Urinary 1-Hydroxypyrene and Polycyclic Aromatic Hydrocarbon Exposure Among Asphalt Paving Workers

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Objectives: Using urinary 1-hydroxypyrene (1-OHP) as a measure of total absorbed dose, the primary objective of this study was to evaluate the total effect of inhalation and dermal PAH exposures while considering other factors such as age, body mass index and smoking that may also have a significant effect on urinary 1-OHP.

Methods: The study population included two groups of highway construction workers: 20 paving workers and 6 milling workers. During multiple consecutive workshifts, personal air and dermal samples were collected from each worker and analyzed for pyrene. During the same work week, urine samples were collected pre-shift, post-shift and at bedtime each day and analyzed for 1-OHP. Distributed lag models were used to evaluate the independent effect of inhalation and dermal exposures that occurred at each of several preceding exposure periods and were used to identify the relevant period of influence for each pathway.

Results: The paving workers had inhalation (mean 0.3 mg/m3) and dermal (5.7 ng/cm2) exposures to pyrene that were significantly higher than the milling workers. At pre-shift on Monday morning, following a weekend away from work, the pavers and millers had the same mean baseline urinary 1-OHP level of 0.4 mg/g creatinine. The mean urinary 1-OHP levels among pavers increased significantly from pre-shift to post-shift during each work day, while the mean urinary 1-OHP levels among millers varied little and remained near the baseline level throughout the study period. Among pavers there was a clear increase in the pre-shift data during the work week, such that the average pre-shift level on day 4 (1.4 mg/g creatinine) was 3.5 times higher than the average pre-shift results on day 1 (0.4 mg/g creatinine). The results of the distributed lag model indicated that the impact of dermal exposure was approximately eight times the impact of inhalation exposure. Furthermore, dermal exposure that occurred during the preceding 32 h had a statistically significant effect on urinary 1-OHP, while the effect of inhalation exposure was not significant.

Conclusions: We found that distributed lag models are a valuable tool for analyzing longitudinal biomarker data and our results indicate that dermal contact is the primary route of exposure to PAHs among asphalt paving workers. An exposure assessment of PAHs that does not consider dermal exposure may considerably underestimate cumulative exposure and control strategies aimed at reducing occupational exposure to asphalt-related PAHs should include an effort to reduce dermal exposure.

Keywords: asphalt; dermal exposure; distributed lag models; hydroxypyrene; paving; pyrene

INTRODUCTION

Asphalt is a semi-solid residue that results from the non-destructive distillation of crude petroleum oil and contains a complex mixture of polycyclic aromatic hydrocarbons (PAHs), some of which are either known or suspected to be carcinogenic (Partanen et al., 1995; Gamble et al., 1999). In the USA, the road paving industry accounts for 87% of domestic asphalt production and employs ~300,000 workers (Asphalt Institute, 1990). Though numerous
epidemiological studies have described an excess risk of cancer among asphalt-exposed workers (Partanen and Boffetta, 1994; Boffetta et al., 1997), there is currently insufficient evidence to establish a causal relationship between occupational asphalt exposure and cancer risk (Chiazze et al., 1991; NIOSH, 2000). The primary limitation of existing epidemiological studies is that the exposure assessments were either weak or absent, lacking quantitative measurements of exposure to asphalt or its constituents (Chiazze et al., 1991; NIOSH, 2000).

Exposure to PAHs can occur due to occupational sources (asphalt industry, coke plants, petrol refineries, aluminum industry) and non-occupational sources (smoking, diesel exhaust, grilled food) and can occur via inhalation, ingestion and dermal contact (Roggi et al., 1997). Historically, the assessment of occupational exposure to PAHs has relied primarily on air monitoring (Jongeneelen, 2001). However, there has been increasing evidence that dermal contact is the primary route of exposure to PAHs (Van Rooij et al., 1993a,b; Quinlan et al., 1995; Viau and Vyskocil, 1995; Borak et al., 2002).

The mounting evidence regarding the importance of dermal PAH exposure has largely been due to the increased use of biological monitoring, which typically evaluates the relationship between urinary 1-hydroxypyrene (1-OHP) and environmental pyrene exposures. Pyrene is a useful indicator of environmental PAH exposure since it is abundant in most PAH mixtures and is strongly correlated with total PAHs in air \( r = 0.87 \) and dermal \( r = 0.65 \) samples (McClean et al., 2004). Pyrene is absorbed through the gastrointestinal tract, lungs and/or skin and then metabolized to 1-OHP, which is ultimately excreted in urine. Urinary 1-OHP has become the most commonly used biological marker of PAH exposure, providing a convenient measure of total absorbed dose.

Urinary 1-OHP and other occupational biomarkers are often evaluated using modeling approaches that examine only the effect of the most recent environmental exposure. However, these approaches require the effect to be fully explained by the most recent exposure without considering the possible effect of preceding exposures. This can be problematic since occupational exposures are often serially correlated, such that the most recent exposure is actually capturing some information about previous exposures. Therefore, because the effects of previous exposures are not directly considered, the independent effect of the most recent exposure is overestimated while the total effect of exposure is underestimated (Pope and Schwartz, 1996).

