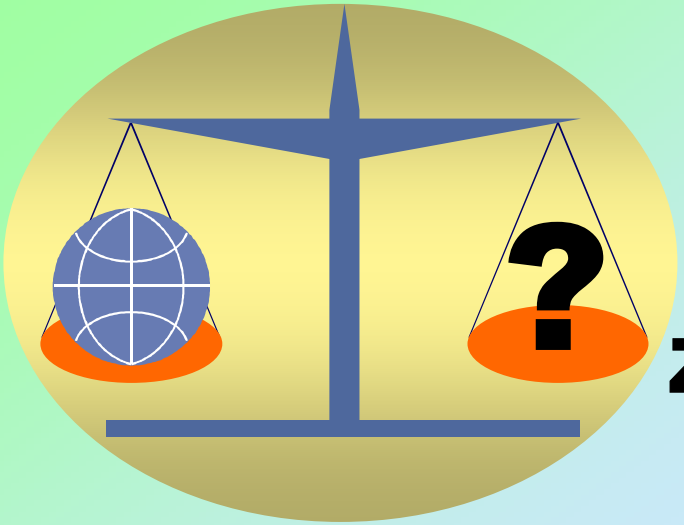

VLIV ZNEČIŠTĚNÉHO OVZDUŠÍ NA ZDRAVOTNÍ STAV POPULACE

Radim J. Šrám

Ústav experimentální mediciny AV ČR
Praha

ARNIKA, Praha, 27. 11. 2008

VÝVOJ ZNEČIŠTĚNÍ OVZDUŠÍ V ČR

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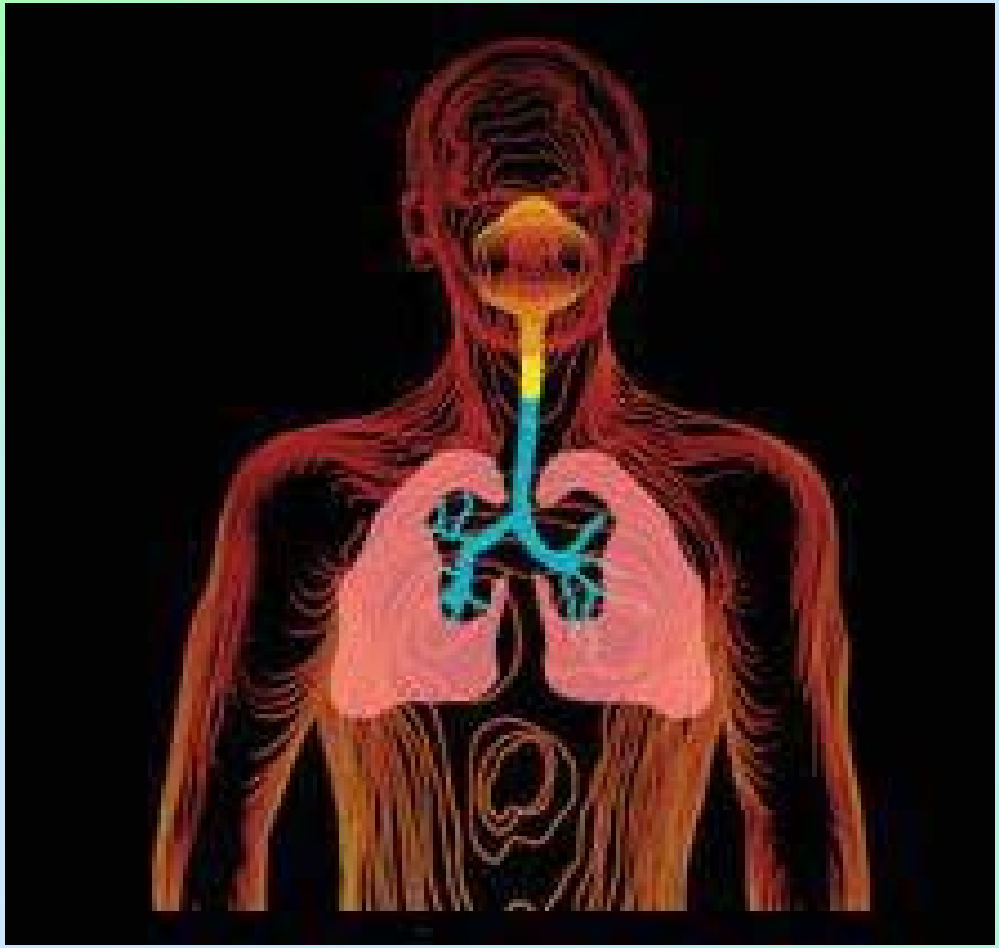
Air particles deposition in the airways



> 10 mm

< 10 mm (PM10)

< 2.5 mm (PM2.5)

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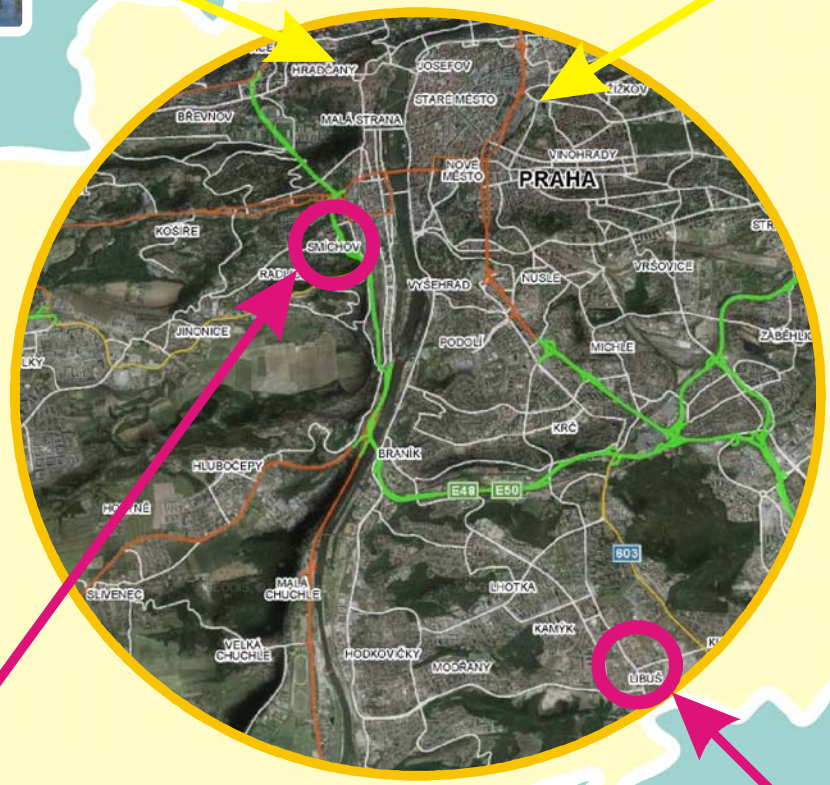
Prague Castle

Old Town Square

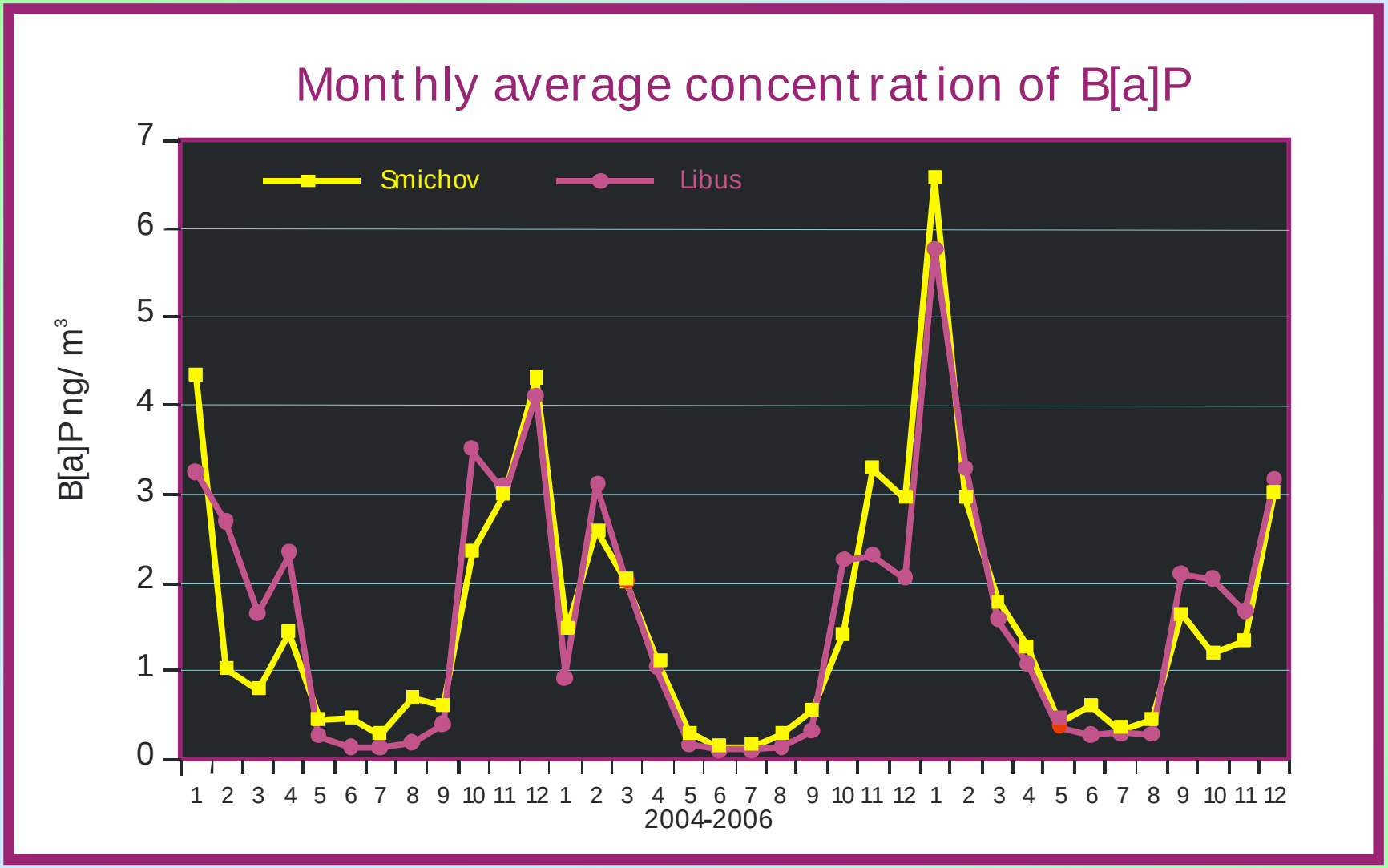


PRAGUE

Prague-Smichov

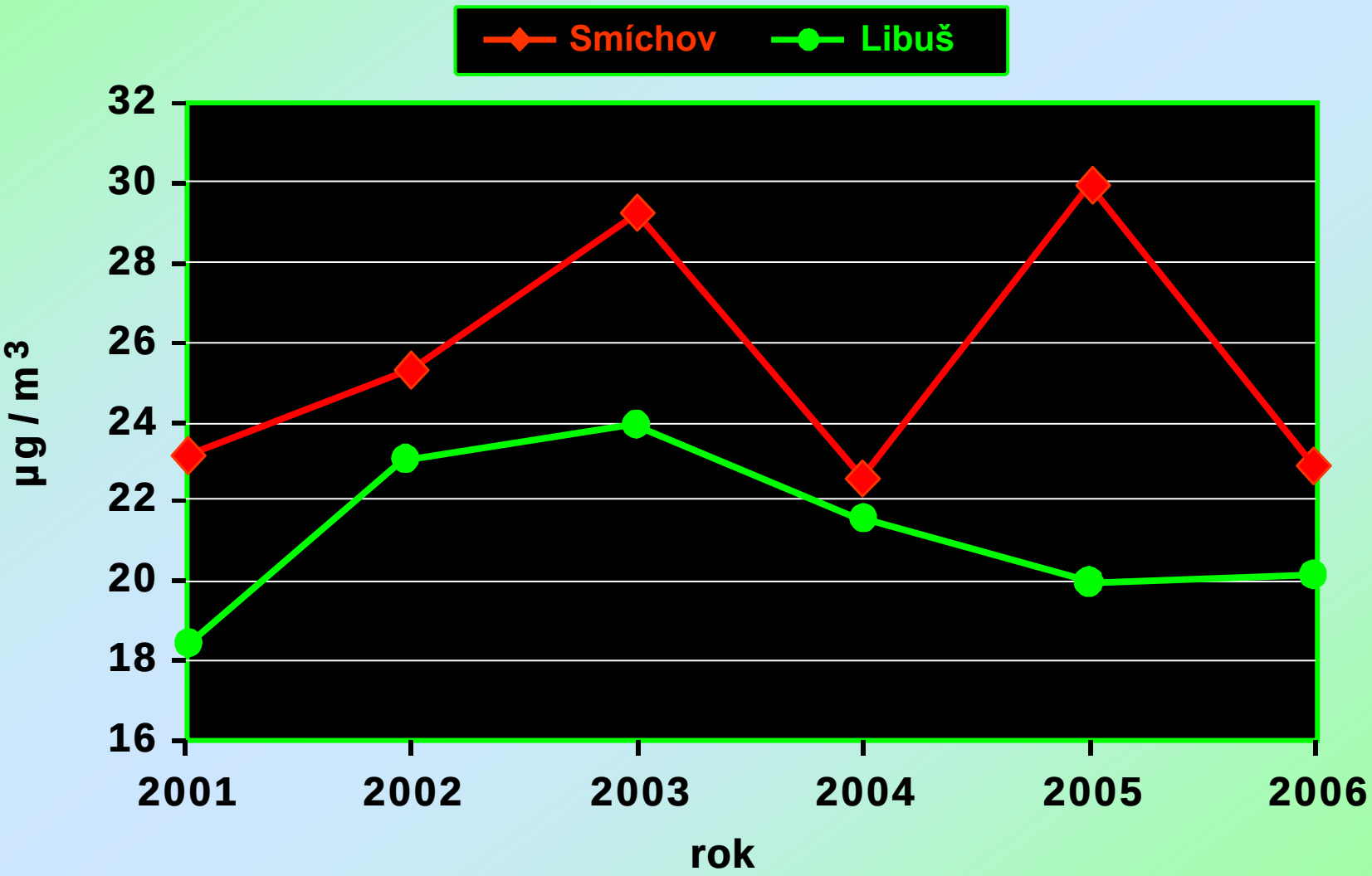
Prague- Libus

STATIONARY MONITORING


Monthly average concentration of B[a]P
Smichov
Libus
B[a]P ng/ m3
0
1
2
3
4
5
6
7
1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3 4 5 6 7 8 9 10 11 12
2004-2006

