

PBMC basophil data available ($n = 16$), the ratio of low-density PBMC basophil/total blood basophil counts was greater in the exacerbation-prone group ($12.2\% \pm 7.2\%$ compared with $4.4\% \pm 5.7\%$, $P = .04$).

Basophils are known to be a significant producer of T_H2 cytokines and are involved in defense against parasites.⁷ Moreover, they traffic to the airways during allergen challenge⁸ and contribute to disease pathology in patients with eosinophilic asthma.⁹ Our findings suggest that the proportion of degranulated basophils can also be associated with recurrent exacerbations. These results will need to be confirmed using a larger cohort and particularly in patients experiencing their first ever exacerbation. Given that early identification of patients with recurrent asthma exacerbations is difficult, the use of basophil proportion and density as a potential marker warrants further exploration.

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REFERENCES

1. Pavord ID, Beasley R, Agusti A, Anderson GP, Bel E, Brusselle G, et al. After asthma: redefining airways diseases. *Lancet* 2018;391:350-400.
2. Rodrigo GJ, Rodrigo C, Hall JB. Acute asthma in adults: a review. *Chest* 2004;125:1081-102.
3. Koga T, Oshita Y, Kamimura T, Koga H, Aizawa H. Characterisation of patients with frequent exacerbation of asthma. *Respir Med* 2006;100:273-8.
4. Cyr MM, Denburg JA. Systemic aspects of allergic disease: the role of the bone marrow. *Curr Opin Immunol* 2001;13:727-32.
5. Subrata LS, Bizzintino J, Mamessier E, Bosco A, McKenna KL, Wikstrom ME, et al. Interactions between innate antiviral and atopic immunoinflammatory pathways precipitate and sustain asthma exacerbations in children. *J Immunol* 2009;183:2793-800.
6. Ygberg S, Nilsson A. The developing immune system—from foetus to toddler. *Acta Paediatr* 2012;101:120-7.
7. Karasuyama H, Yamanishi Y. Basophils have emerged as a key player in immunity. *Curr Opin Immunol* 2014;31:1-7.
8. Dijkstra D, Hennig C, Hansen G, Biller H, Krug N, Hohlfeld JM. Identification and quantification of basophils in the airways of asthmatics following segmental allergen challenge. *Cytometry A* 2014;85:580-7.
9. Suzuki Y, Wakahara K, Nishio T, Ito S, Hasegawa Y. Airway basophils are increased and activated in eosinophilic asthma. *Allergy* 2017;72:1532-9.

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Urinary polycyclic aromatic hydrocarbons and allergic sensitization in a nationwide study of children and adults in the United States



To the Editor:

Allergic sensitization is associated with the development and severity of diseases such as allergic rhinitis and asthma, and approximately 45% of the US population 6 years and older is sensitized to 1 or more allergen.¹ Polycyclic aromatic hydrocarbons (PAHs), a component of diesel exhaust particles, are ubiquitous fused aromatic rings produced by incomplete combustion of organic material.^{2,3} PAHs have been implicated as adjuvants in the pathogenesis of allergic responses.³ Relatively few studies have examined PAHs and allergic sensitization, with most studies limited by small sample size, noninclusion of adults, and varying methods of exposure assessment.⁴ The National Health and Nutrition Examination Survey (NHANES) has been measuring urinary PAH hydroxyl metabolites as a surrogate for PAH exposure in the United States, with results indicating widespread exposure. We hypothesized that PAH exposure increases the risk of allergic sensitization among children and adults in the United States, and used NHANES 2005-2006 data to test this hypothesis.

Ten monohydroxy urinary PAH analytes (1-hydroxynaphthalene, 2-hydroxynaphthalene, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene, 4-hydroxyphenanthrene, 1-hydroxypyrene) were measured in 2005-2006 NHANES from a randomly sampled subpopulation, aged 6 to 85 years ($n = 2638$). We created 3 variables: summation of molecular weight of all 10 PAH metabolites ($\sum_{\text{mol}}\text{PAH}$); summation of molecular weight of 2-ring metabolites ($\sum_{2\text{mol}}\text{PAH}$); and summation of molecular weight for 3- and 4-ring PAH metabolites ($\sum_{3,4\text{mol}}\text{PAH}$) (see this article's Online Repository at www.jacionline.org).

