Hypersensitivity Diseases

Hypersensitivity (also called hypersensitivity reaction or intolerance) is a set of undesirable reactions produced by the normal immune system, including allergies and autoimmunity. They are usually referred to as an over- reaction of the immune system and these reactions may be damaging, uncomfortable, or occasionally fatal. Hypersensitivity reactions require a pre-sensitized (immune) state of the host. They are classified in four groups after the proposal of P. G. H. Gell and Robin Coombs in 1963.

Type I: IgE mediated immediate reaction

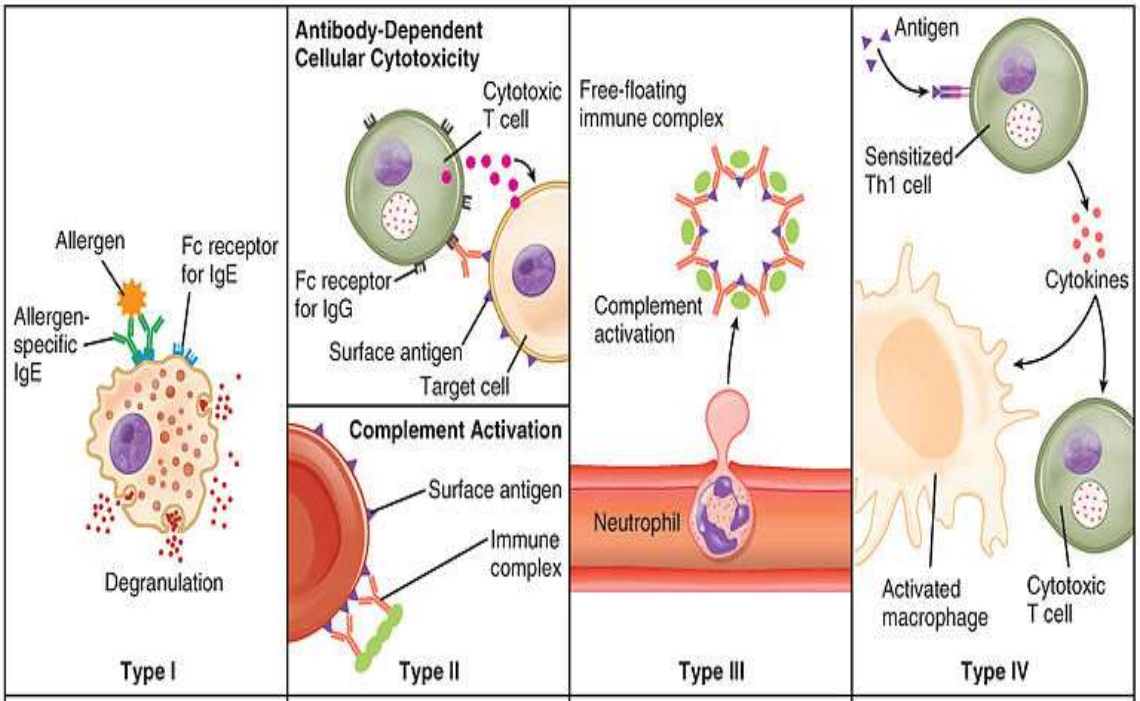
Type II: Antibody-mediated reaction (IgG or IgM antibodies)

Type III: Immune complex-mediated reaction

Type IV: Cytotoxic, cell-mediated, delayed hypersensitivity reaction .

The antigen-specific IgE antibodies can then bind to high-affinity receptors located on the surfaces of mast cells and basophils. Reexposure to the antigen can then result in the antigen binding to and cross-linking the bound IgE antibodies on the mast cells and basophils. This causes the release and formation of chemical mediators from these cells.

