Anti-IgE Monoclonal Antibodies as Tools for Demonstration of Cutaneous IgE Bearing Dendritic Cells

To the Editor:

We read with great interest and benefit the recent article from Lever et al [1] concerning immunophenotyping of the cutaneous infiltrate and the mononuclear cells in peripheral blood in patients with atopic dermatitis.

In this study, using an anti-human IgE monoclonal antibody, the authors observed positive cells in the dermis but failed to demonstrate any staining on dendritic cells in the dermal or epidermal compartments. This is in contrast to the findings of Bruynzeel-Koomen et al [2], as well as to our observations [3] and those of others [4].

It has been well documented that IgE molecules do not bind to type I Fc epsilon receptors (FcεR) by the terminal part of their Fc fragment but by an area between the second and the third constant domain (amino acids 301–375) of both epsilon chains [5] so that IgE molecules are probably reclined when fixed on their receptors [6]. This reclining could be accompanied by a modification of the spatial structure in this area and a concomittant loss of reactivity for those antibodies reacting against the epsilon 1 epitope group (Cε1–Cε2). Moreover, it seems likely that IgE binding on FcεR occurs in a different manner depending on the receptor type (low or high affinity receptors for monomeric or oligomeric IgE molecules) and the cell type bearing the receptor. The characteristics and properties of the FcεR on epidermal Langerhans cells are still unknown and the binding mechanism of IgE molecules on these receptors remains unclear.

Our experience with 4 anti-IgE monoclonal antibodies directed against different epitopes of IgE molecules showed that those antibodies reacting with the so-called ε2 epitope group (Cε3–Cε4) are the most suitable for demonstration of IgE molecules on Langerhans cells [7]. Antibodies against ε1 epitope group reacted with dermal cells but failed to stain Langerhans cells, probably because this domain could be involved in the binding to the receptor or because of a modification of the three-dimensional structure of the epitope in this area during the binding. Another explanation could be the fact that LC bind IgE complexes where some epitopes are involved in the formation of the oligomers and so are not accessible for the antisera.

In other recent studies, Ophir et al [8] demonstrated immunohistoogically and Leung et al [9] immunoelectronmicroscopically the presence of IgE molecules on dendritic epidermal and dermal cells as well as on macrophages.

Since Lever et al did not state precisely the epitope against which their antibody is directed, it could be possible that their reagent failed to demonstrate IgE-bearing dendritic cells because it was reacting with an epitope modified as discussed above.

Thomas Bieber, M.D.
Johannes Ring, M.D.
Ernst Peter Rieber, M.D.
Ludwig-Maxmilians University of Munich

REFERENCES

1. Lever R, Tubitt M, Sanderson A, MacKie R: Immunophenotyping of the cutaneous infiltrate and the mononuclear cells in peripheral blood in patients with atopic dermatitis. J Invest Dermatol 89:4–7, 1987
2. Bruynzeel-Koomen C, van Wichen DF, Toonstra J, Berrens L, Bruynzeel PLB: The presence of IgE molecules on epidermal Langerhans cells in patients with atopic dermatitis. Arch Dermatol Res, 278:199–205, 1986
3. Bieber Th, Ring J, Rieber P: Comparative study of IgE bearing Langerhans cells and serum IgE level in atopic dermatitis (abstr). J Invest Dermatol 89:313, 1987
4. Pigatto PD, Berti E, Altomare GF, Polenghi MM: IgE on skin dendritic cells: A clue for work-related atopic dermatitis. Dermatologica 174:50–51, 1987
5. Geha RS, Helm B, Wood N, Marsh P, Gould H: IgE sites relevant for binding to type 1 Fc epsilon (FcER) receptors on mast cells (abstr). J Allergy Clin Immunol 79:129–1987
6. Holowka M, Baird B: Structural studies on the membrane-bound immunoglobulin E. (IgE)-receptor complex. 2. Mapping of distances between sites of IgE and the membrane surface. Biochemistry 22:3475, 1983
7. Bieber Th, Baier U, Burg G, Ring J, Rieber P: Quantitative assessment of IgE bearing cells in atopic dermatitis (abstr). J Invest Dermatol 89:449, 1987
8. Ophir J, Barker J, Alegre V, McDonald DM: The immunophenotype of dermal IgE bearing cells in atopic dermatitis (abst). J Invest Dermatol 89:313, 1987
9. Leung DYM, Schneberger EE, Siraganian RP, Geha RS, Bhan AK: The presence of IgE on macrophages and dendritic cells infiltrating into skin lesion of atopic dermatitis. Clin Immunol Immunopathol, 42:328–337, 1987

REPLY

We thank Dr. Bieber and his colleagues for their interest in our paper and would make the following comments;

The anti-IgE antibody that we used was produced by New England Nuclear. This is the same antibody with which Dr. Bruynzeel-Koomen has demonstrated epidermal dendritic cells, and the fact that in our preparations we observed positive staining in the dermis of large cells surrounded by smaller lymphocytes gives us confidence that the absence of epidermal staining in our preparations was not due to any technical problem.

The fact that Dr. Bieber, Dr. Bruynzeel-Koomen, and, most recently, Dr. Barker and colleagues [1] have all demonstrated the presence of IgE-bearing dendritic cells in the epidermis indicates that this is certainly found in the epidermis of patients with atopic dermatitis at certain stages of disease progression. Our patients were biopsied in a relatively quiescent stage and the majority had been using topical steroids. These two facts may explain our negative findings.

Rona M. Mackie, M.D., F.R.C.P., FRC Path
Rosemary S. Lever, M.D., M.R.C.P.
Marlyn L. Turbitt, M.Sc., Ph.D.
Western Infirmary
Glasgow, U.K.

REFERENCE

1. Barker JNWN, Alegre VA, MacDonald DM: Surface-bound immunoglobulin E on antigen-presenting cells in cutaneous tissue of atopic dermatitis. J. Invest. Dermatol. *90*, 117–121, 1988

0022-202X/88/$03.50