

Article

Assessment of Benzo(a)pyrene-equivalent Carcinogenicity and Mutagenicity of Residential Indoor *versus* Outdoor Polycyclic Aromatic Hydrocarbons Exposing Young Children in New York City

Kyung Hwa Jung ¹, Beizhan Yan ², Steven N. Chillrud ², Frederica P. Perera ³, Robin Whyatt ³, David Camann ⁴, Patrick L. Kinney ³ and Rachel L. Miller ^{1,3,*}

¹ Division of Pulmonary, Allergy and Critical Care of Medicine, College of Physicians and Surgeons, Columbia University, PH8E, 630 W. 168 St. New York, NY 10032, USA;

E-Mail: kj2237@columbia.edu

² Lamont-Doherty Earth Observatory, Columbia University, 61 Rt, 9W Palisades, NY 10964, USA;

E-Mails: yanbz@ldeo.columbia.edu (B.-Z.Y.); chilli@ldeo.columbia.edu (S.N.C.)

³ Mailman School of Public Health, Department of Environmental Health Sciences, Columbia University, 60 Haven Ave., B-1 New York, NY 10032, USA;

E-Mails: fpp1@columbia.edu (F.P.P.); rmw5@columbia.edu (R.W.); plk3@columbia.edu (P.L.K.)

⁴ Southwest Research Institute, 6220 Culebra Road, San Antonio, TX 78228, USA;

E-Mail: david.camann@swri.edu

* Author to whom correspondence should be addressed; Email: rlm14@columbia.edu;

Tel: 212-305-7759; Fax: 212-305-2277.

Received: 9 March 2010; in revised form: 14 April 2010 / Accepted: 23 April 2010 /

Published: 27 April 2010

Abstract: The application of benzo(a)pyrene (BaP)-toxic equivalent factor to polycyclic aromatic hydrocarbons (PAH) concentrations can provide a more accurate risk assessment from environmental exposure to PAH. We hypothesized that BaP-equivalent toxicity determined following residential air monitoring among young urban children may vary by season. Residential indoor and outdoor air levels of PAH measured over two-weeks in a cohort of 5–6 year old children (n = 260) in New York City were normalized to the cancer and mutagen potency equivalent factor of BaP (BaP = 1). Data are presented as carcinogenic

equivalents (BaP-TEQ) and mutagenic equivalents (BaP-MEQ) for the sum of 8 PAH ($\Sigma_8\text{PAH}$; MW ≥ 228) and individual PAH and compared across heating versus nonheating seasons. Results show that heating compared to nonheating season was associated significantly with higher (BaP-TEQ) $_{\Sigma_8\text{PAH}}$ and (BaP-MEQ) $_{\Sigma_8\text{PAH}}$ both indoors and outdoors ($p < 0.001$). Outdoor (BaP-TEQ) $_{\Sigma_8\text{PAH}}$ and (BaP-MEQ) $_{\Sigma_8\text{PAH}}$ were significantly higher than the corresponding indoor measures during the heating season ($p < 0.01$). These findings suggest that at levels encountered in New York City air, especially during the heating season, residential exposure to PAH may pose an increased risk of cancer and mutation.

Keywords: risk assessment; PAH; BaP-equivalents; TEF; MEF; heating season; indoor; outdoor; and children

1. Introduction

Many polycyclic aromatic hydrocarbons (PAH) are suspected or known carcinogens and mutagens [1-3]. Benzo(a)pyrene (BaP), believed to be the most toxic PAH, has been well-characterized toxicologically. However, less information is available for most of the other PAH. In most risk assessments, many individual PAH have been considered to be of equivalent toxicity as BaP [4]. This approach could result in the overestimation of cancer and mutagen potency of individual PAH because most PAH are considerably less toxic than BaP when analyzed in the same assay systems (e.g., mouse skin, human cell mutagenicity assays) [1-3,5].

Several approaches have been developed to obtain a more accurate assessment of potential risk of exposure to a complex mixture of PAH using toxic equivalency factors based on BaP [1-3,6-8]. One is the carcinogenic equivalency factors (TEF) that can vary at either low or high dose settings. For example, TEF of dibenz(ah)anthracene (DahA) is around 5 at low dose and close to 1 at higher dose based on local tumors induced by subcutaneous injection into mice [9]. Mutagenicity of individual PAH relative to BaP also has been assessed using the mutagenic equivalency factor (MEF) proposed by Durant *et al.* [1,2]. Mutagenic activity, while not as uniformly associated with cancer [10-12], may have implications for other non-cancerous adverse health effects, such as pulmonary diseases [13,14].

TEF and MEF values in combination with measured air concentrations have been used for the calculation of carcinogenic equivalents (TEQ, expressed in ng/m^3) and mutagenic equivalents (MEQ, expressed in ng/m^3) in environmental samples [15-17]. To date, these studies have yielded important reassessments of the contributions of exposure to PAH, including those derived from traffic emissions, on lung cancer risk [17]. However, most pediatric cohort research that addresses the adverse health effects of exposure to air pollution, and PAH specifically, have compared levels of airborne PAH, or their metabolites, with clinical outcomes [18]. Use of the TEQ or MEQ may lead to a more accurate assessment of potential health risk in a pediatric cohort.

