Non-biologic Environmental Factors and Allergy

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Rapid change in asthma prevalence vs Environmental change

- **Number or Percent**
  - 1963: 3.2
  - 1970: 5.7
  - 1983: 10.1
  - 1989: 13.4
  - 1995: 14.4
  - 2000: 12.8

- **Year**
  - 1963
  - 1970
  - 1975
  - 1983
  - 1989
  - 1995
  - 2000

Key:
- **Asthma**
- **Apartment**
- **Nuclear FM**
- **Auto**
- **Smoker**
A model of the pathways in which environmental exposures and individual risk factor lead to susceptibility of asthma

PRENATAL                  POSTNATAL
CHILDHOOD

Risk Factor
- Bronchiolitis
- Preterm/LBW

Increasing Susceptability

Prevalence of Asthma Disease

Genetic Factor
- Parental History of Allergy

Non-Biologic Environmental Factor
- Traffic related air pollution
  - Environmental Tobacco Smoking

Biologic Environmental Factor
- Pollen

Social Factor
- Parent education
  - Social and economical status
Air pollution and allergens

- It is well known that the prevalence of allergic diseases has increased in recent decades in the industrialized world. Exposure to environmental pollutants may partially account for this increased prevalence. In effect, air pollution is a growing public health problem.

- In South Korea, the main source of air pollution due to particles in suspension is represented by motor vehicles – particularly those that use diesel fuel. Diesel exhaust particles (DEPs) are composed of a carbon core upon which high-molecular weight organic chemical components and heavy metals deposit. Over 80% of all DEPs are in the ultrafine particle range (< 0.1 μm in diameter).
Size Distribution of PM

3 main classes of PM

Coarse – PM$_{2.5-10}$ mass
Fine – PM$_{2.5}$ mass
Ultrafine – PM$_{0.1}$ number

Courtesy of David Kittelson and Winn Watts, 2009
Gradients of NO$_2$ and PM from Source

From Beckerman et al 2008
Improvement in PM$_{10}$ concentration in Korea
Improvement in NO$_2$ concentration in Korea
Carcinogenic Potential of Diesel Emissions

Meta-analysis by California Office of Environmental Health Hazard Assessment on diesel exhaust and lung cancer:
- Clear positive relationship between occupational diesel exhaust and lung cancer
- Cigarette smoking removed as confounder
- Consistent with causal relationship
- Association with 40% increased relative risk

IARC CLASSIFIES DIESEL EXHAUST PARTICLES AS DEFINITE CARCINOGENIC TO HUMANS in 2012.
Diesel Exhaust Particles

Unburned Fuel

Vapor Phase Hydrocarbons

Soluble Organic Fraction (SOF)/Particle Phase Hydrocarbons

Elemental Carbon (EC)

Solid Carbon Spheres (0.01 - 0.08 μm diameter) form to make Solid Particle Agglomerates (0.05 - 1.0 μm diameter) With Adsorbed Hydrocarbons

Adsorbed Hydrocarbons

PAHs ...

Dr. John Froines, Director, UCLA Southern California Particulate Center and Health Effects Institute, 1995
Air pollution and allergy

The reactive oxidative species produced in response to air pollution can overwhelm the redox system and damage the cell wall lipids, protein, and DNA, thereby leading to airway inflammation and AHR (Ciencewicki J et al, 2008).

Pro-inflammatory effects in the airways also have been demonstrated including increased numbers of bronchial neutrophils, mast cells, T-lymphocytes with upregulation of adhesion molecules after following acute inhalation of diesel exhaust particles in healthy volunteer (Salvi S et al, 1999).
Air pollution and allergy

One postulated regulatory mechanism based on an experimental murine study is that air pollution can inhibit IFN gamma production, thereby enhancing Th2 cytokine mediated inflammation (Finkelman FD et al, 2004).

