

## Editorial

# Can asthma and allergy be prevented in real life?

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Accepted for publication 20 December 2002

There is a general agreement that a widespread increase in the prevalence of asthma and allergy has occurred during the last 50 years, and especially the last 20 years (1, 2). Several of the studies indicating this are cross-sectional studies with limited level of evidence (3), whereas other studies used identical methods in repeated cross-sectional studies (4) or cohort studies (2). The reported increase in asthma and allergic disease in Europe and the rest of the world has created a general interest and concern in relationship to the possible causes for this increase. Despite increasing knowledge about the genetics of asthma and allergy (5), focus has been put upon the role of the environment and environment–gene interactions (6). The increased prevalence of asthma and allergy has led to a focus upon the environmental factors involved in causing asthma and allergy and the preventive measures which may be taken to prevent the development of asthma and allergy. The effect of the environment starts early. Already during pregnancy it has been shown that smoking has an impact upon reduced lung function in newborn babies of smoking mothers compared with infants of nonsmoking mothers (7). Also allergen exposure during pregnancy has been demonstrated to have an impact upon cellular proliferative responses during late pregnancy (8). Analysing data from an English general practice birth cohort of 24 690 children included between 1988 and 1999, identified exposure to antibiotics *in utero* as a risk factor for asthma as well as hay fever and atopic eczema at the age of 1 year and later in a dose dependent manner (9). Such observations may indicate that preventive measures taken already during pregnancy may be important.

On the contrary, dietary preventive measures taken during pregnancy have not been demonstrated to influence later allergic sensitization or allergic disease in the preschool child (10).

Focus has been put upon the newborn period and infancy as a critical time period for the later development

of allergic diseases and asthma. Holt proposed that during pregnancy Th2 cells were primed *in utero*, and that after birth via immune deviation a switch to an either predominant Th1 (normal) or Th2 (atopic) phenotype occurred with a high risk 'window' for allergic sensitization existing in early postnatal life (11).

This immunologic view favours particularly infancy as an important time period for obtaining an effect of preventive measures upon later development of allergic diseases and asthma. Traditionally preventive measures have been directed against the child at high risk for developing allergic diseases, that is the child with at least one primary relative with manifest allergic disease. The preventive measures have usually included measures as exclusive breast feeding for the first 4–6 months of life, avoidance of solid foods for the same time period, avoidance of exposure to tobacco smoke products also during pregnancy, reduced exposure to allergens such as house dust mites, animal dander and cockroaches during early life. A number of prospective studies have assessed these preventive measures. Høst & Halken recently gave an overview of evidence based recommendations for primary and secondary prevention of allergic diseases reviewing the existing evidence for such recommendations (12).

A renowned interventional case–control study of high risk infants starting at birth on preventive measures for the development of allergic diseases is the 'Isle of Wight Study' initiated by David Hide. At 4 years of age the children taking preventive measures continued to show less allergic symptoms, less sensitization as determined by positive skin prick tests and less eczema (13). As part of an European multicentre study a group of high risk children underwent preventive measures consisting of house dust mite impermeable mattress covers. After 12-month follow-up logistic regression analysis demonstrated an independent preventive effect on development of house dust mite allergy by the prophylactic measures.

In order to prevent sensitization in one child, 15 children were needed to treat (14).

Whereas older studies indicated that early exposure to allergens, both pollen (15) and animal dander (16), could be related to the later development of allergic diseases, and thus supporting the rationale for reducing early exposure to allergens, some cross-sectional studies, first performed on an adult population, indicated that early exposure to animal dander might protect against later allergic sensitization (17). Also cross-sectional studies in children have supported this view (18). Interestingly enough a recent report suggested that the effect of early exposure to allergens might be different in high risk children and normal children. Celedón et al. reported from a study on 448 children with at least one parent with a history of atopy, followed from birth to 5 years of age (19). Among children, whose mother had no history of asthma, exposure to cat or Fel d 1 concentrations  $> 8 \mu\text{g/g}$  dust at 1 month of age, a reduced risk of wheezing between 1 and 5 years of age was found. In children with a mother with a history of asthma such exposures increased the risk of wheezing at the age of 3 years (19). This suggests that preventive measure might have a different effect in high risk children and normal children.

This is in line with the Austrian reports of reduced incidence of asthma and allergic sensitization in children living at farms with animals (20, 21). This has been attributed to the level of endotoxins in farms with animals (22). In a recent study the authors reported that the endotoxin levels in dust samples from the children's mattresses were inversely related to the occurrence of hay fever, atopic asthma and atopic sensitization (23). The endotoxins consisting of bacterial antigens protecting against allergic sensitization is in line with the hygiene hypothesis stating that infections and other causes of Th1 stimulation in early life protect against later allergic sensitization (24). On the other hand it should be mentioned that exposure to bacterial endotoxins during early childhood is related to an increased occurrence of wheezing during 1 year of life (25). Thus the effects of early exposure may have different effects upon different groups of children.

One of the preventive measures included in almost all programs for the prevention of asthma and allergic disease, is the advice of exclusive breast-feeding for the first 4–6 months of life. Finnish studies supported the protective effect (26, 27), in one study a protective effect

for asthma and other allergic disease was found up to 17 years of age (27). This has also recently been cast doubt on. Sears et al. just recently published a cohort study from New Zealand followed from 9 years of age until 26 years. In this study breast feeding did not protect against allergic sensitization or against current asthma between 9 and 26 years of age. On the other hand breast-feeding even seemed to increase the risk (28). Thus several of the different traditional preventive measures to be taken against development of asthma and allergy have during the later years been put under question. This may be related to the increased occurrence of asthma and allergic diseases. Many children, who during earlier times would not have become asthmatic or allergic, have developed these conditions with the present environmental conditions. Different factors may be at work in the development of asthma and allergy in high risk children and low risk children. This may also influence the effect of preventive measures taken.

Most studies performed on the effect of preventive measures in relationship to the development of asthma and allergy have been performed on high risk children. Few studies have been purely observational studies. The study by Wickman et al. (29), published in the present issue of *Allergy*, is therefore of particular interest. In the observational birth cohort study, BAMSE, consisting of 4089 children, an analysis was performed assessing the effect of the families living according to the Swedish primary preventive guidelines for allergic diseases. These guidelines included encouragement of breast-feeding, avoidance of exposure to tobacco smoke and good ventilation and normal dampness in the homes. In this observational noninterventive study the cumulative incidence of recurrent wheezing at 2 years of age was 12.6% and of asthma 6.8% among children with a lifestyle in agreement with all guidelines, compared with 24.1 and 17.9%, respectively in children from families exposed to at least two of the three risk factors (29). In children with heredity to asthma, living according to the guidelines gave a threefold decrease in asthma and in children with no heredity a twofold reduction.

This study may be classified as a real life study, demonstrating the effect of preventive measures in a real life setting. The present study shows that prevention of asthma and allergy may be very effective, and further studies, carefully designed and controlled, followed by real life cohort studies should be encouraged.

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