



# hypersensitivity

By

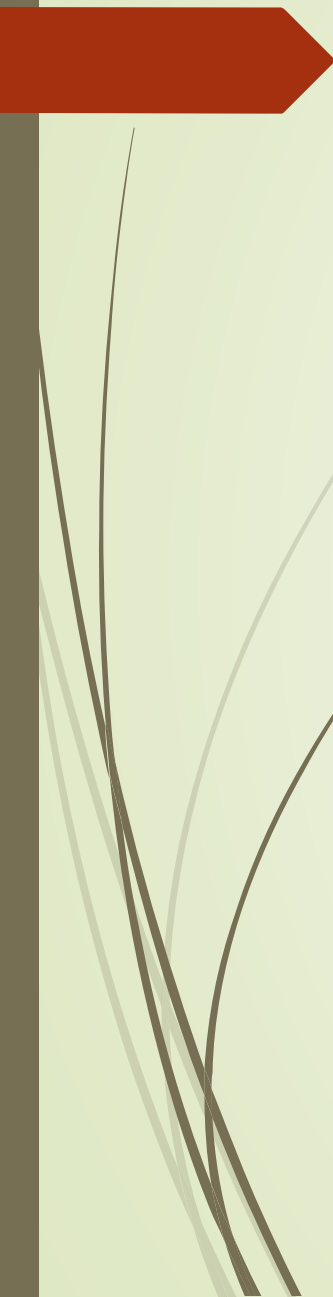
**Lecture 15**

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# Introduction

- **Hypersensitivity**: refers to 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**.
- Increased resistance is called **immunity** and increased susceptibility is called **hypersensitivity**.
- In allergic (hypersensitivity) reactions:
  - • **An antigen-is referred to as allergen or sensitizer**
  - • **Immunization-is referred to as sensitization**
  - • **An individual-is referred to as hypersensitive or allergic**
- **The hypersensitivity may be Immediate or delayed**



| <b>Immediate type<br/>Hypersensitivity Reactions</b>   | <b>Delay type<br/>Hypersensitivity Reactions</b>                                       |
|--|--|
| <ul style="list-style-type: none"><li>• It appears and disappears rapidly.</li></ul>                   | <ul style="list-style-type: none"><li>• It appears slowly &amp; last longer.</li></ul> |
| <ul style="list-style-type: none"><li>• It is induced by the intake of antigen by any route.</li></ul> | <ul style="list-style-type: none"><li>• Only by skin contact</li></ul>                 |
| <ul style="list-style-type: none"><li>• It is antibody mediated B-cell response.</li></ul>             | <ul style="list-style-type: none"><li>• It is T-cell mediated response.</li></ul>      |
| <ul style="list-style-type: none"><li>• Desensitisation easily but short living.</li></ul>             | <ul style="list-style-type: none"><li>• It is difficult but long living.</li></ul>     |

# Hypersensitivity classification

- **Type I hypersensitivity reactions** involve (IgE) antibody against **soluble antigen**, triggering **mast cell degranulation**.
- **Type II hypersensitivity reactions** involve **IgG or IgM** antibodies directed against cellular antigens, **leading to cell damage**
- **Type III hypersensitivity reactions** involve the interactions of IgG, IgM, and, occasionally, IgA<sup>1</sup> antibodies with antigen to form **immune complexes**. **Accumulation of immune complexes in tissue leads to tissue damage**
- **Type IV hypersensitivity reactions** are **T-cell-mediated** reactions that can involve **tissue damage** mediated by activated **macrophages and cytotoxic T cells**.

# Type I hypersensitivity

- When a **pre-sensitized individual** is exposed to an allergen, it can lead to a rapid immune response that occurs almost **immediately**. Such a response is called **an allergy and is classified as a type I hypersensitivity**.
- Allergens may be seemingly harmless substances such as animal dander, molds, or pollen grains.
- Type I hypersensitivity reactions can be either **localized or systemic**.
- **Localized type I hypersensitivity** reactions include **hay fever rhinitis**, hives, and **asthma**.
- Systemic type I hypersensitivity reactions are referred to as **anaphylaxis** or **anaphylactic shock**. **anaphylaxis** shares many symptoms common with the localized type I hypersensitivity reactions, the swelling of the tongue and trachea, blockage of airways, dangerous drop in blood pressure, and development of **shock** can make anaphylaxis especially severe and life-threatening. In fact, **death** can occur within minutes of onset of signs and symptoms.



