

Allergy and the environment

TRAINING FOR HEALTH CARE PROVIDERS



Allergy and the environment

Children's Health and the Environment

CHEST Training Package for the Health Sector

1

<<NOTE TO USER: Please add details of the date, time, place and sponsorship of the meeting for which you are using this presentation.>>

First draft prepared by Ulrike Diez (Germany) and Stephan Boese-O'Reilly (Germany)

With the advice of the Working Group on CHEST Training Packages for the Health Sector

Reviewer: Ondine von Ehrenstein

Learning objectives

After this presentation, individuals will:

- ❖ **Know more about allergies**
- ❖ **Understand how environmental factors influence allergic diseases**
- ❖ **Propose, to parents, proper ways of preventing allergies**

After this talk, we hope that you will be able to satisfy these three learning objectives:

Know more about allergies

Understand the influence of environmental factors for allergic diseases

Propose proper prevention to parents

Allergy and the environment

Atopy

- Tendency to produce IgE antibodies
- No disease, but the inherited likelihood of developing typical symptoms

Sensitivity of target organs:

- Airway hypersensitivity
- Disorder of the skin barrier

Johansson, S.G.O.; et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. *Allergy* 2001; 56: 813-824

Page 816: "Atopy is a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop typical symptoms such as asthma, rhino-conjunctivitis, or eczema/dermatitis."

Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, Motala C, Ortega Martell JA, Platts-Mills TA, Ring J, Thien F, Van Cauwenberge P, Williams HC.: Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol.* 2004 May;113(5):832-6. (Department of Medicine, Unit of Clinical Immunology and Allergy, Karolinska University Hospital, L2:04, S-171 76 Stockholm, Sweden. s.g.o.johansson@ks.se)

The nomenclature proposed in the October 2003 report of the Nomenclature Review Committee of the World Allergy Organization is an update of the European Academy of Allergology and Clinical Immunology Revised Nomenclature for Allergy Position Statement published in 2001. The nomenclature can be used independently of target organ or patient age group and is based on the mechanisms that initiate and mediate allergic reactions. It is assumed that as knowledge about basic causes and mechanisms improves, the nomenclature will need further review.

IgE: Immunoglobulin E

Allergy

- ❑ Most allergens are natural substances, such as pollen
- ❑ Allergens are usually well tolerated by the immune system
- ❑ Allergy is the pathological (disease-producing) reaction of the immune system to allergens

Allergens: Most allergens reacting with IgE and IgG antibody are proteins, often with carbohydrate side chains, but in certain circumstances pure carbohydrates have been postulated to be allergens. In rare instances low molecular weight chemicals, eg. Isocyanates and anhydrides acting as haptens, are still referred to as allergens for IgE antibodies.

Johansson, S.G.O.; et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy 2001; 56: 813-824

Allergy and the environment

Atopic diseases

- ❑ Asthma
- ❑ Allergic rhinitis (hayfever)
- ❑ Allergic conjunctivitis
- ❑ Atopic dermatitis (atopic eczema)
- ❑ Food allergy
- ❑ Allergic urticaria
- ❑ Anaphylaxis

5

Von Ehrenstein, U.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

Page 44: "Atopy, in general, refers to the presence of allergen-specific immunoglobulin E (IgE) antibodies. Atopic diseases are associated with the production of allergen-specific IgE antibodies, including allergic rhinitis ('hay fever'), atopic eczema or dermatitis, and asthma, although only a variable fraction of asthma is atopic. Although these disorders have immunological mediators and reactions in common, they are associated with very different genetic and environmental determinants and risk factors Clinically, their impact varies widely, ranging from a small spot of eczema to a lethal anaphylactic shock. Allergic rhinitis is an allergen (1)-dependent inflammation of the lining of the nose associated with conjunctivitis. It may be chronic, recurrent or seasonal ('hay fever'). Atopic eczema is an inflammatory skin disorder characterised by severe itching, a chronic or chronically relapsing course, and a particular distribution of lesions that changes with age."

Food allergy is an adverse reaction of food, when immunologic mechanisms have been demonstrated.

Johansson, S.G.O.; et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. *Allergy* 2001; 56: 813-824

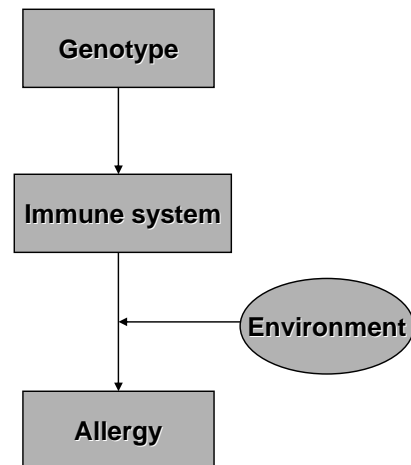
Allergic urticaria is a skin disorder with widespread or localized, circumscribed erythematous skin lesions

Anaphylaxis is an acute, severe reaction, caused by an allergen

Allergy and the environment

Allergy – genotype, the immune system and the environment

Interaction between the environment, genotype and the immune system in how the allergenic phenotype is expressed

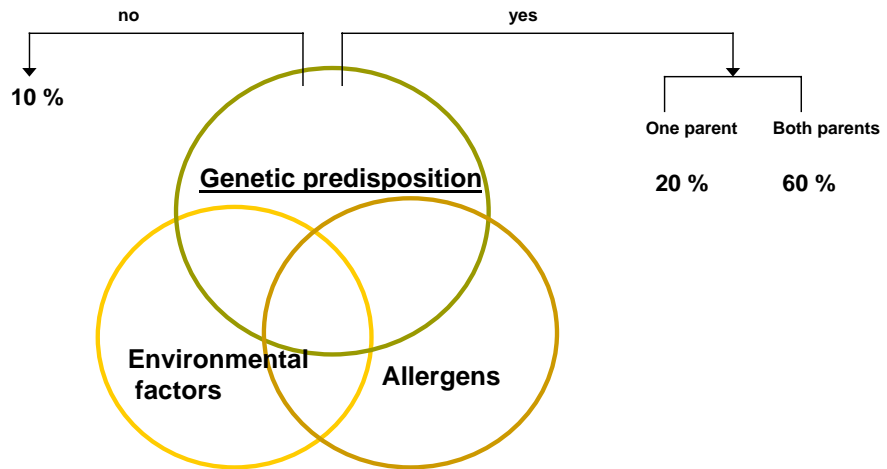


Source: Renz, H: Immunologische Grundlagen allergischer Erkrankungen (Immunological essentials of allergic diseases), in *Paediatrische Allergologie und Immunologie* (edited by Wahn U, Seher R, Wahn V) 3rd ed., Urban & Fischer, Muenchen. After: Von Ehrenstein, U.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

Page 48: "The development of asthma and allergic disease is understood as a complex interaction between environmental influences, genotype and the immune system, with the early life environment modulating immune responses"

Allergy and the environment

Risk factors for allergies



7

Ref.: Bjorgsten B.: Risk factors in early childhood for the development of atopic diseases. *Allergy*. 1994 Jul;49(6):400-7.

The risk of an atopic disease increases for a child with the frequency of atopic diseases of the parents. Mainly the manifestation of an allergy of the mother is of importance. If both parents have the same kind of atopic disease, the risk of a child to develop the same manifestation is 70%.

The atopic phenotype is the result of a complex interaction between genes and environmental factors.

Ref.: Hoffjan S., Nicolae D., Ober C.: Association studies for asthma and atopic diseases: a comprehensive review of the literature. *Respiratory Research* 2003, 4:14

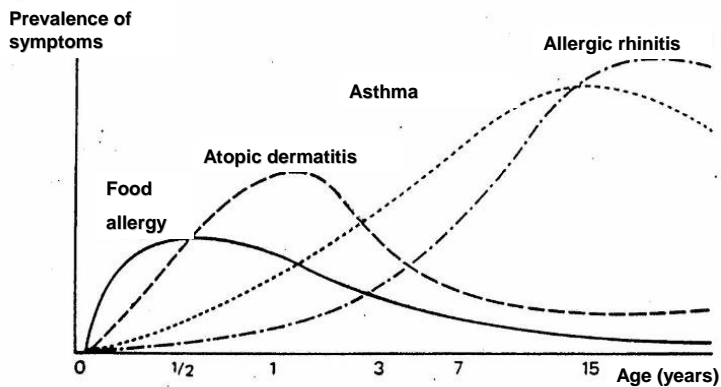
“Hundreds of genetic association studies on asthma-related phenotypes have been conducted in different populations. To date, variants in 64 genes have been reported to be associated with asthma or related traits in at least one study. Of these, 33 associations were replicated in a second study, 9 associations were not replicated either in a second study or a second sample in the same study, and 22 associations were reported in just a single published study. These results suggest the potential for a great amount of heterogeneity underlying asthma. However, many of these studies are methodologically limited and their interpretation hampered by small sample sizes.”

Ref.: von Ehrenstein O.S. et al.: $\alpha 1$ Antitrypsin and the prevalence and severity of asthma. *Arch Dis Child* 89, 230-231, 2004.

„In a random sample of children (aged 9–11 years; $n = 5629$), who were studied according to the ISAAC phase II protocol, heterozygosity of the $\alpha 1$ antitrypsin ($\alpha 1$ -AT) Pi genotypes MS or MZ, or low $\alpha 1$ -AT plasma levels, were not associated with an increased risk of developing asthma. Asthmatics with low levels of $\alpha 1$ -AT were particularly prone to develop airway hyper-responsiveness and reduced lung function“ (p 230).

