Significance of dermal and respiratory uptake in creosote workers: exposure to polycyclic aromatic hydrocarbons and urinary excretion of 1-hydroxypyrene

Eivor Elovaara, Pirjo Heikkilä, Lauri Pyy, Pertti Mutanen, Vesa Riihimäki

Abstract

Objectives—To evaluate workers' exposure in a creosote impregnation plant by means of ambient and biological monitoring.

Methods—Naphthalene (vapour phase) and 10 large molecular polycyclic aromatic hydrocarbons (PAHs) (particulate phase) were measured in the breathing zone air during an entire working week. 1-Hydroxypyrene (1-HP) was measured in 24 hour urine as a metabolite of the pyrene found in neat (dermal exposure) and airborne creosote.

Results—Naphthalene (0-4-4-2 mg/m³) showed 1000 times higher concentrations in air than did the particulate PAHs. In total, the geometric mean (range) of three to six ring PAHs was 4-8 (1-2-13-7) µg/m³; pyrene 0-86 (0-23-2-1) µg/m³; and benzo(a)pyrene 0-012 (0-01-0-05) µg/m³. There was no correlation between pyrene and gaseous naphthalene. The correlations between pyrene and the other nine particulate PAHs were strong, and gave a PAH profile that was similar in all air samples: r = 0-83 (three to six ring PAHs); r = 0-81 (three ring PAHs); r = 0-78 (four to six ring PAHs). Dermal exposure was probably very high in all workers, because the daily output of urinary 1-HP exceeded the daily uptake of inhaled pyrene by ≤50-fold. Urinary 1-HP concentrations were very high, even on Monday mornings, when they were at their lowest (4-22 µmol/mol creatinine). 1-HP seldom showed any net increase over a workshift (except on Monday) due to its high concentrations (16 to 120 µmol/mol creatinine) in the morning samples. 1-HP was always lower at the end of the shift (19 to 85 µmol/mol creatinine) than in the evening (27 to 122), and the mean (SD) change over the working week (47 (18)) was greater than the change over Monday (35 (32)). The timing of 1-HP sampling is therefore very important.

Conclusions—Urinary 1-HP proved to be a good biomarker of exposure to three to six ring PAHs but not to airborne naphthalene. Hence, biomonitoring based on 1-HP has to be completed with exposure assessment for naphthalene as a marker for creosote volatiles that mainly enter the body through the lungs.

Keywords: occupational exposure; naphthalene; pyrene; benzo(a)pyrene; biological monitoring

Creosote oil is a wood preservative derived from coal tar. Occupational exposure, which may take place by inhalation of its vapour as well as aerosol fractions, or through skin contact, is a recognised health hazard. It causes mainly toxic effects to the skin and eyes and is probably carcinogenic to humans. More than 100 different compounds have been analysed in creosote oils, and it has remained unclear which specific chemicals are primarily accountable for the harmful effects. Analysis of polycyclic aromatic hydrocarbons (PAHs) in Finnish creosote impregnation plants has shown that naphthalene and its alkyl derivatives (0-1-11 mg/m³) were the main volatiles in the air, with concentrations 1000 times higher than the particulate PAHs (0-2-46 µg/m³). Pyrene was a major constituent of the large molecular PAHs (four to six rings) of both the neat and airborne creosote.

Complex chemical exposures are a health concern whenever they involve PAHs, a class of compounds considered to have human carcinogenic potential. Workers in industrial operations with high airborne concentrations of PAHs show, in particular, excess rates of lung cancer, and workers exposed specifically to creosote have an excess of skin and bone cancers. The measurement of 1-hydroxypyrene (1-HP) in urine is a method used to monitor exposure not only to its parent compound pyrene, but also as a biomarker for total exposure to PAHs, both of occupational and other origins. The assay for 1-HP offers a method to assess the absorption of pyrene or PAHs by all routes of entry. The importance of the dermal absorption is increasingly considered in studies on occupational exposure to PAHs. In creosote workers, the skin is probably the most important route of exposure to PAHs.

