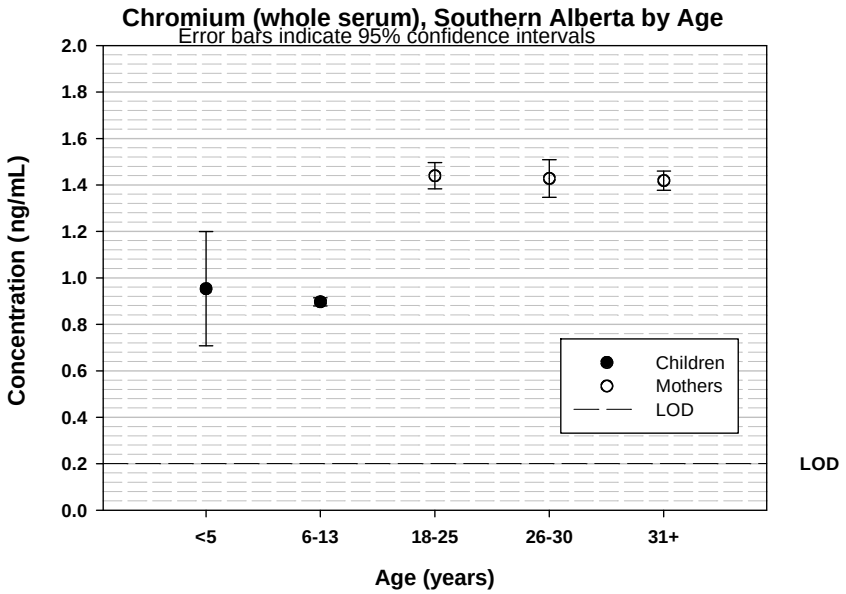


Figure 50

Silver (Ag)

GENERAL INFORMATION

Sources

Silver (Ag) is a naturally occurring chemical element that enters the environment through natural processes, including the natural weathering of rocks.[255,256] In the environment, silver exists in various chemical forms including elemental silver, silver nitrate, silver chloride, silver sulphide, and silver oxide. These silver compounds may also be used in a wide variety of industrial and commercial products such as jewellery, silverware, photographic materials, coins, dental fillings, electronic equipment, medicines and medical devices.[255-259] Silver can be released into our homes and into the environment (air, water and soil) through use or disposal of such products, through mining, and various industrial processes. Absorption, ingestion and inhalation of food, water, soil, and air containing trace levels of silver are the common sources of background silver exposure for the general population.

Possible Health Effects

The human health effects of silver depend on the dose, the form of silver to which we are exposed, the length and timing of exposure, and other physiological factors. At background exposure concentrations silver is not known to cause any adverse health effect.[256] Under a high dose long-term exposure scenario, such as in the case of accidental releases and unusual occupational exposures, silver may cause adverse health effects such as arygria (a blue-grey staining of the skin, eyes, nose and other body tissues), skin rashes, headaches, and coughing or other respiratory problems.[256,260,261] Silver can cross the placental barrier and concentrations have been shown to be higher in neonates and infants than in older children and adults.[262]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations for silver ranged from 0.08 ng/mL to 0.14 ng/mL. Concentrations of silver (Figure 51) are not significantly different between the <5 and 6–13 year age groups. Concentrations of silver in children are lower than in all of the pregnant women.

