# Biomonitoring of Polycyclic Aromatic Hydrocarbons in 2008

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**NVVA-** symposium 2008

#### **Biomonitoring PAH in 2008**

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### Biomonitoring PAH in 2008 Introduction



How to do it?



#### Introduction

### Why biomonitoring?

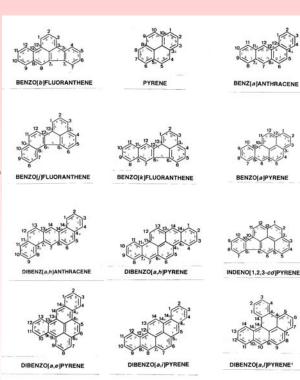
### BM gives estimate of true uptake:

- Individual differences in breathing minute volume
- Individual differences in resorption
- Dermal exposure assessment
- Oral ingestion (by hand-mouth shunt, biting ones nails)



### Biomonitoring PAH Occupational PAH-exposure

- PAH are present as complex combustion mixtures
- In gasphase and particulate matter
- Significant dermal exposure
- Composition varies depending from source
- Carcinogens are the 4-6 ring components





## Biomonitoring PAH Biological indicators of PAHexposure

#### **Suggestions from 1985:**



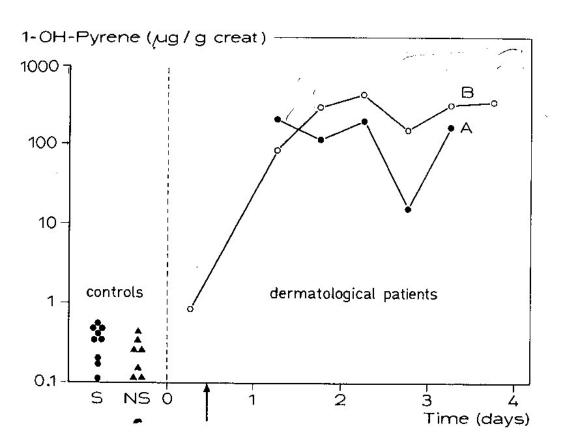
- Metabolites in human urine
  - Pyrene -> 1-hydroxypyrene
  - 2. Phenantrene -> nydroxyphenanthrene
  - 3. Naphtalene -> 1-naphtol
  - 4. Chrysene -> hydroxychrysene
  - 5. BaP -> 3-hydroxybenzo(a)pyrene
- PAH-DNA-adducts in blood cells
  - ♦ BaP -> BaP-adducts
  - ◆ Total PAH -> Aromatic adducts



### Biomonitoring PAH Early data on urinary 1-hydroxypyrene

Int Arch Occup Environ Health (1985) 57:47-55





**Fig. 4.** 1-OH-pyrene in urine samples of 16 non-exposed controls and 2 patients (A and B) undergoing topical treatment with a coal tar ointment. NS = non-smokers, S = smokers

www

## Present status of 1-hydroxypyrene as biological indicator of PAH

### **Early '90:**

Grab sample of papers on biomonitoring of 1-hydroxypyrene

#### 2008:

Search in Pubmed: approx. 600 papers!

AUTHORS	YEAR	OCCUPATIONAL / ENVIRONMENTAL*	
Clonfero et al.	1990	Anode plant	
Jongeneelen et al.	1990	Coke-ovens	
Tolos et al.	1990	Aluminium reduction plant	
Zhao et al.	1990	Coal-burning*	
Buchet et al.	1992	Graphite-electrode & Coke-oven plants	
Buckley et al.	1992	Diet*	
Burgaz et al.	1992	Road pavers	
Gardiner et al.	1992	Carbon black manufacturing	
Jongeneelen et al.	1992	Coke-ovens	
Cenni et al.	1993	Pyrite mine Railway tunnel under construction Earthenware factories	
Granella and Clonfero	1993	Automotive repair	
Grimmer et al.	1993	Coke-oven	
Kanoh et al.	1993	Diesel gas*	
van Rooij et al.	1993a	Coke-oven	
van Rooij et al.	1993b	Wood preservation plant	
Boogaard et al.	1994	Petrochemical plant	
Ferreira Jr. et al.	1994a	Graphite-electrode production Coke-oven	
Ferreira Jr. et al.	1994b	Steel foundry	
		Graphite-electrode production	
Hansen et al.	1994	Iron foundry	
Jongeneelen et al.	1994	PAHs*	
Omland et al.	1994	Iron foundry	
Quinlan et al.	1995	Coal liquefaction	

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# Alternative PAH-metabolites as indicators of exposure