Allergy and the environment

Development of atopic diseases: the atopic march from atopic dermatitis to asthma



Ref.: Von Ehrenstein, O.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertolini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>; page 47:

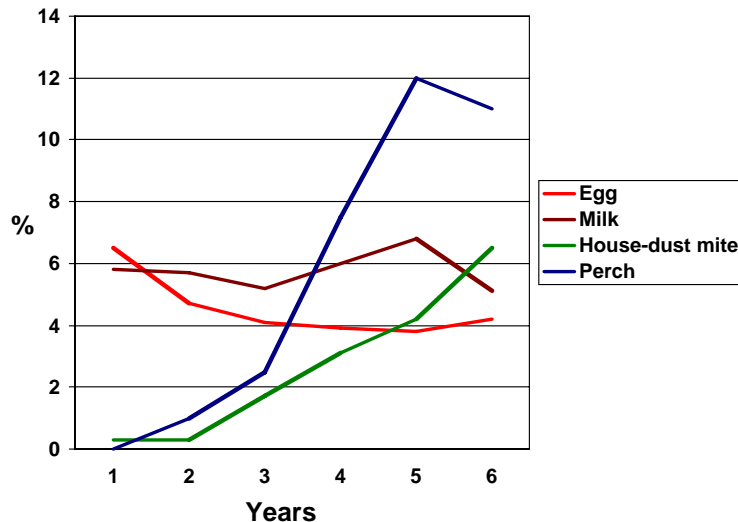
"The spectrum of symptoms of atopic disorders changes with age. During early infancy, IgE antibodies are produced predominantly against cow's milk and chicken egg proteins, and are accompanied by clinical manifestations such as atopic dermatitis, gastrointestinal symptoms and, occasionally, by respiratory symptoms. Sensitisation to house dust mites, cat dander and other indoor allergens becomes more frequent during preschool and school age. Seasonal allergic rhinitis (hay fever) and sensitisation to pollen increases during school age and reaches a peak in adolescence. It is clear that atopy is a strong risk factor for asthma. However, it is also clear that additional factors are required for the development of asthma: while most asthmatics are allergic to at least one inhalant allergen, only a subgroup of allergic children develops persistent airway disease (Woolcock *et al.*, 1995; Holt *et al.*, 1999).

The current understanding of this 'atopic march' is that early onset of sensitisation to food allergens in infancy potentially manifests itself as atopic dermatitis, and may progress to sensitisation to inhalant allergens that may manifest as asthma in a subset of the sensitised children. Obstructive airway diseases and wheezing are frequent among young children. However, in a large birth cohort study in the United States, it was shown that the majority of wheezy infants had transient conditions associated with diminished airway function at birth and did not have an increased risk for asthma or allergies later in life. The authors further concluded that in a substantial minority of children, wheezy episodes were probably related to a predisposition to asthma (Martinez *et al.*, 1995).

Children with atopic parents were particularly at risk for developing atopic disorders, as confirmed in many studies (Sears, 1997)..

Allergy and the environment

Sensitization and age: the atopic march



9

Ref.: Wahn U ;What drives the allergic march? Allergy. 2000 Jul;55(7):591-9.

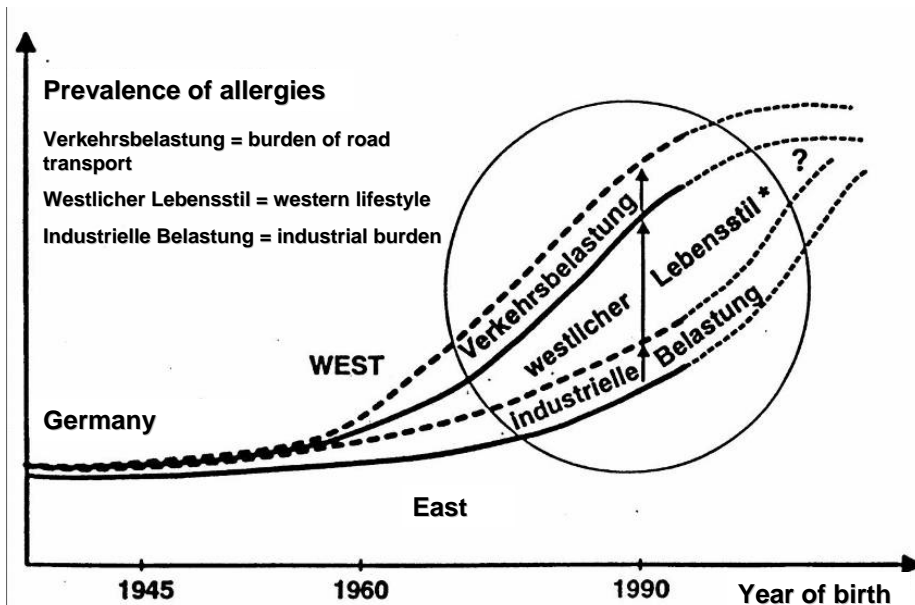
„The "allergic march", which refers to the natural history of *atopic* diseases, is characterized by a typical sequence of sensitization and manifestation of symptoms which appear during a certain age period, persist over years or decades, and often show a tendency for spontaneous remission with age.”

“Although wide individual variations may be observed, atopic diseases tend to be related to the first decades of life, and obviously require a juvenile immune system. In general, no clinical symptoms are detectable at birth, and although the production of IgE antibodies is possible from the 11th week of gestation, no specific sensitization to food or inhalant allergens as measured by elevated serum IgE antibodies can be detected with standard methods. During the first months of life, the first IgE responses to food proteins develop, particularly those to hen's egg and cow's milk. Even in completely breast-fed infants, high amounts of specific serum IgE antibodies to hen's egg may be detected. It has been proposed that exposure to hen's egg proteins occurs via the mother's milk, but this needs further clarification.

Sensitization to environmental allergens from indoor and outdoor sources requires more time and is generally observed between the first and tenth birthdays. The annual incidence of early sensitization depends on the amount of exposure. In a longitudinal birth cohort study in Germany (MAS), a dose-response relationship could be shown between early exposure to cat and mite allergens and the risk of sensitization during the first years of life” (Wahn U. page 592).

Allergy and the environment

Prevalence of allergies and lifestyle



10

Ref.: Wichmann, HE: Environment, lifestyle and allergy: the German answer. *Allergo J.* 1995, 4: 315-16.; Children born in West Germany after 1960 show higher prevalence of allergies: mainly of atopic sensitisation and hay fever. For asthma there are similar significant differences, but in contrast in the Eastern parts there was more obstructive bronchitis in children, for eczema there is partly higher prevalence in Eastern Germany.

Von Ehrenstein, U.: Asthma, allergies and respiratory health. In: *Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe*. Edited by: Giorgio Tamburini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

Page 46-47: "Overall, the epidemiological research indicated relatively high rates and increasing trends mostly in 'western', industrialised and affluent countries. In eastern European countries and in developing countries, the rates were generally lower (review in Matricardi, 2001; ISAAC Steering Committee, 1998a; von Mutius *et al.*, 1992; von Mutius *et al.*, 1994). It was suggested that a 'western lifestyle' is associated with factors determining the manifestation of atopic diseases in childhood. In a unique situation, immediately after the German reunification, significantly lower rates of atopic disorders were found in the eastern than in the western part, while physician-diagnosed bronchitis was more prevalent in the eastern than in the western study area (von Mutius *et al.*, 1992).

Since then tremendous changes have occurred leading to a 'western lifestyle' in the former German Democratic Republic. At the same time, significant increases in the prevalence of hay fever (5.1 % vs. 2.3 %) and atopic sensitisation (26.7 % vs. 19.3 %) were found, whereas the prevalence of asthma and bronchial hyperreactivity remained virtually unchanged (von Mutius *et al.*, 1998b). The authors concluded that important differences in the development of atopic disorders may exist, with factors operating very early in life particularly relevant for the acquisition of childhood asthma, while the development of atopic sensitisation and hay fever may also be affected by environmental factors occurring beyond infancy."

Matricardi, P.M., 2001. Prevalence of atopy and asthma in eastern versus western Europe: Why the difference? *Ann Allergy Asthma Immunol*, Vol 87, pp. 24-7.

ISAAC Steering Committee, 1998a. Worldwide variations in the prevalence of asthma symptoms: The International Study of Asthma and Allergies in Childhood (ISAAC), *Eur Resp J*, Vol 12, pp. 315-35.

von Mutius, E., Fritzsche, C., Weiland, S.K. *et al.*, 1992. Prevalence of asthma and allergic disorders among children in united Germany: A descriptive comparison, *Br Med J*, No 305, pp. 1395-9.

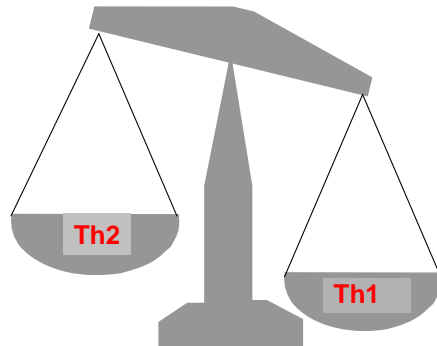
von Mutius, E., Martinez, F.D., Fritzsche, C. *et al.*, 1994. Skin test reactivity and number of siblings, *Br Med J*, Vol 308, pp. 692-5.

von Mutius, E., Weiland, S.K., Fritzsche, C. *et al.*, 1998b. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany, *Lancet*, Vol 351, pp. 862-6.

Allergy and the environment

Early imprinting of the immune system and development of allergies

- ❑ Reduction of T-helper 1 (Th1) cells, which produce interferon- γ and tumour necrosis factor α
- ❑ Predominance of interleukin-4-producing Th2 cells
- ❑ This hypothesis is under permanent discussion



11

Ref.: Renz, H. *Pediatr Pulmonol Suppl.* 2004;26:206-7.
Prenatal influences on the development of allergy and asthma TH1/TH2 balance.

For the reaction of the immune system versus allergens T-cells play a specially important role. Primary TH0 cells are formed to TH1 or TH2-cells under the influence of allergens and other stimuli such as infectious agents. TH1-cells form IFN-gamma, which suppresses the IgE-synthesis from B-cells. TH2-cells excrete IL4 and other cytokines, which stimulate the IgE-synthesis.

The maternal immune system is influenced during pregnancy by an active re-orientation of the lymphocyte-compartments towards a TH2-immune response. The IFN-gamma response of the foetus is suppressed by progesterone. By this the placental-foetal-system of a pregnancy is protected against a graft versus host reaction of the immune system. Through unknown mechanisms this TH2-oriented immune response of the mother is evident as well in the foetus. The newborn are born with a TH2-oriented immune response, which means they produce little IFN-gamma. The immune system of newborns is so far functionally developed, that it can answer with a TH1 as well as with a TH2 immune response.

The TH2-oriented immune of a newborn is shown on the slide above.

TH: T-helper cells

IFN-g: Interferon gamma

TNF-a: tumour necrosis factor

Allergy and the environment

Age 0–1 years

- ▣ Gastrointestinal symptoms: Food allergy
- ▣ Skin symptoms: Atopic dermatitis
- ▣ Breathing problems

12

Newborns are in general healthy.

Food allergy has to be distinguished from food intolerance. If at all children usually only react allergic against one or two substances. Symptoms are vomiting, diarrhoea and colic's.

