




International POPs Elimination Project

Fostering Active and Efficient Civil Society Participation in Preparation for Implementation of the Stockholm Convention

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Reproductive Health Effects Associated with Exposure to PCBs Among Natives of the Russian Arctic

Study of the Impacts of Some Congeners of Polychlorinated Biphenyls (PCBs) on the Reproductive Health of Indigenous Peoples of the Russian Arctic

The North-western Centre of Hygiene and Public Health

Co-ordinator – Alexey Dudarev
E-mail: dudarev@sp.ru

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About the International POPs Elimination Project

On May 1, 2004, the International POPs Elimination Network (IPEN http://www.ipen.org) began a global NGO project called the International POPs Elimination Project (IPEP) in partnership with the United Nations Industrial Development Organization (UNIDO) and the United Nations Environment Program (UNEP). The Global Environment Facility (GEF) provided core funding for the project.

IPEP has three principal objectives:

- Encourage and enable NGOs in 40 developing and transitional countries to engage in activities that provide concrete and immediate contributions to country efforts in preparing for the implementation of the Stockholm Convention;

- Enhance the skills and knowledge of NGOs to help build their capacity as effective stakeholders in the Convention implementation process;

- Help establish regional and national NGO coordination and capacity in all regions of the world in support of longer term efforts to achieve chemical safety.

IPEP will support preparation of reports on country situation, hotspots, policy briefs, and regional activities. Three principal types of activities will be supported by IPEP: participation in the National Implementation Plan, training and awareness workshops, and public information and awareness campaigns.

For more information, please see http://www.ipen.org

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This report is available in the following languages: English, Russian

Abbreviations

PCBs – polychlorinated biphenyls.
Sum_PCB – sum of 15 PCB congeners.
GM – geometric mean.
max – a maximal value.
n – number of observations.
p – value – statistical confidence.
r – correlation coefficient.
NAD – Nenetskiy Autonomous District.
TAD – Taymyrskiy Autonomous District.
CAD – Chukotskiy Autonomous District.
BD – birth defects.
PFs – pregnancy failures.

The project was implemented with financial support from the International POPs Elimination Project, in co-operation with Eco-Accord Centre, at the base of compiled information collected in the course of implementation of several projects. The large scale project of GEF/AMAP/RAIPON - Persistent Organic Pollutants, Food Safety and Indigenous Peoples of the Russian North (2000-2004) - provided the bulk of database materials (2/3) that were used in this project. Another 30% of the information was collected later.

1. Introduction

For the first time in the Russian Federation, large-scale studies, implemented with the participation of the North-western Centre of Hygiene and Public Health in 2001-2005, in the Arctic regions of Russia, revealed that levels of persistent toxic substances (PTS), including polychlorinated biphenyls (PCBs) in environmental media of main areas of residence of Indigenous Peoples of the Russian Far North (Murmansk Oblast, Nenetskiy Autonomous District, Taymyrskiy Autonomous District, Chukotskiy Autonomous District) are fairly high and are compatible with pollution levels in other Arctic regions (Greenland, Alaska, Canada).

The study results revealed high levels of PCBs in individual blood samples of Indigenous residents of the Arctic. These data suggest accelerated human intake of these PTS among Indigenous residents of the Russian Far North, due to contamination of their environment and traditional food.

In the case of Indigenous Arctic peoples, key sources of excessive human intake of PCBs were found to incorporate consumption of polluted fish, sea animals and (sometimes) game animals. These food products are contaminated due to global transfer of pollutants and local pollution sources that cause secondary contamination of food in the course of food storage and cooking.

For the first time, we found that, in all regions, substantial risks of adverse health impacts of PCBs are *inter alia* associated with intensive contamination of indoor environment of residential and public buildings (mainly due to uncontrolled use of technical liquids, 100% of which, according to results of a special sampling study, were contaminated by PCBs.

The traditional food of Indigenous Peoples of the Russian Arctic cannot be assessed as safe. Estimates based on chemical analysis data (PCBs levels in hundreds of samples of traditional

food products) suggest that PCBs intakes by adults (per 1 kg body weight) from traditional food (fish, meat, animal fat and inner animal parts) often substantially exceed recommended limits.

Research studies revealed substantial levels of PTS in blood of pregnant women representatives of Indigenous Peoples of the Far North of the Russian Federation. In many cases, levels of specific highly toxic substances (particularly PCBs) substantially exceeded recommended WHO limits. PCBs are known to impact adversely on reproductive functions and foetal development (ATSDR, 2003). High concentrations of PCBs in blood affect nervous, endocrine and immune systems. Some toxic substances act as hormone-imitators, they suppress production of natural hormones and disrupt hormone-regulated processes such as spermatogenesis, ovulation and sexual development. Due to their solubility in fat, PCBs easily cross the placental barrier and intensely accumulate in the foetus (supplied by maternal blood) or in an infant's body (supplied by breast milk).

Among other adverse effects, that were found to correlate statistically with blood levels of PCBs, it is worth noting substantially higher incidence of low birth weight, cases of premature birth, abortions, stillborn cases, birth defects and alteration of the ratio of boys to girls in newborns.

For the first time, the statistically significant relative risk of premature birth and low birth weight of newborn babies of Indigenous women was found to correlate with elevated levels of PCBs in blood serum (over 4.0 μg/l.)

Average PCBs levels in the blood of mothers with pregnancy failures (birth defects, stillborn babes) are 1.7 – 2.0 times higher than in mothers without pregnancy failures. Some correlation was also found between the incidence of spontaneous abortions and higher PCBs levels in blood.

The above correlation between incidence of pregnancy failures and PCBs impacts is further confirmed by clear dose-dependency - i.e. higher levels of toxic substances in maternal blood cause shorter pregnancy terms and higher incidence of low or very low birth weight cases, as well as a higher incidence of birth defects and other lethal cases.

Effects that had been identified in the course of these research studies need further in-depth study, however, potentially serious adverse health effects for the current generation and particularly for generations to come, necessitate the development and approval of urgent actions to reduce the adverse impacts of PTS on the health of Indigenous Arctic peoples.

First of all, in order to address the problem, it is necessary to develop and implement local and regional programs for identification and elimination of all sources of environmental releases of PTS, to inform local residents on safe methods of storage, processing and cooking of traditional food products, and to modernise prenatal prevention of pregnancy failures.

2. The project description

Aims and objectives

The aim of the project - to assess potential specific impacts of individual PCB congeners (of different types) on the reproductive health of Indigenous Peoples of the Russian Arctic.

Project objectives:

To analyse, using the extended database of 346 puerperae (including personal health status data, reproductive case history, health status of their newborn babies, and personal data on PCBs levels in maternal blood, including individual levels of 15 PCBs congeners):

- menstrual status (age of first menstruation, menstruation duration, menstrual cycle, intensity of menstrual pain and spasms);
- pregnancy failures (premature birth, stillborn babes, ectopic pregnancies);
- foetal pathology (low bight weight, birth defects);
- boy to girl ratios among the newborn babies;
- potential dose - effect dependencies between menstrual status, pregnancy failures, boy/girl ratios and concentrations of different PCB congeners in maternal blood;

3. Materials and methods.

3.1. Research study objects.

The study included pregnant women who were representatives of Indigenous Peoples that permanently reside in the transpolar and subpolar regions of the Russian Far North.

3.2. Geography of the research study and groups under study.

Four regions of residence of pregnant Indigenous women were selected for the mainstream PCB research:

1. Kola Peninsula (Murmansk Oblast). The study area covered Lovozero township, the key settlement of the Lapps, and Krasnostchelie township.
2. The downstream section of the Pechora river (Nenetskiy Autonomous District), with predominantly Nentsy residents. Research studies were conducted in Narian-Mar (pregnant women were transported to the city clinics from different townships, inc. Nelmin Nos, Indiga, etc).
3. Taymyr Peninsula (Taymyrskiy or Dolgano-Nenetskiy Autonomous district). Research studies were conducted in Dudinka (mainly populated by the Nentsy) and in Khatanga township (mainly populated by the Dolgany).
4. Chukotskiy Peninsula (Chukotskiy Autonomous District). Two research areas were selected, with substantial differences in lifestyles of Indigenous Peoples: continental Anadyr district where the reindeer-breeding Chookchi live and the coastal North-eastern part of the peninsula where local Chukchi and Escimo residents traditionally hunt sea animals.

