Environmental determinants of health: Asthma and allergy in children – causes and prevention priorities

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What is a public health problem?

- Needs to affect more than 1% of the population

- Should be associated with serious consequences for;
  - Health
  - Economy
  - The social life

- Contribute to inequalities in health

- Should be possible to prevent
Steps to make

Public health’s approach to health problems in a community has been described as a five-step process:

1. Define the health problem
2. Identify the risk factors associated with the problem
3. Develop and test community-level interventions to control or prevent the cause of the problem
4. Implement interventions to improve the health of the population
5. Monitor those interventions to assess their effectiveness
Haglund, Svanström, KI, revision, Beth Hammarström
The term "allergy" from the Greek *allos* ('other') and *ergon* ('work') was introduced in 1906 in *Munchener Medizinische Wochenschrift* by *Clemens von Pirquet*, who recognized that in both protective immunity and hypersensitivity reactions, an external agent had induced some form of “changed or altered reactivity”
Asthma in children

- Asthma is a chronic lung condition characterized by reversible narrowing and excessive mucus production of the airways.
- This manifests as wheezing, coughing and breathlessness.
- Asthma is an important health cause of school absenteeism.
- The majority of children have well-controlled asthma; however, under-recognition and inappropriate management may lead to considerable ill-health.
- For some children, exercise-induced asthma, night-time cough and sleep disturbance interfere with physical and educational activities thereby reducing their quality of life.
Eczema in children

- Eczema (atopic dermatitis) is a chronic inflammatory condition of the skin, which is common amongst school children and manifests with itching and excoriation.

- Eczema exacerbations may be provoked by allergens. Food allergens (e.g. egg) may cause acute eczema after inadvertent ingestion.

- Inhalant allergens (e.g. house-dust mite, cat dander) as well as staphylococcal skin infection may also contribute to poor eczema control.

- Management of eczema is based on hydrating topical treatment, topical anti-inflammatory treatment and avoidance of specific and nonspecific provocation factors.
Allergic Rhinitis in children

- Rhinitis is defined as an inflammation of the lining of the nose and is characterized by nasal symptoms including rhinorrhoea (nasal secretions), sneezing, nasal blockage and/or itching of the nose.

- Allergic rhinitis is the most common form of noninfectious rhinitis and is usually associated with an IgE-mediated immune response against allergens e.g. grass pollen, house-dust mite or pets.

- It is often associated with eye symptoms (rhinoconjunctivitis) that may be the dominant problem.

- Rhinitis is the most prevalent chronic allergic disease in children.

- The presence of allergic rhinitis commonly exacerbates asthma, increasing the risk of asthma attacks, emergency visits and hospitalizations for asthma.
Food allergy in children

- Food allergy is common amongst school children, with an estimated overall prevalence of 4–7%.
- The symptoms in a child with food allergy can affect many organ systems and may include hives or swelling (facial angioedema), vomiting, abdominal pain, and diarrhoea, hoarseness or voice changes, wheezing, dyspnoea and sneezing and/or cardiovascular problems as dizziness or loss of consciousness.
- Cow’s milk, hen’s egg, peanuts, tree nuts, wheat, soy, fish and crustaceans are the most common foods causing allergic reactions.
- Cow’s milk, egg allergy and wheat allergy may resolve by school age. When persistent, they may cause severe reactions as seen with peanut and tree nuts.
Asthma and allergy

- Atopic eczema is often the earliest sign; not infrequently it is seen during infancy.

- Asthma in connection with infections often makes its debut before two years, while allergic rhinitis afflicts predominantly school children and adults.

- Foodstuffs are common allergens in infants, while allergies to furred animals often start in pre-school children and pollen allergies in schoolchildren and adults.

- Eczema and asthma often improve during the later school years but can recur later in life.
Childhood asthma and allergy – public health problem

- Allergy affects at least one of four schoolchildren, it reduces quality of life and may impair school performance; there is a risk of severe reactions and, in rare cases, death.

- Allergy is a multi-system disorder, and children often have several co-existing diseases, i.e. allergic rhinitis, asthma, eczema and food allergy.

- By the end of 20th century, descriptive data on asthma and allergic diseases indicated a substantial and persistent increase in prevalence. The increase appeared particularly strong in industrialized countries, especially among children.

- There is an increase in the prevalence of allergic disease from south-eastern Europe where it is relatively low (e.g. in Albania) to the northwest (e.g. the United Kingdom). Scandinavia has a middle position between these two extremes.