Dietary restrictions only because of sensitisation are not recommended. A proper history, calendar of symptoms, RAST or PRICK and experienced dietary consultation and diagnostic double-blind provocation are necessary steps to diagnose a food allergy. Food allergies tend to fade fast in early infancy. Exclusive breastfeeding is recommended for the first 6 months of life. If the infant does have a cow's milk allergy, the mother should avoid cows milk products while breastfeeding. Otherwise the infant should be fed with a highly hydrolysed product or a amino acid concentration, late introduction of solid foods (> 6 months of age), and avoiding food with a high allergenic potential, such as eggs, nuts and fish.

Atopic dermatitis: genetic component, disorder of the skin barrier function, neuro-vegetative disorder, age specific sequence of symptoms, typical are the itchiness and the recurring of the symptoms. Atopic dermatitis can fade over time. Signs of type 1 and type 4 allergy. In 33-50% associated with a food allergy. Usually increased total-IgE. Symptoms start in 75% of the cases under the age of 12 months: eczema infantum, disorder of the vascular skin reaction, eczema in the area of the head and face and trunk, often sucking. At the age of 2-3 years half of the children loose the atopic dermatitis, or frequently the typical places of the eczema change.

Allergy and the environment

Age 1–3 years

- ▣ Atopic dermatitis: Change of appearance
- ▣ Fewer gastrointestinal symptoms
- ▣ Hay fever very rare
- ▣ Breathing problems mainly triggered by viral infections



13

Atopic dermatitis: from the second year of life eczema of the extremities and itchiness, in many cases dry skin. 50 % disappear until the age of 10.

Relevant sensitization: Food allergies, house dust mites, mould

Food allergies: Allergens: Egg clear, milk, fish, wheat, soy, peanut. The course of the allergy is influenced by the amount and potency of the allergen, but as well by the individual reaction situation: Infections, physical activities, addition effects by cross reaction; a absolutely consequent diet is often not necessary, e.g. with cows milk allergy: butter and cheese might be tolerated, problem of mixed food: Additives to additives do not have to be declared on the packages. Cows milk should, if possible, not be avoided completely: otherwise replace by trough milk of other animals or soy milk, otherwise a substitution of calcium is necessary. Citrus fruits do not cause a real food allergy, but non-specific skin irritations, they can be replaced by other fruit juices. Cooked vegetables and fruit are usually well tolerated.

Air way symptoms: Children with a disposition of bronchial hyper-responsiveness show clinical symptoms, typically coughing and wheezing leading to airway obstruction, mainly triggered by allergens and airway infections.

Prognosis of early infant wheezing: from the Tuscon Children Respiratory Study: (Wright 2002) infant wheezing has to be considered in different ways. differently. Asthma starts early in childhood, the course is influenced by the maturation of the immune system and air way system: Alveolar system are increasing until the age of 3, the surface of the lung increases trough increase of the alveolar surface until the end of the skeletal growth. Lung volume triples until the end of the first year of life, being then 40% of the size of adults.

Allergy and the environment

Age 3–7 years

- ▣ Asthma manifests mainly at this age
- ▣ Eczema improved in many cases
- ▣ Food allergies less frequent: sensitization to nuts, fish and other food possible
- ▣ Urticaria (food allergies and infections)
- ▣ Hayfever possible



14

In general: Children move more around than infants. It becomes more difficult to control the environmental factors that trigger a disease. Child care takers and teachers should be informed about the allergy of a child, including necessary medication. Allergic symptoms can increase during infections or stress periods. Asthma symptoms can be triggered by physical activity, e.g. swimming in cold water.

Asthma:

Asthma: Attributable part of sensitization (IgE-influenced asthma)

0-2 years of age: 20-30%

School children approx.: 80%

Adults: 40-50%

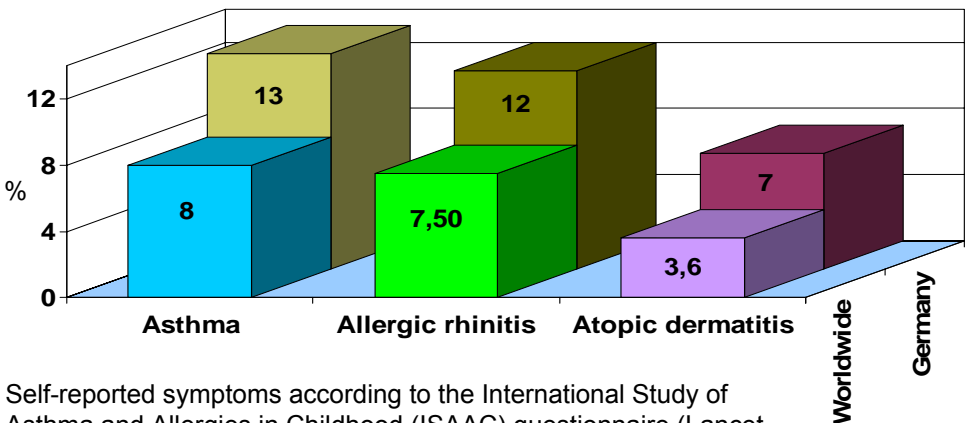
In 80% of the children with asthma the symptoms develop before the age of 5. Triggering factors of asthma are viral infections, allergies against house dust mites, animal epithelia and mould, as well food allergens can play a role. Frequent symptoms are dry cough at night and coughing or shortness of breath during physical activities.

Food allergies: Triggers can be avoided by the child more consciously. Allergy can cause gastro-intestinal symptoms, skin reactions like urticaria to anaphylactic shock. Children do have to carry their own emergency medication with them.

Picture: Fiona (source Stephan Boese-O'Reilly)

Allergy and the environment

12-month prevalence of atopic symptoms at the age of 13–14 years



Self-reported symptoms according to the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (Lancet 1998;351:1225–1232)

15

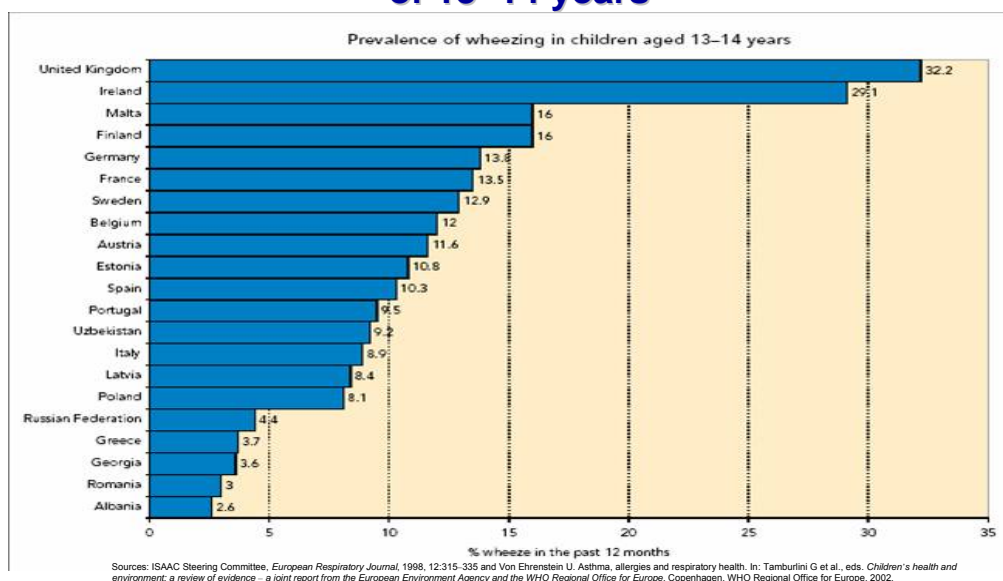
Ref.: The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee: Worldwide variation in prevalence of symptoms of asthma, allergic rhino conjunctivitis, and atopic eczema: ISAAC. Lancet 1998; 351: 1225–1232.

Data from ISAAC study: 13 to 14 years old, 12 month prevalence

	Asthma	Allergic rhinitis	Atopic dermatitis
Worldwide	8	7.5	3.6
Germany	13	12	7

Allergy and the environment

12-month prevalence of atopic symptoms at the age of 13–14 years



16

Ref.: ISAAC Steering Committee, 1998. Worldwide variations in the prevalence of asthma symptoms: The International Study of Asthma and Allergies in Childhood (ISAAC), *Eur Resp J*, 12, 315–35: 1998.

Twelve-month prevalence of self-reported asthma symptoms in children (age group 13–14) from written questionnaires in the ISAAC study 1995–96. “The major differences between populations found in the International study of Asthma and Allergies in Childhood ... are likely to be due to environmental factors” (p 315).

Pic: Von Ehrenstein, U.: Asthma, allergies and respiratory health. In: *Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe*. Edited by: Giorgio Tamburini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

In the original paper data is given for all participating countries and might be used instead of European data given here.

Allergy and the environment

Environmental factors

- ❑ Allergens
- ❑ Infectious agents
- ❑ Pro- and antibiotics
- ❑ Endotoxins
- ❑ Air pollutants
- ❑ Social factors



17

Ref.:

Von Ehrenstein, O.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

Bjorgsten B.: Risk factors in early childhood for the development of atopic diseases. Allergy. 1994 Jul;49(6):400-7.

Wahn U ;What drives the allergic march? Allergy. 2000 Jul;55(7):591-9.

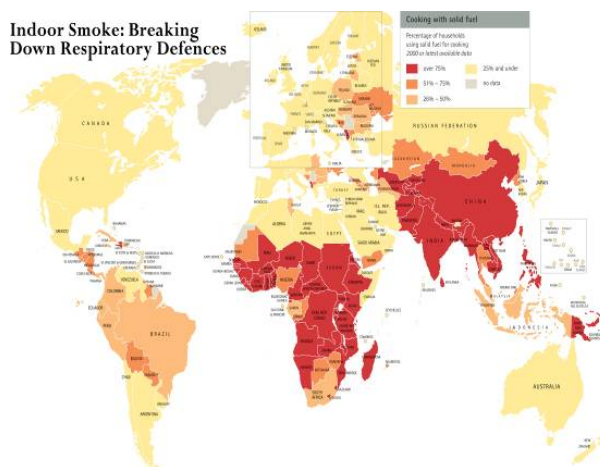
Strachan, D.P.: Hay fever, hygiene, and household size. Br Med J 1989, 299, 1259-60

Picture: Colin and Sebastian (source Stephan Boese-O'Reilly)

Allergy and the environment

Indoor air (worldwide)

- Many children are exposed to indoor smoke, such as from wood or charcoal. Indoor air pollution is a major health hazard for children.
- See the CHEST module on indoor air pollution for more information.