The major mediators and their functions are described as follows:



IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
IgE is bound to mast cells via its Fc portion. When an allergen binds to these antibodies, crosslinking of IgE induces degranulation.	Cells are destroyed by bound antibody, either by activation of complement or by a cytotoxic T cell with an Fc receptor for the antibody (ADCC)	Antigen–antibody complexes are deposited in tissues, causing activation of complement, which attracts neutrophils to the site	Th1 cells secrete cytokines, which activate macrophages and cytotoxic T cells and can cause macrophage accumulation at the site
Causes localized and systemic anaphylaxis, seasonal allergies including hay fever, food allergies such as those to shellfish and peanuts, hives, and eczema	Red blood cells destroyed by complement and antibody during a transfusion of mismatched blood type or during erythroblastosis fetalis	Most common forms of immune complex disease are seen in glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus	Most common forms are contact dermatitis, tuberculin reaction, autoimmune diseases such as diabetes mellitus type I, multiple sclerosis, and rheumatoid arthritis

1. Histamine: This mediator acts on histamine 1 (H1) and histamine 2 (H2) receptors to cause contraction of smooth muscles of the airway and GI tract, increased vasopermeability and vasodilation, enhanced mucus production, pruritus, cutaneous vasodilation, and gastric acid secretion.

2. Tryptase: Tryptase is a major protease released by mast cells. Its role is not completely understood, but it can cleave C3, C3a, and C5 in addition to playing a role in airway remodeling. Tryptase is found in all human mast cells but in few other cells and thus is a good marker of mast cell activation.

3. Proteoglycans: Proteoglycans include heparin and chondroitin sulfate. The role of the latter is unknown; heparin seems to be important in storing the preformed proteases and may play a role in the production of alpha-tryptase.

4. Chemotactic factors: An eosinophilic chemotactic factor of anaphylaxis causes eosinophil chemotaxis; an inflammatory factor of anaphylaxis results in neutrophil chemotaxis. Eosinophils release major basic protein and, together with the activity of neutrophils, can cause significant tissue damage in the later phases of allergic reactions.

Diagnosis of hypersensitivity

Laboratory testing may include:

1- Allergen-specific IgE blood testing: this is testing that is used to help diagnose allergies. The test measures the amount of allergen-specific IgE antibodies in the blood in order to detect an allergy to a particular substance.

The RAST (Radioallergosorbent test) is a laboratory test performed on blood. It tests for the amount of specific IgE antibodies in the blood which are present if there is a "true" allergic reaction.

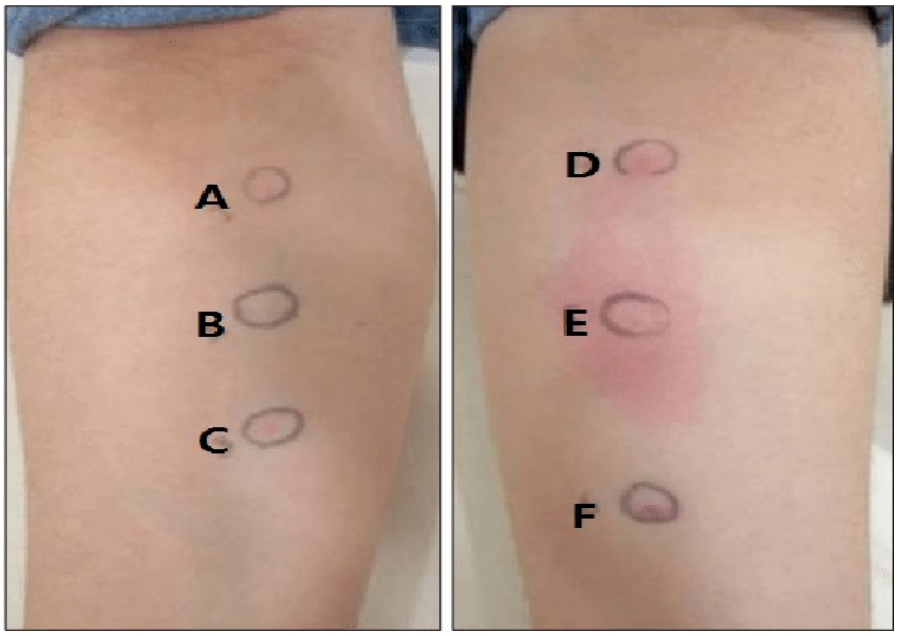
Note: The traditional method for blood testing was the RAST (radioallergosorbent test), but it has been largely replaced with newer IgE-specific immunoassay methods. Some health practitioners, however,

still refer to all IgE allergy blood tests as RAST even though it is not the methodology that the laboratory uses.