As an alternative method of evaluating biomarker data, this study uses distributed lag models to evaluate the effect of inhalation and dermal exposures at each of several preceding exposure periods, thereby resulting in a more accurate estimate of the total effect of each exposure pathway. Though distributed lag models have mainly been used in econometrics and social sciences, this analytical technique has recently been applied to epidemiological studies of air pollution (Pope and Schwartz, 1996; Schwartz, 2000; Braga et al., 2001).

Using urinary 1-OHP as a measure of total absorbed dose, the objectives of this study were to: (i) evaluate the total effect and relative contribution of inhalation and dermal PAH exposures; (ii) assess the effect of inhalation and dermal exposure over different time periods to determine how differences in absorption and/or metabolism may affect total absorbed dose; (iii) evaluate the effect of other factors such as age, body mass index (BMI) and smoking status that may also influence urinary 1-OHP measurements. Understanding how inhalation and dermal exposure to PAHs affects total absorbed dose has significant implications with respect to designing control strategies in the paving industry, as well as to conducting future epidemiological studies of asphalt workers.

**MATERIALS AND METHODS**

**Study population**

The study population included 26 highway construction workers, 20 pavers and six millers. The milling workers used grinding equipment to remove layers of asphalt from old roads in preparation for the paving crews, who later applied hot-mix asphalt while resurfacing the roads. All participants were male, worked for the same company and lived in the Greater Boston area. Written and informed consent was obtained from each study participant prior to sampling and all sampling was conducted in accordance with a standardized human subjects protocol that was approved by the Institutional Review Board at the Harvard School of Public Health.

The details of the paving operation are described elsewhere (McClean et al., 2004). Briefly, each paving crew consisted of 6–8 workers performing four different tasks. The paver operator sat between the hopper and the screw while driving the paving machine. Two screed men stood on a platform attached to the back of the paving machine, each controlling one side of the screw, while 2–3 rakers followed closely using hand tools to fill holes and gaps. One or two rolling machines, each with its own operator, were used to smooth and compact the laid asphalt. The study population included workers from each of the four task categories (paver operators, screed men, rakers and roller operators) in three different crews.

The details of the milling operation are also described elsewhere (McClean et al., 2004). Briefly,
the milling crew consisted of six workers who used a large grinding machine, a smaller trimming machine and a bucket loader to grind away the surface of existing asphalt roads and deposit the ground asphalt into the back of a dump truck. The milling crew was included as a reference group since these highway construction workers do not work with hot-mix asphalt and have very low exposures to pyrene.

Study design

In May and June 1999, multiple exposure samples were obtained from each worker during full work shifts at job sites located within 1 h of Boston. Each day of sampling included the collection of personal air samples (particulate and vapor), dermal patch samples and urine samples. Questionnaire data regarding personal characteristics (e.g. age, height, weight) and non-occupational PAH exposure (e.g. smoking status, dietary information) were also obtained.

Personal air samples. Personal air samples were collected from each worker in accordance with NIOSH Method 5506 (NIOSH, 1998). The air samples were obtained from each worker on three consecutive days for pavers and two consecutive days for millers. The air sampling system consisted of a Teflon filter and cassette holder to collect particulate PAHs, connected in series with an XAD-2 sorbent tube to collect the organic vapor. Using a personal sampling pump operating at 2 l/min, a 37 mm diameter filter (laminated PTFE of 2 μm pore size) was placed in a cassette and attached to each worker’s lapel near the breathing zone. The sorbent tube containing XAD-2 was attached in line and downstream from each filter cassette. Flow rates were checked before, during and after sample collection using a calibrated rotameter. Opaque filter cassettes and foil-wrapped sorbent tubes were used to prevent sample degradation due to sunlight. Samples were transported in coolers and stored at −20°C.

The filter (particulate) and tube (vapor) samples were analyzed separately, each extracted with 4 ml of hexane and ultrasonicated for 60 min. Two milliliters were syringe-filtered, transferred to a clean tube and 2 ml of DMSO was added. The mixture was ‘tumbled’ overnight and the layers were transferred to separate tubes. The DMSO layer was then analyzed for pyrene using high pressure liquid chromatography (HPLC).

Dermal patch samples. Personal dermal patch samples were collected from the wrists of each worker. The dermal samples were obtained from each worker on three consecutive days for pavers and two consecutive days for millers. The skin sampling method was a modification of the method described by Jongeneelen et al. (1988) and Van Rooij et al. (1993c). A soft polypropylene adsorbent material (40 mm diameter) was attached to an exposure pad to create a dermal patch with an effective surface area of 8.71 cm². Using an adhesive backing, the patches were attached to the underside of each wrist and resulted in the collection of two samples per worker per day. Following sample collection, the exposure pads were placed in foil-wrapped Petri dishes, transported in coolers and stored at −20°C.