Therefore, we speculate that air pollution increases AHR through oxidative stress and that AHR was further increased when children were atopic. There are Interactions between allergic sensitization and traffic-related air pollution for development of childhood asthma.
SIZE AFFECTS TOXICITY OF AMBIENT PM

- Exposed rat macrophage cell line *in vitro* to ambient L.A. PM
  3 sizes: PM$_{10-2.5}$ (coarse) PM$_{<2.5}$ (fine) PM$_{<0.15}$ (ultrafine)

Ultrafine PM caused greatest oxidative stress, as indicated by increased hemoxygenase-1

Air Pollutants’ effect on allergen

- Air pollutants not only have a direct or indirect effect upon the individual, but also exert important actions upon aeroallergens. Pollen in heavily polluted zones can express a larger amount of proteins described as being allergenic.

- Through physical contact with the pollen particles, DEPs can disrupt the former, leading to the release of paucimicronic particles and transporting them by air – thus facilitating their penetration of the human airways.
Air pollutants enhancing Th2 cytokine mediated inflammation

**Innate immunity**
- Neutrophil increase
- MIP (IL-8)

**Adaptive immunity**
- CD4+
- CD8+
- Histamine release
- In vitro test
- In vivo test

**Cytokines**
- IL-2
- IL-7, TNF-α, IL-6
- IL-12, IFNγ
- IL-10, IL-4, IL-5

**Antibodies**
- IgE

**Innate immunity**
- APC

**Adaptive immunity**
- MHC class I or II

**Histamine release**
- Neutrophils

**Air pollutants**
- Enhancing Th2 cytokine mediated inflammation
Air pollution concentration prediction

Spatially varying concentrations are typically predicted using:
- Land use regression
- Kriging or other spatial smoothing approach
- Nearest monitor

Air pollution concentration modeled using Mean model (design space)
- Geographically defined (spatially varying) covariates: “Land use regression”
- New covariates derived from physically-based deterministic models

Variance model (geographic space)
- Spatial smoothing
Air Monitoring Station in Seoul
The individual exposure to air pollutants was analyzed using Geostatistical analysis and spatial statistical analysis of ArcGIS (ArcMap 9.3, ESRI Inc., CA, USA). The individual exposure to traffic-related air pollution was calculated by the length of nearby roads and the distance between the habitation and nearby roads.
Highway and Main Road
[Figure] NO2 concentration during recent 3 years by Kriging’s method
Validation of data in the kriging’s method
Air Pollution and Allergy

Air pollutants may induce airway inflammation. Group with susceptible genes are more sensitized on specific allergen due to generation of reactive oxygen species. Asthma is strongly affected by gene susceptabilities. Perinatal air pollution can alter asthma susceptibility.

5% monogenic, the vast majority of cases are due to the interplay or ‘interaction of G-E factors

If we want the effect of air pollution to the susceptible population, gene and environment interaction, environment and environment interaction should be considered,
The Children's Health and Environmental Research (CHEER), a longitudinal follow-up study which was initiated in 2005 to investigate associations between environmental pollutants and children’s health in Korea.

In this study, we report that residential traffic-related air pollutants (TAP) is associated with increased risk of asthma, allergic rhinitis, and allergic sensitization, and with reduced lung function in schoolchildren.
**Association (adjusted hazard ratios) between increase in the pollutant and prevalence of new onset asthma**

<table>
<thead>
<tr>
<th>Distance to main road (m)</th>
<th>N</th>
<th>Wheeze (n=101)</th>
<th>Diagnosed (n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;200</td>
<td>441</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>111–200</td>
<td>448</td>
<td>1.48 (0.76–2.90)</td>
<td>1.31 (0.66–2.60)</td>
</tr>
<tr>
<td>75–110</td>
<td>397</td>
<td>1.92 (0.95–3.86)</td>
<td>1.08 (0.49–2.37)</td>
</tr>
<tr>
<td>&lt;75</td>
<td>369</td>
<td>2.06 (1.07–3.94)</td>
<td>1.70 (0.86–3.56)</td>
</tr>
<tr>
<td>p for trend†</td>
<td></td>
<td>0.023</td>
<td>0.175</td>
</tr>
<tr>
<td>per 100m</td>
<td></td>
<td>1.14 (0.93–1.41)</td>
<td>1.04 (0.84–1.30)</td>
</tr>
</tbody>
</table>