This study was conducted outdoors in a creosote impregnation plant. The purpose was to assess: (a) the workers' exposure through inhaled air by measuring naphthalene, pyrene, benzo(a)pyrene, and eight other PAHs in the breathing zone from whole shift air samples over five days, and (b) the workers' internal exposure with the aid of the urinary 1-HP method. The study focused on different exposure routes (dermal and inhalatory), the variations in individual exposures, and the optimal urine sampling time for 1-HP measurement in an occupational biomonitoring scheme.
Materials and methods

The PAHs used for standardisation were: naphthalene, anthracene, phenanthrene, pyrene, benzo(a)pyrene, and fluoranthene (Fluka, Buchs); benzo(a)fluorene, chrysene, benzo(e)pyrene, dibenzo(ah)anthracene, and benzo(ghi)perylene (Ega-Chemie, Steinheim); and benzo(k)fluoranthene (Community Bureau of Reference, Commission of European Communities, Brussels). The purity was >97% for all PAH standards. 1-Hydroxy-pyrene was from Janssen Chimica, 2340 Beerse, Belgium. β-Glucuronidase and aryl-sulphatase (100 000 Fishman U/ml and 800 000 Roy U/ml) were from Boehringer, Mannheim, Germany. The purity of the solvent chemicals was of high performance liquid chromatography (HPLC) grade.

Subjects and study design

The measurements were carried out in an impregnation plant, where railway ties (sleepers) were impregnated with creosote (imported from Poland). Six men with different jobs volunteered to participate in this study. The five day air sampling period was preceded and followed by a work free period of 64 hours. All workers wore leather protective gloves and cotton overalls, but no one used a respiratory protector. Employees Nos 2 and 3 worked overtime (until 6:30 pm) on Monday, which was an exception from the regular eight hours a day schedule (fig 1).

Air sampling and PAH analyses

Personal breathing zone air samples were taken on five consecutive days in July 1987. Particulate PAHs (air sample volume 200–700 l) were collected during the whole shift (6:00 am to 2:00 pm) in one or two periods on prewashed 37 mm filters (Glassfibre Prefilter SM 13400, Sartorius AG, Goettingen, Germany) at a flow rate of 2 l/min (suction velocity 3.5 cm/s), whereafter the filters were wrapped in aluminium foil, stored in a...
refrigerator, and analysed within seven weeks. The samples were extracted into cyclohexane (60 ml) by a Soxhlet system for eight hours, evaporated to dryness under N₂ flow at room temperature, redissolved in 1 ml of 85% acetonitrile aqueous solution by ultrasonication for four minutes and analysed for PAHs in a single chromatographic run with reversed phase HPLC with fluorescence detection (Perkin Elmer Series 4/Perkin Elmer LS4) with an octadeccylsil P-E HS-3, RP18 (100 × 4.6 mm) column, a Perisorb RP-18 (30 × 2.1 mm) precolumn, and with a linear gradient program from 65% to 85% of acetonitrile in water (1%/min). Measurement was based on peak heights with pure PAH standards (in acetonitrile). The detection limit for benzo(a)pyrene was 5 pg (injection volume 6 μl), which corresponds to an air concentration of about 8 ng/m³ in an air sample of 100 l.

In the gaseous phase, naphthalene (> 99% of its total air concentration) was the only PAH collected (parallel to the filter samples) on XAD-2 resin tubes (yield 88 (9%) and assayed as described by Heikkilä et al.

**BIOLICAL MONITORING**

The workers were asked to collect all urine passed within the 24 hour period into divided samples for the designated periods. Specimens collected at home and at work were stored in the refrigerator until transferred to a deepfreeze (−20°C).

**DETERMINATION OF URINARY 1-HP**

The method of Jongeneelen and coworkers¹³ was used to analyse 1-HP in urine. Thawed urine (5 ml samples, stored for one year at −20°C without preservatives) was adjusted to pH 5-0 with 1N HCl. Sodium acetate buffer (5 ml of 0.2 M, pH 5-0) containing 12.5 μl of β-glucuronidase and arylsulphatase was added for enzymatic hydrolysis (complete) at 37°C for three hours. Mega Bond Elut C-18 cartridges (from Analytichem International, USA) were used for solid phase sample clean up: after priming (5 ml methanol, 10 ml H₂O), the hydrolysed sample was loaded, washed (10 ml H₂O), then 10 ml 20% acetonitrile), and the retained 1-HP was eluted in 10 ml of methanol. If needed, the eluate was concentrated 10-fold to 20-fold by evaporation (under N₂ flow) and redissolved in methanol. The sample tubes were protected from light with aluminium foil. Standards of 1-HP were prepared in pooled blank urine (0, 10, 100, 250, 500, 750, 1000 nmol/l) and carried through the analytical procedures. The 1-HP was analysed with a Shimadzu HPLC system: a manual sample injector (20 μl loop), a ChromSep column (100 × 3 mm ID packed with Chrom-Sphere PAH, Chrompack, Middelburg, Netherlands), and a fluorescence detector (from λ 242 nm to λ 388 nm) were used with acetonitrile-tetrhydrofuran-water (37:5:58 by volume) as the mobile phase of isocratic runs (fig 2). Quantification was based on peak area counts. The coefficient of variation was 4% (for pooled urine with 1-HP 1 μmol/l n = 9) and the recovery of added standards in urine was 65%. Urinary creatinine was determined²⁰ to correct for urine dilution and to express the 1-HP excretion per mol creatinine.

