"Influence of Environmental Factors on Asthma and COPD"

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Disclosures

- Research Funding
  - Environmental Protection Agency
  - NIEHS, NCATS
  - NSF
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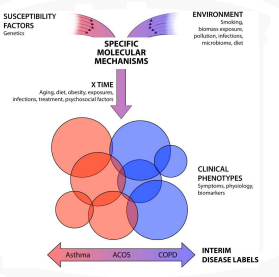
- Other
  - Editor in Chief, Current Allergy and Asthma Reports
  - Associate Editor, JACI
  - Up To Date

Asthma COPD Overlap Syndrome

- Common biological factors/concepts
  - ACOS represents a continuum in airway endotypes ranging from asthma to COPD
  - Tobacco exposure
  - IgE/TH_2 inflammation
  - Bronchial reactivity
- Environmental exposures- "tobacco-like"
  - Smoking
  - Second-hand smoke exposure
  - Particulate matter from biomass use
    - Household Air Pollution
    - Ambient Air PM



Mechanistic basis of immune response to particulate pollutants

Oxidative stress
Innate immune response
Modification of IgE responses

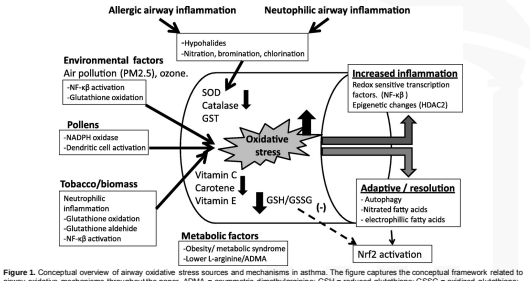
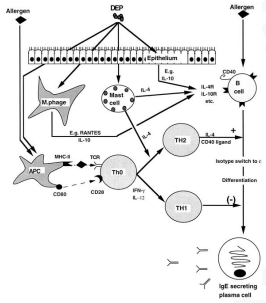


Figure 1. Conceptual overview of airway oxidative stress sources and mechanisms in asthma. The figure captures the conceptual framework related to airway oxidative mechanisms throughout the paper. ADMA = asymmetric dimethylarginine; GSH = reduced glutathione; GSSG = oxidized glutathione; HDAC2 = histone deacetylase–2; NADPH = nicotinamide adenine dinucleotide phosphate; NF-κB = nuclear factor κB; Nrf2 = nuclear factor (erythroid-derived 2)-like 2; PM2.5 = particulate matter < 2.5 μm; SOD = superoxide dismutase.

Annals ATS, 2013
http://www.atsjournals.org/doi/abs/10.1513/AnnalsATS.201305-116AW
Published in: Fernando Holguin; Annals ATS 10, S150-S157.
DOI: 10.1513/AnnalsATS.201305-116AW

Oxidative Stress Mechanisms by which PM, ETS and Biomass impact IgE production



- Initial studies show that DEP associated with IgE production
- Experimental evidence indicates that DEP related ROS from particles drive isotype switch towards IgE
- ROS derives from organic oxidants derived from polyaromatic hydrocarbons
- PAHs and related agents found in most particles produced by low combustion of organic matter-**diesel, tobacco smoke, biomass fuel use**

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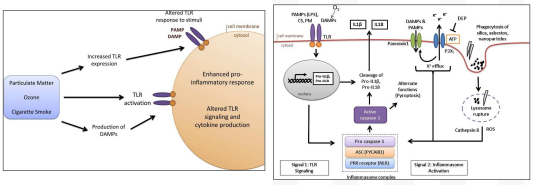
Innate Immune Responses to Environmental Agents



Source: Journal of Allergy and Clinical Immunology 2012; 129:14-24 (DOI:10.1016/j.jaci.2011.11.004)

