"Influence of Environmental Factors on Asthma and COPD"

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- **Research Funding**
  - Environmental Protection Agency
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  - 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/Th2 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

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

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 kappa-light-chain-enhancer of activated B cells; Nrf2 = nuclear factor (erythroid-derived 2)-like 2; PM2.5 = particulate matter < 2.5 µm; SOD = superoxide dismutase.

Annu. ATS, 2013
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DOI: 10.1513/AnnalsATS.201305-116AW
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Innate Immune Responses to Environmental Agents

PM exposure enhances response to inhaled allergens
(diesel exhaust to the left, LPS to the right)

Epidemiological evidence of PM influence in airway disease

Tobacco smoke
Particulate matter
Household air pollution
Table 2. Smoking Status and Incidence of Asthma, Black Women's Health Study, 1995-2011

<table>
<thead>
<tr>
<th>Smoking Status</th>
<th>Cases</th>
<th>Person-Years</th>
<th>Rate Ratio (95% CI)</th>
<th>Multivariable Model (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never active or passive</td>
<td>142</td>
<td>894,071</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Active or passive</td>
<td>275</td>
<td>850,429</td>
<td>1.2 (1.0-1.4)</td>
<td>1.2 (1.0-1.4)</td>
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<tr>
<td>Smoker aged 25 and</td>
<td>329</td>
<td>54,050</td>
<td>1.7 (1.2-2.8)</td>
<td>1.7 (1.2-2.8)</td>
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<tr>
<td>Smoker aged 25-49</td>
<td>238</td>
<td>134,146</td>
<td>1.7 (1.2-2.5)</td>
<td>1.7 (1.2-2.5)</td>
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<tr>
<td>Smoker aged 50 and</td>
<td>166</td>
<td>106,989</td>
<td>1.7 (1.2-2.5)</td>
<td>1.7 (1.2-2.5)</td>
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<tr>
<td>Smoker aged 50-64</td>
<td>52</td>
<td>34,696</td>
<td>1.7 (1.2-2.4)</td>
<td>1.7 (1.2-2.4)</td>
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<tr>
<td>Smoker aged 65+</td>
<td>47</td>
<td>24,749</td>
<td>1.7 (1.2-2.4)</td>
<td>1.7 (1.2-2.4)</td>
</tr>
</tbody>
</table>

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

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

Indoor PM exposure in the US and where biomass is used

Exposure to biomass smoke is known to increase the risk of asthma and related morbidity. In many parts of the world, biomass fuels are the primary source of energy for cooking and heating. This exposure is particularly problematic for children and those with pre-existing respiratory conditions.
Exposure to Household Air Pollution and Lower Respiratory Tract Infection


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

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

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Oxidative Stress Genes

GSTM1

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.

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

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 MA et al. Occup Environ Med doi:10.1136/oem.2010.061747

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Interventions
Focused on Indoor Interventions

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