**International POPs Elimination Project**

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

# DDT an DDE in the Russian Arctic and Reproductive Health of Indigenous Peoples


## Co-ordinator – Alexey Dudarev
## The North-western Centre of Hygiene and Public Health
**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.

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This report is available in the following languages: English

## Contents

## Abbreviations:

DDT – dichlorodiphenyltrichloroethane (1,1,1–trichloro-2,2,-bis(p-chlorophenyl)ethane).
2,4 DDT; 4,4 DDT; 2,4 DDE; 4,4 DDE; 2,4 DDD; 4,4 DDD – DDT metabolites.
n – number of observations.
p – value – statistical confidence of differences observed.
r – correlation coefficient.
RR - relative risk
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 of Eco-Accord Centre, and based on compiled information, collected in the course of implementation of several projects. A large scale project of GEF/AMAP/RAIPON - Persistent Toxic Substances, 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. Other 30% of information was collected later.

We express our gratitude for support in collection of primary data (case history data), taking blood samples and for general assistance in the project implementation to personnel of maternity wards of regional, oblast and district-level clinics of Murmansk Oblast, Nenetskiy, Taymyrskiy and Chukotskiy autonomous districts.

We highly appreciate support in preparatory activities and assistance in organisational arrangements for field work, provided by personnel of state administrations, public heath directorates and sanitary and epidemiological facilities of Murmansk Oblast, Nenetskiy, Taymyrskiy and Chukotskiy autonomous districts.

We express our particular gratitude to the Public Health Institute of Tromse (Norway) for chemical analysis of a part of the blood samples.

# DDT an DDE in the Russian Arctic and Reproductive Health of Indigenous Peoples

## Introduction

For the first time in the Russian Federation, large-scale research studies, implemented with participation of the North-western Centre of Hygiene and Public Health in 2001-2005, in Arctic regions of Russia, revealed that levels of persistent toxic substances (PTS), including DDT 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 and Canada).

The study results revealed high levels of DDT in individual blood samples of Indigenous residents of the Arctic - these data suggest accelerated human intake of 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 DDT 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 DDT are *inter alia* associated with intensive contamination of indoor environment of residential and public buildings (mainly due to uncontrolled use of household insecticide preparations, 100% of which, according to results of a special sampling study, were contaminated by DDT).

Traditional food of Indigenous Peoples of the Russian Arctic cannot be assessed as safe. Estimates based on chemical analysis data (DDT levels in hundreds of samples of traditional food products) suggest that DDT 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 (including DDT) substantially exceeded recommended WHO limits. DDT is known to affect adversely reproductive functions and foetal development (ATSDR, 2002). High concentrations of DDT in blood affect nervous, endocrine and immune systems. Some toxic substances act as hormone-imitators and suppress production of natural hormones and disrupt hormone-regulated processes such as spermatogenesis, ovulation and sexual development. Due to its solubility in fat, DDT easily crosses the placental barrier and intensely accumulates in a foetus (supply by maternal blood) or in an infant's body (supply by breast milk).

## 2. The project description

***Aims and objectives***

**The aim of the project** - to assess potential specific impacts of DDT and its metabolites on reproductive health of Indigenous Peoples of the Russian Arctic.

**Project objectives:**

To analyse, using the extended database of 346 puerperae (women who have just given birth; including personal health status data, reproductive case history, health status of their newborn babies), and personal data on levels of DDT and its metabolites in maternal blood:

- menstrual status (age of the first menstruation, menstruation duration, menstrual cycle, intensity of menstrual pain and spasms);
- pregnancy failures (premature birth, stillborn babes, ectopic pregnancies);
- foetal pathologies (low bight weight, birth defects);
- boys to girls ratios among the newborn babies;
- potential dose - effect dependencies between menstrual status, pregnancy failures, boys/girls ratios and concentrations of DDT and its metabolites in maternal blood

## 3. Material and methods.

### *3.1. Research study objects.*

The study objects incorporated pregnant women - representatives of Indigenous Peoples, permanent residents of 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 Indigenous pregnant women were selected for the mainstream DDT research:

- Cola Peninsula (Murmansk Oblast). The study area covered Lovozero township, the key settlement of the Lapps, and Krasnostchelie township
- 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, including Nelmin Nos, Indiga, etc).
- 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).
- Chukotskiy Peninsula (Chukotskiy Autonomous District). Two research areas were selected, with substantial differences in lifestyles of Indigenous Peoples: continental Anadyr district where 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 Indigenous pregnant 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 (regardless 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 DDT levels in the blood of Indigenous pregnant women of the Arctic, samples of maternal blood and cord blood of the newborns were taken. In parallel with blood sampling, all participants of the study were interviewed in detail.

Table 1. Completed questionnaires and maternal 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. DDT and its metabolites under study in the project*

We measured 2,4 DDT, 4,4 DDT, 2,4 DDE, 4,4 DDE, 2,4 DDD, 4,4 DDD, and the sum of DDT in blood of pregnant women.