The dermal patch samples were cut with a 33.3 mm punch, transferred to labeled culture tubes and 4 ml of DMSO was added. The tubes were then capped and sonicated for 1 h. Following sonication, 3 ml of the extract were transferred to a clean culture tube and 3 ml of hexane was added. The mixture was ‘tumbled’ overnight, the layers were transferred to separate tubes and the DMSO layer was analyzed for pyrene using HPLC.

Urine samples. Three urine samples (pre-shift, post-shift and bedtime) were obtained on consecutive days and an additional pre-shift sample was obtained on the morning of the final day. This resulted in the collection of 10 urine samples from each paving worker and seven urine samples from each milling worker, with the first sample collected at pre-shift on Monday morning, with ~8 h between each sample. All urine samples were collected in sterilized polypropylene specimen containers, transported in coolers and then frozen at −20°C until analysis.

Urine samples were analyzed for 1-OHP by HPLC using a modification of the methods described by Jongeneelen et al. (1987) and Tolos et al. (1989). A 10 ml aliquot of urine was adjusted to pH 5.0 with 1.0 M acetic acid. After 10 ml of CH₃COONa buffer and 25 μl of β-glucuronidase (Sigma G-7770) were added, the mixture was incubated overnight at 37°C. The next day, Sep-Pak C18 cartridges (Waters, lot W8189b1) were primed with 5 ml of methanol and 10 ml of H₂O and the hydrolyzed urine samples were passed through the cartridges. The retained solutes were eluted with 8 ml of methanol and the solvent was evaporated at 40°C using a constant flow of nitrogen (150 ml/min). The residue was dissolved in 2 ml of methanol, transferred to amber HPLC auto sampler vials and stored at −20°C until analysis.

The method was evaluated by pooling urine collected from non-exposed individuals (non-smoking graduate students), splitting it into three 1 l amber glass jars, ‘spiking’ one of the jars with 1 ng/ml 1-OHP and another with 10 ng/ml. The third jar was left unspiked. To determine method recovery and precision, these control urines were run together with each batch of unknown samples. Based on the 21 control urines analyzed at each concentration, the average recoveries were 95 and 89%, while the
relative standard deviations were 12 and 14% for the 1 and 10 ng/ml control urines, respectively.

Because HPLC may respond differently to 1-OHP in urine than to 1-OHP in methanol, a calibration curve was constructed with the pooled urine using the method of standard additions to minimize matrix interference. An intermediate standard was serially diluted in the pooled urine to prepare nominal 1-OHP concentrations of 0, 1, 5, 10, 15 and 20 ng/ml. The resulting data produced a linear standard curve with an intercept close to 0.0. The instrumental limit of detection was ~0.50 ng/ml, calculated as 3 × SD of the smallest standard. All urine samples were analyzed and corrected for creatinine prior to statistical analysis.

Data analysis

All statistical analyses were conducted using SAS statistical software (SAS Institute, Cary, NC) and statistical significance is reported at the 0.05 level. The pyrene data (air and dermal samples) and 1-OHP data (urine) were analyzed using descriptive statistics, graphical displays and distributed lag models for repeated measures data. Following an algebraic transformation of the inhalation and dermal data, the MIXED procedure was used to evaluate the urinary 1-OHP data.

Air and dermal samples. Units for total air exposures are reported in μg/m³. One total air exposure estimate was calculated for each worker on each sampling day by adding the particulate and vapor measurements. Units for dermal exposure are reported in ng/cm². One dermal exposure estimate was calculated for each worker on each sampling day by averaging the left and right wrist measurements. When only one wrist measurement was available, the result from that sample was used in place of the average.

Method limits of detection (LOD) were estimated as three times the SD of the field blanks. In cases where the mean field blanks were significantly different from zero (α = 0.05), the corresponding data were corrected by subtracting the mean field blank from each sample. Negative values that resulted from the subtraction of field blanks were included in all analyses, as were all values less than the detection limits (Gilbert, 1987).

Six individual dermal samples collected from two workers were excluded from analysis (prior to averaging wrists) because there was sufficient evidence to suspect that the samples had been contaminated with diesel fuel. Both workers were rakers on the same paving crew who were observed to be purposefully contaminating the dermal patches with the fuel. These six patches were visibly discolored due to saturation and the resulting values were orders of magnitude higher than all other samples.

To evaluate the correlation between the total air and dermal data, traditional methods of estimating correlation coefficients (i.e. Pearson and Spearman) could not be used due to the repeated measures design of the study. Use of these traditional methods would erroneously ignore the number of subjects as the correct sample size while instead using the total number of observations as the incorrect sample size, thereby increasing the degrees of freedom (Hamlett et al., 2003). As an alternative, all correlation coefficients were estimated using linear mixed effects models as described by Hamlett et al. (2003).

Urine samples. Units for urinary 1-OHP data are reported in μg/g creatinine. Since highly dilute or highly concentrated urine samples are generally not suitable for analysis, urine samples in which the creatinine concentration was either <0.3 or >3.0 g/l were excluded from the data analysis (ACGIH, 2002). These criteria resulted in the exclusion of 10 urine samples.