**STATISTICAL ANALYSIS**

The normality of the distribution of the air analysed data of the original and the log transformed PAH variables was checked. A non-parametric method (Spearman) was used for correlation analysis, because some of the transformed variables (log pyrene, P = 0.068; log of the sum of four to six ring PAHs, P = 0.011) were not normal.

**Results**

Naphthalene was determined in the vapour phase (XAD tube analysis) whereas pyrene and nine other larger PAHs were determined in the particulate phase (filter analysis) of the breathing zone air of six workers during a working week. Table 1 shows the PAHs in creosote oil (dermal exposure) and in whole shift air (eight hour time weighted average (TWA)). The geometric mean (range) air concentration of total particulate PAHs

**Table 1 Studied PAHs in creosote oil* and in workers' breathing zone air**

<table>
<thead>
<tr>
<th>PAH</th>
<th>Concentration in creosote* (pg/m³)</th>
<th>Arithmetic mean (SD)</th>
<th>Geometric mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatic rings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naphthalene</td>
<td>97</td>
<td>1536 (1036)</td>
<td>1254 (1-91)</td>
<td>370-4200</td>
</tr>
<tr>
<td>Phenanthrene</td>
<td>35</td>
<td>4-02 (2-56)</td>
<td>3-25 (2-01)</td>
<td>0-78-100</td>
</tr>
<tr>
<td>Fluorene</td>
<td>44</td>
<td>0-30 (0-35)</td>
<td>0-19 (0-52)</td>
<td>0-04-1-53</td>
</tr>
<tr>
<td>Pyrene</td>
<td>9</td>
<td>0-97 (0-45)</td>
<td>0-86 (0-69)</td>
<td>0-23-2-10</td>
</tr>
<tr>
<td>Chrysene</td>
<td>0-15</td>
<td>0-17 (0-10)</td>
<td>0-14 (1-73)</td>
<td>0-05-0-47</td>
</tr>
<tr>
<td>Benzo(a)fluorene</td>
<td>0-25</td>
<td>0-094 (0-084)</td>
<td>0-068 (1-84)</td>
<td>0-02-0-40</td>
</tr>
<tr>
<td>Benzo(a)pyrene</td>
<td>0-2</td>
<td>0-047 (0-044)</td>
<td>0-036 (2-06)</td>
<td>0-01-0-21</td>
</tr>
<tr>
<td>Benzo(b)fluoranthene</td>
<td>5</td>
<td>0-014 (0-010)</td>
<td>0-014 (2-51)</td>
<td>0-01-0-055</td>
</tr>
<tr>
<td>Benzo(a)pyrene[†]</td>
<td>0-05</td>
<td>0-014 (0-010)</td>
<td>0-012 (1-57)</td>
<td>0-01-0-050</td>
</tr>
<tr>
<td>Dibenzo(a,h)anthracene[†]</td>
<td>0-06</td>
<td>0-010 (0-006)</td>
<td>0-010 (1-16)</td>
<td>0-01-0-020</td>
</tr>
<tr>
<td>Benzo(g,h,i)perylene[†]</td>
<td>0-09</td>
<td>0-012 (0-004)</td>
<td>0-011 (1-28)</td>
<td>0-01-0-025</td>
</tr>
<tr>
<td>Total PAHs excluding naphthalene</td>
<td>81</td>
<td>5-70 (3-36)</td>
<td>4-77 (1-88)</td>
<td>1-23-13-74</td>
</tr>
<tr>
<td>Ratios in creosote oil and in air:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naphthalene†/total 3-6 ring PAHs</td>
<td>1-2</td>
<td>333 (281)</td>
<td>266 (1-9)</td>
<td>69-1556</td>
</tr>
</tbody>
</table>