Source: Gordon B. et al., eds. *Inheriting the world. The atlas of children's health and the environment*. Geneva, World Health Organization, 2004.

18

Ref.: Ezzati M., Kammen D.M.: The Health Impacts of Exposure to Indoor Air Pollution from Solid Fuels in Developing Countries: Knowledge, Gaps, and Data Needs. *energy, indoor air pollution, intervention, public health. Environ Health Perspect* 2002, 110:1057–1068:

“Globally, almost 3 billion people rely on biomass (wood, charcoal, crop residues, and dung) and coal as their primary source of domestic energy. Exposure to indoor air pollution (IAP) from the combustion of solid fuels is an important cause of morbidity and mortality in developing countries.” (p. 1057)

Smith K.R., Samet J.M., Romieu I., Bruce N.: Indoor air pollution in developing countries and acute lower respiratory infections in children. *Thorax* 2000;55:518-532.

“Since acute lower respiratory infection is the chief cause of death in children in less developed countries, and exacts a larger burden of disease than any other disease category for the world population, even small additional risks due to such an ubiquitous exposure as air pollution have important public health implications. In the case of indoor air pollution in households using biomass fuels, the risks also seem to be fairly strong, presumably because of the high daily concentrations of pollutants found in such settings and the large amount of time young children spend with their mothers doing household cooking” (p. 518)

Ref.: Schei M.A., et al.: Childhood asthma and indoor wood smoke from cooking in Guatemala. *J Expo Anal Environ Epidemiol* 14 (Suppl 1): 110-117; 2004.

“Hence use of open fire for cooking, may be an important risk factor for asthma symptoms and severity” (p 110).

Ref.: Melsom T. et al.: Asthma and indoor environment in Nepal: *Thorax* 56; 477-481, 2001.

“The risk of asthma in Nepalese children was lower in subjects exposed to cattle kept inside the house and higher in subjects exposed to passive smoking and indoor use of smoky fuels” (p 477).

Source picture: Inheriting World WHO

Allergy and the environment

Case report: relevance of allergens

Home:



Mould visible: *Aspergillus*, *Penicillium*, 120 000 colony-building units per g of dust



Der p I + Der f I : 35 µg per g of dust

Patient:

15-year-old boy with atopic dermatitis since 2 years of age, 10% of the body surface
Perennial atopic rhinitis declining since 1 year of age

Laboratory: Allergic to

- no reaction to mould

Progress:

Moving house, mould-resistant bed covers and symptomatic treatment



CAP 2, Prick +



CAP 1, Prick ++



CAP 3, Prick +++

Complaints: Itchiness, sleeping problems

On examination: pale, regular developed boy, skin partly lichenified and scratched

Lab results see pictures (cat, birch, mite), pathologic: total IgE 241 kU/l (n < 100), normal: RBC, creatinine, liver values, immunoglobulin.

Indoors: low amount of cat allergen exposure, VOCs regular

Regarded as a likely association between house dust mites and eczema, association to mould not proven.

Symptomatic treatment + climate change (Mediterranean): skin much better afterwards

Picture source; mould and house dust mite: Andrea Mueller, Centre for Environmental Research Leipzig-Halle, Germany, Department of Human Exposure Research and Epidemiology; cat: P. van den Hazel

Allergy and the environment

House-dust mites



Photograph courtesy of Allergopharma

- Size 0.1–0.5 mm
- 1 g of house dust contains a couple of thousand mites
- Optimal conditions: >20°C, relative air humidity 60–80%

Examination of house-dust mite concentration

1. Acarex® test
 2. Microscopic examination
 3. ELISA to determine the house-dust mite concentration
- House-dust mite allergens:
 - *Dermatophagoides pteronyssinus* Der p 1 and Der p 2
 - *Dermatophagoides farinae* Der f 1
- Maximum level: 2–10 µg per g of dust

Ref.: Diebschlag, W., Diebschlag, B.: Hausstaubmilbenallergie, gesundheitliche und hygienische Aspekte (House dust mite allergy, health and hygiene aspects). Muenchen, Utz; 1997.

Chapman MD et al: Immunochemical and molecular methods for defining and measuring indoor allergens in dust and air. *Pediatr. Allergy Immunol* 1995; 6(suppl 7), 8-12

The most common indoor air burden with allergens is in many countries the house dust mite. Early exposure to house dust mite leads to sensitization, but not necessarily to asthma. Sensitization against house dust mite is related with asthma (Wahn U ;What drives the allergic march? *Allergy*. 2000 Jul;55(7):591-9.)

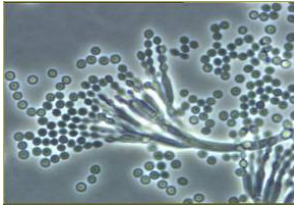
Elimination of the allergen is the primary prevention, to avoid sensitization, has no proven influence on the development of symptoms later in life. But avoiding the allergen is effective in the secondary prevention, which means if somebody is sensitized, to avoid symptoms.

Measuring of house dust mite concentration is possible with various commercial tests, but these tests are usually only used for epidemiological studies. Chemical treatment to reduce the concentration is possible (Benzylbenzoat und tannine-acid). But the main consequence is an encasing of the mattress, bed cover and pillow.

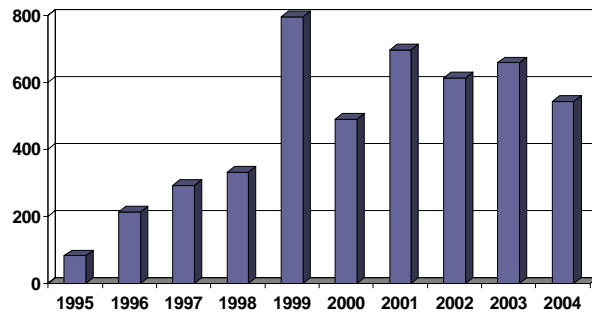
Picture source: House dust mite, Andrea Müller, Centre for Environmental Research Leipzig-Halle, Germany, Department of Human Exposure Research and Epidemiology

Allergy and the environment

Mould exposure in Leipzig, Germany



Number of requests made to the Centre for Environmental Research related to mould problems



Ref.: Schimmelpilzbelastung in Leipzig (mould burden in Leipzig):
Statistics by the Department of Hygiene, Public Health Office Leipzig,
Dr. Schwenke,

Source pictures: mould, Andrea Mueller, Centre for Environmental
Research Leipzig-Halle, Germany, Department of Human Exposure
Research and Epidemiology

Allergy and the environment

Mould exposure and symptoms ($n = 357$)

Complaints	Prevalence
Tiredness or exhaustion	50%
Headache	45%
Blocked nose	42%
Cough	39%
Sleeping problems	37%
Feeling of a dry throat	37%

Source: Rolle-Kampczyk U, Diez U. *Internist Praxis*, 2003, 43:211–219.

22

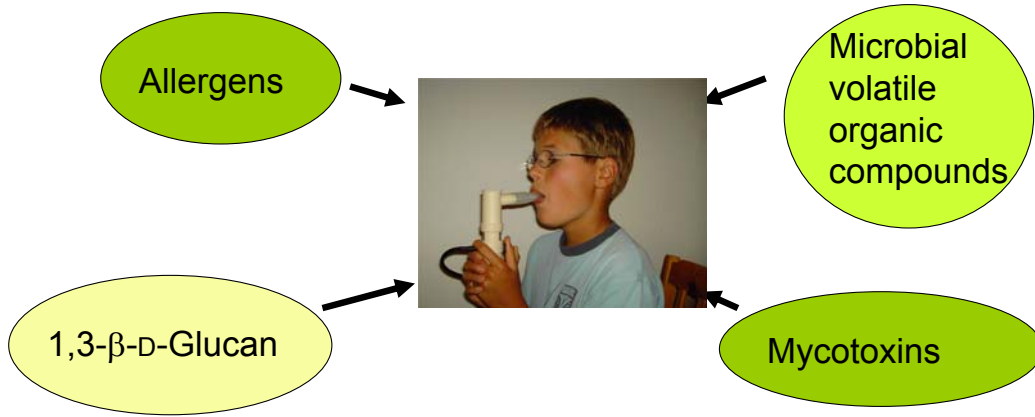
Ref.:

Mould burden and complaints ($n=357$), questioning of participants from people with mould exposure at home by the Department of Human Exposure Research and Epidemiology, Centre für Environmental Research Leipzig-Halle, Germany,

Rolle-Kampczyk, U., Diez, U.: Gesundheitliche Beeinträchtigungen durch Schimmelpilzbelastungen (Health effects due to mould exposure). *internist. praxis* 43 211-219; 2003.

Allergy and the environment

Pathogenic effect of mould



23

Ref.: Innenraumlufthygienekommission des Umweltbundesamtes (Commission on indoor air quality of the Federal Environmental Agency: Leitfaden zur Vorbeugung (Guidelines for prevention), Untersuchung, Bewertung und Sanierung von Schimmelpilzwachstum in Innenraeumen (Examination, classification and rehabilitation of mould grow indoors). Umweltbundesamt (Federal Environmental Agency) Berlin, 2002 (<http://www.umweltbundesamt.de>)

Humidity is good for mould (>68%) as are temperatures between 20 and 30°C. Moulds are very sensitive against cold, typical moulds outdoors are *Alternaria* and *Cladosporium*, and indoors *Aspergillus* and *Penicillium*, spores are 2-100µm big, mainly < 10µm, are inhaled.

Mould allergy: very complex, up to 80 allergens per fungus, can cause allergic rhinitis or asthma, exogenous allergic alveolitis only as occupational health problem. Diagnosis is difficult.

1,3-β-D-Glucan: Polysaccharide from fungal cell walls, in organic dust, might trigger unspecific symptoms and can have immunologic effect.

