

Closing comments: The future of allergy and asthma treatment

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Today we have been discussing the stimulus, the host, and current conventional therapy. In the future, treatment will change.

Patrick Holt¹ has said that in allergic-type inflammation the T_{H2} skewing of early childhood is not switched off. The key events occur during the period when specific T-cell responses to environmental antigens are initiated, and the ensuing T-cell election process (meaning the development of a T_{H2} -type predominance and the allergic reaction) may take several years to complete. His view is that we already know how this process operates and should contemplate controlling it in humans by deliberate administration of allergens to stimulate the development of T_{H1} immunity. I also believe that we know enough about the process to know what areas should be attacked. Whether the process will be allergen specific is moot; alternative therapy may focus on the inflammation itself, or on turning off IgE production as a whole.

The inhibition of allergic inflammation can therefore be considered at a number of different levels. It could be (1) in the form of receptor antagonists of mediators or cytokines, so that the effects of these on the cell receptor are blocked; (2) as inhibitors of chemotaxis, so that the cells do not get to the inflammatory site; (3) as inhibitors of endothelial cell activation, so that the cells are not able to access the inflammatory site; or (4) as antagonists of adhesion molecules.

IgE production may be blocked in a number of ways. For example, if IL-4 is one of the most important molecules in causing antigen-driven B-cell transformation to

an IgE-producing plasma cell, one can potentially block this by synthetic or natural IL-4 antagonists. Numerous cytokines inhibit IL-4 production. Another important signal for IgE production comes through CD40 ligand. Similar strategies can, in a nonantigen specific way, turn off the production of IgE.

I believe that new methodologies in molecular pharmacology are going to be the answer to allergy and asthma. Industry is well aware of this. I have missed this development by a generation. I believe, however, that the future is here now and will happen in the generation after me. When I see a mother and father in the clinic with a 4 year old with life-threatening peanut allergy, I give them encouragement and tell them that there will be many new strategies introduced during their child's lifetime that will turn the reaction off. We will see if this will take place.

REFERENCES

1. Holt PG. A potential vaccine strategy for asthma and allied atopic diseases during early childhood. *Lancet* 1994;344:456-8.

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J Allergy Clin Immunol 1998;102:S106

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0091-6749/98 \$5.00 + 0 1/0/93906