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## Supplemental Material

# House Dust Endotoxin and Peripheral Leukocyte Counts: Results from Two Large Epidemiologic Studies

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**Table S1. Characteristics of the NHANES 2005-2006 study population.**

	Unweighted total N	Weighted %/Mean (SE)
Age (Years)	6,254	37.69 (0.60)
1-5	704	5.7 (0.4)
6-19	2,321	19.1 (0.6)
20-39	1,268	28.1 (0.8)
40-59	968	29.8 (1.3)
60+	993	17.4 (1.4)
Gender		
Male	3,084	48.7 (0.7)
Female	3,170	51.3 (0.7)
Race/Ethnicity		
Non-Hispanic White	2,293	68.9 (2.6)
Non-Hispanic Black	1,724	11.9 (1.8)
Mexican American	1,732	9.4 (1.2)
Other	505	9.8 (1.3)
PIR		
Low (PIR $\leq$ 1.3)	2,174	21.7 (1.6)
Medium (1.3 < PIR $\leq$ 3.5)	2,357	40.6 (1.4)
High (PIR > 3.5)	1,456	37.7 (2.5)
BMI		
Underweight (BMI < 18.5)	1,181	12.4 (0.5)
Normal (18.5 $\leq$ BMI < 25)	1,963	31.9 (1.0)
Overweight (25 $\leq$ BMI < 30)	1,419	26.4 (0.6)
Obese (BMI $\geq$ 30)	1,451	29.3 (1.2)
Smoking Status <sup>a</sup>		
Current	769	25.9 (1.5)
Past	806	25.3 (0.9)
Never	1,652	48.8 (1.6)
Current Asthma		
Yes	573	8.9 (0.6)
No	5,660	91.1 (0.6)
COPD		
Yes	280	7.5 (0.4)
No	5,974	92.5 (0.4)
Anti-inflammatory Medication		
Yes	436	8.4 (0.5)
No	5,818	91.6 (0.5)
Atopic <sup>b</sup>		
Yes	2,888	44.5 (1.0)
No	3,134	55.5 (1.0)
WBC (1,000/uL)	6,254	7.43 (0.05)
Monocytes (1,000/uL)	6,235	0.58 (0.01)
Lymphocytes (1,000/uL)	6,235	2.34 (0.03)
Basophils (1,000/uL)	6,235	0.04 (0.00)
Eosinophils (1,000/uL)	6,235	0.22 (0.00)
Neutrophils (1,000/uL)	6,235	4.24 (0.05)
C-reactive protein (mg/dL) <sup>d</sup>	6,077	0.14 (0.01)
Cotinine (ng/mL) <sup>c</sup>	5,764	57.74 (2.85)

BMI = body mass index; COPD = chronic obstructive pulmonary disease; PIR = poverty-to-income ratio; WBC = white blood cells.

<sup>a</sup> Only available for participants aged 20 years or above.

<sup>b</sup> Sensitized to at least 1 allergen-specific IgE.

<sup>c</sup> Only available for participants aged 3 years or above.

<sup>d</sup> Median CRP displayed in place of mean due to non-normality.

**Table S2. Bivariate analysis of total leukocyte and serum C-reactive protein levels in participant subgroups in NHANES 2005-2006 study population.**

Outcome	Subsample	N	Mean	SE	P-value <sup>a</sup>
WBC (1000/uL)	COPD	280	8.044	0.114	<.001
	Non-COPD	5,974	7.379	0.054	
	Current Asthma	573	7.407	0.161	0.87
	No Current Asthma	5,660	7.429	0.048	
	Current Smokers	769	8.251	0.107	<.001
	Former Smokers	806	7.150	0.128	
	Never Smokers	1,652	7.153	0.073	
	Cotinine < 10 ng/mL	4,665	7.138	0.050	<.001
	Cotinine ≥ 10 ng/mL	1,099	8.097	0.100	
	Atopic	2,888	7.389	0.081	0.57
	Non-Atopic	3,134	7.441	0.058	
	C-reactive Protein <sup>b</sup> (mg/dl)	COPD	281	0.395	0.059
Non-COPD		5,814	0.131	0.008	
Current Asthma		559	0.216	0.022	<.001
No Current Asthma		5,515	0.136	0.008	
Current Smokers		769	0.218	0.012	0.56
Former Smokers		804	0.181	0.020	
Never Smokers		1,645	0.192	0.010	
Cotinine < 10 ng/mL		4,674	0.133	0.006	<.001
Cotinine ≥ 10 ng/mL		1,102	0.185	0.015	
Atopic		2,862	0.141	0.010	0.62
Non-Atopic		3,086	0.141	0.014	

