Atopy and Allergy

Mucosal contact with allergen results in uptake by an antigen-presenting cell (APC) and presentation in the form of an allergenic peptide held in the groove of the major histocompatibility complex (MHC) class II molecule to a helper T lymphocyte. This then provides help for a previously committed B cell, which is capable of recognizing the antigen, to make IgE antibody.

Factors determining IgE rather than IgG production are not fully understood; however, the nature of the antigen-presenting cells may be relevant. In atopic eczema and allergic rhinitis Langerhans cells which are HLA-DR positive and bear high-affinity IgE receptors have been described. Class switching to IgE is promoted by cytokines IL-4 and IL-13 and is inhibited by interferon γ. In atopics increased levels of T_H2 type T cells producing IL-4 have been described, e.g. in vernal conjunctivitis.

A second signal required for IgE expression is delivered by a soluble fragment of FcεRII (CD23). This is also upregulated by IL-4. Class switching with the production of mRNA for IgE has been described within 30 min of allergen contact. Initial IgE production probably takes place in the local lymphoid tissues. Once produced, the IgE is rapidly and avidly bound by its Fc piece to mast cells and basophils, which are then sensitized. Subsequent contact with the same allergen results in cross-linking of IgE molecules by their Fab portion, calcium ion influx, cell degranulation and mediator release.

Certain mediators exist preformed in granules within the cell, others are formed after activation by phospholipase A_2 breakdown of the cell membrane to release arachidonic acid. This is then metabolized by the cyclo-oxygenase or lipoxygenase pathways, depending on the cell type, to produce prostaglandins and thromboxanes, or leukotrienes respectively. Recent research suggests that there is a third phase of cytokine production taking place in the mast cell during the hours after degranulation. This involves *de novo* protein synthesis and results in the generation of several cytokines, including IL-3, IL-4 and IL-5. Storage of IL-4 has also been demonstrated within mast cells and its release can occur on degranulation.

Degranulation of mast cells and basophils can also occur following cross-linking of adjacent membrane-bound IgE molecules by anti-IgE, by anti-idiotype, or by lectins.

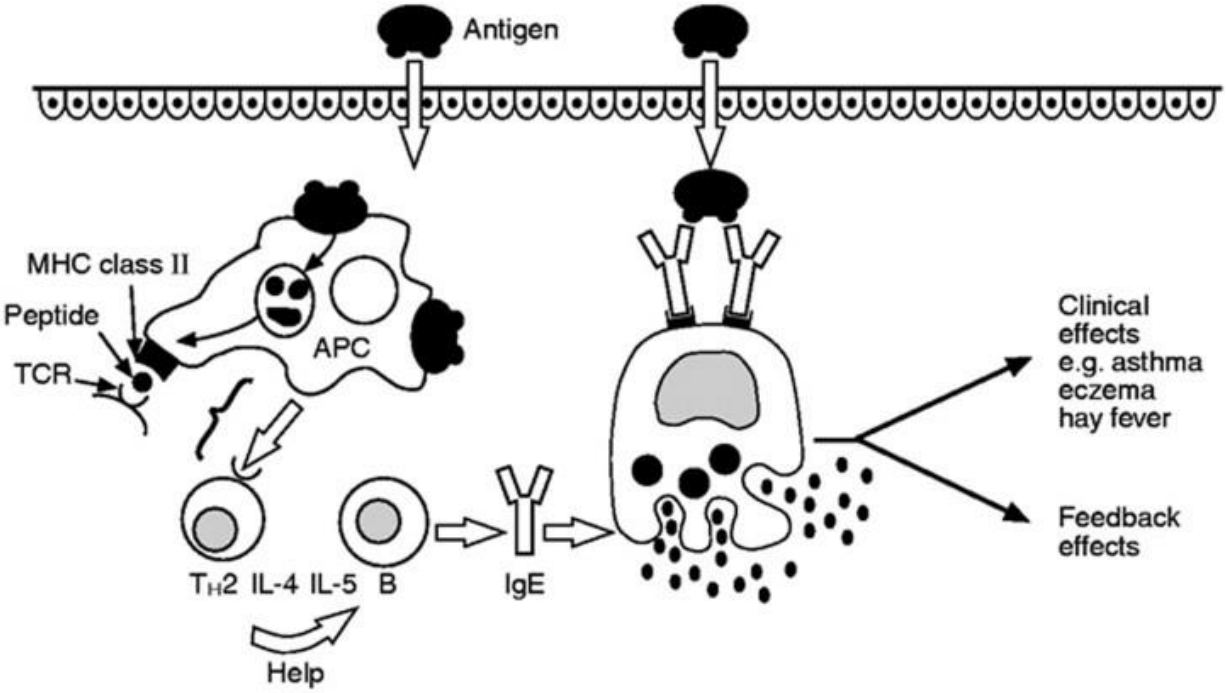
Fab portions of anti-idiotype could occupy IgE antigen-binding sites without causing cross-linking and degranulation, and can thus theoretically protect against allergen challenge.

Type I hypersensitivity reactions underlie all atopic disorders (eg, atopic dermatitis, allergic asthma, rhinitis, conjunctivitis) and many allergic disorders (eg, anaphylaxis, some cases of angioedema, urticaria, latex and some food allergies). The terms atopy and allergy are often used interchangeably but are different:

- **Atopy is an exaggerated IgE-mediated immune response; all atopic disorders are type I hypersensitivity disorders.**
- **Allergy is any exaggerated immune response to a foreign antigen regardless of mechanism.**

Thus, all atopic disorders are considered allergic, but many allergic disorders (eg, hypersensitivity pneumonitis) are not atopic. Allergic disorders are the most common disorders among people.

Atopic disorders most commonly affect the nose, eyes, skin, and lungs. These disorders include conjunctivitis, extrinsic atopic dermatitis (the most common type of eczema), immune-mediated urticaria, immune-mediated angioedema, acute latex allergy, some allergic lung disorders (eg, allergic asthma, IgE-mediated components of allergic bronchopulmonary aspergillosis), allergic rhinitis, and allergic reactions to venomous stings.


Antigen
MHC class II
Peptide
TCR
APC
Clinical
effects
e.g. asthma
eczema
hay fever
Feedback
effects
TH2 IL-4 IL-5 B
IgE
Help