- Hydroxyphenantrenes in urine
  - ◆ 3-ring PAH, mainly gas-phase
  - ♦ First experienced in 1995
  - ♦ 20 papers
  - Mainly in Germany
- 1- and 2-hydroxynaphtalene in urine
  - 2-ring PAH, stricktly gas-phase PAH
- 6-hydroxychrysene in urine
  - ♦ New in 2006
  - ♦ 3 papers
- 3-hydroxybenz(a)pyrene in urine
  - ♦ New in 2007
  - ♦ 2 papers



#### **Biomonitoring PAH**

### Conclusions on urinary metabolite monitoring

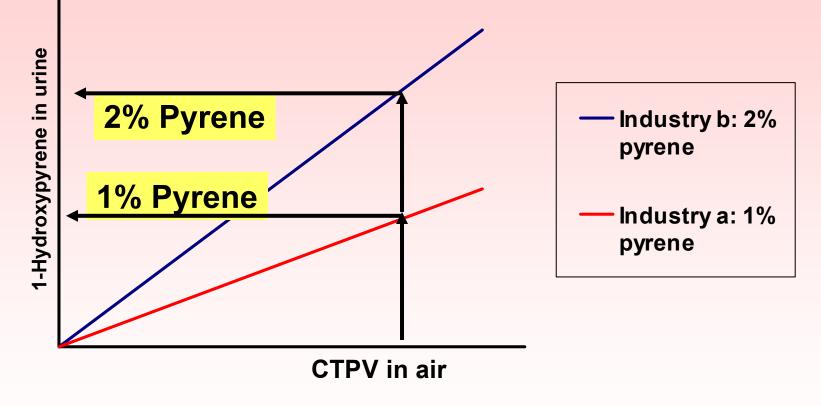
- \* 1-Hydroxypyrene is prefered indicator
  - Many reference data for benchmarking
  - Analytical method has proven to be solid
  - 4-ring PAH = representative of carcinogenic PAH
- Series of PAH-metabolites is sometimes useful
  - 3-OH-BaP at cokeoven
  - OH-naphtalene light products



### Health-based exposure limit

- Dose response data on urinary 1-OH-Pyrene and cancer not available
- Concentration in urine at the airborne exposure limit of PAH = 2.3 25.0 umol/mol (5 papers)
- \* LoOEL of early genotoxic effects = 1.0 1.9 umol/mol (4 papers)
- ❖ Be aware: there is a background in urine
  - Smokers: 95-percentile = 0.7 umol/mol
  - Non-smokers: 95-percentile = 0.3 umol/mol
- Interference: Pyrene content is not fixed

### Pyrene content in PAHmixtures is not constant



Level of urinary 1-hydroxypyrene is dependant of the content of pyrene in CTPV

### Conclusion on health-based limit

- Not yet possible
  - Dose-response data are poor
  - PAH-profile is different in various industries/sources

- Alternative approach:
  - Control based limits. Already recommended by HSE and ACGIH



## HSE (UK): Control-based exposure limit

### 1998 Survey results



pp. 395–403, 2006 with the permission Stationery Office 93/annhyg/mel010

This study showed that 90% of workers in 'good practice'

A industries have levels below 4.0 pmol/mol (excl. creosote exposed an workers)

BMGV 4 \( \text{pmol/mol (8 \text{pg/g})} \)



### Biological Monitoring Guidance Value - HSE (UK)

#### **HSE** concluded in 2004:

- Suitable monitoring method
- Sufficient data
- Guidance Value can be set for 'good occupational practice'

BMGV for PAH was set as 4.0 µmol/mol hydroxypyrene in urine



## ACGIH (USA): Biological Exposure Index

#### **ACGIH** concluded in 2005:

- Health-based BEI scientifically not justified
- Control exposure toward reference value
  - Reference level as 99-percentile of controls = 1.0 μg/L = approx. 0.49 μmol/mol
  - Warrants occupational exposure
- ❖ Adjust to the actual ratio pyrene/B(a)p
  - ◆ Default ratio pyrene/B(a)p = 2.5
  - Formula: { 1-OHP<sub>adj</sub> =1-OHP \* actual ratio/default ratio}



## Biomonitoring of PAH as a tool for hygienists

### **Examples:**

- 1. Test of efficacy of control measures
  - a) Reduction of exposure by improved dermal protection
  - b) Reduction of exposure by using an air stream helmet
- Detection of PAH uptake of PAH among wetsuit wearing windsurfers



# Biomonitoring PAH as a tool for hygienists Reduction of dermal exposure: example 1a

Figure 1. The effect of extra hygienic measures on the urinary 1-hydroxypyrene excretion of cokeoven workers at the top side (\(\sigma\)---\(\sigma\), coke side