Results represent air sampling of five days and six men (n = 30): NA = not analysed. *Data from a previous publication (Nyhus, et al 1992).* According to the overall evaluation of carcinogenicity to humans as classified by IARC (1987), *Carcinogenicity not classifiable (group 3)*; possibly carcinogenic (group 2B); likely for this PAH there is an occupational limit value (10 μg/m³, 8h TWA) in Finland; *probable carcinogenic (group 2A).*
The significance of urine profiles of HP1, HP2, Cn1, and Cn2 containing 1-37 pg/M3 (n = 30) to HP12 (0-21) pg/M3 (n = 0-95) in relation to the particulate PAHs. The naphthalene concentrations were generally higher than the concomitant concentrations of pyrene. It is thus evident that the air profiles of gaseous naphthalene, and the pyrene bound to air particulates, were not similar. Variation between workers was considerable and higher for naphthalene than for the other PAHs in air.

The actual relations between pyrene and other PAHs in breathing zone air were evaluated from the air analysis data that represent altogether 48 sampling periods during the five day working week (table 2). The particulate PAHs, subgrouped for correlation analysis by molecular size, were compared with the pyrene concentration of the same sample. The correlation coefficients by pyrene and the three ring PAHs (r = 0.81), the four to six ring PAHs (r = 0.83), and the sum of the nine other particulate PAHs (r = 0.78) indicated that the PAH profile of all samples was very similar. As concentrations of the five to six ring PAHs were mostly near or below the limits of detection, no separate values were calculated for these. The best correlation (r = 0.86) was found between pyrene and the other four ring PAHs (chrysene + benzo(a)fluorene + benzo(a)pyrene + benzo(k)fluoranthene + benzo(a)pyrene + benzo(ghi)perylene + dibenz(a,h)anthracene, the sum of phenanthrene + fluorene).

Values are arithmetic mean (SD) (n = 48); *r* = Spearman correlation coefficient; †The sum of chrysene + benzo(a)fluorene + benzo(a)pyrene + benzo(k)fluoranthene + benzo(a)pyrene + benzo(ghi)perylene + dibenz(a,h)anthracene, the sum of phenanthrene + fluorene.

![Figure 2 HPLC profiles of extracts from (A) a pooled blank urine with a known amount of the standard added to contain 1 μmol/l of 1-hydroxypyrene (HP), and (B) a pooled urine sample from workers exposed to creosote.](group.bmj.com)
end of the shift. In the morning samples of Tuesday to Saturday (after 16 hours off), the urinary 1-HP was often higher in the middle or at the end of the shift. It was thus characteristic for 1-HP that it never reached peak excretion during the shift, a phenomenon more or less explained by the apparent dermal absorption continuing even after working hours. The net increases in individual 1-HP urine concentrations were calculated over (a) one working day (Monday), (b) one working week (Monday morning → Friday end of shift), and (c) before shifts (Monday → Friday).

To compare, on a molar basis, the pyrene inhaled over a working day with the 1-HP excreted in urine (table 4), the respiratory pyrene dose per working day was calculated by taking into account the uptake of both particulate and gaseous pyrene (the concentration of the gaseous pyrene is known to be maximally about 50% of the total pyrene24 25 27).

Pyrene dose = $C_{\text{total}} \times V \times T \times R$

where $C_{\text{total}} = 2 \times C_{\text{particulates}}$ pyrene concentration in air (μg/m3), $V = 25$ l/min ventilation rate (assumed), $T = $ daily exposure time, $R = 50\%$ retention (assumed). Moreover, urinary excretion of 1-HP (as μmol/mol creatinine at different times or nmol/24 h) did not show any significant correlation with the concentration of pyrene in the breathing zone air. As some of the workers apparently did not provide complete 24 hour urine samples on all the experimental days, we rejected uncertain data. Then, of all the possible correlations calculated by linear regression analysis, the best one was shown between daily pyrene uptake (through inhalation) and the amount of 1-HP in 24 hour urine: $r = 0.34$, $n = 9$.

### Discussion

In view of the ambient and biological monitoring, it is evident that the workers were exposed both through the lungs and the skin to neat and airborne creosote. Hence, it is important to note that the chemical profiles of liquid creosotes differ from their airborne profiles, a factor complicating exposure assessment for creosote.