COPD = chronic obstructive pulmonary disease

<sup>a</sup>P-values compare mean biomarker levels across subsamples and are calculated using Wald's F-test.

<sup>b</sup>Median C-reactive protein displayed in place of mean due to non-normality. P-values use Log<sub>10</sub> transformed values to compare groups.

**Table S3. Bivariate analysis of absolute counts of leukocyte subtypes within participant subgroups in NHANES 2005-2006 study population.**

Absolute cell count	Subsample	N	Mean	SE	P-value <sup>a</sup>
Monocytes (1,000/uL)	COPD	279	0.609	0.019	0.03
	Non-COPD	5,956	0.573	0.007	
	Current Asthma	571	0.578	0.015	0.84
	No Current Asthma	5,643	0.576	0.007	
	Current Smokers	766	0.603	0.010	<.001
	Former Smokers	802	0.570	0.012	
	Never Smokers	1,640	0.547	0.009	
	Cotinine < 10 ng/mL	4,651	0.563	0.008	<.001
	Cotinine ≥ 10 ng/mL	1,094	0.596	0.010	
	Atopic	2,879	0.573	0.009	0.41
Non-Atopic	3,126	0.579	0.008		
Lymphocytes (1,000/uL)	COPD	279	2.167	0.037	<.001
	Non-COPD	5,956	2.356	0.031	
	Current Asthma	571	2.304	0.061	0.45
	No Current Asthma	5,643	2.346	0.030	
	Current Smokers	766	2.402	0.023	<.001
	Former Smokers	802	2.067	0.075	
	Never Smokers	1,640	2.143	0.057	
	Cotinine < 10 ng/mL	4,651	2.250	0.037	0.008
	Cotinine ≥ 10 ng/mL	1,094	2.366	0.021	
	Atopic	2,879	2.288	0.026	0.17
Non-Atopic	3,126	2.368	0.052		
Eosinophils (1,000/uL)	COPD	279	0.248	0.009	0.007
	Non-COPD	5,956	0.221	0.004	
	Current Asthma	571	0.294	0.016	<.001
	No Current Asthma	5,643	0.215	0.003	
	Current Smokers	766	0.236	0.006	<.001
	Former Smokers	802	0.212	0.006	
	Never Smokers	1,640	0.204	0.003	
	Cotinine < 10 ng/mL	4,651	0.215	0.003	<.001
	Cotinine ≥ 10 ng/mL	1,094	0.239	0.007	
	Atopic	2,879	0.256	0.006	<.001
Non-Atopic	3,126	0.197	0.004		
Basophils (1,000/uL)	COPD	279	0.050	0.005	0.049
	Non-COPD	5,956	0.042	0.002	

	Current Asthma	571	0.046	0.004	0.25
	No Current Asthma	5,643	0.042	0.002	
	Current Smokers	766	0.049	0.003	0.01
	Former Smokers	802	0.037	0.004	
	Never Smokers	1,640	0.040	0.003	
	Cotinine < 10 ng/mL	4,651	0.039	0.002	0.002
	Cotinine ≥ 10 ng/mL	1,094	0.047	0.002	
	Atopic	2,879	0.042	0.002	0.86
	Non-Atopic	3,126	0.042	0.002	
Neutrophils (1,000/uL)	COPD	279	4.974	0.102	<.001
	Non-COPD	5,956	4.181	0.049	
	Current Asthma	571	4.184	0.113	0.54
	No Current Asthma	5,643	4.244	0.045	
	Current Smokers	766	4.958	0.087	<.001
	Former Smokers	802	4.252	0.088	
	Never Smokers	1,640	4.217	0.043	
	Cotinine < 10 ng/mL	4,651	4.065	0.040	<.001
	Cotinine ≥ 10 ng/mL	1,094	4.846	0.081	
	Atopic	2,879	4.228	0.059	0.73
	Non-Atopic	3,126	4.249	0.052	

COPD = chronic obstructive pulmonary disease.