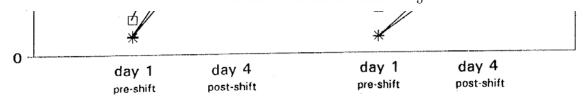


Ann. occup. Hyg., Vol. 38, No. 3, pp. 247-256, 1994
Elsevier Science Ltd
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0003-4878/94 \$7.00+0.00

0003-4878(94)E0025-U

REDUCTION OF URINARY 1-HYDROXYPYRENE EXCRETION IN COKE-OVEN WORKERS EXPOSED TO POLYCYCLIC AROMATIC HYDROCARBONS DUE TO IMPROVED HYGIENIC SKIN PROTECTIVE MEASURES

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### Biomonitoring PAH as a tool for hygienists

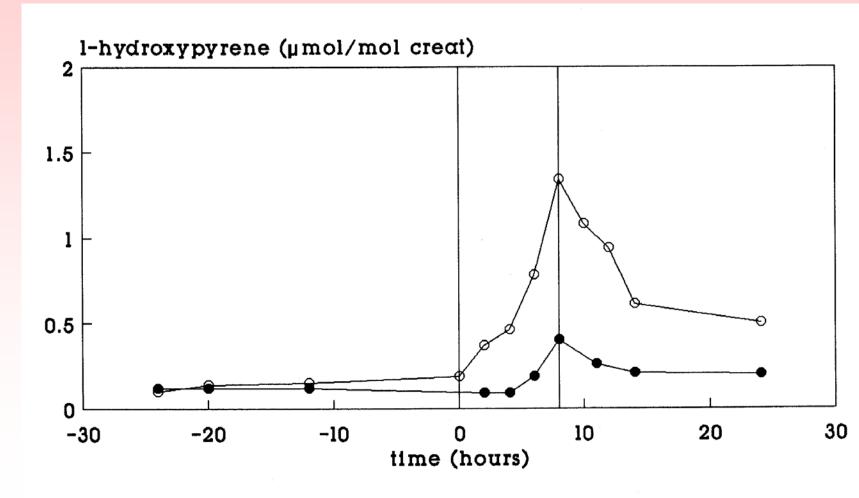
### Protection factor of air-streamhelmet on cokeoven: example 1b

- Question: What is protection of an airstream helmet at cokeoven?
- Cokesoven: diffuse emission of PAH
- Volunteer. 2 times a 8h-shift on deck
  - ◆ 1. With air stream helm
  - ♦ 2. Without air stream helm
- 2 series of ca. 10 urine samples over 48 hour
- Bioindicator of PAH: 1-hydroxypyrene in urine





# Biomonitoring PAH as a tool for hygienists Assigned protection factor of air-streamhelmet on cokeoven: example 1b



- air stream helmet

air stream helmet

BM of PAH as a tool for hygienists

PAH exposure among windsurfers:

example 2

In the Netherlands
Rhine delta lakes
may have a sludge
layer of 0,5 m,
contaminated with
PCB's, PAH
and heavy metals

Are windsurfers exposured to PAH?

