

EDITORIAL

Why do allergic individuals accumulate more eosinophils at the site of an IgE-mediated reaction than do normal subjects?

Since the time of Prausnitz and Kustner, investigators of allergic reactions have known that sera of allergic individuals can passively transfer skin reactivity to specific allergens. In the 1930s the Prausnitz–Kustner reaction was utilized to investigate the effect of prolonged administration of allergy extracts on the levels of blocking (IgG) antibody and of reaginic activity in the sera of individuals treated with immunotherapy. In the 1960s it was shown that IgE is a member of the immunoglobulin family and is responsible for reaginic activity. It was also shown that injection of antibodies to IgE triggers weal-and-flare reactions in human skin. Also during the 1960s, investigations utilizing the skin-window procedure showed that eosinophils infiltrate skin-test sites and it was found that more eosinophils were present in the skin-window sites of allergic patients [1]. Finally, in the 1970s it was recognized that cutaneous allergen challenge not only produces an immediate reaction, but also a late-phase cutaneous reaction, the latter being even more marked than the former in terms of the intensity of the inflammatory response [2,3].

In studies of the Prausnitz–Kustner reaction, virtually all investigators have made the tacit assumption that there is no difference in the responsiveness of the recipient; in other words, one sees the same type of responses in recipients who are allergic, as well as in recipients who are not allergic. However, in most studies investigators took pains to perform the Prausnitz–Kustner reaction on normal individuals because of the potential complications which could arise from ongoing reactions in allergic subjects. The possibility that there might be differences between the response of allergic and normal individuals to passively transferred antibodies was first raised by Eidinger *et al.* in 1962 [1] and again shown by Henocq and Vargaftig in 1986 [4]. Henocq and Vargaftig [4] noticed a striking accumulation of eosinophils in response to intracutaneous PAF-acether in allergic subjects which was markedly different from that seen in normal subjects, and their study resurrected the possibility that there are differences in the ability of normal and allergic subjects in the recruitment of eosinophils to sites of inflammatory lesions.

In the present manuscript, the authors have induced immediate and late cutaneous reactions in healthy and

atopic individuals by anti-IgE challenge and have utilized the skin-window technique to determine whether the pattern of cells obtained at 24 hr differs between these groups [5]. They found that challenge with anti-IgE is characterized by a significant accumulation of eosinophils only in atopic subjects. Interestingly, they also showed that cetirizine significantly inhibited this phenomena while terifenadine did not. These observations support the hypothesis that there is a difference between allergic and normal individuals in their ability to recruit eosinophils and further suggests that cetirizine has the unusual property, for an antihistamine, to inhibit eosinophilic accumulation at the site of an allergic lesion. In view of the increasing evidence that eosinophils play a critical role in the pathophysiology of allergic reactions, this effect of cetirizine could be of considerable importance.

Finally, what might account for this difference in the responsiveness of normal and allergic subjects? An obvious candidate is the occurrence of increased numbers of mast cells or an increased activity of mast cells at the site of the lesion. As mast cells have now been shown to produce a variety of cytokines, including IL-5 [6,7], the possibility exists that the mast cells of allergic individuals may be able to produce greater quantities of an eosinophil-specific chemo-attractant than do those of non-allergic individuals. Alternative hypotheses are that certain cells within the skin are able to bind IgE and produce an eosinophil specific chemo-attractant in response to antigen challenge or mast cell derived products stimulate another cell to produce an eosinophil chemo-attractant. However, it remains to be shown whether cells (other than mast cells), able to bind IgE and to be stimulated by antigen, exist at these local sites. The mast cell seems to be a very attractive candidate because of its possession of a high-affinity receptor for IgE. Clearly, Drs Henocq and Rihoux have identified an interesting difference between allergic and normal subjects and have highlighted a potentially important area for research.

References

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