Impact of air pollution on human health

R. J. Sram

The Czech Academy of Sciences, Institute of Experimental Medicine, Prague, Czech Republic

Conference „Fighting Air Pollution“, Ostrava, November 19, 2018
## THE FREQUENCY OF CHILDREN WITH DELIVERY WEIGHT LESS THAN 2500 G

<table>
<thead>
<tr>
<th>Year</th>
<th>Teplice</th>
<th>Ústí n.L.</th>
<th>Jablonec</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>1882</td>
<td>1546</td>
<td>8.3</td>
<td>1591</td>
</tr>
<tr>
<td>1983</td>
<td>1511</td>
<td>8.3</td>
<td>1551</td>
</tr>
<tr>
<td>1984</td>
<td>1374</td>
<td>9.2</td>
<td>1460</td>
</tr>
<tr>
<td>1985</td>
<td>1351</td>
<td>7.9</td>
<td>1510</td>
</tr>
<tr>
<td>1986</td>
<td>1408</td>
<td>6.5</td>
<td>1532</td>
</tr>
</tbody>
</table>
# Morbidity of Children in the Mining Districts in the Region of Northern Bohemia (1988)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Morbidity of Children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Cases/100</td>
</tr>
<tr>
<td></td>
<td>Czech Republic</td>
</tr>
<tr>
<td>Urinary &amp; Kidney (chronic)</td>
<td>0.89</td>
</tr>
<tr>
<td>Respiratory (unspecific)</td>
<td>0.54</td>
</tr>
<tr>
<td>Allergy</td>
<td>1.70</td>
</tr>
<tr>
<td></td>
<td>(0-6 yrs. old)</td>
</tr>
<tr>
<td>Mental illness</td>
<td>0.53</td>
</tr>
<tr>
<td>Skin</td>
<td>0.65</td>
</tr>
<tr>
<td>Urinary &amp; Kidney (chronic)</td>
<td>1.42</td>
</tr>
<tr>
<td>Respiratory (unspecific)</td>
<td>0.45</td>
</tr>
<tr>
<td>Mental illness</td>
<td>2.00</td>
</tr>
<tr>
<td>Endocrine</td>
<td>1.17</td>
</tr>
<tr>
<td></td>
<td>(7-15 yrs. old)</td>
</tr>
<tr>
<td>Skin</td>
<td>0.73</td>
</tr>
<tr>
<td>Other Chronic</td>
<td>0.92</td>
</tr>
</tbody>
</table>

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Air Pollution in the Teplice District, Czech Republic derives from the use of locally mined coal for industry and home heating, and is higher in winter than summer.

$\text{SO}_2$, $\text{NO}_x$, PM10 (PAHs)
TEPLICE PROGRAM

IMPACT OF AIR POLLUTION ON HUMAN HEALTH

TEPLICE
(coal power plant
open pit mines
industry)

Model district

PRACHATICE
(agricultural
area)

Control district
January – February, 1994

Average Fine Mass Concentration = 52.6 µg/m³
GENOTOXICITY AND EMBRYOTOXICITY OF URBAN AIR PARTICULATE MATTER IN VITRO

Characterization of biologically active pollutants

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CONTRIBUTION OF THE MAJOR PAH-DNA ADDUCTS TO THE TOTAL DNA ADDUCTS LEVEL FROM URBAN SAMPLES

(Binková et al. 1999)

PAH-DNA adducts derived from

anti - BPDE  CHRY
B[b]F       B[a]A
B[k]F       I[c,d]P

Total radioactivity from all DNA adducts detected approx. 50 %

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AIR POLLUTION
PREGNANCY OUTCOME
PREGNANCY OUTCOME - RISK OF c-PAHs

AMBIENT EXPOSURE
to 15 ng c-PAHs/m³/month
(2.8 ng B[a]P/m³)

INDOOR EXPOSURE (50-60%)
approximately to 9 ng c-PAHs/m³/month
(1.7 ng B[a]P/m³)

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IMPACT OF IUGR

- Child Mortality
- Child Morbidity
- Delayed Growth
- Non-Insulin Dependent Diabetes
- Hypertension
- Ischemic Heart Disease
AIR POLLUTION

LIFE EXPECTANCY

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Life expectancy at birth - males