Serum IgE levels to 15 allergens (*Alternaria alternata*, *Aspergillus fumigatus*, Bermuda grass, common silver birch, cat dander, German cockroach [*Blattella germanica*], dog dander, dust mite [*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*], mouse urinary protein, oak, common ragweed, rat urinary protein, Russian thistle, and rye grass) were measured and considered positive if greater than or equal to 0.35 kU/L.

Logistic regression was used for the multivariable analysis of urinary PAH and allergen-specific IgEs. All models were adjusted for age, sex, race/ethnicity, poverty income ratio, serum cotinine, and urinary creatinine. For each PAH significantly associated with sensitization to a specific allergen, we tested for an interaction between PAH and dust levels of the corresponding indoor allergen.

The characteristics of study participants are presented in [Table 1](#). Forty-two percent of participants had 1 or more positive IgE to allergens: most commonly to dust mite and rye grass, and least commonly to mouse or rat. All PAHs were significantly correlated with each other, with naphthalene metabolites being the least correlated with other metabolites (see [Fig E1](#) in this article's Online Repository at www.jacionline.org).

A comparison of the means for $\sum_{\text{mol}}\text{PAH}$, $\sum_{2\text{mol}}\text{PAH}$, and $\sum_{3,4\text{mol}}\text{PAH}$ between individuals with and without sensitization revealed higher mean PAH concentrations in those sensitized to cockroach for all PAHs, and higher mean $\sum_{\text{mol}}\text{PAH}$ and $\sum_{2\text{mol}}\text{PAH}$ for *D. farinae* and rat urinary protein. We found no

TABLE I. Main characteristics of study participants in NHANES 2005-2006, subsampled for urinary PAH metabolite analysis

Variable	Mean $\pm$ weighed SE or N (weighted %)	Variable	N (weighted %)
N	2593	Allergen-specific IgEs*	
Age (y)	39 $\pm$ 0.9	(1 or more IgE positive)	1098 (42%)
Sex: female	1308 (51%)	+ Cockroach	315 (10%)
Poverty income ratio, ≤ 1	555 (13%)	+ Dust mite (<i>D pteronyssinus</i>)	509 (19%)
Race		+ Dust mite (<i>D farinae</i>)	507 (19%)
Black, non-Hispanic	685 (12%)	+ Cat	287 (12%)
Hispanic	717 (12%)	+ Dog	297 (12%)
Other	125 (6%)	+ Mouse	35 (0.8%)
White, non-Hispanic	1066 (70%)	+ Rat	29 (1.0%)
Urinary creatinine (mg/dL)	127 $\pm$ 2	+ Aspergillus	205 (6%)
Serum cotinine (ng/mL)	60.9 $\pm$ 2.6	+ Alternaria	230 (8%)
Total IgE (kU/L)	131 $\pm$ 7	+ Oak tree	300 (11%)
		+ Birch tree	254 (10%)
		+ Ragweed	396 (14%)
		+ Russian thistle	296 (10%)
		+ Rye grass	527 (17%)
		+ Bermuda grass	403 (13%)
Urinary PAHs (ng/L)			
	Geometric mean (95% CI)		
1-Hydroxynaphthalene	2641 (2388-2922)		
2-Hydroxynaphthalene	3626 (3351-3923)		
2-Hydroxyfluorene	316 (297-338)		
3-Hydroxyfluorene	124 (115-134)		
9-Hydroxyfluorene	308 (289-328)		
1-Hydroxyphenanthrene	152 (143-161)		
2-Hydroxyphenanthrene	65 (61-70)		
3-Hydroxyphenanthrene	103 (96-109)		
4-Hydroxyphenanthrene	29 (26-32)		
1-Hydroxypyrene	98 (91-106)		
Σ PAH	9238 (8537-9997)		
Σ_2 PAH	7350 (6724-8033)		
$\Sigma_{3,4}$ PAH	1287 (1199-1381)		

*A positive IgE defined as ≥ 0.35 kU/L.**TABLE II.** Multivariable analysis of urinary PAH metabolites and allergic sensitization in NHANES 2005-2006, ages 6-85+ years