We hypothesized that BaP-equivalent toxicity, when assessed using residential monitoring in a pediatric urban cohort, varies by season due to higher emissions from heating sources and more frequent stagnant meteorological conditions in the winter. Our approach was to calculate BaP-TEQ and

BaP-MEQ to estimate residential indoor and outdoor PAH carcinogenic and mutagenic hazards in young inner city children, known to be at greater risk for adverse health consequences from exposure to air pollution [18–20]. BaP-TEQ is based specifically on the report by Nisbet and Lagoy [3] and was determined at relatively low doses compared to other reports and may be an more appropriate method for reassessing the potential risk of airborne exposure to PAH in urban settings [3,6,7].

2. Experimental Section

Study design. Children were primarily of African-American and Dominican ethnicity and lived in Northern Manhattan and the South Bronx, geographical areas where exposure to traffic-related air pollution has been implicated in asthma and other diseases [19]. 260 children from the parent Columbia Center for Children’s Environmental Health (CCCEH) cohort study was included in this analysis [18,20] if they were age 5–6 years beginning October 2005 and resided in Northern Manhattan and the South Bronx during pregnancy and continued to live in Northern Manhattan and the Bronx at enrollment as described [21]. The study was approved by the Columbia University Institutional Review Board and informed consent obtained.

Residential monitoring. Boxes containing up to three vacuum pumps and valves to control flow were used to collect two-week integrated indoor and outdoor PAH samples at each of 260 homes between October 2005 and May 2009. Indoor air monitors were placed in a room where the child spent most of his or her time (e.g., child’s bedroom or main living area of the apartment), at a height of about 1.2 m and at least 0.3 m from the walls. At one third of homes, selected randomly but evenly across all 4 meteorological seasons, simultaneous outdoor sampling was conducted by placing samplers out of windows securely hung 0.9 m from the outside wall with a window unit that was designed so as not to appreciably affect air exchange rates of the apartment (*i.e.*, subject can have the window open or closed).

Particulate phase of PAH on a quartz microfiber filter was collected in a cassette attached downstream from a cyclone with a 2.5 μm aerodynamic-diameter cut point (model SCC 1.062, BGI, Inc.). Gas phases of PAH were collected on polyurethane foam (PUF) cartridge back-up, as previously described [21,22]. The residential air sampling pumps operated continuously at 1.5 L/min for two weeks, leading to an average sampling volume of 30.1 m^3 . The air flow rates were checked at the beginning and end of sampling to ensure that a constant flow rate was maintained throughout the sampling period. Eight 4-ring to 6-ring PAH were selected as target compounds due to their abundance in traffic emissions and their possible carcinogenicity and mutagenicity [23,24]. The eight PAH monitored were: benz[a]anthracene (BaA), chrysene/iso-chrysene (Chry), benzo[b]fluoranthene (BbFA), benzo[k]fluoranthene (BkFA), benzo[a]pyrene (BaP), indeno[1,2,3-c,d]pyrene (IP), dibenz[a,h]anthracene (DahA), benzo[g,h,i]perylene (BghiP). A single soxhlet extraction of both the filters and PUFs together was analyzed at Southwest Research Institute (San Antonio, TX) as described [23]. Two deuterated compounds (anthracene- d_{10} and p-terphenyl- d_{14}) were used as surrogate standards for recovery and chrysene- d_{12} and perylene- d_{12} were used as internal standard for quantification.

Calculation of BaP-equivalent concentrations. BaP-TEQ (carcinogenic equivalents, ng/m^3) and BaP-MEQ (mutagenic equivalents, ng/m^3) were calculated by multiplying the concentrations of each

PAH compound with its TEF for cancer potency relative to BaP [3] and MEF relative to BaP [1-2], respectively. BaP-TEQ and BaP-MEQ levels for the sum of nonvolatile PAH ($\Sigma_8\text{PAH}$; $\text{MW} \geq 228$) were calculated as follows:

- $(\text{BaP-TEQ})_{\Sigma_8\text{PAH}} = [\text{BaA}] \times 0.1 + [\text{Chry}] \times 0.01 + [\text{BbFA}] \times 0.1 + [\text{BkFA}] \times 0.1 + [\text{BaP}] \times 1 + [\text{IP}] \times 0.1 + [\text{DahA}] \times 5 + [\text{BghiP}] \times 0.01.$
- $(\text{BaP-MEQ})_{\Sigma_8\text{PAH}} = [\text{BaA}] \times 0.082 + [\text{Chry}] \times 0.017 + [\text{BbFA}] \times 0.25 + [\text{BkFA}] \times 0.11 + [\text{BaP}] \times 1 + [\text{IP}] \times 0.31 + [\text{DahA}] \times 0.29 + [\text{BghiP}] \times 0.19.$

Quality control. Each air monitoring result was assessed and flagged if there are any issues of sampling conditions such as tube disconnection from the pump, late-takedown, pump failure, switch error, and any other human errors. Once flagged, air monitoring data were given a quality assurance (QA) score of 1 (0: highest quality) and further examined for additional score for erroneous length of sampling time, erroneous flow rate of pump, and missing documentation. If a final QA score is ≥ 3 , the data was excluded, sampling was redone. Flagged data were included for analysis if they passed a quality control test ($\text{QA} \leq 2$), as described [25]. Five failed the quality control test.