Values are adjusted for age, gender, keeping of pets, and city.
* Estimated 5-year-averaged concentrations of air pollutants at the residential addresses.
†p-value for the trend of adjusted HRs
### Association (adjusted hazard ratios) between increase in the pollutant and prevalence of new onset asthma

<table>
<thead>
<tr>
<th>Length of main roads within a 200m buffer</th>
<th>New onset asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>0</td>
<td>447</td>
</tr>
<tr>
<td>1-150</td>
<td>319</td>
</tr>
<tr>
<td>151-300</td>
<td>464</td>
</tr>
<tr>
<td>&gt;300</td>
<td>425</td>
</tr>
<tr>
<td><strong>p for trend†</strong></td>
<td>0.010</td>
</tr>
<tr>
<td>per 100m</td>
<td>1.21(1.05-1.14)</td>
</tr>
</tbody>
</table>

Values are adjusted for age, gender, keeping of pets, and city.

* Estimated 5-year-averaged concentrations of air pollutants at the residential addresses.

†p-value for the trend of adjusted HRs
Effect of bronchiolitis and PM$_{10}$ exposure on the risk of doctor diagnosed asthma

<table>
<thead>
<tr>
<th>Bronchiolitis</th>
<th>PM$_{10}$</th>
<th>0–50 $\mu g/m^3$</th>
<th>≥ 50 $\mu g/m^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>Odds ratio</td>
<td>1.0</td>
<td>1.61</td>
</tr>
<tr>
<td></td>
<td>95% Confidence interval*</td>
<td>(0.93 – 2.80)</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>Odds ratio</td>
<td>3.52</td>
<td>8.53</td>
</tr>
<tr>
<td></td>
<td>95% Confidence interval*</td>
<td>(1.05 – 13.5)</td>
<td>(4.69 – 15.55)</td>
</tr>
</tbody>
</table>

* adjusted for gender, ETS, family history of allergy, and preterm birth
Effect of bronchiolitis and road proximity exposure on the risk of doctor diagnosed asthma

<table>
<thead>
<tr>
<th>Bronchiolitis</th>
<th>&gt;300m</th>
<th>75–300m</th>
<th>&lt;75m</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>1.00</td>
<td>1.54</td>
<td>1.79</td>
</tr>
<tr>
<td>yes</td>
<td>6.35</td>
<td>6.98</td>
<td>9.84</td>
</tr>
</tbody>
</table>

* adjusted for gender, ETS, family history of allergy, and preterm birth
Climate change and allergy

- Climate change in part gives rise to variations in the temperature pattern characterizing the different seasons of the year. Thus, plants may vary their pollination calendar, advancing and prolonging their pollination period.
- In addition, in the presence of high CO\textsubscript{2} concentrations and temperatures, plants increase their pollen output with the subsequent risk of allergic sensitization among the exposed human population.
Atmospheric Carbon Dioxide Increase in the Future

Atmospheric Carbon Dioxide

Observed and Projected Values Relative to Pre-Industrial Levels

1700 1900 AD 2100 2300
Ozone formation increases with temperature

- Ozone is the primary component of smog
- Ozone formation:
  \[ \text{NO}_2 + \text{VOCs} \rightarrow \text{ozone} \]
  (Heat/ light)
- Warmer temperatures favor ozone formation
Warmer weather increases spore release and pollen dispersal

- Increased production
- Increased dispersion
(a) 1 hr $O_3$ concentration 1995 summer

(b) 1 hr $O_3$ concentration 2055 summer
O$_3$ increase in the future

- O$_3$ generates oxidative stress and associates with asthma development.
- O$_3$ concentration in summer in South Korea was predicted using GEOS–Chem chemical transport model. 2°C increase was predicted at 2055 summer compared to 1995 summer. 8 hour mean concentration will be remarkably increased. Especially in Yougnam district, 53 days are observed exceeding 8 hr mean O$_3$ standard criteria.
Conclusions

- There are individuals who are especially susceptible to air pollution.
- Non-biologic environmental factors have contribution to allergy development, interacting with biologic environmental factors and genetic factors.
- Management of non-biologic environmental factors, therefore, is very important for protecting vulnerable children’s health in South Korea.
Thanks for attention

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