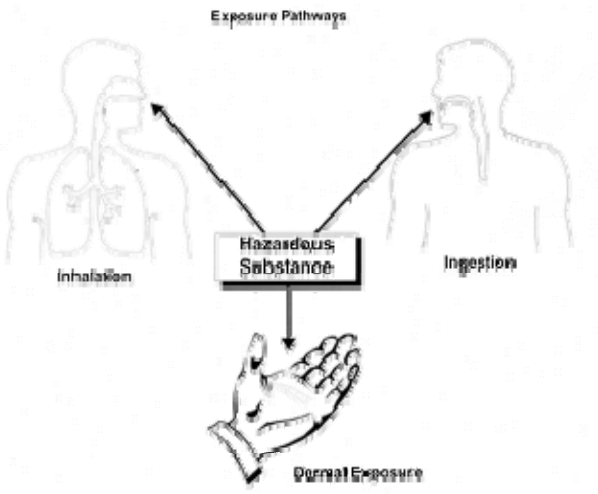

Relevantie van huidblootstelling in de praktijk

Frans Jongeneelen

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Introduction –

Background

- CEFIC-LRI Project: Development of generic PBPK-model for BEGV estimation

  – Inhalation
  – Dermal absorption

  → Estimated blood and/or Urine concentration

- This work has triggered improvements of the Skinperm model
  – Time-dependant transport over skin layers
  – Gives insight in the process of uptake

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Introduction –

Historical development of methods and techniques for exposure assessment

Period	Method/technique
early days	Area or stationairy monitoring
from 1975	Personal monitoring
from 1975	Biomonitoring (internal dose)
from 1985	Sampling of dermal load

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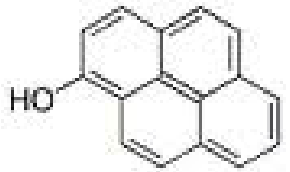
Historic development of exposure assessment methods – PAHs as example

Period	Assessment methods
From 1950	**Sampling of Benzene Soluble Matter (BSM) at fixed spots**
1975	**Personal sampling introduced**
1978	**Analysis of 16 EPA-PAH**
1985	**Biomonitoring with urinary 1-hydroxypyrene**
1988	**Sampling of dermal exposure with pads directly mounted on different skin sites**



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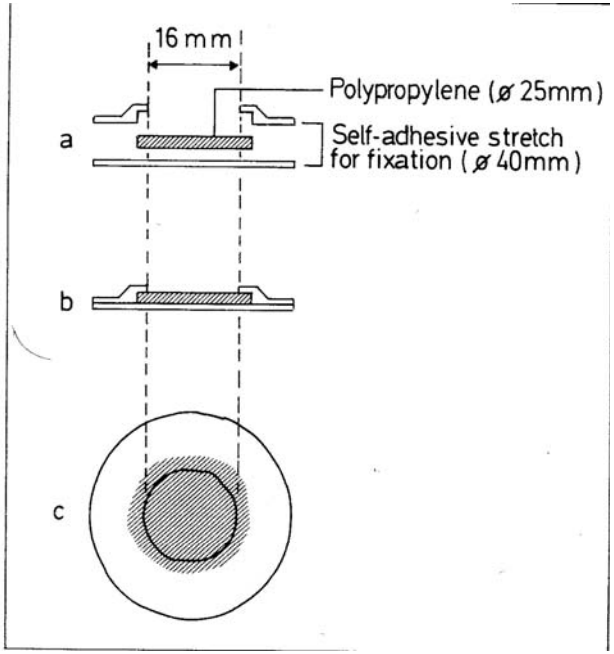
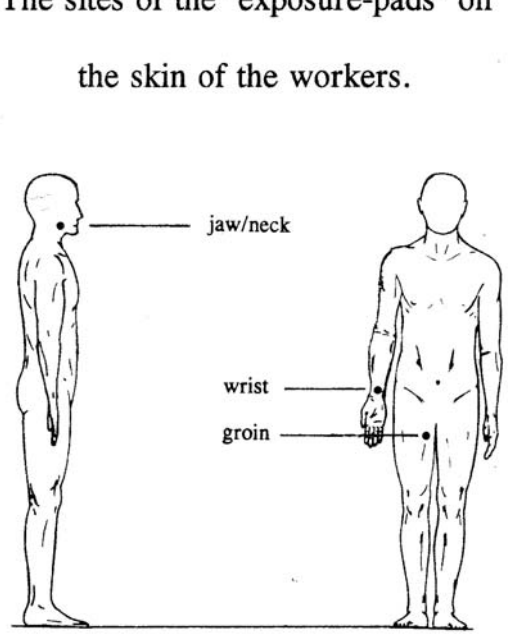
Dermal exposure assessment of PAH –
Pads mounted on skin

