Environmental factors and allergy in children

Yuichi Adachi, MD, PhD
Department of Pediatrics, Graduate School of Medicine and Pharmaceutical Science, University of Toyama, Japan
I have the following financial conflicts of interest to disclose concerning the presentation.

- Research Funding from the Japanese Ministry of Health, Labor, and Welfare, the Japanese Ministry of the Environment, and Environmental Restoration and Conservation Agency, Japan
- Lecture fees and consultant fees from GSK, MSD, Kyorin, AstraZeneca, and Novartis
Human evolution and environment changes
## Environmental factors associated with allergy

<table>
<thead>
<tr>
<th>Route</th>
<th>Exposure</th>
<th>Factors within exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled</td>
<td>Household dust</td>
<td>HDM products, LPS, pet allergen</td>
</tr>
<tr>
<td></td>
<td>Products of tobacco smoke</td>
<td>PM$_{2.5}$, volatile organic compounds (benzene, formaldehyde)</td>
</tr>
<tr>
<td></td>
<td>Traffic fumes</td>
<td>PM$_{2.5}$, SO$_2$, oxides of nitrogen</td>
</tr>
<tr>
<td></td>
<td>Pollens</td>
<td>Trees, plants, fungi</td>
</tr>
<tr>
<td></td>
<td>Swimming pool</td>
<td>Chloride, humidity, exercise</td>
</tr>
<tr>
<td>Ingested</td>
<td>Fish</td>
<td>Omega 3 and 6 fatty acids, fat soluble vitamins, allergenic protein, pesticides</td>
</tr>
<tr>
<td></td>
<td>Fruit</td>
<td>Water soluble vitamins, allergenic proteins, pesticides</td>
</tr>
<tr>
<td></td>
<td>Dairy products</td>
<td>Vitamin D, allergenic proteins</td>
</tr>
</tbody>
</table>

HDM, house dust mite; LPS, lipopolysaccharide; VOC, volatile organic compound;
Prevalence of allergic diseases in Japanese school children

In 11 western districts in Japan


More pollens can cause more pollinosis?

Cedar and cypress pollen counts are associated with the prevalence of allergic diseases in Japanese schoolchildren

K. Yoshida¹, Y. Adachi², M. Akashi³, T. Itazawa², Y. Murakami⁴, H. Odajima⁴, Y. Ohya⁵ & A. Akasawa¹

¹Division of Allergy, Tokyo Metropolitan Children’s Medical Center, Tokyo; ²Department of Pediatrics, University of Toyama, Toyama; ³Department of Pediatrics, Saitama City Hospital, Saitama; ⁴Department of Pediatrics, Fukuoka National Hospital, Fukuoka; ⁵Division of Allergy, National Center for Child Health and Development, Tokyo, Japan

Japanese Cedar  Japanese Cypress

Cedar pollen dispersal precedes cypress pollen dispersal, and 70% of patients with cedar pollinosis are also allergic to cypress pollen because of a cross-reactivity between them.

From Prof Sahashi N
Pollen counts

Japanese cedar

Japanese cypress

counts/cm²

0–1000
1001–2000
2001–3000
3001–4000
>4000

0–500
501–1000
1001–2000
2001–3000
>3000

from Association of Pollen Information in Japan

Prevalence of allergic rhinoconjunctivitis

6-7 years old

13-14 years old

Allergic rhinoconjunctivitis according to the definition of ISAAC questionnaire

Association between pollen counts and prevalence of allergic rhinoconjunctivitis

6-7 years old

R=0.48
P=0.001

13-14 years old

R=0.18
P=0.24

Japanese cedar pollen (counts/cm²)

Association between pollen counts and prevalence of allergic rhinoconjunctivitis

Differences in prevalence rates of allergic rhinoconjunctivits between children aged 6-7 yrs and 13-14 yrs

(PR at 13-14 yrs old) – (PR at 6-7 yrs old)

R=-0.52
P<0.001

Which pollen drives the prevalence of allergic rhinitis?

![Graph showing the prevalence of allergic rhinitis over age with high exposure to cedar pollen.

- High exposure to cedar pollen
- Cedar pollen

Prevalence (%) against Age (yr)
Which kind of pollen drives the prevalence of allergic rhinitis?

- High exposure
- Low exposure to cedar pollen

- Cedar pollen
- Cypress pollen
## Associations between pollen counts and prevalence of bronchial asthma

<table>
<thead>
<tr>
<th></th>
<th>Japanese cedar</th>
<th>Japanese cypress</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient (SE)</td>
<td>P-value</td>
</tr>
<tr>
<td>6–7 years old</td>
<td>0.49 (0.16)$^\dagger$</td>
<td>0.003</td>
</tr>
<tr>
<td>13–14 years old</td>
<td>0.11 (0.15)$^\dagger$</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Coefficient is for each pollen count increment of 1000 counts/cm². SE = standard error.

$^\dagger$Adjusted for the gender ratio, mean annual temperature, mean annual relative humidity, cypress pollen counts, and prevalence of allergic rhinoconjunctivitis.