The study covered pregnant Indigenous women who, in 2001-2002, were hospitalised in maternity wards of clinics in Olenegorsk (Murmansk Oblast), Narian-Mar (NAD), Dudinka and Khatanga township (TAD), Anadyr, Ugolnye Kopi township and Lavrentia township (CAD). Several women were examined at Kamchatka Peninsula, in the maternity ward of the oblast-level clinic of Petropavlovsk-Kamchatski. To collect information on control groups, similar studies were conducted among pregnant women in Norilsk (TAD) and Urgench (the environmental crisis area of the Aral Sea, Uzbekistan).

There are 117 human settlements of Indigenous Peoples within the study area. Ethnic groups of these settlements (containing a relatively small overall number of residents) represent almost 2/3 of the overall ethnic composition of Indigenous Peoples of the Russian Arctic. As a result, the

selected regions under study allowed us to assemble a representative sample of key ethnic/genetic groups of the whole Russian North that follow traditional local household, social and cultural lifestyles and have specific diets.

In order to estimate PCBs levels in the blood of pregnant Indigenous women of the Arctic, samples of maternal blood and cord blood of the newborn were taken. In parallel with blood sampling, all participants of the study were interviewed in detail.

Table 1. Completed questionnaires and blood samples analysed

Study areas	**n**
Murmansk Oblast	16
Nenetskiy AD (NAD)	38
Taymyrskiy AD (TAD)	69
Chukotskiy AD (CAD) – coastal zone	59
Chukotskiy AD (CAD) – continental zone	67
Kamchatka	8
Norilsk (TAD)	59
Urgench (the Aral Sea zone)	30
Total	**346**

3.3. Polychlorinated biphenyls under study (PCBs).

Fifteen congeners of polychlorinated biphenyls (PCBs) were measured in samples of blood of pregnant women and cord blood of their newborn babies: # 28(31), 52, 99, 101, 105, 118, 128, 138, 153, 156, 170, 180, 183 and 187, and overall PCBs levels were measured.

3.5. Analytical methods and quality control.

PCBs levels in blood samples were measured by the "Taifun" R&D facility in Obninsk (Kaluga Oblast), the Arctic Monitoring Regional Centre in St.-Petersburg, Unilab Analysis AC in Tromce (Norway) and by the Toxicology Centre of Quebec (Canada).

Qualitative analysis of PCBs was conducted by gas chromatography with electron capture detection (ECD). In addition, samples with abnormal composition of pollutants or abnormally high contamination levels were analysed by GC-MS to ascertain presence of the pollutants analysed. In the latter case, the same purified extracts were used that were analysed by GC-ECD.

All solvents were additionally rectified. All gases, used for analytical purposes, were at least of 5-0 purity grade. All standard samples of PCBs for graduation purposes were produced by Ultra Scientific (USA) with ISO 9001 certification.

The quality of analytical services of all four laboratories, that participated in the project, was confirmed in the course of testing of PCBs samples in the framework of international round robin tests including the ones conducted under the auspices of AMAP.

3.6. Questioning and interviewing methodologies.

Interviewing of pregnant women and collection of blood samples (simultaneously with sampling of cord blood) were particularly important in terms of coverage of the "risk group".

Pregnant Indigenous women were interviewed in maternity wards of clinics by medical staff members who underwent special training. Questionnaires contained information on ethnic groups, living conditions, marital status, employment, income levels, diets (particularly traditional ones), unhealthy habits, application of insecticides, hunting, fishing and health status. In addition, questionnaires incorporated sections on reproductive case history of the women surveyed (outcomes of pregnancies, parameters of their newborn babies, individual features of menstrual cycle, prior health problems) and data from the medical records of their newborn children.

3.7. Methods of statistical and epidemiological analysis.

Standard data processing methodologies were used to process medical data (with application of MKB-10 , the International Classification of Diseases (ICD), Revision 10 (1989), and dose load data to analyse effects. We applied correlation analysis, dispersion analysis and factor analysis, as well as risk analysis methods.

SPSS and Excel software was used for computerised data processing.

4. Results and discussion.

The report provides results of chemical analysis of PCBs in maternal blood and further analysis of PCBs impacts on maternal and foetal health (at the base of tests of maternal blood only). All analysed effects, including weight of the newborn, depend on maternal health, as results of testing of cord blood would not allow us to analyse impacts of PCBs on maternal health. Besides that, a close correlation was confirmed between PCBs levels in a mother's body and her foetus, because PCBs can easily penetrate the placentary barrier.

4.1 PCBs levels in maternal blood.

In geographic terms (see Table 2), the highest levels of almost all PCB congeners were found in blood of women residents of the North-western coastal areas of Chukotka. These results are clearly associated with their diets (fat of sea mammals, containing high levels of PCBs). However, close to maximal levels (in the overall array) were registered in continental Chukotka (congeners 99; 101; 118; 128; 156; 183), in NAD (congeners 128; 156; 170; 180; 187), in TAD (congeners 128; 156; 183), i.e. in reindeer breeding regions, where food chains were probably not contaminated by globally transferred PCBs. In reindeer breeding regions people eat venison which is lean and therefore contains a lower accumulation of organochlorine substances. We may assume that congeners 128; 156 – 187 in these regions are of local origin. These pollutants may be associated with secondary contamination of food by specific PCBs mixtures that were applied earlier (or are still present) nearby areas of residence, hunting or fishing of Indigenous Peoples.

Table 2. Geometric mean and maximal concentrations (µg/L) of individual PCB congeners in maternal blood by regions.

# PCB congener µg/L		Murmansk Oblast	NAD	TAD	CAD (cont.)	CAD (coast.)	Kamchatka	Norilsk	Aral Sea Zone	Total
	n	16	38	69	67	59	8	59	30	346
#28/31	G/mean	0.025	0.021	0.044	0.042	0.080	0.032	0.007	0.021	0.038
	Max	0.113	0.058	0.111	0.173	1.122	0.048	0.061	0.200	1.122
#52	G/mean	0.009	0.018	0.041	0.027	0.060	0.012	0.007	0.011	0.029
	Max	0.040	0.107	0.120	0.196	1.454	0.020	0.074	0.146	1.454
#99	G/mean	0.105	0.084	0.151	0.109	0.380	0.096	0.163	0.059	0.165
	Max	0.204	0.230	0.360	0.728	0.875	0.186	0.493	0.550	0.875
#101	G/mean	0.032	0.032	0.060	0.052	0.081	0.014	0.009	0.017	0.044
	Max	0.142	0.281	0.370	0.689	0.754	0.027	0.076	0.344	0.754
#105	G/mean	0.071	0.062	0.107	0.094	0.204	0.052	0.069	0.013	0.099
	Max	0.273	0.152	0.630	0.777	3.43	0.084	0.275	0.179	3.430
#118	G/mean	0.244	0.143	0.278	0.243	0.455	0.177	0.253	0.057	0.259
	Max	0.603	0.300	0.856	1.398	1.490	0.255	1.355	0.595	1.490
#128	G/mean	0.010	0.017	0.022	0.017	0.018	0.016	0.004	0.005	0.014
	Max	0.065	0.150	0.170	0.158	0.138	0.027	0.079	0.078	0.170
#138	G/mean	0.258	0.192	0.249	0.152	0.441	0.114	0.192	0.039	0.226
	Max	0.566	0.560	0.740	0.720	1.177	0.194	0.584	0.320	1.177
#153	G/mean	0.302	0.617	0.489	0.311	1.633	0.316	0.337	0.049	0.587
	Max	0.497	2.390	1.610	1.667	4.810	0.518	1.398	0.260	4.810
#156	G/mean	0.038	0.061	0.090	0.040	0.070	0.059	0.020	0.016	0.052
	Max	0.109	0.350	0.280	0.255	0.235	0.122	0.148	0.160	0.350
#170	G/mean	0.054	0.153	0.099	0.057	0.185	0.061	0.042	0.009	0.091
	Max	0.152	1.120	0.320	0.245	0.685	0.094	0.217	0.090	1.120
#180	G/mean	0.114	0.274	0.172	0.087	0.319	0.091	0.102	0.013	0.162
	Max	0.283	1.300	0.560	0.350	1.039	0.121	0.359	0.060	1.300
#183	G/mean	0.013	0.032	0.035	0.021	0.058	0.015	0.003	0.001	0.026
	Max	0.051	0.190	0.350	0.389	0.139	0.029	0.032	0.015	0.389
#187	G/mean	0.035	0.092	0.072	0.033	0.135	0.033	0.012	0.002	0.058
	Max	0.125	0.620	0.230	0.152	0.397	0.057	0.063	0.017	0.620
Sum_ PCB	G/mean	1.350	1.820	1.912	1.290	4.120	1.071	1.219	0.455	1.868
	Max	3.004	6.470	5.160	5.762	10.918	1.617	4.690	2.435	10.918