Roční průměry PM2.5

Praha - Smíchov a Libuš 2001- 2006



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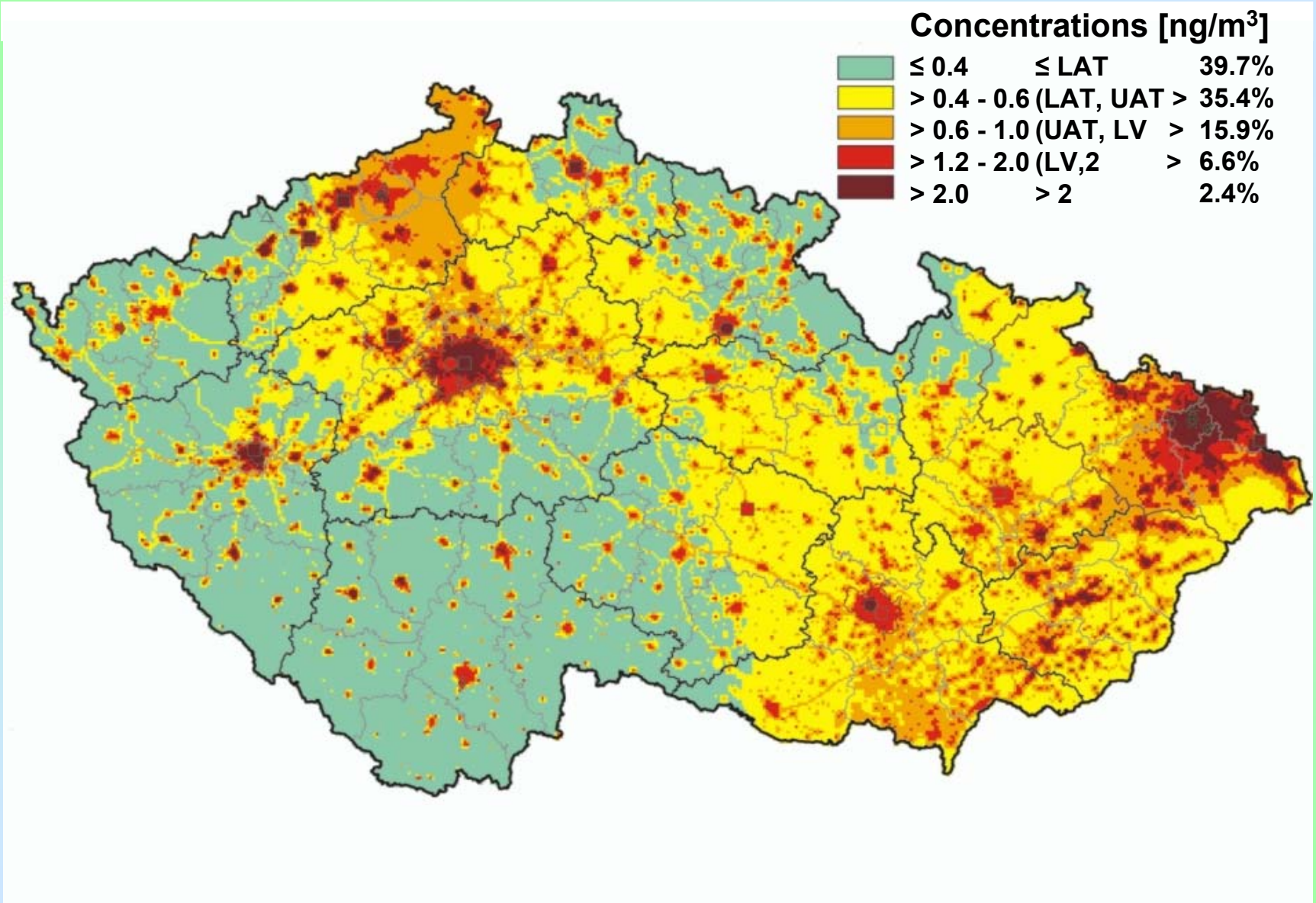
B[a]P - 2006



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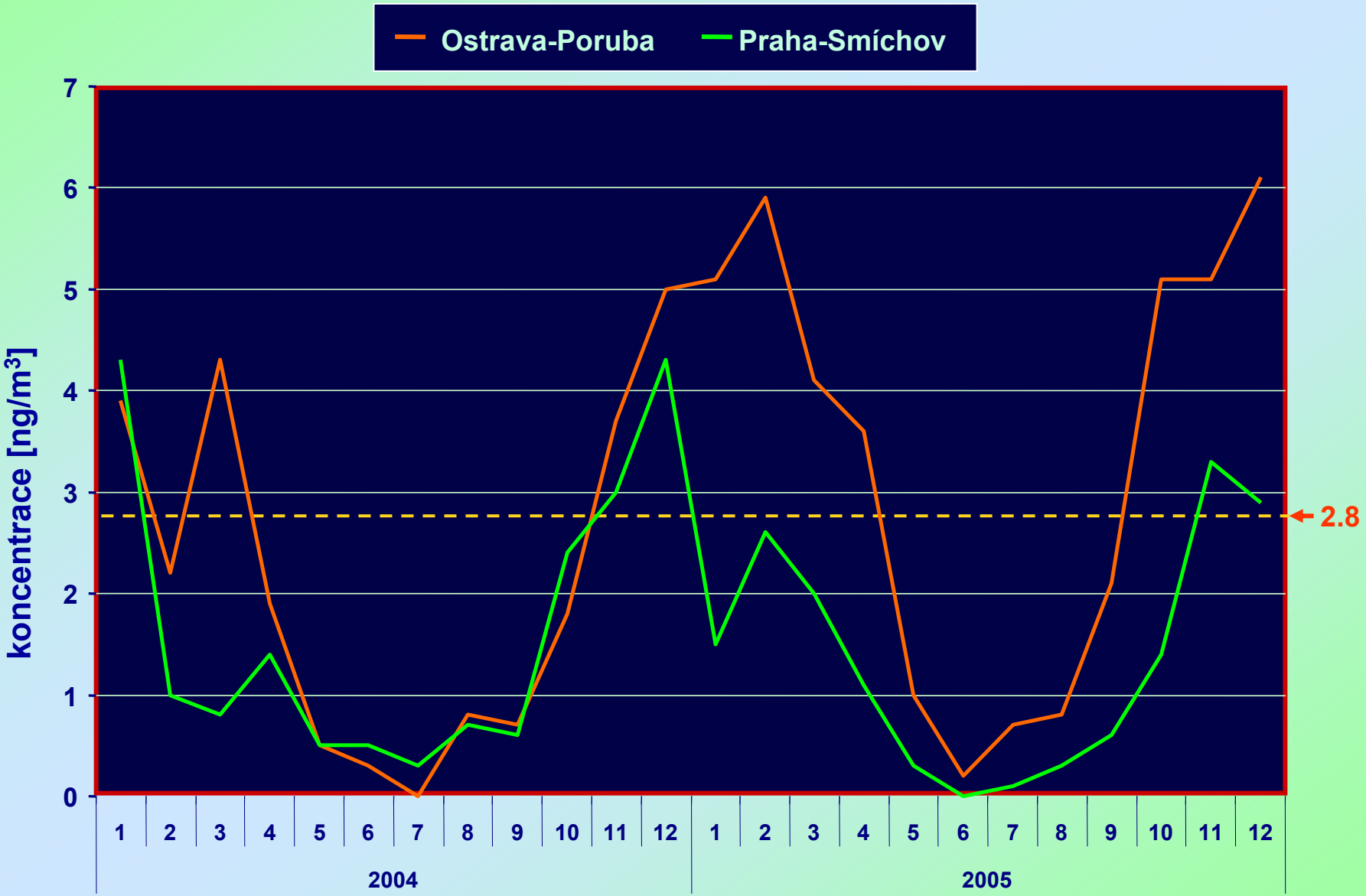
KONCENTRACE B[a]P



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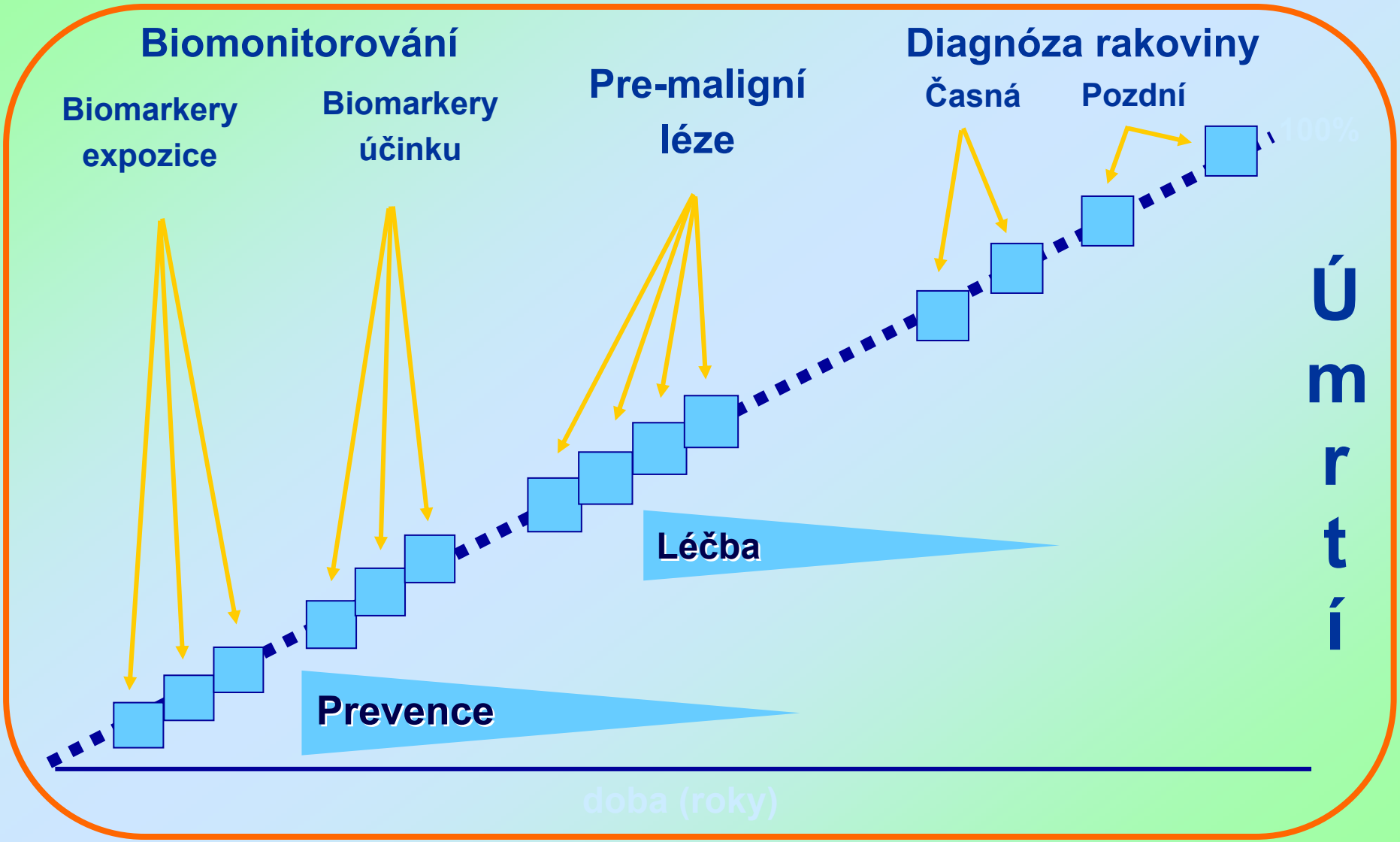
BIOMARKERS

