Endocrine Disruptors (EDs)

- Exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations (IPCS, 2002)
- A variety of chemical classes, incl. natural and synthetic hormones, pesticides, compounds used in the plastics industry and in consumer products, and other industrial by-products and pollutants.
- Often widely dispersed in the environment.
- Some are persistent, can be transported long distances across national boundaries, and have been found in virtually all regions of the world (e.g. POPs).
- Others are rapidly degraded in the environment or human body or may be present for only short periods of time but at critical periods of development (e.g. phthalates).
- Interfere with reproduction, immune functions, neurobehavior, development of cancer, at all levels of biological organization and at key stages of life cycles.

Polychlorinated Biphenyls (PCBs)

- Persistent lipophilic organochlorine compounds, with endocrine disrupting properties
- Bioaccumulate in the food chain
- More than 1 million tons of PCBs produced worldwide
- Plasticizers, adhesives, heat transfer fluids, flame retardants
- Ubiquitous in the environment
- Food of animal origin as the primary source of exposure
- The major dietary sources of PCBs are fish and fish products and meat and meat products
- Toxic compounds – endocrine, immune, nervous and reproductive systems
- Developmental toxicants
- Children – a most vulnerable population (in utero exposure, breast feeding).

Obesity, Obesogens

- Obesity is a major global health problem.
- Associated with many serious health risks
- Fundamental basis = an imbalance of energy intake and expenditure the early life experience (e.g. quality of intrauterine life) being the important risk factor in obesity development.
- ……the role of in utero and early life exposures to synthetic chemicals (e.g. EDs) that may have the capacity to disrupt energy balance, in the development of obesity and related metabolic diseases
- Obesogens = chemical agents with ED properties that inappropriately regulate and promote lipid accumulation and adipogenesis to favour weight gain and obesity (Grun and Blumberg, 2007).
- Exposure to dietary and environmental chemicals, may further exacerbate the effects of imbalances in diet and exercise, resulting in an increased susceptibility to obesity and obesity-related disorders.
- A first set of candidate obesogens – e.g. persistent organic pollutants (POPs), perfluoroalkyl compounds, bisphenol A, and phthalates.
Adipose Tissue, Adipokines

- **Adipose tissue** = an active secretory organ
- **Adipokines** = metabolically active proteins
  - produced by fat cells (adipocytes),
  - affecting metabolically active tissues
  - regulating several neuroendocrine axes
- **Leptin**
  - the regulator of food intake and energy expenditure at the hypothalamic level
  - an indicator of total fat mass
  - High circulating levels of leptin in obese subjects suggest leptin resistance in obesity, an inability of high circulating leptin levels to suppress appetite and increase energy utilisation.
- **Adiponectin**
  - a key molecule in "metabolic syndrome"
  - a regulatory effect on insulin sensitivity
  - Decreased levels in obese and overweight patients

Aim

- to assess the effect of prenatal and postnatal exposure to PCBs on the levels of selected adipokines in 7-year-old children, born and living in Michalovce region.
Methods

- Cohort of children, born and living in the Michalovce region (N=450) followed from birth.
- At 7 years of age:
  - Fasting blood samples collection
  - Levels of leptin and adiponectin measured in blood (N=267) using ELISA method.
  - Selected PCB congeners in cord blood and at the age of 6 years were analyzed by high-resolution gas chromatography (HR-GC).
- Administration of questionnaire:
  - Data on health status and socio-demographic and environmental characteristics.
- Multiple linear regression was used for assessment of the association between prenatal and current PCB exposures and the levels of adipokines (STATA 6.0 for Windows).

Range of PCB 153 concentration in cord serum (P10, median, P90; ng/L), using observed and estimated concentrations, ENRIECO/OBELIX birth cohorts

1094 mothers
Sum of PCBs in ng/g serum lipids:
Mean: 620
Median: 430
Limits of the quartiles: 276, 430, 701, 12095
Leptin levels and weight at 7 years

Spearman $r = 0.64$, $p < 0.001$

Pre- and postnatal exposure to PCB153 and leptin levels at 7 years

Prenatal PCB153 exposure

Postnatal PCB153 exposure (6Y)

Spearman $r = -0.28$, $p < 0.001$

Exposure to PCB153 and adiponectin levels at 7 years

Prenatal PCB153 exposure

Postnatal PCB153 exposure (6Y)

Spearman $r = -0.15$, $p = 0.0172$

Multiple linear regression

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Leptin</th>
<th>Adiponectin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter estimate</td>
<td>SE</td>
<td>$p$ value</td>
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<tr>
<td>Log (PCB153 6Y)</td>
<td>-0.45</td>
<td>0.101</td>
</tr>
<tr>
<td>Gender (0, 1)</td>
<td>0.45</td>
<td>0.213</td>
</tr>
<tr>
<td>Ethnicity (0, 1)</td>
<td>-0.87</td>
<td>0.315</td>
</tr>
</tbody>
</table>

Log (PCB153 cord) -0.07 0.041 0.101
Gender (0, 1) 0.03 0.062 0.625
Ethnicity (0, 1) 0.08 0.093 0.374
Conclusions

- Obesity is not simply a product of overeating and lack of exercise.
- Our preliminary findings support the hypothesis that exposures to endocrine disruptors in infancy and childhood interfere with metabolic pathways.
- We did not find the effect of prenatal PCB exposure, but postnatal – current PCB exposure was found to be associated with the levels of leptin in 7-year old children.
- Although the human PCB exposure is slowly decreasing worldwide, the risk of deleterious health effects on human population is still present.
- Without direct intervention at the most heavily contaminated environmental components (rationally based remediation) and appropriate education regarding consumption of PCB contaminated food, a decrease in health risks is unlikely.