Allergic sensitization	$\Sigma_{\text{mol}}\text{PAH}$		$\Sigma_{2\text{mol}}\text{PAH}$		$\Sigma_{3,4\text{mol}}\text{PAH}$	
	OR	95% CI	OR	95% CI	OR	95% CI
Cockroach	1.49*	(1.1-2.0)	1.48*	(1.1-2.0)	0.99	(0.6-1.7)
Dust, <i>D farinae</i>	1.29*	(1.0-1.7)	1.28*	(1.0-1.6)	1.37	(0.8-2.4)
Dust, <i>D pteronyssinus</i>	1.15	(0.9-1.5)	1.14	(0.9-1.5)	1.25	(0.7-2.3)
Mouse	1.03	(0.4-2.9)	1.04	(0.4-2.8)	0.59	(0.1-4.3)
Rat	1.74†	(1.2-2.5)	1.73†	(1.2-2.5)	0.64	(0.2-2.4)
Aspergillus, <i>A fumigatus</i>	1.36	(0.9-2.1)	1.36	(0.9-2.1)	1.18	(0.6-2.4)
Alternaria, <i>A alternata</i>	1.20	(0.8-1.8)	1.22	(0.8-1.8)	1.04	(0.5-2.2)
Cat	1.01	(0.7-1.4)	1.01	(0.8-1.4)	1.50	(0.8-2.7)
Dog	0.92	(0.6-1.4)	0.92	(0.7-1.3)	1.38	(0.6-3.0)
Oak tree	0.92	(0.6-1.3)	0.95	(0.7-1.3)	0.67	(0.3-1.4)
Birch tree	0.91	(0.6-1.4)	0.93	(0.6-1.4)	1.08	(0.6-1.9)
Ragweed	1.00	(0.7-1.4)	1.04	(0.8-1.4)	0.72	(0.4-1.4)
Russian thistle	1.02	(0.5-1.9)	1.06	(0.6-1.8)	0.49	(0.2-1.4)
Rye grass	1.01	(0.7-1.4)	1.04	(0.8-1.4)	0.87	(0.4-1.7)
Bermuda grass	1.00	(0.6-1.8)	1.04	(0.6-1.7)	0.65	(0.3-1.3)

All models adjusted for age, sex, race/ethnicity, poverty income ratio, serum cotinine, and urinary creatinine.

* $P < .05$.† $P < .01$.

significant association between PAHs and sensitization to any of the other allergens (see Table E1 in this article's Online Repository at www.jacionline.org).

In a multivariable analysis, each log-unit increment in $\Sigma_{\text{mol}}\text{PAH}$ was significantly associated with 49% increased odds of sensitization to cockroach, 29% increased odds of sensitization

to *D. farinae*, and 74% increased odds of sensitization to rat urinary protein (Table II). Similar results were found for $\sum_{2\text{mol}}\text{PAH}$. Notably, the number of subjects sensitized to rat urinary protein ($n = 29$ or 1%) was small. No significant associations were found with any of the other allergens or for $\sum_{3,4\text{mol}}\text{PAH}$. We found no significant interaction between urinary PAH and allergen levels on sensitization to cockroach, *D. farinae*, or rat urinary protein (see Table E2 in this article's Online Repository at www.jacionline.org).

Our results expand those of previous analyses in NHANES, in which $\text{PM}_{2.5}$ was associated with sensitization to indoor allergens but not to outdoor allergens⁵ (PAHs are components of $\text{PM}_{2.5}$). In one study, having high urinary PAH metabolites at both ages 5 and 9 years was more significantly associated with cockroach sensitization than having high PAH at either time point,⁶ suggesting that persistent PAH exposure may be particularly relevant to cockroach allergy. Consistent with these results, we found that PAH was significantly associated with cockroach sensitization. In contrast to our results for mouse allergy, urinary PAH metabolites measured at age 5 years were significantly associated with mouse sensitization at age 5 years in a previous study of inner-city children.⁴ This could be explained by differences in the prevalence of sensitization to mouse urinary protein between our study (1%) and that previous report (ie, 14% at age 9 years⁶).