### *3.4. Methods of blood sampling, storage and transportation of blood samples.*

To take blood samples, we used laboratory items, specially tested for absence of persistent organochlorine compounds, including DDT:

| Laboratory items | Manufacturers |
|---|---|
| Vacutainer 10 mL lavender (BD366457; $K_3$EDTA) for Organochlorines | Becton Dickinson Vacutainer System (USA) |
| Vacutainer Brand Holder Portable-tube | Becton Dickinson Vacutainer System (USA) |
| Needles Vacutainer Sterile | Becton Dickinson Vacutainer System (USA) |
| 7 mL Clear Vial, screw cap for storage of plasma/serum (for Organochlorines) | Supelco (USA) |
| Transfer pipettes 3,5 ml № 86.1172.001 for transfer of plasma/serum | Sarstedt (Germany) |

Techniques of sampling of maternal and foetal blood

Maternal blood was taken from the ulnar vein, while foetal blood was taken from the cord in several consecutive stages. Blood samples were taken by vacutainers - vacuum tubes with screw-mounted needles for dosed intravenous blood sampling. Further operations with blood samples require special tubes and containers, tested for absence of compounds that might affects analytical results. Processing of blood samples requires also a centrifuge (3000 r.p.m). Samples should be stored in a freezer at temperatures not higher than $-20^0$C. Frozen blood samples were transported in special containers that prevent their defrosting.

Samples of maternal blood were collected at 1st to 3rd day after the childbirth. Cord blood samples were taken in the course of deliveries, immediately after the cord dressing. Samples of maternal and cord blood were tested by the same methods.

Only single-use instruments were used for taking blood samples.

The blood sampling set incorporates:
1 needle holder
1 needle
3 vacutainers (6; 7 and 10 ml)
2 plastic vials with screw caps
2 plastic pipettes
5 labels

### *3.5. Analytical methods and quality control.*

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

Quantitative analysis of DDT 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 purified by rectification. All gases, used for analytical purposes, were at least of 5-0 purity grade. All standard samples of DDT for graduation purposes were produced by Promochem and had ISO 9001 certification.

Quality of analytical services of all four laboratories that participated in the project was confirmed in the course of testing of samples in the framework of international ring-tests, including the ones, conducted under auspices of AMAP.

### *3.6. Questioning and interviewing methodologies.*

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

Indigenous pregnant 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 medical records of their newborn children.

### *3.7. Statistical and epidemiological analysis methods.*

Standard data processing methodologies were used to process the raw epidemiological data collected.

Research results were input into a computer database. Statistical data processing was conducted by Microsoft Excel 2003, and SPSS applied software, with application of parametric and nonparametric statistics, correlation analysis (Pearson and Spearman correlation coefficients), regression analysis and significance tests (Student and Mann-Whitney).

In order to assess specific risk factors, we used principles of epidemiological statistics. To estimate risks, we calculated relative risks (RR) by Mantel-Haensel and 95% confidence interval with application of 4-field tables for "case-control" analysis and $\chi 2$ test.

## 4. Results and discussion.

The report provides results of chemical analysis of DDT in maternal blood and further analysis of DDT impacts on maternal and foetal health (based on 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 DDT on maternal health. Besides that, a close correlation was confirmed between DDT levels in a mother's body and her foetus, because DDT can easily penetrate the placental barrier.

### *4.1. PCBs levels in maternal blood.*

Geographic differences of DDT levels in maternal blood are shown in Table 2.

Table 2. Concentrations of DDT and its metabolites in maternal blood, by regions (µg/l)

| µg/l | | CAD (cont.) | CAD (coast.) | Murmansk Oblast | NAD | TAD | Norilsk | The Aral Sea zone | Kamchatka | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | 67 | 59 | 16 | 38 | 69 | 59 | 30 | 8 | 346 |
| 2,4 DDE | G.mean | 0.001 | 0.003 | 0.001 | 0.002 | 0.003 | 0.033 | 0.002 | 0.010 | 0.003 |
| | max | 0.040 | 0.090 | 0.001 | 0.147 | 0.210 | 0.222 | 0.017 | 0.010 | 0.222 |
| 4,4 DDE | G.mean | 1.425 | 2.411 | 2.059 | 1.589 | 1.497 | 3.164 | 7.792 | 1.745 | 2.161 |
| | max | 6.350 | 6.980 | 6.559 | 5.440 | 7.650 | 19.645 | 20.762 | 2.453 | 20.762 |
| 2,4 DDD | G.mean | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.009 | 0.002 | 0.010 | 0.003 |
| | max | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.321 | 0.080 | 0.010 | 0.321 |
| 4,4 DDD | G.mean | 0.008 | 0.010 | 0.007 | 0.005 | 0.004 | 0.002 | 0.008 | 0.013 | 0.007 |
| | max | 0.178 | 0.302 | 0.102 | 0.140 | 0.182 | 0.040 | 0.500 | 0.021 | 0.500 |
| 2,4 DDT | G.mean | 0.006 | 0.004 | 0.006 | 0.003 | 0.004 | 0.002 | 0.004 | 0.010 | 0.005 |
| | max | 0.541 | 0.184 | 0.055 | 0.750 | 0.235 | 0.360 | 0.028 | 0.010 | 0.750 |
| 4,4 DDT | G.mean | 0.203 | 0.209 | 0.250 | 0.241 | 0.186 | 0.334 | 0.220 | 0.058 | 0.220 |
| | max | 1.090 | 1.200 | 0.801 | 1.850 | 0.850 | 6.267 | 3.660 | 0.339 | 6.267 |
| ∑ DDT | G.mean | 1.702 | 2.732 | 2.365 | 1.929 | 1.779 | 3.690 | 8.212 | 1.887 | 2.512 |
| | max | 7.115 | 8.052 | 7.517 | 7.377 | 8.019 | 25.911 | 21.407 | 2.488 | 25.911 |

the most high concentrations.