Period	Assessment method
1988	**Sampling of dermal exposure of PAH with pads directly mounted on different skin sites**





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Early insight in relevance of dermal exposure

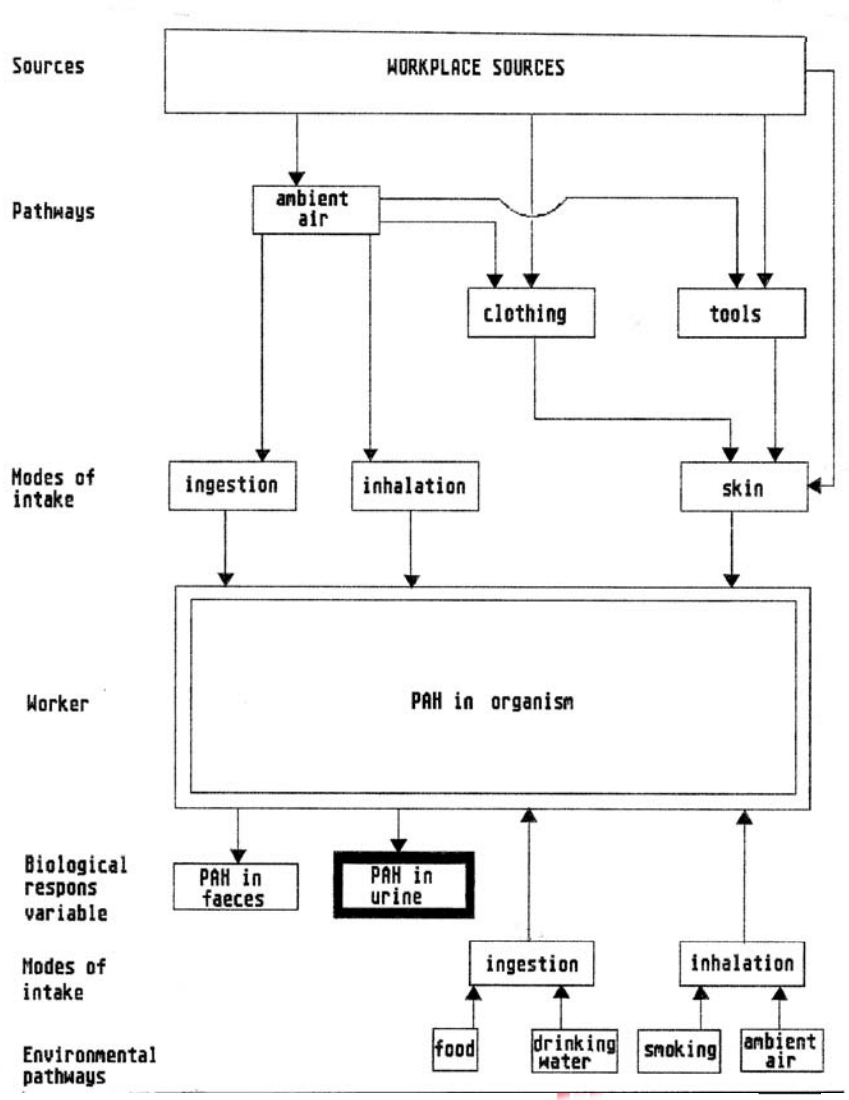
Mass balance studies

Dermal absorbed dose =

Excreted dose - Inhaled dose

<u>Cokeovenworkers</u>:

Approximately 50% of dose of PAH is due to dermal exposure



Examples

Studies of dermal exposure of PAH using biomonitoring

- **A two-route uptake study**
- **Trans-dermal uptake of bitumen fume**
- **An intervention study**

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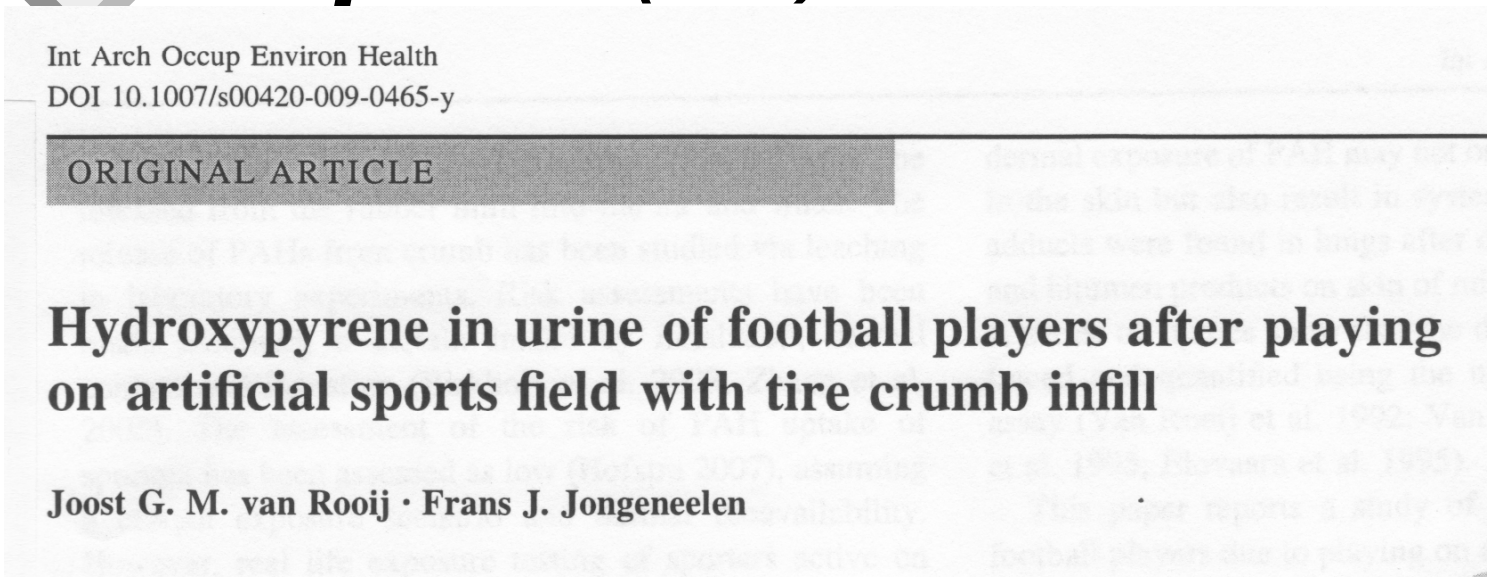
Studies of dermal exposure of PAH

example 1 (2009)



Int Arch Occup Environ Health
DOI 10.1007/s00420-009-0465-y

ORIGINAL ARTICLE

Hydroxypyrene in urine of football players after playing on artificial sports field with tire crumb infill

Joost G. M. van Rooij · Frans J. Jongeneelen

Are football players on a artificial field exposed to PAH?

- **Inhalation of dust of rubber scrumb?**
- **Dermal uptake?**

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Example 1

PAH exposure among football players on a artificial ground

Background:

An artificial sporting field contains crumb infill of scrap rubber tyres

Rubber tyre crumb contains contaminants as PAH, accelerators and zinc

Are sporters exposed to PAH?

Study design:

Training + match during 2,5 h on artificial pitch with tyre infill.