Lake: Ketelmeer

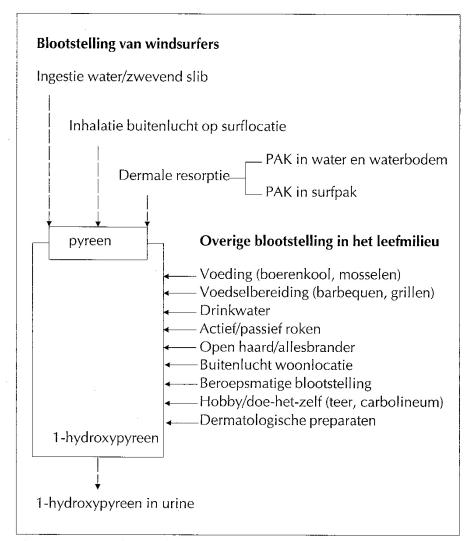


### BM of PAH as a tool for hygienists

Routes of exposure of windsurfers wearing a wetsuit

#### **Exposure to PAH:**

- Swallowing water
- Dermal uptake
- Inhalation

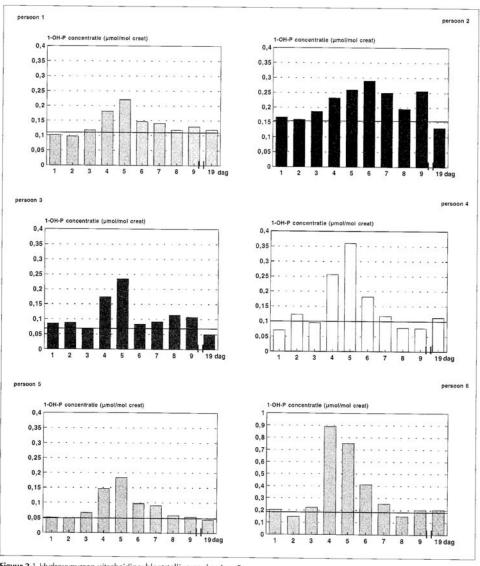


**Figuur 1** Overzicht van blootstellingswegen voor PAK bij windsurfers



Biomonitoring PAH as a tool for hygienists Results: 1-OH-Pyrene in urine of windsurfers

- Increased level on the active surfing days 4 and 5
- Reason:
  - By skin uptake?
  - By swallowing water?



Figuur 2 1-Hydroxypyreen uitscheiding; blootstelling op dag 4 en 5



### Some PAH-biomonitoring studies with new data/approach or information



### Nice new PAH biomonitoring study 1 Urinary 1-hydroxypyrene in newborn

### "Trans-placental" exposure in 42 mothersbabies couples (Sartorelli et al; 1984)

	Smoking (N=31)	Non-smoking (N=11)
Mothers (N=42)	0,23 (0,11)	0,15 (0,10)
Babies (N=42)	0,20 (0,15)	0,15 (0,17)

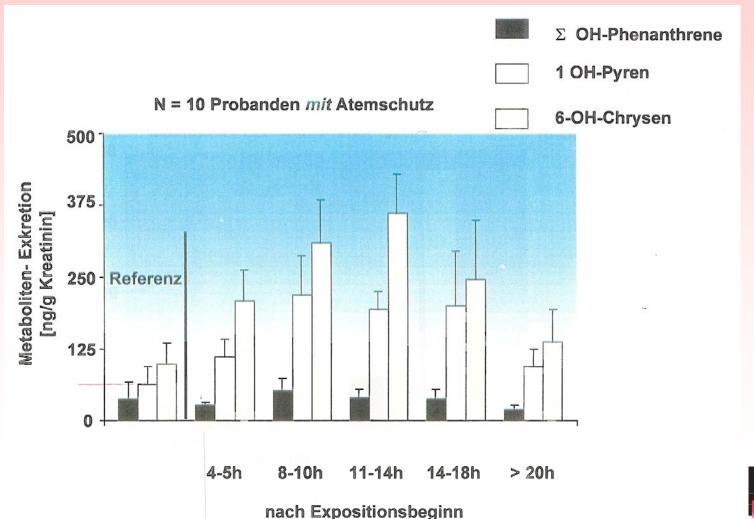


# Nice new PAH biomonitoring study 2 Dermal uptake of PAH in bitumen fume

- Study of Knecht, 2001
- Experimental design
  - 10 male, non-smoking volunteers with respirators were during 4 hrs exposed to 20 mg/m³ bitumen fume
  - Urine analysed for three PAHmetabolites



# Nice new PAH biomonitoring study 2 Dermal uptake of PAH in bitumen fume: results





# Nice new PAH biomonitoring study 3 Association between urinary 1hydroxypyrene and genotoxic effects

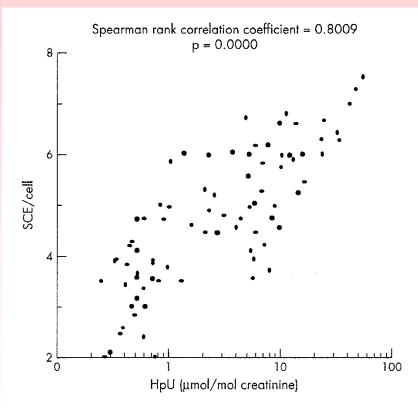
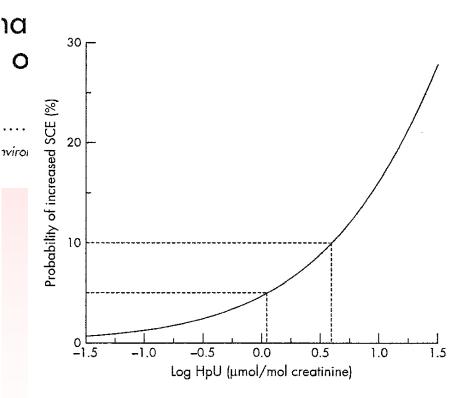


Figure 1 Relation between SCE in lymphocytes and HpU concentration in post-shift urine of exposed and control population (n = 85).