Maximal personal concentrations of ∑DDT for the regions of study reached 8 µg/l in blood serum of Indigenous women of the Russian Arctic and 26 µg/l in blood serum of women - residents of Norilsk. In the area nearby Urgench (the Aral Sea zone of pesticide contamination in Uzbekistan) ∑DDT levels in blood serum of pregnant Uzbek women reached 21 µg/l. These results suggest the presence of local DDT sources in the Russian North.

Average levels of DDT and its metabolites in maternal blood are fairly similar for four main regions of the Russian North (1.7 - 2.7 µg/l for ∑DDT levels in serum and 1,4-2,4 µg/l for 4,4 DDE).

Percentage shares of individual DDT metabolites in ∑DDT levels in maternal blood are similar in all Northern regions (see Table 3). The most stable DDT metabolite - 4,4 DDE makes the highest contribution to ∑DDT levels – from 82% to 95%.

The 4,4 DDE/4,4 DDT ratios of 5.5 to 9 for main regions suggest a relatively recent contamination (10-15% of newly released 4,4 DDT), while ratio of 14.4 in Kamchatka, and particularly ratio of 22 in the Aral sea zone suggest rather old pollution (only 4 - 6% of newly released 4,4 DDT).

Percentage shares of unstable DDT metabolites are generally negligible (shares of 2,4 DDE do not exceed 0.5%, except in Norilsk, where its shares reach 1.5%; while shares 2,4 DDT were registered at the level of a few hundredth of 1%, except Norilsk and Kamchatka, where its shares reach 1% and 0.5%, respectively; shares of 4,4 DDT do not exceed 1.3%; and shares of 2,4 DDT do not exceed 2%).

Table 3. Average percentage shares of DDT metabolites in ∑DDT levels in maternal blood (by regions)

| µg/l | | CAD (cont.) | CAD (coast.) | Murmansk Oblast | NAD | TAD | Norilsk | The Aral Sea zone | Kamchatka | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | 67 | 59 | 16 | 38 | 69 | 59 | 30 | 8 | 346 |
| 2,4 DDE | % of ∑ DDT | 0.13% | 0.30% | 0.02% | 0.42% | 0.53% | 1.55% | 0.03% | 0.51% | 0.52% |
| 4,4 DDE | % of ∑ DDT | 84.42% | 88.24% | 88.41% | 81.78% | 86.15% | 86.42% | 95.20% | 92.53% | 88.27% |
| 2,4 DDD | % of ∑ DDT | 0.05% | 0.03% | 0.02% | 0.04% | 0.04% | 1.07% | 0.06% | 0.51% | 0.27% |
| 4,4 DDD | % of ∑ DDT | 1.05% | 1.28% | 0.41% | 0.84% | 0.68% | 0.08% | 0.28% | 0.68% | 0.60% |
| 2,4 DDT | % of ∑ DDT | 1.78% | 0.61% | 0.25% | 1.86% | 1.18% | 0.21% | 0.07% | 0.51% | 0.70% |
| 4,4 DDT | % of ∑ DDT | 12.61% | 9.59% | 10.94% | 15.07% | 11.54% | 10.72% | 4.32% | 6.43% | 9.68% |
| 4,4DDE/ 4,4DDT | ratio | 6.70 | 9.20 | 8.08 | 5.43 | 7.47 | 8.06 | 22.05 | 14.39 | 9.12 |

the most high concentrations.

### *4.2. Reproductive health and DDT impacts*

Analysis of impacts of individual DDT metabolites and ∑DDT on maternal and foetal health was based on the overall database array, including 346 records. The attempt to separate control groups (Norilsk and the Aral Sea zone) failed as it was impossible to detect effects in the both groups due to small samples.

Analysis of DDT effects incorporated several key dimensions: we compared average (geometric mean) concentrations in groups with and without analysed effects, assessed dose-effect correlations in 4 gradually increasing dose ranges and estimated relative risks of adverse effects of exposure to the pollutants.

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;
- spontaneous abortions - 36;
- stillborn cases and birth defects - 16.

Stillborn cases and birth defects were merged into one parameter under analysis due to their low incidence in the study sample. 16 such cases incorporated 13 stillborn cases and 3 birth defects.

Menstrual status of the women was assessed by the following indicators:

- Age of the first menstruation (< 13 years; 13 years and over);
- Menstrual cycle (< 28 days; 28 days and more);
- Menstruation duration (< 4 days; 4 days and over);
- Menstruation pain and spasms (yes/no).

Boys/girls ratios among the newborn babes of women from groups of mothers with different DDT dose loads were analysed separately.