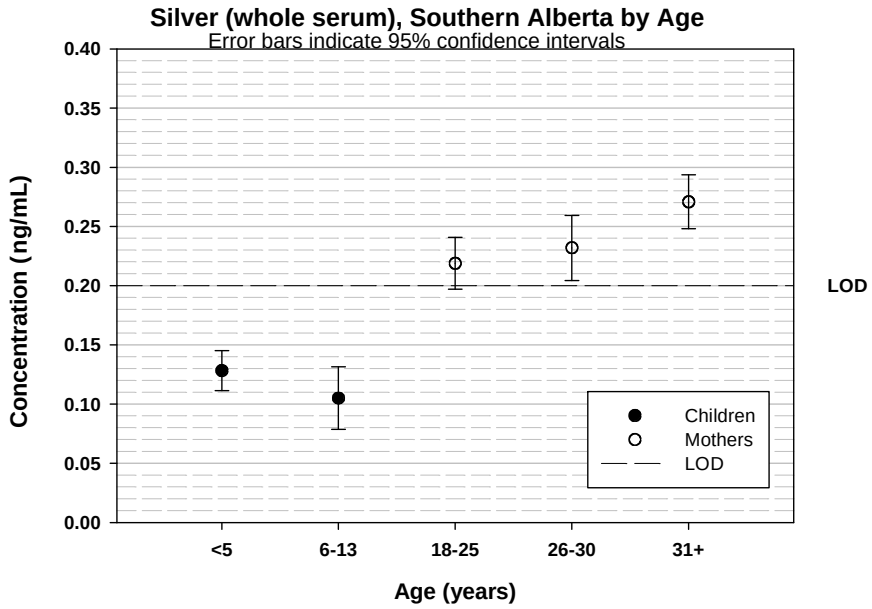


Figure 51

Vanadium (V)

GENERAL INFORMATION

Sources

Vanadium (V) is a naturally occurring chemical element that can be found in mineral rocks. In the environment it exists in the form of various vanadium compounds such as vanadium oxide, vanadium sulphate and vanadium chloride. These vanadium compounds are used in or found in a wide variety of products including steel products, aircraft engines, automobile parts, rubber, plastics and ceramics.[263] Vanadium can be released into the environment (air, water and soil) through use or disposal of such products and also through mining, burning of fuel oils, and various other industrial processes. Absorption, ingestion and inhalation of food, water, soil and air containing trace concentrations of vanadium are the background sources of exposure for the general population. People may be exposed to higher vanadium concentrations in occupational settings where vanadium-containing products are manufactured or used.[263]

Possible Health Effects

The human health effects of vanadium depend on the dose, the form of vanadium present in the environment, the length and timing of exposure, and other physiological factors. Background concentrations of vanadium in humans are not known to cause any adverse health effects.[263] Under a high dose long-term exposure scenario, such as in the case of accidental releases and unusual occupational exposures, vanadium may cause adverse health effects such as eye irritation, sore throat and coughing or other respiratory problems.[263]

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentration for vanadium ranged from 0.28 ng/mL to 0.34 ng/mL. Vanadium concentrations (Figure 52) are essentially the same between the <5 and 6–13 year age groups. Concentrations are not significantly different between the children and the pregnant women. Vanadium was measured in whole blood of children aged nine to thirteen living near Prague. The median was 0.042 ng/mL (range: 0.024–0.226 ng/mL) in control children[264], but these values cannot be directly compared to the serum values in the present study.

