PINCHE POLICY RECOMMENDATIONS ON REPRODUCTIVE EFFECTS

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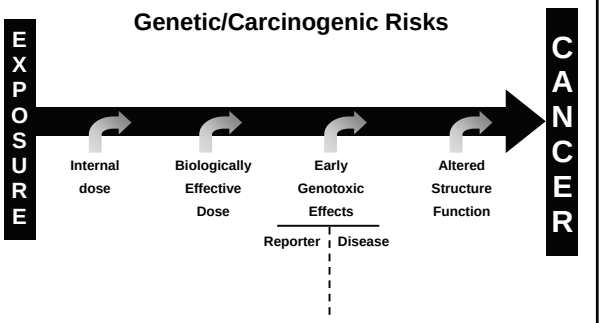
HUMAN BIOMARKERS



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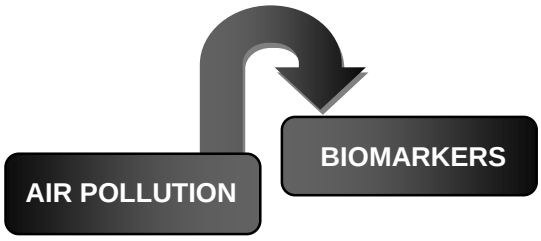
Environ Health Perspect 74: 3-9, 1987



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BIOMARKERS OF EXPOSURE

DNA ADDUCTS	Hb ADDUCTS	ALBUMIN ADDUCTS	COMET ASSAY
↓	↓	↓	↓
AIR POLLUTION	SMOKING ETS	SMOKING ETS	AIR POLLUTION
CZECH REP.			MEXICO
POLAND			BELGIUM
MEXICO			
USA-NY			

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BIOMARKERS OF EFFECTS

CHROMOSOMAL ABERRATIONS	MICRONUCLEI	HPRT
↓	↓	↓
AIR POLLUTION	AIR POLLUTION	SMOKING
FISH NY ?	RUSSIA	
	INDIA	
CHEMICAL PLANT LITHUANIA	BELGIUM	
FORMALDEHYDE CZECH REP.	CZECH REP.	

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BIOMARKERS OF SUSCEPTIBILITY

GENETIC POLYMORPHISMS

metabolic genotype
CYP1A1, CYP1B1, CYP 2E1
ADH2, ADH3
GSTM1, GSTT1, GSTP1
NAT1, NAT2, EPHX

DNA repair
XPD, hOGG1, ERCC2, AGT

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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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AIR POLLUTION → PREGNANCY OUTCOME

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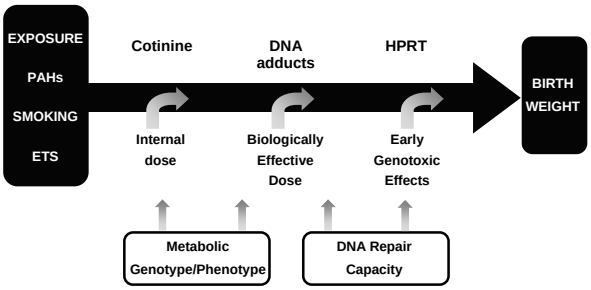
PREGNANCY OUTCOME



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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 →

9-OH-B[a]P	B[j]F
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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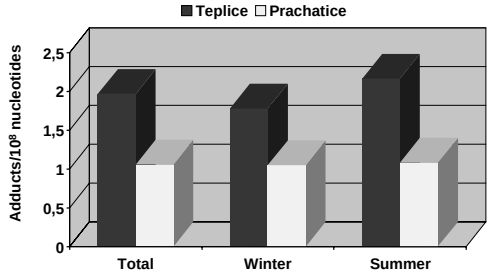
TOTAL DNA ADDUCT LEVELS IN PLACENTA

Effect of district and season



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FACTORS AFFECTING DNA ADDUCTS IN PLACENTA

- Air pollution - carc. PAHs
- Diet - vitamin C
- Life style - smoking
- Genotypes - GSTM1, NAT2, EPHX, CYP1A1
- Pregnancy outcome - IUGR
- Education
- Passive smoking