Length of life - years

year 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 00 01 02 03 04 05 06 07 08 09 10 11 12 13

ČR Ústecký kraj Teplice Jižní Morava Ostrava Praha
Life expectancy at birth - females

Length of life - years

Year: 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 00 01 02 03 04 05 06 07 08 09 10 11 12 13

ČR  Ústecký kraj  Teplice  Jižní Morava  Ostrava  Praha
EFFECT OF AIR POLLUTION TO POPULATION OF MINING DISTRICTS

1) Constantly decreased life expectancy of males and females

2) Constantly increased mortality to cardiovascular diseases

3) In children born in seventieth and eightieth we should expect in later adulthood the increased incidence of:
   hypertension, ischemic heart disease, diabetes of 2nd grade,
   affected the sperm quality

4) Damage of genetic material (DNA) will unfavorably affect generations yet unborn
PM2.5
<table>
<thead>
<tr>
<th>Organization</th>
<th>Standard (µg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU</td>
<td>25</td>
</tr>
<tr>
<td>USA</td>
<td>12</td>
</tr>
<tr>
<td>WHO</td>
<td>10</td>
</tr>
</tbody>
</table>
Obr. IV.1.4 Pole roční průměrné koncentrace PM$_{2.5}$, 2016
B[a]P

Acceptable risk level: 0.12 ng B[a]P/m³

Increasing tendency in B[a]P emissions - implementation of climate mitigation policies promoting the use of biomass burning for domestic heating
Obr. IV.2.1 Pole roční průměrné koncentrace benzo[a]pyrenu, 2016
## AIR POLLUTION 2010 – 2017

(CHMI)

<table>
<thead>
<tr>
<th>Locality</th>
<th>PM10 µg/m³</th>
<th>PM2.5 µg/m³</th>
<th>B[a]P ng/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostrava-Poruba</td>
<td>39.9 ± 41.4 / 27.4 ± 15.9</td>
<td>32.2 ± 37.0 / 21.7 ± 15.9</td>
<td>3.8 ± 6.2 / 2.5 ± 0.7</td>
</tr>
<tr>
<td>Ostrava-Bartovice</td>
<td>61.7 ± 45.6 / 35.1 ± 27.0</td>
<td>46.7 ± 38.2 / 35.5 ± 29.8</td>
<td>7.2 ± 8.1 / 9.6 ± 6.0</td>
</tr>
<tr>
<td>Karvina</td>
<td>54.3 ± 50.0 / 35.3 ± 26.8</td>
<td>X / 27.0 ± 19.2</td>
<td>6.3 ± 8.8 / 3.9 ± 1.4</td>
</tr>
<tr>
<td>Prague-Smichov</td>
<td>37.9 ± 20.1 / 31.0 ± 26.3</td>
<td>21.1 ± 14.2 / 22.0 ± 17.7</td>
<td>X</td>
</tr>
<tr>
<td>Prague-Libus</td>
<td>27.4 ± 16.9 / 21.1 ± 16.8</td>
<td>20.3 ± 13.1 / 16.7 ± 12.9</td>
<td>0.9 ± 1.2 / 0.9 ± 0.3</td>
</tr>
<tr>
<td>Ceské Budejovice</td>
<td>25.2 ± 16.9 / 18.5 ± 13.9</td>
<td>X / 14.6 ± 10.4</td>
<td>1.5 ± 1.8 / 1.3 ± 0.5</td>
</tr>
</tbody>
</table>

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Měsíční koncentrace benzo[a]pyrenu (2012)

- Radvanice
- Poruba
- Karviná

Vliv na fragmentaci DNA spermií
- Výsledek těhotenství
- 2,8
- 7,5

Roční limit B[a]P (31.12.2013): 1 ng/m³

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CHILDREN RESPIRATORY MORBIDITY

(URI + bronchitis + laryngitis + pneumonia + tonsillitis + otitis media)

Incidence/child in 5 districts

Years of age

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COMPARISON OF ‘NO ASTHMA’ VS. ‘ASTHMA’ T-TEST RESULTS

In the Venn diagrams shown below, the t-test results obtained using all experiments either with a p-value cutoff of 0.01 or a p-value cutoff of 0.01 and at least a 1.5 fold change are compared.