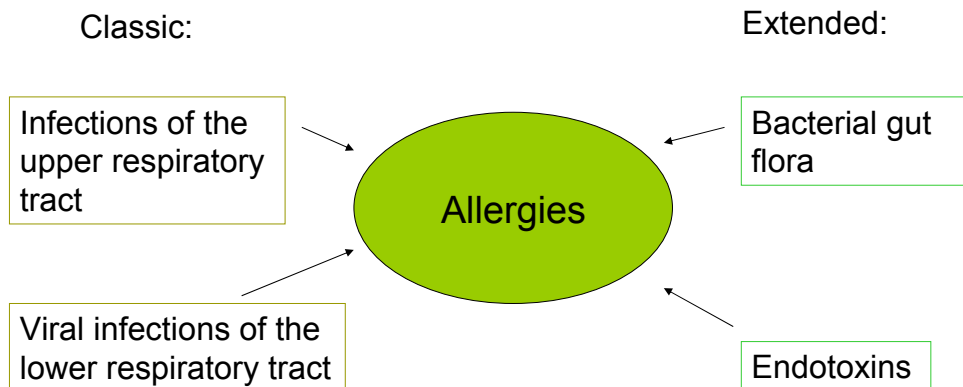
MVOC (Microbial volatile organic compound): occur in very low doses, cause the typical smell of mould. Exposure with mould can be indicated by MVOC analysis.

Mycotoxins: secondary metabolism products, immune-modulating, estrogenic, toxic, carcinogenic effects.

Picture: Jonathan (source: Ulrike Diez)

Allergy and the environment

Hygiene hypothesis



24

Ref.:

Strachan, D.P.: Hay fever, hygiene, and household size. Br Med J 1989, 299, 1259-60

Martinez, F.D., Holt, P.G.: Role of microbial burden in aetiology of allergy and asthma. Lancet 199, 354, Suppl. 2, 12-15

Martinez, F.D.: The coming-of-age of the hygiene hypothesis. Respir. Res 2001, 2, 129-132.

Von Ehrenstein, O.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

Page 53: "Early exposure to infections or sibship size: Many epidemiological studies have shown associations between changing patterns of childhood infections and atopic disorders, even when considering the reduced total burden of infections in early infancy, as well as the decline of certain infections, in many affluent countries. A protective effect of infections on atopy was suggested by Strachan (1989), who described an inverse association between the number of older siblings and hay fever. ... It has been hypothesised that the lack of immunological challenge during early infancy in many industrialised countries may result in an increased propensity to develop atopy, the so-called 'hygiene hypothesis' (Strachan, 1989; Martinez and Holt, 1999)."

Allergy and the environment

Infections

□ Some studies show that “infections” have a protective effect

- Certain viral infections in early childhood might lower the risk of atopy and asthma (MAS study in Germany: Illi et al., BMJ 2001;322:390–5)

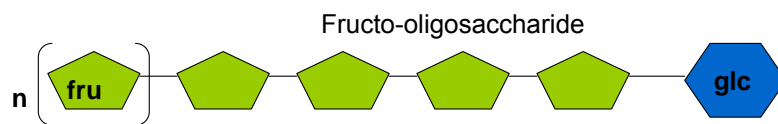
Ref.: Illi S. et al: Early childhood infectious diseases and the development of asthma up to school age: a birth cohort study. BMJ 322:390–5, 2001

“The total burden of infection as well as certain viral infections, namely repeated episodes of runny nose and viral infections of the herpes type, before the age of 3 years showed an inverse relation with the development of asthma by the age of 7. The data support the hypothesis that repeated viral infections early in life may stimulate the immature immune system towards the Th1 phenotype, thereby reducing the risk of asthma and atopy” (p 394).

Allergy and the environment

Probiotics and antibiotics

- ❑ Gut flora of neonates shows regional differences
- ❑ Infants 12 months old with atopic disorder have more *Clostridium* bacteria and fewer *Bifidus* bacteria
- ❑ Applying antibiotics during the first and second year of life disturbs the gut flora: allergies increase
- ❑ Development of pre- and probiotic food



26

Ref.:

Kalliomaki M, Salminen S, Arvilommi H, Kero P, Koskinen P, Isolauri E.: Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. *Lancet*. 2001 Apr 7;357(9262):1076-9.

Isolauri, E. et al.: Probiotics in the management of atopic eczema. *Clin. And Exp. Allergy*, 2000, Vol. 30, 1604-1610.

Composition of gut flora influences the optimal development of the immune system

Breastfed infants have more *Bifidus* bacteria and less *E. coli* in the gut.

Infant food is partly added with pre-biotic fibre material to enhance the growth of *Bifidus* bacteria in the gut.

Pro-biotica: living bacteria, e.g. *Bifidus* bacteria, that are added to the food.

Allergy and the environment

Farming

□ Some studies show that farming has a protective effect

- Factors directly or indirectly related to farming as the parental occupation decrease the risk of children becoming atopic and developing symptoms of allergic rhinitis (Braun-Fahrlander 1999)
- Reduced risk of hayfever and asthma among children of farmers (von Ehrenstein 2000)
- Reduced risk of asthma (Melsom 2001)
- Long-term and early live exposure to stables and farm milk induces a strong protective effect against the development of asthma, hayfever and atopic sensitization (Riedler 2001)
- Regular childhood exposure to animal buildings reduces the risk of nasal allergies (Radon 2004)
- Decreased prevalence of asthma among farm-reared children (Adler 2005)

27

Von Ehrenstein, O.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>:

"The evidence is conflicting about a lower risk for atopic diseases in rural as compared with urban areas. ... Recent studies from Europe independently found that children who lived on a farm during childhood had a substantial reduction in risk for hay fever and asthma compared with their peers in non-farming families in the same rural regions. Increased exposure to livestock was related to a decreased risk for atopic diseases. Findings from a recent study from Austria, Switzerland and Germany suggest that exposure to stables and farm milk starting very early in life has a strong protective effect against the development of asthma, hay fever and atopic sensitisation. Certain components (lipopolysaccharides) of the cell wall of Gram-negative bacteria, which were found to be more prevalent in farming environments, were suggested to be involved in the modulation of the immune response, possibly protecting against the development of atopy. These reports that exposure to environmental bacterial products that do not directly cause specific diseases may influence the pattern of immune responses in humans provide a new framework for understanding the 'hygiene hypotheses'."

Ref.: Braun-Fahrlander C., Gassner M., Grize L., Neu U., Sennhauser F.H., Varonier H.S., Vuille J.C., Wutrich B.: Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. *Clinical and Experimental Allergy* 1999, 29, 28-34.

Ref.: [Von Ehrenstein O.S.](#), [Von Mutius E.](#), [Illi S.](#), [Baumann L.](#), [Bohm O.](#), [von Kries R.](#): Reduced risk of hay fever and asthma among children of farmers. *Clin Exp Allergy*. 2000 Feb;30(2):153-7.

"Factors related to environmental influences on a farm such as increased exposure to bacterial compounds in stables where livestock is kept prevent the development of allergic disorders in children" (p 153).

Ref.: Melsom T. et al.: Asthma and indoor environment in Nepal: *Thorax* 56; 477-481, 2001.

"The risk of asthma in Nepalese children was lower in subjects exposed to cattle kept inside the house and higher in subjects exposed to passive smoking and indoor use of smoky fuels. Childhood exposure to micro organisms or allergens from cattle may protect against the development of atopic disease" (p 477).

Ref.: Riedler J. et al: Exposure to farming in early life and development of asthma and allergy: a cross sectional study. *Lancet* 358; 1129-1133, 2001.

Ref.: Schei M.A., et al.: Childhood asthma and indoor wood smoke from cooking in Guatemala. *J Expo Anal Environ Epidemiol* 14 (Suppl 1): 110-117; 2004.

"Hence use of open fire for cooking, may be an important risk factor for asthma symptoms and severity" (p 110).

Ref.: [Radon K.](#), [Ehrenstein V.](#), [Praml G.](#), [Nowak D.](#): Childhood visits to animal buildings and atopic diseases in adulthood: an age-dependent relationship. *Am J Ind Med* 46:349-56, 2004.

Ref.: [Adler A.](#), [Tager I.](#), [Quintero D.R.](#): Decreased prevalence of asthma among farm-reared children compared with those who are rural but not farm-reared. *J Allergy Clin Immunol*. 115:67-73, 2005.

"Asthma, but not other manifestations of allergy, is less commonly reported among farm-reared children. Early exposures may be more important than those occurring later. Without ongoing exposures, their effects on disease expression may diminish over time" (p 67).

Allergy and the environment

Endotoxins

- ▣ Lipopolysaccharides of cell membranes from gram-negative bacteria
- ▣ **Effect:** binding to receptors of antigen-presenting cells
- ▣ Complex of intracellular signal mechanisms activated
- ▣ Cytokines and immune mediators ↑
- ▣ Interferon- gamma ↑ : sensitization ↓, atopic rhinitis ↓, asthma ↓
- ▣ On the other side: patients with asthma have ↑ complaints



Time of exposure important

Ref.:

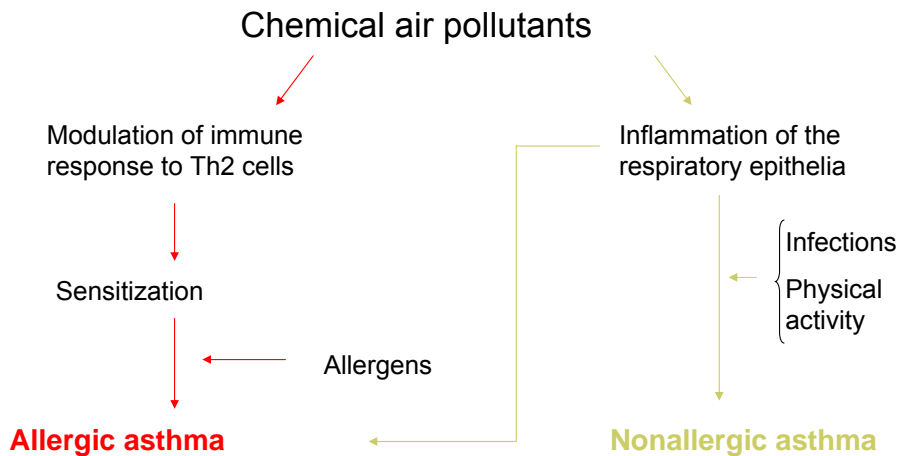
Braun-Fahrlander, C. et al.: Environmental exposure to endotoxin and its relation to asthma in school-age children. N Engl. J. Med. 2002, Vol. 347, No 12, 869-877.

The discovery of the endotoxin effect did lead to the extension of the hygiene hypothesis. Endotoxin occurs e.g. in animal farms.

IFN: Interferon

Allergy and the environment

Asthma and air pollutants



29

Ref.:

Von Ehrenstein, O.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>

Many air pollutants can in this way play a role in asthma, but as with infections of the lower and upper respiratory tract. Which effect each pollutant on the air way system has, depends on the chemical properties, like solubility, and with particles as well from the particle size.