Shapiro–Wilks tests and graphical displays indicated that the urinary 1-OHP data were not normally distributed. However, a log transformation of the data did result in an approximately normal distribution. Accordingly, all modeling was conducted using the log transformed urinary 1-OHP data.

Distributed lag models. Distributed lag models allow us to evaluate the possibility that each urinary 1-OHP measurement is not only influenced by the most recent inhalation and dermal exposures, but also by exposures that occurred during previous exposure periods. For notational and conceptual purposes, time t will refer to time intervals of 8 h each; inhalation and dermal samples were collected during each time interval, whereas urine samples were collected at the end of each time interval. Accordingly, the unconstrained lag model evaluating q + 1 exposure periods for the ith subject at time interval t is described as:

\[
\ln(Y_{it}) = \alpha + \beta_0 X_{it} + \beta_1 X_{it-1} + \cdots + \beta_q X_{it-q} + \text{covariates}_i + \varepsilon_{it} \quad (1)
\]

where the outcome \(Y_{it}\) may depend on the most recent exposure \(X_{it}\) as well as previous exposures \(X_{it-1}, X_{it-2}, \ldots, X_{it-q}\), while \(\varepsilon_{it}\) represents the residual error term. The total effect of exposure \(X\) is the sum of its impact during the most recent period and its impact on previous days, i.e. \(\beta_0 + \beta_1 + \cdots + \beta_q\). However, because \(X_{it}\) is correlated with \(X_{it-1}, X_{it-2}, \ldots, X_{it-q}\), the high degree of collinearity in this unconstrained model would result in unstable estimates of the values of \(\beta_q\). To reduce the degree of collinearity and as an alternative to the unconstrained model, a polynomial
distributed lag function can be used to constrain $\beta_j$ to a polynomial function of lag $j$:

$$\beta_j = \sum_{d=0}^{\infty} C_d j^d$$

(2)

Accordingly, for the analysis of the urinary 1-OHP data, $\beta_j$ was restricted to be a cubic function ($d=3$) of $j$, since this provides maximum flexibility within the bounds of a biologically plausible relationship. For the cubic function, (2) can be rewritten as:

$$\beta_j = C_0 + C_1 j + C_2 j^2 + C_3 j^3$$

(3)

To evaluate the effect of the most recent exposure and the effect of six lag periods ($j = 0, 1, \ldots, q = 6$), substituting $\beta_j$ from (3) into our original model (1) gives us:

$$\ln(Y_{it}) = \alpha + C_0 X_{it} + (C_0 + C_1 + C_2 + C_3)X_{it-1} + \cdots + (C_0 + 6C_1 + 6^2 C_2 + 6^3 C_3)X_{it-6} + \text{covariates}_i + \varepsilon_{it}$$

(4)

If we then factor out each $C_k$ (for $k = 0, 1, 2, 3$), then we have:

$$\ln(Y_{it}) = \alpha + C_0 (X_{it} + X_{it-1} + \cdots + X_{it-6}) + \cdots + C_3 (X_{it-1} + 2X_{it-2} + \cdots + 6^2 X_{it-6}) + \text{covariates}_i + \varepsilon_{it}$$

(5)

Finally, we can define $d+1$ new variables $Z_{it}$ to be the weighted sum of the exposure variable $X$ and its lags, such that:

$$Z_{it0} = X_{it} + X_{it-1} + \cdots + X_{it-6}$$

$$Z_{it1} = X_{it-1} + 2X_{it-2} + \cdots + 6X_{it-6}$$

$$Z_{it2} = X_{it-2} + 2^2X_{it-3} + \cdots + 6^2X_{it-6}$$

$$Z_{it3} = X_{it-3} + 2^3X_{it-4} + \cdots + 6^3X_{it-6}$$

(6)

and we can estimate the model:

$$\ln(Y_{it}) = \alpha + C_0 Z_{it0} + C_1 Z_{it1} + C_2 Z_{it2} + C_3 Z_{it3} + \text{covariates}_i + \varepsilon_{it}$$

(7)

The coefficients of the $Z$ values (i.e., $C_0$, $C_1$, $C_2$, $C_3$) are the parameters of the polynomial distributed lag model, which can be used to obtain the $\beta_j$ value according to (3). The appeal of the polynomial distributed lag model is that it is highly flexible and allows for a wide variety of distributed lag effects (increasing, decreasing or a combination thereof), thus allowing the data to dictate the pattern while reducing the high degree of collinearity that would result from using an unrestricted lag model (Pope and Schwartz, 1996). A more complete description of polynomial distributed lag models is available elsewhere (Harvey, 1990; Pope and Schwartz, 1996).