R. J. Sram 2008

LIDSKÉ BIOMARKERY

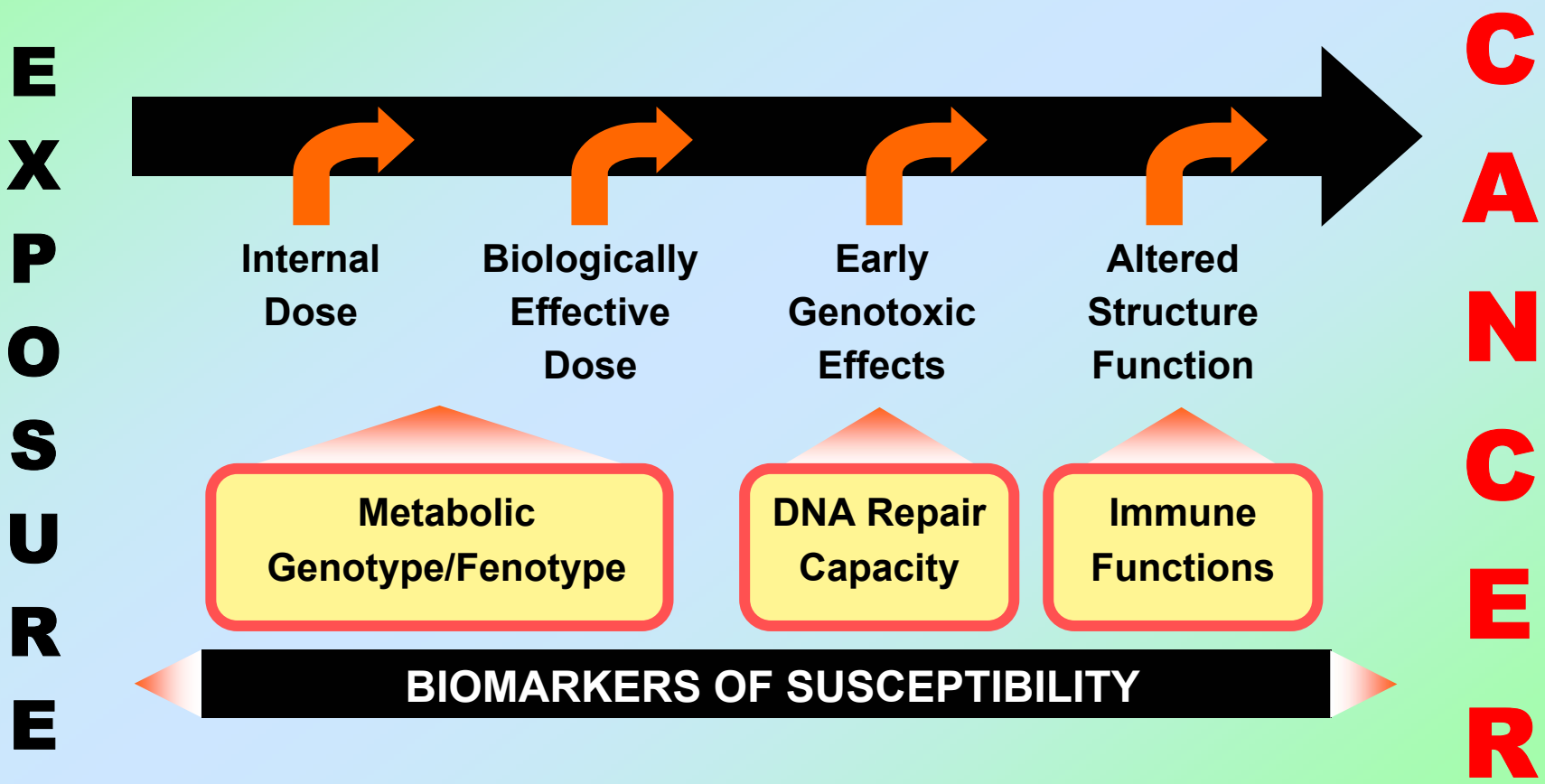


R. J. Šrám 2006

R.J. Albertini 1998

HUMAN BIOMARKERS

Genetic/Carcinogenic Risks



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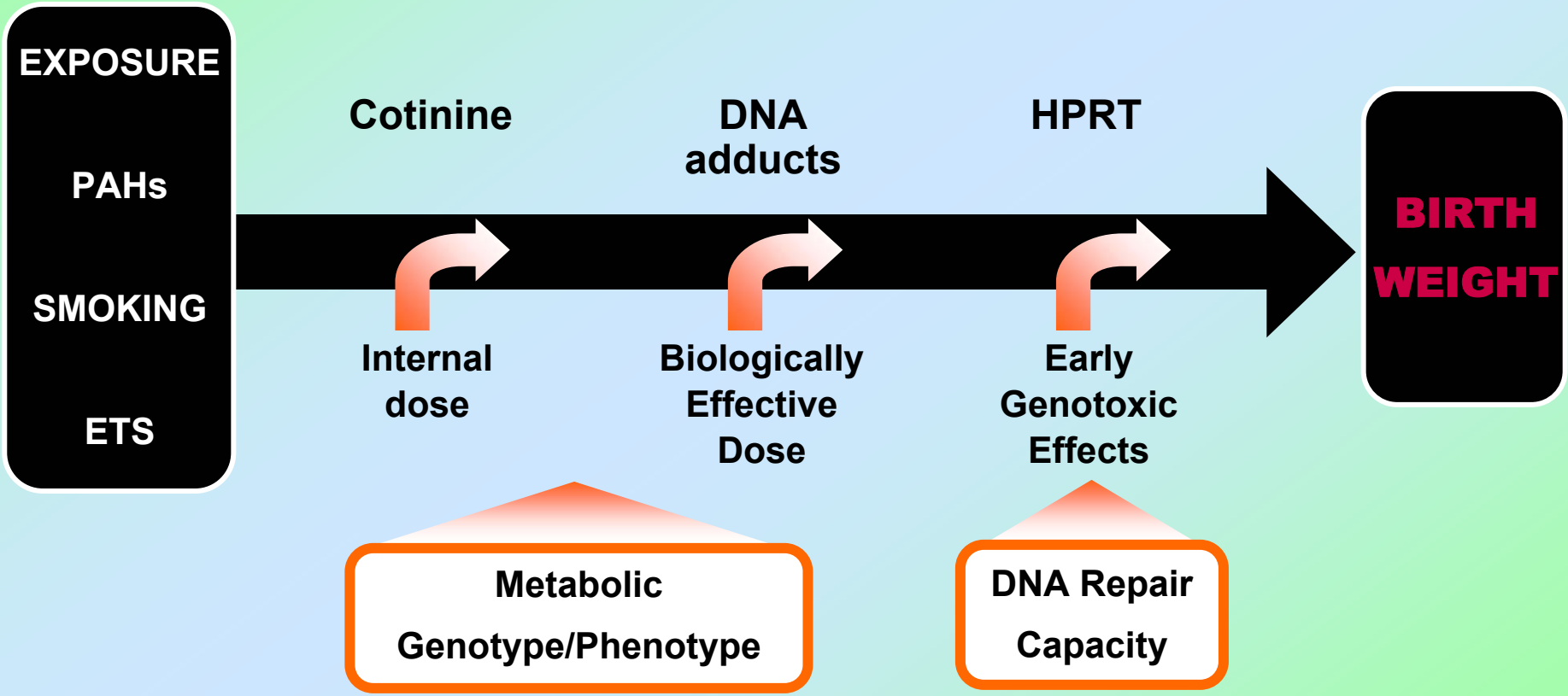
Environ Health Perspect 74: 3-9, 1987

PREGNANCY OUTCOME



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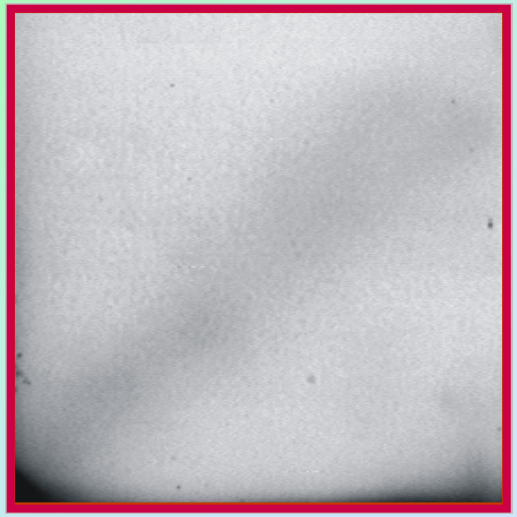
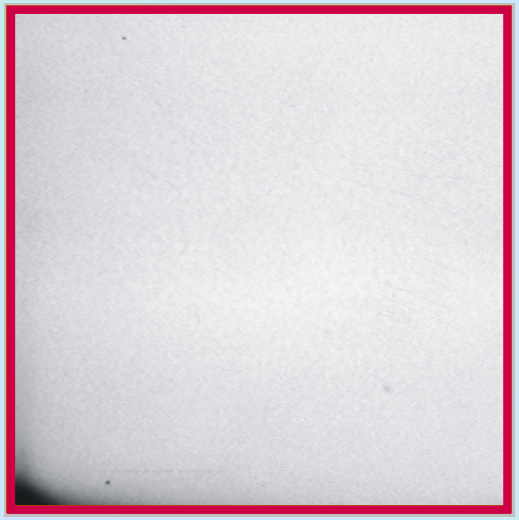
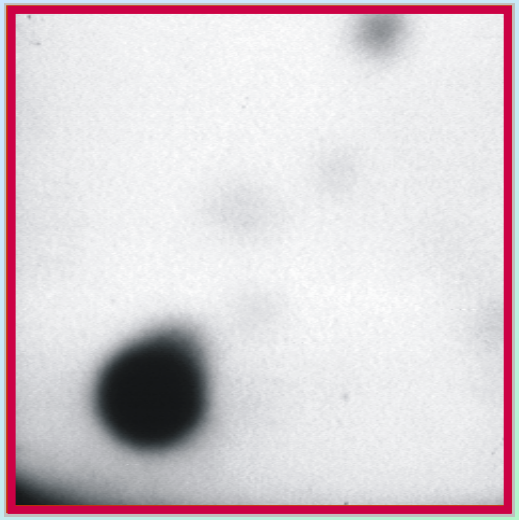
Autoradiographs of thin layer chromatograms with DNA adduct pattern of:



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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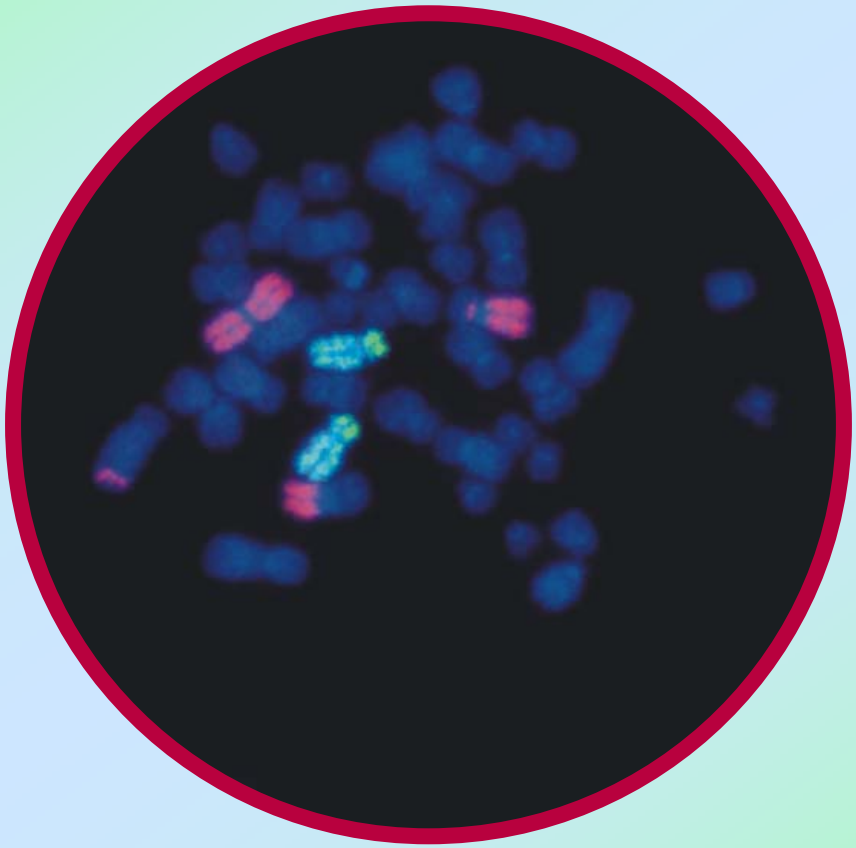
CYTOGENETIC ANALYSIS

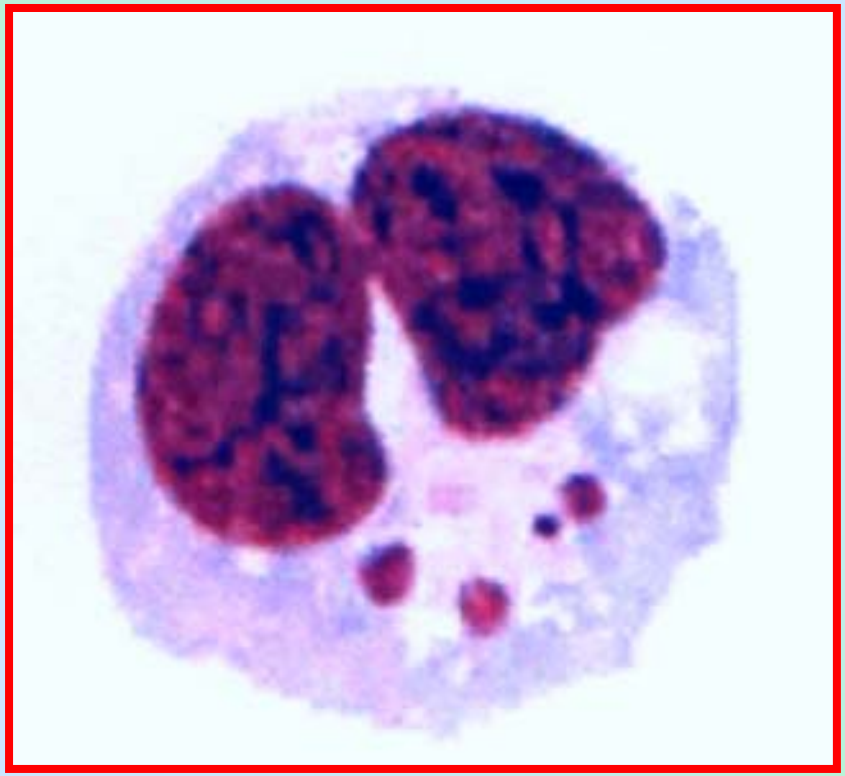
FISH analysis



t(Ab);t(Ab);t(Ba)

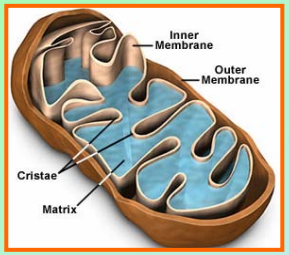
Three translocations between chromosome 1 and unpainted chromosomes