Our data seem driven primarily by naphthalene, which (as in previous studies^{4,7}) comprises the largest average percent of total PAH concentration (see Table E3 in this article's Online Repository at www.jacionline.org). Although using urinary PAH metabolites is beneficial in aggregating exposure from all routes (respiratory, skin, gastrointestinal), specific routes may be more important for allergic sensitization. Naphthalene exposure has been reported to occur almost exclusively by inhalation, with only approximately 2% in the particulate phase.² Thus, vaporous PAH may be more likely to reach the distal airways. An additional limitation of urinary PAH measures is that differences in the metabolism of parent PAH compounds, from intraindividual metabolism differences to intrinsic parent PAH differences, could result in preferential tissue secretion of certain PAHs (eg, higher molecular weight PAHs more excreted in feces^{7,8}). Moreover, air pollution is a heterogeneous mixture, and thus naphthalene may be a surrogate marker of other unmeasured exposures.

The cross-sectional design of our study precludes causal inferences, and the timing of PAH measurements (ie, prenatal vs postnatal) may be important. Perzanowski et al⁹ found that increased prenatal exposure to $\sum_8\text{PAH}$ nonvolatile modified the effect of cockroach allergen on cockroach sensitization in children, particularly in those with null genotype for glutathione S-transferase M1 (GSTM1).⁹ We did not find a significant interaction between postnatal cockroach allergen exposure and urinary PAH metabolites on cockroach sensitization. Although we used a single PAH measurement, estimated to reflect exposure in the previous 24 to 72 hours,⁸ comparison to previous NHANES cycles suggests similar exposure levels across NHANES cohorts (see Table E4 in this article's Online Repository at www.jacionline.org).

In summary, $\sum_{\text{mol}}\text{PAH}$ and $\sum_{2\text{mol}}\text{PAH}$ were associated with cockroach, dust mite, and rat sensitization in a large US representative sample. Given the ubiquity of PAHs and the importance of allergic sensitization in atopic diseases, our findings are highly relevant to public health and should further encourage investigation into molecular mechanisms and

environmental exposure routes, as well as policies aimed at promoting clean air in the United States and worldwide.

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REFERENCES

1. Salo PM, Arbes SJ Jr, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. *J Allergy Clin Immunol* 2014;134:350-9.
2. Kim KH, Jahan SA, Kabir E, Brown RJ. A review of airborne polycyclic aromatic hydrocarbons (PAHs) and their human health effects. *Environ Int* 2013;60:71-80.
3. Saxon A, Diaz-Sanchez D. Air pollution and allergy: you are what you breathe. *Nat Immunol* 2005;6:223-6.
4. Miller RL, Garfinkel R, Lendor C, Hoepner L, Li Z, Romanoff L, et al. Polycyclic aromatic hydrocarbon metabolite levels and pediatric allergy and asthma in an inner-city cohort. *Pediatr Allergy Immunol* 2010;21:260-7.
5. Weir CH, Yeatts KB, Sarnat JA, Vizuete W, Salo PM, Jaramillo R, et al. Nitrogen dioxide and allergic sensitization in the 2005-2006 National Health and Nutrition Examination Survey. *Respir Med* 2013;107:1763-72.
6. Jung KH, Lovinsky-Desir S, Perzanowski M, Liu X, Maher C, Gil E, et al. Repeatedly high polycyclic aromatic hydrocarbon exposure and cockroach sensitization among inner-city children. *Environ Res* 2015;140:649-56.
7. Li Z, Sandau CD, Romanoff LC, Caudill SP, Sjodin A, Needham LL, et al. Concentration and profile of 22 urinary polycyclic aromatic hydrocarbon metabolites in the US population. *Environ Res* 2008;107:320-31.
8. Strickland P, Kang D, Sithisarankul P. Polycyclic aromatic hydrocarbon metabolites in urine as biomarkers of exposure and effect. *Environ Health Perspect* 1996;104:927-32.
9. Perzanowski MS, Chew GL, Divjan A, Jung KH, Ridder R, Tang D, et al. Early-life cockroach allergen and polycyclic aromatic hydrocarbon exposures predict cockroach sensitization among inner-city children. *J Allergy Clin Immunol* 2013;131:886-93.

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Relations between epidermal barrier dysregulation and *Staphylococcus* species-dominated microbiome dysbiosis in patients with atopic dermatitis



To the Editor:

Atopic dermatitis (AD) is an inflammatory skin disease that affects 25% of children and 10% of adults,¹ with an increasing prevalence in industrialized countries and a higher risk of allergic rhinitis and asthma later in life.² Genetic factors, such as filaggrin-null mutations, as well as environmental factors,

METHODS

Study population

NHANES 2005-2006 is a cross-sectional nationwide survey representative of the US noninstitutionalized, civilian population. To provide reliable estimates, certain groups such as non-Hispanic blacks, Mexican Americans, adolescents, older adults (≥ 60 years), and persons with low income are oversampled. The survey was conducted using a complex, multistage, clustered, and stratified probability sample design of approximately 10,000 persons.