- highest geometrical mean values and maximal concentrations.

From the range of 15 PCB congeners that were analysed in the framework of the project (see Table 3), two congeners contain 3 chlorine atoms, one congener contains four chlorine atoms, four contain five chlorine atoms, four contain six chlorine atoms and four contain seven chlorine atoms. Therefore, we can compare effects of low-chlorine and high-chlorine content congeners.

Three congeners (# 105;118; and156) belong to dioxin-like compounds.

Table 3. PCB congeners under study in the project

# PCB congener	Cl atoms	Ortho-Cl	Para-Cl	Meta-Cl	Planar/non-planar compounds
# 28	3	1	2	0	planar
# 31	3	1	1	1	
# 52	4	2	0	2	non-planar
# 99	5	2	2	1	
# 101	5	2	1	2	
# 105	5	1	2	2	dioxin-like, planar
# 118					
# 128	6	2	2	2	non-planar
# 138					
# 153					
# 156	6	1	2	3	dioxin-like, planar
# 170	7	2	2	3	non-planar
# 180					
# 183	7	3	2	2	non-planar
# 187					

All 15 PCB congeners may be subdivided to 4 groups:

- # 28 – 101. Five congeners with different chemical structures and optical properties and with relatively low molecular weight compared to other congeners studied.
- # 105; 118; 156. Three dioxin-like planar congeners with 2 para chlorine atoms and (at least) 2 meta chlorine atoms, that define their high activity.
- # 128-153. Three chemically identical non-planar congeners; optical isomers.
- # 170 – 187. Four high-chlorine content non-planar congeners with almost identical chemical structures.

The percentages of individual PCB congeners in overall PCBs levels in maternal blood (see Table 4) are almost similar in all northern regions (there are some differences, compared to the Aral Sea region). Congener #153 makes the highest contribution – from 20% to 35%. The shares of five congeners (99, 118, 138, 153 and 180) reach up to 75% of the summed PCBs levels.

The low chlorine content group contributes 14.7% to the overall level. Dioxin-like congeners contribute 22%. The "128-153" group contributes 44.3% and the "170-187" group contributes 18 % of the summed PCBs levels.

Table 4. Average percentages of individual PCB congeners in overall PCBs levels in maternal blood (by regions)

# PCB congener	Murmansk Oblast	NAD	TAD	CAD	Norilsk	The Aral Sea zone	Total	
# **28_31**	1.8	1.2	2.3	2.3	0.6	4.5	2	14.7 %
# **52**	0.7	1	2.2	1.6	0.6	2.3	1.5	
# **99**	7.8	4.6	7.9	9	13.3	13	8.8	
# **101**	2.3	1.8	3.1	2.5	0.7	3.8	2.4	
# **105**	5.3	3.4	5.6	5.6	5.6	2.9	5.3	19.2 %
# **118**	18.1	7.9	14.5	13.1	20.8	12.6	13.9	
# **128**	0.8	0.9	1.2	0.7	0.3	1	0.8	44.3 %
# **138**	19.1	10.5	13	11	15.8	8.5	12.1	
# **153**	22.3	33.9	25.6	35.6	27.7	10.7	31.4	
# **156**	2.8	3.4	4.7	2.1	1.6	3.6	2.8	2.8 %
# **170**	4	8.4	5.2	4.5	3.4	1.9	4.9	18 %
# **180**	8.5	15	9	7.5	8.4	2.8	8.6	
# **183**	1	1.8	1.8	1.5	0.2	0.2	1.4	
# **187**	2.6	5	3.8	3.1	0.9	0.5	3.1	
Sum_PCB	100%	100%	100%	100%	100%	100%	100%	100%

4.2 Reproductive health and PCBs impacts

The analysis of impacts of individual PCB congeners on maternal and foetal health was based on the overall database array containing 346 records. The attempt to separate control groups (Norilsk and the Aral Sea zone) failed as it was impossible to detect effects in both groups due to small sample size.

The analysis of the effects of the 15 individual congeners and total PCBs levels incorporated several dimensions:

1. In groups with effects under analysis and in the rest of the data array (without such effects), average (geometric mean) concentrations were compared with use of a t-criterion to assess statistical significance of differences;
2. In four subsequently increasing dose ranges, effects were assessed by "yes/no" criterion:
   - Spontaneous abortions.
   - Stillborn babes and birth defects,

   or by time intervals –
   - Pregnancy duration (< 37 weeks; 37-40 weeks);
   - Age of the first menstruation (< 12 years; 13-14 years; 15 years and over);
   - Menstruation duration (< 4 days; 4 –5 days; 6 days and over);
   - Menstruation pain and spasms (never; sometimes; often);

   or by quantitative parameters –
   - Birth weight (< 2500 g; 2500-2999 g; 3000 g and more)

The statistical significance of the dose-effect relationships was assessed by correlation coefficients.

From the overall array of 346 pregnant women with database records, the following pregnancy failures were registered:

- premature birth (< 37 weeks): 41 women
- low birth weight (< 2500 g): 22 women
- spontaneous abortions: 36 women
- stillborn cases and birth defects: 16 women

Note that stillborn cases and birth defects were merged into one parameter under analysis due to their low numbers in the study sample. Sixteen such cases incorporated 13 stillborn cases and 3 birth defects.

Some effects under analysis (e.g. menstrual cycle alterations) are not referred to in this report, as no congener demonstrated statistically significant dose-effect dependency for a given parameter.

3. Boy/girl ratios among the newborn babes was analysed separately.

4.2.1. Pregnancy failures (PFs).

The concentrations of PCB congeners in blood of women with pregnancy failures are shown in Table 5.

Table 5. Comparative concentrations of PCB congeners (µg/l) in blood serum of pregnant women with/without pregnancy failures.