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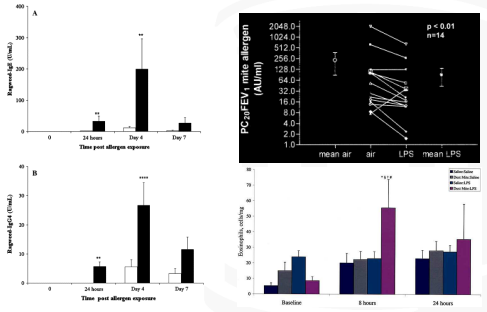
PM exposure enhances response to inhaled allergens

(diesel exhaust to the left, LPS to the right)



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Epidemiological evidence of PM influence in airway disease

Tobacco smoke

Particulate matter

Household air pollution

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Coogan, PF et al "Active and Passive Smoking and the Incidence of Asthma in the Black Women's Health Study", American Journal of Respiratory and Critical Care Medicine, Vol. 191, No. 2 (2015), pp. 168-176.

Table 2. Smoking Status and Incidence of Asthma, Black Women's Health Study, 1995–2011

Smoking Status	Cases	Person-Years	Basic Model (Age and Questionnaire Cycle) [*HR (95% CI)*]	Multivariable Model [*HR (95% CI)*]*
Never active or passive	142	84,071	1.0	1.0
Passive only	677	284,103	1.36 (1.13–1.63)	1.21 (1.00–1.45)
Exposed before age 20 only	225	105,193	1.26 (1.02–1.56)	1.17 (0.94–1.45)
Exposed at age 20 or older only	180	72,745	1.39 (1.11–1.74)	1.24 (0.99–1.56)
Exposed before and after 20	272	106,165	1.43 (1.16–1.75)	1.18 (0.96–1.46)
Former smoker	423	139,885	1.71 (1.41–2.08)	1.36 (1.11–1.67)
Current smoker	281	85,741	1.72 (1.40–2.11)	1.43 (1.15–1.77)

Am J Respir Crit Care Med, 2015 http://www.atsjournals.org/doi/abs/10.1164/rccm.201406-1108OC
Published in: Patricia F. Coogan; Nelsy Castro-Webb; Jeffrey Yu; George T. O'Connor; Julie R. Palmer; Lynn Rosenberg; *Am J Respir Crit Care Med* 191, 168-176.
DOI: 10.1164/rccm.201406-1108OC

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Association between Residential Proximity to Fuel-Fired Power Plants and Hospitalization Rate for Respiratory Diseases

Liu X, Lessner L, and Carpenter DO; Environmental Health Perspectives 120(6), 2012

Table 2. Crude hospital discharge rates for asthma, ARI, and COPD according to age and exposure after excluding extremes of MHI status.

		Hospital discharge rate per 100,000 (95% CI)		
Exposure	Person-years	Asthma	ARI	COPD
Age < 10 years				
Clean	8,661,904	359 (355, 363)	404 (400, 409)	
Fuel only	567,857	381 (365, 397)	414 (397, 431)	
Waste only	8,939,610	452 (448, 457)	474 (470, 479)	
Fuel and waste	3,355,019	509 (501, 517)	551 (544, 559)	
Age ≥ 10 years				
Clean	56,609,900	512 (510, 513)	147 (146, 148)	1,222 (1,219, 1,225)
Fuel only	3,962,094	570 (563, 578)	154 (151, 158)	1,390 (1,379, 1,402)
Waste only	60,539,925	589 (597, 601)	169 (168, 170)	1,401 (1,398, 1,404)
Fuel and waste	21,653,627	672 (669, 676)	192 (191, 194)	1,627 (1,622, 1,633)

Table 3. Adjusted RRs of hospital discharge for asthma, ARI, and COPD as a function of residence in ZIP codes with different exposure status.

