

Atopic dermatitis and food allergy in Europe – prevalence and risk factors

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It has been established by many epidemiologic surveys published in recent years that the prevalence of atopic disorders, not only rhinitis and asthma, but also atopic dermatitis (AD), is increasing in childhood, mainly in the more developed societies (1, 2). Already, 25–30% of all children at the age of 11 years suffer from an atopic disease. In the very young age group, the predominant manifestations of atopy are AD and food allergy (FA), and AD is the first sign of the atopic march (3). Interestingly, a large proportion of children with AD experience later in life other respiratory allergic manifestations such as rhinitis or asthma. Although AD is well known since ancient times, it has been rather neglected until recent years, when this common and frustrating disorder has led to research in many countries. In fact, due to its peculiar natural history, which is characterized by a high prevalence of asthma, AD is an ideal disorder to investigate the risk factors for the development of asthma in atopic children (3, 4).

Several epidemiologic studies have shown that the prevalence of AD in children varies from 9% to 15% (5) and have confirmed the increase of AD in European children in the last decades. An analysis of the prevalence of allergic diseases among Swedish conscripts has confirmed the increase of AD in the last decades. The prevalence of these disorders was quite similar in 1973–8 (males born between 1955 and 1960). Since then, there has been a threefold increase in the prevalence of flexural dermatitis (from 0.8% to 2.6%), asthma (from 2%

to 6%), and hay fever (from 5% to 15%) up to 1993, while the prevalence of contact dermatitis has increased much less (6).

Other epidemiologic surveys performed in Germany have provided new information on the prevalence of atopic disease in children in this European country. Behrendt et al. have shown that the prevalence of AD was significantly higher in the former East Germany (15.7%) than in the former West Germany (12.9%) (7). However, another study did not show a higher lifetime prevalence of AD in Leipzig (East Germany) than Munich (West Germany) (8). Schafer et al. performed a cross-sectional survey in Bavaria, looking at the risk and prevalence of atopic disease in relationship to atopy in parents. Overall, 8.3% of the children had AD, and the relative risk for the child was seven times higher if the mother also suffered or had suffered from AD (9). Studies from other European countries have reported the following data: The prevalence of AD is 7% in Denmark (10), 23.6% in Norway (11), 20% in the UK (12), and 20% in Switzerland (13). In Italy, according to our recent data, the prevalence of AD is 5%; the period prevalence according to age is 10% in children below 2 years of age, 5% at 2–6 years, 4% at 6–12 years, and 1% over 12 years (14).

Moreover, we have demonstrated a significantly higher prevalence of AD ($P < 0.005$) in children living in northern (7%) than in southern Italy (2%). There was no significant difference in the prevalence of AD according to the number of inhabitants in the cities where the children lived,

but the prevalence was significantly higher ($P < 0.05$) in children living in city centers (5%) or in residential areas (5%) than in those living in inner areas (3%) (14).

Our data agree with recent data showing that in northern and eastern Europe the highest 12-month prevalences of wheezing and flexural dermatitis were in Scandinavia and the lowest in Albania, Georgia, Romania, Russia, and Uzbekistan (6).

The baseline data of 818 infants with AD, under 12 years of age with a positive family history of atopic disease and with a negative history of asthma, from 12 European countries plus Canada enrolled in the ETAC (early treatment of atopic child) study, a large multicenter, multinational randomized study investigating the possible preventive effects of cetirizine for the prevention of asthma, confirmed the crucial role of the environment in early life for IgE sensitization. Profound differences in IgE sensitization to domestic allergens were found in different countries. Early exposure to potent allergens such as that of cat fur was associated with a highly significant increase of IgE antibodies to cats. Evaluation of both baseline and follow-up data of the enrolled infants up to the age of 5 years will offer information to elucidate the natural history from atopic dermatitis to asthma.

Early exposure to cow's milk and egg was associated with a higher rate of sensitization to these potent allergens. In countries with a lower prevalence of breast-feeding, there was a higher rate of sensitization to cow's milk and egg.

In addition, children with more severe AD, as defined by the Scorad index, had a higher rate of sensitization to cow's milk and egg, confirming the important role played by food allergy in AD.

Although the risk of AD is certainly genetically determined, this factor cannot explain the reported increase in prevalence of the disease, because the genetic background has not changed. Therefore, the reason for this increase must be in the interaction, in genetically predisposed individuals, between the environment, in terms of the time, and the amount of allergen exposure, in the presence of nonspecific indoor and outdoor air pollution and irritants (6, 15).

Experimental, epidemiologic, and clinical observations strongly support the hypothesis that the condition under which the primary encounter with an allergen takes place influences the immune response; i.e., whether tolerance or sensitization is triggered (16–18).

A number of interesting data have been accumulated on the effect of some environmental factors that, encountered in early childhood, may modulate the sensitization to allergens. For

instance, geographic differences modulate the prevalence of AD in the same country, thus stressing the crucial role of the environment in this disorder.

Allergic disease is more common in industrialized countries than in rural areas of developing countries and in the same country according to the rate of industrialization (6).

There is also a relationship between lifetime prevalence of AD and socioeconomic status, showing that the disease is more common in more privileged families. In the UK, Williams et al. have shown that the prevalence of AD was significantly higher for each age group in the higher social class and was lowest in the underprivileged social class (19). This study was confirmed in Switzerland by Wüthrich, who reported a prevalence of AD of 15.6% in the children of the higher social classes and of 9.6% in those of the lowest social classes (13). The Italian data showing a higher prevalence of AD in the north than the south agree with these studies. The main family income is higher in the north, where there is much heavy industry, than in the south, which is mostly rural, and the main employment is in agriculture and fishing (14).

In addition, the results of several reports performed in the last decade clearly suggest that factors such as crowding (number of persons per room) and family size (number of siblings) may be associated with the decrease in the prevalence of AD. Domestic crowding is usually related to low socioeconomic conditions and would be expected to be associated with increased exposure to common infections (20).

A low standard of living with domestic crowding and frequent infections during early infancy could trigger T-cell immune responses, expressing the TH1 phenotype and protecting against atopic sensitization. On the other hand, a high standard of living without crowding and fewer infections during the first months could enhance an immune response of the TH2 type in children with an atopic propensity, making them more vulnerable to adjuvants, such as pollutants (21–23).

There is strong evidence to support the epidemiologic observation that pollution may enhance sensitization, as well as triggering symptoms of the respiratory tract. Exposure to tobacco smoke is by far the best identified risk factor for the development of asthma (24).

In conclusion, AD is an ideal “experiment of Nature” by which to investigate the environmental factors influencing the allergic march.

Knowledge of the main risk factors both for atopic sensitization and for the onset of asthma is imperative to promote studies in the prevention of

asthma in these highly atopic children. Preliminary data from the ETAC study have stressed the crucial role of allergen exposure early in life in promoting allergic sensitization.

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