# Estimation of individual dermal and respiratory uptake of polycyclic aromatic hydrocarbons in 12 coke oven workers

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**Abstract**

**Twelve workers from a coke plant in The Netherlands participated in an intensive skin monitoring programme combined with personal air sampling and biological monitoring during five consecutive eight hour workshifts. The purpose of the study was to make a quantitative assessment of both the dermal and respiratory intake of polycyclic aromatic hydrocarbons (PAHs). Pyrene was used as a marker compound for both dermal and respiratory exposure to PAHs. The biological measure for the internal exposure to PAHs was urinary 1-OH-pyrene concentration. Measurements on exposure pads at six skin sites showed that mean total skin contamination of the 12 workers ranged between 21 and 166 μg pyrene a day. The dermal uptake of pyrene ranged between 4 and 34 μg/day, which was about 20% of the pyrene contamination on skin. The mean concentration of total pyrene in the breathing zone air of the 12 coke oven workers ranged from 0·1 to 5·4 μg/m³. The mean respiratory uptake of pyrene varied between 0·5 and 32·2 μg/day. Based on the estimates of the dermal and respiratory pyrene uptake it is concluded that an average 75% (range 28%–95%, n = 12) of the total absorbed amount of pyrene enters the body through the skin. Because of the difference in the pyrene:benzo(a)pyrene ratio between the air samples and the skin contamination samples, the dermal uptake of benzo(a)pyrene was also estimated. This was about 51% of the total absorbed amount (range 8%–92%, n = 12). The total excreted amount of urinary 1-OH-pyrene as a result of exposure to PAHs during the five consecutive workshifts varied between 36 and 239 nmol. A multiple regression model of the mass balance between pyrene dose (both dermal and respiratory) and 1-OH-pyrene excretion confirmed the relevance of the dermal exposure route. The variation in urinary 1-OH-pyrene excretion was determined more by the dermal pyrene dose than by the respiratory dose. The model showed an estimate of the percentage of the absorbed amount of pyrene that is metabolised and excreted as 1-OH-pyrene in urine. For the 12 workers this percentage varied between 13% and 49% depending on smoking habits and consumption of alcohol. The results of this study indicate that among coke oven workers, the skin is the main route of uptake of PAHs. Preventive measures to reduce exposure to PAHs should be focused more on the reduction of dermal contamination by PAHs than on the reduction of inhaled dose.**

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Coke oven workers are highly exposed to polycyclic aromatic hydrocarbons (PAHs). In coke ovens bituminous coal is destructively distilled to produce coke. The emissions from a coke oven are complex mixtures of gases, liquids, and solid particles. The airborne particulate matter on top of a coke battery contains about 15% of PAHs by weight.[1]

Epidemiological studies have shown that exposures in the coke production industry give rise to lung and skin cancer in humans. The possible agent is coal tar fume, which contains high concentrations of PAHs; these are carcinogenic in experimental animals.[2,3]

To control occupational exposure to PAHs, threshold limit values (TLVs) based on airborne concentrations are set in many countries. For example, the TLV in the United States is based on the benzene soluble fraction of sampled dust (TLV = 0·2 mg/m³).[4] The German technical guiding concentration (TRK) is based on the benzo(a)pyrene concentration in air (TRK = 2 μg/m³).[5]

Besides the respiratory tract, the skin might also

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*Table 1 Personal data and characteristics of workers*

| Personal code | Function/ work location | Age (y) | Alcohol* | Smoking† | Height (cm) | Body weight (kg) | Respiration volume (l/min)‡ | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Intensive activities | Non-intensive activities |
| 1 | Push side | 24 | 1 | 0 | 187 | 75 | 34·4 (2·8) | 21·6 (5·2) |
| 2 | Push side | 46 | 1 | 1 | 178 | 86 | 25·3 (2·8) | 18·5 (5·2) |
| 3 | Supervisor | 33 | 0 | 1 | 182 | 94 | 28·3 (4·2) | 17·8 (3·9) |
| 4 | Top side | 28 | 1 | 0 | 176 | 78 | 21·6 (3·5) | 19·9 (4·5) |
| 5 | Supervisor | 42 | 1 | 0 | 182 | 93 | 37·7 (3·5) | 13·8 (4·5) |
| 6 | Quencher car | 59 | 0 | 1 | 180 | 100 | 15·5 (3·5) | 15·0 (4·5) |
| 7 | Coke screening | 52 | 1 | 1 | 176 | 84 | 32·9 (4·9) | 10·5 (3·1) |
| 8 | Push side | 29 | 1 | 1 | 176 | 70 | 19·3 (2·8) | 14·8 (5·2) |
| 9 | Miscellaneous | 28 | 0 | 1 | 170 | 80 | 15·7 (4·0) | 13·5 (4·0) |
| 10 | Miscellaneous | 25 | 0 | 0 | 173 | 68 | 20·7 (3·5) | 12·4 (4·5) |
| 11 | Coke side | 27 | 0 | 1 | 178 | 87 | 20·3 (3·5) | 8·4 (4·5) |
| 12 | Coke side | 20 | 0 | 1 | 160 | 52 | 36·9 (3·5) | 26·4 (4·5) |

*Alcohol use during week of measurements; 1=yes, 0=no.
†Smoking of tobacco; 1=yes, 0=no.
‡Values are converted to the atmospheric pressure and saturation at body temperature (BTPS). Durations of the work periods (h) with physically intensive and non-intensive work activities are given in parentheses.

be an important route of body entry of PAHs. Application of tars containing PAHs on to the skin of mice induced local papillomas and skin carcinomas, and also systemic DNA damage in tissues such as the lungs and heart.[6 7] Application of coal tar ointment to the skin of healthy male volunteers resulted in a six to 10-fold increase in the urinary 1-OH-pyrene excretion rate (unpublished data). This metabolite of pyrene is increasingly being used and accepted as a biological indicator of the internal dose of PAHs.[8-12]