Mean recovery of deuterated surrogate standards was 97.9% ($\pm 17\%$ Standard deviation, SD) and 102.6% ($\pm 15\%$, SD) for d10 anthracene and d14-p-terphenyl, respectively in all batches except for one. In one batch of measures, the mean recovery efficiency exceeded 130% in some samples (attributed to evaporation during storage) and adjustment was made downward by the multiplier 100/ (mean recovery) and included for the data analysis. The limit of detection (LODs) for 8 individual PAH was 0.03 ng/m^3 .

Statistical analysis. Descriptive statistics were used to describe overall BaP-TEQ and BaP-MEQ concentrations for individual PAH and $\Sigma_8\text{PAH}$ indoors and outdoors. Due to the non-normal distributions of individual PAH and the sum of 8 PAH ($\Sigma_8\text{PAH}$) concentrations, Mann-Whitney and Wilcoxon signed ranks test were conducted. Heating season was defined as any sampling that was initiated October 1st through April 30st as described [21]. Indoor and outdoor comparisons were based on the subset of homes in which both indoor and outdoor air concentrations were measured simultaneously. Analyses were conducted using SPSS software (SPSS; Chicago, IL, version 17).

3. Results

Residential indoor and outdoor BaP-equivalents

The BaP-equivalent (BaP-TEQ and BaP-MEQ) concentrations calculated for $\Sigma_8\text{PAH}$ and individual PAH measured in this study are shown in Table 1. The levels of indoor $(\text{BaP-TEQ})_{\Sigma_8\text{PAH}}$ and $(\text{BaP-MEQ})_{\Sigma_8\text{PAH}}$ ranged from $0.098\text{--}8.348 \text{ ng/m}^3$ and $0.069\text{--}19.72 \text{ ng/m}^3$, respectively. For all samples studied, the largest contribution of individual PAH to $(\text{BaP-TEQ})_{\Sigma_8\text{PAH}}$ and $(\text{BaP-MEQ})_{\Sigma_8\text{PAH}}$ was made by BaP, followed by DahA for $(\text{BaP-TEQ})_{\Sigma_8\text{PAH}}$ and IP and BghiP for $(\text{BaP-MEQ})_{\Sigma_8\text{PAH}}$ (Table 1). In outdoor air, the contribution of BbFA to $(\text{BaP-MEQ})_{\Sigma_8\text{PAH}}$ was substantially elevated when compared to indoor air, making it the dominant compound contributing to $(\text{BaP-MEQ})_{\Sigma_8\text{PAH}}$.

Table 1. BaP-equivalent carcinogenicity and mutagenicity risks assessed in 5–6 year old residential indoor and outdoor air.

Analyte	n	BaP-TEQ Levels, ng/m ³					BaP-MEQ Levels, ng/m ³				
		^a TEF	Median	Mean	SD	Range	^b MEF	Median	Mean	SD	Range
Σ ₈ PAH	255	NA	0.299	0.478	0.709	0.098–8.348	NA	0.376	0.590	1.325	0.069–19.72
BaP	255	1	0.121	0.198	0.363	0.015–4.494	1	0.121	0.198	0.363	0.015–4.494
BaA	255	0.1	0.006	0.009	0.010	0.002–0.132	0.082	0.005	0.007	0.009	0.001–0.108
Chry	255	0.01	0.001	0.001	0.002	0.000–0.021	0.017	0.001	0.002	0.003	0.000–0.036
BbFA	255	0.1	0.019	0.028	0.034	0.004–0.346	0.25	0.047	0.069	0.084	0.010–0.865
BkFA	255	0.1	0.006	0.010	0.013	0.002–0.140	0.11	0.007	0.010	0.014	0.002–0.154
IP	255	0.1	0.028	0.044	0.094	0.002–1.400	0.31	0.087	0.136	0.291	0.006–4.340
DahA	255	5	0.083	0.180	0.212	0.055–1.741	0.29	0.005	0.010	0.012	0.003–0.101
BghiP	255	0.01	0.004	0.008	0.033	0.001–0.517	0.19	0.084	0.156	0.624	0.016–9.828
Outdoor											
Σ ₈ PAH	82	NA	0.277	0.450	0.389	0.109–1.932	NA	0.360	0.528	0.454	0.062–2.394
BaP	82	1	0.091	0.133	0.133	0.016–0.748	1	0.091	0.133	0.133	0.016–0.748
BaA	82	0.1	0.007	0.011	0.011	0.001–0.059	0.082	0.005	0.009	0.009	0.001–0.048
Chry	82	0.01	0.001	0.002	0.002	0.0003–0.008	0.017	0.002	0.004	0.003	0.001–0.013
BbFA	82	0.1	0.039	0.048	0.043	0.006–0.237	0.25	0.097	0.121	0.108	0.015–0.592
BkFA	82	0.1	0.010	0.015	0.017	0.002–0.114	0.11	0.011	0.017	0.018	0.002–0.125
IP	82	0.1	0.027	0.035	0.031	0.003–0.197	0.31	0.085	0.107	0.095	0.010–0.611
DahA	82	5	0.083	0.199	0.188	0.075–1.021	0.29	0.005	0.012	0.011	0.004–0.059
BghiP	82	0.01	0.005	0.007	0.007	0.001–0.039	0.19	0.087	0.126	0.126	0.010–0.739

^aTEF: toxic equivalency factors for cancer potency relative to BaP (Nisbet and LaGoy, 1992)

^bMEF: mutagenic potency factor relative to BaP (Durant *et al.*, 1996 and 1999)

BaP-TEQ: Carcinogenic equivalents calculated from the cancer potency relative to BaP (TEF) multiplied by the concentration of PAH in a sample.