	Asthma				ARI				COPD	
	Age < 10 years		Age ≥ 10 years		Age < 10 years		Age ≥ 10 years		Age ≥ 10 years	
Exposure	RR (95% CI)	*p*-Value	RR (95% CI)	*p*-Value	RR (95% CI)	*p*-Value	RR (95% CI)	*p*-Value	RR (95% CI)	*p*-Value
Clean	1.00		1.00		1.00		1.00		1.00	
Fuel only	1.01 (0.91, 1.12)	0.85	1.11 (1.02, 1.20)	0.01	1.03 (0.93, 1.14)	0.56	1.15 (1.05, 1.27)	0.003	1.17 (1.06, 1.29)	0.002
Waste only	1.11 (1.03, 1.19)	0.005	1.07 (1.00, 1.14)	0.04	1.13 (1.05, 1.21)	0.001	1.09 (1.02, 1.17)	0.01	1.16 (1.08, 1.26)	0.0001
Fuel and waste	1.19 (1.11, 1.28)	< 0.0001	1.18 (1.11, 1.26)	< 0.0001	1.24 (1.15, 1.33)	< 0.0001	1.21 (1.13, 1.30)	< 0.0001	1.26 (1.17, 1.37)	< 0.0001

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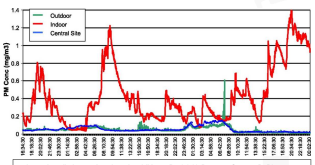
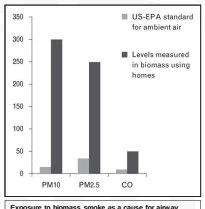
Indoor PM exposure in the US and where biomass is used



Indoor Air Pollution and Asthma in Children. Patrick N. Breysse; Gregory B. Diette; Elizabeth C. Matsui; Arlene M. Butz; Nadia N. Hansel; Meredith C. McCormack. *Proc Am Thorac Soc.* **2010,** 7, 102-106.

Figure 1. Comparison of particulate matter (PM) concentrations simultaneously measured indoors, immediately outdoors, and at a central monitoring site.



Exposure to biomass smoke as a cause for airway disease in women and children. Kodgule, Rahul; Salvi, Sundeep. Current Opinion in Allergy & Clinical Immunology. 12(1):82-90, February 2012.

Figure 3. Comparison of US-EPA standard for ambient air and levels measured air in homes exposed to biomass smoke PM10, PM2.5 and CO. Levels expressed as mcg/m3 x 10 for PM10, mcg/m3 for PM2.5 and ppm for CO.

Exposure to Household Air Pollution and Lower Respiratory Tract Infection

Smith KR, et al, Lancet. 2011 Nov 12;378(9804):1717-26

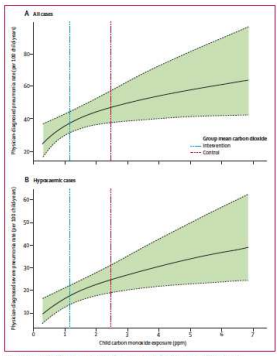
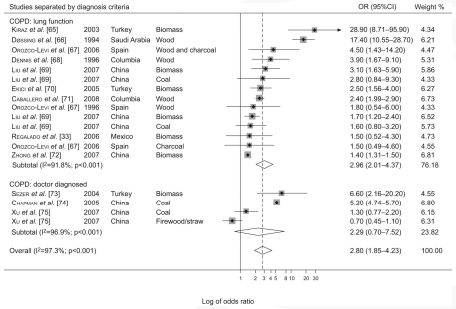


Figure 4: Exposure-response for personal carbon monoxide concentrations in study children for physician-diagnosed pneumonia (A) and physician-diagnosed severe (hypoxaemic) pneumonia (B)

Forest plot showing risk of chronic obstructive pulmonary disease (COPD) in populations exposed to solid fuel smoke.



