Hypersensitivity adverse reactions that we see in clinical practice (Fig. 1). Become the ‘umbrella’ term to cover all reproducible are not IgE mediated. Hypersensitivity has therefore not exclusive to IgE.

With the realisation that delayed hypersensitivity reactions (IgE) antibody in 1968 by Johansson and Ishizaka, allergy can either be antibody or cell mediated. IgE-mediated allergy is mediated by IgE as in pollen allergic rhinitis, while non-IgE mediated allergy may be IgG mediated as in allergic alveolitis or cell-mediated as in allergic contact dermatitis.

Atopy is a personal or familial (genetic) tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop ‘classic’ allergic diseases such as asthma, rhinoconjunctivitis or eczematous dermatitis. To help illustrate this, IgE responses to pollen and cat dander are more frequent in atopic families, whereas IgE responses to bee venom and drugs are not more frequent in atopic families. Hence poli-nosis is referred to as an atopic disease whereas venom anaphylaxis is not an atopic disease.

Atopy phenotype is the (genetic) predisposition to a predominance of Thelper 2 (TH2) (IgE-producing) T-lymphocyte lineage type immune responses and development of classic IgE allergies. This seems to be coded on chromosome 5 (interleukin 4 & 5-induced IgE synthesis) and chromosome 11 (IgE Fc receptor production).

The allergic march is the chronological progression from one allergic manifestation to the next as an atopic child grows up. We see mainly food allergy and atopic eczema in infancy, while asthma develops in the middle childhood years and allergic rhinitis manifests in the teens.

Allergens are usually specific protein antigens (peptides) that stimulate immune hypersensitivity by reacting with IgE or IgG antibodies and T-cells. In certain circumstances low-molecular-weight sugars, metals and isocyanates act as haptenics by attaching to other proteins, and so induce an immune response. Allergens enter the body via inhalation, ingestion, skin contact or injection (drugs and venom).

Anaphylaxis is a severe life-threatening, generalised or systemic hypersensitivity reaction. The reaction develops over a short period of time (within minutes) and starts with itching of the gums/throat, palms and soles. There is usually associated urticaria, initially localised which then becomes generalised. This progresses to multiple-organ involvement with asthma, hypotension and circulatory collapse. The term allergic anaphylaxis is used where an immunological component is evident, and IgE-mediated with IgE or non-IgE-mediated when IgG immune complex, complement-related or immune cell-mediated mechanisms are evident. If no immune mechanism is evident, this is termed non-allergic anaphylaxis (previously referred to as anaphylactoid reaction).

The most extensively studied immune response is that mediated by IgE. The IgE-mediated allergic response (Fig. 2) comprises three stages, as seen in typical IgE-mediated allergic diseases such as asthma, allergic rhinoconjunctivitis and anaphylaxis.
• **Initial allergic sensitisation.** On initial exposure, antigen-presenting cells (APC) present the allergen peptide to T-cells (TH2 cells) which then induce B-lymphocytes to produce antigen-specific IgE. These bind to mast cell and basophil high-affinity IgE receptors. (This process can take up to 6 weeks to develop allergen-specific IgE.)

• **Early-phase (immediate hypersensitivity) reaction (up to 2 hours).** Re-exposure to the allergen then induces mast cells and basophils to degranulate, releasing preformed inflammatory mediators (histamine, tryptase and heparin) along with newly synthesised mediators (leukotrienes and cytokines). Histamine is the best studied of these mediators. It induces smooth-muscle constriction (bronchospasm), vascular permeability (swelling), mucus secretion (mucorrhoea) and sensory nerve stimulation (itch).

• **Late phase reaction (2-24 hours after allergen exposure).** Further mediator production (leukotrienes, cytokines, histamine) then occurs with infiltration of inflammatory cells (eosinophils releasing major basic protein, eosinophil cationic protein and more leukotrienes). TH2 lymphocytes also release cytokines that further stimulate IgE production, eosinophil chemo-attraction and increase mucosal mast cell numbers.

This rapid spiral of pro-inflammatory events is called the allergic inflammatory cascade, resulting in chronic allergic inflammation, airway irritability, mucosal damage and tissue remodelling.

**Basics of allergic disease management**

**Prevention of allergic disease** by avoiding or minimising exposure to the offending allergens:

- **Primary prevention** — preventing allergic sensitisation by avoiding any exposure to allergen in infancy
- **Secondary prevention** — preventing expression of the allergic disease by removing allergen after initial exposure and sensitisation
- **Tertiary prevention** — targets the effective control of allergen exposure in established disease.

Appropriate medication to control symptoms in established disease by dampening immune responses and subsequent cascade of pro-inflammatory mediators. Examples include preventer and reliever medications in asthma, eczema and rhinitis.

**Allergen immunotherapy** to induce immune tolerance to specific allergens and effectively ‘cure’ the allergy in established disease that is not controlled with conventional medication (antihistamines, low-dose steroids, etc.).

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**Further reading**