MICRONUCLEI

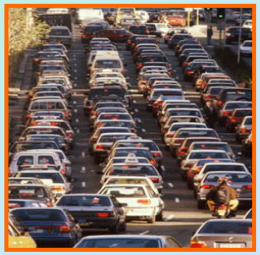


Reactive oxygen species

Endogenous sources



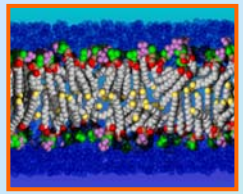
Exogenous sources

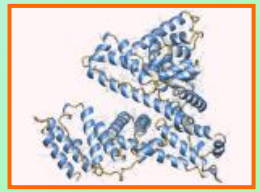



$O_2^{\cdot-}$ —SOD→ H_2O_2 —Catalase→ $H_2O + O_2$

H_2O_2 —GPX→ H_2O

H_2O_2 → $OH^{\cdot}$





Lipid peroxidation **DNA oxidation** **Protein oxidation**

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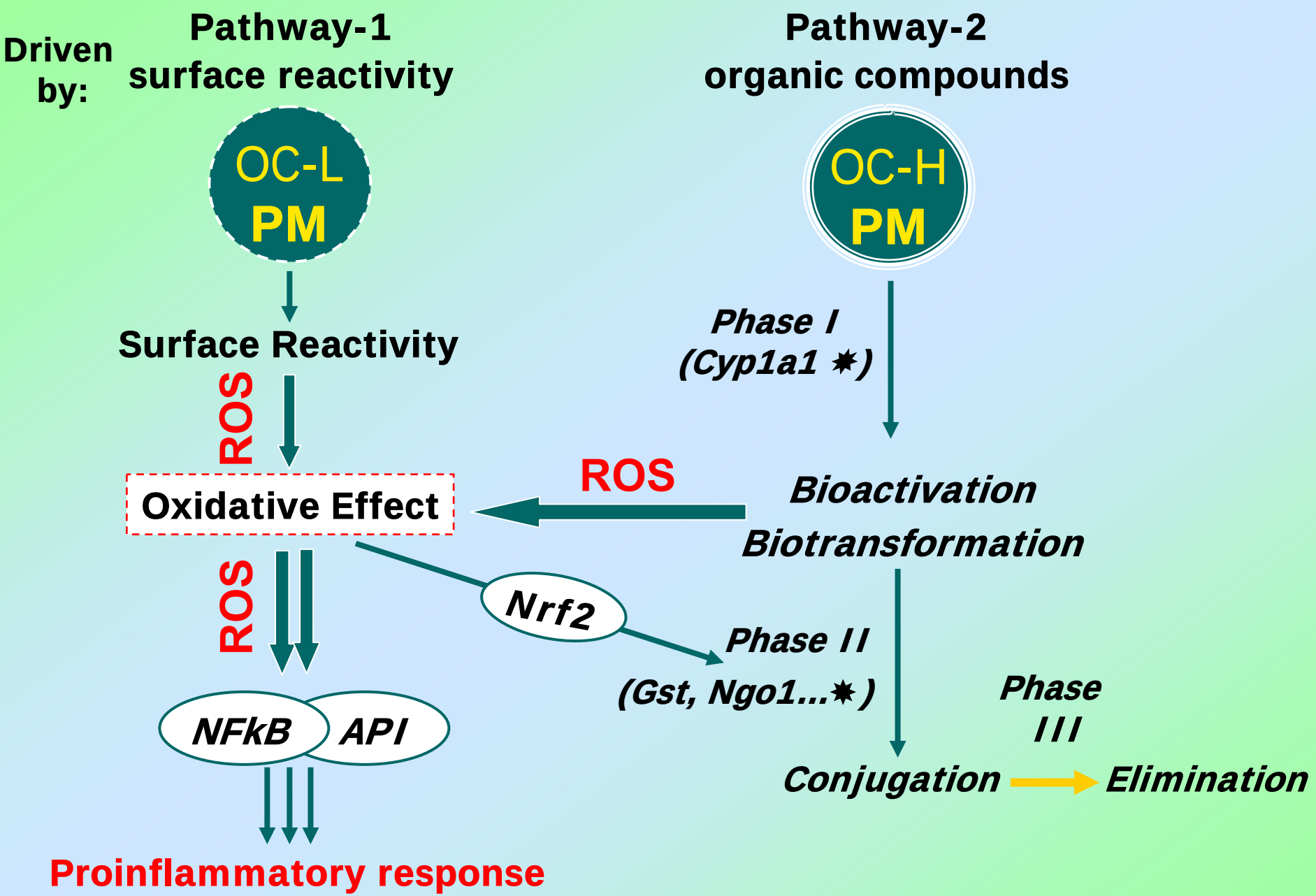
Driven by:
Pathway-1
surface reactivity
Pathway-2
organic compounds
OC-L
PM
OC-H
PM
Surface Reactivity
ROS
Phase I
(Cyp1a1 ✸)
ROS
Oxidative Effect
Bioactivation
Biotransformation
ROS
Nrf2
Phase II
(Gst, Ngo1...✸)
Phase
III
NFkB
API
Conjugation
Elimination
Proinflammatory response

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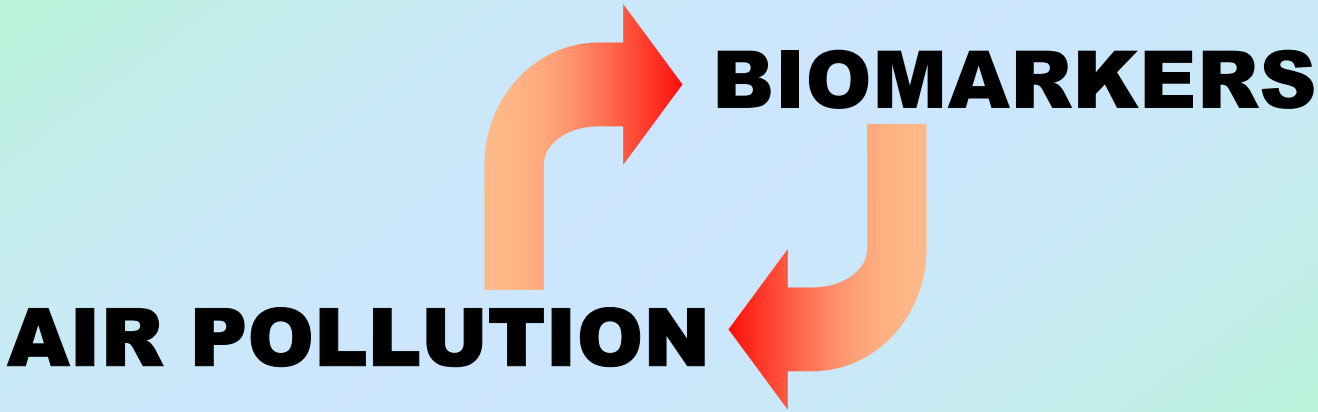

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Human studies and biomarkers of exposure, effect and susceptibility

- 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, folic acid
- 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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c-PAHs CONCENTRATIONS
PERSONAL MONITORING

(median and range)

Group	N	Age (years)	B[a]P ng/m^3	carcPAU ng/m^3
EXPOSED	53	31.6 ± 7.2	1.6 (0.3 - 8.7)	9.7 (3.1 - 58.2)
Smokers	19	32.9 ± 7.0	1.6 (0.3 - 7.5)	10.8 (3.1 - 43.6)
Nonsmokers	34	30.9 ± 7.3	1.5 (0.3 - 8.7)	8.7 (3.1 - 58.2)
CONTROLS	52	29.6 ± 9.1	0.8 (0.3 - 2.8)	5.8 (3.1 - 19.3)
Smokers	7	37.6 ± 14.2	0.3 (0.3 - 1.4)	3.3 (3.1 - 8.2)
Nonsmokers	45	28.3 ± 7.6	0.9 (0.3 - 2.8)	6.1 (3.1 - 19.3)

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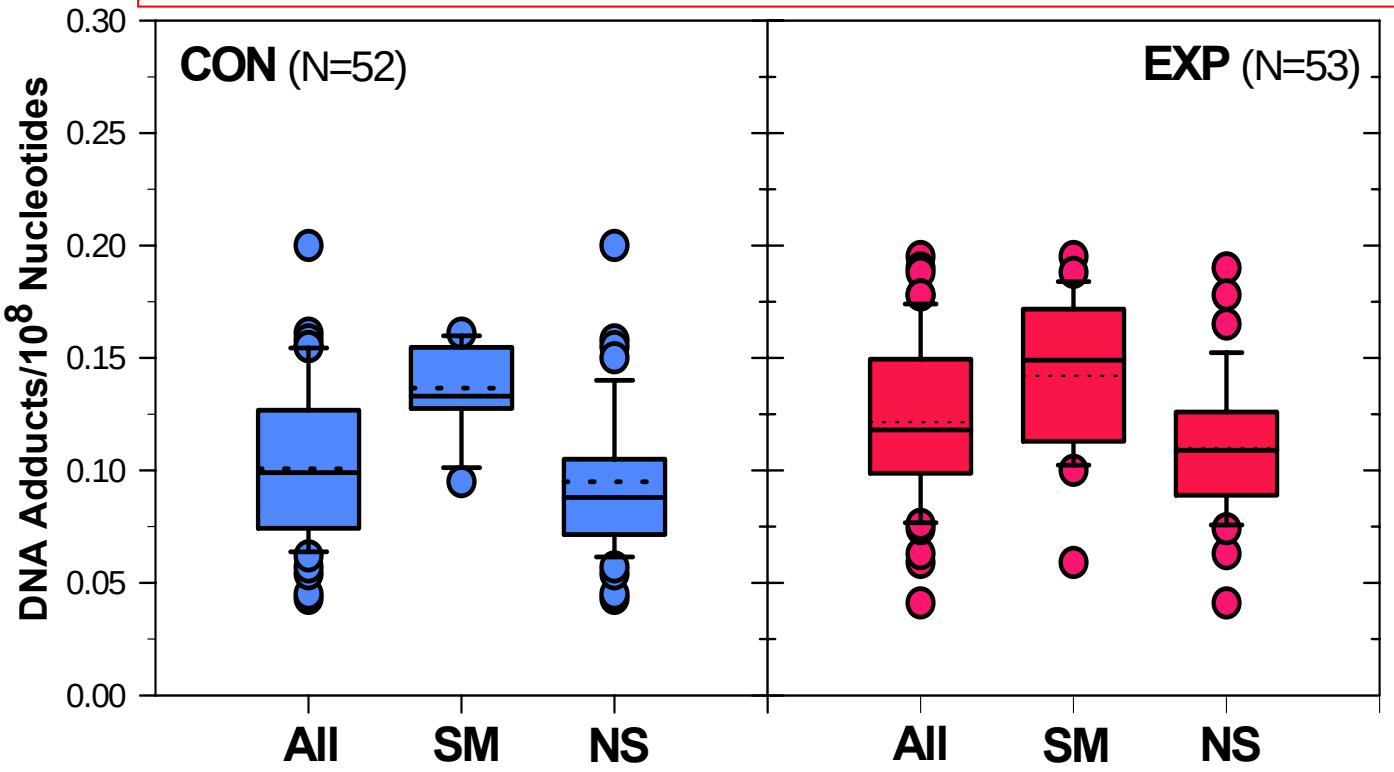
„LIKE“ B[a]P-DNA ADDUCT



EXP vs CON: P<0.01

Smokers vs Nonsmokers within groups: P<0.01

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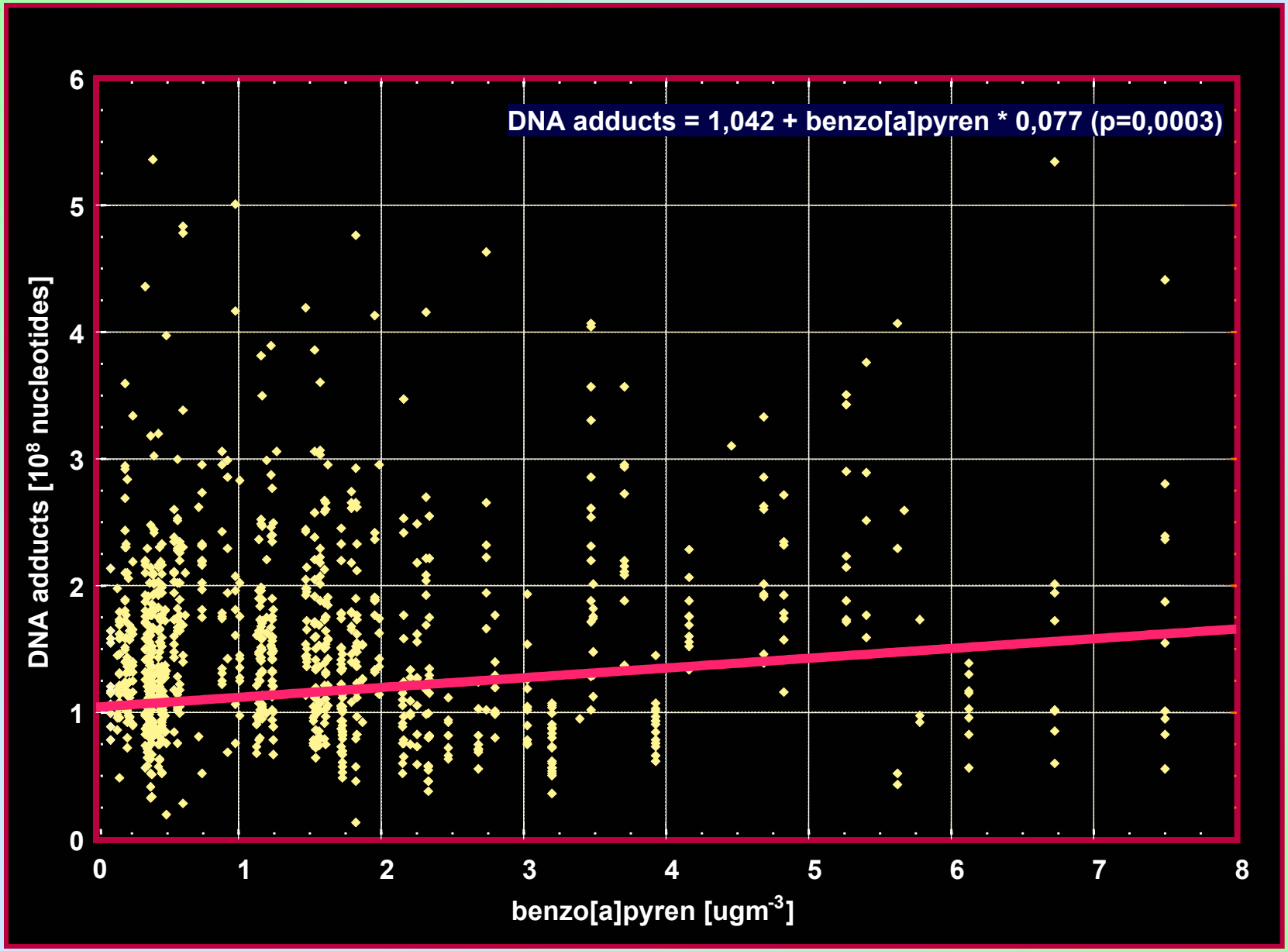
IMPACT OF ENVIRONMENTAL POLUTION TO DNA ADDUCTS