Om P. Kurmi et al. Eur Respir J 2012;40:239-254

Summary of Epidemiology

- Particulate matter from organic biomass burning similar across several sources
  - Low temperature combustion with polyaromatic hydrocarbons
  - Endotoxins
  - Similar in tobacco smoke, much ambient PM (coal, diesel), and biomass burning
- PM associated with:
  - LRTI
  - COPD
  - Asthma
- Markedly increased levels in indoor environments
  - Seen in US
  - Much greater where biomass is used

Oxidative Stress Genes

GSTM1

Effect of glutathione-S-transferase M1 genotypes on allergen induced responses to diesel exhaust and secondhand smoke

Gilliland FD, Li Y-F, Diaz-Sanchez D. Lancet 2004 (363) 9403, 119-125
Gilliland FD, Li Y-F, Gong H, Diaz-Sanchez D. Am J Respir Crit Care Med 2006, 174, 1335-1341

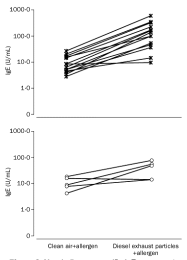


Figure 3. Nasal allergen-specific IgE response to allergens plus clean air and allergen plus diesel exhaust particles for GSTM1 absent (upper) and present (lower) genotypes Y axis is log scale of median IgE concentrations.

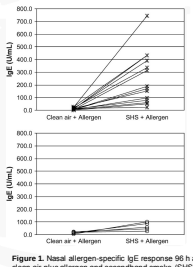
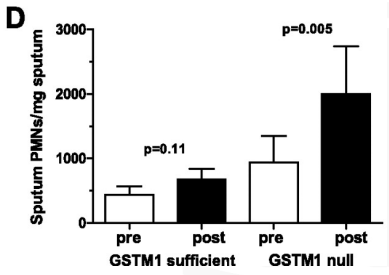


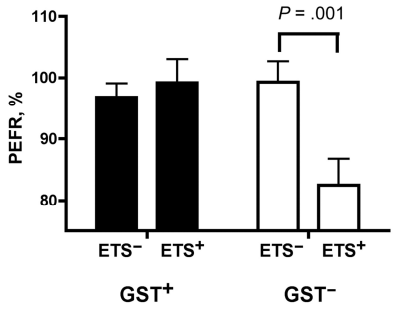
Figure 1. Nasal allergen-specific IgE response 96 h after clean air plus allergen and secondhand smoke (SHS) plus allergen by *GSTM1* genotype. *Asterisks*, *GSTM1* null; *open circles*, *GSTM1* present.

Baseline versus post-CCRE (endotoxin) responses (mean±SEM) in airway sputum (PMNs/mg sputum) in GSTM1 sufficient and GSTM1 null volunteers.



Dillon M A et al. Occup Environ Med
doi:10.1136/oem.2010.061747

Dual GSTM1/GSTP1 genotype and peak expiratory flow in teenagers and young adults with asthma.



Palmer C N et al. Pediatrics 2006;118:710-716

PEDIATRICS

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Interventions

Focused on Indoor Interventions

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Interventions focused on the environmental causes of disease

- Antioxidant
  - NRF2 based interventions
  - Specific radical scavengers
  - Results of early studies mixed, yet to see significant phase III type studies
- Avoidance of PM
  - Strong evidence that policy measures to decrease ambient air PM related to better health outcomes
  - Indoor biomass use of better cookstove ventilation being studied
  - Decrease of active smoking and second hand tobacco smoke exposure works

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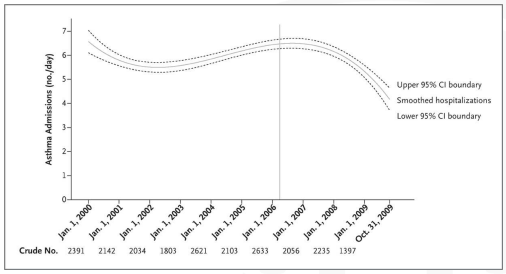
DAILY HOSPITAL ADMISSIONS FOR ASTHMA AMONG CHILDREN BETWEEN JANUARY 2000 AND OCTOBER 2009



MACKAY D ET AL. N ENGL J MED 2010;363:1139-1145

The NEW ENGLAND JOURNAL of MEDICINE