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SUMMARY

- Results indicate disease specific and region-dependent gene expression profiles.
- Gene expression profiles for asthma children are different between the polluted and control regions.
- In each region were observed specific transcripts comparing asthma vs. no asthma, 17 transcripts in the control region, 12 transcripts in the polluted region.
- Comparing “no asthma” or “asthma” groups, a strong region effect was observed (57 and 92 transcripts with > 1.5 fold changes).
- Asthma bronchiale in Prachatice – the allergic type of asthma response to allergens.
- Asthma bronchiale in Ostrava - the nonallergic type of asthma induced by irritants as air pollution, ETS, viruses.
BIOMARKERS
HUMAN BIOMARKERS

Genetic/Carcinogenic Risks

- Internal Dose
- Biologically Effective Dose
- Early Genotoxic Effects
- Altered Structure Function

- Metabolic Genotype/Fenotype
- DNA Repair Capacity
- Immune Functions

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Environ Health Perspect 74: 3-9, 1987
Autoradiographs of thin layer chromatograms with DNA adduct pattern of:

- DNA isolated from lymphocytes of subject sampled in January 2004 (1st sampling period)
- Water blank
- Positive control (DNA isolated from the lung of rats intraperitoneally treated with 100 mgB[a]P/kg b.w.)
CYTOGENETIC ANALYSIS

FISH analysis

t(\text{Ab}); t(\text{Ab}); t(\text{Ba})

Three translocations between chromosome 1 and unpainted chromosomes

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Reactive oxygen species

Endogenous sources

\[ \text{O}_2^- \rightarrow \text{SOD} \rightarrow \text{H}_2\text{O}_2 \rightarrow \text{OH}^* \rightarrow \text{DNA oxidation} \]

Exogenous sources

\[ \text{H}_2\text{O} + \text{O}_2 \rightarrow \text{H}_2\text{O} \rightarrow \text{H}_2\text{O} + \text{O}_2 \]

Lipid peroxidation
DNA oxidation
Protein oxidation

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EXPOSURE VS. BIOMARKERS

STATIONARY MONITORING

PERSONAL MONITORING – 8 h, 24 h, 48 h

BIOMARKERS

hours (SCGE)
weeks (DNA adducts)
months (chromosomal aberrations)

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HUMAN STUDIES AND BIOMARKERS OF EXPOSURE, EFFECT AND SUSCEPTIBILITY

- PM2.5 Stationary monitoring
- c-PAHs Personal monitoring
  Stationary monitoring

- VOC Personal monitoring
  Stationary monitoring

- Cotinine

- Triglycerids, Total, HDL and LDL cholesterol

- Vitamins A, C, E

- DNA adducts by $^{32}$P-postlabeling

- Chromosomal aberrations
  conventional, FISH, micronuclei

- Oxidative damage
  8-oxodG, 15-F2T-isoP, proteins, SCGE

- Genetic polymorphisms

- Gene expression

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PERSONAL MONITORING IN PRAGUE

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PERSONAL SAMPLING OSTRAVA
January 11 – 28, 2010

B[a]P 14.6 ng/m$^3$

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Autoradiographs of thin layer chromatograms with DNA adduct pattern of:

- DNA isolated from lymphocytes of subject sampled in January 2004 (1st sampling period)
- Water blank
- Positive control (DNA isolated from the lung of rats intraperitoneally treated with 100 mgB[a]P/kg b.w.)

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## DNA adducts

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>B[a]P ng/m³</th>
<th>B[a]P –“like”</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009</td>
<td>2010</td>
<td>2009</td>
<td>2010</td>
</tr>
<tr>
<td>Prague</td>
<td>64</td>
<td>0.80 ± 0.55</td>
<td>2.86 ± 1.87</td>
<td>0.21 ± 0.06</td>
</tr>
<tr>
<td>Ostrava</td>
<td>98</td>
<td>2.73 ± 2.60*</td>
<td>14.8 ± 13.3*</td>
<td>0.28 ± 0.08*</td>
</tr>
<tr>
<td>Controls</td>
<td>42</td>
<td>0.80 ± 0.62</td>
<td>0.10 ± 0.03</td>
<td>0.76 ± 0.20</td>
</tr>
</tbody>
</table>