Occupational dermal contamination with PAHs has been measured with exposure pads (polypropylene filter in plaster material) as a pseudoskin monitoring technique in several work environments. Among road paving workers skin contamination with pyrene, after a workshift of eight hours, ranged up to 1400 ng/cm$^2$.[13] In the primary aluminium industry contamination of skin with pyrene was found in the range of 6 to 192 ng/cm$^2$, and benzo(a)pyrene in the range of 2 to 34 ng/cm$^2$.[14] In these studies substantial contamination (up to 106 ng/cm$^2$) was also detected on exposure pads that were pasted underneath "protective" working clothes. Determination of total PAHs in skin oil showed a mean contamination of 97 ng/cm$^2$ on the foreheads of roofing workers.[15]

Among primary aluminium workers we found that the contamination of skin with PAHs showed a better correlation with urinary 1-OH-pyrene excretion than PAH concentration in breathing zone air.[14] A quantitative assessment of the dermal intake could not be made, however.

In the present study among 12 coke oven workers, we conducted an intensive skin monitoring programme combined with personal air sampling to make a quantitative assessment of both skin contamination and respiratory intake. A model to estimate the dermal dose of pyrene based on measurements of contamination with PAHs is described. A mass balance of input (estimated dermal and respiratory pyrene dose) and output (1-OH-pyrene in urine) is presented.

## Study design and methods

The study was carried out among 12 workers at a coke plant in The Netherlands in September 1990. The 12 workers belong to one crew and represent operating, maintainance, and supervisory personnel. Table 1 gives the personal data for the workers.

The coke plant, which comprises two batteries, consists of 110 ovens in parallel rows and produces about 600 000 tonnes of coke a year. Five crews of 18 workers and a group of special maintainance personnel work in the vicinity of the battery. The coal is destructively distilled at a temperature of around 1270°C for 18 to 19 hours to produce coke. On average about 47 ovens are worked for each shift of eight hours. About 95% of the workers wear overalls during working hours; these are dry cleaned after periods of three to five workshifts. Those who work in the vicinity of the ovens are provided with an air stream helmet. About 60% of the workers use it more than four hours a workshift; 20% do not use the air stream helmet.

Environmental monitoring to determine contamination of skin with PAHs and the concentration of PAHs in breathing zone air was conducted during five consecutive eight hour workshifts (1400–2200). The biological monitoring programme to determine the internal exposure of the workers to PAHs lasted seven days (the same five workshifts followed by a two day period off work. Interviews were conducted by a trained interviewer with a questionnaire about personal characteristics including age, weight, height, smoking habits, and alcohol consumption.

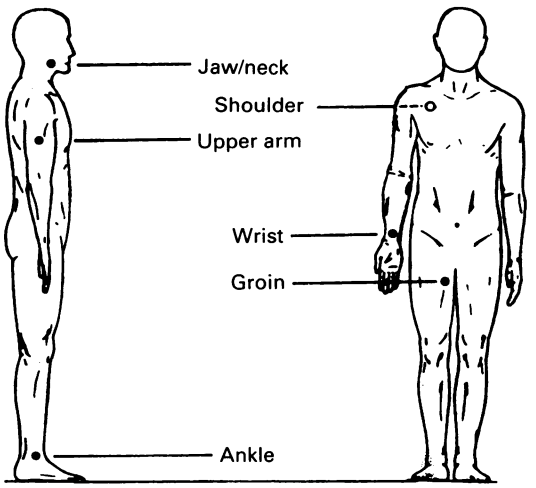


*Figure 1 Skin sites where exposure pads are mounted for the monitoring of dermal contamination with PAHs.*

MONITORING OF SKIN CONTAMINATION

Skin contamination of the workers was measured with an exposure pad on six skin sites: the jaw/neck, shoulder, upper arm, wrist, groin, and ankle (fig 1). The exposure pads were round monitoring devices (diameter 60 mm) with a small monitoring area (diameter 18 mm). Flexible polypropylene filter material (Gelmann Sciences) was used as adsorbing material in the exposure pad. The design of the exposure pad has been published elsewhere.[13] At the beginning of the shift (1400) pads were pasted on the skin and immediately after work (2200) they were removed, packed in aluminium foil and stored at −20°C until analysis. The effective monitoring area of the exposure pad (1·77 $cm^2$) was punched out and ultrasonically extracted for 10 minutes with dichloromethane (10 ml). After centrifugation (2000 rpm for five minutes), the extract was analysed for pyrene and benzo(a)pyrene by high performance liquid chromatography (column Vydac C18, temperature 40°C) with multiple shift fluorescence detection (LS-4, Perkin Elmer). The recoveries of pyrene and benzo(a)pyrene from exposure pads was 80% and 100% respectively.

MONITORING OF BREATHING ZONE AIR

During working hours, airborne particulates in the breathing zone air were collected on a Teflon filter (PTFE filter: diameter 25 mm, pore size 0·5 $\mu$m, Millipore) with samplers that were equipped with a cone over the face. In conjunction with a suction flow of 2 l/min (Dupont air samplers, models P4000 and S2500), a suction velocity of 1·25 m/s was produced in the face entrance. Three of the 12 workers (workers 4, 8, and 12) wore an adsorbent tube directly behind the sampler to trap the gaseous phase on days 2, 3, and 5. The adsorbent tube contains XAD-2 resin as adsorbent (ORBO 43, Supelco, USA).

After sampling, the PTFE filters and the adsorbent tubes were stored in the dark at −20°C until analysis. The samples were analysed for pyrene and benzo(a)pyrene within three weeks after sampling. The filters and XAD-2 adsorbents (from both the front and back section of the adsorbent tubes) were extracted and analysed in a similar way to the exposure pads. The recovery of pyrene and benzo(a)pyrene on the PTFE filters was 70% and 100% respectively. No benzo(a)pyrene was detected in extracts of the XAD-2 adsorbents; the recovery of pyrene was 70%.

