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Natural course of house dust mite allergy

House dust is a complex mixture containing many different foreign proteins, as well as a variety of arthropods, nematodes, bacteria, fungi and human skin scales. When Voorhorst and Spieksma established that dust mites were the most important source of allergens in house dust in the Netherlands, they also developed the technique for growing quantities of mites. This made it possible to purify a major allergen (Der p 1) to measure the airborne exposure and to study the immune response. Initial studies focused on isotype specific antibodies and T-cell responses. With more detailed understanding, it became clear that germinal centres were not a good site for generating IgE B-cells (Aalberse and Platts-Mills, JACI 2004). Indeed, those immunisation regimes or adjuvants that effectively induce high titer IgG antibodies and germinal centre formation generally switch off IgE production. The route to produce high titer IgE antibody production to inhalants is a direct switch from IgM B-cells to IgE B-cells with subsequent generation of IgE plasma cells. Further, these plasma cells are predominantly sequestered in secluded sites within the bone marrow, which are protected from the regulatory effects of T-cells. Thus, even with prolonged avoidance of exposure or high dose immunotherapy, IgE antibody levels only change slowly.

It is important to remember that mite growth is dependent upon temperature and humidity as well as on the availability of suitable nests. While high levels of mite allergens are found in most temperate climate countries, there are also many areas where mites do not flourish, primarily because of low humidity (e.g. northern Scandinavia, the mountain states of the United States and apartments in Chicago). In birth cohorts, it is possible to follow the development of serum IgE antibodies. In general, very little happens in the first two years, and hospitalisation for bronchiolitis or wheezing at that age is not significantly related to mite allergy (Heymann *et al*, JACI 2004). By contrast, by age 7 years, sensitisation is common and is increasingly strongly associated with asthma (Sporik *et al*, NEJM 1990). However, increasing evidence suggests that the risk of acute or severe asthma is associated with the titer of serum IgE antibodies. This evidence relates to cat, cockroach and dust mite allergens (Commins *et al*, AJRCCM 2012). Furthermore, there is increasing evidence that the contribution of rhinovirus to acute episodes of asthma is restricted to allergic subjects and is strongly influenced by the titer of IgE antibodies to inhalant allergens, particularly dust mites (Soto-Quiros *et al*, JACI 2012).

Children living in what we might call “pre-hygiene” societies today do not have a high prevalence of asthma, and yet many authors have documented positive mite skin tests in these populations. Recently, we have reported on populations of this kind in rural Kenya, Ghana and Ecuador (Stevens *et al*, CEA 2011). The striking feature in each case is that the titers of IgE antibodies to mite are low or very low. Thus, one could

argue that the effect of hygiene (i.e. clean water, shoes and anti-helminth treatment) is to allow high titer IgE antibodies to indoor allergens, as well as a fall in total IgE. Taken together, dust mites are more than just a model for other perennial exposures. In many countries, dust mites dominate all other forms of sensitisation, as judged by prevalence and most of all by titer. The best explanation for this is that the particles carrying dust mite allergens, endotoxin and mite and bacterial DNA are a remarkably effective immunogen for the production of IgE antibodies.