Seven football players collected all urine voidings over a 3-day period including the pre-sporting day.

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Example 1

PAH exposure among football players on a artificial ground

Player F

Pre

Post

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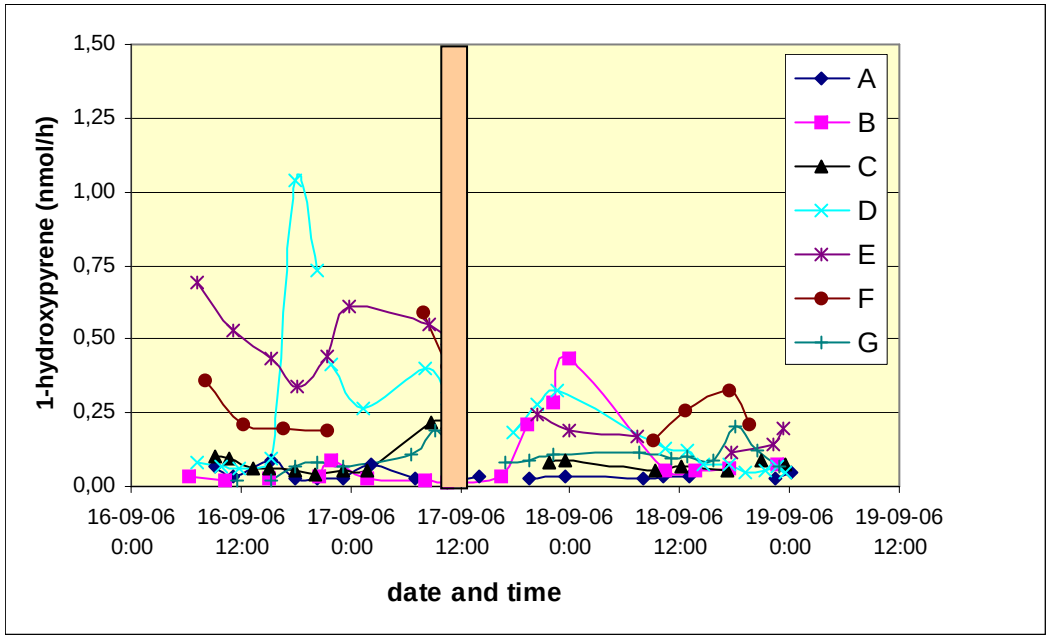
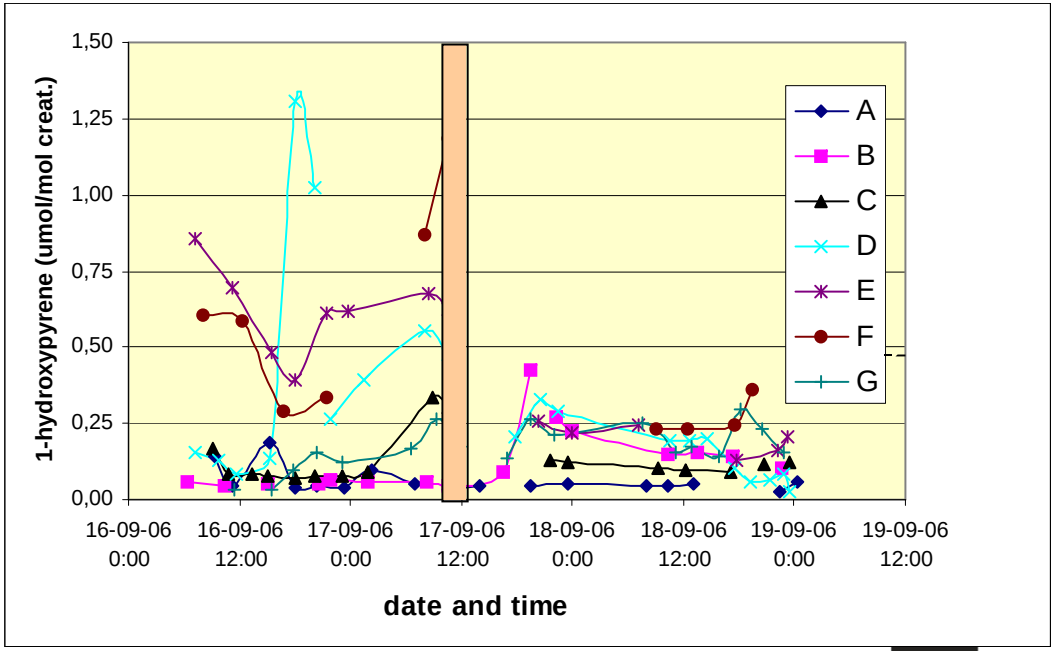
Example 1