To determine the average daily respiratory volume of the workers, the workshift was divided into time with intensive and time with non-intensive physical activity (see table 1). In both periods the respiratory volume of the workers and the temperature of exhaled air was measured with a portable gas meter (Zentralwerkstatt Göttingen GmbH, Göttingen, Germany) for 10 minutes by the method of Kofranyi and Michaelis.[16] To be able to compare the results of the measurements the volumes were converted to the atmospheric pressure at the moment of measurement and to saturation at body temperature (BTPS).[17]

BIOLOGICAL MONITORING

During the five workdays, spot urine samples were collected before (1400) and immediately after the workshift (2200). In the two day period off work after the work week urine was collected at the same times. The urine samples were stored at −20°C until analysis. Metabolites in urine were deconjugated by enzymatic hydrolysis and a solid phase sample clean up was applied. Analysis by HPLC allows the determination of the sum of free and conjugated 1-OH-pyrene in urine at the nmol/l level. The reproducibility of the analysis of urinary 1-OH-pyrene was determined by a repeated analysis of 30 randomly selected urine samples and this gave a coefficient of variation of 12%. A full description of the method is presented elsewhere.[18] Urinary 1-OH-pyrene concentrations were corrected for creatinine. Correction for very low or high creatinine values is not reliable. Therefore, urine samples with a creatinine concentration outside the range of 4–34 mmol/l were excluded from the analyses.

CALCULATIONS OF THE DERMAL DOSE

The absorbed amount of PAHs at a skin region after a workshift of eight hours, is assumed to be equal to the total contamination of the skin region as measured with exposure pads minus the remain-

der after eight hours:

(1) $X_{absorbed,j} = X_{contamination,j} - X_{remainder,j}$

where $X_{absorbed,j}$ = amount of pyrene absorbed at skin region; (ng/cm²); $X_{contamination,j}$ = pyrene contamination on skin region$_j$ (ng/cm²); $X_{remainder,j}$ = amount of pyrene remaining on skin region$_j$ (ng/cm²).

The remaining PAHs on the skin after a workshift is assumed to be determined by two rate processes—namely, the contamination rate and the dermal absorption rate. The differential equation describing the remainder of PAHs on a skin region, based on a zero order contamination and a first order absorption process, is:

(2) $\frac{dX_{remainder,j}}{dt} = m_j - k_{a,j} \star X_{remainder,j}$

where $m_j$ = pyrene contamination rate at a skin region$_j$ (ng/cm²/h); $k_{a,j}$ = pyrene absorption rate constant at a skin region$_j$ (l/h); t = time after start of exposure (h)

The pyrene contamination rate is calculated by dividing the pyrene contamination of the exposure pad (ng/cm²) by the hours of exposure. The contamination of the exposure pad at a skin site, as measured in the skin monitoring programme, is taken to represent the dermal contamination of a whole skin region during the workshift of eight hours. Each skin region represents a percentage of the total body area (see table 2).[19] The total body surface of a worker is based on weight and height, and calculated with the formula proposed by Du Bois and Du Bois:[20]

(3) total body area = $71{\cdot}84 \star \text{weight}^{0{\cdot}425} \star \text{height}^{0{\cdot}725}$

where total body area is expressed in cm², weight in kg, and length in cm.

Table 2 presents the mean absorption rate constant of four or more fused ring PAHs at various skin sites as determined after application of coal tar ointment to the skin of healthy volunteers (unpublished data). A combination of formula (1) and the integrated form of equation (2) leads to an equation that enables calculation of the absorbed amount of pyrene at a skin region during a workshift:

(4) $X_{absorbed\ j,\ T} = \left( (m_j * T) - \frac{m_j}{k_{a,j}} * (1 - e^{-k_{a,j} * T}) \right)$

where T = duration of workshift (h)

The total amount of pyrene absorbed through the skin during the workshift is calculated as:

(5) Dermal dose = $\sum_{j=1}^{n} (X_{absorbed\ j,\ T} \star area_j)$

where dermal dose = total absorbed amount of pyrene during the workshift (ng); area$_j$ = area of skin region$_j$ (cm²); n = number of skin regions.

*Table 2 Area of skin regions and PAH absorption rate constants used in dermal dose calculations*

| *Skin site of exposure pad* | *Skin region* | *% Of total body area** | *PAH absorption rate constant†* |
|---|---|---|---|
| Jaw/neck | Head<br>Neck | 6·8 | 0·065 (0·008) |
| Shoulder | Shoulder<br>Back<br>Chest | 22·8 | 0·135 (0·027) |
| Upper arm | Upper arms | 9·7 | 0·070 (0·007) |
| Wrist | Forearms | 6·7 | 0·070 (0·007) |
| | Hands | 5·6 | 0·037 (0·005) |
| Groin | Hips<br>Thighs | 27·1 | 0·053 (0·010) |
| Ankle | Calves<br>Feet | 19·9 | 0·036 (0·003) |

*Adapted from Popendorf and Lettingwell[19]
†Mean dermal absorption rate constant of four or more fused ring PAHs (1/h) (SEM) as determined in a previous study (unpublished data)

STATISTICAL ANALYSIS

Exposure variables are presented as the geometric mean (GM) because this is considered more representative of a skewed distribution of data than the arithmetic mean (AM). Data below the detection limit were processed as having the numerical value of half of the detection limit. Correlations were assessed with Spearman's rank correlation analysis ($r_S$). Multiple regression analysis was carried out to study the relation between both dermal and inhalatory exposure and internal dose. The residuals were checked for the normal distribution assumption. None of the analyses showed major deviation from this assumption. Statistical analyses were performed with the SAS computer software package, version 6.0.