# PCB congener	**Pregnancy < 37 weeks**			**Birth weight < 2500 g**			**Spontaneous abortions**			**Stillborn cases and birth defects**			**No PFs**	
n	41 (11.8%)			22 (6.4%)			36 (10.4%)			16 (4.6%)			296 (85.5%)	
	GM	max	P – value	GM	max	P - value	GM	max	P - value	GM	max	P - value	GM	max
#28_31	0.009	0.100	> 0.05	0.016	0.131	> 0.05	0.007	0.129	> 0.05	0.014	0.152	> 0.05	0.011	1.122
#52	0.010	0.111	> 0.05	0.009	0.196	> 0.05	0.004	0.070	> 0.05	0.009	0.111	> 0.05	0.007	1.454
#99	0.132	0.724	< 0.01	0.103	0.728	> 0.05	0.074	0.534	> 0.05	0.200	0.768	< 0.05	0.078	0.875
#101	0.010	0.230	> 0.05	0.017	0.510	> 0.05	0.004	0.142	> 0.05	0.009	0.120	> 0.05	0.009	0.754
#105	0.034	0.630	> 0.05	0.032	0.777	> 0.05	0.017	0.250	> 0.05	0.113	0.380	< 0.001	0.032	3.430
#118	0.200	0.538	< 0.001	0.231	1.398	< 0.05	0.149	0.750	> 0.05	0.352	1.070	< 0.001	0.122	1.490
#128	0.004	0.170	> 0.05	0.006	0.158	> 0.05	0.002	0.080	> 0.05	0.001	0.138	> 0.05	0.002	0.170
#138	0.168	0.560	< 0.01	0.187	0.720	< 0.01	0.114	0.740	> 0.05	0.297	0.883	< 0.01	0.104	1.177
#153	0.497	2.701	< 0.01	0.439	2.390	> 0.05	0.291	2.368	> 0.05	0.743	3.899	< 0.05	0.234	4.810
#156	0.011	0.330	> 0.05	0.006	0.330	> 0.05	0.016	0.270	> 0.05	0.004	0.260	> 0.05	0.009	0.350
#170	0.045	0.530	> 0.05	0.034	0.530	> 0.05	0.033	0.530	> 0.05	0.052	0.685	> 0.05	0.029	1.120
#180	0.106	1.300	> 0.05	0.122	1.300	> 0.05	0.104	1.300	> 0.05	0.215	1.039	< 0.01	0.071	1.110
#183	0.007	0.090	> 0.05	0.008	0.090	> 0.05	0.007	0.090	> 0.05	0.008	0.100	> 0.05	0.007	0.389
#187	0.021	0.340	> 0.05	0.025	0.340	> 0.05	0.030	0.340	> 0.05	0.023	0.210	> 0.05	0.017	0.620
SumPCB	1.679	6.082	< 0.05	1.668	5.981	> 0.05	1.410	5.160	> 0.05	2.333	9.125	< 0.05	1.247	10.918

It is clear, that PCB levels in the blood of women with pregnancy failures are higher, compared to women who had normal pregnancies and gave birth to healthy children. Significant differences of geometric mean concentrations of congeners # 99; 118; 138; 153; 180 or 75% of the overall PCBs levels were identified in the group of women with pregnancies under 37 weeks, and in the group of women with stillborn babies and birth defects, compared to the group of women without pregnancy failures. In the group of women with low weight newborns, statistically significant differences were found for only two congeners (118 and 138 that contributed 14% and 12%, respectively, to the overall PCB levels). In the group of women with spontaneous abortions, no significant differences for any congener were found in comparison to the control group. In the case of summed PCBs levels, statistically significant differences were identified for groups of women with prematurely born children and women with stillborn babies and birth defects.

Dose - effect relationships (for subsequently increasing dose ranges) for 15 individual congeners are shown in Table 6.

Table 6. Pregnancy failures vs. levels of individual PCB congeners in maternal blood (correlation coefficients).

# PCB congener	**Pregnancies under 37 weeks**	**Birth weight under 2500 g**	**Spontaneous abortions**	**Stillborn cases and birth defects**
n, %	41 (11.8%)	22 (6.4%)	36 (10.4%)	16 (4.6%)
# 28/31	0.20	0.42	- 0.51	0.93
# 52	0.39	0.85	0.66	- 0.18
# 99	0.72	0.44	0.28	0.98
# 101	0.27	0.61	- 0.64	0.03
# 105	0.43	0.62	- 0.65	0.97
# 118	0.39	0.91	- 0.29	0.89
# 128	0.22	0.84	- 0.22	0.09
# 138	0.78	0.53	0.44	0.99
# 153	0.83	0.88	0.90	0.99
# 156	0.53	0.34	0.94	- 0.31
# 170	0.65	0.93	0.92	0.8
# 180	0.85	0.28	0.82	0.99
# 183	0.84	0.99	0.76	0.65
# 187	0.94	0.77	0.99	0.79
Sum PCBs	0.96	0.66	0.98	0.99

- statistically significant ($r > 0.7$) dependency of effects on PCB levels in blood.

Among pregnancy failures, premature birth cases (pregnancies under 37 weeks) demonstrate close statistical linkages with only five congeners, four of which have high chlorine contents.

Decreasing birth weight was found to depend significantly on increasing levels of seven congeners in maternal blood (five of these congeners have high chlorine contents).

Incidence of spontaneous abortions clearly depends on increasing doses of six congeners (starting from #153) with high chlorine contents. Low chlorine content congeners seem to have no impacts on incidence of spontaneous abortions. Therefore, elevated levels of PCB congeners with high chlorine contents more significantly affects such parameters as premature birth, low birth weight and incidence of spontaneous abortions.

Higher blood levels of 10 of 15 PCB congeners were found to correlate closely with the incidence of stillborn cases and birth defects (regardless of chemical structure and the optical properties of these congeners).

For all four groups of congeners, dose - effect relationships were observed for all PFs only in the case of the group of non-planar congeners with the highest chlorine contents (congeners 183 and 187). In addition, pregnancy failures were analysed for four groups of congeners.

Table 7. Concentrations of PCB congeners (total group levels) in maternal blood vs. pregnancy failures.

		#28 - 101	**#105-118, 156**	**#128 - 153**	**#170 - 187**
Pregnancy < 37 weeks	GM	0.257	0.321	0.724	0.225
	max	0.978	0.880	3.257	2.260
	p	< 0.001	< 0.01	< 0.01	> 0.05
	n	41	41	41	41
Birth weigh < 2500 g	GM	0.235	0.371	0.664	0.246
	max	1.198	2.323	3.100	2.260
	p	> 0.05	> 0.05	> 0.05	> 0.05
	n	22	22	22	22
Spontaneous abortions	GM	0.146	0.245	0.448	0.239
	max	0.743	1.260	2.784	2.260
	p	> 0.05	> 0.05	> 0.05	< 0.05
	n	36	36	36	36
Stillborn cases and birth defects	GM	0.300	0.510	1.067	0.410
	max	1.024	1.600	4.920	1.949
	p	< 0.05	< 0.05	< 0.05	< 0.01
	n	16	16	16	16
No adverse effects	GM	0.150	0.219	0.372	0.134
	max	4.074	4.579	5.800	2.940
	n	296	296	296	296

Figure 1.