**Figure 2** Probability of increased SCE as a function of HpU concentration in post-shift urine.



# Nice new PAH biomonitoring study a Toxicokinetic modeling for refined estimation of uptake by route. Example

Research. Inhalation uptake

2. Dermal uptake
PBTK Modeling Demonstrates Contribution of Derma
Components to Earnsport in abouty centrations

David Kim,<sup>1</sup> Melvin F Andersen,<sup>2</sup> Yi-Chun E. Chao,<sup>1</sup> Peter P. Egeghy,<sup>1\*</sup> Steph Leena A. Ny Ander-Fatorage in body

<sup>1</sup>Department of Environmental Sciences and Engineering, School of Public Health, The Univ Chapel Hill, No. Caroling, \$6,000 Public

→ Kinetic model demonstrates uptake by different routes (PBTK-model)

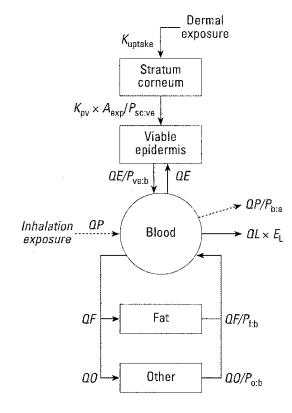
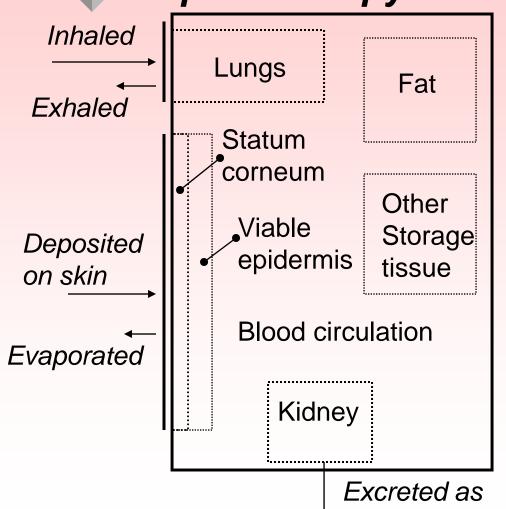


Figure 1. Schematic of the physiologically based toxicokinetic (PBTK) models for the study of naphthalene toxicokinetics. Pulmonary uptake of naphthalene in the personal breathing-zone and pulmonary clearance from the blood compartment are added to a previously published dermatotoxicokinetic model (Kim et al. 2006b). Abbreviations in the PBTK model:  $K_{\rm uptake}$ , input rate constant for dermal exposure;  $K_{\rm py}$ , permeability coefficient for the viable epidermis;  $A_{exp}$ , exposed surface area; P<sub>sc:ve</sub>, stratum corneum:viable epidermis partition coefficient; QE, blood flow rate to skin; Pverh, viable epidermis:blood partition coefficient; QP, pulmonary ventilation rate;  $P_{b:a}$ , blood:air partition coefficient; QF, blood flow rate to fat;  $P_{f-b}$ , fat:blood partition coefficient; QO, blood flow rate to other tissue;  $P_{o:b}$ , other tissue:blood partition coefficient;  $E_{\rm I}$ , extraction ratio.

### Our present research work

Example: CBTK-model for predicting the urine concentration as a result of inhalation and/or dermal exposure of pyrene (CEFIC-LRI funded study)



Urinary excretion of pyrene as metabolite = f(Net inhalation, Net dermal uptake, elimination)



Excreted as hydroxypyrene in urine

### Our present research work Outline CEFIC-LRI funded study

Input Tool Output

DNEL or equivalent Toxicity limit value of compound

Computer Program

Databases with:

- 1. CBPK & PBPK models
- 2. Chemical & physical data
- 3. Toxicokinetic data

Biomonitoring
Equivalent
Guidance
Value (BEGV)
in biological
specimen

Compound

Route(s) of exposure

Biological specimen of choice



### What will the near future bring?

- Hydroxy-PAH series in urine. Series of 16 priority PAH of EPA as hydroxy-PAH?
- \* Total PAH-dose as expressed as b(a)p-equivalents (BEQ) ?
  - viz. TCDD-equivalents (TEQ) for dioxines
- Modeling for refined exposure assessment. PBTK modeling with probablistic distributions of parameters?
- Introduction of markers for target dose or biological effective dose?
- Introduction of individual assessement of risk on PAHinduced cancer using genomics (= sequence information on the human genome)? Not in the near future!

Only God knows what will be brought. However, in the lobby we can try to change that.

### Biomonitoring PAH More info?

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### Thank you