Naphthalene is the main component in the air of workplaces where creosote is used, and it reflects well the ambient concentration of the main creosote volatiles to which, notably, pyrene and PAHs do not belong. 4 5 This was also evident from our findings indicating that the concentrations of naphthalene vapour were about three orders of magnitude higher, and much more variable, than those of particulate pyrene in personal air samples. Not unexpectedly, the correlation of naphthalene with pyrene in air was non-existent. It is thus evident that 1-HP is not a biomarker for the major volatile fraction of airborne creosote.

Pyrene occurs characteristically with the group of large molecular PAHs, and it is found among the PAHs (chrysene, benzo(k)fluoranthene, benzo(a)pyrene, benzo(g,h,i)perylene), specifically implicated in the aetiology of human lung cancer. 29 30 A methodological difference in the PAH air sampling technique between our study and for example, the study of Tjoe Ny et al. 17 is that they used glass fibre filters backed by XAD-2 tubes for quantitative (indoor) trapping of PAHs in a Söderberg potroom of an aluminium smelter. They reported that, in total, 48% pyrene, 24% total PAHs, but no benzo(a)pyrene, were found on XAD tubes. Despite these methodological differences, and also the very different types of work environments with widely different airborne concentrations of pyrene ($\leq 100$ times) and benzo(a)pyrene ($\leq 3000$ times), their findings as well as ours support the conclusion that

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### Table 3 Summary of the results from ambient and biological exposure monitoring of creosote workers

| Worker No | Pyrene in air (μg/m3) | Monday morning before work | Tuesday morning to Saturday | End of shift† | Evening (after work)† | Weekend (morning)‡ | Changes: working day Monday§ | Changes: working week¶ | Changes: before shifts Friday minus Monday
<table>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.90 (2.24)</td>
<td>4</td>
<td>16 (7)</td>
<td>19 (10)</td>
<td>27 (8)</td>
<td>12 = 4 = 7</td>
<td>12 = 26 = 18</td>
<td>96 = 63 = 96</td>
<td>58 = 58 = 58</td>
</tr>
<tr>
<td>2</td>
<td>1.09 (3.92)</td>
<td>9</td>
<td>120 (20)</td>
<td>85 (18)</td>
<td>122 (63)</td>
<td>115 = 38 = 13</td>
<td>96 = 63 = 96</td>
<td>58 = 58 = 58</td>
<td>58 = 58 = 58</td>
</tr>
<tr>
<td>3</td>
<td>1.25 (4.44)</td>
<td>16</td>
<td>89 (16)</td>
<td>70 (25)</td>
<td>95 (25)</td>
<td>85 = 34 = 18</td>
<td>10 = 56 = 58</td>
<td>51 = 53 = 51</td>
<td>56 = 56 = 56</td>
</tr>
<tr>
<td>4</td>
<td>1.39 (4.49)</td>
<td>17</td>
<td>77 (9)</td>
<td>71 (31)</td>
<td>119 (50)</td>
<td>9 = 5 = ND = 6</td>
<td>24 = 53 = 51</td>
<td>56 = 56 = 56</td>
<td>56 = 56 = 56</td>
</tr>
<tr>
<td>5</td>
<td>0.53 (0.22)</td>
<td>22</td>
<td>104 (40)</td>
<td>64 (20)</td>
<td>113 (78)</td>
<td>74 = 47 = ND</td>
<td>28 = 23 = 56</td>
<td>56 = 56 = 56</td>
<td>56 = 56 = 56</td>
</tr>
<tr>
<td>6</td>
<td>0.65 (0.31)</td>
<td>9</td>
<td>58 (10)</td>
<td>79 (29)</td>
<td>105 (60)</td>
<td>ND</td>
<td>38 = 59 = 50</td>
<td>50 = 50 = 50</td>
<td>50 = 50 = 50</td>
</tr>
<tr>
<td>All workers</td>
<td>0.97 (0.45)</td>
<td>13</td>
<td>77 (37)</td>
<td>64 (23)</td>
<td>97 (35)</td>
<td>35 (32)</td>
<td>47 (18)</td>
<td>56 (25)</td>
<td>56 (25)</td>
</tr>
</tbody>
</table>

Values are the mean (SD); *whole shift TWAs of five days; †n = three days, Monday, Wednesday and Friday; §Saturday, Sunday and Monday; ¶difference between urine specimens, Monday end of shift (2.00 pm) minus Monday morning; ‡difference between urine specimens, Friday end of shift minus Monday morning; ND = not determined.