Results

1) in nmol/h



2) in µmol/mol creat



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Example 1

Individual results of pre- and post sporting

persoon	*Uitscheiding 1-hydroxypyreen (nmol/uur)*							
	ACHTERGROND (zaterdag tot zondag 10:00 uur)							*Ná zondag 10:00 uur*
	N	*GM*	*gsd*	*Min*	*Max*	*95th Percentile*	*UTL 95%,95%**	*Aantal monsters > UTL 95%,95%*
A	8	0,04	1,7	0,02	0,09	0,10	0,22	**0**
B	7	0,03	1,7	0,02	0,09	0,07	0,17	**3**
C	9	0,07	1,6	0,04	0,22	0,16	0,32	**0**
D	*9*	*0,22*	*2,9*	*0,06*	*1,04*	*1,28*	*5,72*	*0*
E	*7*	*0,50*	*1,3*	*0,34*	*0,69*	*0,74*	*1,13*	*0*
F	*5*	*0,28*	*1,6*	*0,19*	*0,59*	*0,63*	*2,21*	*0*
G	7	0,06	2,2	0,02	0,19	0,23	0,95	**0**

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Example 1

Conclusion

Uptake of PAH by football players active on artificial grounds with rubber crumb infill is minimal

If there is any uptake, it is low and within the range of environmental PAH-exposure.

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Study of dermal exposure to PAH

Example 2: Dermal uptake of bitumen fume

- **Study of Walter & Knecht, 2007**
- **Experimental design**
  - **10 male non-smoking volunteers, wearing only short pants and shoes were exposed during 8 hrs to approx 20 mg/m³ bitumen fume (= 18 mg/m³ vapor + 2,5 mg/m³ aerosol)**
  - **One experiment with powered respirator (= dermal only), another without respirator**
  - **Urine was sampled and analysed for metabolites of three PAH in bitumen**