*R. J. Sram 2018*
Three translocations between chromosome 1 and unpainted chromosomes
# Genomic frequency of translocations (FISH)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>B[a]P ng/m³ 2009</th>
<th>B[a]P ng/m³ 2010</th>
<th>% AB.C. 2009</th>
<th>% AB.C. 2010</th>
<th>F_G/100 2009</th>
<th>F_G/100 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prague</td>
<td>60</td>
<td>0.80 ± 0.55</td>
<td>2.86 ± 1.87</td>
<td>0.27 ± 0.18</td>
<td>0.23 ± 0.15</td>
<td>1.43 ± 1.15</td>
<td>1.39 ± 1.03</td>
</tr>
<tr>
<td>Ostrava</td>
<td>98</td>
<td>2.73 ± 2.60</td>
<td>14.8 ± 13.3*</td>
<td>0.26 ± 0.19</td>
<td>0.22 ± 0.18</td>
<td>1.44 ± 1.23</td>
<td>1.25 ± 1.18</td>
</tr>
<tr>
<td>Controls</td>
<td>42</td>
<td>0.80 ± 0.62</td>
<td></td>
<td>0.21 ± 0.16</td>
<td></td>
<td>1.13 ± 1.01</td>
<td></td>
</tr>
</tbody>
</table>
FREQUENCY OF MICRONUCLEI

(impact of 3-weeks stay in Ostrava region, January 2010)

<table>
<thead>
<tr>
<th>Groups</th>
<th>sampling</th>
<th>(N) (6000 b./person)</th>
<th>% AB.B. S MN</th>
<th>MN/1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>controls</td>
<td>I.</td>
<td>4</td>
<td>0.81 ± 0.15</td>
<td>8.32 ± 1.63</td>
</tr>
<tr>
<td></td>
<td>II.</td>
<td>4</td>
<td>0.80 ± 0.14</td>
<td>8.47 ± 1.55</td>
</tr>
<tr>
<td>exposed</td>
<td>I.</td>
<td>4</td>
<td>0.74 ± 0.43</td>
<td>7.96 ± 4.92</td>
</tr>
<tr>
<td></td>
<td>II.</td>
<td>4</td>
<td>1.14 ± 0.55</td>
<td>12.91 ± 6.49 *</td>
</tr>
</tbody>
</table>

* \(p < 0.05\)

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# Oxidative stress (in winter)

## 15-F2t-isoprostane (pg/ml)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>B[a]P ng/m³</th>
<th>15-2Ft-IsoP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prague</td>
<td>60</td>
<td>0.80 ± 0.55</td>
<td>165.9 ± 41.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.86 ± 1.87</td>
<td>256.5 ± 104.7*</td>
</tr>
<tr>
<td>Ostrava</td>
<td>98</td>
<td>2.73 ± 2.60*</td>
<td>279.3 ± 303.6*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.8 ± 13.3*</td>
<td>279.5 ± 124.5</td>
</tr>
</tbody>
</table>

* p < 0.05
QUESTIONS

Dose-effect relationship?

Possible adaptive response?
1) 100 mothers  
    100 newborns  
    Summer 2013  
    Karvina (exposed)  
    Ceske Budejovice (control)  
    100 mothers  
    100 newborns  
    Winter 2014  
    Karvina (exposed)  
    Ceske Budejovice (control)

2) Impact of diet  
   10 mothers – diet for 7 days  
   Each season & location
NUTRITIONAL QUALITY OF DIET

VEGETABLES
% days with RDI 300 g/day

FRUITS
% days with RDI servings

MILK, DIARY PRODUCTS
% days with RDI servings
EXPOSURE TO PM 2.5 AND B[a]P

PM2.5

\[\text{µg/m}^3\]

<table>
<thead>
<tr>
<th></th>
<th>Summer</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceske Budejovice</td>
<td>$\leq 30$</td>
<td>$\leq 50$</td>
</tr>
<tr>
<td>Karvina</td>
<td>$\leq 30$</td>
<td>$\leq 50$</td>
</tr>
</tbody>
</table>

\[p < 0.001\]

B[a]P

\[\text{ng/m}^3\]

<table>
<thead>
<tr>
<th></th>
<th>Summer</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceske Budejovice</td>
<td>$\leq -2$</td>
<td>$\leq 2$</td>
</tr>
<tr>
<td>Karvina</td>
<td>$\leq -2$</td>
<td>$\leq 2$</td>
</tr>
</tbody>
</table>

\[p < 0.001\]