### Table 4 Crude approximation of daily pyrene uptake through dermal or inhalatory routes in six creosote workers

| Worker No | Smoking | Visible contamination on clothing | Pyrene uptake through inhalation* (nmol/day) | 1-HP in 24 h urine† (nmol/mol creatinine) | Molar ratio: 1-HP in 24 h urine/ pyrene uptake through inhalation
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>Very low</td>
<td>58 (3)</td>
<td>281 (40)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>Low</td>
<td>9 (3)</td>
<td>151 (27)</td>
<td>22 (5)</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>Moderate</td>
<td>91 (37)</td>
<td>630 (150)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>High</td>
<td>169 (20)</td>
<td>728 (16)</td>
<td>11 (1)</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>High</td>
<td>30 (9)</td>
<td>1038 (790)</td>
<td>32 (17)</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>High</td>
<td>46 (16)</td>
<td>576 (31)</td>
<td>13 (4)</td>
</tr>
</tbody>
</table>

Values are mean (SD) of three workdays (Monday, Wednesday, and Friday; *See the text for the calculations on pyrene concentrations measured in worker’s breathing zone air (no correction was made for the pyrene uptake in tobacco smoke); †indicative of total pyrene metabolism in the body, of which smoking may account at most for 20 nmol/24 h urine (Jongeneelen et al 1990)*.
there is a strong correlation between pyrene and the total PAHs in the air. In our study, the particulate concentrations of benzo(a)pyrene in air were even at maximum (0.05 µg/m³) low compared with its occupational limit value (10 µg/m³), and also low in view of the resultant respiratory doses (≤ 0.3 µg/8 h working day) that were exceedingly lower than—for example, in a meal high in benzo(a)pyrene (about 5 µg). Based on the 1-HP urine data, it is evident that the major uptake of carcinogenic PAHs was attributable to creosote exposure through the skin. Although ambient monitoring of benzo(a)pyrene is of indisputable value as a measure of exposure to an actual carcinogen, it was, compared with pyrene, an insensitive PAH marker for the assessment of differences between workers in external exposures to total PAHs in a work environment like the present one.

Although exposure to creosote is typically associated with working outdoors, our findings as well as those of others14 15 25 32 point out that the urinary concentrations of 1-HP in creosote workers are very high in comparison with workers exposed to PAHs from other work environments—for example, at a coke plant,16 31 34 an aluminium plant,17 in asphalt road surfacing,18 19 and others.35 36 Also in the light of our own laboratory data, the urinary 1-HP concentrations in creosote workers were very high compared with the controls (mean (SD) 0·27 (0·24) µmol/mol creatinine, geometric mean 0·20, n = 27) measured in people from urban and rural areas in Estonia. Zhao et al have shown that the correlations between urinary 1-HP and the ambient concentration of both pyrene (r = 0·987) and benzo(a)pyrene (r = 0·959) were highly significant in the workers of coke and steel plants, whereas in our study 1-HP and pyrene did not correlate (r ≤ 0·34).

The daily uptake of inhaled pyrene was far too small to explain the high daily urinary output of 1-HP (table 4). This becomes more evident when it is borne in mind that in humans the urinary 1-HP may maximally account for 10% of inhaled pyrene. After creosote oil was given to rats (4 to 80 mg/rat, intragastrically) only 5% to 3% of the pyrene therein was recovered in 24 hour urine as 1-HP (unpublished own results). In another study on rats the percentage was 10 times lower (≤ 0·4%). Hence, the observed lack of relation between 1-HP and inhaled pyrene may best be explained by additional exposure through the skin. The dirtiness of the creosote work was also obvious.

From therapeutic coal tar treatment of patients' skin it is known that pyrene is readily absorbed and excreted at high urinary concentrations of 1-HP.12 22 32 In view of the study by van Rooij et al25 it may be concluded that skin is the main route of PAH uptake in creosote workers.

