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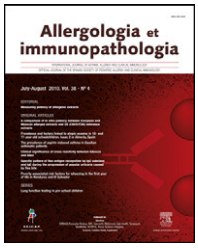

EDITORIAL

Is atopy the common factor mediating changes in the prevalence of different allergic diseases?

The prevalence of allergic disease has been increasing for at least the past 40 years and has now reached epidemic proportions in many countries.[1–3] The underlying cause of the observed increase in allergies remains unknown; and opinion is divided on the role of atopy in the pathogenesis of asthma, eczema and rhinoconjunctivitis. Indeed it is not clear whether rising prevalence of diseases such as asthma, food allergy and eczema is connected, or whether it is due to separate processes. Thus in some countries such as the UK asthma prevalence has fallen in the last decade while food allergy continues to increase.

The international study of asthma and allergies in childhood epidemiological research programme (ISAAC) was established in 1991 to look at epidemiological factors associated with asthma, eczema and rhinoconjunctivitis. It is the largest allergy survey ever undertaken, with almost 2,000,000 participants in 105 countries.[3] This large cross-sectional study has provided a powerful and unique opportunity to explore, on a global scale, the epidemiological factors involved in allergic disease. In the current edition of Allergologia et Immunopathologia Asher et al. present data from the third phase of the ISAAC study and examine time trends in the prevalence of asthma, eczema and rhinoconjunctivitis symptoms over a seven-year period.[4]

The key question which Asher et al. have addressed is whether the relationship between asthma, eczema and rhinoconjunctivitis has changed over a seven-year period. The study has already established significant rises in the prevalence of some of these diseases over this short follow-up period, but it is not clear whether these are due to separate processes.[3] If they are due to separate processes then one might expect the relationship between the diseases to change over time. Asher et al. provide robust data confirming that over a period of seven years the prevalence of asthma, eczema and rhinoconjunctivitis symptoms has remained in a near constant relationship to each other across 106 centres in 56 countries. The authors suggest that these findings could represent chance; might relate to the short interval between studies or alternatively suggest that the ''three diseases regulate themselves for prevalence and severity''.

At first these results may seem uninteresting; why would we expect the relationships between these diseases to change over such a short follow-up period? The reason is that relationships between the diseases vary in different populations examined cross-sectionally, so one might expect them to be differentially influenced by environmental changes. There are no consistent associations with gene polymorphisms for each of these conditions, so one might expect the environmental influences interacting with such polymorphisms to differ. The findings of Asher et al. suggest two major possibilities – either environmental influences are the same for these three conditions, or there has been insufficient time for the environmental factors to change sufficiently to differentially affect prevalence rates. This may be particularly relevant if the changing environmental factors influence disease development from very early in life. However, anaphylaxis admissions in children appear to have risen faster than the prevalence of asthma, eczema or hay fever in some regions during the 1990s, over a similar time period.[5] In this context, the data reported by Asher et al. are quite intriguing, and give us potentially important insights into these allergic diseases. They suggest that the environmental exposure(s) which have led to increased disease prevalence between ISAAC I and ISAAC III surveys may be similar across asthma, eczema and hay fever, and that they may all be acting through one specific mechanism.

The most obvious candidate for a unifying factor is atopy – if rising atopy underlies rising prevalence of these diseases, and the relationship between atopy and disease is similar for all three conditions, then this would explain their constant inter-relationship. Atopy does seem to be more common than previously, in some countries– for example in NHANES II and III, a 2.1–5.5 fold increase in IgE sensitisation to common allergens was shown over an 18-year period.[6] Moreover, ISAAC phase II showed a significant correlation between demonstrable atopy and asthma, eczema and rhinoconjunctivitis across both affluent and non-affluent populations.[7–9] This was despite relatively poor participation rates with average participation for skin prick or IgE testing at between 60 and 70% (range 13–100%).[7–9] The strongest correlations between atopy and disease were

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seen in more affluent countries with the odds ratio for allergic disease in atopic individuals from affluent countries being 4.0 (CI 3.5–4.6), 2.7 (CI 2.3–3.1), and 2.2 (CI 1.8–2.6) for asthma, eczema, and allergic rhinoconjunctivitis respectively.[7,9] So while a significant proportion of asthma, eczema and rhinoconjunctivitis is not associated with systemic evidence of atopy, it is not possible at this stage to exclude atopy as the common underlying factor influencing changes in allergic disease prevalence.

One important limitation of the findings of Asher et al. is the lack of local detail. Genetic variations in responses to environmental factors, and local variations in exposure may lead to different changes in the relationship between the three diseases over time in different populations. There is some evidence for this in Figure 3, where some centres have changing relationships between asthma, eczema and rhinoconjunctivitis over time although overall there is no clear global trend.[4] The importance of gene-environment interactions in allergic disease suggests that summative data from large-scale projects such as ISAAC might miss important genotype-specific associations.[10] So it is possible that different relationships between these diseases may be seen in specific populations, exposed to specific environmental stimuli.[11] Further work is therefore needed, especially in populations that have undergone specific environmental changes during the interval between ISAAC I and ISAAC III.[12] The differing interactions between genetic, epigenetic and environmental factors are difficult to explain; and population specific risk factors are hard to tease out when examined on a global scale.

Over the past 30 years allergy research has often relied on large cross-sectional studies and cohort studies to provide insights into the causes of allergic disease. With the prevalence of these diseases at epidemic proportions, and the burden conferred by them a major public health issue, the time has surely come to move towards an increased focus on intervention studies for the primary and secondary prevention of these diseases. In many regions of the world, each child born today has a high risk of lifelong allergic disease, which is largely irreversible. Prevention of atopy may change this, and the number of completed primary prevention trials is really very small in proportion to the scale and duration of the problem.[13] Data such as those presented by Asher et al. suggest that targeting a single mechanism may be effective in reducing the prevalence of all allergic diseases, and we would suggest that the most likely mechanism in that regard is atopy. Going forward, there needs to be greater work to look at specific interventions to prevent atopic immune responses from establishing themselves in the developing infant.

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