## Results

MONITORING OF SKIN CONTAMINATION

The exposure pads mounted on the jaw/neck and the wrist showed the highest pyrene contamination compared with the other skin sites (shoulder, groin, ankle, and upper arm), on which the pyrene contamination was an average threefold lower (see table 3). The pyrene contamination on exposure pads mounted underneath protective clothing reached 23 ng/cm². The pyrene contamination on the skin of coke oven workers showed a high dispersal.

Figure 2B shows the interday variation of the pyrene contamination for the exposure pads on the jaw/neck of worker 4 (top side of oven) and worker 11 (coke side of oven) during the five workshifts.

Based on the measurements on the exposure pads at six skin sites, total pyrene skin contamination was calculated (see table 4). The mean total skin contamination of the 12 workers after an exposure of eight hours ranged between 21 and 166 $\mu$g

*Table 3 Pyrene contamination (ng/cm²) on exposure pads pasted on to six skin sites of coke oven workers*

| Personal code | Function/ work location | Skin site: Jaw/neck | Shoulder | Upper arm | Wrist | Groin | Ankle |
|---|---|---|---|---|---|---|---|
| 1 | Push side | 6·7 (4·9–8·9) | 2·2 (0·7–4·2) | 3·0 (2·0–3·7) | 11·1 (5·8–19·4) | 0·5 (0·1–0·7) | 1·4 (1·3–1·4) |
| 2 | Push side | 7·2 (2·1–19·0) | 2·4 (1·3–3·4) | 1·3 (0·9–2·1) | 13·3 (2·0–29·7) | 0·8 (0·7–1·7) | 2·3 (0·3–7·3) |
| 3 | Supervisor | 8·6 (5·9–10·6) | 2·5 (1·4–4·9) | 3·3 (1·8–5·8) | 6·1 (2·0–16·4) | 4·7 (2·5–7·3) | 1·4 (1·4–1·4) |
| 4 | Top side | 16·5 (12·0–28·7) | 3·0 (2·0–4·7) | 1·9 (0·4–4·1) | 5·2 (2·0–7·9) | 5·7 (2·3–10·7) | 3·1 (1·4–7·6) |
| 5 | Supervisor | 4·2 (2·1–8·9) | 3·9 (2·1–18·6) | 0·9 (0·3–1·7) | 6·0 (4·0–11·6) | 2·9 (0·7–7·3) | 1·4 (1·3–1·4) |
| 6 | Quencher car | 1·5 (0·1–4·8) | 1·1 (0·1–2·8) | 0·4 (0·1–1·1) | 1·5 (0·7–2·0) | 0·7 (0·7–0·7) | 1·7 (1·4–2·4) |
| 7 | Coke screening | 2·1 (2·1–2·1) | 0·8 (0·1–2·8) | 0·7 (0·1–2·5) | 2·0 (2·0–2·0) | 0·8 (0·7–1·3) | 1·4 (1·4–1·4) |
| 8 | Push side | 5·5 (3·5–7·2) | 1·4 (0·1–4·8) | 3·9 (1·7–6·6) | 11·0 (8·3–16·1) | 4·3 (2·3–7·3) | 5·6 (4·4–8·1) |
| 9 | Miscellaneous | 4·9 (0·1–50·9) | 1·1 (0·1–3·1) | 3·0 (1·3–9·0) | 3·7 (1·7–7·1) | 2·7 (1·1–4·8) | 1·6 (1·3–2·5) |
| 10 | Miscellaneous | 10·6 (2·1–29·0) | 1·1 (0·1–3·4) | 1·8 (0·9–4·4) | 9·4 (2·0–31·2) | 1·4 (0·7–3·8) | 1·4 (1·4–1·4) |
| 11 | Coke side | 15·9 (12·7–18·8) | 1·6 (0·1–7·8) | 1·4 (0·1–4·8) | 18·8 (15·8–23·5) | 15·3 (8·2–23·3) | 1·7 (1·3–3·4) |
| 12 | Coke side | 14·0 (8·1–21·2) | 3·5 (3·0–4·1) | 4·2 (2·5–8·1) | 9·3 (5·7–13·1) | 0·9 (0·7–1·6) | 2·9 (1·4–7·5) |
| Overall mean (n = 60) | | 6·5 (0·1–50·9) | 1·9 (0·1–18·6) | 1·8 (0·1–9·0) | 6·4 (0·7–31·2) | 2·1 (0·1–23·3) | 2·0 (0·3–8·1) |

Results are geometric mean (range); n = 5.

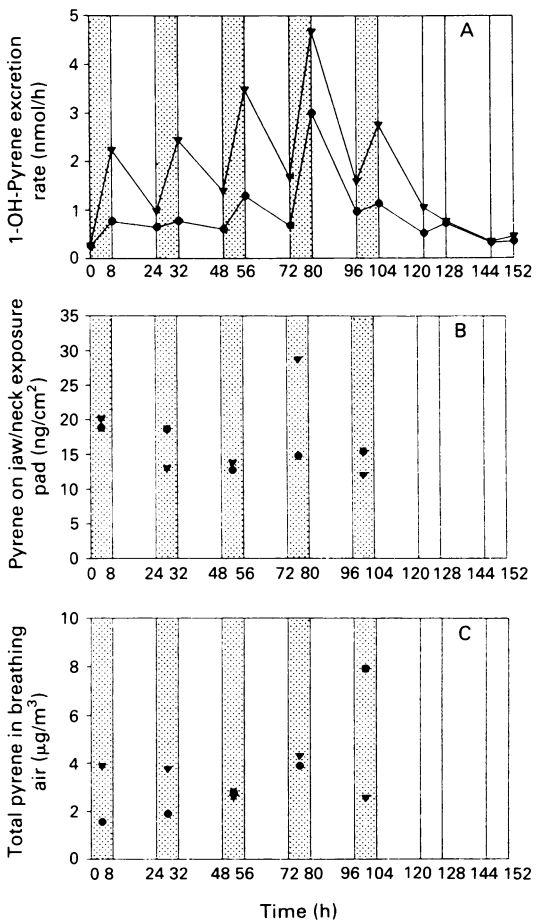


*Figure 2 (A) Urinary 1-OH-pyrene excretion; (B) pyrene contamination on exposure pads at the jaw/neck; and (C) pyrene breathing zone air concentrations of a top side worker (●---●) and a coke side worker (▼---▼) during a period of seven days. The shaded areas are eight hour workshifts.*

pyrene (GM, n = 5). The highest pyrene skin contamination was found among workers at the coke side and top side of the ovens; this reached 166 µg and 101 µg respectively (GM, n = 5).