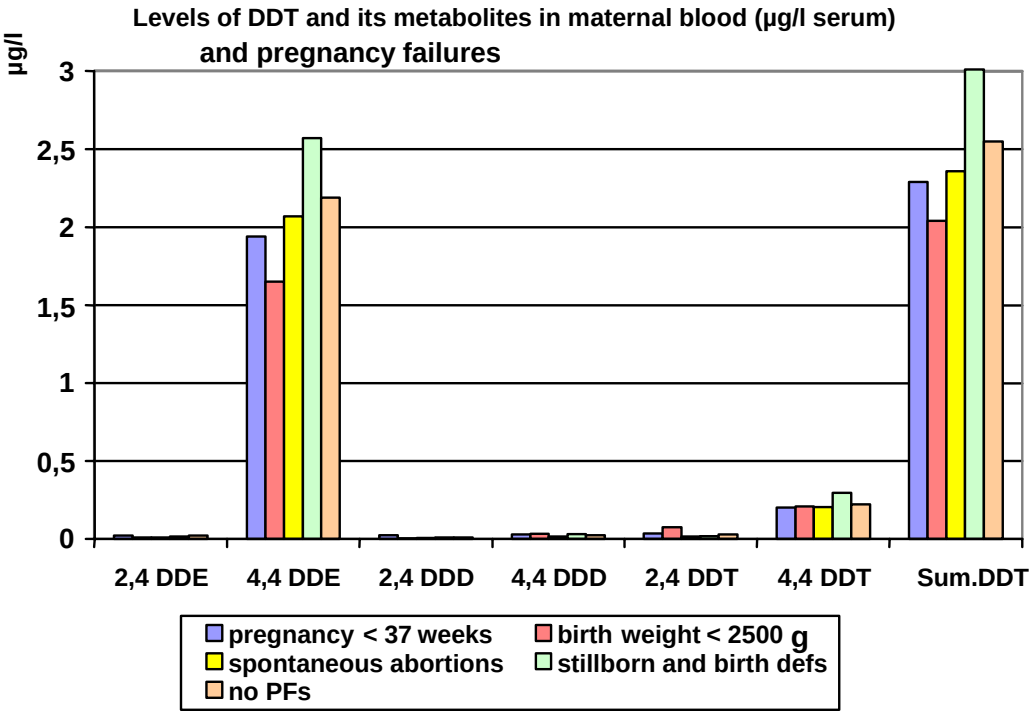
#### 4.2.1. Pregnancy failures (PFs).

Levels of DDT metabolites in blood of women with pregnancy failures (PFs), comparatively to relevant levels in blood samples of women without PFs, are shown in Table 4 and Fig. 1.

Table 4. Comparative concentrations of DDT metabolites (μg/l) in blood serum of women with/without pregnancy failures.

| | **Pregnancy < 37 weeks** | | | **Birth weight < 2500 g** | | | **Abortions** | | | **Stillborn cases and birth defects** | | | **No PFs** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| n | 41 (11.8%) | | | 22 (6.4%) | | | 36 (10.4%) | | | 16 (4.6%) | | | 296 (85.5%) | |
| | g. mean | max | P - value | g. mean | max | P - value | g. mean | max | P - value | g. mean | max | P - value | g. mean | max |
| **2,4 DDE** | 0.02 | 0.15 | > 0.05 | 0.01 | 0.12 | < 0.05 | 0.01 | 0.10 | < 0.05 | 0.02 | 0.09 | > 0.05 | 0.02 | 0.22 |
| **4,4 DDE** | 1.94 | 9.57 | > 0.05 | 1.65 | 12.00 | > 0.05 | 2.07 | 19.65 | > 0.05 | 2.57 | 19.65 | > 0.05 | 2.19 | 20.76 |
| **2,4 DDD** | 0.02 | 0.28 | > 0.05 | 0.01 | 0.01 | < 0.01 | 0.01 | 0.09 | > 0.05 | 0.01 | 0.09 | > 0.05 | 0.01 | 0.32 |
| **4,4 DDD** | 0.03 | 0.30 | > 0.05 | 0.03 | 0.18 | > 0.05 | 0.02 | 0.18 | > 0.05 | 0.03 | 0.19 | > 0.05 | 0.02 | 0.50 |
| **2,4 DDT** | 0.03 | 0.75 | > 0.05 | 0.08 | 0.75 | > 0.05 | 0.02 | 0.14 | < 0.05 | 0.02 | 0.08 | > 0.05 | 0.03 | 0.75 |
| **4,4 DDT** | 0.20 | 1.42 | > 0.05 | 0.21 | 1.42 | > 0.05 | 0.21 | 6.27 | > 0.05 | 0.29 | 6.27 | > 0.05 | 0.22 | 3.66 |
| **∑DDT** | 2.29 | 10.58 | > 0.05 | 2.04 | 12.27 | > 0.05 | 2.36 | 25.91 | > 0.05 | 3.01 | 25.91 | > 0.05 | 2.55 | 21.41 |

Figure 1.




It is clear, that levels of such DDT metabolites as 2,4 DDE, 2,4 DDD, 4,4 DDD and 2,4 DDT are too low for a meaningful assessment of their health impacts. We focused on 2 main DDT metabolites with 10 to 100 times higher levels in maternal blood.