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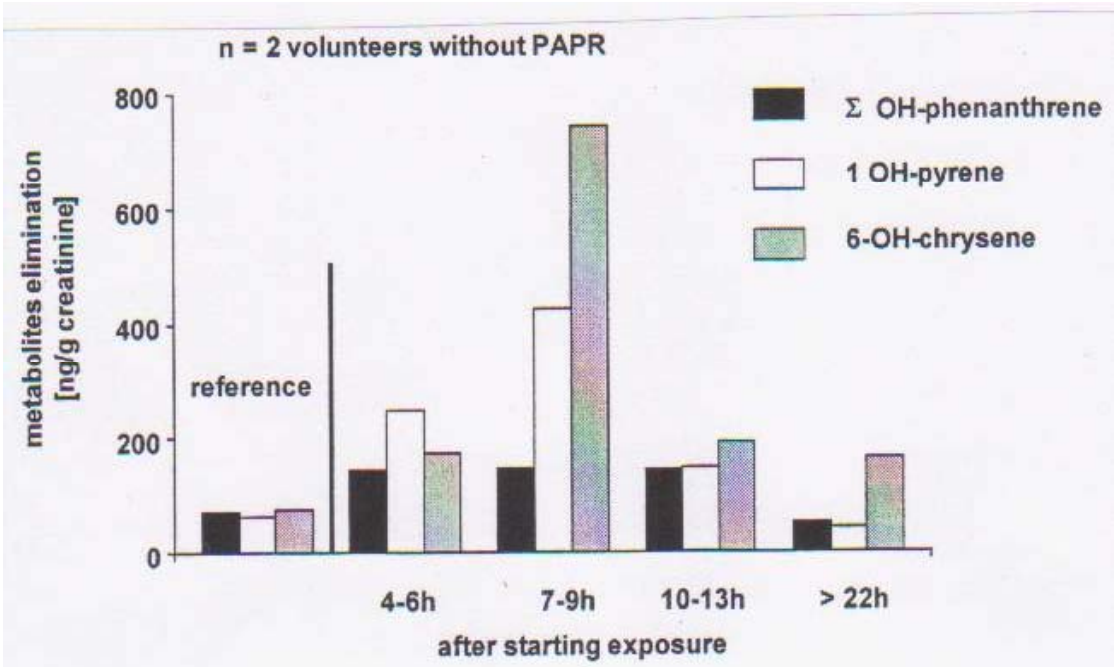
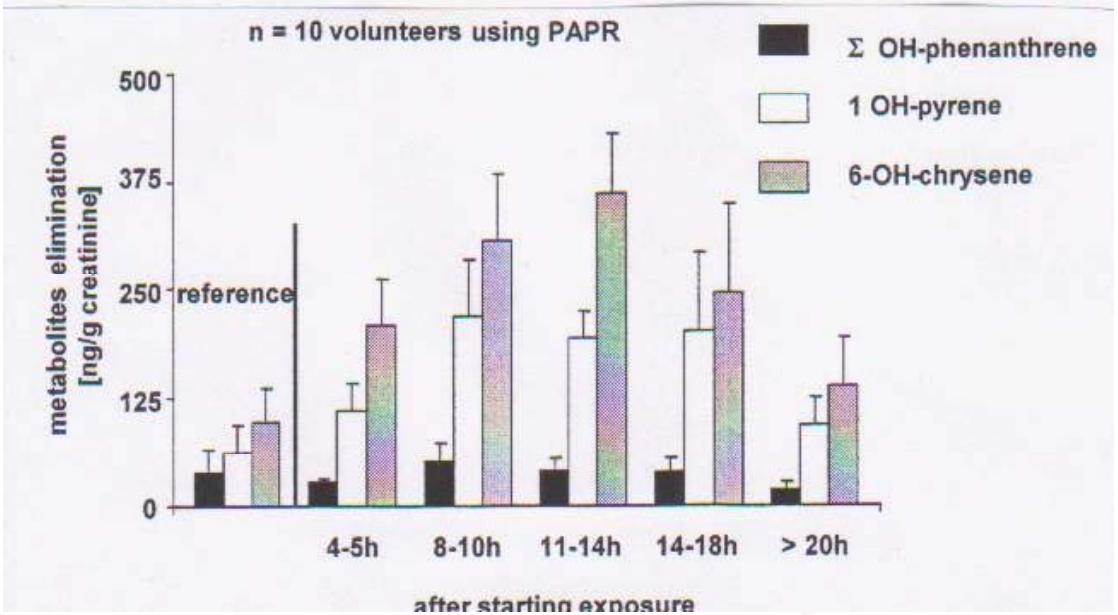
Example 2

Dermal uptake of PAH in bitumen fume: results

Conclusion: Approx. 50% enters through skin





Study of dermal exposure to PAH

Example 3: Intervention study of effect of skin protective measures

Pergamon

Ann. occup. Hyg., Vol. 38, No. 3, pp. 247–256, 1994
Elsevier Science Ltd

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

JOOST G. M. VANROOIJ,*† MONIKA M. BODELIER-BADE,* PIET M. J. HOPMANS‡ and FRANS J. JONGENEELEN§

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Study of dermal exposure to PAH

Example 3: intervention study of effect of extra skin protection

- 13 cokeoven workers
- Monitoring in two 2 weeks
  - Week 1: Normal dermal protection
  - Week 2: Extra dermal protection
- Extra dermal protection: simple measures
  - Each shift clean overall + socks + underwear
  - Increased hands and face washing
- Cross-over study design