Application of formula (5) resulted in an estimate of the daily dermal dose of pyrene after an exposure of eight hours that ranged between 4 and 34 µg. The highest mean dermal pyrene doses were for a worker at the coke side and the worker at the top side of the oven. These were 34 µg and 22 µg respectively (GM, n = 5). Thus about 22% of the pyrene contamination on the skin of a worker enters the body (range 20·3%-25·2%, n = 12). Table 4 presents the dermal weekly dose of pyrene for each worker, which is the sum of five daily skin doses. This varied between 119 and 893 nmol pyrene.

### MONITORING OF BREATHING ZONE AIR

Personal air measurements of both gaseous and particulate pyrene showed an amount of pyrene in the gas phase equivalent to 29% of the amount of particle bound pyrene (GM, range 13%-46%, n = 9). The concentration of total pyrene, both particulate and gaseous, in the breathing zone air of the workers, of which only particulate pyrene was sampled, was calculated assuming that the amount of pyrene in the gas phase was 29% of the sampled particulate pyrene.

The weekly average concentration of total pyrene in the breathing zone air of the 12 coke oven workers ranged from 0·1 to 5·4 µg/m³ (GM, n = 5). The worker at the top side of the oven had a pyrene concentration in breathing zone air of 3·0 µg/m³ (GM, n = 5). The two coke side workers had mean pyrene concentrations in breathing zone air of 3·3 and 5·4 µg/m³ (GM, n = 5). Figure 2C shows the total pyrene concentration in breathing zone air of worker 4 and worker 11 during five workshifts. The concentration for worker 4 varied between 1·5 and 7·9 µg/m³, whereas worker 11 had

*Table 4 Estimates of daily pyrene exposure, pyrene uptake during five days (input), and total urinary 1-OH-pyrene excretion during seven days (output) for 12 coke oven workers*

| | | Daily exposure | | Input (five days) | | Output (seven days) |
|---|---|---|---|---|---|---|
| Personal code | Function/ work location | Pyrene; skin contamination (μg) | Pyrene; breathing zone air concentration (μg/m³) | Pyrene; dermal dose (nmol) | Pyrene; respiratory dose (nmol) | 1-OH-Pyrene; excretion in urine (nmol) |
| 1 | Push side | 58·8 | 0·46 | 339 | 66 | 58 |
| 2 | Push side | 84·9 | 1·01 | 473 | 102 | 98 |
| 3 | Supervisor | 83·4 | 1·15 | 474 | 143 | 163 |
| 4 | Top side | 101·0 | 3·01 | 551 | 362 | 96 |
| 5 | Supervisor | 76·1 | 0·21 | 492 | 27 | 76 |
| 6 | Quencher car | 27·5 | 0·29 | 162 | 22 | 58 |
| 7 | Coke screening | 21·2 | 0·09 | 119 | 12 | 43 |
| 8 | Push side | 93·1 | 1·38 | 486 | 125 | 102 |
| 9 | Miscellaneous | 58·3 | 1·27 | 342 | 173 | 133 |
| 10 | Miscellaneous | 60·2 | 0·82 | 323 | 101 | 36 |
| 11 | Coke side | 165·9 | 3·33 | 893 | 238 | 235 |
| 12 | Coke side | 62·6 | 5·37 | 354 | 918 | 239 |

a rather constant pyrene concentration in his breathing zone air of 3·3 μg/m³ (GM, n = 5).

The daily respiratory dose was calculated as:

(6) Respiratory pyrene dose = $((pyr_{part} \star RF_{lung,part}) + (pyr_{gas} \star RF_{lung,gas}) + (pyr_{part} \star RF_{GI\text{-}tract})) \star RV$

where $pyr_{part}$ = particulate pyrene concentration in breathing zone air (μg/m³); $RF_{lung,part}$ = resorption factor of inhaled particulate pyrene that is deposited in the lungs = deposited fraction ⋆ particle elution = 0·125 ⋆ 1 = 0·125; $pyr_{gas}$ = gaseous pyrene concentration in breathing zone air (μg/m³); $RF_{lung,gas}$ = resorption factor of inhaled gaseous pyrene in the lungs = 0·7; $RF_{GI\text{-}tract}$ = resorption factor of inhaled particulate pyrene that is swallowed (gastrointestinal tract) = swallowed fraction ⋆ absorption efficiency = 0·625 ⋆ 0·40 = 0·25; RV = total respiration volume during an eight hour workshift (m³).

For the estimation of exposure to particle bound chemicals it is generally assumed that about 25% of inspired particulates is exhaled, 12·5% is deposited in the lower respiratory tract, and 62·5% is eliminated from the lungs and swallowed.[21] It is assumed that the elution of pyrene from the deposited particles in the lower respiratory tract is 100%, and that of the swallowed fraction of the particle bound pyrene 40% is absorbed in the gastrointestinal tract.[22 23] A resorption factor of 70% is assumed for inhaled gaseous pyrene.