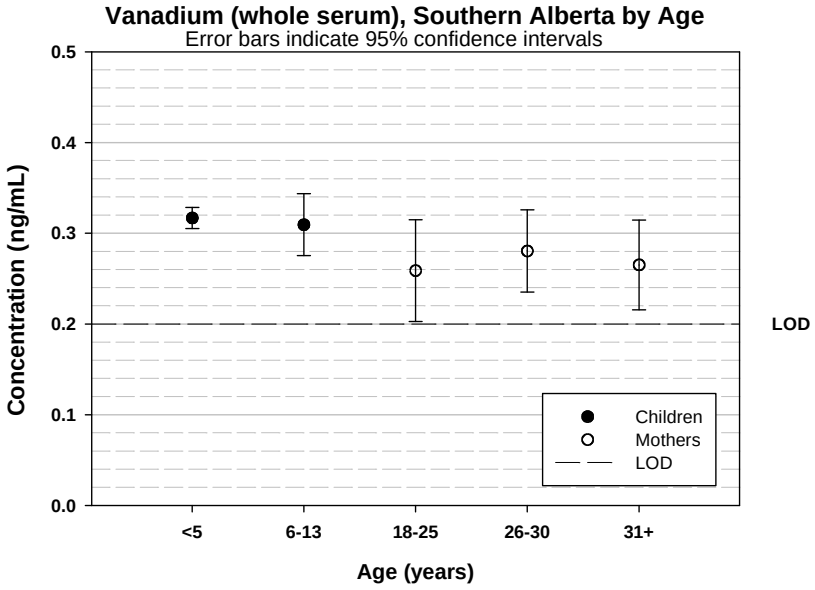


Figure 52

MINERAL MICRONUTRIENTS

Mineral micronutrients are metals needed in small quantities to sustain life. Although high exposure to micronutrients may also represent health risks and Health Canada sets allowable limits for many of these metals in natural health products, the normal public health focus is to ensure populations are receiving an adequate supply. Thus, exposure sources and possible health effects arising from very high exposure to mineral micronutrients have not been reviewed here, and nutritional aspects are beyond the scope of the current report. In general, however, humans ingest mineral micronutrients in the diet, including fruits and vegetables, animal products, and drinking water. The ultimate source of mineral micronutrients is soil and water. Thus, human serum concentrations are anticipated to vary by region with local soil and drinking water chemistry.

Boron (B)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean boron concentration in blood serum of children in Alberta ranged from 29 ng/mL to 33 ng/mL. Boron concentrations (Figure 53) are essentially the same between the <5 and 6–13 year age groups, but concentrations in all children are significantly higher than in all pregnant women.

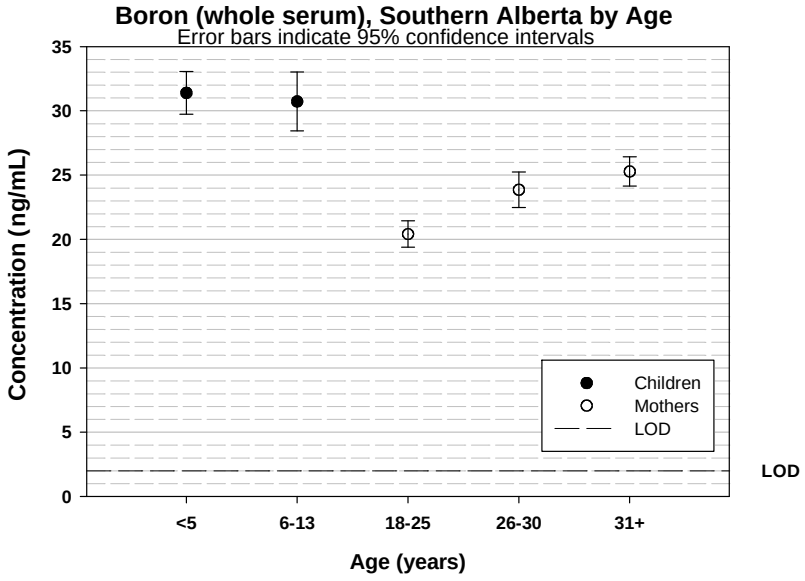


Figure 53

Cobalt (Co)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations of cobalt (Co) ranged from 0.16 ng/mL to 0.20 ng/mL. There was no difference in concentration between the <5 and 6–13 year age groups (Figure 54). However, the concentrations of cobalt in children are lower than those in all of the pregnant women. Mean concentrations of cobalt in the children are below the LOD of 0.2 ng/mL. Serum cobalt concentrations of healthy children with a mean age of twelve living in Iran were 50 ng/mL.[251] Serum cobalt in Bulgarian children with a mean age of 12.9 was determined to be 407 ng/mL.[265] Serum cobalt was measured in a Chinese study to be 164.1 ng/mL (one year olds), 85.7 ng/mL (three year olds), 120.8 ng/mL (seven year olds), and 84.2 ng/mL (twelve year olds).[254] It is not clear why other studies have found such high concentrations of cobalt compared to the current study.