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c-PAHs TRANSPLACENTAL EXPOSURE

DNA adducts ……..	+
HPRT mutations……..	+
Birth weight……..	-
Birth length……..	-
Head circumference……..	-

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Perera et al. 2002, 2004

ASSOCIATION BETWEEN DNA ADDUCTS AND BIRTH WEIGHT (G)

ALL (N = 199)			TEPLICE (N = 90)		
	g	P		g	P
DNA adducts	- 12.3		DNA adducts	3.7	
Gestation age (40)	167.7	< 0.001	Gestation age (40)	159.0	< 0.01
Smoking	- 198.5	< 0.01	Smoking	- 235.6	< 0.05
EPHX - medium	- 76.8		GSTM1	- 25.4	
EPHX - high	- 141.0		EPHX - medium	-165.3	
			EPHX - high	-183.1	

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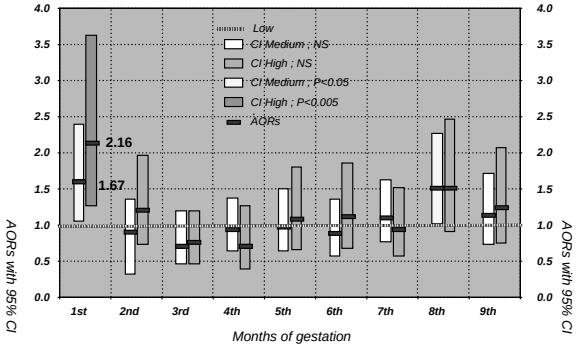
CARCINOGENIC PAHs & IUGR IN TEPLICE



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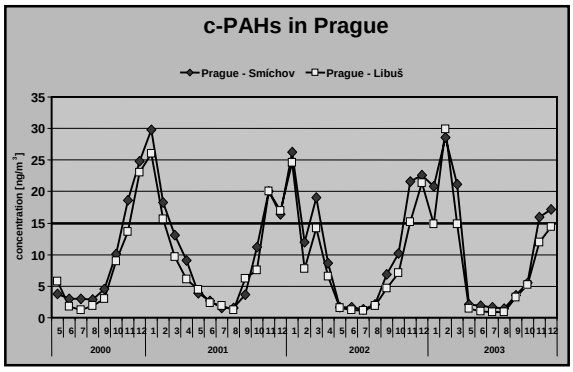

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EXPOSURE TO PAHs (ng/m^3)

	B[a]P	c-PAHs
Prague	1.7	11.4
Teplice	1.5	10.7
Prachatice	0.7	4.4
New York*	0.5	3.6
Cracow*	5-10	52
Tongliang*	15	

*(* Perera et al. 2005)*

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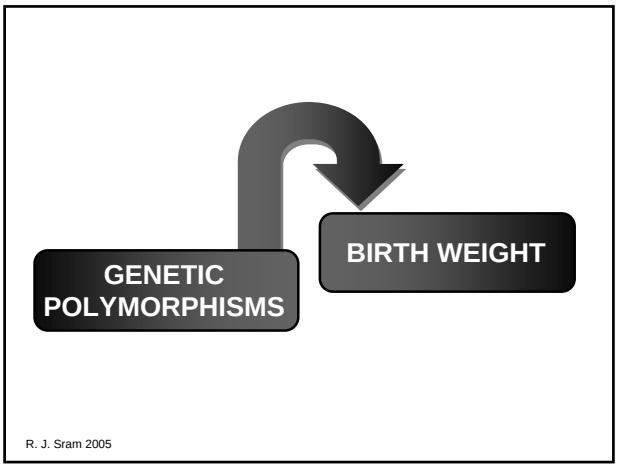

METHODS

Material for analysis

Locality	N
Teplice	672
Prachatice	229
Prague	112
Total	1013

Genetic polymorphisms
(PCR-based RFLP assays)