PAH exposure

Ten monohydroxy urinary PAH analytes (1-hydroxynaphthalene, 2-hydroxynaphthalene, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene, 4-hydroxyphenanthrene, 1-hydroxypyrene) were measured in a randomly sampled subpopulation, aged 6 years and older ($n = 2638$; 2593 with positive weights), via capillary gas chromatography combined with high-resolution mass spectrometry and were reported as ng/L urine. For each analyte, values below the lower limit of detection (LLD) were assigned the LLD divided by the square root of 2. Geometric means were calculated for each metabolite, as previously described.^{E1} Each analyte was converted to molecular weight.^{E2} In addition, on the basis of previous analyses^{E2,E3} and calculated spearman correlation coefficients for the PAH analytes (Fig E1), we created 3 variables: summation of molecular weight of all 10 PAH metabolites ($\sum_{\text{mol}} \text{PAH}$); summation of molecular weight of 2-ring naphthalene metabolites ($\sum_{2\text{mol}} \text{PAH}$); and summation of molecular weight for 3-ring (fluorene and phenanthrene) and 4-ring (pyrene) PAH metabolites ($\sum_{3,4\text{mol}} \text{PAH}$). Variables were log10-transformed for analyses. Variation in urine dilution was adjusted for by including urinary creatinine in models as a separate covariate, as previously described.^{E2,E4,E5}

Allergic sensitization

IgE level to each of 15 aeroallergens (*Alternaria alternata*, *Aspergillus fumigatus*, Bermuda grass, common silver birch, cat dander, German cockroach [*Blattella germanica*], dog dander, household dust mite [*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*], mouse urinary protein, oak, common ragweed, rat urinary protein, Russian thistle, and rye grass) was measured in serum using the Pharmacia Diagnostics ImmunoCAP 1000 System (Pharmacia, Uppsala, Sweden). For each allergen, an IgE was considered positive if greater than or equal to 0.35 kU/L.

Informed consent was obtained from all study participants. NHANES was approved by the Institutional Review Board of the National Center for Health Statistics of the Centers for Disease Control and Prevention. Data from the survey and operation details are publicly available from the Centers for Disease Control and Prevention at <https://www.cdc.gov/nchs/nhanes/htm>.

Statistical analysis

To account for the complex sample design, sampling weights, stratification, and clusters were used for data analyses. Spearman rank

correlation coefficients were obtained for urinary PAH metabolites (Fig E1). Urinary PAH metabolites, including summation molecular weight variables, were log10-transformed for analyses. Difference in means between sensitized and nonsensitized subjects were assessed via proc surveyreg between log10-transformed molecular weight PAH. The differences are reported as differences in geometric means between those sensitized and unsensitized for each specific allergen. Logistic regression was used for the multivariable analysis of urinary PAHs and each allergen-specific IgE. All models were adjusted for age, sex, race/ethnicity (as Hispanic, non-Hispanic black, non-Hispanic white, and others), poverty income ratio (≤ 1 vs >1), serum cotinine (in ng/mL), and urinary creatinine (in mg/dL).

Previous findings suggest that urinary PAHs modify the estimated effect of an indoor allergen on allergic sensitization (ie, urinary PAH may interact with cockroach allergen on the development of cockroach sensitization).^{E3} Thus, for each urinary PAH significantly associated with sensitization to a particular allergen, we conducted an exploratory analysis of interaction between such urinary PAH and dust levels of the corresponding indoor allergen (collected from the participants' bed and bedroom floor). SAS version 9.4 (SAS Institute, Inc, Cary, NC) and SAS SURVEY procedures were used for data analysis. We set α at 0.05 given *a priori* associations of PAH and allergic sensitization, and elected against Bonferroni corrections given that allergens and PAH are correlated (ie, dependent).

