The immunology of fetuses and infants
What drives the allergic march?

Allergy 55 (7), 591-599 (2000)

U. Wahn
The Department of Pediatric Pneumology and Immunology, Humboldt University, Berlin

“The ‘allergic march’, which refers to the natural history of atopic diseases, is characterized by a typical sequence of sensitization and manifestation of symptom which appear during a certain age period, and persist over years or decades.”

“Atopy refers to those allergic conditions which tend to cluster in families, including hay fever, asthma, and eczema, and which are associated with the production of specific IgE antibodies to common environmental allergens.”

There is evidence of the prevalence of certain atopic phenotypes in children aged 6 and 13 years.

Most investigators seem to agree that a complex interaction between genetic and environmental factors regulates the manifestation and development of different atopic features.

The natural history of atopic diseases

Atopic diseases tend to be related to the first decades of life, and obviously require a juvenile immune system.

“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.

Hereditary factors

“It has been known for many years that atopic diseases run in families.”
“The risk of neonates developing atopic symptoms during the first two decades of life strongly depends on the manifestation of the disease in their parents and siblings.”

Genetic studies conclude that “both asthma and other allergic diseases are genetically heterogeneous disorders each of the atopic phenotypes is probably the result of a polygenic inheritance and a complex inter-action between genes and environmental factors.”

**Early immunologic markers**

“The production of IgE is known to be largely genetically controlled.”

Those at risk of developing atopic disease have a low TH1 response and a high TH2 response.

**Environment and lifestyle**

“During the last decade, a number of environmental and lifestyle factors have been found to be significantly associated with certain atopic phenotypes.”

**Allergen exposure**

Although exposure to environmental allergens as a risk factor for sensitization and manifestation of atopy and asthma is established, recent investigations suggest that factors other than allergen exposure are important in determining which children develop asthma. [IMPORTANT]

**Adjuvant factors**

Studies suggest that both traffic and passive tobacco smoke exposure are important risk factors in developing atopy and asthma.

**Lifestyle and the development of atopic disease**

The risk of atopic sensitization and disease manifestation early in life is particularly high in Western, industrialized countries with relatively high standards of living.

Recent studies have shown that the prevalence of symptoms of allergic rhinitis and of allergen-specific IgE antibodies is much lower among the offspring of farmers than among other children in these areas.
Several studies have found that the critical period during which lifestyle influences the development of atopy is probably the first years of life.

The lifestyle factors which have been proposed so far

“The hypothesis which has attracted the most interest is the proposal that a decline in certain childhood infections or a lack of exposure to infectious agents during the first years of life, could have caused the recent epidemic of atopic disease and asthma.” [WOW!]

“Infections are known to have long-lasting, nonspecific systemic effects on the nature of the immune response to antigens and allergens.”

“For example, recovery from natural measles infection reduces the incidence of atopy and allergic responses to house-dust mites to half that seen in vaccinated children.”

“Obviously, the fact that certain infections induce a systemic and nonspecific switch to Th1 activities could be responsible for an inhibition of the development of atopy during childhood.”

Prenatal or perinatal bacterial infections are modulators of the atopic march.

Often, preterm birth is now the result of bacterial infections during pregnancy, and these low-birth-weight infants have a lower prevalence of atopic eczema.

Intestinal microflora might well be the major source of microbial stimulation of the immune system in early childhood, as they enhance Th1-type responses. [Antibiotic use during early childhood would destroy this microflora Th1 driven response].

Other lifestyle-related factors

The lifestyle-related factors which might be associated with the atopic march in children.

1. Obesity.
2. Immobility (systemic).
3. Children tend to watch television longer nowadays rendering them less mobile.
(4) “Recent reports describe an association of the use of antibiotics during the first 2 years of life with an increased risk of asthma.”

(5) “The hypothesis has been proposed that the use of omega-6 instead of omega-3 dietary fatty acids in certain populations might cause an increased risk of allergic inflammation.”

**Principles for prevention today**

The primary prevention measures which are suitable for everybody include: breast-feeding in infancy and introduction of solid food after the fourth month of life, the avoidance of smoking and passive smoke exposure of children.

**KEY POINT SUMMARY FROM DAN MURPHY**

(1) Atopic disorders (hay fever, asthma, and eczema, etc.) are significantly increasing in all Western industrialized countries.

(2) Atopy is dependent upon both genetic and environmental factors,

(3) The mother’s diet (especially eggs and dairy) during pregnancy may predispose the infant to atopy.

(4) The critical period during which lifestyle influences the development of atopy is the first years of life.

(5) A decline in certain childhood infections and during the first years of life could have caused the present global epidemic of atopic disease and asthma.

(6) Healthy intestinal microflora in early childhood enhance the desireable Th1-type response. [Destroyed by antibiotics].

(7) The use of antibiotics during the first 2 years of life increase the risk of asthma.

(8) A high omega-6 to omega-3 dietary fatty acids ratio increases risk of allergic inflammation.