As can be seen at Fig. 1, levels of 4,4 DDE, 4,4 DDT and ∑DDT in blood of women with PFs (including premature birth, low birth weight and spontaneous abortions), were lower in comparison to women who had no PFs, excluding stillborn cases and birth defects. Levels of DDT metabolites in blood of women with such PFs as stillborn cases and birth defects were by about 20% higher than in the control group, but no statistically significant differences were identified.

Therefore, no significant differences in average blood levels of DDT and its metabolites were observed between the group of women with PFs and women of the control group.

Dose - effect relationships (for gradually increasing dose ranges) for DDT are shown in Table 5.

Table 5. Dose-effect relationships between PFs and levels of DDT metabolites in maternal blood (correlation coefficients)

| | Pregnancies under 37 weeks | Birth weight less than 2500 g | Spontaneous abortions | Stillborn cases and birth defects |
|---|---|---|---|---|
| n (%) | 41 (11.8%) | 22 (6.4%) | 36 (10.4%) | 16 (4.6%) |
| 4,4 DDE | -0.31 | -0.71 | -0.50 | 0.14 |
| 4,4 DDT | 0.39 | -0.33 | -0.77 | 0.92 |
| ∑DDT | -0.62 | -0.90 | -0.85 | 0.20 |

- statistically significant ($r > 0.7$) dose - effect dependencies.

The data of Table 5 clearly demonstrate that incidence of PFs does not depend on growing levels of DDT and its main metabolites ($r < 0.7$), or it may be even reversely proportional to growing DDT doses ($r > 0.7$). Stillborn cases and birth defects represent the only exception. However, the latter pathologies demonstrate some correlation with growing doses of 4,4 DDT that does not contribute substantially to overall DDT levels.

In other words, growing blood levels of ∑DDT and its main component - 4,4 DDE (80-90%) are not associated with higher incidence of pregnancy failures. A close positive correlation was found between growing doses of 4,4 DDT in maternal blood and higher incidence of stillborn cases and birth defects.

Estimated relative risks of pregnancy failures under impacts of DDT are shown in Table 6.

Table 6. Relative risks of pregnancy failures under impacts of DDT

| | RR | 95% CI | p-value |
|---|---|---|---|
| **4.4 DDE in maternal blood (2.3 µl/l in blood serum)** | | | |
| Pregnancies under 37 weeks | 0.80 | 0.41-1.55 | 0.51 |
| Birth weight less than 2500 g | 0.79 | 0.33-1.91 | 0.60 |
| Spontaneous abortions | 0.81 | 0.40-1.64 | 0.56 |
| Stillborn cases and birth defects | 0.90 | 0.33-2.47 | 0.84 |
| **4.4 DDT in maternal blood (0.23 µg/l in blood serum)** | | | |
| Pregnancies under 37 weeks | 0.81 | 0.42-1.55 | 0.52 |
| Birth weight less than 2500 g | 0.86 | 0.36-2.04 | 0.74 |
| Spontaneous abortions | 0.86 | 0.43-1.71 | 0.49 |
| Stillborn cases and birth defects | 1.48 | 0.52-4.16 | 0.46 |
| **∑DDT in maternal blood (2.5 µg/l in blood serum)** | | | |
| Pregnancies under 37 weeks | 0.83 | 0.43-1.59 | 0.56 |
| Birth weight less than 2500 g | 0.80 | 0.34-1.91 | 0.62 |
| Spontaneous abortions | 0.76 | 0.38-1.52 | 0.44 |
| Stillborn cases and birth defects | 1.67 | 0.59-4.69 | 0.33 |

The data of Table 6 demonstrate no higher relative risks (odd's ratio) of pregnancy failures if blood levels of DDT and its metabolites exceed the above concentrations, except for stillborn cases and birth defects. In the latter case, relative risks exceed 1.5, however, the lower margin of confidence interval (95% CI) and p-value suggest lack of a credible dependence.

### 4.2.2. Reproductive (menstrual) case history of the women surveyed.

Reproductive case history parameters were analysed in pairs - for two separate groups of women under study (see Table 7, Fig. 2 and 3).

Table 7. Concentrations of DDT and its metabolites in maternal blood (µg/l serum) for two groups with different menstrual status parameters