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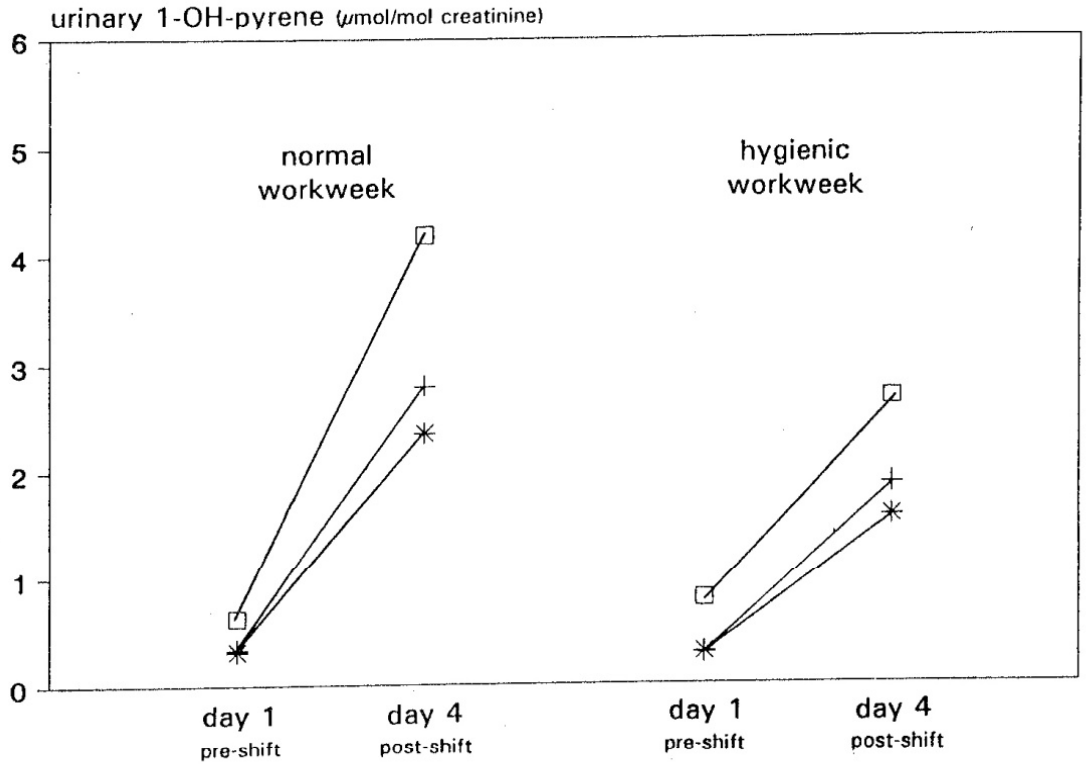
Study of dermal exposure to PAH

Example 3: intervention study of effect of extra skin protection

Figure 1. The effect of extra hygienic measures on the urinary 1-hydroxypyrene excretion of cokeoven workers at the top side (□---□), coke side (+---+) and push side (---*) of the oven (median value, N=4).*



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Risk assessment of dermal exposure

Relevant items

- Dermal exposure or dermal load
  - How large is the exposed skin surface ?
  - What is the (regional) dermal load rate of the skin ?
  - Duration and frequency of exposure ?

- Absorbed dermal dose
  - What is the resulting dose that is transdermally absorbed (systemic available) given the dermal exposure scenario ?

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Risk assessment of dermal exposure

Estimation of absorbed dermal dose

- Classical estimate: simple fractional absorption
  - Default: 100% absorption
- Modelling of absorption as time- and concentration dependant proces is closer to true absorption proces
  - A skin model with evaporation and diffusion through different aerial and skin layers to blood perfused dermis is urgently needed

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Risk assessment of dermal exposure

How can modelling improve the estimation of absorbed dermal dose ?

- The SKIN PBPK model – *Wil ten Berge*
  - A model with evaporation and different aerial and skin layers
- Examples of estimated uptake of vapors - *Daan Huizer*
  - ethanol, NMP, glycolethers

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