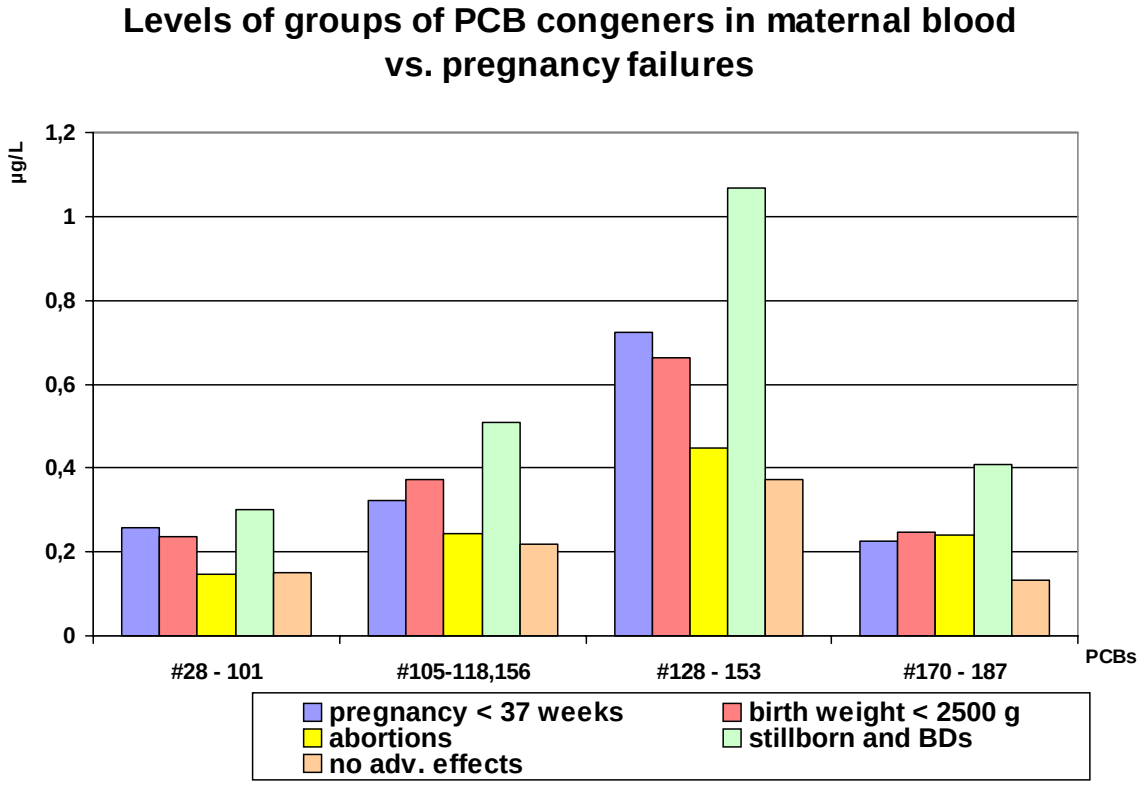


Table 7 and Figure 1 show that the average concentration of grouped PCB congeners in the blood of women without PFs are statistically significantly lower than PCBs levels in the blood of women with:

- prematurely born children (for groups of congeners 28-101; 105-156 and 128-153);
- stillborn cases and birth defects – for all four groups of congeners.

PCBs levels in the blood of women, who had spontaneous abortions and low birth weight of their newborn children, were also higher than relevant levels of the control group, but these differences were not statistically significant.

4.2.2. Reproductive case history of the women.

Reproductive case history parameters were analysed for two separate groups of women under study (women with parameters under analysis and the ones without such parameters).

Table 8. Comparative analysis of concentrations of PCB congeners (μg/L) in the blood serum of the women surveyed (for separate groups with different reproductive case history parameters)..

# PCB congener	**Age of first menstruation under 13 years**		**Age of first menstruation - 13 years or more**		P - value
n	99 (28.6%)		247 (71.4%)		
	GM	max	GM	max	
#28_31	0.012	0.120	0.007	1.122	> 0.05
#52	0.007	0.196	0.004	1.454	> 0.05
#99	0.102	0.780	0.067	0.875	< 0.01
#101	0.009	0.689	0.005	0.754	> 0.05
#105	0.039	0.777	0.023	3.430	> 0.05
#118	0.157	1.490	0.119	1.398	< 0.05
#128	0.002	0.158	0.001	0.170	> 0.05
#138	0.135	0.940	0.099	1.177	< 0.05
#153	0.341	4.810	0.219	4.076	< 0.05
#156	0.012	0.350	0.006	0.260	> 0.05
#170	0.039	1.120	0.019	0.685	< 0.05
#180	0.094	1.110	0.057	1.300	< 0.05
#183	0.008	0.190	0.004	0.389	> 0.05
#187	0.023	0.620	0.011	0.397	< 0.05
SumPCB	1.463	10.330	1.222	10.918	> 0.05

# PCB congener	**Menstruation duration < 4 days**		**Menstruation duration of 4 days or more**		P – value
	n = 61 (17.6%)		n = 285 (82.4%)		
	GM	max	GM	max	
#28_31	0.009	0.200	0.008	1.122	> 0.05
#52	0.007	0.087	0.005	1.454	> 0.05
#99	0.047	0.793	0.084	0.875	< 0.05
#101	0.004	0.370	0.006	0.754	> 0.05
#105	0.011	0.693	0.032	3.430	< 0.05
#118	0.059	0.991	0.151	1.490	< 0.001
#128	0.001	0.050	0.005	0.170	< 0.05
#138	0.051	0.924	0.128	1.177	< 0.001
#153	0.121	4.076	0.291	4.810	< 0.01
#156	0.005	0.190	0.008	0.350	> 0.05
#170	0.019	0.465	0.025	1.120	> 0.05
#180	0.045	0.827	0.074	1.300	> 0.05
#183	0.004	0.139	0.006	0.389	> 0.05
#187	0.012	0.282	0.014	0.620	> 0.05
Sum_ PCB	0.949	9.176	1.373	10.918	< 0.01

# PCB congener	**Menstruation with pain and spasms**		**Menstruation without pain and spasms**		P - value
	n = 146 (42.2%)		n = 200 (57.8%)		
	GM	max	GM	max	
#28_31	0.003	0.152	0.018	1.122	< 0.001
#52	0.002	0.196	0.011	1.454	< 0.001
#99	0.054	0.790	0.097	0.875	< 0.001
#101	0.002	0.510	0.014	0.754	< 0.001
#105	0.014	3.430	0.041	0.693	< 0.001
#118	0.087	1.355	0.171	1.490	< 0.001
#128	0.001	0.158	0.003	0.170	> 0.05
#138	0.085	0.967	0.130	1.177	< 0.001
#153	0.170	4.076	0.330	4.810	< 0.001
#156	0.004	0.350	0.011	0.280	> 0.05
#170	0.012	1.120	0.039	0.685	< 0.001
#180	0.042	1.300	0.091	1.039	< 0.001
#183	0.002	0.190	0.010	0.389	< 0.001
#187	0.006	0.620	0.027	0.350	< 0.001
SumPCB	1.008	10.918	1.537	10.330	< 0.001

Reviewing the data in Table 8, it is necessary to note that women with early age of first menstruation (under 13 years) certainly have higher blood levels of seven PCB congeners (including five of the most common ones that contribute 75% to the overall PCB levels). Women with menstruation duration under four days certainly have lower blood levels of six congeners (# 99 - 153, including four of the most common ones). Women with menstruation pain and spasms certainly have lower blood levels of almost all congeners, except congeners # 128 and 156 that make an almost negligible contribution to overall PCB levels.

Dose - effect dependencies (in four subsequently increasing dose ranges) for all 15 PCB congeners are shown in Table 9.

Table 9. Reproductive health status parameters of women under study vs. blood levels of individual PCB congeners (correlation coefficients).

# PCB congener	Age of first menstruation under 13 years	Menstruation duration < 4 days	Menstruation without pain and spasms
n, %	99 (28.6%)	61 (17.6%)	200 (59.7%)
# 28/31	0.90	- 0.04	0.84
# 52	0.59	0.83	0.92
# 99	0.49	- 0.56	0.99
# 101	0.95	- 0.87	0.82
# 105	0.89	- 0.65	0.93
# 118	0.76	- 0.73	0.82
# 128	0.96	- 0.85	0.93
# 138	0.65	- 0.55	0.98
# 153	0.29	- 0.46	0.94
# 156	0.88	- 0.99	0.98
# 170	0.86	- 0.49	0.94
# 180	0.91	- 0.25	0.99
# 183	0.59	- 0.99	0.99
# 187	0.74	- 0.68	0.89
Sum_ PCB	0.64	- 0.52	0.96

- statistically significant ($r > 0.7$) dependence of effects on blood levels of PCB congeners.

Among other reproductive health status parameters of the women surveyed, higher blood levels of eight of the 15 PCB congeners show a statistically significant correlation with early age of first menstruation (under 13 years), while higher doses of six congeners correlate with decreasing numbers of women with menstruation duration under four days (regardless individual congeners). Higher doses of any of 15 individual congeners show a statistically significant correlation with decreasing numbers of women with menstruation pain and spasms.

We also analysed the reproductive health status of the women under study for four groups of PCB congeners.

Figure 2.