Our study showed difficulties in selecting appropriate sampling times for biological monitoring of creosote workers. It was evident that the highest concentrations of 1-HP were consistently found in late evening samples but not at the end of the shift, and that the baseline excretion concentration could be determined only after the weekend. Similar conclusions may be drawn from the data presented by van Rooij et al.26 Assessment of daily uptake by the net increase of 1-HP in urine as a change within shift has been the common practice in many laboratories. However, it was hardly applicable even on Monday. When the workers had been exposed on the day before sampling, this method was not valid at all, because the 1-HP values were mostly higher in the morning than at the end of shift. Hence, the change within shift showed mostly a net decrease (Tuesday to Friday). Also Bos, Jongeneelen, and coworkers5 32 studied workers who creosoted wood and found that, instead of a net increase, a decrease occurred in urinary 1-HP excretion over the workshifts. Evidently, biomonitoring based on the urine sampling both before and after work may represent rather meaningless sampling times for assessment of exposure to pyrene, especially in workers with apparent skin exposure. Another complicating factor is that in humans the excretion process of 1-HP is biphasic, showing two relatively long half-lives: a shorter one (one to two days) for the readily available (for metabolism and then excretion) body pyrene and a longer one (16 days) for the slowly available component. Both elimination components imply pyrene accumulation, and consistent with this the average net increase in urinary 1-HP over a workday was less than the change within a working week or within the samples taken before shifts (Friday minus Monday values).

The Monday morning concentrations of 1-HP (13 (7) µmol/mol creatinine) were very high in all the men studied, a finding characteristic for creosote workers.14 16 25 32 The concentrations were so high that they exceeded not only the upper limits reported for normal 1-HP excretion of unexposed non-smokers 0·66 and smokers 1·3 µmol/mol,14 but also the biological exposure limits of 2·3 and 4·3 µmol/mol for coke oven workers7 27 and for workers in a Sörderberg potroom,27 respectively.

Biotransformation of pyrene into 1-HP by human liver preparations in vitro has shown large differences between people.10 It is not clear to what extent differences between people in pyrene biochemistry may cause variation in the urinary excretion rates of 1-HP in general, or in the present workers who reported different intakes of alcoholic beverages and tobacco. Alcohol consumption, medication, and age are known to have little effect on the elimination kinetics of 1-HP in humans.16 19 Also the daily amounts of 1-HP excretion that may come from the diet21 seem relatively unimportant in creosote workers.

Although smoking is known to increase the 1-HP concentrations in urine,14 16 19 it seems to be a negligible source of pyrene exposure in creosote workers. Smoking is thus not a problem to the use of this biomarker. Nevertheless, smoking is a high risk factor in lung cancer; together with occupational
exposure it may efficiently enhance the pulmonary expression of cytochrome P-450 enzymes required for the activation of procarcinogens both in tobacco smoke and in inhaled creosote.

Profiles of PAHs such as those of pyrene and known carcinogenic PAHs vary in different work environments. This is important to know when 1-HP is used to assess exposure to carcinogenic PAHs. For example, the urinary excretion of 1-HP among the creosote workers of our study was almost comparable with the concentrations in the Söderberg potroom workers. In the potroom workplace, the inhalable concentrations of benzo(a)pyrene were high (< 95 μg/m³) in contrast with our study where they were low (≤ 0.05 μg/m³).

Knowledge of the PAH profiles, both of the source and the airborne fractions, is thus necessary whenever 1-HP is used as a single biomarker of exposure to total PAHs and for the prediction of cancer risks associated with PAHs in various work environments.

Conclusions

Ambient concentrations of pyrene were predictive of particulate PAHs but not of naphthalene. The ratio of naphthalene to three to six ring PAHs was two orders of magnitude higher in inspired air than in creosote oil. Naphthalene may thus be used as an ambient marker for those volatiles of creosote that enter the body mainly through the lungs. The urinary excretion of 1-HP was high in all workers, and it showed greater variation between the workers than did the inhaled pyrene. Conspicuous diurnal elimination kinetics showed that the timing of 1-HP sampling is very critical. For the assessment of exposure to pyrene and PAHs 1-HP is a valid biomarker, but not for pyrene if monitored by the ambient method alone, as this ignores the dermal route that in the case of airborne large molecular PAHs seems to be very important. Specific knowledge of the PAH profile in air and creosote oil in the workplace is needed to allow any statement on a worker’s actual exposure to carcinogens. In this study, exposure to carcinogenic PAHs through air was low but not necessarily through the skin in view of the results that indicated high dermal uptake of pyrene. Individual measurements of exposures along with hygienic improvements are needed to lower and control dermal exposure in creosote workers.

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Significance of dermal and respiratory uptake in creosote workers


Significance of dermal and respiratory uptake in creosote workers: exposure to polycyclic aromatic hydrocarbons and urinary excretion of 1-hydroxypyrene.

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