

# Allergy



John Tregoning, Imperial College London, UK

**Allergy** is a harmful, misguided and over-zealous immune response to **antigens** that causes tissue damage and disease. It is a form of hypersensitivity, which can be classified into four types, based on the immune reactant, the antigen type and the effector mechanism (**Table 1**): it can be considered as a type of autoimmunity. An extreme example of allergy is **anaphylaxis**. Antigens that can induce an allergic response are called **allergens**, and they are often derived from non-infectious or non-microbial sources. There is no single unique structural motif (or family of motifs) that define a protein as being **allergenic**, but commonly they are small, soluble, stable and can have peptidase activity. Due to the structural similarities of some (unrelated) proteins an individual who is allergic to one protein may be allergic to another protein from very different species e.g. Latex, kiwi and birch pollen allergies are linked.

Hypersensitivity Type	Immune Reactant	Antigen Type	Effector	Example
1: Allergy	<u>IgE</u>	Soluble antigen	Mast cells	Anaphylaxis
2: Drug Allergy	IgG	Drug bound to erythrocytes	Complement/ Phagocytosis	Penicillin Allergy
3: Serum Sickness	IgG	Soluble Antigen	Immune complexes	<u>Arthus</u> reaction in skin
4: Delayed type hypersensitivity	T cells	Soluble antigen or cell associated Ag	Inflammation, cell death	Chronic asthma, contact dermatitis

**Table 1: Types of hypersensitivity reaction.** Hypersensitivity is defined by three factors, the immune reactant, the antigen type, and the effector.

## Sensitisation to allergy

Sensitisation to allergy is a form of immune memory priming. Both **T-** and **B cells** need to be primed to cognate antigen (in this case the allergen). The factors that cause an allergic response are not fully understood, but the environment, the site and the type of **antigen presenting cell** are critical to the outcome. A skewing of the response towards **T helper 2 (Th2)** is also critical.

# Allergy



John Tregoning, Imperial College, London, UK

## The Allergic Response

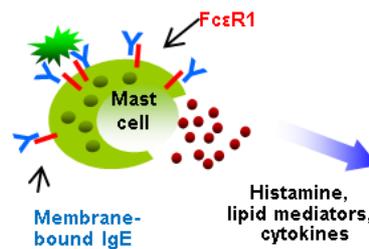
Allergic responses have two phases: the acute and the chronic, observed as **Wheal** and **Flare**.

### **Wheal: Acute allergic reaction**

This generally occurs rapidly after allergen exposure (<1hour). It is caused by the degranulation of mast cells and the release of histamine and other mediators. Histamine causes local inflammation and the symptoms of an 'allergic attack', acute local redness and swelling. **Mast-cell** degranulation is caused by the binding of allergen to **IgE** (pre-bound to **FcεR1** receptors on the mast-cell surface). Since IgE is pre-bound, this reaction is very rapid in onset.

### **Flare: Chronic Allergic reaction**

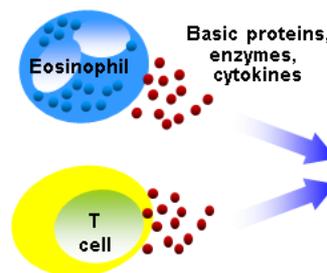
This generally occurs within 6-12 hours of the initial allergen exposure. It is the cellular response and is caused by the recruitment of T cells, **eosinophils** and more mast cells to the point of exposure. These cells once recruited release enzymes, toxic proteins and more cytokines leading to more inflammation.



### Acute Allergic Reaction

- Wheezing
- Urticaria
- Sneezing, rhinorrhea
- Conjunctivitis

**Acute:** Allergen Specific IgE is pre-bound to the FcεR1 receptor on mast cells. Circulating allergen binds the IgE causing receptor cross linking and mast cell degranulation.



### Chronic Allergic Reaction

- Further wheezing
- Sustained blockage of the nose
- Eczema

**Chronic:** Recruitment and activation of allergen specific T cells and other cells by mast cell derived mediators