The quality of air is of special relevance for children, because:

Children breath more frequently than adults. The lung volume (per minute) is approx. 7 litres / minute; newborns approx. 10 litres / minute.

Children are especially at risk from pollutants, e.g. from car exhaust, as they breath at a different height.

TH2: T-helper cells 2

Allergy and the environment

Asthma and outdoor air pollutants

Pollutant	SO ₂ and dust	NO _x , ozone, volatile organic compounds
T-cell response	Th1 stimulation	Th2 stimulation
Effect on the airways	Inflammation	Inflammation
Diagnosis	Bronchitis	Asthma

30

Ref.: Leitfaden Umweltmedizin (Guidelines Environmental Medicine).
Editors Boese-O'Reilly S., Kammerer S., Mersch-Sundermann V,
Wilhelm M. Urban und Fischer Verlag, Muenchen, 2. edition 2001

Ref.: [Trasande L](#), [Thurston GD](#) : The role of air pollution in asthma and other pediatric morbidities. J Allergy Clin Immunol 115:689-99, 2005.

„A growing body of research supports the role of outdoor air pollutants in acutely aggravating chronic diseases in children, and suggests that the pollutants may have a role in the development of these diseases. This article reviews the biologic basis of children's unique vulnerability to highly prevalent outdoor air pollutants, with a special focus on ozone, respirable particulate matter (PM 2.5 [<2.5 microm in diameter] and PM 10 [<10 microm in diameter]), lead, sulfur dioxide, carbon monoxide, and nitrogen oxides” (p 689).

SO₂: sulphur dioxide

NO_x: Nitric-oxide

O₃: Ozone

TH: T-helper cell

Allergy and the environment

Emissions from road transport

- NO_x, ozone, particulate matter, soot and benzene are air pollutants. Children's exposure to air pollutants in urban areas originates mainly from emissions from road transport.
- Some studies show an association between exposure to road transport and asthma or related symptoms (Duhme 1998, Nicolai 2003, Hwang 2005, Gauderman 2005)

31

Ref.: Duhme H., et al: Asthma and Allergies among children in West and East Germany: a comparison between Muenster and Greifswald using the ISAAC phase I protocol. Eur Respir J 11, 840-847, 1998: "... exposures such as truck traffic in a residential street or actives smoking were positively associated with symptoms" (p 840).

Ref.: Nicolai T., Carr D., Weiland S.K., Duhme H., von Ehrenstein O., Wagner C., von Mutius E.: Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. Eur Respir J 2003; 21: 956–963.

"Random samples of schoolchildren (n=7,509, response rate 83.7%) were studied using the International Study of Asthma and Allergies in Childhood phase-II protocol with skin-prick tests, measurements of specific immunoglobulin E and lung function. Traffic exposure was assessed via traffic counts and by an emission model which predicted soot, benzene and nitrogen dioxide (NO₂). Traffic counts were associated with current asthma, wheeze and cough. In children with tobacco-smoke exposure, traffic volume was additionally associated with a positive skin-prick test. Cough was associated with soot, benzene and NO₂, current asthma with soot and benzene, and current wheeze with benzene and NO₂. No pollutant was associated with allergic sensitisation. High vehicle traffic was associated with asthma, cough and wheeze, and in children additionally exposed to environmental tobacco smoke, with allergic sensitisation. However, effects of socioeconomic factors associated with living close to busy roads cannot be ruled out" (p.956).

Ref.: Hwang B-F., Lee Y-L., Lin Y-C., Jaakkola J.J.K., Guo Y.L.: Traffic related air pollution as a determinant of asthma among Taiwanese school children. Thorax 2005;60:467-473

"To assess the effect of air pollutants on the risk of asthma among school children, a nationwide cross sectional study of 32 672 Taiwanese school children was conducted in 2001. In a two stage hierarchical model adjusting for confounding, the risk of childhood asthma was positively associated with O₃ (adjusted OR 1.138, 95% confidence interval (CI) 1.001 to 1.293), CO (adjusted OR 1.045, 95% CI 1.017 to 1.074), and NO_x (adjusted OR 1.005, 95% CI 0.954 to 1.117). Against our prior hypothesis, the risk of childhood asthma was weakly or not related to SO₂ (adjusted OR 0.874, 95% CI 0.729 to 1.054) and PM₁₀ (adjusted OR 0.934, 95% CI 0.909 to 0.960). The results are consistent with the hypothesis that long term exposure to traffic related outdoor air pollutants such as NO_x, CO, and O₃ increases the risk of asthma in children" (p. 467).

Ref.: Gauderman WJ, Avol E, Lurmann F et al: Childhood asthma and exposure to traffic and nitrogen dioxide. Epidemiology 2005; 16; 737-743: "These results indicate that respiratory health in children is adversely affected by local exposure to outdoor NO₂ or other freeway-related pollutants.

NO_x: Nitric oxide

O₃: Ozone

PM: Particulate matter

Allergy and the environment

Particulate matter

- ▣ Solid particulates from combustion of organic matter and dust
- ▣ Mixture of suspended solid and liquid particles with different sizes
- ▣ Particles < 10 micro-metres (µm) diameter (PM10) can be produced by road traffic, industry, heating
 - Keep suspended for longer periods
 - more likely to be inhaled and penetrate airways
 - Can damage airways
- ▣ Respiratory diseases, both acute and chronic, have been clearly associated with temporarily high concentrations of particulate matter
- ▣ Many studies show an association between exposure to particulate and asthma or related symptoms (Schwartz 1994)

32

Ref.: Tambulini, G.: Environmental hazards in specific settings and media: an overview. In: Von Ehrenstein, U.: Asthma, allergies and respiratory health. In: Children's health and environment: A review of evidence - a joint report from the European Environment Agency and the WHO Regional Office for Europe. Edited by: Giorgio Tambulini, Ondine S. von Ehrenstein, Roberto Bertollini. WHO Regional Office for Europe, ISBN 92-9167-412-5, Copenhagen 2002, <http://www.euro.who.int/ecehrome>. Page 35:

"Particulate matter includes solid particulates resulting from combustion of organic matter and dust, originating from the mechanical breakdown of solid matter. Particulate air pollution is a mixture of suspended solid and liquid particles that vary in size. The particle size is the primary determinant of the level at which they are deposited in the respiratory apparatus. Particles smaller than 10 micro-metres (µm) diameter (PM10), such as those produced by motor vehicle exhaust, remain suspended for longer periods and are more likely to be inhaled and to penetrate into and damage the lungs. Respiratory diseases, both acute and chronic, have been clearly associated with temporarily high concentrations of particulate matter, in children as well as in adults.

Aerosol are suspensions of solid or liquid particles in a carrier gas.

Air is a aerosol.

Arctic: some 100 particles per cm³

Countryside: some thousand particles per cm³

Downtown: some hundred thousand particles per cm³

Particle sources: in town: road traffic, industry, heating

Indoors: Smoking, heating. Contents: Smoke, metals, minerals.

Size distribution of particles: 80% are smaller than 0,1µm , contribute to the total mass with less than 5%. PM 2,5: particle < 2,5 µm, PM 10 particle < 10 µm,

Ref.: Schwartz J. et al: Acute effects of summer air pollution on respiratory symptom reporting in children. Am J Respir Crit Care Med 150, 1234-1242, 1994.

"Significant associations were found between incidence of coughing symptoms and incidence of lower respiratory symptoms and PM10" (p. 1234).

PM: Particulate matter

Allergy and the environment

Ozone

- ▣ Ozone (O₃) is a air pollutant related to emissions from road transport
- ▣ Some studies show an association between exposure to ozone and asthma or related symptoms (Schwartz 1994, Thurston 1997, McConnell 2002, Hwang 2005)

33

Ref.: Schwartz J. et al: Acute effects of summer air pollution on respiratory symptom reporting in children. *Am J Respir Crit Care Med* 150, 1234-1242, 1994.

“Significant associations .. Were also found between ... ozone and incidence of cough ... “ (p. 1234).

Ref.: Thurston GD, Lippmann M, Scott MB, Fine JM. Summertime haze air pollution and children with asthma. *American Journal of Respiratory and Critical Care Medicine* 1997;155:177

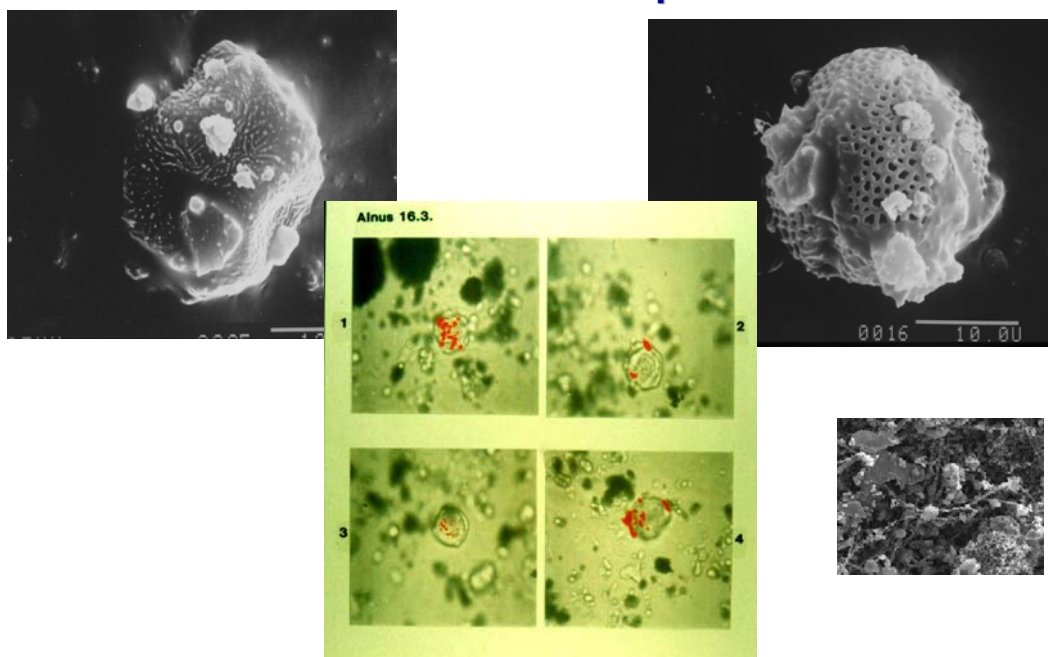
Ref.: McDonnell R, Berhane K, Gilliland F et al: Asthma in exercising children exposed to ozone: a cohort study. *Lancet* 2002;359:386-91.

