MODELING IMMUNOTHERAPY FOR ALLERGY

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Type I hypersensitivity, which functions to protect the organism from parasites, is caused by binding of antigen to IgE antibodies pre-attached to the cell surface of tissue mast cells and their circulating counterparts, the basophils. In "allergy," type I hypersensitivity is inappropriately induced by protein-based foreign substances (such as pollen) or protein components of insect stings, which in the normal course of events would be cleared from the organism without causing any damage. Paradoxically, a successful clinical treatment of allergy involves repeated immunization of allergic persons with low doses of the allergen—immunotherapy. Investigation of the available experimental evidence leads to the conclusion that the phenomena of immunotherapy are best addressed in terms of the interplay among the mechanism(s) of immune memory—Th1/Th2 cross-regulation—and the physical compartmentalization of the immune system. These conclusions are illustrated with a numerical simulation. © 1996 Society for Mathematical Biology

1. Introduction. Type I hypersensitivity is caused by binding of antigen to IgE antibodies pre-attached to the cell surface of tissue mast cells and their circulating counterparts, the basophils. Multivalent antigen binding to the pre-attached IgE promotes their cross-linking. Extensive cross-linking (Dembo et al., 1978) results in a release of a variety of mediators that collectively cause increased vascular permeability, vasodilation, smooth muscle contraction and local inflammation. Because these reactions occur rapidly, within minutes of repeat exposure to antigen, type I hypersensitivity is also called immediate hypersensitivity. In their benign form these reactions are thought to protect the organism from parasites (Abbas et al., 1991).

Type I hypersensitivity is inappropriately induced by protein-based foreign substances (such as pollen) or protein components of insect stings that in the normal course of events would be cleared from the organism without causing any damage. In its most extreme systemic form, anaphylaxis, mast cell/basophil-derived mediators can restrict airways to the point of asphyxiation and produce lethal cardiovascular collapse (Abbas et al., 1991). Such outcomes are fortunately rare. However, more moderate allergic responses
are widespread, e.g. an estimated 20% of the U.S. population suffers from an allergy to some common substance (Lichtenstein, 1993). The list of allergy-inducing substances includes foods, plant pollen (hay fever), antibiotics and protein components of insect bites.

An often successful clinical treatment of allergy involves repeated immunization of allergic persons with low doses of allergen—immunotherapy (Ishizaka, 1976). The treatment, if successful, continues for years. Observable outcomes of this treatment are (a) an increase in the concentration of circulating IgG antibodies, (b) slow (half-life = years) decrease in the concentration of circulating IgE antibodies and (c) suppression of the secondary IgE responses after long-term treatment (Ishizaka, 1976; Graft et al., 1987) (Fig. 1). The primary purpose of this paper is to formulate a hypothesis for understanding immunotherapy for pollen antigens and to explore some of its aspects via mathematical modeling.

2. Formulation of the Hypothesis. Continuous production of allergen-specific antibody in allergic individuals (Ishizaka, 1976; Graft et al., 1987) indicates that type I hypersensitivity is an immune memory phenomenon. This fact plays an important role in our model.