- In parallel with this increase the possibilities of treating allergic disorders have improved appreciably. The development of steroid preparations for inhalation in the treatment of asthma, and the development of effective anti-histamine preparations for the treatment of hay fever have been particularly important.
Prevalence of asthma symptoms in 6-7 yr old children (ISAAC Phase III)

Modified: Asher MI. Lancet 2006, V. 368:733-43
Childhood asthma and allergy – major public health problem in Sweden

- Allergic disorders are the most common longterm health problems among children in Sweden
- In The Children’s Environmental Health Survey 2003, 26% of parents of 4-year-old children and 28% of parents of 12-year-old children stated that their children had some kind of allergy disease
- The prevalence of allergic disorders varies geographically. Asthma and hay fever are, with some exceptions, most common in northern Sweden, where the rate of increase has also been highest
- Mortality from allergic disorders has declined during the past few decades thanks to improved medical treatment
- The number of serious allergic reactions (anaphylactic shock) leading to hospitalization increased threefold between 1987 and 2002
Proportion of self-reported allergic disorders among boys and girls aged 4 and 12 years, respectively, according to Children’s Environmental Health Survey 2003, Sweden

Determinants of childhood allergy / asthma

Respiratory infections
- Male sex
- ETS

Allergens
- Heredity +
- Air pollution

Micro-biological exposure
- Heredity -
- Certain gut flora
- Certain viruses
- Diet / breast feeding

"Western life style"
- Urban environment

Rural environment
- Presence of older siblings

High risk

Low risk

Adopted and modified from the presentation by Prof. Göran Pershagen, 2009
<table>
<thead>
<tr>
<th>Gene</th>
<th>Locus</th>
<th>Predicted primary function</th>
<th>Suggested role in asthma</th>
<th>Publication</th>
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<tbody>
<tr>
<td>ADAM33</td>
<td>20p13</td>
<td>Metalloproteinase</td>
<td>Airway remodelling</td>
<td>Van Eerdewegh et al. Nature 2002</td>
</tr>
<tr>
<td>PHF11</td>
<td>13q14</td>
<td>Zinc finger transcription factor</td>
<td>Immunoregulation</td>
<td>Zhang et al. Nature Genetics 2003</td>
</tr>
<tr>
<td>DPP10, DRPR3</td>
<td>2q14</td>
<td>Dipeptidyl peptidase</td>
<td>Cytokine processing</td>
<td>Allen et al. Nature Genetics 2003</td>
</tr>
<tr>
<td>GPRA / NPSR1</td>
<td>7p14</td>
<td>G-protein coupled receptor</td>
<td>Immunoregulation, neural regulation</td>
<td>Laitinen et al. Science 2004</td>
</tr>
<tr>
<td>HLA-G</td>
<td>6p21</td>
<td>Human leukocyte antigen</td>
<td>Antigen presenting, Immunoregulation</td>
<td>Nicolae et al. 2005 American Journal of Human Genetics</td>
</tr>
<tr>
<td>CYFIP2</td>
<td>5q33</td>
<td>Cytoplasmic protein interaction</td>
<td>T cells</td>
<td>Noguchi et al. AJRCCM 2005</td>
</tr>
<tr>
<td>ORMDL3</td>
<td>17q21</td>
<td>Transmembrane protein anchored in the ER</td>
<td>Unknown</td>
<td>Moffatt et al. Nature 2007</td>
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</tbody>
</table>

Adopted from the presentation by Prof. Göran Pershagen, 2009
The substantial increases in the incidence of asthma over the past few decades and the geographic variation in both base prevalence rates and the magnitude of the increases support the thesis that environmental changes play a large role in the current asthma epidemic.

Although genetic predisposition is clearly evident, gene-by-environment interaction probably explains much of the international variation in prevalence rates for allergy and asthma.

Environmental factors such as infections and exposure to endotoxins may be protective or may act as risk factors, depending in part on the timing of exposure in infancy and childhood.
Prenatal risk factors for asthma and allergy

**Prenatal tobacco smoke**

- Prenatal maternal smoking has been consistently associated with early childhood wheezing, and there is a dose–response relation between exposure and decreased airway calibre in early life.

- Prenatal maternal smoking is also associated with increased risks of food allergy.

- This effect is increased when combined with postnatal smoke exposure.
Prenatal risk factors for asthma and allergy

Diet and nutrition

- Higher intake of fish or fish oil during pregnancy is associated with lower risk of atopic disease (specifically eczema and atopic wheeze) up to age 6 years

- Higher prenatal vitamin E and zinc levels have been associated with lower risk of development of wheeze up to age 5
Prenatal risk factors for asthma and allergy

Stress

- A number of animal models have suggested that prenatal maternal stress acts through regulation of the offspring’s hypothalamic–pituitary–adrenal axis to decrease cortisol levels, which may affect the development of an allergic phenotype.
Antibiotic use

- The association between prenatal antibiotic treatment and subsequent development of atopic disease has been examined in 2 ways: with treatment as a dichotomous predictor (i.e., any antibiotic use) and by number of courses of antibiotics during pregnancy.

- Longitudinal cohort studies examining any antibiotic use showed a greater risk of persistent wheeze and asthma in early childhood and a dose–response relation between number of antibiotic courses and risk of wheeze or asthma.
Prenatal risk factors for asthma and allergy

Mode of delivery

- Development of atopy was 2 to 3 times more likely among infants delivered by emergency cesarean section, although no such association occurred with elective cesarean section.