<sup>a</sup> P-values compare mean biomarker levels across subsamples and are calculated using Wald's F-test.

**Table S4. Sensitivity analysis of the change in leukocytes and serum C-reactive protein associated with a 10-fold increase in house dust endotoxin concentration in NHANES 2005-2006 study population.<sup>a</sup>**

Participant Subgroup	White Blood Cells (1000/uL)				C-reactive Protein <sup>e</sup>				
	N	$\beta$	SE	P-value	N	$\beta$	SE	10 <sup><math>\beta</math></sup>	P-value
Overall	5,080	0.175	0.050	0.003	5,092	0.024	0.017	1.056	0.17
COPD									
Yes	203	-0.002	0.437	0.997	204	0.114	0.064	1.300	0.10
No	4,877	0.176	0.054	0.005	4,888	0.016	0.018	1.037	0.40
Atopy <sup>b</sup>									
Yes	2,414	0.222	0.095	0.03	2,421	0.030	0.020	1.070	0.16
Yes	2,556	0.138	0.057	0.03	2,561	0.020	0.028	1.048	0.48
Current asthma									
Yes	400	0.257	0.267	0.35	401	0.083	0.044	1.211	0.08
No <sup>c</sup>	4,665	0.171	0.041	0.001	4,676	0.016	0.019	1.036	0.42
Current asthma type <sup>d</sup>									
Atopic	268	0.352	0.307	0.27	269	0.042	0.055	1.102	0.46
Non-atopic	122	0.119	0.282	0.68	122	0.116	0.080	1.305	0.17
No asthma	4,566	0.167	0.041	0.001	4,577	0.018	0.021	1.042	0.40
Wheeze									
Atopic	350	0.348	0.164	0.05	350	0.051	0.060	1.124	0.41
Non-atopic	247	0.462	0.296	0.14	247	0.208	0.054	1.614	0.002
No wheeze	4,372	0.126	0.053	0.03	4,384	0.008	0.023	1.019	0.72

COPD = chronic obstructive pulmonary disease.

<sup>a</sup> Adjusted for age, gender, race/ethnicity, cotinine, PIR, and BMI. Overall data includes participants with missing stratification status.

<sup>b</sup> Sensitized to at least 1 allergen-specific IgE.

<sup>c</sup> Includes participants who either answered 'no' to doctor-diagnosed asthma, or who answered 'yes' to doctor-diagnosed asthma but 'no' to 'Do you still have asthma?'

<sup>d</sup> Captures the same participants as the 'Current asthma' categorization above with the exception that it only includes participants with non-missing data for atopic status.

<sup>e</sup> Linear analysis performed on Log<sub>10</sub> transformed C-reactive protein values (raw values in mg/dl). 10 <sup>$\beta$</sup>  represents expected ratio increase in C-reactive protein for every 10-fold increase in HDE concentration.

**Table S5. Linear regression of the change in white blood cells and serum C-reactive protein associated with a 10-fold increase in house dust endotoxin concentration within demographic strata in NHANES 2005-2006 study population.<sup>a</sup>**