- CYP 1A1 MspI
- CYP 1A1 Ile/Val
- MTHFR
- MS
- GSTM1
- GSTT1
- GSTP1
- EPHX

LOGISTIC REGRESSION ANALYSIS
MULTIPLE REGRESSION ANALYSIS

BW LBW (<2500 g) Prematurity (06037 wks)	c-PAHS Smoking ETS Genotypes	Cases (LBW, Prematurity, IUGR) Controls

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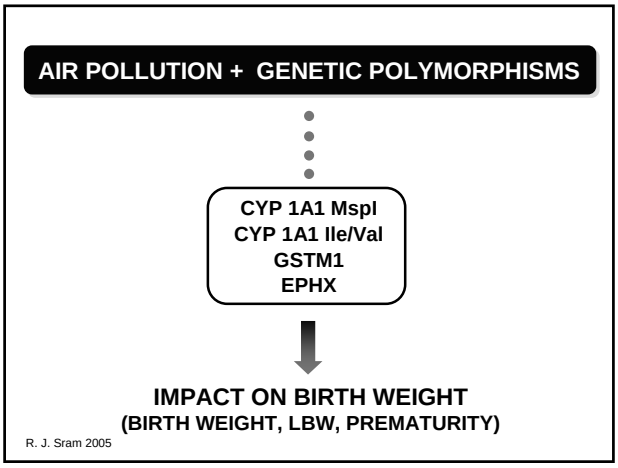

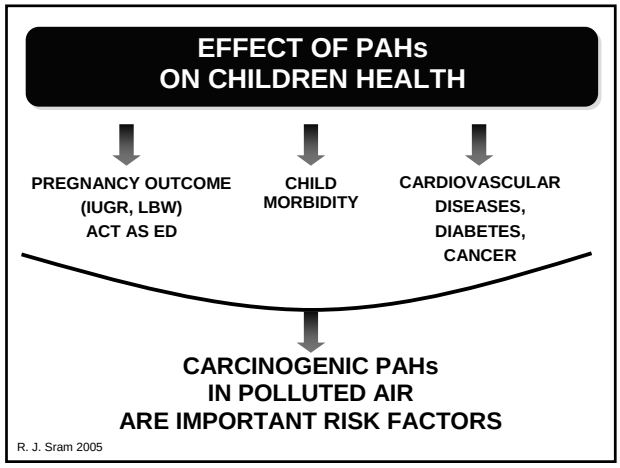

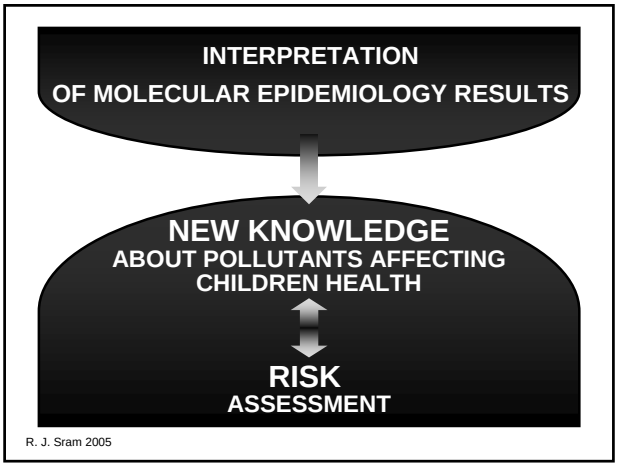

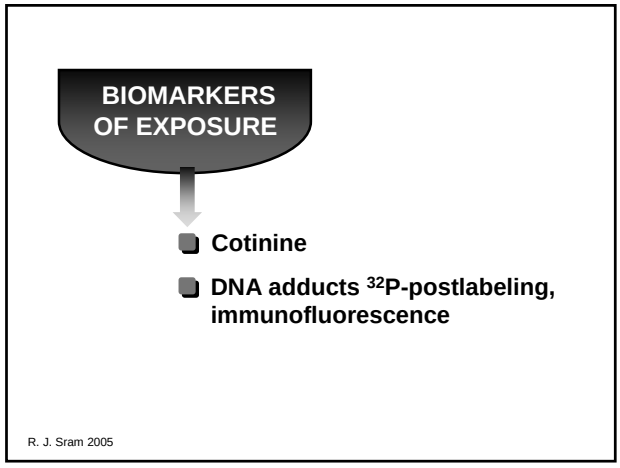

BIOMARKERS OF EFFECT

- **Chromosomal aberrations** (conventional, FISH)
- **Micronuclei**
- **HPRT**

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BIOMARKERS OF SUSCEPTIBILITY