REFERENCES

- E1. Grainger J, Huang W, Patterson DG Jr, Turner WE, Pirkle J, Caudill SP, et al. Reference range levels of polycyclic aromatic hydrocarbons in the US population by measurement of urinary monohydroxy metabolites. *Environ Res* 2006;100:394-423.
- E2. Scinicariello F, Buser MC. Urinary polycyclic aromatic hydrocarbons and childhood obesity: NHANES (2001-2006). *Environ Health Perspect* 2014;122:299-303.
- E3. Perzanowski MS, Chew GL, Divjan A, Jung KH, Ridder R, Tang D, et al. Early-life cockroach allergen and polycyclic aromatic hydrocarbon exposures predict cockroach sensitization among inner-city children. *J Allergy Clin Immunol* 2013;131:886-93.
- E4. Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham LL, Pirkle JL. Urinary creatinine concentrations in the U.S. population: implications for urinary biologic monitoring measurements. *Environ Health Perspect* 2005;113:192-200.
- E5. Peters KO, Williams AL, Abubaker S, Curtin-Brosnan J, McCormack MC, Peng R, et al. Predictors of polycyclic aromatic hydrocarbon exposure and internal dose in inner city Baltimore children. *J Expo Sci Environ Epidemiol* 2017;27:290-8.
- E6. Centers for Disease Control and Prevention. Fourth report on human exposure to environmental chemicals. Atlanta, GA: U.S. Department of Health and Human Services; 2009.
- E7. Li Z, Sandau CD, Romanoff LC, Caudill SP, Sjodin A, Needham LL, et al. Concentration and profile of 22 urinary polycyclic aromatic hydrocarbon metabolites in the US population. *Environ Res* 2008;107:320-31.

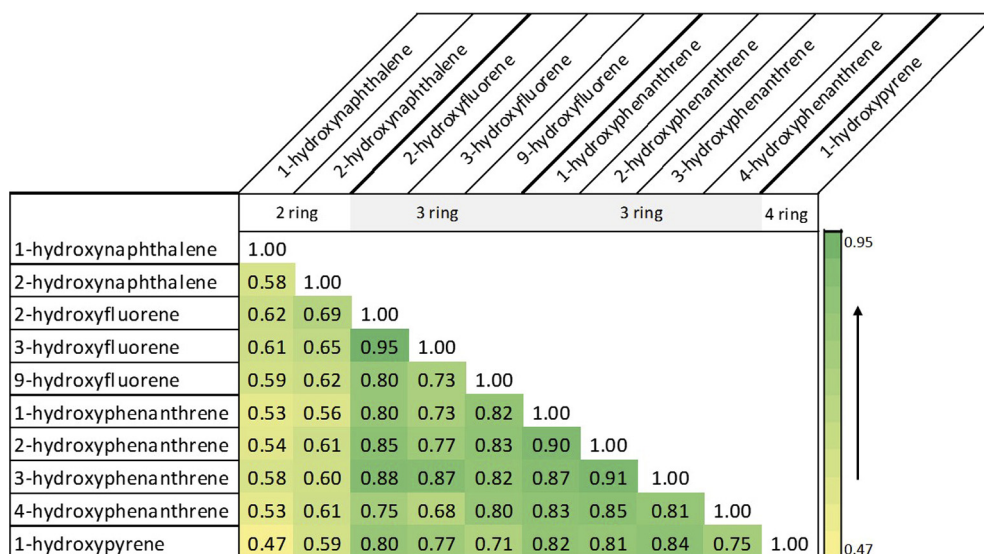


FIG E1. Spearman correlation coefficients for urinary PAH metabolites in NHANES 2005-2006. All *P* values are less than .001. Correlations are colored on the basis of strength of correlation, from yellow (lowest correlation of $r = 0.47$) to green (highest correlation of $r = 0.95$).