Participant Subgroup	White Blood Cells (1000/uL)					C-reactive Protein <sup>b</sup>					
	N	$\beta$	SE	P-value	Interaction P-value <sup>a</sup>	N	$\beta$	SE	$10^\beta$	P-value	Interaction P-value <sup>a</sup>
Juveniles	2,077	0.178	0.145	0.2388	0.71	2,081	0.034	0.037	1.081	0.3760	0.40
Adults	3,397	0.177	0.062	0.0119		3,405	0.038	0.021	1.093	0.0876	
Females	2,770	0.116	0.066	0.0988	0.47	2,775	0.026	0.028	1.061	0.3622	0.86
Males	2,704	0.242	0.108	0.0407		2,711	0.031	0.023	1.074	0.1917	
Mexican Americans	1,424	0.066	0.112	0.5631	0.60	1,425	-0.015	0.036	0.967	0.6921	0.67
Non-Hispanic Blacks	1,535	0.052	0.094	0.5899		1,536	0.011	0.026	1.026	0.6663	
Non-Hispanic Whites	2,069	0.233	0.078	0.0090		2,079	0.037	0.023	1.089	0.1274	
Other Race	446	0.187	0.155	0.2480		446	0.068	0.047	1.170	0.1677	

<sup>a</sup> P-value of interaction term in non-stratified model.

<sup>b</sup> Linear analysis performed on  $\text{Log}_{10}$  transformed C-reactive protein values (raw values in mg/dl).  $10^\beta$  represents expected ratio increase in C-reactive protein for every 10-fold increase in household dust endotoxin concentration.



**Table S6. Linear regression of the change in count of leukocyte subtypes associated with a 10-fold increase in house dust endotoxin within demographic strata in NHANES 2005-2006 study population.**

Outcome	Subsample	N	$\beta$	SE	P-value	Interaction P-value <sup>a</sup>
Monocyte Count (1,000/ $\mu$ L)	Juveniles	2,077	0.011	0.010	0.31	0.049
	Adults	3,380	0.013	0.006	0.04	
	Females	2,755	0.017	0.004	0.001	0.61
	Males	2,702	0.015	0.008	0.08	
	Mexican Americans	1,422	0.007	0.009	0.44	0.94
	Non-Hispanic Blacks	1,527	0.010	0.009	0.27	
	Non-Hispanic Whites	2,066	0.016	0.006	0.02	
	Other Race	442	0.031	0.015	0.05	
Lymphocyte Count (1,000/ $\mu$ L)	Juveniles	2,077	0.061	0.073	0.41	0.13
	Adults	3,380	0.047	0.026	0.10	
	Females	2,755	0.061	0.033	0.09	0.41
	Males	2,702	0.086	0.023	0.002	
	Mexican Americans	1,422	0.011	0.036	0.76	0.21
	Non-Hispanic Blacks	1,527	0.026	0.028	0.37	
	Non-Hispanic Whites	2,066	0.093	0.032	0.01	
	Other Race	442	0.020	0.068	0.77	
Eosinophil Count (1,000/ $\mu$ L)	Juveniles	2,077	0.017	0.019	0.39	0.09
	Adults	3,380	0.001	0.007	0.90	
	Females	2,755	0.011	0.004	0.01	0.64
	Males	2,702	0.001	0.012	0.91	
	Mexican Americans	1,422	0.015	0.012	0.23	0.86
	Non-Hispanic Blacks	1,527	0.008	0.005	0.13	
	Non-Hispanic Whites	2,066	0.006	0.009	0.49	
	Other Race	442	-0.005	0.018	0.79	
Basophil Count (1,000/ $\mu$ L)	Juveniles	2,077	-0.002	0.004	0.66	0.37
	Adults	3,380	0.0002	0.002	0.94	
	Females	2,755	-0.001	0.002	0.75	0.76
	Males	2,702	0.0003	0.003	0.93	
	Mexican Americans	1,422	0.002	0.003	0.59	0.70
	Non-Hispanic Blacks	1,527	-0.004	0.003	0.20	
	Non-Hispanic Whites	2,066	0.0003	0.003	0.92	
	Other Race	442	0.005	0.006	0.47	
Neutrophil Count (1,000/ $\mu$ L)	Juveniles	2,077	0.085	0.084	0.33	0.34
	Adults	3,380	0.121	0.045	0.02	
	Females	2,755	0.034	0.063	0.60	0.50
	Males	2,702	0.140	0.085	0.12	

Mexican Americans	1,422	0.044	0.111	0.70	0.69
Non-Hispanic Blacks	1,527	0.033	0.077	0.68	
Non-Hispanic Whites	2,066	0.116	0.050	0.04	
Other Race	442	0.139	0.103	0.20	

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<sup>a</sup> P-value of interaction term in non-stratified model.