- **Genetic polymorphisms** Metabolic genotype, DNA repair
- **DNA repair** Comet (SCGE)
- **Vitamins**

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IMPACT OF AIR POLLUTION ON BIOMARKERS

- **DNA adducts**
- **Chromosomal aberrations, micronuclei**
- **Genetic polymorphisms**
- **DNA repair**

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AIR POLLUTION c-PAHs

- **Significant group of air pollutants**
- **New risk factors for human population**
- **Risk assessment**

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IMPACT OF AIR POLLUTION – EPIDEMIOLOGIC STUDIES

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TRAFFIC RELATED POLLUTANTS & ADVERSE RISK OUTCOMES

- **POLLUTANTS**
- **TRAFFIC DENSITY**
- **LOW SOCIOECONOMIC STATUS**

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(Wilhelm and Ritz 2003, Ponce et al. 2005)

AIR POLLUTION & LBW

Pollutant	Results
TSP	50 – 100 µg/m^3 ↑ *Wang et al. 1997, Bobak and Leon 1999, Bobak 2000 (Ha et al. 2001)*
SO_2	50 – 100 µg/m^3 ↑ *Wang et al. 1997, Bobak and Leon 1999, Bobak 2000 (Ha et al. 2001, Maisonet et al. 2001)*
CO	> 5.5 ppm, 1 ppm ↑ *Ritz and Yu 1999, Maisonet et al. 2001*

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AIR POLLUTION & PREMATURE BIRTH

Pollutant	Results
TSP	50 – 100 µg/m^3 ↑ *Xu et al. 1995, Bobak 2000*
PM10	50 µg/m^3 ↑ *Ritz et al. 2000*
SO_2	50 – 100 µg/m^3 ↑ *Xu et al. 1995, Bobak 2000*

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AIR POLLUTION & IUGR

Pollutant	Results
PM10	> 40 µg/m^3 *Dejmek et al. 1999, 2000*
PM2.5	> 27 mg/m^3 *Dejmek et al. 1999, 2000*
c-PAHs	> 15 ng/m^3 *Dejmek et al. 2000 (Vassilev et al. 2001)*

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PINCHE RECOMMENDATIONS ON REPRODUCTIVE EFFECTS

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PINCHE RECOMMENDATIONS FOR AIR POLLUTANTS

- **Air pollution significantly affect children health already from the time of conception**
- **EU policy should recognize the risk of PM $_{2.5}$ and c-PAHs for children**
- **It should be understood that the susceptibility of children to air pollution is determined by genetic polymorphisms**

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PINCHE RECOMMENDATIONS FOR AIR POLLUTANTS

- **Determine EU regions with concentrations of $PM_{2.5}$ and c-PAHs over a proposed limit**
- **Propose EU environmental policy for these risk regions to decrease exposure to $PM_{2.5}$ and c-PAHs**

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PINCHE RECOMMENDATIONS FOR $PM_{2.5}$

- **EU proposed "cap" annual average $PM_{2.5}$ conc. 25 μg/m³- corresponds to the monthly concentrations inducing IUGR**
- **Limit value should be obligatory, according to risk assessment for adverse reproductive outcomes**

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PINCHE RECOMMENDATIONS FOR c-PAHs

- **c-PAHs should be recognized as the significant risk for children health**
- **Environmental exposure to c-PAHs should be obligatory monitored**
- **c-PAHs concentrations higher than 15 ng/m3 should be understood as the risk for pregnancy outcomes**
- **EU should propose a limit value for c-PAHs (B[a]P) according to the risk assessment for children health**

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