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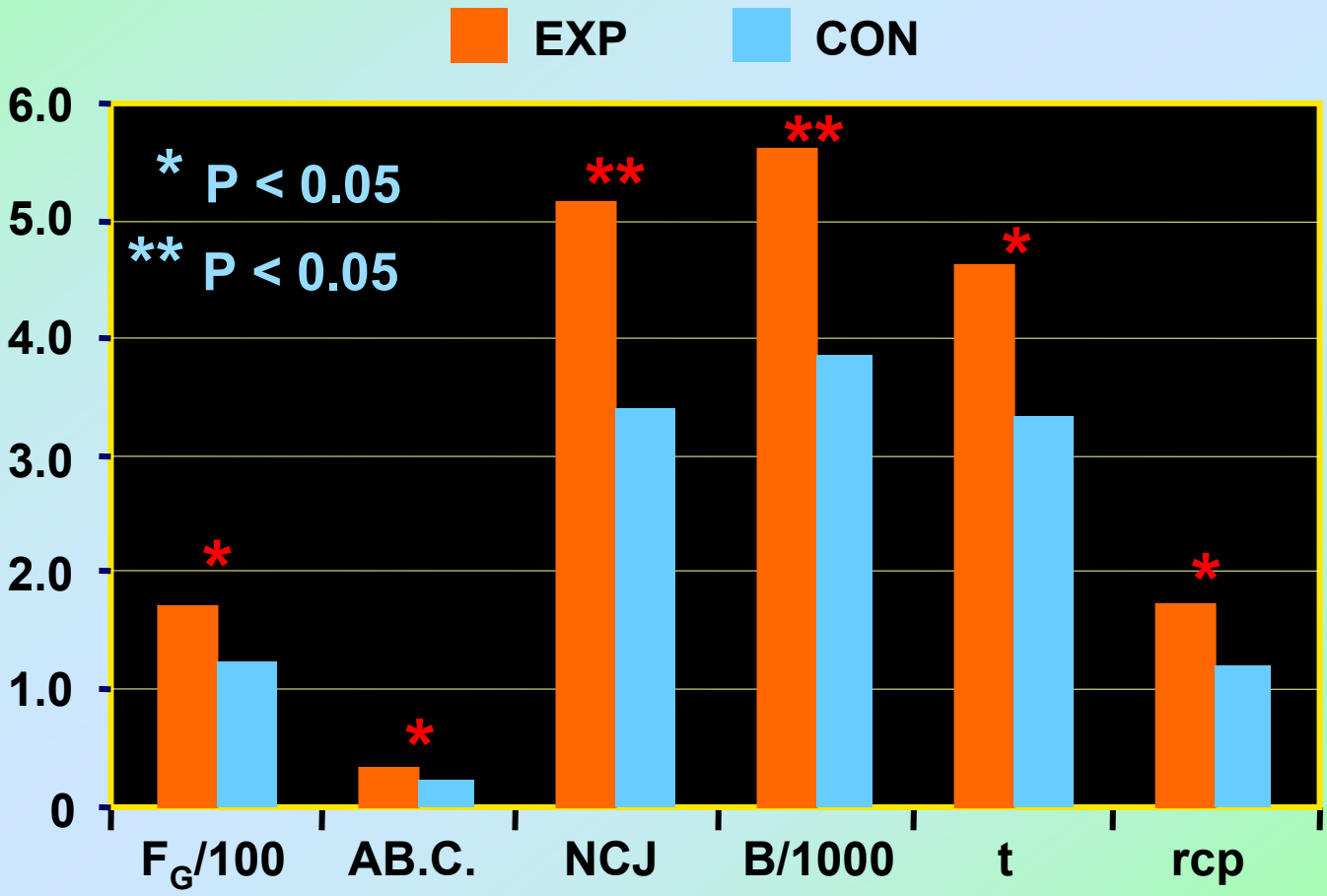
CYTOGENETIC ANALYSIS

FISH



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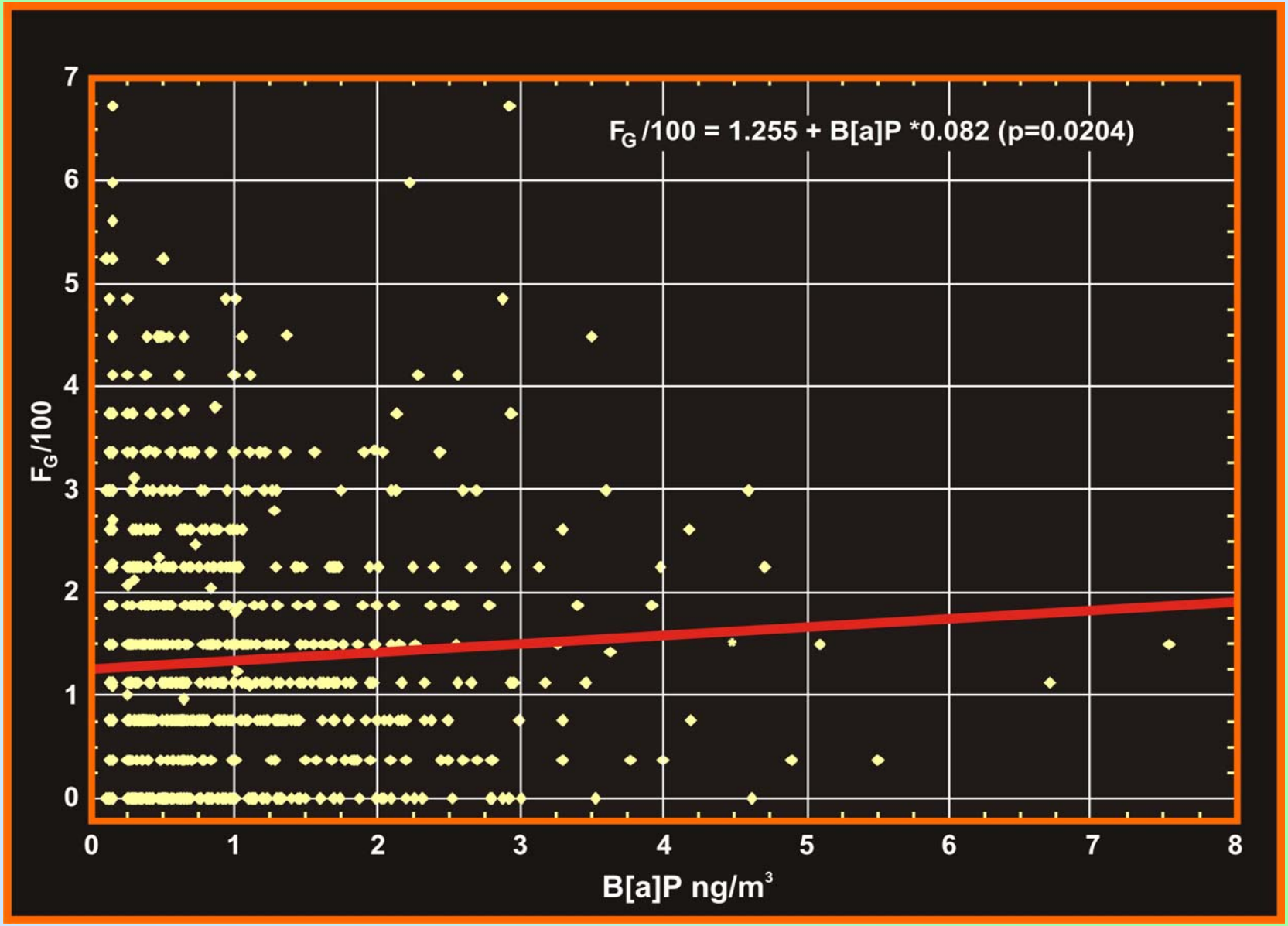
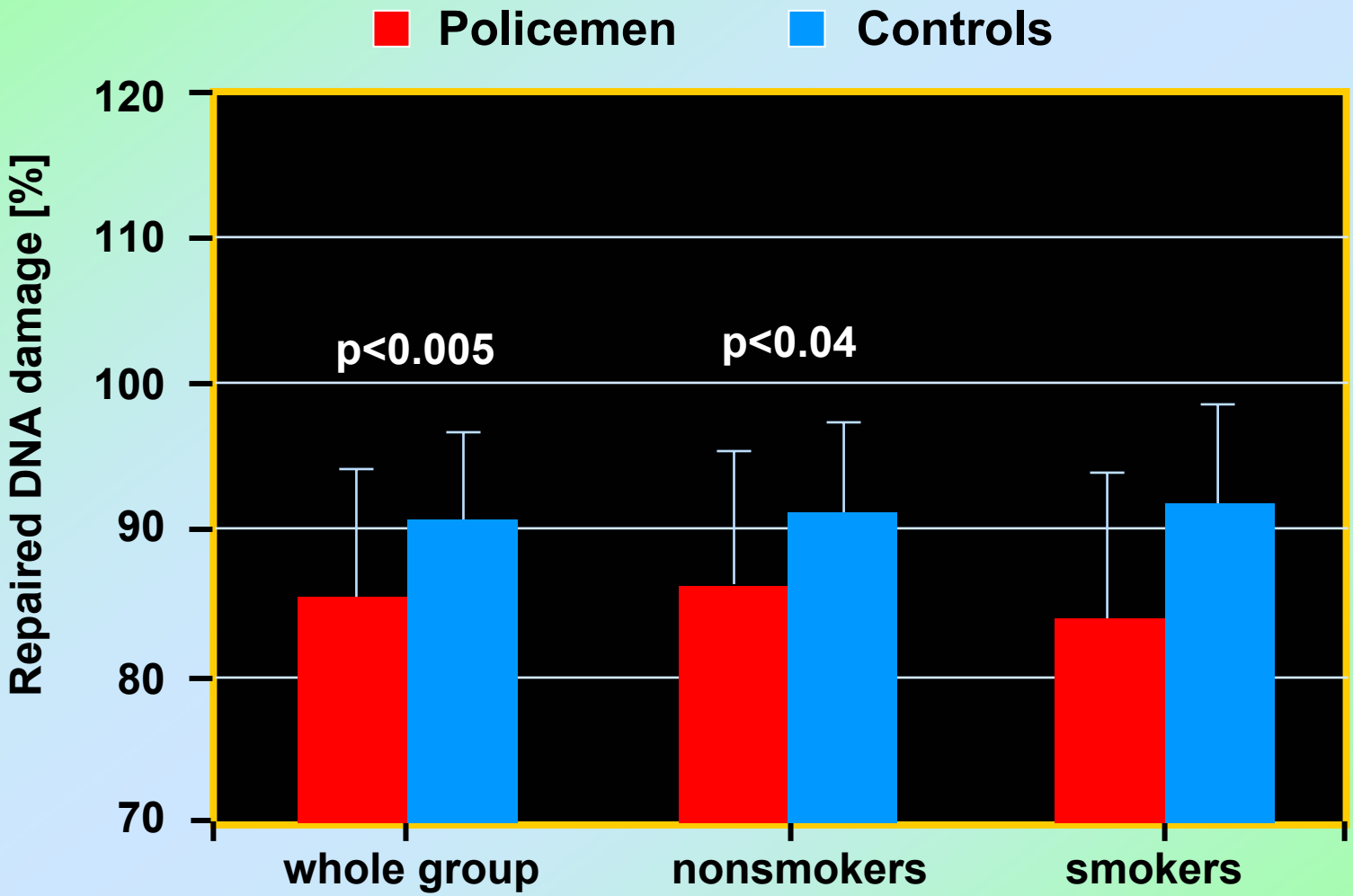
IMPACT OF ENVIRONMENTAL POLUTION TO CHROMOSOMAL ABERRATIONS - FISH



SCGE repair capacities of DNA damage



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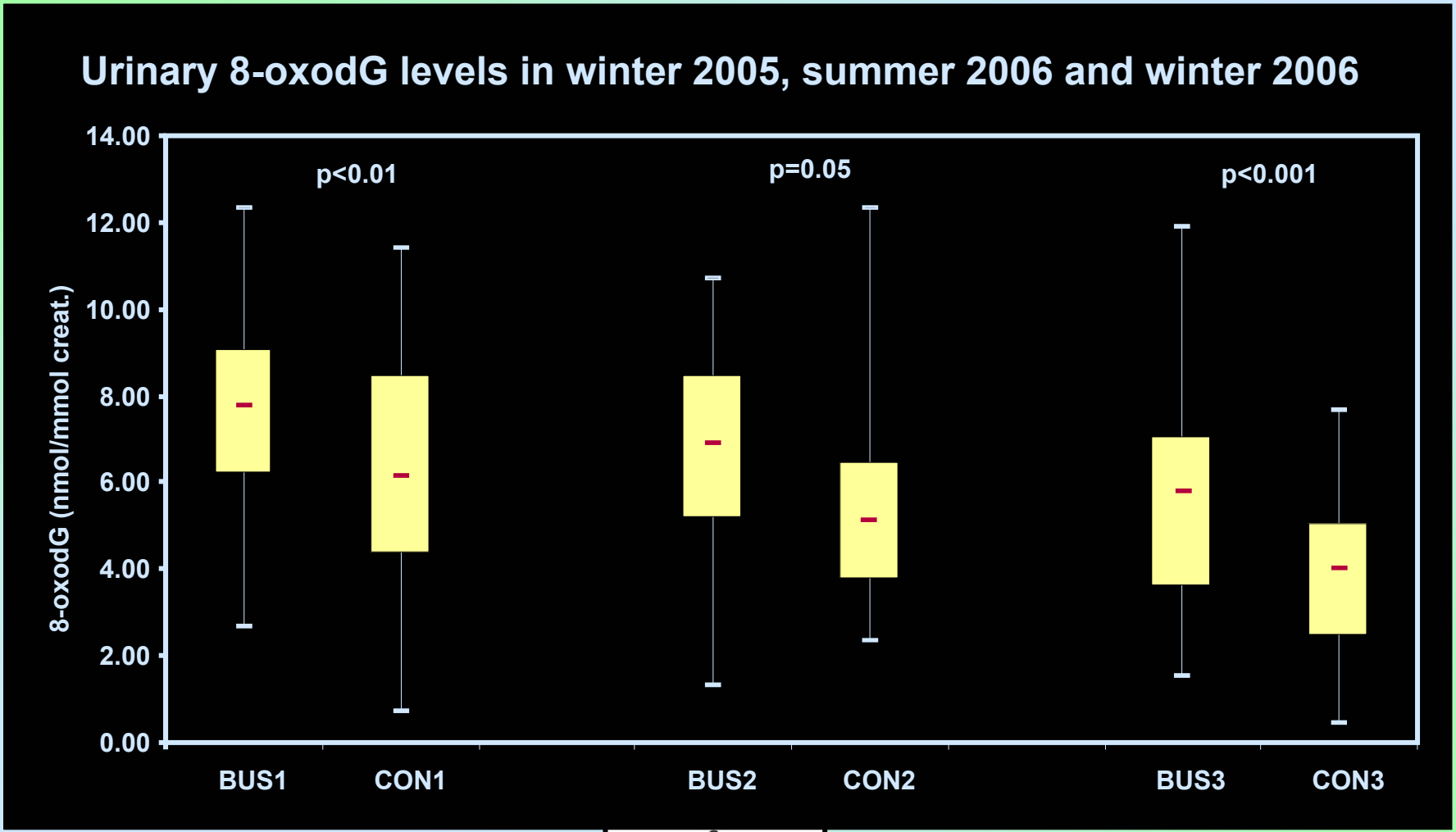
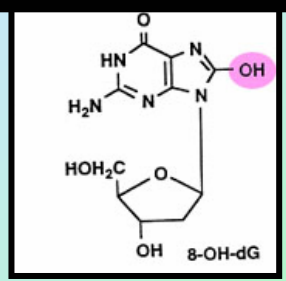
8-oxodG in urine of bus drivers and controls





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Correlation between oxidative stress markers and other factors