**Table S7. Population characteristics of the Agricultural Lung Health Study subset.**

Characteristic	Overall (N=1708) N (%)	Asthma cases (N=645) N (%)	Non-cases (N=1063) N (%)
<b>Participant Type<sup>a</sup></b>			
Farmer	966 (56.6)	322 (49.9)	644 (60.6)
Spouse	742 (43.4)	323 (50.1)	419 (39.4)
<b>Age (years)</b>			
20-39	16 (0.9)	7 (1.1)	9 (0.8)
40-59	693 (40.6)	268 (41.6)	425 (40.0)
60+	999 (58.5)	370 (57.4)	629 (59.2)
<b>Gender</b>			
Male	938 (54.9)	305 (47.3)	633 (59.5)
Female	770 (45.1)	340 (52.7)	430 (40.5)
<b>State</b>			
Iowa	1178 (70.0)	463 (71.8)	715 (67.3)
North Carolina	530 (30.0)	182 (28.2)	348 (32.7)
<b>Smoking Status</b>			
Never	1086 (64.7)	448 (70.3)	638 (61.2)
Former	504 (30.0)	165 (25.9)	339 (32.5)
Current	89 (5.3)	24 (3.8)	65 (6.2)
Missing	29	8	21
<b>Currently living on farm</b>			
Yes	1301 (77.5)	486 (76.4)	815 (78.2)
No	377 (22.5)	150 (23.6)	227 (21.8)
Missing	30	9	21
<b>Currently farming</b>			
Yes	1009 (60.1)	356 (55.9)	653 (62.6)
No	671 (39.9)	281 (44.1)	390 (37.4)
Missing	28	8	20
<b>Race</b>			
White	1660 (98.3)	628 (98.7)	1032 (98.1)
Black	15 (0.9)	5 (0.8)	10 (1.0)
Other	13 (0.8)	3 (0.5)	10 (1.0)
Missing	20	9	11
<b>BMI</b>			
Underweight (BMI < 18.5)	10 (0.6)	3 (0.5)	7 (0.7)
Normal (18.5 ≤ BMI < 25)	328 (19.2)	94 (14.6)	234 (22.0)
Overweight (18.5 ≤ BMI < 25)	569 (33.3)	194 (30.1)	375 (35.3)
Obese (BMI ≥ 30)	801 (46.9)	354 (54.9)	447 (42.1)
<b>Dust collection season</b>			
Winter	419 (24.5)	136 (21.1)	283 (26.6)
Spring	452 (26.5)	142 (22.0)	310 (29.2)
Summer	463 (27.1)	185 (28.7)	278 (26.2)
Fall	374 (21.9)	182 (28.2)	192 (18.1)

<sup>a</sup> Farmers and spouses do not represent a married pair. Rather, they are farmers or a spouse of a farmer from independent households.

**Table S8. Leukocyte counts for the Agricultural Lung Health Study subset**

Cell Counts (1,000/uL)	Mean (SE)		Mean (SE)
	Combined (N=1708)	Asthma cases (N=645)	Non-cases (N=1063)
WBC (1,000/uL)	6.11 (0.04)	6.22 (0.06)	6.05 (0.05)
Monocytes (1,000/uL)	0.48 (0.01)	0.48 (0.01)	0.48 (0.01)
Lymphocytes (1,000/uL)	2.01 (0.02)	2.01 (0.03)	2.00 (0.02)
Basophils (1,000/uL)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
Eosinophils (1,000/uL)	0.20 (0.004)	0.23 (0.01)	0.18 (0.01)
Neutrophils (1,000/uL)	3.41 (0.03)	3.47 (0.06)	3.37 (0.04)