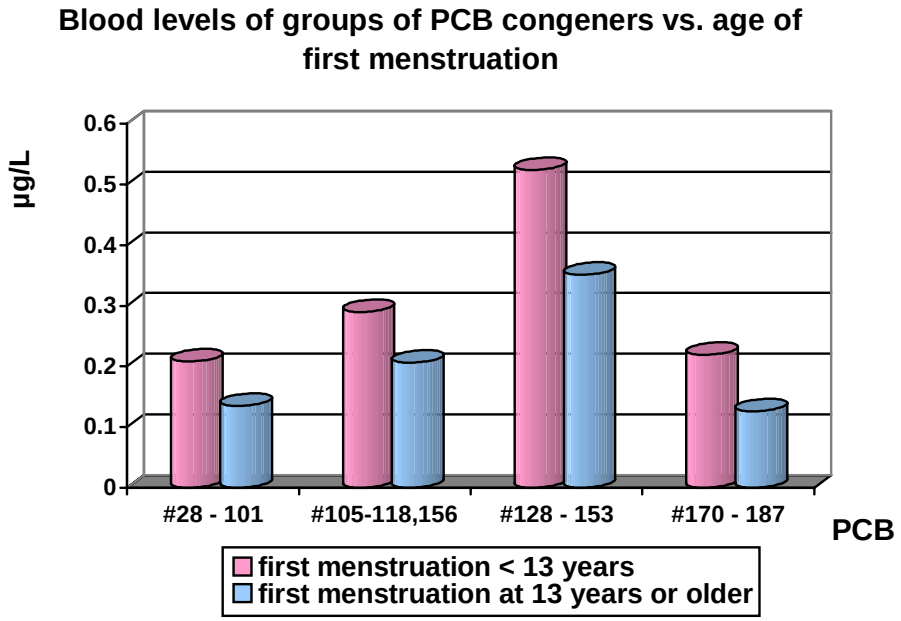


Figure 3.

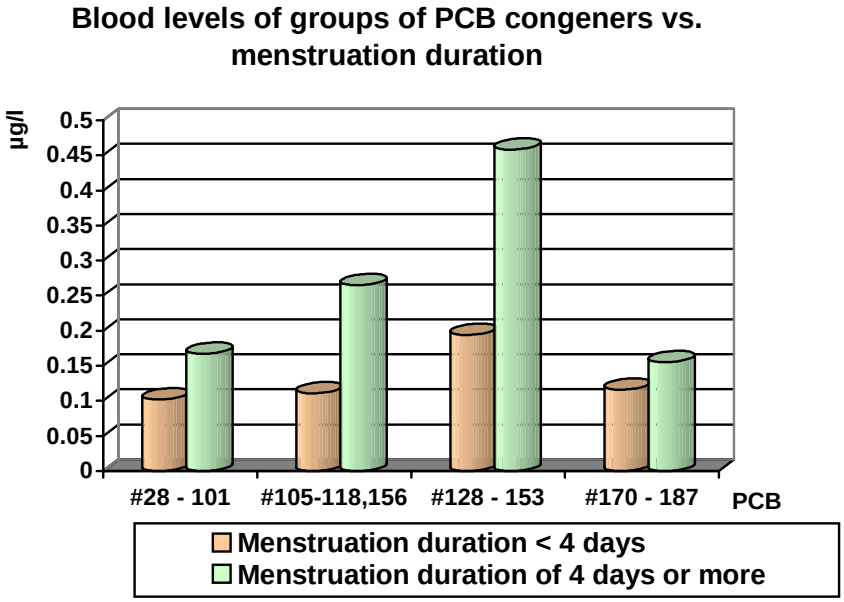
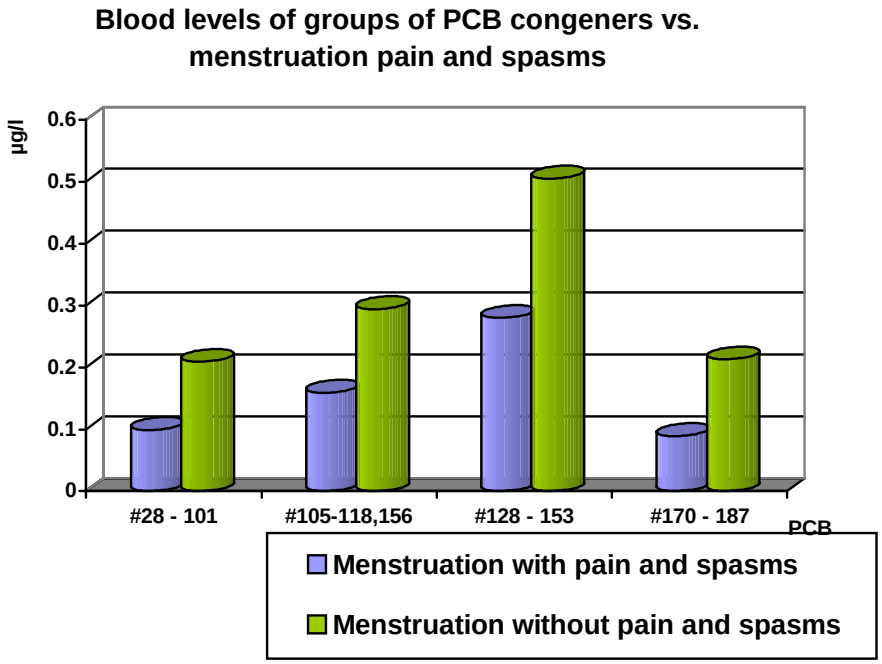


Figure 4.



Figures 2-4 demonstrate certainly higher levels of PCBs (in all four groups of congeners) among women with earlier age of first menstruation, with menstruation duration over 4 days and menstruation without pain and spasms.

4.2.3. Boy/girl ratio of the newborn children.

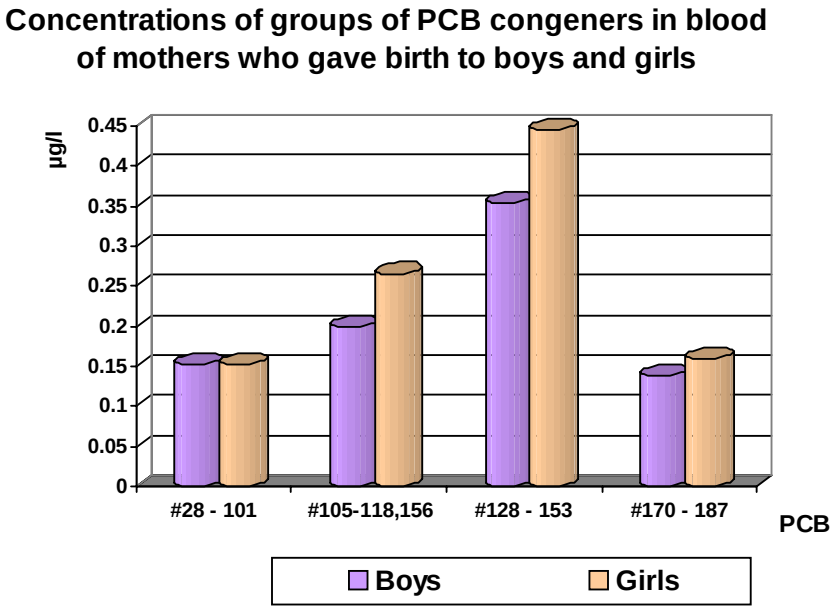
Table 10. Comparative analysis of the concentrations of PCB congeners (µg/L) in blood serum of women who gave birth to boys and girls.