$^\S$Adjusted for the gender ratio, mean annual temperature, mean annual relative humidity, cedar pollen counts, and prevalence of allergic rhinoconjunctivitis.

This ecological analysis showed that exposure to pollens could lead to the development of allergic airway diseases in a dose-dependent manner.

## Environmental factors associated with allergy

<table>
<thead>
<tr>
<th>Route</th>
<th>Exposure</th>
<th>Factors within exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled</td>
<td>Household dust</td>
<td>HDM products, LPS, pet allergen</td>
</tr>
<tr>
<td></td>
<td>Products of tobacco smoke</td>
<td>PM$_{2.5}$, volatile organic compounds (benzene, formaldehyde)</td>
</tr>
<tr>
<td></td>
<td>Traffic fumes</td>
<td>PM$<em>{2.5}$, SO$</em>{2}$, oxides of nitrogen</td>
</tr>
<tr>
<td></td>
<td>Pollens</td>
<td>Trees, plants, fungi</td>
</tr>
<tr>
<td></td>
<td>Swimming pool</td>
<td>Chloride, humidity, exercise</td>
</tr>
<tr>
<td>Ingested</td>
<td>Fish</td>
<td>Omega 3 and 6 fatty acids, fat soluble vitamins, allergenic protein, pesticides</td>
</tr>
<tr>
<td></td>
<td>Fruit</td>
<td>Water soluble vitamins, allergenic proteins, pesticides</td>
</tr>
<tr>
<td></td>
<td>Dairy products</td>
<td>Vitamin D, allergenic proteins</td>
</tr>
</tbody>
</table>

HDM, house dust mite; LPS, lipopolysaccharide; VOC, volatile organic compound;
Asian dust storms（黄砂）

Asian dust storms (黄砂)

Transport of desert dust

Deserts in Asian Continent

Westerlies

Movement and diffusion

Chemical changes

Long range transport

Gravity deposition

Incorporated into rain

Deserts in Asian Continent

Japan

Japanese Ministry of the Environment
Composition of desert dust

Electron microscopic images of desert dust

Quartz: silica, aluminum
Chemical compounds: $\text{NO}_3^-$, $\text{SO}_4^{2-}$, PAH
Biological materials: bacteria, fungi, viruses
Increasing frequency of transport of desert dust
## Composition of desert dust

### Water soluble components in particles

<table>
<thead>
<tr>
<th>Particles</th>
<th>SO$_4^{2-}$</th>
<th>NO$_3^-$</th>
<th>Cl$^-$</th>
<th>NH$_4^+$</th>
<th>Na$^+$</th>
<th>Ca$^{2+}$</th>
<th>Mg$^{2+}$</th>
<th>LPS</th>
<th>β-Glucan</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD1$^a$</td>
<td>9.2</td>
<td>13</td>
<td>11</td>
<td>0.96</td>
<td>72</td>
<td>14</td>
<td>1.5</td>
<td>0.061</td>
<td>0.214</td>
</tr>
<tr>
<td>ASD2$^b$</td>
<td>16</td>
<td>50</td>
<td>54</td>
<td>0.023</td>
<td>35</td>
<td>23</td>
<td>5.2</td>
<td>0.355</td>
<td>28.16</td>
</tr>
</tbody>
</table>

Concentration of water soluble components in particles (µg/mg)  
LPS and β-glucan (ng/ml)

### Polycyclic aromatic hydrocarbons (PAH) in particles

<table>
<thead>
<tr>
<th></th>
<th>BaP</th>
<th>BkF</th>
<th>BghiP</th>
<th>BbF</th>
<th>IdP</th>
<th>Chr</th>
<th>Flu</th>
<th>Perylene</th>
<th>Coronene</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD1$^a$</td>
<td>439</td>
<td>296</td>
<td>569</td>
<td>170</td>
<td>377</td>
<td>734</td>
<td>1443</td>
<td>118</td>
<td>308</td>
</tr>
<tr>
<td>ASD2$^b$</td>
<td>660</td>
<td>455</td>
<td>672</td>
<td>350</td>
<td>552</td>
<td>1122</td>
<td>1972</td>
<td>192</td>
<td>844</td>
</tr>
</tbody>
</table>

ASD1: May 1-3, 2011, ASD2: May 12-14, 2011

Effects of storm dust on lung eosinophilia

CD1 mice

Intrathoraccheal instillation

2 w 2 w 2 w

Saline  Storm dust  OVA  dust + OVA

Effects on inflammatory cells in the airway (HE stain)

Desert-dust exposure is associated with increased risk of asthma hospitalization in children

Kanatani KT, Ito Isao, Al-Demaimy WK, Adachi Y, Hathwes WC, Ramsdell JW, Toyama Asian Desert Dust and Asthma Study Team

Am J Respir Crit Care Med 182:1475;2010

Desert dust data:
obtained by the Light Detection and Ranging (LIDAR) system

Outcome:
Hospitalization of children aged 1-15 years for asthma exacerbation in 8 hospitals in Toyama during Feb to Apr, 2005 to 2009

△: LIDAR  ○: Hospitals
Light Detection And Ranging (LIDAR)

Non-mineral dust particles (spherical particles)

Mineral dust particles (nonspherical particles)

Not-scattered light

Scattered light

Polarized laser beam

Desert dust is distinguished from other spherical particles by the differences in the patterns of reflected light.