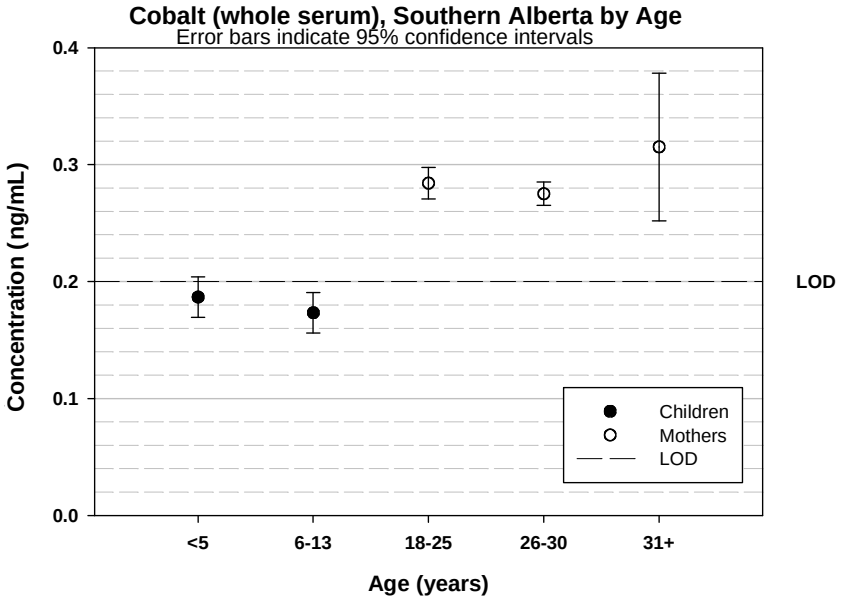


Figure 54

Copper (Cu)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations of copper (Cu) ranged from 1070 ng/mL to 4516 ng/mL. Concentrations of copper (Figure 55) were not significantly different between the <5 and the 6–13 year groups. One sample in the 6-13 year group had a very high concentration of copper, resulting in a large standard deviation that could not be explained by our quality control program. The concentrations in the <5 year group are lower than the concentrations in all of the pregnant women. Copper concentrations were measured in the serum of Iranian children of an average age of twelve to be 610 ng/mL.[251] Copper in the serum of healthy Argentinian children aged four to ten years was measured to be 997 ng/mL.[266] Mean serum concentrations measured in Greek children were 1859 ng/mL (<5 years), 1564 ng/mL (six to ten years), and 1525 ng/mL (>ten years).[267] A Swedish study of healthy children aged four to sixty five months determined serum copper to be 1380 (±350) ng/mL.[253] Copper serum concentrations were measured in a Chinese study in newborns (548 ng/mL), one year olds (1344 ng/mL), three year olds (1516 ng/mL), seven year olds (1289 ng/mL), and twelve year olds (1059 ng/mL).[254]