BaP-MEQ: Mutagenic equivalents calculated from the mutagenic potency relative to BaP (MEF) multiplied by the concentration of PAH in a sample.

Σ₈PAH includes benzo(a)pyrene (BaP), benz(a)anthracene (BaA), chrysene/iso-chrysene (Chry), benzo(b)fluoranthene (BbFA), benzo(k)fluoranthene (BkFA), indeno(1,2,3-c,d)pyrene (IP), dibenz(a,h)anthracene(DahA), and benzo(ghi)perylene(BghiP).

Seasonal variations in BaP-equivalents

Heating compared to nonheating season was associated significantly with higher (BaP-TEQ) $_{\Sigma 8\text{PAH}}$ and (BaP-MEQ) $_{\Sigma 8\text{PAH}}$ both indoors and outdoors (Figure 1-a and Figure 1-b; $p < 0.001$, Mann-Whitney test). This pattern was apparent when the individual 8 PAH were assessed ($p < 0.001$).

In addition, during the heating season, outdoor (BaP-TEQ) $_{\Sigma 8\text{PAH}}$ and (BaP-MEQ) $_{\Sigma 8\text{PAH}}$ were significantly higher than the corresponding indoor measures (Table 2; $p < 0.01$, Wilcoxon signed ranks test). A similar pattern was not observed during the nonheating season (Table 2; $p > 0.05$, Wilcoxon signed ranks test). Similarly, most individual 8 PAH (except BaP and IP) were higher outdoors compared to indoors during the heating season ($p < 0.05$). BbFA and Chry were significantly higher outdoors than indoors regardless of season ($p < 0.05$, Wilcoxon signed ranks test).

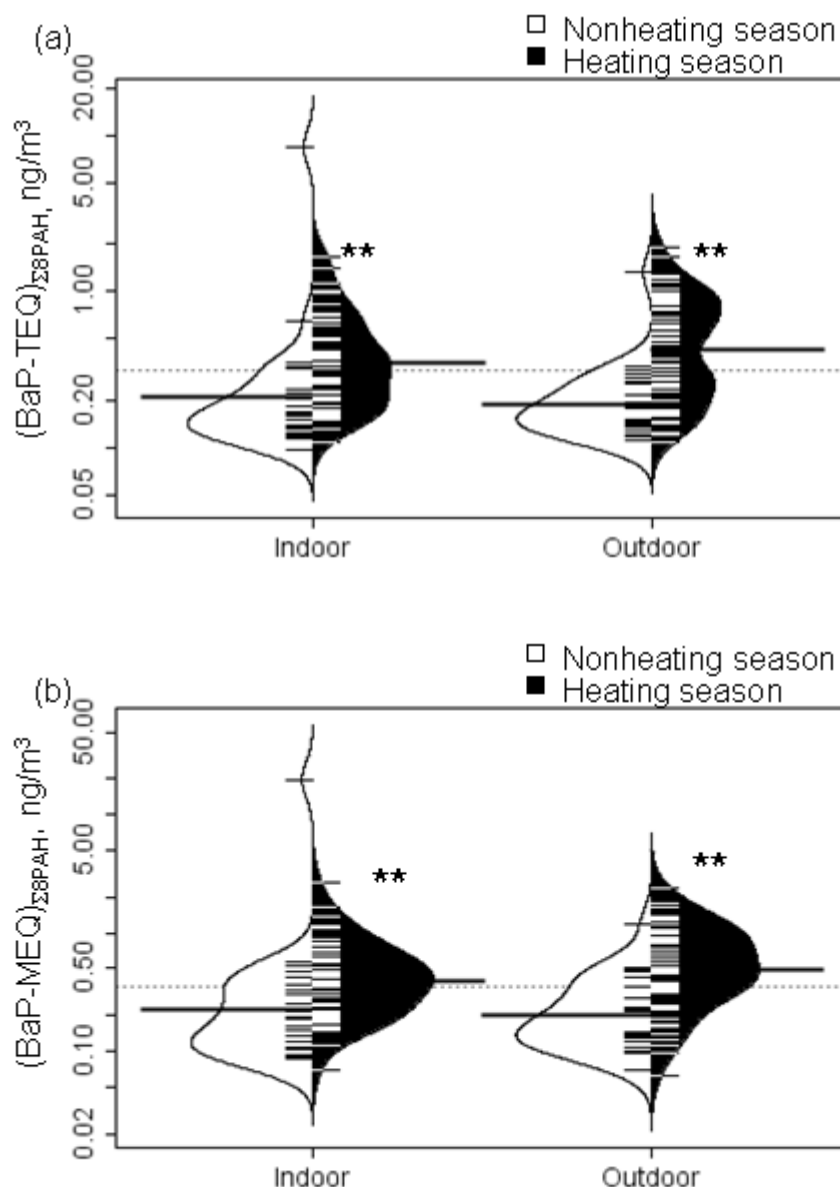
Table 2. Relationship between indoor and outdoor BaP-equivalent carcinogenicity and mutagenicity risks, stratified by season.