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PAHs IN DIET – CHEMICAL ANALYSIS

• ¼ of consumed diet
• Daily intake: 1.58 kg
**PAHs in diet**

2 + 3-rings PAHs: NA, AC, ACL, FL, PHE, AN
4-rings PAHs: FA, PY, BaA, CHR, BcF, 5MC
5 + 6-rings PAHs: BbFA, BkFA, BjFA, BaP, DBahA, IP, BghiP, CPP, DBalP, DBaeP, DBaIP, DBahP

* Error bars indicate minimum and maximum concentration
PAHs in human breast milk

Relationship between atmospheric pollution in the residential area and concentrations of polycyclic aromatic hydrocarbons (PAHs) in human breast milk

Jana Pulkrobova, Michal Stupak, Andrea Svarcova, Pavel Rosner, Andrea Rossnerova, Antonin Ambroz, Radim Sram, Jana Hajslova

2 + 3-rings PAHs: NA, AC, ACL, FL, PHE, AN
4-rings PAHs: FA, PY, Baa, CHR, BcF, 5MC
5 + 6-rings PAHs: BbFA, BkFA, BjFA, BaP, DBahA, IP, BghiP, CPP, DBalP, DBaeP, DBaIP, DBahP
INTAKE OF B[a]P FROM AMBIENT AIR AND DIET

**Graph:**
- **X-axis:** Months - August 2013, September 2013, October 2013.
- **Y-axis:** ng/day.
- **Legend:**
  - Orange: Diet
  - Yellow: Ambient Air
- **Locations:** Ceske Budejovice, Karvina.

**Bar Charts:**
- **X-axis:** Months - August 2013, September 2013, October 2013.
- **Y-axis:** Percentage (%).
- **Legend:**
  - Orange: Diet
  - Yellow: Ambient Air
- **Locations:** Ceske Budejovice, Karvina.
The first such complex study on the assessment of human exposure to PAHs in the Czech Republic

The first data on the levels of OH-PAHs in urine of the Czech population
- Approximately 2x higher median ΣOH-PAHs in urine from winter period in Karvina compared to Ceske Budejovice

HUMAN EXPOSURE
- The importance to monitor both the dietary intake together with exposure via inhalation was documented
- In summer period the major part of exposure (60 – 90%) is via diet while in winter more than 60% is via inhalation
- Newborns – milk contribute by about 20 – 50% of the total exposure depending on the season
DNA ADDUCTS IN NEWBORNS

**B[a]P-like DNA adducts**

<table>
<thead>
<tr>
<th></th>
<th>Summer</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceske Budejovice</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Karvina</td>
<td>71</td>
<td>73</td>
</tr>
</tbody>
</table>

*p<0.01*

**Total DNA adducts**

<table>
<thead>
<tr>
<th></th>
<th>Summer</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceske Budejovice</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Karvina</td>
<td>71</td>
<td>73</td>
</tr>
</tbody>
</table>

*p<0.01*

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DNA adducts in newborns vs. vegetables intake by mothers

![Graph showing DNA adducts in newborns vs. vegetables intake by mothers]
## OXIDATIVE STRESS IN NEWBORNS

<table>
<thead>
<tr>
<th>Season</th>
<th>Location</th>
<th>N</th>
<th>8-oxodG mmol/mmol creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUMMER</td>
<td>Ceske Budejovice</td>
<td>99</td>
<td>4.7 ± 1.4</td>
</tr>
<tr>
<td></td>
<td>Karvina</td>
<td>71</td>
<td>4.7 ± 2.4</td>
</tr>
<tr>
<td>WINTER</td>
<td>Ceske Budejovice</td>
<td>99</td>
<td>4.2 ± 1.5</td>
</tr>
<tr>
<td></td>
<td>Karvina</td>
<td>73</td>
<td>5.7 ± 2.9 ***</td>
</tr>
</tbody>
</table>

*** p<0.001
MORBIDITY OF CHILDREN AT 2 YS OF AGE
**Comparison of locality and season**

- **Karvina winter genes**
  - MUC6 ▲ inflammatory immune response
  - SERPINA13 ▲ blood coagulation inflammation Parkinson disease
  - FBOX7 ▲ oxidative stress in neuron Parkinson disease