# PCB congener	**Newborn boys** n = 187 (54%)		**Newborn girls** n = 159 (46%)		P - value
	GM	max	GM	max	
#28_31	0.012	1.122	0.009	0.173	> 0.05
#52	0.006	1.454	0.005	0.196	> 0.05
#99	0.075	0.778	0.077	0.875	> 0.05
#101	0.009	0.754	0.006	0.510	> 0.05
#105	0.022	3.430	0.036	0.777	> 0.05
#118	0.108	1.355	0.157	1.490	< 0.01
#128	0.002	0.079	0.002	0.170	> 0.05
#138	0.096	1.177	0.126	1.176	< 0.05
#153	0.224	4.041	0.282	4.810	> 0.05
#156	0.011	0.270	0.006	0.350	> 0.05
#170	0.025	0.610	0.022	1.120	> 0.05
#180	0.058	0.913	0.076	1.300	> 0.05
#183	0.008	0.350	0.005	0.389	> 0.05
#187	0.022	0.339	0.013	0.620	> 0.05
SumPCB	1.251	10.918	1.329	10.330	> 0.05

Statistically significant differences in PCB concentrations between groups of women who gave birth to boys and girls were identified for two congeners only (# 118 and 138). No dose - effect relationships between changes of boys/girls ratios and growing dose ranges were identified for all congeners.

Average concentrations of groups of PCB congeners in maternal blood are shown at Figure 5.

Figure 5.



Mothers who gave birth to girls demonstrate markedly higher PCB levels (for all groups of congeners), but the increase is not statistically significant.

Boys/girls ratios were analysed separately for 4 dose ranges and for 4 groups of congeners (Figures 6-10).

Figure 6.

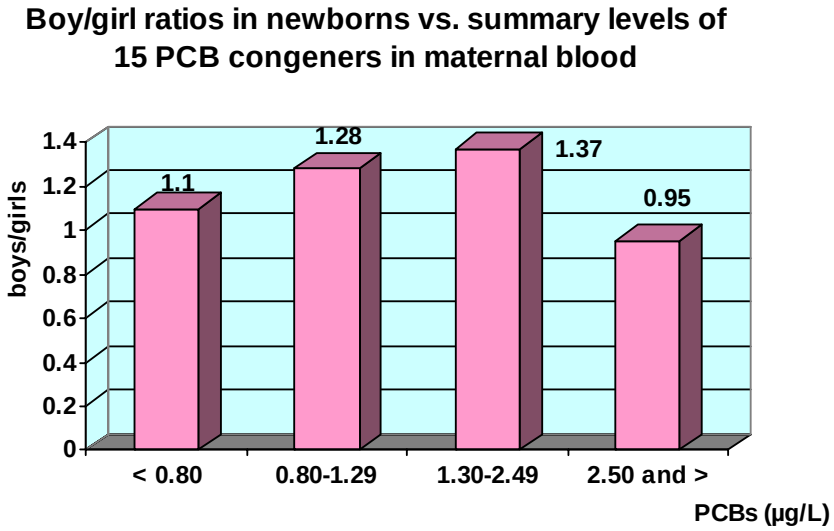


Figure 7.

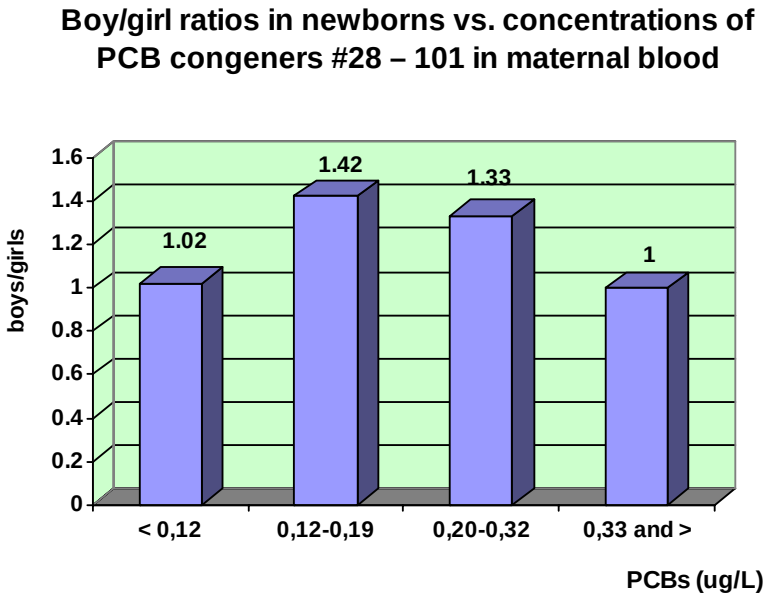


Figure 8.

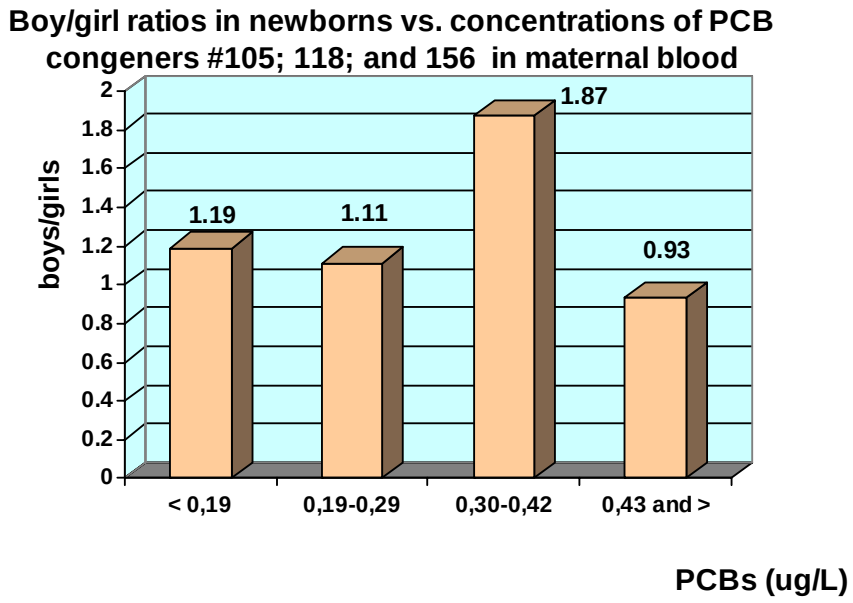


Figure 9.

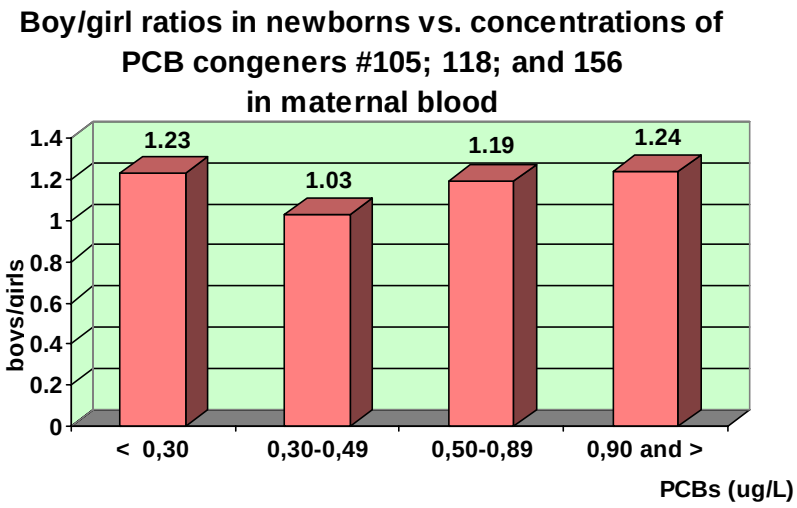
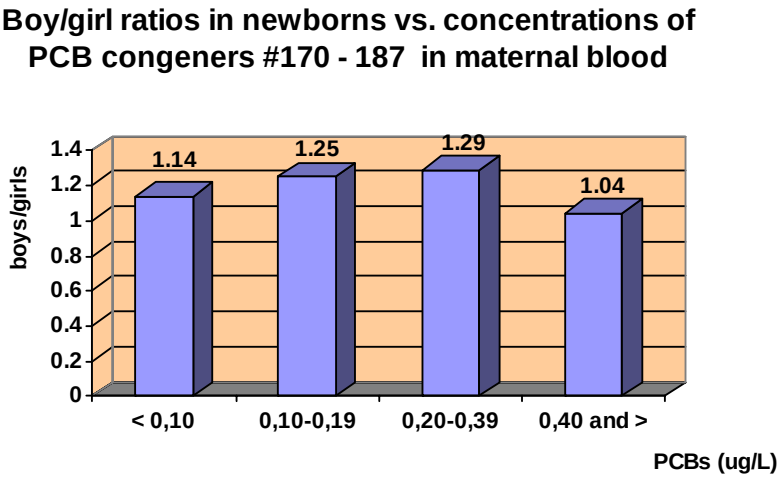


Figure 10.