Season	Measure	Indoor, ng/m ³ (n ^a = 55; n ^b = 26)		Outdoor, ng/m ³ (n ^a = 55; n ^b = 26)		p
		Average $\pm$ SD	Median	Average $\pm$ SD	Median	
Heating	(BaP-TEQ) $_{\Sigma 8\text{PAH}}$	0.460 $\pm$ 0.365	0.346	0.558 $\pm$ 0.407	0.485	0.002**
	(BaP-MEQ) $_{\Sigma 8\text{PAH}}$	0.521 $\pm$ 0.448	0.388	0.660 $\pm$ 0.480	0.500	0.001**
Nonheating	(BaP-TEQ) $_{\Sigma 8\text{PAH}}$	0.515 $\pm$ 1.602	0.163	0.232 $\pm$ 0.233	0.167	0.989
	(BaP-MEQ) $_{\Sigma 8\text{PAH}}$	0.975 $\pm$ 3.826	0.174	0.260 $\pm$ 0.230	0.173	0.989

**($p < 0.01$) for Wilcoxon Signed Ranks test.

n^a: Number for heating season, n^b: Number for nonheating season

Heating season was defined as any sampling that was initiated October 1st through April 30th.

Figure 1. Seasonal variations in (a) $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ and (b) $(\text{BaP-MEQ})_{\Sigma 8\text{PAH}}$.

Note: Mann-Whitney test was performed to compare heating season and nonheating concentrations $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ and $(\text{BaP-MEQ})_{\Sigma 8\text{PAH}}$ indoors and outdoors. The white and black lines show individual observations, while the white and black area shows the distribution. The dotted line indicates the overall geometric mean and the thicker solid line shows the geometric mean concentration of indoors and outdoors for each season. Mann-Whitney test, $**p < 0.001$. $\Sigma_8\text{PAH}$ includes benz(a)anthracene (BaA), chrysene/iso-chrysene (Chry), benzo(b)fluoranthene (BbFA), benzo(k)fluoranthene (BkFA), benzo(a)pyrene (BaP), indeno(1,2,3-c,d)pyrene (IP), dibenz(a,h)anthracene(DahA), and benzo(ghi)perylene (BghiP).

4. Discussion and Conclusions

Our objective was to estimate the potential carcinogenic and mutagenic risks of residential exposure to PAH for a cohort of inner city young children based on BaP-equivalent concentration (BaP-TEQ and BaP-MEQ). We found a significant effect of heating season on BaP-TEQ and BaP-MEQ possibly due to higher emissions from heating sources and more frequent stagnant meteorological conditions in the winter. While an effect of heating season has been documented in small studies [15,16], this is the first paper to examine seasonal differences in carcinogenic and mutagenic risks based on residential exposure of a large cohort of urban children.

The indoor $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ levels observed in this study were considerably lower than those reported for other homes impacted heavily by industrial and traffic emissions in Ohura *et al.* [15]. $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ risk levels depend not only on concentrations of individual 8 PAH, but also the composition of PAH mixtures affected by varying emission sources. While $\Sigma 8\text{PAH}$ concentrations measured in the Ohura study were 1.3–2.2 times higher than those measured in this study, $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ levels were 2–3.5 times higher. Consistent with Ohura *et al.* [15], we observed that BaP was the dominant compound contributing to $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$, accounting for 45% of indoor $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ and 35% of outdoor $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$.

While the contributions of the sum of IP and BghiP to $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ both indoors and outdoors were only 11–12%, their contributions to $(\text{BaP-MEQ})_{\Sigma 8\text{PAH}}$ were much higher considerably (45–48%). Considering that these compounds are considered tracers of vehicular emissions [26], exposure to traffic emissions may impact the mutagenicity risk to a greater extent than the carcinogenic risk.

Both indoors and outdoors, higher $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ and $(\text{BaP-MEQ})_{\Sigma 8\text{PAH}}$ risks were observed in the heating season, compared to the nonheating season. The heating season may be associated with (1) increased use of fossil fuel combustion for residential heating (2) reduced air exchange rates (AERs) [27], (3) reduced PAH transformation through photochemical/chemical reaction due to a lower temperature and ozone concentration [28], (4) gas/particle partitioning in favor of the particulate phase with lower temperature and (5) frequent stagnant meteorological conditions such as a lower mixing height. Presumably some combination of these characteristics of heating season led to changes in either concentrations or relative composition that was pertinent to the calculation of these measures.

Several studies reported that heavier 5–7 ring PAH have higher airborne measures outdoors compared to indoors, due to the presence of major outdoor emission sources (*i.e.*, traffic sources, industry, and power generation etc) of those compounds [15,29]. Heavier PAH concentrations indoors are strongly affected not only by the outdoor concentrations but also by outdoor-to-indoor AERs that were shown to be lower during winter than summer when residential windows usually are shut [15,27,29]. Similar trends were obtained for $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ and $(\text{BaP-MEQ})_{\Sigma 8\text{PAH}}$ during the heating season. This result suggests that children are subjected to higher carcinogenic and mutagenic risks derived from PAH when they play outside more so than inside the home during the heating season. When compared to other urban outdoor values measured in the winter season [15–17], outdoor $(\text{BaP-TEQ})_{\Sigma 8\text{PAH}}$ and $(\text{BaP-MEQ})_{\Sigma 8\text{PAH}}$ observed in this study were 2–5 times lower during the heating season.