The distributed lag models required some assumptions regarding inhalation and dermal exposures that occurred away from work. Though inhalation and dermal measurements were obtained during the 8 h work shifts (corresponding to the time periods preceding the post-shift urine samples), exposure measurements were not available during the remaining 16 h of the day (corresponding to bedtime and pre-shift samples). Since the workers did not have occupational exposure during this time, inhalation and dermal exposures to pyrene were assumed to be 0. Similarly, since the first urine sample was always collected on Monday morning, the same rationale was used to assume 0 exposure during the 56 h prior to collection of the Monday morning pre-shift sample (representing the most recent exposure period and six lagged exposure periods during the weekend).

**Linear mixed effects models.** Since multiple urine samples were collected from each worker, linear mixed effects models were used to evaluate the distributed lag effect of inhalation and dermal exposure. This relationship was evaluated while controlling for the effect of age, BMI and smoking status (current smoker versus non-smoker). The repeated measures design and the use of linear mixed effects models allowed each worker to serve as their own control while evaluating changes in urinary 1-OHP over time. If we allow $\lambda_j$ to represent the effect of inhalation exposure ($I_{ij}$) and $\delta_j$ to represent the effect of dermal exposure ($D_{ij}$), then the final linear mixed effects model can be described as follows:

$$\ln(Y_{it}) = \alpha + \lambda_0 I_{it} + \lambda_1 I_{it-1} + \lambda_2 I_{it-2} + \lambda_3 I_{it-3} + \delta_0 D_{it} + \delta_1 D_{it-1} + \delta_2 D_{it-2} + \delta_3 D_{it-3} + \gamma_1 \text{AGE}_i + \gamma_2 \text{BMI}_i + \gamma_3 \text{SMOKER}_i + \varepsilon_{it}$$

where $Y_{it}$ represents the urinary 1-OHP measurement of the $ith$ worker at time $t$. The $\gamma$ values represent the fixed effects for AGE (yr), BMI (kg/m$^2$) and SMOKER (yes/no). Inhalation and exposures were initially evaluated using six lag periods. However, based on the observed results it was clear that the evaluation of six lag periods was not reasonable in all cases. For instance, dermal inhalation exposure was shown to have a positive effect on urinary 1-OHP out to a maximum of three lag periods. To avoid the inclusion of irrelevant lag periods, the number of lags included in the final model for each exposure pathway was adjusted according to...
the biological plausibility of the observed results. Models were fitted using a heterogeneous autoregressive covariance matrix which yielded the lowest Akaike’s Information Criteria diagnostic values compared with the other covariance matrices examined (e.g. independence, compound symmetry and homogeneous autoregressive).

RESULTS

Table 1 presents the summary statistics for the pyrene exposure data. The summary statistics are stratified by exposure pathway and for paving workers are also stratified by task. In total air samples, pyrene was detected above the LOD of 0.01 \( \mu g/m^3 \) in 97% of the paving samples (mean 0.3 \( \mu g/m^3 \)), but only 18% of the milling samples. In dermal samples, pyrene was detected above the LOD of 2.3 ng/cm\(^2\) in 61% of the paving samples (mean 5.7 ng/cm\(^2\)), but only 27% of the milling samples. Exposure measurements for pavers were significantly higher than for millers for inhalation (\( P = 0.001 \)), while differences were marginally significant for dermal exposure (\( P = 0.1 \)). Additionally, there was a strong correlation between the inhalation and dermal exposure measurements obtained for paving workers (\( r = 0.66 \)).

Table 2 presents the summary statistics for the pre-shift, post-shift and bedtime urinary 1-OHP data for each day of the study period. Figure 1 shows the mean urinary 1-OHP results for pavers and millers. At pre-shift on Monday morning (following a weekend of no exposure) pavers and millers were found to have the same mean 1-OHP level of 0.4 \( \mu g/g \) creatinine. Among paving workers there was a clear increase from pre-shift to post-shift during each day of the study period. There was also a clear increase in the pre-shift data during the work week, such that the average pre-shift results on day 4 were 3.5 times higher than the average pre-shift results on day 1. However, among the milling workers the urinary 1-OHP levels remained around the baseline value with very little change between pre-shift and post-shift and very little change during the work week.

Figure 2 shows the urinary 1-OHP results averaged during the preceding 16 h. For dermal exposure, the results of Model 3 were very similar to the results of Model 2, with the only real differences being a slight reduction in the total effect of dermal exposure (from 0.41 to 0.37) and the fact that the largest effect shifted from the most recent dermal exposure (0–8 h) in Model 2 to the first lagged dermal exposure (8–16 h) in Model 3. Conversely, for inhalation exposure, the results of Model 3 were quite different from the results of Model 1. When inhalation exposure was included in the model without dermal exposure (Model 1) the results indicated that the total effect of inhalation (3.5) was significant, with a positive effect being observed during the preceding 32 h. However, when dermal exposure was added to the model (Model 3) the total effect of inhalation was reduced to 0.77 and was not significant, with a positive effect being observed during the preceding 16 h.
Table 1. Summary statistics for Pyrene data

<table>
<thead>
<tr>
<th>Task</th>
<th>Inhalation (LOD = 0.01 µg/m³)</th>
<th>Dermal (LOD = 2.3 ng/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Detect %</td>
</tr>
<tr>
<td>Paving</td>
<td>59</td>
<td>97</td>
</tr>
<tr>
<td>Paver Operators</td>
<td>9</td>
<td>100</td>
</tr>
<tr>
<td>Roller Operators</td>
<td>11</td>
<td>82</td>
</tr>
<tr>
<td>Rakers</td>
<td>24</td>
<td>100</td>
</tr>
<tr>
<td>Screedmen</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Milling</td>
<td>11</td>
<td>18</td>
</tr>
</tbody>
</table>

*a*For summary statistics, multiple measurements from each worker included as individual samples.