- **Karvina winter pathways**
  - *porphyrin and chlorophyll metabolism*
  - heme synthesis, transportation, and metabolism
  - *NRF2 pathway*
  - cellular defense against oxidative stress
  - *Neurotrophin signaling pathway*
  - brain development processes

**Influence of B[a]P and PM2.5**

- **CB Summer** vs. **Karvina Summer** relationship with locality and season

- **PM2.5**
  - both localities: Karvina 27, CB 263

- **B[a]P**
  - both localities: Karvina 11, CB 361

**Karvina**

- **TAF15** neurological disease (B[a]P)
- **FBXO41** immune system (PM2.5)

**CB**

- The most of genes were correlated in control locality.
Exposure to B[a]P represents a significant health risk for the population of the Czech Republic (62 % living in regions with the exposure > 1 ng/m3/year)

PM2.5 and B[a]P concentrations were higher in Karvina in both seasons

DNA adducts were significantly higher in newborns from Karvina in both seasons

DNA oxidative damage in newborns was higher in Karvina during winter

Increased concentrations of PAHs metabolites in children urine were associated with decreased birth length, birth weight and head circumference

Diet may be a significant source of PAHs exposure, especially when their concentrations in ambient air are lower

Morbidity of children at 2 ys of age was higher in a more polluted district
DUE TO A HIGH AIR POLLUTION CZECH REPUBLIC SEEMS TO BE A PARADISE TO STUDY THE IMPACT OF PM2.5 AND PAHs EXPOSURE TO HUMAN HEALTH, ESPECIALLY TO CHILD DEVELOPMENT
ACKNOWLEDGEMENT

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M. Dostal

J. Pavlikova
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Thank you for your attention

R.J. Sram, 2018
ACKNOWLEDGEMENT

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CHANGES IN THE TRANSCRIPTOME OF PREGNANT MOTHERS
CONCENTRATIONS OF POLLUTANTS
(months)

Prague

Ceske Budejovice

B[a]P (ng/m$^3$)

benzene (µg/m$^3$)

PM2.5 (µg/m$^3$)

R. J. Sram 2018
## DNA ADDUCTS IN MOTHERS AND NEWBORNS (\(^{32}\text{P}-\text{postlabeling}\))

(Prague vs. Ceske Budejovice)

<table>
<thead>
<tr>
<th>Adducts/10^8 nucl.</th>
<th>N</th>
<th>Peripheral blood mothers</th>
<th>Cord blood</th>
<th>Placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average ± S.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>B[a]P-like</td>
<td>Total</td>
<td>B[a]P-like</td>
</tr>
<tr>
<td>Prague</td>
<td>80</td>
<td>0.24±0.18</td>
<td>1.23±1.09</td>
<td>0.23±0.18</td>
</tr>
<tr>
<td>Ces. Budejovice</td>
<td>76</td>
<td>0.44*±0.39</td>
<td>1.59*±1.46</td>
<td>0.41*±0.41</td>
</tr>
</tbody>
</table>

R. J. Sram 2018
Lipid peroxidation (15-F$_{2t}$-isoprostane)

<table>
<thead>
<tr>
<th>pg/ml of plasma</th>
<th>Peripheral blood mothers</th>
<th>Cord blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prague</td>
<td>80</td>
<td>304.7 ± 211.9</td>
</tr>
<tr>
<td>Ceske Budejovice</td>
<td>76</td>
<td>147.0 ± 125.0*</td>
</tr>
</tbody>
</table>
MICRONUCLEI IN NEWBORNS

PRAGUE
(86)
2.17 MN/1000 BC

CESKE BUDEJOVICE
(92)
3.82 MN/1000 BC

TOWN
(40)
3.45 MN/1000 BC

VILLAGES
(52)
4.11 MN/1000 BC
Cord blood

Change: 104 genes

Increased expression in CB:
genesis related to metabolism
of xenobiotics

Decreased expression in CB:
genesis related to immune response
and autoimmune diseases
Studies of transcriptome indicate a new knowledge about a possible effect of air pollution to children's health.

Surprisingly, the monthly exposure to B[a]P > 2.8 ng/m³ increased IUGR as well as the deregulation of genes in newborns.

We should try to learn what is the impact of those data for the child development, specifically the effect of c-PAHs and PM2.5 exposures to respiratory morbidity.
N.D. Saenen et al.