These risks measured and calculated here raise significant concerns for public health. For example, applying the World Health Organization (WHO) suggested unit risk of $8.7 \times 10^{-5} (\text{ng}/\text{m}^3)^{-1}$ for lifetime

(70 years) PAH exposure [30], the corresponding lifetime lung cancer risks were found to be 4.2×10^{-5} ($= 0.478 \text{ ng/m}^3 \times 8.7 \times 10^{-5} (\text{ng/m}^3)^{-1}$) and 5.1×10^{-5} ($= 0.590 \text{ ng/m}^3 \times 8.7 \times 10^{-5} (\text{ng/m}^3)^{-1}$) when the average indoor (BaP-TEQ) $_{\Sigma 8\text{PAH}}$ and (BaP-MEQ) $_{\Sigma 8\text{PAH}}$ concentration were used, respectively. Hence, if 1,000,000 people were exposed to 0.478 ng/m^3 of indoor (BaP-TEQ) $_{\Sigma 8\text{PAH}}$ for 70 years, then 42 people may develop lung cancer. An excess lung cancer risk from lifetime exposure to (BaP-MEQ) $_{\Sigma 8\text{PAH}}$ concentration would be 51 cases among one million individuals exposed. The estimated cancer risks from air pollution in NYC did not exceed a health-based guideline (8.7×10^{-5}) calculated based on the maximum permissible level of 1 ng/m^3 of BaP [30]. However, it should be noted that the risk estimates presented are very uncertain, and could be understood only as a crude estimation of cancer risk from the PAH inhalation.

We acknowledge study limitations. The potential risk of PAH exposure based on TEQ or MEQ may be underestimated if the interaction of some PAHs are synergistic rather than additive. Chemical degradation of PAH by ambient oxidants (ozone, hydroxyl radical, or nitrogen oxides) in the atmosphere as well as on the filters during sampling could also underestimate the potential risks due to reduced measured PAH levels, as shown in several studies [28,31–36]. For example, BaP concentrations collected without denuder that can remove atmospheric oxidants such as ozone and OH radical can be underestimated by more than 200% of the measured value at high ozone levels in summer [28,31]. Also PAH collected on the filters may be decomposed through heterogeneous chemical reactions with ozone during an extended sampling period [28,34–36]. Furthermore, nitrated/oxygenated PAH compounds have not been measured in this study, underestimating the full carcinogenic and mutagenic potential of PAH exposure. Those PAH compounds formed by photochemical/chemical reactions are known to be more toxic than their parent PAH based on tumorigenicity of PAH in a newborn mouse assay [8,37,38]. Young children can be exposed to PAH through other routes besides inhalation. These include ingesting food, nondietary ingestion of dust or soil through hand-to-mouth activity, or dermal contact with soil polluted by PAH [39,40]. Although inhalation is an important pathway for inner-city children because of high levels of PAH measured in indoor and outdoor air, dietary ingestion and non-dietary ingestion pathways are thought to be more important for young children's exposure to heavier PAHs [39,40]. Thus, the values reported in this study may need to be considered as the lower limit of estimated potential PAH health risk resulted from inhalation of air. Further investigations are needed whether BaP-equivalent levels are associated with any observed health outcomes (*i.e.*, respiratory or allergic symptoms *etc.*) within the cohort.

In conclusion, we found that heating season is an important contributor to the potential risk of PAH exposure. This finding has implications for the design of environmental health studies that focus on air pollution exposure and young children living in the inner city.

Acknowledgements

Support from NIH R01ES013163, P50ES015905, P01ES09600, R01ES08977, the Educational Foundation of America, the John & Wendy Neu Family Foundation, the New York Community Trust, and the Trustees of the Blanchette Hooker Rockefeller Fund.