| **Case history parameters** | | **4,4 DDE** | **4,4 DDT** | **∑DDT** |
|---|---|---|---|---|
| age of the first menstruation - less than 13 years | geom. mean | 1.96 | 0.23 | 2.33 |
| | mean deviation | 0.20 | 0.03 | 0.22 |
| | t | 0.99 | 0.48 | 0.81 |
| | p-value | > 0.05 | > 0.05 | > 0.05 |
| | n | 99 | 99 | 99 |
| age of the first menstruation - 13 years or more | geom. mean | 2.25 | 0.21 | 2.59 |
| | mean deviation | 0.21 | 0.03 | 0.22 |
| | n | 247 | 247 | 247 |
| | | | | |
| menstrual cycle < 28 days | geom. mean | 2.30 | 0.26 | 2.67 |
| | mean deviation | 0.34 | 0.09 | 0.42 |
| | t | 0.44 | 0.56 | 0.43 |
| | p-value | > 0.05 | > 0.05 | > 0.05 |
| | n | 68 | 68 | 68 |
| menstruation cycle of 28 days or more | geom. mean | 2.13 | 0.21 | 2.47 |
| | mean deviation | 0.18 | 0.02 | 0.19 |
| | n | 278 | 278 | 278 |
| | | | | |
| menstruation duration - less than 4 days | geom. mean | 2.10 | 0.16 | 2.36 |
| | mean deviation | 0.51 | 0.03 | 0.52 |
| | t | 0.15 | 0.87 | 0.34 |
| | p-value | > 0.05 | > 0.05 | > 0.05 |
| | n | 61 | 61 | 61 |
| menstruation duration of 4 days or more | geom. mean | 2.18 | 0.23 | 2.55 |
| | mean deviation | 0.16 | 0.03 | 0.18 |
| | n | 285 | 285 | 285 |
| | | | | |
| menstruation with pain and spasms | geom. mean | 2.50 | 0.23 | 2.89 |
| | mean deviation | 0.31 | 0.05 | 0.34 |
| | t | 1.62 | 0.32 | 1.68 |
| | p-value | > 0.05 | > 0.05 | > 0.05 |
| | n | 146 | 146 | 146 |
| menstruation without pain and spasms | geom. mean | 1.94 | 0.21 | 2.27 |
| | mean deviation | 0.15 | 0.02 | 0.16 |
| | n | 200 | 200 | 200 |

Figure 2.

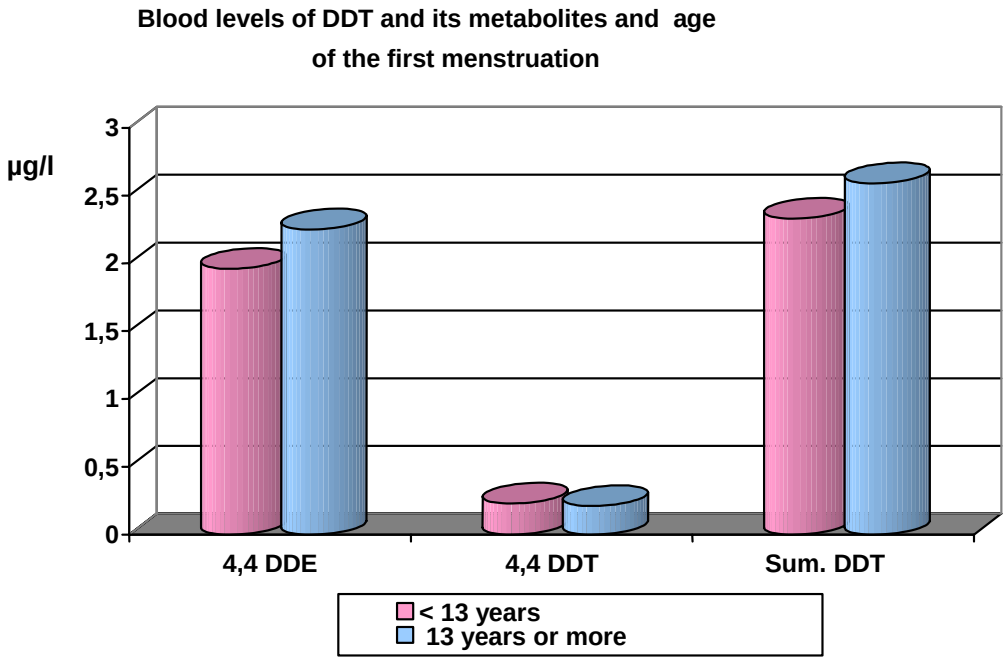
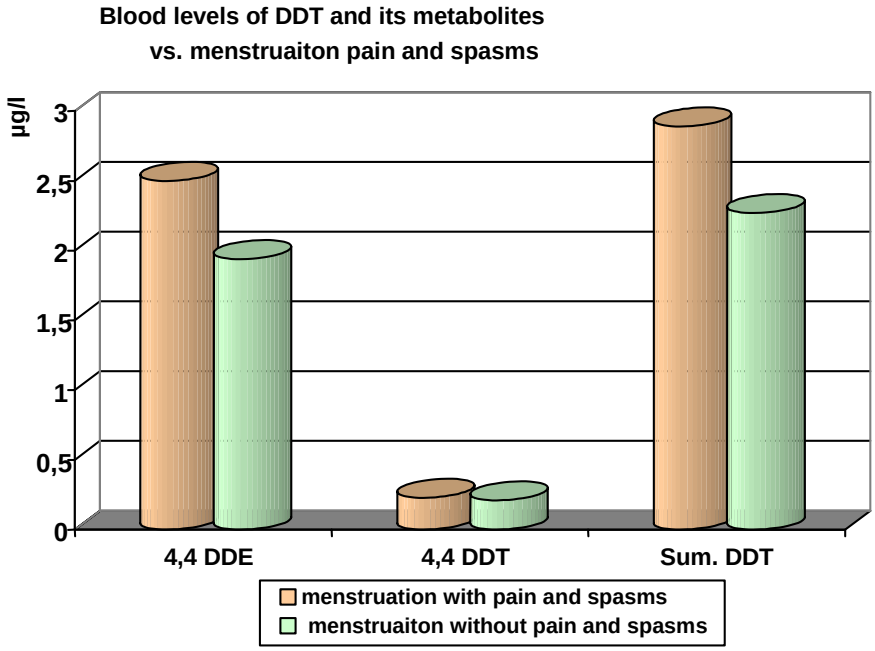



Figure 3.