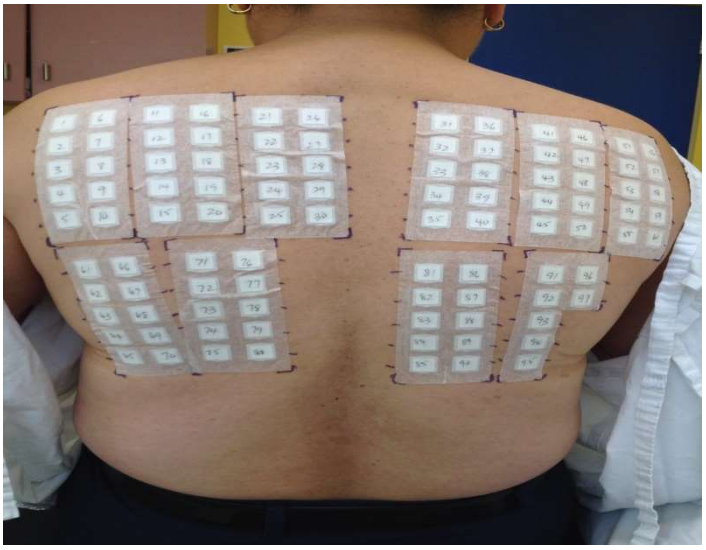
Other types of allergy tests:

1. ***Skin prick or scratch tests*** are done in an allergist's or dermatologist's office and must be done by a trained professional. They are often used to detect airborne allergies such as pollens, dust, and molds. Because of the potential for a severe reaction, skin prick tests are not usually used for food allergies. The person being tested must not have significant eczema or be taking antihistamines or certain antidepressants for several days before the skin prick test. False positives can arise with even a non-allergic person if the dosage of the allergen is high enough.

2. ***Intradermal allergy skin tests*,** using injections that form a bubble under the skin, may be done but they are not widely accepted because of a high false-positive rate.



3. ***Patch testing*:-** Delayed hypersensitivity skin and patch tests are the easiest methods of testing for type IV delayed hypersensitivity. A concentration of the suspected allergen is applied to the skin under a nonabsorbent adhesive patch and left for 48 hours. If burning or itching develops more rapidly, the patch is removed. A positive test consists of redness with some hardening and swelling of the skin and sometimes vesicle (blister-like) formation. Some reactions will not appear until after the patches are removed, so the test sites are also checked at 72 and 96 hours.



4- ***Oral food challenges*** **are** considered the "gold standard" for diagnosing food allergies. They are labor-intensive and require close medical supervision because reactions can

be severe, including life-threatening anaphylaxis. Food challenges involve giving a person small amounts of unmarked potential food allergens in capsule or intravenous form and watching for allergic reactions. Negatives are confirmed with larger meal-sized portions of food.

5- ***Food elimination*** is another way to test for food allergies: eliminating all suspected foods from the diet, then reintroducing them one at a time to find out which one(s) are causing the problem.

2- **Total IgE testing** is sometimes done to look for an ongoing allergic process. It is a blood test that detects the total amount of IgE protein (including allergy antibodies) but does not identify specific allergens. Conditions besides allergies can also cause the IgE level to rise.

3- **Complete blood count (CBC) and WBC differential**—these tests include the measurement of eosinophils, a type of white blood cell. The level of eosinophils may be increased in a person with allergies.

4- Histamine and/or tryptase blood tests may be used to help diagnose anaphylaxis or mast cell activation.

6- **The MELISA® test** (Memory Lymphocyte Immuno Stimulation Assay) measures hypersensitivity to numerous metals, including mercury, by placing a series of metals into contact with the white blood cells of the person being tested and then monitoring the reaction. An innovative diagnostic tool.

Treatment

The treatment of immediate hypersensitivity reactions includes the management of anaphylaxis with intramuscular adrenaline (epinephrine), oxygen, intravenous (IV) antihistamines, support blood pressure with IV fluids, avoid latex gloves and equipment in patients who are allergic, and surgical procedures such as tracheotomy if there is severe laryngeal edema.