References

1. Durant, J.; Lafleur, A.; Busby, W.; Donhoffner, L.; Penman, B.; Crespi, C. Mutagenicity of C24H14 PAH in human cells expressing CYP1A1. *Mutat. Res.-Genet. Toxicol. E. M.* **1999**, *446*, 1-14.
2. Durant, J.; Busby, W.; Lafleur, A.; Penman, B.; Crespi, C. Human cell mutagenicity of oxygenated, nitrated and unsubstituted polycyclic aromatic hydrocarbons associated with urban aerosols. *Mutat. Res.-Genet. Tox.* **1996**, *371*, 123-157.
3. Nisbet, I.; LaGoy, P. Toxic equivalency factors (TEFs) for polycyclic aromatic hydrocarbons (PAHs). *Regul. Toxicol. Pharmacol. RTP* **1992**, *16*, 290-300.
4. Marty, M.A.; Alexeeff, G.V.; Collins, J.F.; Blaisdell, R.J.; Rosenbaum, J.; Lee, L. Airborne emissions from industrial point sources and associated cancer risks of selected carcinogens in California. In *The Emissions Inventory: Perception and Reality Proceedings of an International Specialty Conference*; Air & Waste Management Association: Pittsburgh, PA, USA, 1994; pp. 1086-1097.
5. Wynder, E.; Hoffmann, D. A study of tobacco carcinogenesis. X. Tumor promoting activity. *CA-Cancer J. Clin.* **1959**, *24*, 289-301.
6. Chu, M.M.L.; Chen, C.W. Evaluation and estimation of potential carcinogenic risks of polynuclear aromatic hydrocarbons. Presented at *the Symposium on Polycyclic Aromatic Hydrocarbons in the Workplace*; Pacific Rim Risk Conference: Honolulu, HI, USA, 1984.
7. Clement, Comparative potency approach for estimating the cancer risk associated with exposure to mixtures of polycyclic aromatic hydrocarbons (Interim Final Report). *Prepared for EPA under Contract 68-02-4403*; ICF-Clement Associates: Fairfax, VA, USA, April 1988.
8. Collins, J.; Brown, J.; Alexeeff, G.; Salmon, A. Potency equivalency factors for some polycyclic aromatic hydrocarbons and polycyclic aromatic hydrocarbon derivatives. *Regul. Toxicol. Pharmacol.* **1998**, *28*, 45-54.
9. Pfeiffer, E.H. Oncogenic interaction of carcinogenic and non-carcinogenic polycyclic aromatic hydrocarbons. In *Air Pollution and Cancer in Man*; Mohr, V., Schmahl, D., Tomatis, L., Eds.; IARC Scientific Publication 16. World Health Organization: Lyon, France, 1977.
10. Kier, L.; Brusick, D.; Auletta, A.; Von Halle, E.; Brown, M.; Simmon, V.; Dunkel, V.; McCann, J.; Mortelmans, K. The Salmonella typhimurium/mammalian microsomal assay. A report of the US Environmental Protection Agency Gene-Tox Program. *Mutat. Res.* **1986**, *168*, 67-238.
11. Zeiger, E. Mutagens that are not carcinogens: faulty theory or faulty tests? *Mutat. Res.-Genet. Toxicol. E. M.* **2001**, *492*, 29-38.
12. Zeiger, E. Identification of rodent carcinogens and noncarcinogens using genetic toxicity tests: premises, promises, and performance. *Regul. Toxicol. Pharmacol.* **1998**, *28*, 85-95.
13. DeMarini, D.; Brooks, L.; Warren, S.; Kobayashi, T.; Gilmour, M.; Singh, P. Bioassay-directed fractionation and salmonella mutagenicity of automobile and forklift diesel exhaust particles. *Environ. Health Perspect.* **2004**, *112*, 814.
14. Seagrave, J.; McDonald, J.; Gigliotti, A.; Nikula, K.; Seilkop, S.; Gurevich, M.; Mauderly, J. Mutagenicity and in vivo toxicity of combined particulate and semivolatile organic fractions of gasoline and diesel engine emissions. *Toxicol. Sci.* **2002**, *70*, 212.

15. Ohura, T.; Amagai, T.; Fusaya, M.; Matsushita, H. Polycyclic aromatic hydrocarbons in indoor and outdoor environments and factors affecting their concentrations. *Environ. Sci. Technol.* **2004**, *38*, 77-83.
16. Ohura, T.; Noda, T.; Amagai, T.; Fusaya, M. Prediction of personal exposure to PM 2.5 and carcinogenic polycyclic aromatic hydrocarbons by their concentrations in residential microenvironments. *Environ. Sci. Technol.* **2005**, *39*, 5592-5599.
17. Nielsen, T.; Jørgensen, H.; Larsen, J.; Poulsen, M. City air pollution of polycyclic aromatic hydrocarbons and other mutagens: occurrence, sources and health effects. *Sci. Total Environ.* **1996**, *189*, 41-49.
18. Miller, R.; Garfinkel, R.; Horton, M.; Camann, D.; Perera, F.; Whyatt, R.; Kinney, P. Polycyclic aromatic hydrocarbons, environmental tobacco smoke, and respiratory symptoms in an inner-city birth cohort. *Chest* **2004**, *126*, 1071-1078.
19. Perera, F.; Illman, S.; Kinney, P.; Whyatt, R.; Kelvin, E.; Shepard, P.; Evans, D.; Fullilove, M.; Ford, J.; Miller, R. The challenge of preventing environmentally related disease in young children: community-based research in New York City. *Environ. Health Perspect.* **2002**, *110*, 197-204.
20. Perera, F.P.; Rauh, V.; Whyatt, R.M.; Tsai, W.Y.; Tang, D.; Diaz, D.; Hoepner, L.; Barr, D.; Tu, Y.H.; Camann, D.; Kinney, P. Effect of prenatal exposure to airborne polycyclic aromatic hydrocarbons on neurodevelopment in the first 3 years of life among inner-city children. *Environ. Health Perspect.* **2006**, *114*, 1287-1292.
21. Jung, K.H.; Patel, M.M.; Kinney, P.L.; Chillrud, S.N.; Whyatt, R.; Hoepner, L.; Yan, B.; Garfinkel, R.; Ross, J.; Camann, D.; Perera, F.P.; Miller, R.L. Effects of season and indoor heating on indoor and outdoor residential levels of airborne polycyclic aromatic hydrocarbons, absorbance and particulate matter 2.5 in an inner city cohort of young children. *J. Allergy Clin. Immunol.* **2010**, *125*, AB81.
22. Whyatt, R.; Garfinkel, R.; Hoepner, L.; Holmes, D.; Borjas, M.; Williams, M.; Reyes, A.; Rauh, V.; Perera, F.P.; Camann, D.E. Within-and between-home variability in indoor-air insecticide levels during pregnancy among an inner-city cohort from New York City. *Environ. Health Perspect.* **2007**, *115*, 383-389.
23. Tonne, C.; Whyatt, R.; Camann, D.; Perera, F.; Kinney, P. Predictors of personal polycyclic aromatic hydrocarbon exposures among pregnant minority women in New York City. *Environ. Health Perspect.* **2004**, *112*, 754-760.
24. Boffetta, P. Cancer risk from occupational and environmental exposure to polycyclic aromatic hydrocarbons. *Cancer Causes Control.* **1997**, *8*, 442-472.
25. Choi, H.; Jedrychowski, W.; Spengler, J.; Camann, D.; Whyatt, R.; Rauh, V.; Tsai, W.; Perera, F. International studies of prenatal exposure to polycyclic aromatic hydrocarbons and fetal growth. *Environ. Health Perspect.* **2006**, *114*, 1744.
26. Miguel, A.; Pereira, P. Benzo (k) fluoranthene, benzo (ghi) perylene and indeno (1, 2, 3-cd) pyrene. New tracers of automotive emissions in receptor modeling. *Aerosol. Sci. Tech.* **1989**, *10*, 292-295.
27. Kinney, P.L.; Chillrud, S.N.; Ramstrom, S.; Ross, J.; Spengler, J.D. Exposures to multiple air toxics in New York City. *Environ. Health Perspect.* **2002**, *110*, 539-546.