TABLE E1. Comparison of mean urinary PAHs between subjects with and without allergic sensitization to select aeroallergens in NHANES 2005-2006, ages 6-85+ years

Allergic sensitization	$\sum_{\text{mol}} \text{PAH}$		$\sum_{2\text{mol}} \text{PAH}$		$\sum_{3,4\text{mol}} \text{PAH}$	
	Difference	P value	Difference	P value	Difference	P value
Cockroach	4142	.008	3631	.005	311	.03
Dust, <i>D. farinae</i>	2164	.03	1862	.03	266	.08
Dust, <i>D. pteronyssius</i>	1210	.17	1033	.16	188	.19
Mouse	-3162	.23	-2825	.22	-318	.29
Rat	8502	.005	7782	.005	295	.45
Aspergillus, <i>A. fumigatus</i>	2301	.13	1990	.12	302	.11
Alternaria, <i>A. alternata</i>	1715	.16	1600	.13	246	.12
Cat	819	.56	648	.55	244	.15
Dog	89	.99	-3	1.0	203	.27
Oak tree	-1406	.17	-1090	.18	-144	.24
Birch tree	-1209	.26	-1040	.28	-6	.89
Ragweed	-239	.86	0	1.00	-28	.83
Russian thistle	-434	.83	-188	.89	-141	.45
Rye grass	-231	.83	-96	.91	23	.86
Bermuda grass	215	.85	342	.77	-19	.87

Difference (mean positive sensitization - mean negative sensitization) expressed as difference in geometric means. For each allergen, sensitization is defined as serum-specific IgE ≥ 0.35 kU/L. P value obtained via proc surveyreg of molecular weight means, boldface numbers with P value $<.05$.

TABLE E2. Multivariable analysis of $\sum_{\text{mol}}\text{PAH}$ and allergic sensitization, with additional adjustment for house dust allergen levels

Allergic sensitization	Model 1	Model 2
Cockroach		
$\sum_{\text{mol}}\text{PAH}$	1.49* (1.09-2.03)	1.58* (1.08-2.32)
Indoor dust allergen: Bla g 1		2.48* (1.05-5.82)
Dust mite (Der f 1)		
$\sum_{\text{mol}}\text{PAH}$	1.29* (1.01-1.65)	1.24 (0.93-1.65)
Indoor dust allergen: Der f 1		1.001 (1.00-1.00)
Rat		
$\sum_{\text{mol}}\text{PAH}$	1.74† (1.22-2.47)	1.67* (1.09-2.52)
Indoor dust allergen: Rat n 1		0.994 (0.82-1.20)

Results displayed as odds ratio (95% CI). All models adjusted for age, sex, race/ethnicity, poverty income ratio, serum cotinine, and urinary creatinine.

* $P < .05$.

† $P < .01$.

TABLE E3. Mean percent, by molecular weight, of urinary PAH metabolite group by total mean molecular weight in NHANES 2005-2006

Urinary PAH metabolite	% Mean molecular weight*
∑naphthalene	89.7 ± 0.4
∑fluorene	4.1 ± 0.2
∑phenanthrene	5.0 ± 0.2
Pyrene	1.3 ± 0.1

* $\sum$ molecular weight for metabolite group/ $\sum$ all 10 PAH metabolites molecular weight $\times$ 100; means calculated using survey sample weights.

TABLE E4. Comparison between geometric means (95% CI) of polycyclic aromatic hydrocarbon urinary monohydroxyl metabolites (ng/L) in persons aged 6 years and older in our current study compared with previous studies/NHANES cycles

PAH urinary monohydroxyl metabolite	2005-2006 [*]	2003-2004 ^{E6}	2001-2002 ^{E7}	1999-2000 ^{E1}
1-Hydroxynaphthalene	2641 (2388-2922)	2680 (2360-3050)	2050 (1790-2340)	—
2-Hydroxynaphthalene	3626 (3351-3923)	3180 (2760-3670)	2470 (2110-2890)	—
2-Hydroxyfluorene	316 (297-338)	304 (262-354)	318 (277-366)	441 (330-590)
3-Hydroxyfluorene	124 (115-134)	126 (108-148)	134 (115-155)	408 (302-551)
9-Hydroxyfluorene	308 (289-328)	267 (234-305)	219 (191-251)	—
1-Hydroxyphenanthrene	152 (143-161)	156 (140-173)	140 (125-158)	154 (128-186)
2-Hydroxyphenanthrene	65 (61-70)	59 (53-67)	54 (46-64)	98.4 (83-117)
3-Hydroxyphenanthrene	103 (96-109)	115 (104-128)	105 (93-118)	127 (112-144)
4-Hydroxyphenanthrene	29 (26-32)	25 (23-28)	42 (31-56)	—
1-Hydroxypyrene	98 (91-106)	89 (80-100)	50 (43-57)	79.8 (69-92)

^{*}Current study.