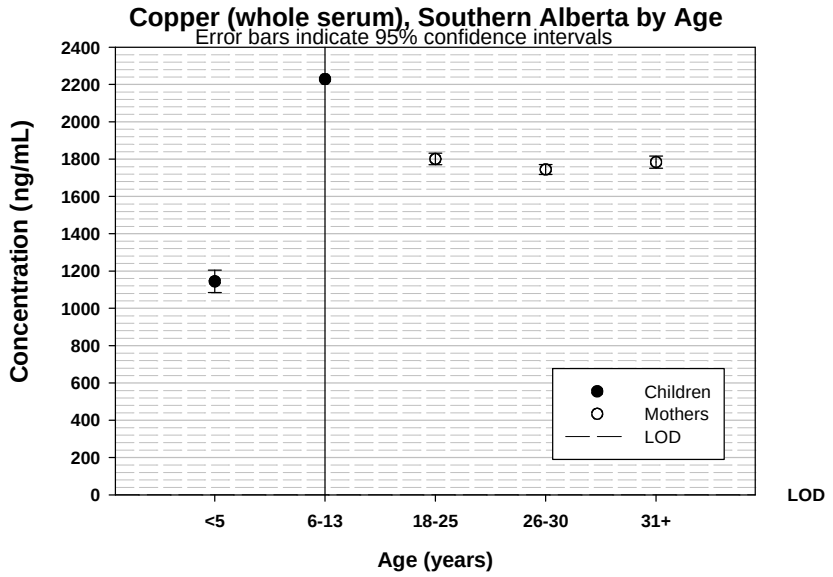


Figure 55

Iron (Fe)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations for iron (Fe) ranged from 1266 ng/mL to 1318 ng/mL. The concentrations of iron (Figure 56) in the <5 and 6–13 year age groups are not significantly different. Concentrations between the children and the pregnant women are not statistically different. All concentrations are above the limit of detection of 10 ng/mL. A study of Nigerian children determined serum iron to be 949 ng/mL (<five years old) and 1206 ng/mL (five to eight years).[268] A Turkish study measured serum iron in healthy one to four year olds to be 720.4 ng/mL.[269] Serum iron was measured in Taiwanese preschool children aged three to six living in Taichung city as 2430 ng/mL. Those children living in ten urban townships had mean serum iron concentrations of 3180 ng/mL.[252] A Swedish study measured serum iron concentrations in children aged four to sixty five months to be 1150 (± 380) ng/mL.[253] Iron concentrations were measured in a Chinese study to be 1455 ng/mL (one year olds), 1513 ng/mL (three year olds), 1369 ng/mL (seven year olds), and 1553 ng/mL (twelve year olds).[254]

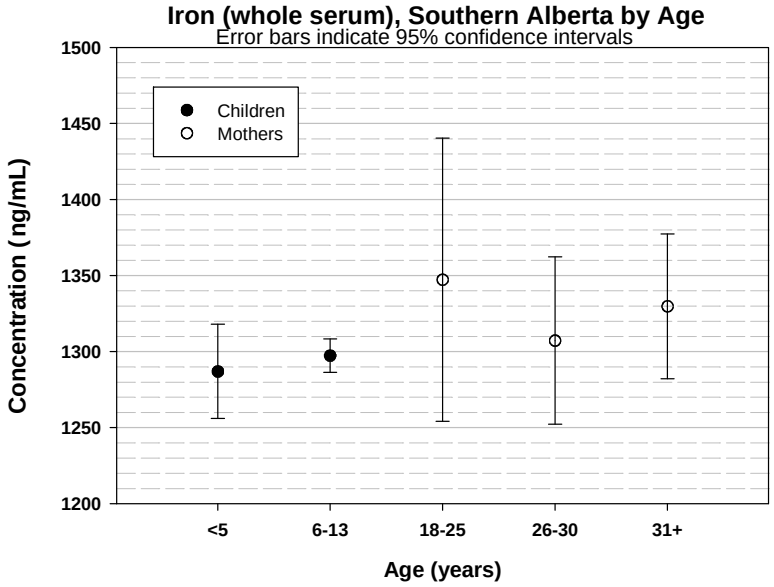


Figure 56

Molybdenum (Mo)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentrations of molybdenum (Mo) ranged from 2.46 ng/mL to 3.58 ng/mL. Molybdenum concentrations (Figure 57) in the <5 year group are higher than those in the 6–13 year group, and concentrations in all children samples were significantly higher than those in all pregnant women samples. A Chinese study examining trace elements in children's serum determined molybdenum concentrations to be 30 ng/mL (one year olds), 16.6 ng/mL (three year olds), 21.0 ng/mL (seven year olds) and 15.0 ng/mL (twelve year olds).[254] These values are greater than those measured in the present study.