*b*Total inhalation exposure during entire workshift (sum of particulate and vapor).

*c*Dermal exposure during entire workshift (average of left and right wrists).

*d*Not shown due to low level of detection.
Table 2. Average urinary 1-OHP\(^a\) (µg/g creatinine) by job and sampling period

<table>
<thead>
<tr>
<th>Job</th>
<th>Statistic</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-shift</td>
<td>Post-Shift</td>
<td>Bedtime</td>
<td>Pre-shift</td>
</tr>
<tr>
<td>Pavers(^b) (20 workers)</td>
<td>Mean ± SD</td>
<td>0.4 ± 0.4</td>
<td>1.6 ± 1.6</td>
<td>1.3 ± 1.6</td>
<td>0.8 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>0.12</td>
<td>1.0</td>
<td>0.74</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>16</td>
<td>17</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Millers(^b) (6 workers)</td>
<td>Mean ± SD</td>
<td>0.4 ± 0.3</td>
<td>0.4 ± 0.4</td>
<td>0.4 ± 0.4</td>
<td>0.4 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>0.32</td>
<td>0.31</td>
<td>0.20</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

\(^a\)Urine samples with a creatinine concentration <0.3 g/l or >3.0 g/l were excluded.

\(^b\)Fewer measurements were obtained from millers due to practical limitations.
Figure 3 shows the contributions of inhalation exposure and dermal exposure at the mean inhalation and dermal exposure levels according to the results of Model 3. The error bars show the 95% confidence intervals for each of the estimates. Each lag period represents an 8 h period of exposure, where lag 0 represents the most recent exposure period (0–8 h), lag 1 represents the preceding 8–16 h, etc.

As mentioned, each of the models described above also evaluated the effect of age, BMI and smoking status. The results of Model 3 indicate that age had a positive effect on urinary 1-OHP ($P = 0.08$), BMI had a negative effect on urinary 1-OHP ($P = 0.06$) and smokers tended to have higher urinary 1-OHP levels as compared with non-smokers ($P = 0.09$). The effects of age, BMI and smoking were all marginally significant and were retained in the final models. It should be noted that consistent results were observed without adjusting the urinary 1-OHP concentrations for creatinine.

The effect of diet was initially included in the models and evaluated the effect of grilled food versus...
Table 3. Results of distributed lag models evaluating urinary 1-OHP among pavers (ln µg/g creatinine)

<table>
<thead>
<tr>
<th>Term</th>
<th>Lag (j)</th>
<th>$X_j$</th>
<th>Model 1</th>
<th></th>
<th>Model 2</th>
<th></th>
<th>Model 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Effect (SE)</td>
<td>Contribution</td>
<td>Effect (SE)</td>
<td>Contribution</td>
<td>Effect (SE)</td>
<td>Contribution</td>
</tr>
<tr>
<td>Intercept</td>
<td>$\alpha$</td>
<td></td>
<td>1.5 (0.9)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>0–8 hours</td>
<td>$\lambda_0$</td>
<td>0</td>
<td>0.09</td>
<td>1.7 (0.4)</td>
<td>0.16</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>8–16 hours</td>
<td>$\lambda_1$</td>
<td>1</td>
<td>0.09</td>
<td>1.1 (0.4)</td>
<td>0.10</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>16–24 hours</td>
<td>$\lambda_2$</td>
<td>2</td>
<td>0.09</td>
<td>0.5 (0.4)</td>
<td>0.05</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>24–32 hours</td>
<td>$\lambda_3$</td>
<td>3</td>
<td>0.05</td>
<td>0.3 (0.6)</td>
<td>0.01</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>3.5 (1.2)</td>
<td>0.32</td>
<td>–</td>
<td>–</td>
<td>0.77 (1.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Dermal</td>
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</tr>
<tr>
<td>0–8 hours</td>
<td>$\delta_0$</td>
<td>0</td>
<td>1.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.12 (0.02)</td>
<td>0.20</td>
</tr>
<tr>
<td>8–16 hours</td>
<td>$\delta_1$</td>
<td>1</td>
<td>1.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.12 (0.02)</td>
<td>0.20</td>
</tr>
<tr>
<td>16–24 hours</td>
<td>$\delta_2$</td>
<td>2</td>
<td>1.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.09 (0.02)</td>
<td>0.15</td>
</tr>
<tr>
<td>24–32 hours</td>
<td>$\delta_3$</td>
<td>3</td>
<td>1.1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.05 (0.02)</td>
<td>0.06</td>
</tr>
<tr>
<td>32–40 hours</td>
<td>$\delta_4$</td>
<td>4</td>
<td>1.1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.02 (0.02)</td>
<td>0.02</td>
</tr>
<tr>
<td>40–48 hours</td>
<td>$\delta_5$</td>
<td>5</td>
<td>1.1</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.01 (0.02)</td>
<td>0.01</td>
</tr>
<tr>
<td>48–56 hours</td>
<td>$\delta_6$</td>
<td>6</td>
<td>0.4</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.001 (0.04)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>0.41 (0.08)</td>
<td>0.64</td>
<td>0.37 (0.10)</td>
<td>0.56</td>
<td></td>
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<tr>
<td>Covariates</td>
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</tr>
<tr>
<td>AGE</td>
<td>$\gamma_1$</td>
<td></td>
<td>0.02 (0.01)</td>
<td>0.02 (0.01)</td>
<td>0.02 (0.01)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>$\gamma_2$</td>
<td></td>
<td>–0.1 (0.03)</td>
<td>–0.05 (0.03)</td>
<td>–0.06 (0.03)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMOKER</td>
<td>$\gamma_3$</td>
<td></td>
<td>0.2 (0.3)</td>
<td>0.6 (0.3)</td>
<td>0.5 (0.3)</td>
<td></td>
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</tr>
</tbody>
</table>