The respiratory volume during the hours of work is based on the measured respiratory volume of the workers during physically intensive and non-intensive working hours, which varied between 8·4 and 37·7 l/min (see table 1), calculated with the formula:

$$(7) \quad RV = \frac{(WP_i \star rv_i) + (WP_{n-i} \star (rv_{n-i})}{1000}$$

where WP = workshift with physically intensive (i) or non-intensive (n-i) activities (hours); rv = respiration volume during physically intensive (i) or non-intensive (n-i) activities (l/hour)

The average respiratory volume of the 12 monitored workers during a workshift of eight hours ranged between 6·9 and 15·2 m³ (AM, 10·1 (SD 2·7) m³/8 h; n = 12).

The estimated daily respiratory pyrene dose of the 12 workers varied between 0·5 and 33·3 μg (GM, n = 5). The highest mean respiratory doses during a workshift of eight hours were calculated for a worker at the coke side of the oven (33·3 μg pyrene (GM, n = 5), and the worker at the top side of the oven (12 μg pyrene (GM, n = 5)).

Table 4 presents the results of the calculations of the respiratory weekly dose. For the 12 workers, the respiratory weekly dose of pyrene, which is the sum of the five workshifts, varied between 12 and 918 nmol. The top side worker (worker 4) and a coke side worker (worker 12) had the highest respiratory weekly doses of 362 and 918 nmol pyrene respectively.

## BIOLOGICAL MONITORING

Figure 2A shows the rate of 1-OH-pyrene excretion in urine of worker 4 and worker 11 during a period of seven days. The urinary 1-OH-pyrene excretion rate was calculated as:

(8) $uOHP_{rate} = uOHP_{conc} \star C_{creat} \star bw$

where $uOHP_{rate}$ = urinary 1-OH-pyrene excretion rate (nmol/hour); $uOHP_{conc}$ = urinary 1-OH-pyrene concentration (nmol/mmol creatinine); $C_{creat}$ = excretion rate constant of creatinine (mmol/hour/kg); bw = body weight (kg).

Creatinine excretion depends on body weight and shows a rather constant excretion rate of 25 mg/24 h/kg body weight,[24] which is equivalent to 0·009 mmol/h/kg body weight. To estimate the total amount of 1-OH-pyrene excreted as a result of a five day period of exposure to PAHs, we determined the area under the curve after correction for background 1-OH-pyrene excretion. Table 4 presents the total excreted amount of 1-OH-pyrene for

*Table 5 Multiple regression analysis of the mass balance: pyrene input urinary 1-OH-pyrene output**

| *Independent variables†* | *Parameter estimate* | *Standard error* | *Partial $r^2$* | *F* | *p Value* |
|---|---|---|---|---|---|
| Dermal pyrene weekly dose (nmol) | 0·14 | 0·019 | 0·82 | 53·2 | 0·0001 |
| Respiratory pyrene weekly dose (nmol) | 0·13 | 0·025 | 0·11 | 27·3 | 0·0008 |
| Smoking (yes = 1, no = 0) | 67·2 | 12·3 | 0·04 | 30·1 | 0·0006 |
| smoking/alcohol use (both = 1, not both = 0) | -45·2 | 14·6 | 0·02 | 9·6 | 0·015 |

Dependent variable: Excreted urinary 1-OH-pyrene during seven days, corrected for background excretion (nmol).
*n = 12
†Use of alcohol and quetelet index were excluded from the model ($p > 0·05$).

12 coke oven workers over seven days as a result of exposure to PAHs during five consecutive workshifts. It ranged from 36 to 239 nmol. The two workers at the coke side of the ovens showed the highest 1-OH-pyrene excretion (235 and 239 nmol).

A MASS BALANCE

To determine the relation between the pyrene dose (both dermal and respiratory) and urinary 1-OH-pyrene excretion, we conducted a multiple regression analysis on the data (table 5). The regression analysis was performed with weekly doses of pyrene, which is the pyrene exposure during five consecutive workshifts, and the 1-OH-pyrene excretion over seven days to reduce the influence of interindividual differences in elimination half life of pyrene on the relation. Besides the dermal and respiratory weekly dose, smoking habits, alcohol consumption during the week of measurements and the quetelet index (as a measure for fat content) were entered in the regression model. The smoking of cigarettes, drinking of alcohol, and fat content may influence urinary 1-OH-pyrene excretion.

The multiple regression analysis showed that the dermal pyrene dose, the respiratory pyrene dose, smoking, and the interaction between smoking and the drinking of alcohol significantly determine urinary 1-OH-pyrene excretion (see table 5). The effects of alcohol and fat content were not significant at $p < 0·05$ ($p = 0·42$ and $p = 0·09$ respectively) and consequently were removed from the model.

Ninety nine per cent of the variation in urinary 1-OH-pyrene excretion was explained by the regression model rather than left to residual error. The estimated parameters of the dermal and respiratory pyrene weekly dose were 0·14 (SD 0·019) and 0·13 (SD 0·025) respectively. Based on the parameter estimates it was concluded that for non-smokers about 13% of the total absorbed pyrene was metabolised and excreted as 1-OH-pyrene in urine. For workers who smoked but did not drink alcohol, this percentage was on average twofold higher (AM = 27%, range 18%-49%, n = 5). For workers who both smoked and drank, it was estimated that about 21% (AM, range 17%-30%, n = 3) of the total absorbed pyrene was excreted as 1-OH-pyrene in urine.

## Discussion

Data on PAH contamination of the skin of exposed workers are limited. It is striking to see the many studies that have been performed, with PAHs applied to skin of experimental animals and to human skin (in vitro) and the little effort that has been made to assess the skin contamination and to determine its relevance among exposed workers. Wolff and co-workers studied PAHs in skin oil of roofing workers.[15] We have measured contamination with PAHs among road paving workers and primary aluminium workers.[13 14] The relevance of these measurements is shown in the present study, in which monitoring of skin contamination is combined with biological monitoring.