- Potential reasons for these findings include maternal stress and differences in the infant’s gut microflora associated with different modes of delivery.
Breastfeeding

- Exclusive breastfeeding for at least 3 months is associated with lower rates of asthma between 2 and 5 years of age, with the greatest effect occurring among those with a parental history of atopy
Lung function

- Decreased airway calibre in infancy has been reported as a risk factor for transient wheezing, perhaps related to prenatal and postnatal exposure to environmental tobacco smoke.

- Furthermore, the presence of airways with decreased calibre has been associated with increased bronchial responsiveness and increased symptoms of wheeze.

- Several studies have suggested an association between reduced airway function in the first few weeks of life and asthma in later years.
Childhood risk factors for asthma and allergy

Family structure

- Family size and the number and order of siblings may affect the risk of development of asthma

- Later-born children in large families would be expected to be at lower risk of asthma than first-born children, because of exposure to their older siblings’ infections

- Some studies on allergy showed that although large family size (more than 4 children) is associated with a decreased risk of asthma, birth order is not involved
Childhood risk factors for asthma and allergy

Socio-economic status

- Children of parents with lower socio-economic status have greater morbidity from asthma

- Some studies have reported associations of lower socio-economic status with greater airway obstruction and symptoms but not with a diagnosis of asthma

- Parental stress has also been prospectively associated with wheezing in infancy, and family difficulties have been linked to asthma.
## Childhood risk factors for asthma and allergy

### Farm-related exposures

Allergy in children of farmers in Austria, Germany and Switzerland

<table>
<thead>
<tr>
<th>Exposure during first year of life</th>
<th>Asthma OR (95%CI)</th>
<th>Hay fever OR (95%CI)</th>
<th>Sensitization OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit to stable</td>
<td>0.51 (0.14 – 1.86)</td>
<td>0.25 (0.05 – 1.13)</td>
<td>0.56 (0.25 – 1.27)</td>
</tr>
<tr>
<td>No milk from farm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No visit to stable</td>
<td>0.48 (0.21 – 1.1)</td>
<td>0.24 (0.10 – 0.56)</td>
<td>0.43 (0.24 – 0.77)</td>
</tr>
<tr>
<td>Milk from farm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit to stable</td>
<td>0.14 (0.04 – 0.48)</td>
<td>0.20 (0.08 – 0.50)</td>
<td>0.32 (0.17 – 0.62)</td>
</tr>
<tr>
<td>Milk from farm</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

From Riedler et al. 2001

Adopted from the presentation by Prof. Göran Pershagen, 2009
Childhood risk factors for asthma and allergy

Life-style factors

*Anthroposophy*

Rudolf Steiner  
Steiner schools  
Holistic medicine  
Biodynamic diet  
Restrictive use of: antibiotics  
  antipyretics  
vaccinations

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Allergy in children of Steiner schools and Public schools

From Alm et al. 1999

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Childhood risk factors for asthma and allergy
Air pollution and asthma/allergy

- Acute respiratory symptoms
- Lung function effects
- Development of asthma
- Sensitization

Adopted from the presentation by Prof. Göran Pershagen, 2009
General conclusions

- Protective factors for asthma and allergy in children are associated with farming and an anthroposophic life style.

- Exposure to traffic related air pollution may affect respiratory symptoms, lung function and sensitization in children.

- Interactions between environmental exposures and genetic factors are important for induction asthma and allergy in children.

- There is a substantial potential for prevention of allergy among children by reducing smoking among women in childbearing ages.
Example of longitudinal study on allergy in children
THE BAMSE BIRTH COHORT
7,221 born children
Non-responders (25.5%)
Example of cross-sectional study on allergy in children

The International Study of Asthma and Allergies in Childhood (ISAAC) – the largest worldwide multicentre cross-sectional study on protective and risk factors related to asthma, rhinoconjunctivitis and eczema in children

- Two age groups of children: 6-7 years and 13-14 years
- 56 countries
- 156 participating centres (target sample size – 3,000 children per each age group per centre)
Public Health Action
(example from the Global Allergy and Asthma European Network (GA2LEN) Task Force)

**Action points for all children with allergic disease at school**

- Schools should enquire about allergic disease at the registration of new pupils, and parents should inform the school of any new allergy diagnosis.
- A written allergy management plan should be obtained from the doctor, including allergens/triggers to avoid, medications and contact information.
- The allergic child should be readily identifiable to all school staff.
- Reasonable measures should be instituted to ensure appropriate allergen avoidance.
- Tobacco smoking should be banned.
- School staff should be educated in allergen avoidance and recognition and emergency treatment of allergic reactions.
- Relieving and emergency medication should be available at all times.
- School staff should be indemnified against prosecution for the consequences of administering emergency or relieving medication.
- Ensure protective measures continue on school trips/holidays.

From Muraro A, et al., Allergy, 2010;65:681-89