*Model 1 evaluates the effect of inhalation exposure while controlling for age, BMI, and smoking status.
*Model 2 evaluates the effect of dermal exposure while controlling for age, BMI, and smoking status.
*Model 3 evaluates the effect of both inhalation and dermal exposure while controlling for age, BMI, and smoking status.
*Mean exposure level at each lag period for each exposure pathway.
*To evaluate model results at mean exposure levels, the contribution was calculated by multiplying each effect estimate by its corresponding mean exposure.
*Number of lags included in final models adjusted according to biological plausability of observed results.
DISCUSSION

Although most studies evaluating PAH exposure have focused primarily on inhalation exposure, an increasing number have presented evidence suggesting that dermal exposure is actually the primary route of exposure to PAHs (Van Rooij et al., 1993a,b; Boogaard and van Sittert, 1995; Quinlan et al., 1995; Moen et al., 1996; Borak et al., 2002). In coke oven workers, after evaluating pyrene exposure data (air and dermal) and urinary 1-OHP data, Van Rooij et al. (1993a) estimated that ∼75% of the total absorbed dose was attributable to dermal exposure. In creosote facility workers, Borak et al. (2002) found that >90% of urinary 1-OHP could be attributed to dermal exposure. Accordingly, the primary objective of this analysis was to evaluate the extent to which urinary 1-OHP (absorbed dose) is affected by inhalation and dermal exposure among asphalt paving workers.

The dermal data are presented in units of ng/cm², which represents the amount of PAH per square centimeter of exposed skin (at the wrist) during each work shift. The wrist measurements are not intended to represent total body dermal exposure, since exposures of most other parts of the body are likely to be lower than of the wrist. However, the wrist samples do provide a useful tool for characterizing and comparing the intensity of daily dermal exposures.

Urinary 1-OHP by job

The paving workers had inhalation and dermal exposures that were significantly higher than the milling workers, while Fig. 1 shows that the urinary 1-OHP levels appear to be consistent with these differences in pyrene exposure.

At pre-shift on day 1, pavers and millers were found to have the same mean 1-OHP level (0.4 μg/g creatinine). This baseline level is probably due to non-occupational exposures such as smoking, diet and/or other environmental exposures. It is unlikely to be attributable to occupational exposure since these samples were always collected following a weekend away from work. Also, since we know that the pyrene exposures associated with each job are significantly different, we would not expect these 1-OHP levels to be identical for pavers and millers if they were actually job related.

While the millers showed little deviation from the baseline 1-OHP level during the work week, the pavers showed a clear increase from pre-shift to post-shift during each day of the study period. Among pavers, there was also a clear increase in the daily pre-shift data during the work week, such that the average pre-shift results on day 4 were 3.5 times higher than the average pre-shift results on day 1.

Urinary 1-OHP by task

Among paving workers, the pyrene data presented in Table 1 indicate that the task-based means ranged from 0.06 to 0.6 μg/m³ for inhalation exposure (roller operators < rakers < screed men < paving operators)
while the task-based means ranged from 2.1 to 7.7 ng/cm² for dermal exposure (roller operators < paving operators < rakers < screed men). In a separate analysis of these exposure data (McClean et al., 2004), both the inhalation and dermal exposures were found to vary significantly by paving task.