Based on the estimates of the individual dermal and respiratory dose of pyrene (table 4) it is concluded that 28%-95% (GM 75%, n = 12) of the total absorbed amount of pyrene enters the body through the skin. Three major assumptions were made to obtain these estimates and need some comment. Firstly, an important aspect of the dermal dose estimations is whether the amount on the exposure pad indeed reflects the contamination of the natural skin. It is possible that the adsorption characteristics of the polypropylene filter in the exposure pad differ from the adsorption characteristics of natural skin. Among workers exposed to creosote, the exposure pad measurements tend to underestimate the pyrene contamination on natural skin (unpublished observations). Secondly, another assumption that might underestimate the actual dermal dose is that the absorption of pyrene stops after the workers have left their work place. All the contamination may not, however, be removed by a shower after work. This underestimation is probably limited, however, because in a previous study we found that the decontamination efficiency of a washing procedure to remove coal tar ointment from skin, with warm tap water and a cleaner for tar and oil-like contamination, was more than 99% (unpublished data). A third source of inaccuracy might be the absorption rate constants used in the calculations. These are based on the disappearance

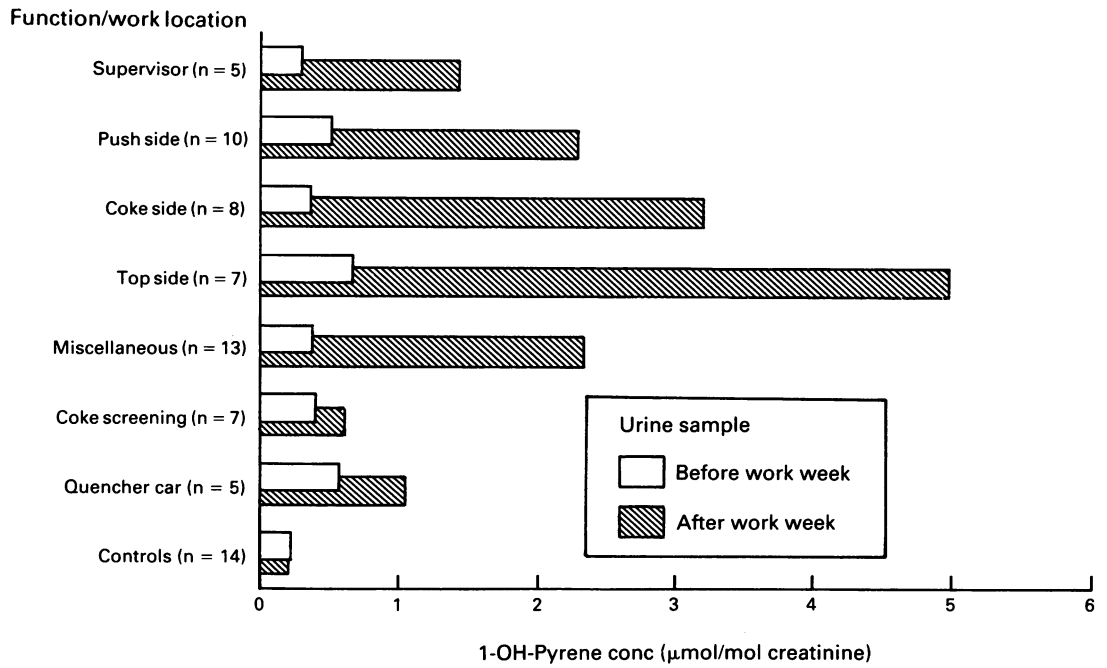


*Figure 3 Concentrations of 1-OH-pyrene in urine of all workers of the coke plant sampled before and after five consecutive workshifts (geometric mean).*

of PAHs from the surface after coal tar ointment application on various regions of the skin of volunteers (n = 4); unpublished observations). Although the interindividual differences in the absorption rate constants were minor (7%) in comparison with skin site differences (69%), the standard error of the mean PAHs absorption rate constant at a skin site was rather high (see table 2). The presented dermal pyrene dose estimates based on variation in absorption rate constants between skin regions did not differ significantly from the calculated dose based on one overall average absorption rate constant of 0.066/h (results not shown). Guy and Maibach calculated that the dermal doses of hydrocortisone, malathion, and parathion were overestimated two to three times when regional differences in penetration rate were neglected and only the penetration rate of the forearm was used in the calculations.[25] Finally, the estimates of the respiratory dose show that the variation in respiration volume between the workers may have a great impact on the dose. When the estimated respiratory pyrene dose of workers 11 and 12 were compared, the dose of worker 12 was shown to be fourfold higher although the mean pyrene breathing zone air concentration was only a factor of 1·6 higher. The eight hour respiration volume for worker 12 was 15·2 $m^3$ and for worker 11 only 6·9 $m^3$, despite comparable work activities.

The simultaneous measurement of dermal exposure to pyrene, inhalatory pyrene exposure, and total body burden (urinary 1-OH-pyrene) enables a mass balance assessment to control the quality of both the dermal and respiratory dose estimates. The presented regression model of the mass balance between both dermal and respiratory pyrene dose and urinary 1-OH-pyrene, fits well (the coefficient of determination ($r^2$) = 0·99). The model also shows comparable estimates of the fraction of both the dermal and respiratory pyrene dose that is excreted as 1-OH-pyrene in urine (0·14 and 0·13 respectively; see table 5). This supports the dose estimates, because it might be expected that the fraction of pyrene, which is metabolised into 1-OH-pyrene and excreted in urine after it has entered the systemic circulation, is independent of the route of entry. It also indicates that the dermal pyrene dose, which is on average three times higher than the respiratory pyrene dose, determines most of the internal dose. The smoking of cigarettes was found to increase the urinary 1-OH-pyrene excretion after occupational exposure to PAHs. This might be caused by an underestimation of the respiratory dose or by an increased metabolic conversion of pyrene. The socalled hand-mouth shunt or a decreased clearance of particle bound pyrene from the ciliated surface of the respiratory tract may lead to an underestimation of the respiratory dose of

workers who smoke cigarettes. The significant interaction between smoking and the use of alcohol, however, suggests that the effect of smoking on urinary 1-OH-pyrene excretion is more likely to be a toxicokinetic effect.