Ref.: Hwang B-F., Lee Y-L., Lin Y-C., Jaakkola J.J.K., Guo Y.L.: Traffic related air pollution as a determinant of asthma among Taiwanese school children. *Thorax* 2005;60:467-473

“To assess the effect of air pollutants on the risk of asthma among school children, a nationwide cross sectional study of 32 672 Taiwanese school children was conducted in 2001. In a two stage hierarchical model adjusting for confounding, the risk of childhood asthma was positively associated with O₃ (adjusted OR 1.138, 95% confidence interval (CI) 1.001 to 1.293) ... The results are consistent with the hypothesis that long term exposure to traffic related outdoor air pollutants such as NO_x, CO, and O₃ increases the risk of asthma in children” (p. 467).

Allergy and the environment

Pollen and ultrafine particles



34

Slide copied from module transport

Generally the association between air pollution from motorised transport and asthma and allergies is complex. It is well established that children with asthma and allergies of the respiratory tract are especially sensitive to high air pollution episodes and especially to soot and ultra-fine particles: Symptoms-scores, hospital admissions, drug use etc. increase with air pollution.

The introduction of allergic disease is a more complex issue. While it is well established that genetic factors play a major role, the causes for the tremendous increase in atopy prevalence is not so well understood. Immunological mechanisms at an early stage of life (Hygiene-Hypothesis) are important, but fine particles and some irritant gases also contribute when they hit during a vulnerable time window in early life. Epidemiological findings on that are still somewhat contradictory but this could well be because of the fact that this time window is not yet exactly defined.

This slide highlights the atmospheric reactions between pollen (and other natural allergens) and ultra-fine particles. (Photos kindly provided by Herwig Schinko, Linz).

Center: Light microscopy of alder pollen. Their surface is covered by fine particles (soot). The soot in this picture is in red (after electronical transformation of picture data by picture analysis system "LUCIA"). Note the sometimes very high burden of soot on airborne pollen grains. Specimen taken from the Burkard pollen trap situated in the center of Linz.

Source: Herwig Schinko und Roland Schmidt: Assoziation von Luftallergenen und partikulären Aerosolen in Linz 1991 - II. Teil. City of Linz, 1994, Linz.

Raster-electron microscopic pictures of birch (left) and willow (right) (pictures also provided by Schinko). Take note of the anorganic particles on the pollen surfaces.

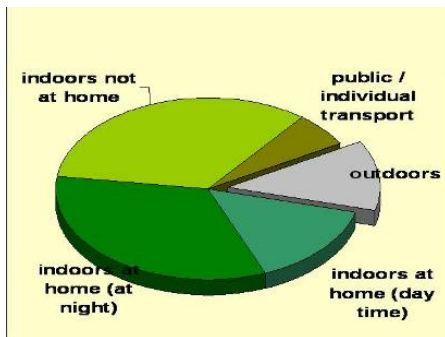
Bottom right: raster electron microscopy of soot on a filter.

Soot and pollen interact in the air (especially under damp conditions) or in the airways. Soot sticks to the pollen surface and induces swelling and rupturing of pollen grains. Allergenic pollen structures previously coated by the pollen surface become free in the ruptured pollen particles. Parts of pollen that are substantially smaller than the whole pollen grain remain airborne for a considerably longer period of time and reach deeper parts of the airways upon inhalation.

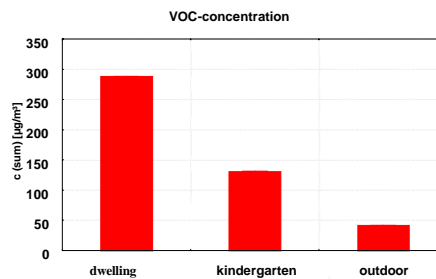
Allergy and the environment

Exposure to volatile organic compounds (VOC) indoors versus outdoors

- 85–90% of people's time is spent indoors



- VOC concentration 6 times higher indoors than outdoors



Herbarth O et al. Effect of volatile organic compounds in- and outdoors on allergies. In: Brebbia CA et al., eds. *Air pollution VI*. Southampton, WIT Press, 1998.

35

Ref.:

Herbarth, O. et al.: Effect of volatile organic compounds in- and outdoors on allergies. In: Brebbia CA, Ratto CF, Power, H (eds) *Air pollution VI*, Southampton: WIT Press Boston; 1998

Preschool children spend on average 85% of the day indoors, while newborn infants remain indoors for as much as 95% of the day.

The right graphic shows the concentration of volatile organic compounds (VOC, added total burden of 26 substances in $\mu\text{g}/\text{m}^3$ air) measured in 301 homes of newborns, 131 kindergartens and 41 outdoor in 1995 in Leipzig, Germany. Clear differences could be observed, whereby the residential premises were affected with the higher levels of VOCs.

VOC: volatile organic compounds

Allergy and the environment

VOC concentration and exposure

Author	VOC	Sources
Wieslander et al. 1997	Aliphatic chains (C8ŠC11)	Painting of walls, ceilings, relation to the intensity of painting (number of rooms)
	Formaldehyde	Painting of wooden parts, carpets
	Butanol	Painting of wooden parts
Hoffman et al. 2000	Benzene C9 bindings	Tobacco smoke in the environment, etc. , renovation activities
Diez et al. 2000	Aliphatic chains (C9, C11, C12)	Painting
	Styrole	Glued carpet
	Benzene	Tobacco smoke in the environment
Wolkoff 1999	Aldehydes, formaldehyde	Carpet, plastic furniture
	Styrole, terpene, aldehydes, acrylic	Furniture painting
	Aldehyde	Linoleum

36

Particularly high exposure levels were recorded indoors when renovations have been carried out, such as painting, new furnishing and/or replacing floor coverings.

Ref.: Wieslander, G., Norbaeck, G., Bjoernsson, E., Janson, C., Boman, G.: Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces. Int Arch. Environ., Health 1997, 69, 115-124.

Ref.: Hoffmann, K., Krause, C., Seifert, B., Ullrich, D.: The German Environmental Survey 1990/1992 (GerES II): Sources of personal exposure to volatile organic compounds. J. Expo. Anal. Environ. Epidemiol. 2000, 10, 115-125.

Ref.: Diez, U., Kroessner, T., Rehwagen, M., Richter, M., Wetzig, H., Schulz, R., Borte, M., Metzner, G., Krumbiegel, P., Herbarth, O.: Effects of indoor painting and smoking on airway symptoms in atopy risk children in the first year of life – results of the LARS-study. Int. J. Hyg. Environ. Health 2000, 2003, 23-28.

Ref.: Wolkoff, P.: How measure and evaluate volatile organic compound emissions form building products. A perspective. The Science of the Total Environment 1999, 227, 197-213.

Ref.: Rumchev K., Spickett J., Bulsara M., Phillips M., Stick S.: Association of domestic exposure to volatile organic compounds with asthma in young children. Thorax 59; 746-751, 2004.

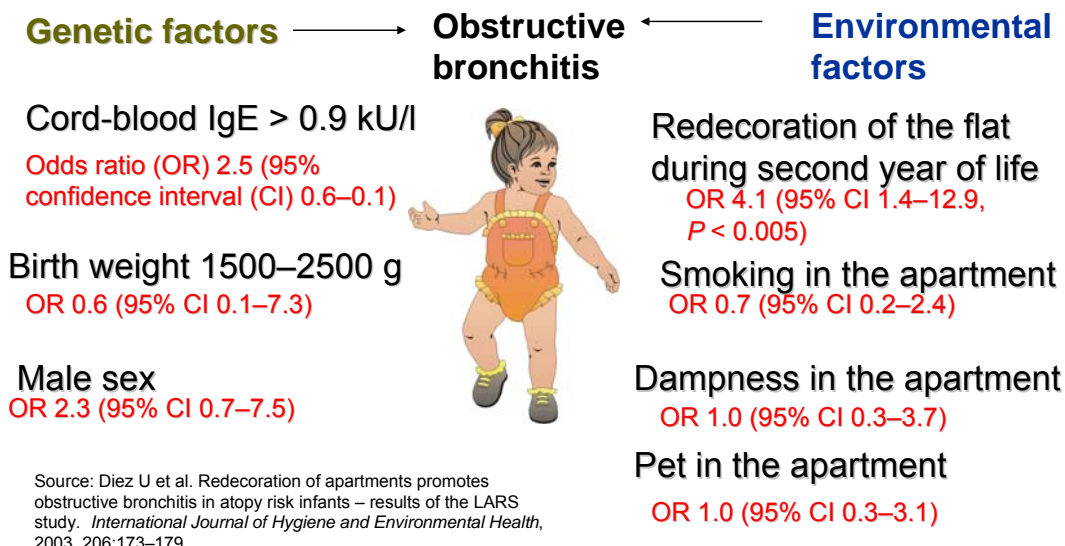
“Domestic exposure to VOCs at levels below currently accepted recommendations may increase the risk of childhood asthma” (p 746).

VOC: volatile organic compounds

Allergy and the environment

Effect of redecoration

(Leipzig Allergy Risk in Children Study; cohort at 2 years of age)



37

Ref.: Data from LARS study.

Diez, U., Rehwagen, M., Rolle-Kampczyk, U., Wetzig, H., Schulz, R., Richter, M, Lehmann, I., Borte, M., Herbarth, O.: Redecoration of apartments promotes obstructive bronchitis in atopy risk infants – Results of the LARS study. *Int. J. Hyg. Environ. Health* 206, 173-179, 2003.

OR: Odds ratio

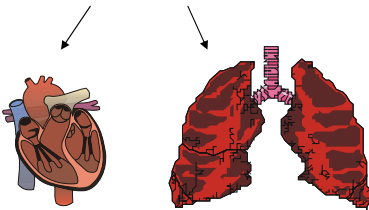
The Leipzig Allergy Risk Children Study (LARS) is a birth cohort study which included atopy risk children at birth. At the age of two years the influence of indoor activities like renovation during the first year was introduced by questionnaires. The relationships between exposure and obstructive bronchitis were calculated by logistic regressions models.

The figure described the relationship between genetic and environmental factors on obstructive bronchitis in the 2nd year of life. Each factor is adjusted against each other, significant OR are indicated by * ($p < 0.05$).