Figure 2 shows the task-based urinary 1-OHP levels, which were also found to vary significantly by paving task (P = 0.01). The results of the linear mixed effects model indicated that the rank order of the task-based urinary 1-OHP levels was identical to the rank order of the task-based dermal exposures (roller operators < paving operators < rakers < screed men). A closer look at the paving operators is particularly interesting given that the paving operators had the highest inhalation exposures but the second lowest dermal exposures. Consistent with dermal exposure, the paving workers also had the second lowest urinary 1-OHP levels. This is evident in Fig. 2 and was confirmed by the results of the linear mixed effects model.

A work-shift increase in urinary 1-OHP levels is observed to varying extents for each paving task (Fig. 2). For screed men and rakers, the tasks with the highest dermal exposure, there is a clear increase in 1-OHP levels from pre-shift to post-shift during each day of the study period; however, the daily spike in 1-OHP level is less pronounced for the paver operators and not particularly evident for the roller operators. It is possible that the effect of non-occupational exposures is more graphically evident for the paver operators and roller operators.

Distributed lag models

The use of polynomial distributed lag models allowed the analysis of 1-OHP levels while evaluating the effect of inhalation and dermal exposure during the preceding 56 h, divided into seven 8 h time periods. Because the inhalation and dermal measurements were only obtained during the 8 h work shifts, this modeling approach required an assumption that inhalation and dermal exposure were 0 during all 8 h periods that were spent away from work. This included the 8 h period between post-shift and bedtime, the 8 h period between bedtime and pre-shift (the next day) and all six 8 h periods during the preceding weekend.

Figure 3 shows the mean contribution of each exposure pathway during each lag period. The results indicate that the preceding 16 h of inhalation exposure had a positive effect on urinary 1-OHP, although the effect estimates were not significant for either of the two 8 h lag periods. The fact that the largest effect estimate was observed for the most recent inhalation exposure suggests that the absorption, metabolism and excretion of inhaled pyrene was quite rapid. The results also indicate that the preceding 56 h of dermal exposure had a positive effect on urinary 1-OHP, although the effect estimates were only significant for the most recent exposure and for the first three lag periods (0–32 h). The fact that the largest effect estimate was observed for the first lag period (8–16 h), as well as the fact that the effect estimates were very similar during each of the first three exposure periods (0–24 h), suggests that the absorption of pyrene by dermal contact was slower than by inhalation. These results are consistent with Viau and Vyskocil (1995), who estimated that the excretion of urinary 1-OHP peaks between 10 and 15 h after dermal exposure to pyrene.

The results of Model 3 indicate that the impact of dermal exposure was eight times that of inhalation exposure, while controlling for the effect of age, BMI and smoking. In fact, the total effect of dermal exposure was significant while the total effect of inhalation exposure was not significant. Also, while the total effect of dermal exposure was very similar between models (Model 2 versus Model 3), the total effect of inhalation exposure was considerably different between models (Model 1 versus Model 3). Model 1 was constructed such that inhalation exposure was evaluated without controlling for the effect of dermal exposure, just as Model 2 evaluated dermal exposure without controlling for the effect of inhalation exposure. By including both inhalation and dermal exposure in the model together, Model 3 allowed us to evaluate the effect of each exposure pathway while controlling for the effect of the other.

A comparison of the models indicates that the total effect of inhalation exposure was considerably decreased (82% reduction) once dermal exposure was added to the model, while the total effect of dermal exposure was reduced by only 7% once inhalation exposure was added to the model. Since we know that inhalation exposure and dermal exposure are correlated, it appears that the effect of inhalation from Model 1 was largely due to confounding, since dermal exposure was not evaluated in the model. If dermal exposure had not been measured and included in this analysis, the total effect of inhalation would have been underestimated due to the correlation with dermal exposure. However, the results of Model 3 indicate that the dermal pathway is actually the primary route of exposure to PAHs among this group of workers.

In addition to evaluating the effect of inhalation and dermal exposure on urinary 1-OHP, each of the three models also found a marginally significant effect of age, BMI and smoking. The results of Model 3 indicate that BMI had a negative effect on urinary 1-OHP, suggesting that the excretion of urinary 1-OHP decreases as BMI increases. Since pyrene is very lipid-soluble, one possible explanation for this
association is that increased BMI may result in increased storage of pyrene in fatty tissue such that less of the pyrene is metabolized to 1-OHP and excreted. This finding is consistent with Roggi et al. (1997), who also found that BMI significantly influences the levels of urinary 1-OHP.

CONCLUSIONS

This study represents one of the first applications of distributed lag models to biological monitoring data. The results of this urinary 1-OHP analysis suggest that among this group of paving workers the impact of dermal exposure was eight times the impact of inhalation exposure. Dermal exposure that occurred during the preceding 32 h had a statistically significant effect on urinary 1-OHP, while the effect of inhalation exposure was not significant. These findings are consistent with a growing body of literature suggesting that dermal contact is the primary route of occupational exposure to PAHs. Accordingly, an assessment of occupational exposure to PAHs that does not consider dermal exposure may considerably underestimate cumulative exposure. Similarly, control strategies aimed at reducing occupational exposure to asphalt-related PAHs should include an effort to reduce dermal exposure.

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REFERENCES