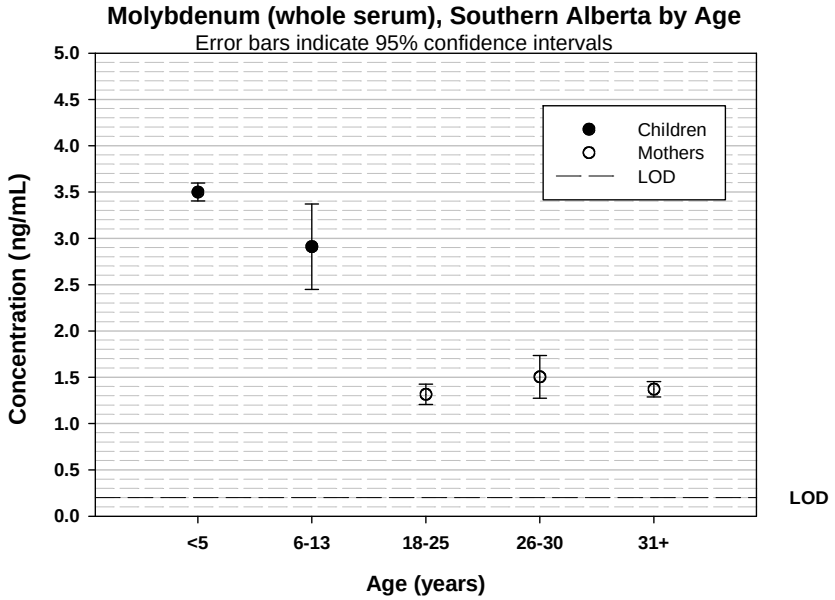


Figure 57

Nickel (Ni)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, mean concentration of Nickel (Ni) ranged from 1.16 ng/mL to 1.32 ng/mL. Nickel concentrations (Figure 58) are essentially the same between the <5 and 6–13 year age groups, but concentrations in the children were higher than those in the pregnant women. Serum nickel was measured in Iranian children of an average age of twelve and the mean determined to be 56 (±57) ng/mL.[251] A Swedish study determined mean serum nickel concentrations in healthy children aged four to sixty five months to be 0.66 (±0.45) ng/mL.[253] A Chinese study measured serum nickel concentrations to be 21.9 ng/mL (one year olds), 18.4 ng/mL (three year olds), 21.0 ng/mL (seven year olds), and 15.0 ng/mL (twelve year olds).[254]

