# Increased frequency of diabetes and other forms of dysglycemia in the population of specific areas of eastern Slovakia chronically exposed to contamination with polychlorinated biphenyls (PCB).

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**Introduction**

Some studies suggest that exposure to organochlorine pollutants may affect glucose metabolism and insulin secretion and action [1-5]. Considerable pollution of water, soil and food chain in Eastern Slovakia was caused by a chemical factory, which was manufacturing PCBs in 1959-1985. The aim of the present preliminary evaluation of data obtained within the EC project PCBRISK was to search for further interrelations between long-term organochlorine pollution and disturbances in glucose homeostasis in large cohorts of population from three districts of Eastern Slovakia.

**Materials and Methods**

**Population:** a total of 2050 adults, 835 males (44.9 ± 0.4 years, BMI = 27.4 ± 0.1 kg/m$^2$) and 1215 females (44.7 ± 0.3 years, BMI = 26.6 ± 0.1 kg/m$^2$) from three districts of Eastern Slovakia were examined. Some data were not obtained from negligible number of subjects due to technical reasons.

**Baseline samples and oral glucose tolerance test:** Fasting baseline blood samples were obtained from all 2050 participating subjects. A standard oral glucose tolerance test (75g glucose) was performed in 1222 willing subjects without previous evidence of diabetes or other dysglycemia. Blood for estimation of glucose and insulin concentrations was collected just before and 60 and 120 min after the glucose load.

**Glucose, insulin and organochlorines:** Plasma glucose concentrations were measured using a glucose oxidase method (Analyser Boehringer Mannheim, Germany). Insulin concentrations in plasma were determined using electrochemiluminiscence immunoassay (Elecsys 1010, Roche, Germany). Diabetes mellitus and other dysglycemias were classified according to the ADA criteria from November 2003[6].

Serum concentrations of α,β,γ-HCH, HCB, DDE, DDT and 15 PCB-congeners were measured as described in this volume by Kočan et al.

**Statistical evaluation:** The data were statistically evaluated by the SPSS program 11.0.0 and with the subprogram "Answer Tree". Differences were considered significant at $p<0.05$. Due to intersexual differences in organochlorine metabolism, several parameters were statistically evaluated for males and females separately.

**Results:** The sum of the PCBs measured, HCB, βHCH, DDE and DDT correlated with one another in females ($p = 0.007 – 0.000$, $r = 0.09 – 0.57$). The correlations of these same pollutans were similar in males ($p = 0.002 – 0.000$, $r = 0.11 – 0.55$), except βHCH, which did not correlate with the sum of PCBs.
Increased frequency of impaired fasting glucose (IFG) and diabetes mellitus (DM) was observed in the second and third PCB tertile, in those subjects with medium and high levels of PCB and other relevant compounds (Fig. 1). Increased prevalence of isolated impaired fasting glucose and other dysglycemias was observed also in subjects with high concentrations of PCBs among 1222 those who underwent the oral glucose tolerance test (Fig. 2).

**Fig. 1:** Prevalence of normal fasting glucose (NFG), impaired fasting glucose (IFG) and diabetes mellitus (DM) in fasting state in 2047 subjects stratified into tertiles of the sum of PCB in ng/g serum lipids (p-values were calculated using the chi-square test, significance vs. low PCB tertile).

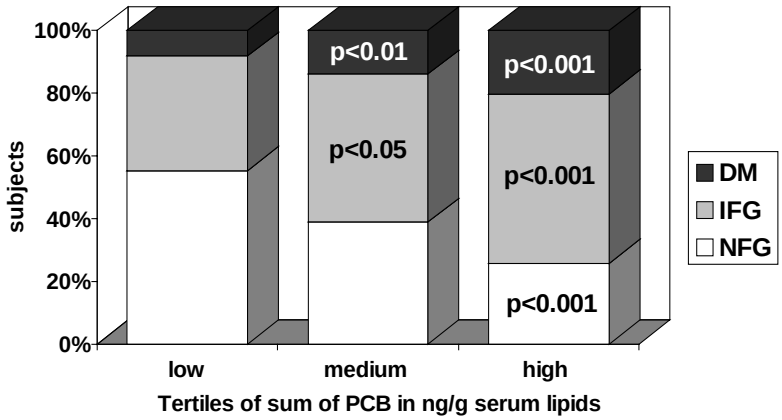
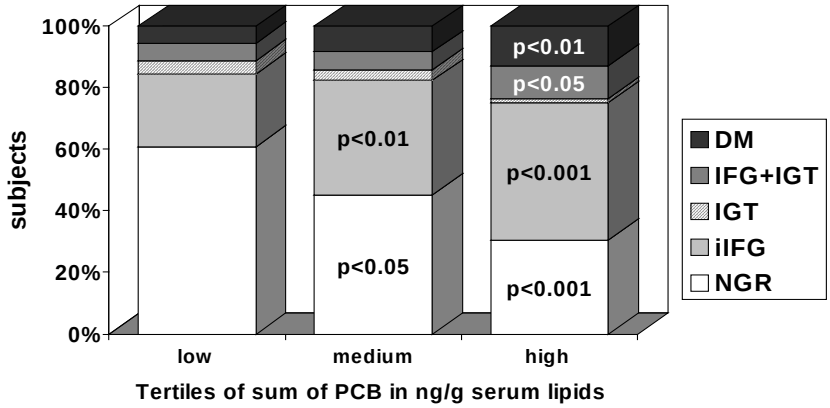


**Fig. 2:** Prevalence of normal fasting glucose (NFG), isolated impaired fasting glucose (iIFG), impaired glucose tolerance (IGT), combined IFG and IGT and diabetes mellitus (DM) in oral glucose tolerance test in 1222 subjects stratified into tertiles of the sum of PCB in ng/g serum lipids ( p-values were calculated using the chi-square test, significance vs. low PCB tertile).