		15-F_{2t}-IsoP	8-oxodG	carbonyl	B[a]P	cPAHs	PM2.5	PM10
15-F_{2t}-IsoP	R P	- -	0.212 <0.001	0.083 0.165	0.172 p<0.01	0.180 p<0.01	0.168 p<0.01	0.116 p<0.05
8-oxodG	R P	0.212 <0.001	- -	0.057 0.338	0.009 0.874	0.009 0.874	0.212 <0.001	0.307 <0.001
carbonyl	R P	0.083 0.165	0.057 0.338	- -	-0.371 <0.001	-0.379 <0.001	-0.404 <0.001	-0.030 0.613

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VLIV OVZDUŠÍ

NA RESPIRAČNÍ ONEMOCNĚNÍ U DĚTÍ

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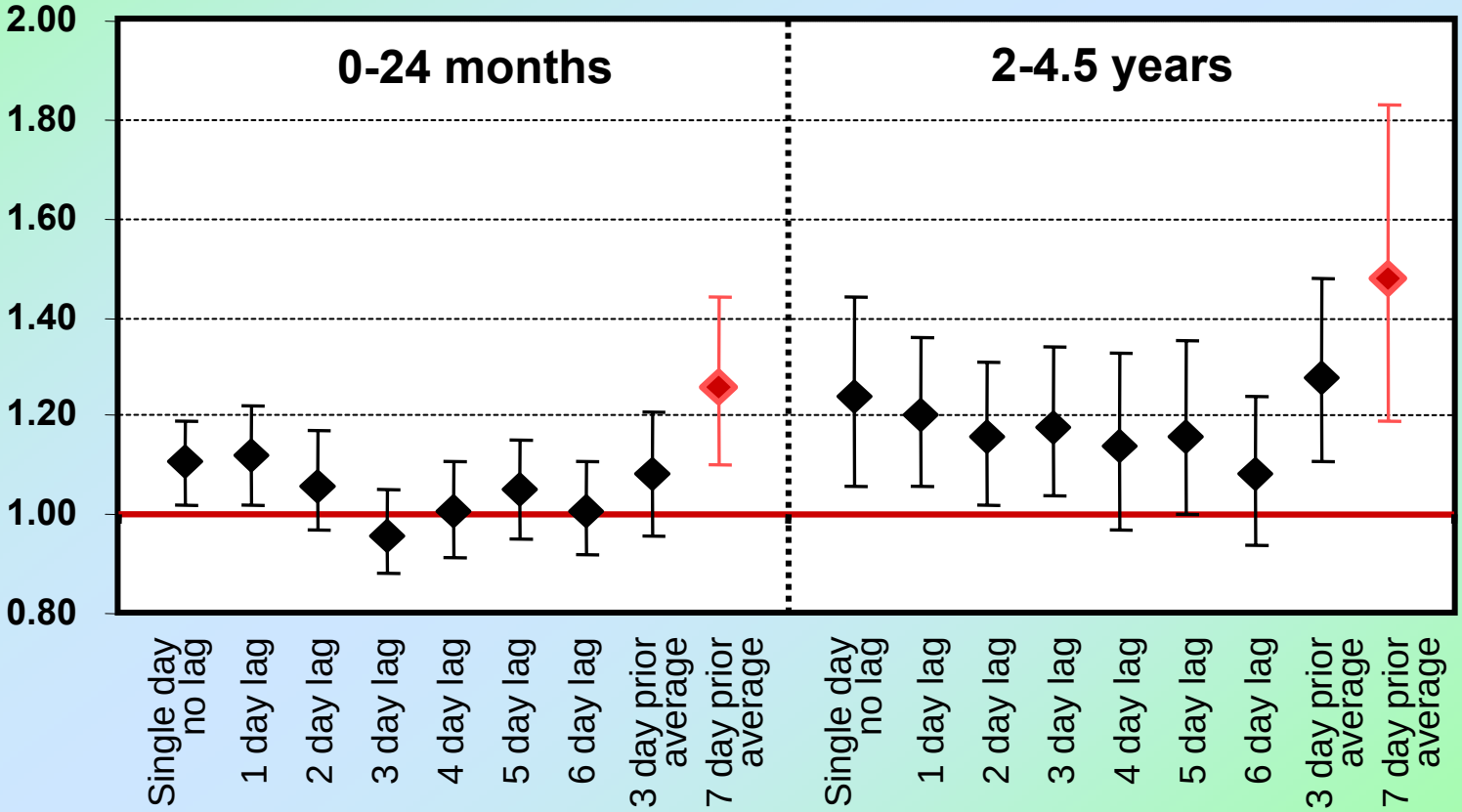
Bronchitidy RR, 95% CI's, akutní expozice PAU,
multivariátní analýza



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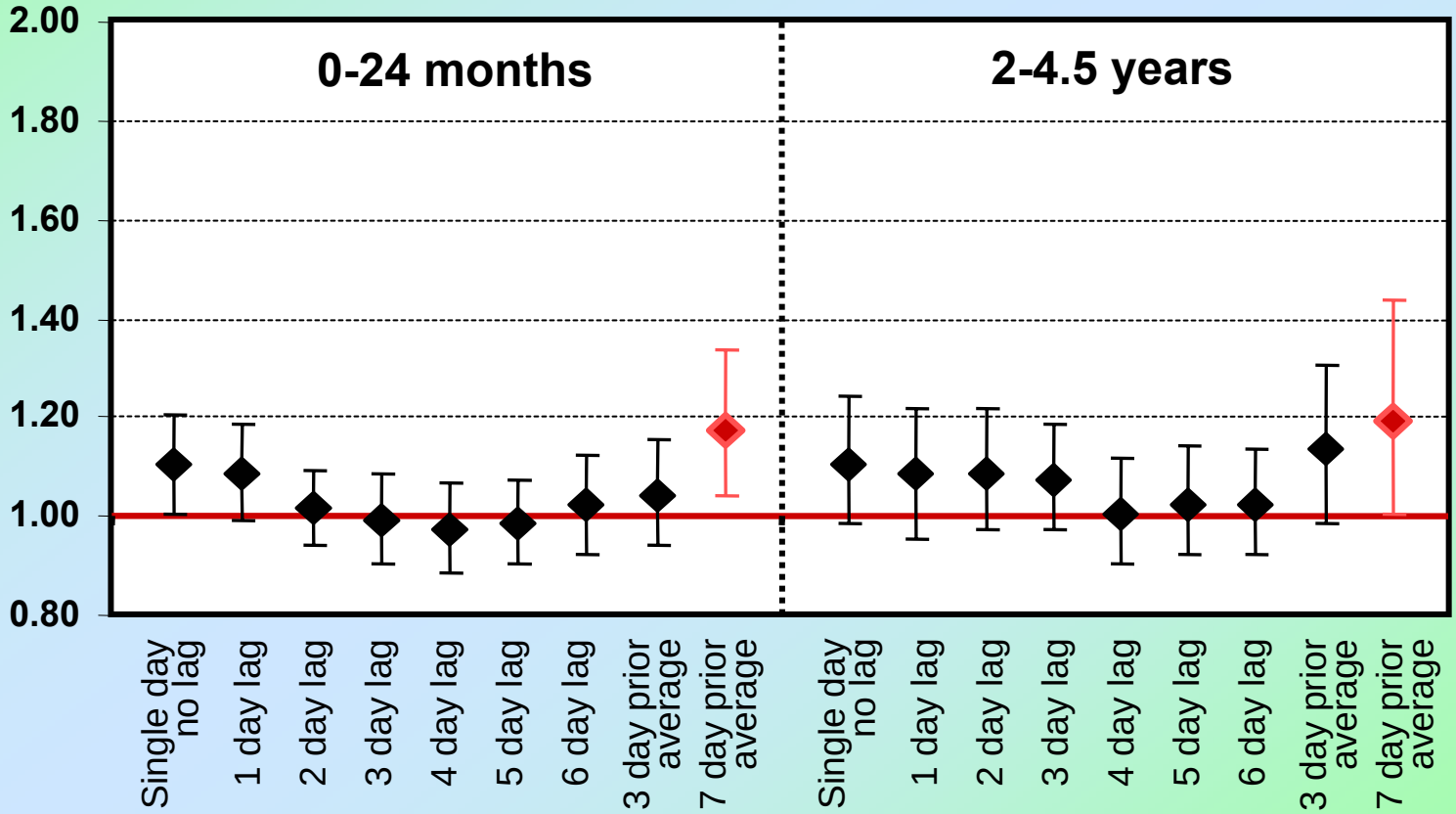
Bronchitidy RR, 95% CI's, akutní expozice PM2.5,
multivariátní analýza



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Význam

první léta života dítěte
jsou kritickou periodou
dýchacího ústrojí a imunity

VLIV OVZDUŠÍ

NA 8-oxodG V MOČI DĚTÍ

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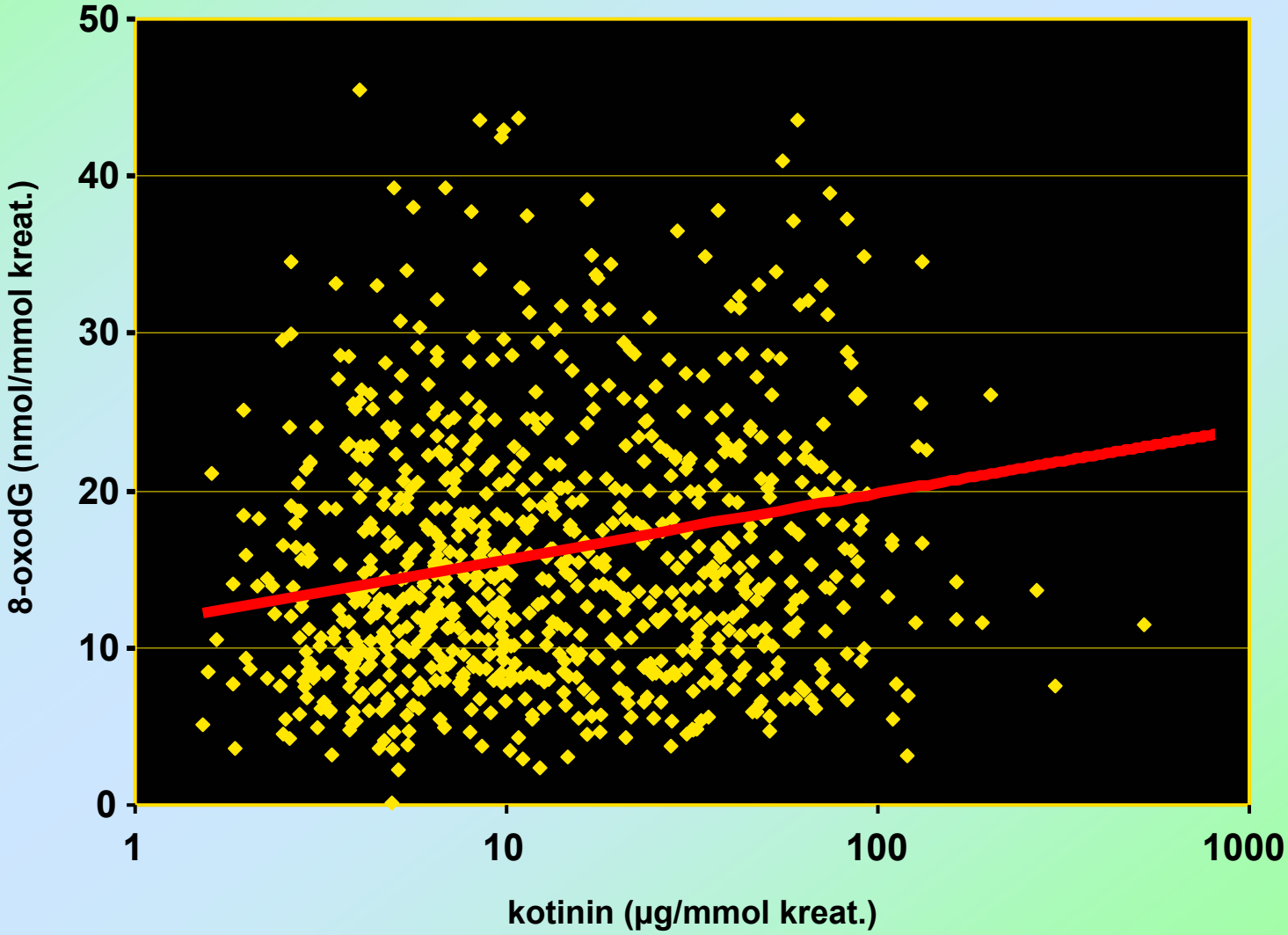
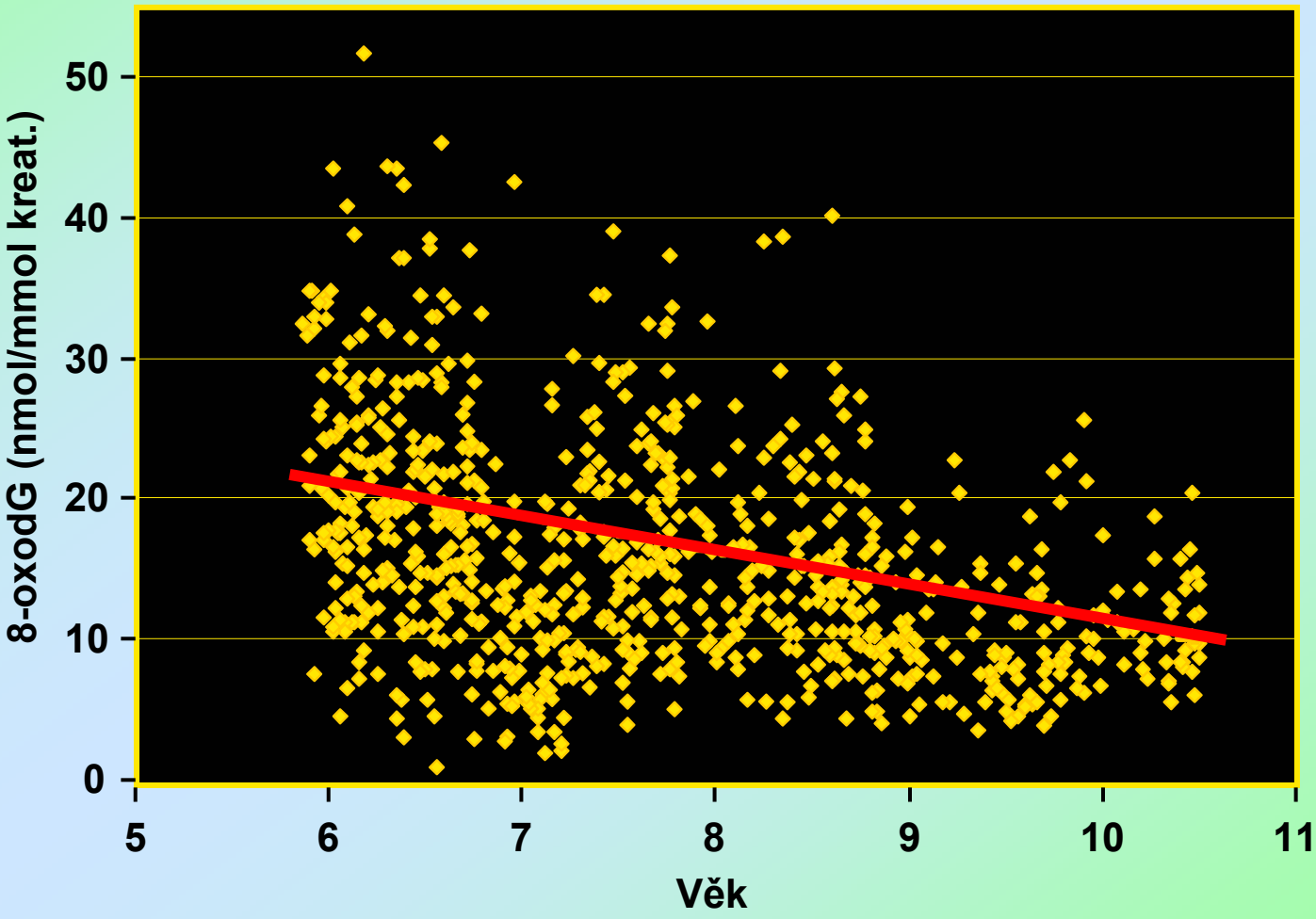
Vztah 8-oxodG a kotininu