As for data of Table 7 and Fig. 2 and 3, it is worth to note that no significant differences in blood levels of DDT and its metabolites were found between pairs of women's groups for all menstrual status parameters (including age of the first menstruation, menstruation cycle, menstruation duration, menstruation pain and spasms). Women, who reported menstruation pain and spasms, have higher levels of DDT and its metabolites in blood, these differences are rather marked, but they do not reach the necessary level ($t < 2$).

Dose - effect relationships (in 4 gradually increasing dose ranges of DDT and its metabolites) are shown in Table 8.

Table 8. Menstruation case history parameters vs. blood levels of DDT and its metabolites (correlation coefficients).

| | Age of the first menstruation - less than 13 years | Menstruation duration - less than 4 days | Menstrual cycle < 28 days | Menstruation with pain and spasms |
|---|---|---|---|---|
| n (%) | 99 (28.6%) | 61 (17.6%) | 68 (19.7%) | 146 (40.3%) |
| 4,4 DDE | -0.50 | 0.11 | 0.25 | 0.93 |
| 4,4 DDT | 0.33 | -0.38 | 0.86 | 0.28 |
| ∑ DDT | -0.70 | 0.33 | -0.12 | 0.99 |

- statistically significant ($r > 0.7$) dose - effect dependencies.

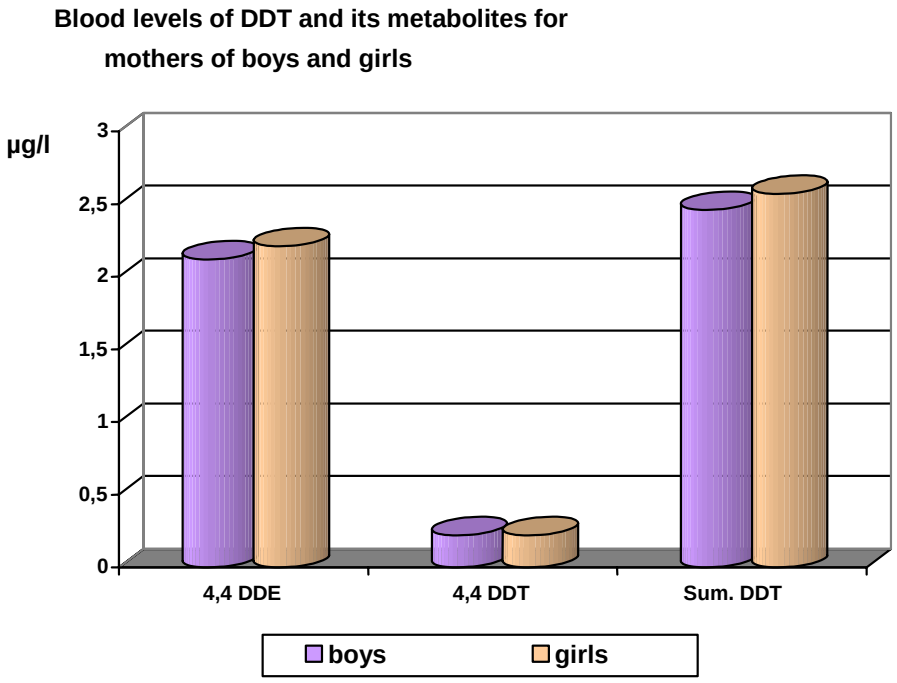
Among menstruation status parameters, higher blood levels of DDT and its metabolites do not correlate with menstruation duration. A statistically significant correlation was found between ∑DDT and age of the first menstruation (at higher DDT doses the age of the first menstruation increases). Growing doses of 4,4 DDE and ∑DDT closely correlate with increasing numbers of women, who reported menstruation pain and spasms. Menstrual cycle shows a significant correlation only with growing doses of 4,4 DDT that makes a minor contribution to the overall DDT level.

#### 4.2.3. Boys/girls ratio of the newborn children.

Table 9. Levels of DDT and its metabolites in maternal blood (μg/l serum) vs. boys/girls ratio of the newborn.

| Case history parameters | | 4,4 DDE | 4,4 DDT | ∑DDT |
|---|---|---|---|---|
| boys | geom. mean | 2.12 | 0.22 | 2.46 |
| | mean deviation | 0.21 | 0.04 | 0.24 |
| | t | 0.26 | 0.16 | 0.32 |
| | p-value | > 0.05 | > 0.05 | > 0.05 |
| | n | 187 | 187 | 187 |
| girls | geom. mean | 2.21 | 0.22 | 2.57 |
| | mean deviation | 0.24 | 0.02 | 0.25 |
| | n | 159 | 159 | 159 |