*In Utero* Fine Particle Air Pollution and Placental Expression of Genes in the Brain-Derived Neurotrophic Factor Signaling Pathway: An ENVIRONAGE Birth Cohort Study EHP 123:834-840 (2015)

PM2.5 15-19 μg/m³

deregulation of genes *BDNF* and *SYN1* in placenta
D. Tang et al. Molecular and neurodevelopmental benefits to children of closure of a coal burning power plant in China. PLOS One 9(2014)e91966

<table>
<thead>
<tr>
<th></th>
<th>2002 (N=110)</th>
<th>2005 (N=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH-DNA adducts</td>
<td>0.324±0.139</td>
<td>0.204±0.081*</td>
</tr>
<tr>
<td>BDNF, ug/dL</td>
<td>752.9±463.1</td>
<td>1266.6±619.8*</td>
</tr>
<tr>
<td>Gesell Scores Average</td>
<td>99.4±10.7</td>
<td>100.3±7.2</td>
</tr>
<tr>
<td>Motor</td>
<td>97.5±11.5</td>
<td>97.8±7.8</td>
</tr>
<tr>
<td>Adaptive</td>
<td>98.7±14.9</td>
<td>101.2±11.0</td>
</tr>
<tr>
<td>Language</td>
<td>102.1±12.8</td>
<td>100.5±9.8*</td>
</tr>
<tr>
<td>Social</td>
<td>99.4±11.8</td>
<td>101.8±6.8</td>
</tr>
</tbody>
</table>

*p < 0.05
1) Increased prenatal exposure to PAHs reduced left hemisphere white matter

2) Reduced white matter measures of the left hemisphere were associated with significantly higher scores for externalizing problems of the CBCL (child behavior checklist), as well as externalizing symptoms that included ADHD symptoms and conduct disorder problems.

3) Higher prenatal PAH exposure was associated with reduced processing speed during intelligence testing.
PAHs and cognitive functions


→ 170 children in Cracow

→ Exposure: PAH-DNA adducts, prenatal PAHs 43.0±55.3 ng/m3

→ At age 7 ys Wechsler Intelligence Scale for Children

→ Depressed verbal IQ index, cord blood adducts RR=3.0 (95%CI: 1.3, 6.8)

→ Breast feeding 6 months – protective effect RR=0.3 (95%CI: 0.1, 0.9)

→ Conclusion: PAHs are harmful to the developing fetal brain
Zvýšené koncentrace PM2.5 zvyšují výskyt:
- autismu
- poruch kognitivních funkcí u dětí
- onemocnění depresí
- incidence demence
- Parkinsonovy choroby
- ovlivňují koncentraci proteinu BDNF
Zvýšené koncentrace PAHs:

- ovlivňují hladinu BDNF
- redukují bílou hmotu mozku
- snižují kognitivní funkce u dětí
- zvyšují výskyt ADHD
CONCLUSIONS

DUE TO A HIGH AIR POLLUTION CZECH REPUBLIC
SEEMS TO BE A PARADISE TO STUDY THE IMPACT
OF PM2.5 AND PAHs EXPOSURE TO HUMAN HEALTH
AIR POLLUTION

IMPACT ON SPERM

R. J. Sram 2009
DNA adducts

chromosomes

chromatine

R. J. Sram 2009
SCSA® - Acridine Orange Stained DNA

Native DNA Stainability (green fluorescence)

Fragmented DNA (red fluorescence)
Policemen patrolling the streets in Prague centre with heavy traffic

The level of air pollution will be assessed on the basis of information from two sources:
- data from stationary measuring stations AIM Prague
- for 48 h using personal sampling devices (URG Corp, USA)

![Box plots showing the distribution of det DFI, high DFI, and HDS percentages for February and May, with statistical significance indicated by P≤0.001.]

<table>
<thead>
<tr>
<th>Category</th>
<th>February</th>
<th>May</th>
</tr>
</thead>
<tbody>
<tr>
<td>det DFI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>high DFI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**N=46**

- dDFI < 15%: Feb 30, May 42
- dDFI 15 – 30%: Feb 16, May 4
- dDFI >30%: Feb 2, May 2
- HDS >15%: Feb 10, May 4

R. J. Sram 2009