Japanese Ministry of the Environment
Results during the period
6 Asian dust events and 620 hospitalizations
Relationship between asthma hospitalization and dust exposure

OR 1.83
95%CI (1.3-2.6)
P=0.0006

Relationship between asthma hospitalization and dust exposure

The OR was still high after adjustment by meteorological factors, air pollutant levels, and pollen counts.

<table>
<thead>
<tr>
<th>Meteorological factors</th>
<th>Air pollution</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Average temperature</td>
<td>• NO$_2$</td>
</tr>
<tr>
<td>• Temperature difference within the day</td>
<td>• SO$_2$</td>
</tr>
<tr>
<td>• Temperature difference from the previous day</td>
<td>• Ozone</td>
</tr>
<tr>
<td>• Average air pressure</td>
<td>• Pollens</td>
</tr>
<tr>
<td>• Air pressure difference from the previous day</td>
<td></td>
</tr>
<tr>
<td>• Humidity</td>
<td></td>
</tr>
<tr>
<td>• Wind speed</td>
<td></td>
</tr>
</tbody>
</table>
The associations were particularly strong for schoolboys. OR 3.9
95%CI (1.1-13.2)

This study suggested that heavy dust events were significantly associated with the increased risk of asthma exacerbation for children with asthma. Physicians, patients, and the general public, including schools and preschools, should be adequately informed of the health implications of heavy desert dust exposure to minimize the deleterious effects of the dust.

Forecast system for Asian dust storm (Japanese Meteorological Agency)
Effects of air pollution on health

Short-term effects

Respiratory

Cardiovascular

Long-term effects

Lung cancer

Cardiovascular

Lung development
A birth cohort study involving 100,000 parent-child pairs, was launched in 2011 in order to evaluate the impact of various environmental factors on children's health and development. Health outcomes and exposure measurements will continue until the participating children become 13 years old.
Effects of Asian dust to allergy-like symptoms in pregnant women

• Objective
  – To examine the association between ambient desert dust exposure and allergy symptoms.

• Methods
  – Pregnant women participating in the Japan Environment & Children’s Study (JECS) were recruited in Kyoto, Toyama and Tottori in Japan.
  – Asian dust days were defined using the LIDAR system data.

• Covariates
  – $SO_2$, $NO_2$, meteorological variables
Effects of Asian dust to allergy-like symptoms in pregnant women

• Data acquisition
  – Web-based questionnaire for behavior and allergic symptoms was sent to the participant’s mobile phone in the evening on the Asian dust days and the control days.

• Outcome
  – Allergy-like symptoms by Allergy CONTROL Score™
# Relative risk of allergy symptom development

## Allergy CONTROL Score™

<table>
<thead>
<tr>
<th>Organ</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>itching</td>
</tr>
<tr>
<td></td>
<td>watering</td>
</tr>
<tr>
<td></td>
<td>reddening</td>
</tr>
<tr>
<td>Nose</td>
<td>sneezing</td>
</tr>
<tr>
<td></td>
<td>itching</td>
</tr>
<tr>
<td></td>
<td>running</td>
</tr>
<tr>
<td>Blocked nose</td>
<td></td>
</tr>
<tr>
<td>Bronchial system/lung</td>
<td>cough</td>
</tr>
<tr>
<td></td>
<td>wheezing</td>
</tr>
<tr>
<td></td>
<td>difficulty of breathing</td>
</tr>
</tbody>
</table>

**Desert dust level on the day**

**OR1.24 (95%CI: 1.16-1.32)**

Effects of duration of outdoor activities on the development of symptoms

Effect of being allergic to Japanese cedar pollen on the development of symptoms

This may indicate that the co-existence of allergen and dust in the air is important for the dust to exert its effects.

Summary

• Exposure to pollen in the early life is a risk factor for the development of allergic airway diseases.
• Asian dust is also a risk factor for exacerbation of allergic symptoms in children and pregnant women. Asian dust might work as an adjuvant.
• The general public should be adequately informed of the health implications of these air pollutions to minimize the deleterious effects on health.
• To evaluate long-term effects of exposure to environmental factors on allergy, further multidisciplinary studies are needed.
Environment and Allergy

- Outdoor pollution
- Indoor pollution
- Allergen
- Genetic factor
- Direct effect
- Time window
- Epigenetic effect
- Diet
- Virus/Bacteria
These studies were supported by the Environment Research and Technology Development Fund from the Ministry of Environment, Japan [C-1152 (2011-2013)]. The findings and conclusions of these studies are solely the responsibility of the authors and do not represent the official views of Japanese government.