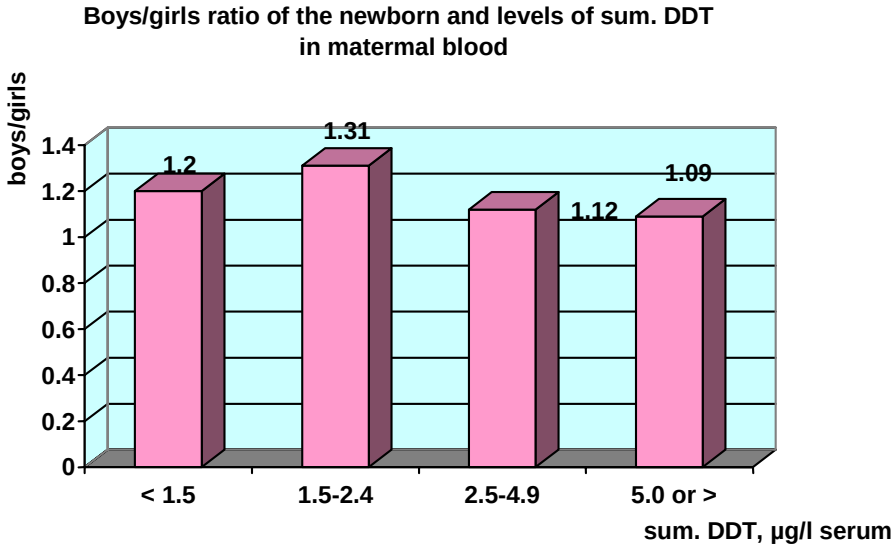
Fig. 4.




Data of Table 9 and Fig. 4 demonstrate no differences of blood level of DDT and its metabolites for mothers of boys and mothers of girls.

No dose - effect relationships were identified in gradually increasing dose ranges between DDT levels and boys/girls ratio (Fig. 5).

Figure 5.



## 5. Conclusions.

1. DDT levels in maternal blood

Average levels of DDT and its metabolites in maternal blood of Indigenous women were found to be fairly similar in four main regions of the Russian North (1.7 - 2.7 μg/l for ∑DDT levels in serum and 1,4-2,4 μg/l for 4,4 DDE).

Maximal personal concentrations of ∑DDT for the regions of study reached 8 μg/l in blood serum of Indigenous women of the Russian Arctic and 26 μg/l in blood serum of women - residents of Norilsk. In the area nearby Urgench (the Aral Sea zone of pesticide contamination in Uzbekistan) ∑DDT levels in blood serum of pregnant Uzbek women reached 21 μg/l. These data clearly suggest the presence of local DDT sources in the Russian North.

Percentage shares of individual DDT metabolites in ∑DDT levels in maternal blood are similar in all Northern regions (see Table 3). The most stable DDT metabolite - 4,4 DDE makes the highest contribution to ∑DDT levels – from 82% to 95%.

4,4 DDE/4,4 DDT ratios of 5.5 to 9 for main regions of the North suggest a relatively recent contamination (10-15% of newly released 4,4 DDT in ∑DDT levels), while ratio of 14.4 in Kamchatka, and particularly ratio of 22 in the Aral sea zone suggest rather old pollution (only 4 - 6% of newly released 4,4 DDT).

2. Pregnancy failures (PFs)

No significant differences in average blood levels of DDT and its metabolites were observed between the group of women with PFs and women of the control group. Levels of 4,4 DDE, 4,4 DDT and ∑DDT in blood of women with PFs (including premature birth, low birth weight and spontaneous abortions), were even somehow lower in comparison to women who had no PFs, excluding stillborn cases and birth defects. Levels of DDT metabolites in blood of women with such PFs as stillborn cases and birth defects were by about 20% higher than in the control group, but no statistically significant differences were identified.

Incidence of PFs and growing doses of DDT and its metabolites either do not correlate ($r < 0.7$), or demonstrate a negative correlation.

No credible increase of relative risks (RR) of pregnancy failures was identified in the range of studied concentration of DDT and its metabolites in maternal blood.

3. Reproductive (menstrual) case history of the women studied

No significant differences in blood levels of DDT and its metabolites were found between pairs of groups of women for all menstrual status parameters (including age of the first menstruation, menstruation cycle, menstruation duration, menstruation pain and spasms). Women, who reported menstruation pain and spasms, have higher levels of DDT and its metabolites in blood, but these differences are not statistically significant.

Growing doses of 4,4 DDE and ∑DDT were found to correlate closely with increasing numbers of women, who reported menstruation pain and spasms.

4. Boys/girls ratio of the newborn

There are no differences in blood levels of DDT and its metabolites between mothers of boys and mothers of girls.

No dose - effect relationships were identified in gradually increasing dose ranges between levels of DDT and its metabolites and boys/girls ratio of the newborn.

## Final conclusions

Analysis of the study database on 346 puerperae (women who have just given birth; mainly representatives of Indigenous Peoples of the Russian North) does not allow us to identify a significant correlation between incidence of pregnancy failures, changes in menstrual status parameters or changes in boys/girls ratio of the newborn children and DDT levels in maternal blood (including its main metabolites - 4,4 DDE and 4,4 DDT) in the dose range under study. A limited sample of the study and relatively low doses do not allow us to make a definite conclusion on causal relations between doses and the health problems studied.