Vztah 8-oxodG a věku dítěte



Multivariate model of effect of PM2.5 on 8-oxodG levels (linear regression)

Region	Pollutant	Period (days before sampling			
		3-day (-4;-6)		7-day (-1;-7)	
		R	p	R	p
All	Intercept		33.56		33.94
	PM2.5	0.16	<0.05	0.16	0.08
	Child age	-2.74	<0.0001	-2.74	<0.001
	Cotinine (above/below 20 ng/mg)	3.20	0.001	3.23	0.005
	Allergic rhinitis	1.34	0.41	1.28	<0.005
Teplice	Intercept	28.57		29.81	
	PM2.5	0.24	<0.01	0.23	<0.05
	Child age	-2.51	<0.001	-2.56	<0.001
	Cotinine (above/below 20 ng/mg)	4.41	<0.005	4.321	0.005
	Allergic rhinitis	7.59	0.01	7.64	0.01
Prachatice	Intercept	43.71		45.22	
	PM2.5	-0.13	0.30	-0.20	0.21
	Child age	-3.07	<0.001	-3.09	<0.001
	Allergic rhinitis	-3.03	0.06	-3.02	0.06

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Multivariate model of effect of B[a]P on 8-oxodG levels (linear regression)

Region	Pollutant	Period (days before sampling			
		3-day (-4;-6)		3-day (-1;-7)	
		R	p	R	p
All	Intercept	34.01		34.94	
	B[a]P	-1.44	0.03	1.20	0.08
	Child age	-2.65	<0. 001	-2.74	<0.001
	Cotinine (above/below 20 ng/mg)	3.04	<0.005	3.49	<0.01
	Allergic rhinitis	1.19	0.47	1.27	0.55
Teplice	Intercept	31.09		31.30	
	B[a]P	1.73	<0.05	2.13	<0.05
	Child age	-2.54	<0.001	-2.71	<0.001
	Cotinine (above/below 20 ng/mg)	4.42	<0.005	4.58	0.01
	Allergic rhinitis	7.76	<0.01	8.46	<0.05
Prachatice	Intercept	40.25		42.18	
	B[a]P	-0.02	0.98	-0.99	0.36
	Child age	-3.05	<0.001	-2.97	<0.001
	Allergic rhinitis	-1.62	0.22	-4.18	0.05

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8-oxodG V MOČI DĚTÍ

- zvýšen při expozici pasivnímu kouření
- snižuje se s věkem dětí
- je ovlivněn etnicitou a vzděláním matky
- zvýšen expozicí PM2.5 a PM10 7 dní před odběrem
- zvýšen expozicí k-PAU 1-3 a 7-9 dní před odběrem
- zvýšen u dětí s alergickou rhinitidou

VLIV OVZDUŠÍ NA VÝSLEDKY TĚHOTENSTVÍ

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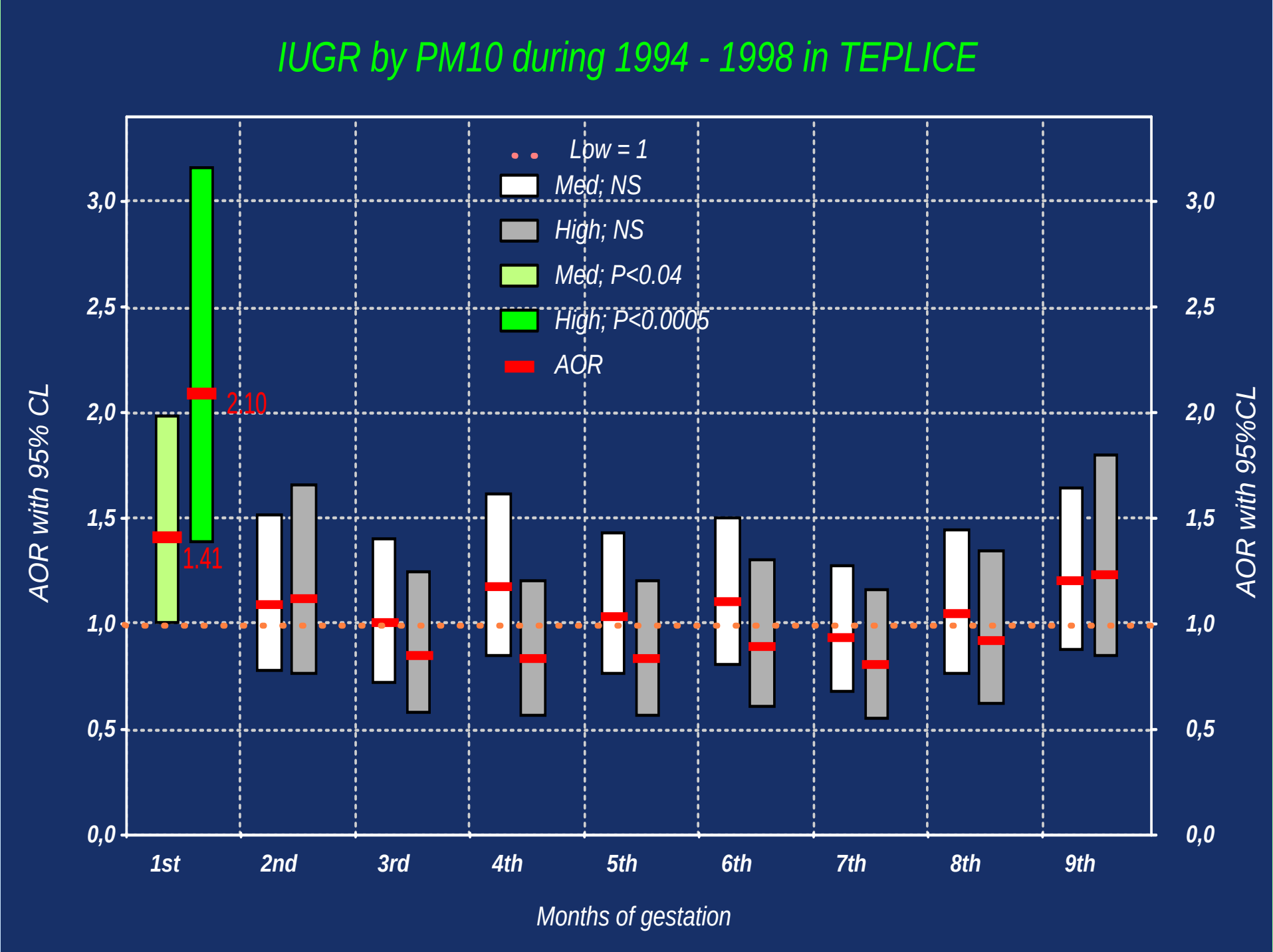
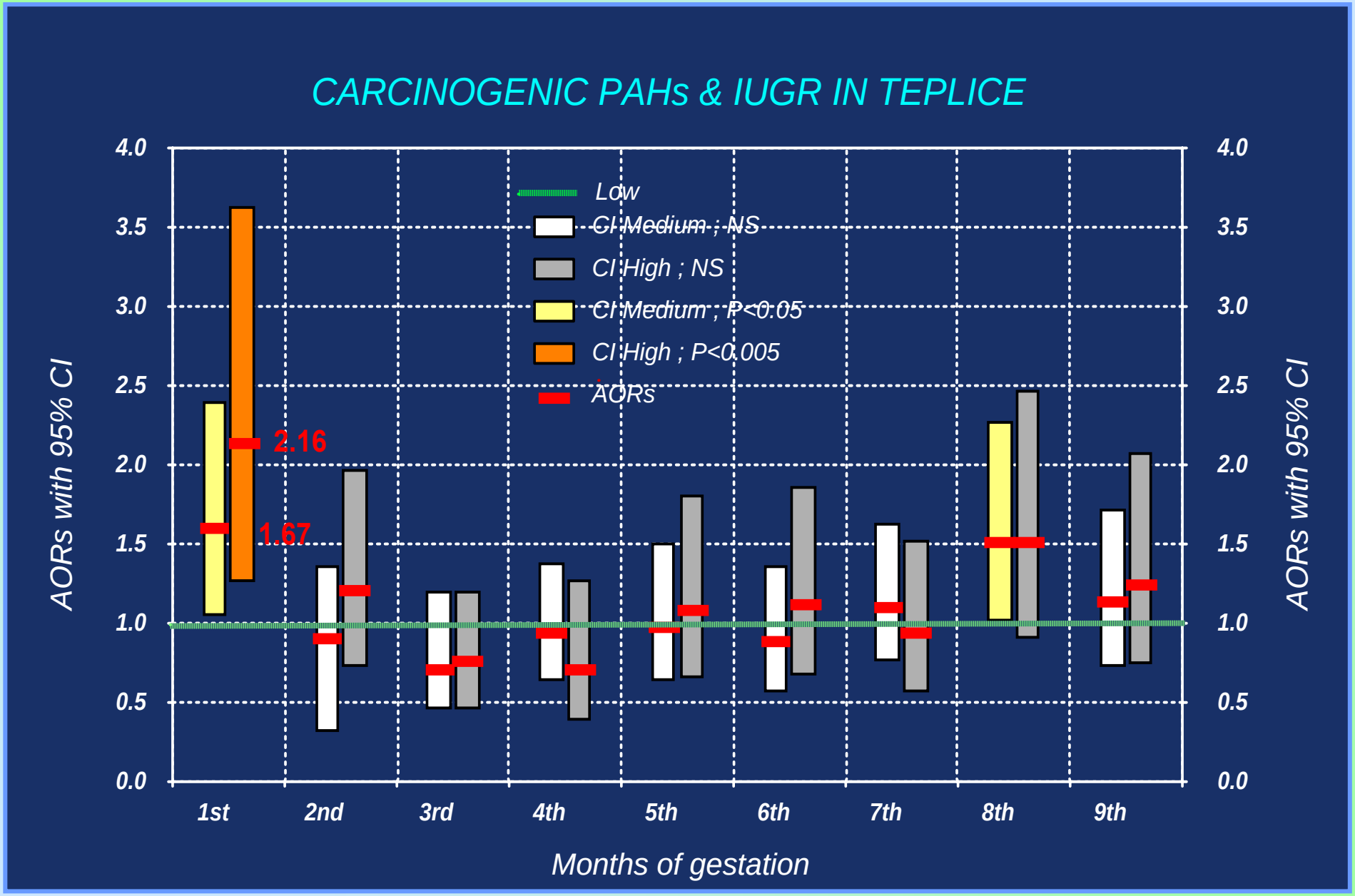

IUGR by PM10 during 1994 - 1998 in TEPLICE
Low = 1
Med; NS
High; NS
Med; P<0.04
High; P<0.0005
AOR
2.10
1.41
3,0
2,5
2,0
1,5
1,0
0,5
0,0
AOR with 95% CL
1st
2nd
3rd
4th
5th
6th
7th
8th
9th
Months of gestation


CARCINOGENIC PAHs & IUGR IN TEPLICE
AORs with 95% CI
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Low
CI Medium ; NS
CI High ; NS
CI Medium ; P<0.05
CI High ; P<0.005
AORs
2.16
1.67
1st
2nd
3rd
4th
5th
6th
7th
8th
9th
Months of gestation

R. J. Sram 2007

OVLIVNĚNÍ VÝVOJE DĚTÍ

VLIV FAKTORŮ ŽP A ŽIVOTNÍHO STYLU:

- porodní hmotnost
- genotyp
- nemocnost
- dýchací funkce
- neuropsychické funkce