Allergy and the environment

Effects of environmental tobacco smoke

Prenatal



Postnatal



- Sudden infant death syndrome
- Asthma
- Atopic sensitization
- Ear infection
- Reduced sense of smell
- Complications during anaesthesia
- Meningitis

38

Ref.:

Diez U.: Einfluss ausgewählter Schadstoffbelastungen auf die kardiopulmonale Entwicklung bis zum Ende des ersten Lebensjahres – ein Beitrag zur pädiatrischen Umweltmedizin. Habilitationsschrift 2002, Universität Leipzig. (Influence of selected pollutants on the cardio-pulmonary development until the end of the first year of life – a contribution to paediatric environmental medicine. Habilitation script 2002, University of Leipzig, Germany)

Bornhaeuser, A.; Poetschke-Langer, M. et al.: Passivrauchende Kinder in Deutschland – Frühe Schädigungen für ein ganzes Leben (Passive smoking children in Germany – Early damage for a whole life). DKFZ (German Cancer Research Institute) Heidelberg 2003, <http://www.dkfz.de>

C.M. Courage: Environmental tobacco smoke. In: G. Tamburlini; O.S. von Ehrenstein, R. Berthollini: Children's health and environment. A review of evidence. S.44-65, Environmental issue report No 29, WHO Regional Office for Europe, Copenhagen 2002.

Cigarette smoke consists of over 4000 substances, smoking during pregnancy damages the child pre-natal with post-natal consequences, disturbed are the growth. One of the reasons is an insufficient supply with oxygen. Infants of smokers have significantly higher COHb values; CO substitutes O₂ from haemoglobin, which shifts the oxygen binding curve and thereby causes an O₂ lack in the tissue. The foetus is compensating it with an increase of the blood pressure and the after load. At birth the heart is relatively bigger, the growth of the lung is diminished. Cigarette smoke contains also substances that have an influence on the immune regulation and further carcinogenic substances. Neuronal disturbances that happened in utero in the arousal centre might contribute to SIDS (Sudden Infant Death Syndrome).

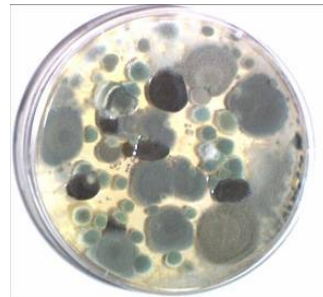
SIDS: Sudden infant death syndrome

Picture source: Ulrike Diez

Allergy and the environment

Environmental medicine – diagnostic procedures

- ▣ **History:** smoking, mould, renovation, indoor environment, pets
- ▣ **Measurements:** formaldehyde, volatile organic compounds (VOC), microbial VOC, mould, house-dust mite allergens, cat allergens
- ▣ **Biomonitoring:** VOC metabolites, mycotoxins



39

Ask about the change of pattern of symptoms due to season, time of the day, time of the year, holidays ...

Source pictures: mould, Andrea Mueller, Centre for Environmental Research Leipzig-Halle, Germany, Department of Human Exposure Research and Epidemiology

3M-Monitor(Neuss, Germany) for measurement of VOC:, Martina Rehwagen, Centre for Environmental Research Leipzig-Halle, Germany, Department of Human Exposure Research and Epidemiology

HCHO: Formaldehyde

VOC: Volatile organic compounds

MVOC: Microbial volatile organic compound

Allergy and the environment

Preventing allergy

- ❑ Exclusive breastfeeding for 4–6 months
- ❑ Solid foods after the sixth month (juice, cereals)
- ❑ No pets (with “hair”) at home
- ❑ Cool and dry sleeping rooms (few house-dust mites)
- ❑ No mould at home
- ❑ Smoke-free environment for children
- ❑ Minimize chemical exposure

Ref.: Guidelines of the GPA (Association for Allergological Paediatrics and Environmental Health)

Primary prevention: Target group: infants at risk to develop allergies, reduction of sensitization rates for pre-disposed individuals. -> reduction of the incidence of allergies.

Secondary prevention: Target group: sensitized non symptomatic infants and infants with early signs of disease. -> avoid the disease manifestation and a change of symptoms.

Tertiary prevention: Improve the clinical picture of the manifested allergic disease. To avoid recurrent problems, secondary diseases and a chronification.

The following topics are not proven enough: Diet: pro-biotica, whether for the pregnancy or after birth. Hydrolysed formula for prevention. Vaccination. Early exposure to cats.

Breast feeding – Ref.: Oddy W.H. et al: Association between breast feeding and asthma in 6 year old children: findings of a prospective birth cohort study. BMJ 319:815-819, 1999.

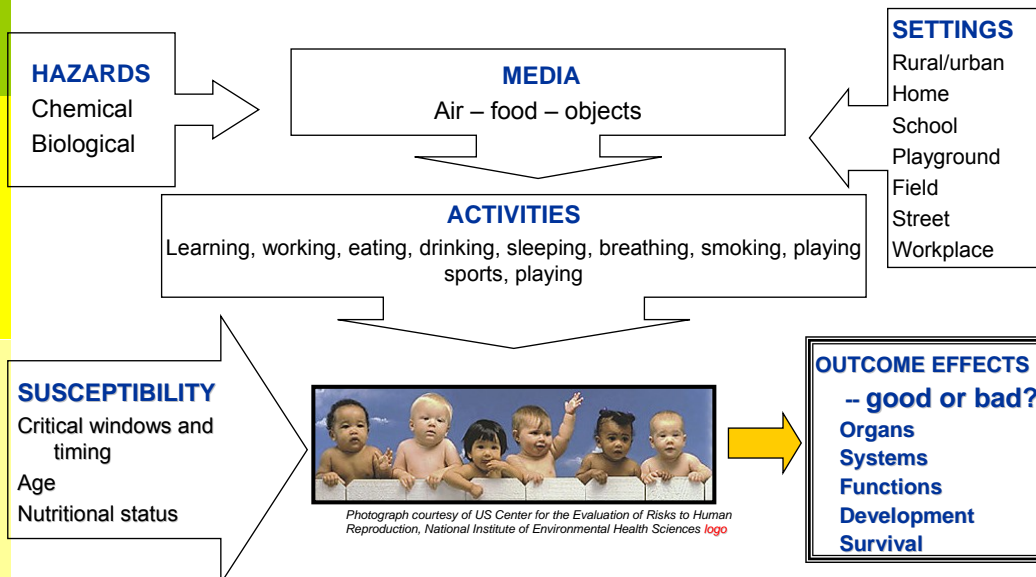
Pets – Ref.: Lau S. et al.: Longitudinal study on the relationship between cat allergen and endotoxin exposure, sensitization, cat-specific IgG and development of asthma in childhood--report of the German Multicentre Allergy Study (MAS 90). Allergy. 60:766-73, 2005: „We could confirm that high cat allergen exposure in a cohort with lower community prevalence of cats is associated with higher serum IgG and IgE levels to cat in schoolchildren. Sensitization to cat allergen (IgE) is a risk factor for childhood asthma. While exposure to cat allergen during infancy is associated with sensitization (IgE), only in the very highly exposed children the likelihood of sensitization (IgE) is decreased and high IgG levels to cat without IgE were associated with low risk of wheeze. However, cat-specific IgG ab levels did not protect children with IgE-mediated sensitization from wheeze” (p 766).

House dust mites - Ref.:Morgan W.J. et al: Results of a Home-Based Environmental Intervention among Urban Children with Asthma. NEJM 351:1068-1080, 2004 : „Among inner-city children with atopic asthma, an individualized, home-based, comprehensive environmental intervention decreases exposure to indoor allergens, including cockroach and dust-mite allergens, resulting in reduced asthma-associated morbidity“ (p. 1068).

Chemical exposure – Ref.: Sherriff A., Farrow A., Golding J. , the ALSPAC Study Team, Henderson J. : Frequent use of chemical household products is associated with persistent wheezing in pre-school age children. Thorax 60; 45-49; 2005: “Conclusion: These findings suggest that frequent use of chemical based products in the prenatal period is associated with persistent wheezing in young children. Follow up of this cohort is underway to determine whether TCB is associated with wheezing, asthma, and atopy at later stages in childhood” (p 45).

Allergy and the environment

The complex environment of children and adolescents



41

In this summary slide, we see the complexity of the issues related to children's environmental health. Hazards (physical, chemical, biological – in many cases favored by social factors) are introduced into environmental media (water, air, food, soil objects, toys) with variable efficiency in different settings (urban and rural: home, school, field, playground, street, workplace). A child's activities brings him into contact with these hazards.

<<READ SLIDE>>

Depending upon the individual susceptibility of the child based upon age, general health and social supports, the exposure may cause harm from subtle changes in function to death.

Children's environmental health is the field which synthesizes these complexities and attempts to make fundamental changes to improve children's environments and prevent environmental illnesses.

Allergy and the environment

Health and environment professionals have a crucial role



Photograph courtesy of WHO

- Diagnose and treat
- Publish and conduct research
 - Sentinel cases
 - Community-based intervention
- Educate
 - Patients and families
 - Colleagues and students
- Advocate
- Serve as role models

42

US example: Task Force on Environmental Health Risks and Safety Risks to Children
Asthma and the Environment: A Strategy to Protect Children:
RESEARCH

Strengthen and accelerate focused research into the environmental factors that cause or worsen childhood asthma. Strengthen and accelerate research into the environmental factors that may contribute to the onset of asthma in children.

Expand and accelerate research to develop and evaluate environmental strategies that will improve the quality of life of people with asthma.

PUBLIC HEALTH PROGRAMS

Implement public health programs that foster improved use of current scientific knowledge to reduce environmental exposures to prevent and reduce the severity of symptoms for those with asthma.

Promote clinician and patient implementation of national guidelines for reducing environmental risks that worsen asthma.

Expand support for state and local public health action.

Reduce children's exposure to environmental tobacco smoke and other indoor triggers in their homes.

Establish school based asthma programs that help reduce or eliminate allergens and irritants and that promote student's self management of asthma and full participation in school activities.

Continue to reduce outdoor air pollution.

SURVEILLANCE

Establish a coordinated, integrated, and systematic nationwide asthma surveillance system for collecting and analyzing health outcome and risk factor data at the state, regional and local levels.

DISPROPORTIONATE IMPACT ON THE POOR AND MINORITIES

Identify the reasons for and eliminate the disproportionate burden of asthma among different racial and ethnic groups and those living in poverty.

Improve asthma management for children within the medicaid program.

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