Figures 6 – 10 suggest some increase in the boy/girl ratio (from 1 to 1.37-1.87) in line with growing PCB levels in three initial dose ranges for summary PCBs, congeners # 28-101; the group of dioxin-like congeners, and congeners # 170-187. In the fourth dose range, the ratio decreases. The dependence follows a parabolic pattern - initially, numbers of newborn boys exceed numbers of girls and then (in the maximal range of PCBs levels in maternal blood), the numbers of newborn girls became close to numbers of newborn boys. In the case of congeners # 128-153, no such dependence was identified.

Therefore, the above results confirm the regularity we had identified earlier (i.e. higher PCB levels in maternal blood affect boy/girl ratios in newborns). At relatively low levels of toxic substances, boy/girl ratios increase somehow, while further increases in PCBs results in growing more newborn girls and ratios closer to 1.0. This phenomenon has been discussed in the scientific literature in connection with the impacts of dioxin-like compounds on parental health (D.L. Davis et al. 1998; Ryan et al, 2002). However, in the course of implementing our project, we, for the first time, made a quantitative assessment of the changes in boy/girl ratios in newborns with application of criteria based on concentrations of summed PCB congeners in maternal blood.

5. Conclusions.

Pregnancy failures.

Premature birth (pregnancies < 37 weeks).

- Summary PCB levels in maternal blood, as well as the level of five PCB congeners (# 99; 118; 138; 153; 180), that contribute 75% to the summary PCB contents, are statistically significantly higher than in the control group.

- Dose - effect dependencies for incidence of premature birth cases were identified for summary PCB levels and for congeners # 99; 153; 180-187 (three of them have high chlorine contents).
- Average blood levels of grouped PCB congeners ("28-101", "105-156" and "128-153") are statistically significantly higher than in the control group.

Low birth weight (< 2500 g).

- Significant differences in blood levels of PCBs, compared to the control group, were found for only two congeners (# 118 and 153).
- Percentage shares of low weight newborn children were found to increase with growing levels of seven congeners in maternal blood; the correlation was statistically significant (five of these congeners have high chlorine contents).
- Average blood levels of grouped PCB congeners are higher than in the control group, but these differences are not statistically significant.

Spontaneous abortions.

- No statistically significant differences were found compared to the control group (for all individual PCB congeners and summary PCB contents).
- The incidence of spontaneous abortions clearly depends on increasing doses of summary PCBs and six PCB congeners with high chlorine contents (starting from congener # 153).
- The average blood levels of grouped PCB congeners are higher than in the control group, but these differences are not statistically significant.

Stillborn cases and birth defects.

- Levels of summary PCBs and five key PCB congeners in maternal blood are higher than in the control group. The results are statistically significant.
- Higher blood levels of summary PCBs and 10 of 15 PCB congeners are closely linked with the incidence of these pathologies, regardless of the chemical structure of individual congeners.
- Average levels of grouped PCB congeners (all 4 groups) are higher than in the control group. The results are statistically significant.

Reproductive case history.

1. Early age of first menstruation (under 13 years).
   - Blood levels of seven PCB congeners (including five key congeners) are higher than in the control group. The results are statistically significant.
   - Higher blood levels of eight of 15 PCB congeners (including key congeners # 99; 138; 153) show a statistically significant correlation with early age of first menstruation.
   - Average levels of grouped PCB congeners (all 4 groups) are higher than in the control group and the results are statistically significant.

2. Menstruation duration under four days.
   - Lower blood levels of six congeners (congeners # 99 - 153, including four key congeners), were associated with menstruation duration under four days compared to the control group. The results were statistically significant.
   - Higher concentrations of six PCB congeners correlate with a lower proportion of women with menstruation duration under four days (regardless of the types of these congeners).

- The average levels of grouped PCB congeners (all four groups) are lower in women with menstruation duration under four days than in the control group. These differences are statistically significant for three groups but not for the group of congeners "170-187".

3. Menstruation pain and spasms.
   - Blood levels of almost all congeners (except PCB congeners # 128 and 156) are statistically significantly lower.
   - There is a clear inverse correlation between doses of each of all 15 congeners and the proportion of women, who reported menstruation pain and spasms.
   - Average levels of grouped PCB congeners (all four groups) are lower than in the control group. The differences are statistically significant.

Boy/girl ratios in newborns.

- Higher levels of PCB 118 and 138 were found in the blood of mothers of girls, compared to mothers of boys. The differences were statistically significant.
- Average blood levels of grouped PCB congeners (all four groups) were higher among mothers of girls, compared to mothers of boys, but these differences were not statistically significant.
- Analysis of dose - effect relationships suggests some increase of boy/girl ratios (from 1 to 1.37-1.87) with increasing PCB levels in three initial dose ranges for summary PCBs, congeners # 28-101; the group of dioxin-like congeners and congeners # 170-187. In the fourth dose range, the ratio decreased. The dependence follows a parabolic pattern - initially, the numbers of newborn boys exceed the numbers of girls and then (in the maximal range of PCBs levels in maternal blood), numbers of newborn girls became close to numbers of newborn boys. In the case of congeners #128-153, no such dependence was identified.

Final conclusions.

1. Adverse impacts of 15 PCB congeners on the reproductive health status of women and the health status of newborn children were identified for individual PCB congeners, groups of congeners with similar chemical structure, and summary PCB levels. These impacts may develop at relatively low levels of PCBs in blood serum (less than 1 μg/L).

2. Levels of summary PCBs, grouped PCB congeners, and individual PCB congeners in the blood of women with pregnancy failures are higher compared to the control group (women with normal pregnancies and healthy newborn children), however, these differences are not statistically significant in all cases.

3. Higher levels of the majority of individual PCB congeners, all 4 groups of PCB congeners and summary PCBs were registered in the blood of women with low birth weight newborns, stillborn cases and newborn children with birth defects. The results were statistically significant.

4. No statistically significant relationships were found between levels of PCB congeners, summary PCB levels and incidence of spontaneous abortions and low birth weight cases.

5. Early age of first menstruation was found to be statistically significantly dependent on higher levels of the majority of PCB congeners.

6. Concentrations of the majority of PCB congeners are lower in the blood of women with menstruation duration under four days.

7. Lower summary PCB levels, groups of PCB congeners and all individual congeners were registered in blood of women who reported menstruation pain and spasms. These correlations were statistically significant.

8. The average blood levels of grouped PCB congeners were higher among mothers of girls, compared to mothers of boys, but these differences were not statistically significant.

9. The study results confirm an effect on boy/girl ratios. At relatively low levels of PCBs boy/girl ratios increase. Higher PCB levels results in growing shares of newborn girls and boy/girl ratios closer to 1.0.

10. We have not identified specific impacts of individual PCB congeners on the reproductive health status of women under study and the health status of their newborn children. In comparison with control groups, effects of medium-range congeners (congeners # 99 – 153) are more marked, while in the course of assessment of dose - effect relationships, the effects of PCB congeners with higher chlorine contents (congeners # 153 – 187) are more marked.

11. Analysis of effects of grouped PCB congeners demonstrates that dioxin-like congeners and other congeners, planar and non-planar ones, congeners with high and low chlorine contents may induce development of reproductive pathologies. Further studies would be necessary to get a deeper understanding of the problem.