AIR POLLUTION

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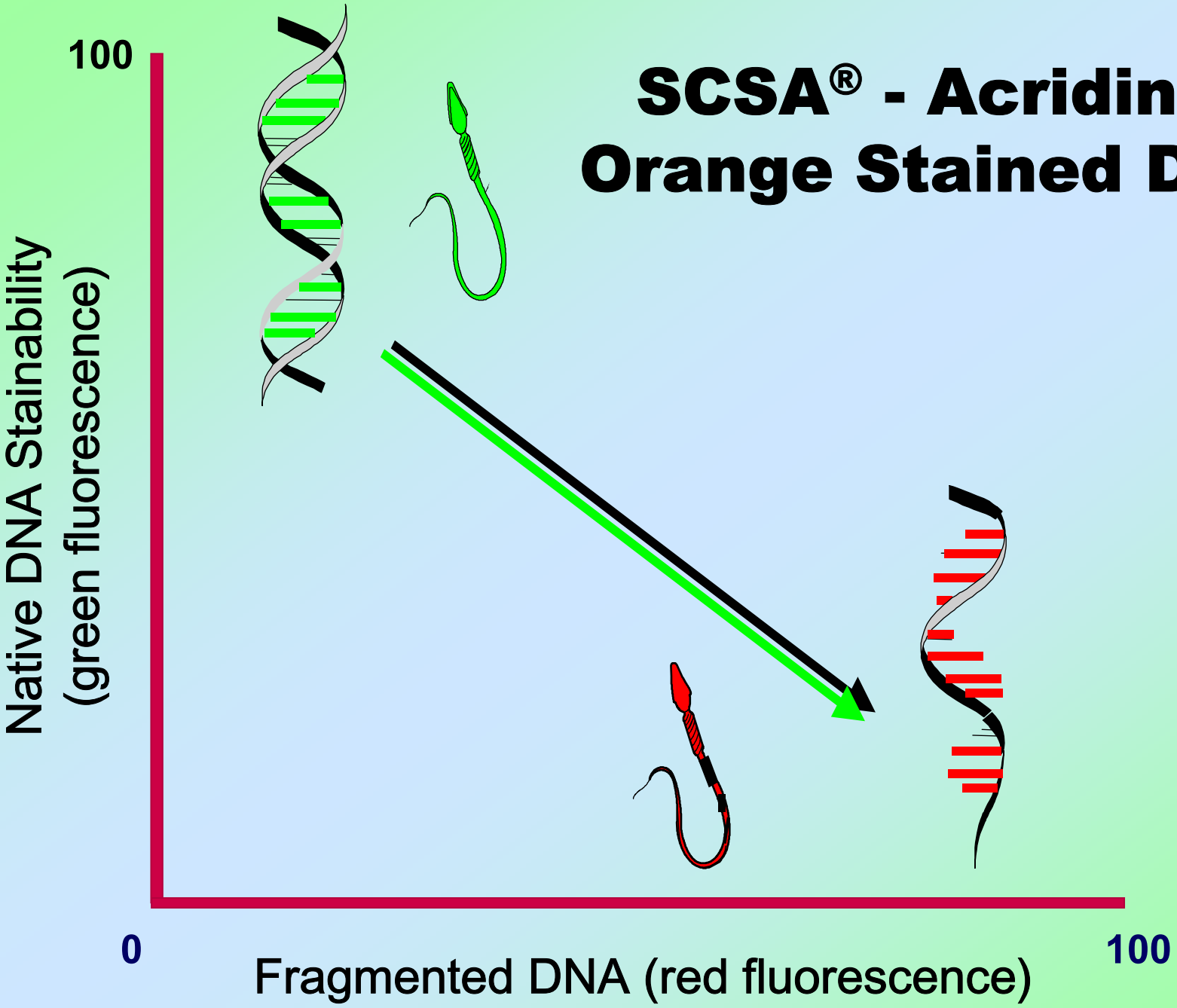
SCSA® - Acridine Orange Stained DNA



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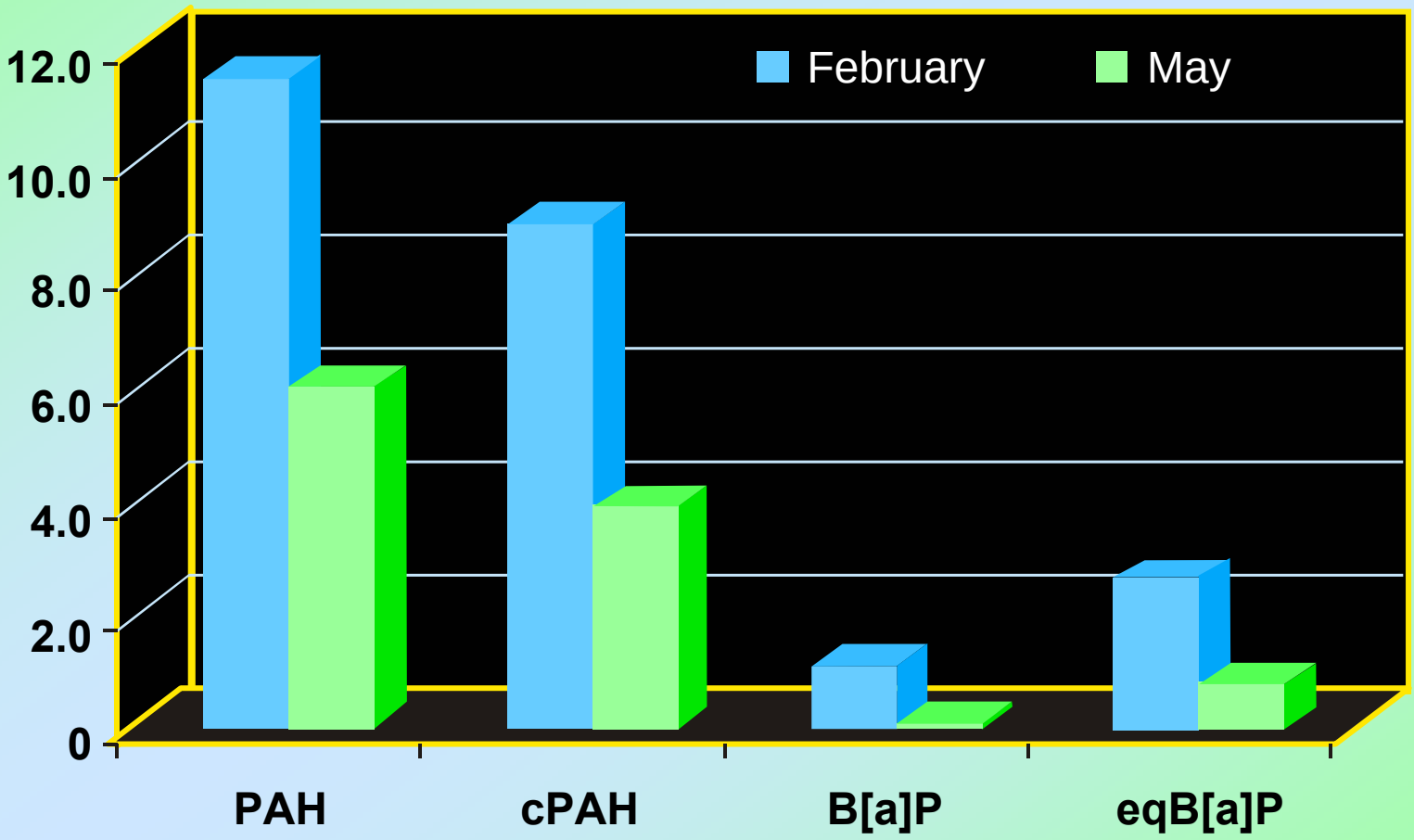
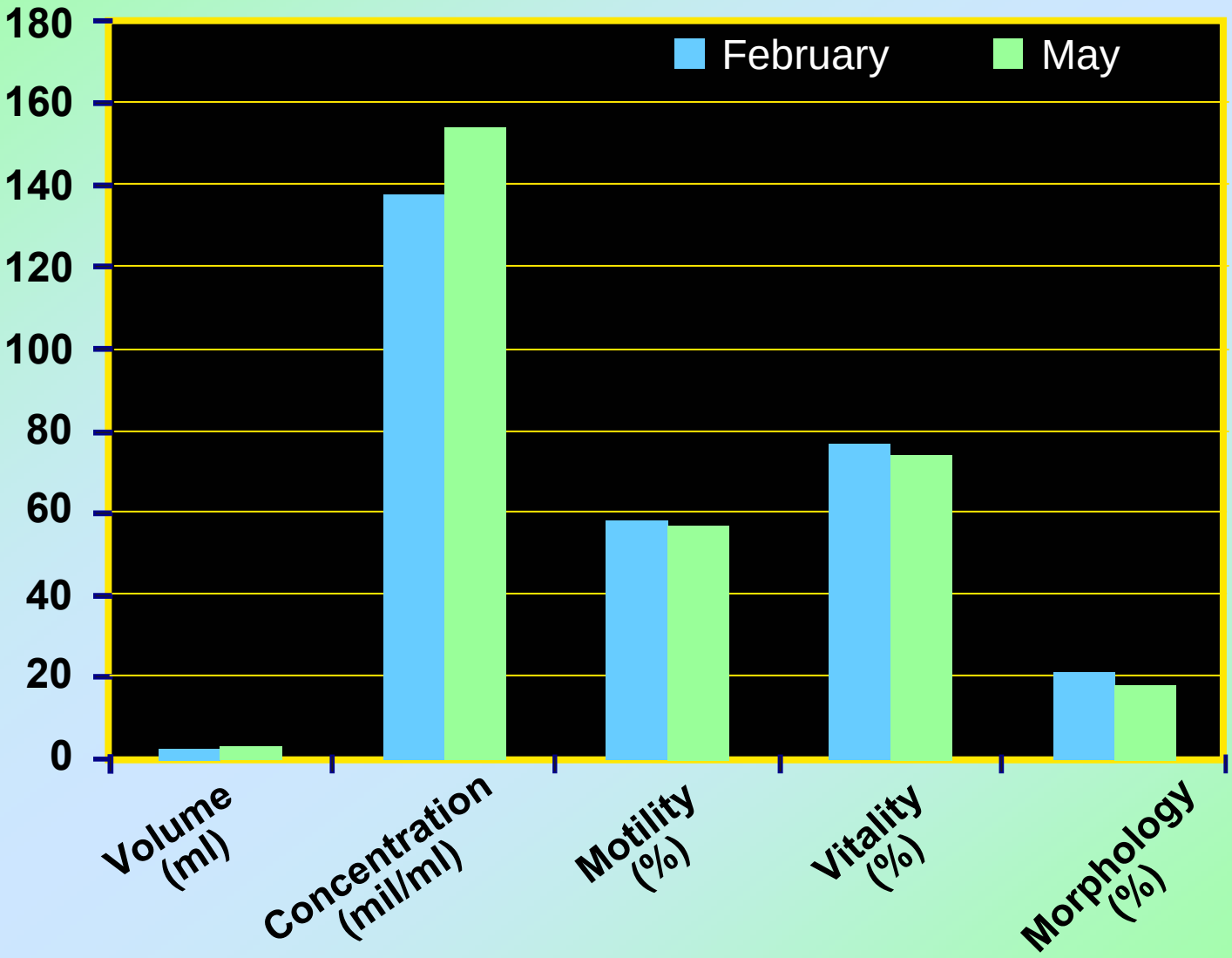
Air pollutions Prague 2007 (ng/m^3)



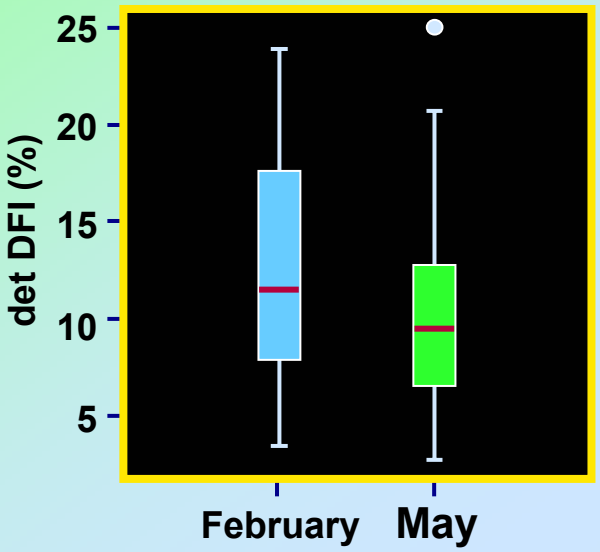
Sperm analysis



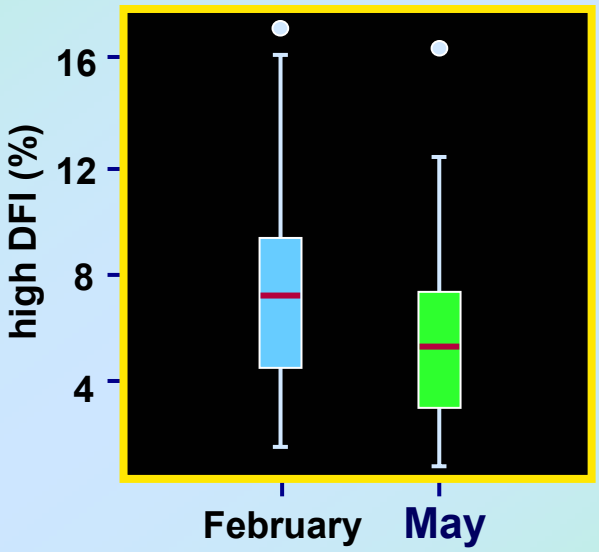
Policemen patrolling the streets in Prague centre with heavy traffic

The level of air pollution will be assessed on the basis of information from two source:

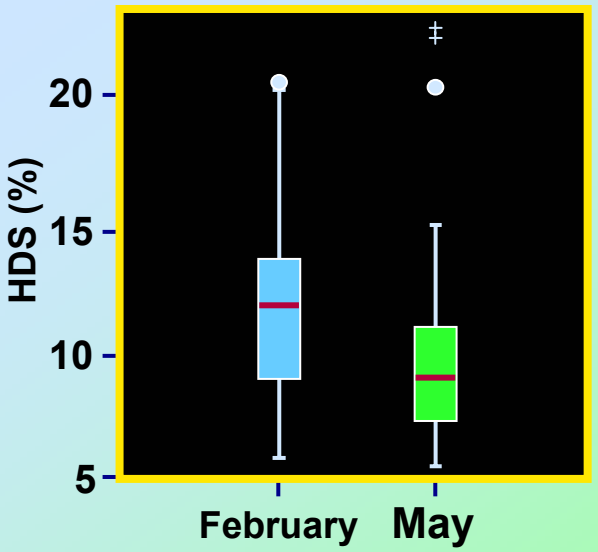
- **-data from stationary measuring stations AIM Prague**
- **-for 48 h using personal sampling devices (URG Corp, USA)**



P≤0.001



P≤0.001



P≤0.001

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

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AIR POLLUTION RISK ASSESSMENT

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ACCORDING TO MOLECULAR EPIDEMIOLOGY STUDIES

concentrations
> 1 ng B[a]P/m^3
in polluted air

RISK FOR HUMAN HEALTH

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NOVÉ POZNATKY

- **VLIV ENVIRONMENTÁLNÍ EXPOZICE k-PAU – RIZIKO GENOTOXICITY**
- **VZTAH MEZI EXPOZICÍ k-PAU, DNA adukty a chromosomovými aberacemi (FISH), snížením DNA reparace**
- **VÝZNAM OXIDAČNÍHO POŠKOZENÍ PRO NEMOCNOST DĚTÍ**

VÝZNAM OXIDAČNÍHO POŠKOZENÍ

→ **U DĚTÍ**

zvyšuje výskyt respiračních onemocnění

(bronchitidy, astma)

ovlivňuje imunitu

→ **U DOSPĚLÝCH**

zvyšuje výskyt nádorových onemocnění

aterosklerosy

diabetes

→ **URYCHLUJE PROCES STÁRNUTÍ**

POŠKOZENÍ GENOMU

POČÁTEK NEMOCI

NUTNOST PREVENCE !

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