

Editorial

The immunology of fetuses and infants

Numerous studies indicate that the prevalence of atopic disorders – bronchial asthma, atopic dermatitis, and allergic rhinoconjunctivitis – has increased worldwide over the last few decades (1, 2). This increase in the prevalence of atopic disorders has been assumed to depend on an interaction between genetic and environmental factors (3). The increase in allergy prevalence is particularly seen during childhood, since newborn infants and young children are more susceptible to the effects of environmental pollutants than adults (1).

Our knowledge of atopic diseases among children – “the atopic march” – indicates that the development starts early, maybe already *in utero* (4–6). Interest in the *in utero* milieu in relation to the development of allergy goes back to the beginning of the 19th century (7). Furthermore, in the 1920s, Ratner, a US pediatrician, published several studies describing his attempts to intervene in fetal sensitization in order to reduce the development of allergy in the offspring (8). The interest in fetal sensitization intensified after the discovery of IgE (9). Thus, it was found that the fetus can produce IgE already from the 11th to 12th weeks of gestation (10). It has also been generally accepted that IgE does not pass the placental barrier; therefore, the IgE in cord blood is assumed to be of fetal origin (11). However, there are few studies showing the presence of antigen-specific IgE antibodies in cord blood (12).

Over the last decade, our knowledge of molecular biology in relation to allergic inflammation has increased dramatically. Thus, the immune responses can be classified as Th1 or Th2 depending upon the predominant profile of cytokine production (13). Several studies have shown that IgE-mediated allergic diseases are associated with expression of Th2-like cytokine responses (13). The immunologic milieu of the placenta is constitutively skewed away from Th1 and shifted toward the Th2 phenotype during pregnancy (4, 5, 14). These Th2-cytokine-dominated immune responses seem to be preserved in early periods of infancy (15). The initial exposure of neonates to environmental allergens, via breast-feeding, inhalation, and/or digestion, at the time when the immune system is biased toward the Th2-skewed cytokine phenotype, contributes to the preferential development of the Th2 pathogenic responses, as found in atopic allergy (15, 16). An increased IgE level in cord blood, the presence of cord-blood mononuclear cell proliferation in response to various allergens (17, 18), and the presence

of activated and memory T cells at birth (15, 16) suggest that the risk of such a development may be amplified by prenatal exposure.

Although our knowledge of the immune events in allergic inflammation and the development of atopic disorders has increased, our understanding of the immunologic events that lead to tolerance and health is still a matter of dispute (19). The immune inter-relationship between the mother and the fetus/newborn infant during the pre- and postnatal periods seems to be of importance for such a development (4, 5, 20, 21). However, much research in the field of epidemiologic allergy has so far focused on the impact of various factors of exposure. It is now becoming evident that various so-called protective factors deserve more attention. The inverse relation between the development of atopic disorders and being raised on a farm with cows (22), or of being born into a family with an anthroposophic lifestyle (23), is a significant observation. New knowledge gained from such studies may later have a great impact on allergy-preventive measures with regard to both dietary recommendations (i.e., maternal diet during pregnancy and lactation and infant feeding during the first year of life) and factors of the indoor environment (i.e., keeping of animals, exposure to tobacco smoke).

In *Allergy Review Series VI*, “The immunology of fetuses and infants”, leading pediatric allergologists will present up-to-date summaries of the immunology of the fetus and the infant in relation to IgE sensitization and clinical allergy during infancy (24–27). This will offer new insights into this exciting field of allergology and stimulate further research.

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