The subjects with the medium and high levels of PCBs were significantly older than those with low PCB levels (low: 40.3 ± 0.5, medium: 45.0 ± 0.4, high: 49.2 ± 0.4; p<0.001) however, no significant differences in BMI were observed in BMI between PCB tertiles.

Variables determining the glucose homeostasis status such as fasting glucose, 120min glucose, fasting insulin and 120 min insulin concentrations correlated with the levels of HCB, βHCH, DDE and DDT in males (p =0.02 – 0.000, r = 0.11 – 0.28) and in females (p = 0.003 – 0.000, r = 0.11 – 0.26). In females and males, only weak correlation and no correlation respectively, was observed between concentrations of glucose and insulin and the PCB sum. When controlling for age, the most correlations disappeared in females remaining weak between concentrations of glucose and insulin on the one side and HCB and DDT on the other side (p = 0.004 – 0.045, r = 0.07 – 0.11).

Statistical analysis of the data provided a good model for prediction fasting plasma glucose and insulin in males and in females (Table 1 - 4).

**Table 1.** Linear regression analysis for fasting plasma glucose in females

| **Fasting glucose** | **Unstandardized coefficients** | | **t** | **95% CI for B** | **significance** |
|---|---|---|---|---|---|
| **females** | **B** | **SE** | | | |
| **constant** | 3.36 | 0.24 | 13.894 | 2.89 – 3.84 | p < 0.0001 |
| **BMI** | 0.065 | 0.009 | 7.040 | 0.047– 0.083 | p < 0.0001 |
| **HCB** | 1.14E-04 | 0.41E-04 | 2.762 | 0.33E-04 – 1.94E-04 | p = 0.006 |
| **βHCH** | 2.28E-03 | 1.01E-03 | 2.261 | 0.30E-03 – 4.26E-03 | p = 0.024 |
| **DDT** | 12.27E-04 | 4.88E-04 | 2.513 | 2.69E-04 – 21.8E-04 | p = 0.012 |
| **age** | 9.4E-03 | 4.5E-03 | 2.089 | 0.57E-03 – 18.2E-03 | p = 0.037 |

**Table 2.** Linear regression analysis for fasting plasma glucose in males

| **Fasting glucose** | **Unstandardized coefficients** | | **t** | **95% CI for B** | **significance** |
|---|---|---|---|---|---|
| **males** | **B** | **SE** | | | |
| **constant** | 1.69 | 0.57 | 2.966 | 0.57 – 2.81 | p =0.003 |
| **BMI** | 0.134 | 0.022 | 6.112 | 0.091 – 0.177 | p < 0.0001 |
| **βHCH** | 7.30E-03 | 1.85E-03 | 3.943 | 3.67E-03 – 10.93E-03 | p < 0.0001 |
| **age** | 1.95E-02 | 0.77E-02 | 2.521 | 0.43E-02 – 3.47E-02 | p = 0.012 |

**Table 3.** Linear regression analysis for fasting plasma insulin in females

| **Fasting insulin** | **Unstandardized coefficients** | | **t** | **95% CI for B** | **significance** |
|---|---|---|---|---|---|
| **females** | **B** | **SE** | | | |
| **constant** | -6.784 | 1.314 | -5.163 | -9.362 – -4.206 | p < 0.0001 |
| **BMI** | 0.547 | 0.049 | 11.146 | 0.451 – 0.643 | p < 0.0001 |
| **DDT** | 9.34E-03 | 2.83E-03 | 3.295 | 3.78E-03 – 14.9E-03 | p = 0.001 |

**Table 4.** Linear regression analysis for fasting plasma insulin in males

| **Fasting insulin** | **Unstandardized coefficients** | | **t** | **95% CI for B** | **significance** |
|---|---|---|---|---|---|
| **males** | **B** | **SE** | | | |
| **constant** | -11.937 | 1.652 | -7.226 | -15.18 – -8.69 | p < 0.0001 |
| **BMI** | 0.713 | 0.061 | 11.616 | 0.593 – 0.834 | p < 0.0001 |
| **DDE** | 2.79-04 | 1.03E-04 | 2.722 | 0.78E-04 – 4.81E-04 | p = 0.007 |

**Discussion:** A relation between environmental pollution and disorders of glucose metabolism has been found in population chronically exposed to organochlorine compounds. An increased frequency of diabetes and other dysglycemias was found in subjects with high concentrations of PCBs and other pollutants. The serum levels of PCBs, HCB, HCHs, DDT and DDE were associated with each other, suggesting simultaneous exposure. The interactive effects of compounds on human health cannot be excluded. Therefore the dissociation of the impact of individual pollutants might be difficult.

Some parameters such as age and BMI may confound associations between serum organochlorines concentration and disease. They are associated with concentrations of pollutants and are also risk factors for diabetes mellitus and other dysglycemias. Also a disease itself e.g. diabetes may modify the toxokinetics, metabolism and distribution of some pollutants.

Therefore in the prediction model of linear regression analysis also age and BMI were included. In females, predictive parameters for fasting plasma glucose, besides age and BMI, are the concentrations of HCB, βHCH and DDT. In males the predictive parameters are BMI, βHCH and age. The predictive parameters for fasting plasma insulin, besides BMI, are DDT and DDE for females and males, respectively.

In this work we revealed an evidence for a causal relationship between disturbances of glucose metabolism and environmental pollution with organochlorine compounds. For definitive statements further analysis are necessary.

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