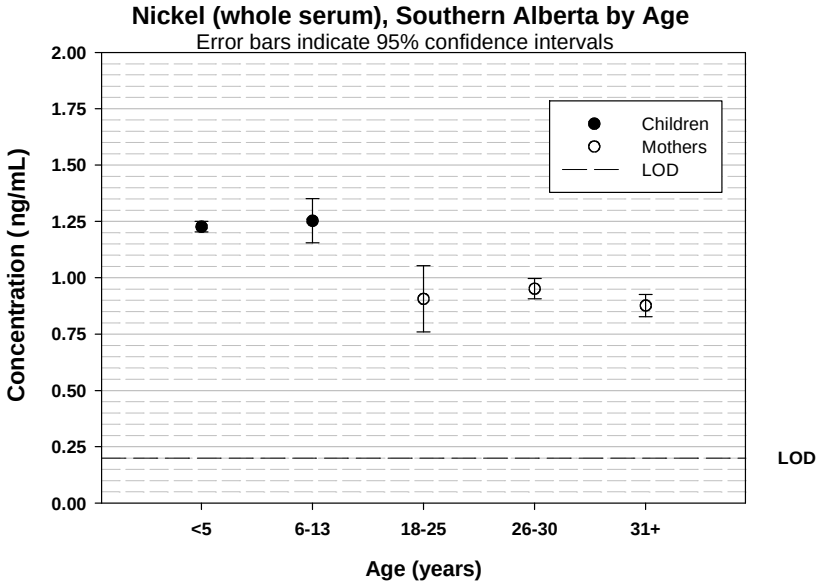


Figure 58

Selenium (Se)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, the mean concentration of selenium (Se) ranged from 111 ng/mL to 124 ng/mL. Concentrations of selenium (Figure 59) are essentially the same between the <5 and 6–13 year age groups, but concentrations were significantly lower than in all pregnant women. All concentrations are greater than the limit of detection of 0.5 ng/mL. Serum selenium measured in healthy Swedish children aged four to sixty five months was 98 (± 32) ng/mL.[253] A study of Tehranian children determined serum selenium concentrations to be 63.72 (±20.29) ng/mL (<four years) and 75.82 (±13.42) ng/mL (four to sixteen years).[270] Mean serum selenium concentrations in New Zealand children aged five to fourteen were determined in the 2002 National Children's Nutrition Survey to be 75.8 ng/mL.[271]

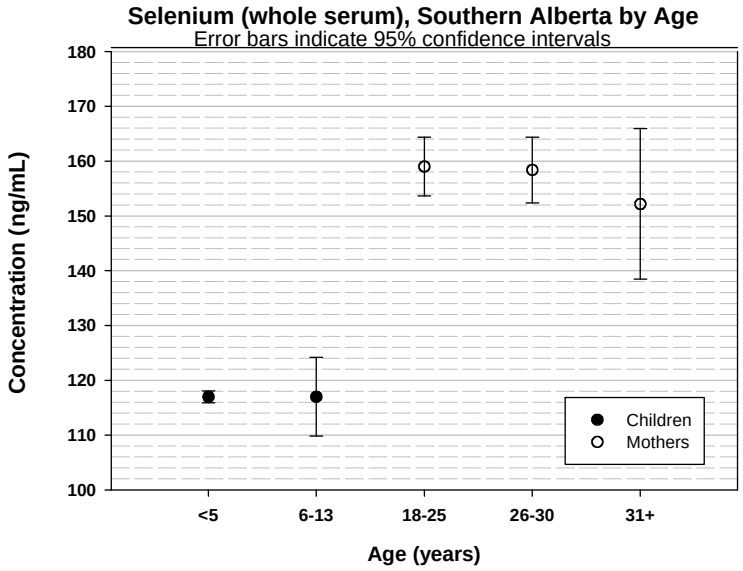


Figure 59

Zinc (Zn)

BLOOD SERUM CONCENTRATIONS IN CHILDREN IN ALBERTA

Concentrations and Trends

Overall, the mean concentration of zinc (Zn) ranged from 809 ng/mL to 869 ng/mL. Concentrations of zinc (Figure 60) are essentially the same between the <5 and the 6–13 year age groups, but concentrations in all pregnant women are significantly higher than those in the children. All concentrations are well above the limit of detection of 5 ng/mL. A Swedish study determined serum zinc concentrations in children aged four to sixty five months to be 970 (± 180) ng/mL.[253] Serum zinc was determined in a control group of Indian children aged six months to five years to be 1095 (± 173) ng/mL.[272] A study of healthy Belgian children determined serum zinc concentrations to be 759 ng/mL (<one year old) and 837 ng/mL (one to four years old).[273] A Chinese study determined serum zinc concentrations to be 1090 ng/mL (newborns), 1018 ng/mL (one year olds), 1198 ng/mL (three year olds), 1178 ng/mL (seven year olds), and 1037 ng/mL (twelve year olds).[254]