28. Schauer, C.; Niessner, R.; Poschl, U. Polycyclic aromatic hydrocarbons in urban air particulate matter: decadal and seasonal trends, chemical degradation, and sampling artifacts. *Environ. Sci. Technol.* **2003**, *37*, 2861-2868.
29. Ohura, T.; Amagai, T.; Sugiyama, T.; Fusaya, M.; Matsushita, H. Characteristics of particle matter and associated polycyclic aromatic hydrocarbons in indoor and outdoor air in two cities in Shizuoka, Japan. *Atmos. Environ.* **2004**, *38*, 2045-2054.
30. WHO, Air quality guidelines for Europe. *WHO Regional Publications, European Series, No. 23*, 1987.
31. Goriaux, M.; Jourdain, B.; Temime, B.; Besombes, J.; Marchand, N.; Albinet, A.; Leoz-Garziandia, E.; Wortham, H. Field comparison of particulate PAH measurements using a low-flow denuder device and conventional sampling systems. *Environ. Sci. Technol.* **2006**, *40*, 6398-6404.
32. Lodovici, M.; Venturini, M.; Marini, E.; Grechi, D.; Dolara, P. Polycyclic aromatic hydrocarbons air levels in Florence, Italy, and their correlation with other air pollutants. *Chemosphere* **2003**, *50*, 377-382.
33. Marr, L.; Dzepina, K.; Jimenez, J.; Reisen, F.; Bethel, H.; Arey, J.; Gaffney, J.; Marley, N.; Molina, L.; Molina, M. Sources and transformations of particle-bound polycyclic aromatic hydrocarbons in Mexico City. *Atmos. Chem. Phys.* **2006**, *6*, 1733-1745.
34. Brorström, E.; Grennfelt, P.; Lindskog, A. The effect of nitrogen dioxide and ozone on the decomposition of particle-associated polycyclic aromatic hydrocarbons during sampling from the atmosphere. *Atmos. Environ.* **1983**, *17*, 601-605.
35. Pitts, J., Jr.; Lokensgard, D.; Ripley, P.; van Cauwenberghe, K.; van Vaeck, L.; Shaffer, S.; Thill, A.; Belser, W., Jr. "Atmospheric" epoxidation of benzo[a]pyrene by ozone: formation of the metabolite benzo[a]pyrene-4,5-oxide. *Science* **1980**, *210*, 1347-1349.
36. Tsapakis, M.; Stephanou, E. Collection of gas and particle semi-volatile organic compounds: use of an oxidant denuder to minimize polycyclic aromatic hydrocarbons degradation during high-volume air sampling. *Atmos. Environ.* **2003**, *37*, 4935-4944.
37. Busby, W.; Stevens, E.; Martin, C.; Chow, F.; Garner, R. Comparative lung tumorigenicity of parent and mononitro-polynuclear aromatic hydrocarbons in the BLU: Ha newborn mouse assay. *Toxicol. Appl. Pharmacol.* **1989**, *99*, 555-563.
38. Wislocki, P.; Bagan, E.; Lu, A.; Dooley, K.; Fu, P.; Han-Hsu, H.; Beland, F.; Kadlubar, F. Tumorigenicity of nitrated derivatives of pyrene, benz[a]anthracene, chrysene and benzo[a]pyrene in the newborn mouse assay. *Carcinogenesis* **1986**, *7*, 1317-1322.
39. Chuang, J.; Callahan, P.; Lyu, C.; Wilson, N. Polycyclic aromatic hydrocarbon exposures of children in low-income families. *J. Expo. Anal. Env. Epid.* **1999**, *9*, 85-98.
40. Vyskocil, A.; Fiala, Z.; Cháer, V.; Krajak, L.; Ettlerova, E.; Bukac, J.; Viau, C.; Emminger, S. Assessment of multipathway exposure of small children to PAH. *Environ. Toxicol. Pharmacol.* **2000**, *8*, 111-118.