To determine whether the 12 intensively monitored workers had exposure levels representative of the other workers of the plant, we collected spot urine samples of 56 other workers who also worked in the vicinity of the coke ovens. Spot urine samples of these workers were collected just before and at the end of five consecutive eight hour workshifts. Control urine samples were available from administrative personnel of the plant (n = 14). Figure 3 shows the urinary 1-OH-pyrene concentrations per function or work location of the coke oven workers and controls (in $\mu$ mol/mol creatinine). The 1-OH-pyrene concentrations in urine of the 12 selected workers were within the range as measured among the other PAH exposed workers of the plant. The results show that workers in the vicinity of the ovens, especially at the top side, were mostly exposed to PAHs. About 46% of the workers who work in the vicinity of the ovens of the coke plant had a urinary 1-OH-pyrene concentration that exceeded the recently proposed biological exposure limit of 2·3 $\mu$mol/mol creatinine.[26] The urinary 1-OH-pyrene concentrations measured among coke oven workers of this plant ranged between 0·2 and 9·3 $\mu$mol/mol creatinine. The concentrations measured in another coke plant were of the same range: 0·3–11·3 $\mu$mol/mol creatinine.[27]

Most of the data on exposure of workers to PAHs at other coke plants are confined to air concentrations of PAHs, generally benzo(a)pyrene. The mean concentration of benzo(a)pyrene in breathing zone air of the 12 coke oven workers varied between 0·01 and 13·9 $\mu$g/m$^3$ (data not shown), which is within the range measured in other studies.[1 27-31]

The particulate pyrene concentrations in breathing zone air measured in this study are comparable with those measured in a previous study among coke oven workers of another coke plant in The Netherlands.[27] Data on gaseous pyrene in breathing zone air samples of coke oven workers are scarce. In the present study, the percentage of gaseous pyrene in total pyrene varied between 11% and 30% (GM 21%, n = 9). Björseth and coworkers reported a mean 5% in stationary air samples at the battery top.[1] Regression analysis of the benzo(a)pyrene concentration in air (GM of measurements during five workshifts in $\mu$g/m$^3$) and the end of week urinary 1-OH-pyrene concentration ($\mu$mol/mol creatinine) of the 12 workers and controls gave the relation: (end-of-week 1-OH-pyrene) = 0·54 + 1·34 $\star$ (benzo(a)pyrene in air). With this formula the urinary 1-OH-pyrene concentration was estimated for workers, when exposed to the German technical guiding concentration of 2 $\mu$g benzo(a)pyrene/m$^3$. This gave a biological exposure limit of 3·2 $\mu$mol 1-OH-pyrene/mol creatinine (95% confidence interval 2·4–4·1), which is similar to the value of 2·3 $\mu$mol/mol as proposed by Jongeneelen.[26]

Data on dermal contamination with PAHs for coke oven workers of other coke plants are not available. Among the coke oven workers the mean daily pyrene contamination on skin ranged between 21 and 166 $\mu$g/day. This is lower than the mean pyrene skin contamination as estimated for primary aluminium workers (about 400 $\mu$g/day)[14]. The pyrene contamination on exposure pads worn by the coke workers is comparable with those worn by road paving workers, except for the pyrene contamination on the wrist pad, which is on average three times higher among road paving workers[13]. Table 3 shows that the pyrene contamination on exposure pads worn by coke oven workers who have a comparable work location and work activities, varies in extent and dispersal (compare for example, workers 11 and 12). Apparently, both the extent and dispersal of PAH contamination on skin of workers exposed to PAHs are not only determined by work environment, but also by function and personal factors. Personal factors that might influence skin contamination by PAHs are personal hygiene, individual working methods, the use of protective clothing, and the frequency of laundering.

The suitability of pyrene as a marker compound for PAHs in air samples is shown in a previous study. Particulate pyrene correlated well with the sum of 11 PAHs ($r$ = 0·88, n = 47)[27]. In our present study, a significant correlation between pyrene and benzo(a)pyrene in both breathing zone air samples and skin exposure samples was found. The Spearman correlation coefficients were 0·94 (n = 58) and 0·73 (n = 378) respectively; however, the ratio pyrene: benzo(a)pyrene (wt/wt) was 2·1 (GM, range 0·6–16·2) in breathing zone air samples and 6·3 (GM, range 0·15–165) in skin contamination samples. Because of the difference in the ratio pyrene: benzo(a)pyrene between breathing zone air samples and skin contamination samples, we also estimated the dermal and respiratory uptake of benzo(a)pyrene by applying the presented formulae. This showed that the percentage of the total absorbed amount of benzo(a)pyrene that enters the body through skin ranged from 8%–92% (GM = 51%, n = 12).

The correlation between the PAH concentration in breathing zone air and the estimated PAH uptake by skin was rather low. For pyrene the Spearman correlation coefficient was 0·59 (p = 0·045, n = 12) and for benzo(a)pyrene 0·55 (p = 0·067, n = 12). Because of the high uptake of

PAHs through the skin we suggest that exposure is assessed by a biological monitoring method, which gives a more accurate assessment of the internal PAH exposure of a worker than breathing zone air measurements. This study confirms that the measurement of 1-OH-pyrene in urine as an indicator of internal PAH exposure, is a powerful biological monitoring method.

In summary, we have found that among coke oven workers, the uptake of PAHs through skin is very relevant in terms of the internal dose. For pyrene an average 75% (range 28%–95%) of the total dose was absorbed through skin. For benzo(a)pyrene it was 51% (range 8%–92%). Our results indicate that preventive measures to reduce exposure to PAHs should be focused more on the reduction of dermal contamination with PAHs than on the reduction of the inhaled dose.

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