

## Hypersensitivity reactions

Excessive or inappropriate immune response resulting in a disease.

### What are the possible causes of hypersensitivity reactions based on its definition?

1. Immune response directed against host tissue (autoimmunity). inappropriate immune response جهاز المناعة يهاجم مكونات الجسم نفسه
2. Immune response against commensal microbes or environmental antigens. inappropriate immune response جهاز المناعة يهاجم كائنات غير مسببة للمرض أو بروتينات غير ضارة للجسم
3. Inadequate control of immune response against pathogenic microbes. excessive or inappropriate immune response جهاز المناعة يربي قنبلة ليقتل فأراً

### Classification of hypersensitivity reactions is based on:

1. Type of immune response (antibody vs. cellular)
2. Mechanism of tissue injury (types of immune mediators that cause damage to the body)

### Overview of hypersensitivity reactions:

Type	Immune mediator of pathology	Mechanism of tissue injury	Examples
Immediate (type 1)	IgE	Mast cells and their mediators (vasoactive amines, lipid mediators and cytokines)	Allergic reactions, anaphylaxis, asthma, eczema الحساسية
Antibody mediated (type 2)	IgM, IgG against antigens bound to cells or tissues	Phagocytosis, antibody-dependent cell mediated cytotoxicity (ADCC), receptor blocking or complement mediated lysis	ABO incompatibility, Rh incompatibility
Antibody mediated (type 5)	Stimulating antibodies against antigens bound to cells or tissues	Overactivity in the target organ	Graves' disease مرض يسبب زيادة نشاط الغدة الدرقية
Immune complex mediated (type 3)	Circulating immune complexes of antigens and IgM or IgG	Ag-Ab complexes activate the complement and Fc receptors resulting in activation and recruitment of leukocytes	Systemic lupus erythematosus الحمى الذؤابية, rheumatoid arthritis التهاب المفاصل الرثوي
Cell mediated (type 4)	CD4+ T cells or CD8+ cytotoxic T lymphocytes	Macrophage activation resulting in cytokine mediated inflammation or direct cell killing by cytotoxic T lymphocytes	Tuberculosis

### Important notes regarding each type of hypersensitivity reactions:

#### Type 1 (immediate type, allergies) تفاعلات الحساسية

Allergy occurs in genetically predisposed individuals (عند الأفراد ذوي الاستعداد الجيني). These individuals are termed "atopic" since they have "atopy". Atopy is the genetic predisposition to allergy. Atopic individuals produce large quantities of IgE after minor exposure to environmental benign antigens (allergens).

#### Examples of these allergens (مسببات الحساسية عند الأفراد ذوي الاستعداد الجيني):

- A. Dust mites غُتَّ غبار المنزل
- B. Peanut الفول السوداني
- C. Dyes
- D. Creams
- E. Fragrances in the products for skin care
- F. Eggs
- G. Pollens حبوب اللقاح
- H. Spores
- I. Drugs

This is the only material required for the exam. No other source is needed

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Upon exposure to allergen, cross-linking of IgE at mast cells and basophils cause degranulation with release of the following mediators:

- A. Histamine: increased permeability of venules, contraction of intestinal, bronchial and arterial smooth muscles.
- B. Leukotrienes and prostaglandins: bronchoconstriction, increased vascular permeability, and mucus production.
- C. Cytokines (IL-4, IL-5 and IL-13): recruitment and activation of inflammatory cells.

Allergic conditions:

- A. Allergic rhino-conjunctivitis (hay fever حمى القش): respiratory exposure
- B. Asthma (الربو): respiratory exposure
- C. Food allergy: gastrointestinal exposure
- D. Atopic dermatitis (eczema): skin exposure
- E. Anaphylaxis (الحساسية المفرطة): introduction of an allergen into the blood directly

### Management of allergy:

Identification of the causative allergen and its avoidance.

خليها قاعدة عامة في الحياة... إذا موضوع معين ولا شخص معين بسببلك حساسية، أحسن حل تعرف ما هو هذا الشيء وتجنبه تماماً

Symptomatic: anti-inflammatory agents, anti-histamines, EPIPEN (epinephrine) in anaphylaxis to prevent shock.

### Diagnosis:

Very high levels of IgE

Skin testing to determine the exact allergen causing the disease.

### Type 2 hypersensitivity reaction example:

#### Rh incompatibility

Georgina married Christian. Georgina blood group is A negative (lacking D antigen), while Christian blood group is A positive (having D antigen). The first child had D antigen and Georgina got exposed to fetal red blood cells having D antigen. Since these antigens are foreign to her, she reacted by the formation of anti-D antibodies. During the second pregnancy of a child who had the D antigen, anti-D from Georgina will cross the placenta and bind to D antigen on the red blood cells of the second child causing hemolysis (hemolytic disease of the fetus/newborn).

The solution, for cases similar to Georgina/Christian situation, give the mother anti-D during her first and subsequent pregnancies to cover the D antigens and prevent the formation of anti-D in the mother.

### Type 5 hypersensitivity reaction:

Similar to type 2 (antibody will bind to antigens fixed to cells or tissues). The difference is that these antibodies will affect the function of the affected tissue.

Example: Graves' disease

Auto-antibodies will bind thyroid stimulating hormone (TSH) receptor on the thyroid gland causing excessive secretion of the thyroid hormones (زيادة إفراز هرمونات الغدة الدرقية).

### Type 3 hypersensitivity reaction:

Failure of the immune mechanisms to clear immune complexes due to ongoing excessive production (e.g., chronic antigenemia), will end up in activating the complement system and recruiting leukocytes with inflammation and tissue damage. Immune complex deposition is most likely where there is high blood pressure and turbulence (e.g., glomerular capillaries, brain, joints).

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**Type 4 hypersensitivity reaction:**

An exaggerated interaction between Ag and the normal T cell mediated immune responses. It is characterized by T cell response driving an inflammatory reaction involving macrophages.

**Autoimmune disease summary:**

Autoimmunity can be defined as adaptive immune responses directed against self-antigens. It arises as a result of loss of self-tolerance.

The autoimmune responses can involve auto-antibodies or self-reactive T cells, which can cause tissue damage through hypersensitivity reactions type 2, 3, 4 or 5.

Auto-antibodies can be found in some healthy individuals; however, their very low levels and low affinities for self-antigens do not allow the development of autoimmune disease.

Genetic factors play a role in the development of autoimmune disease including factors such as HLA type.

The auto-antigens are impossible to be eradicated from self. So, autoimmune disease will be active for a long time (chronicity).

In general, women are more susceptible than men to autoimmunity (overall more than 75%).

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