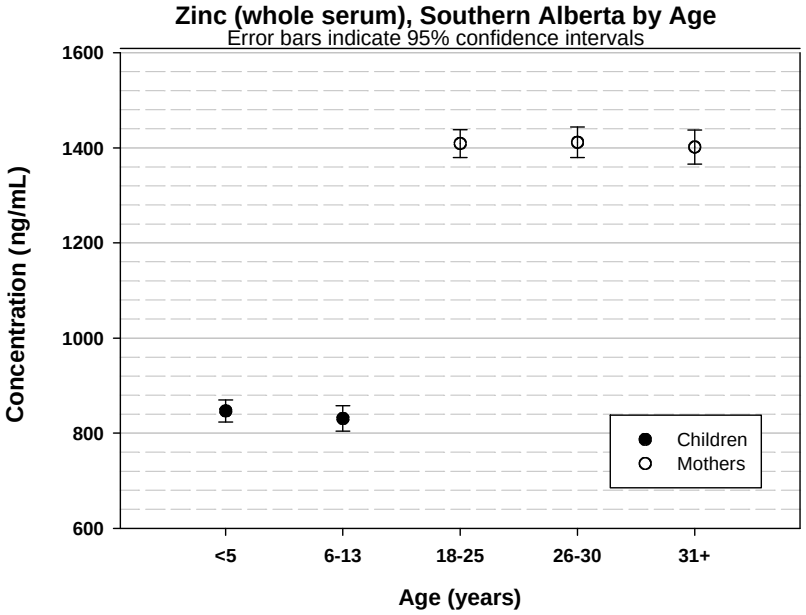


Figure 60

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Glossary Of Terms

Bioaccumulation	Accumulation of substances in an organism (plant, animal or human) above what is in the environment (e.g., water, air, food).
Man-made Chemicals	Chemicals that are produced by human activities, either intentionally or non-intentionally, and which are not normally found in the environment.
Naturally Occurring Chemicals	Chemicals that are present or produced naturally in the environment. Some man-made chemicals are also naturally occurring.
Serum	The clear yellowish liquid part of whole blood. It is obtained by clotting the whole blood and then separating the liquid from the solids.
Metabolite	A substance produced from another precursor substance through metabolic transformation (by enzymes or microorganisms in our bodies)
Aliquot	A small portion of the total sample
Persistent	Resistant to degradation processes in our bodies or in the environment
Lipid	Synonym of "fat"
Lipophilic	"Fat loving" – can be easily dissolved in lipids
Background Concentration of Chemicals	A subjective term normally used to describe the baseline concentration of a chemical in humans or the environment where there has been no occupational or accidental exposure to high concentrations.
LOD	Limit of detection
LOQ	Limit of quantitation
Mean Concentration	Also known as the average concentration, or arithmetic mean.
Median Concentration	For a list of concentrations arranged from lowest value to highest concentration, the middle concentration (or the average of the two middle concentrations) is the median.
Geometric Mean Concentration	For a list of n numbers, the numbers are multiplied and then the n^{th} root of the resulting product is taken.

Conversion Of Measurement Units

Units	Abbreviations	Values/Conversions
liter	L	
deciliter	dL	10^{-1} L
milliliter	mL	10^{-3} L
microliter	μL	10^{-6} L
gram	g	
microgram	μg	10^{-6} g
nanogram	ng	10^{-9} g
picogram	pg	10^{-12} g
1 μg/g serum[1,2]	equivalent to approximately 1 μg/mL or 1 mg/L serum	
1 ng/g serum[1,2]	equivalent to approximately 1 ng/mL or 1 μg/L serum	
1 pg/g serum[1,2]	equivalent to approximately 1 pg/mL or 1 ng/L serum	

[1] Can also be reported per mass of serum lipid. In such a case, the denominator is the mass of lipid (fat) in the volume or mass of serum analyzed. This is only done for chemicals that are known to associate primarily with lipids.
[2] Serum concentrations can be reported by mass or volume. The final units reported depend on whether the lab analyzed a specific mass, or specific volume, of serum. For the sake of comparison among studies in this report 1 g of serum can be considered approximately equivalent to 1 mL of serum.