## Skin Test of Type I Hypersensitivity



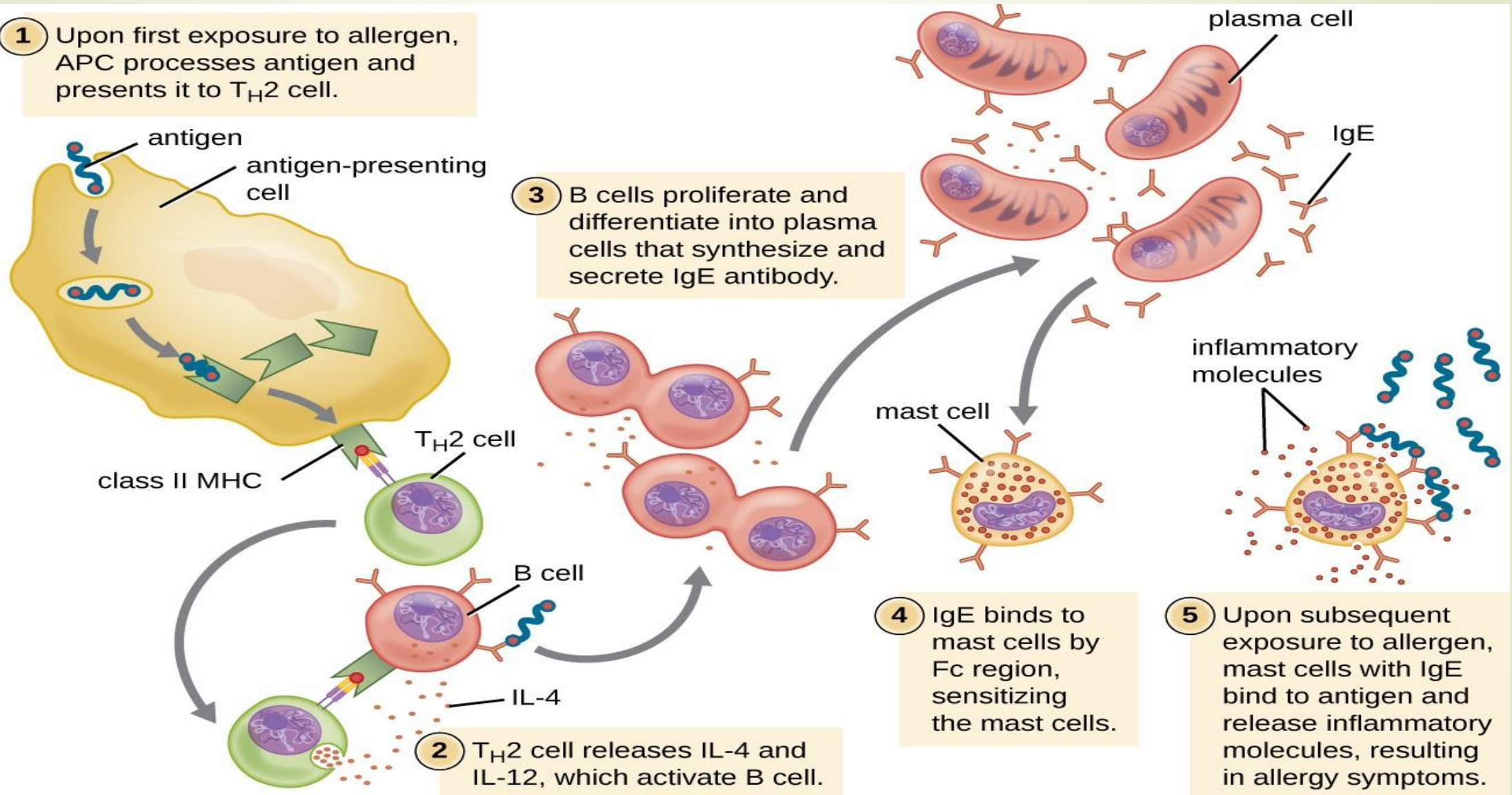
# Type I hypersensitivity mechanism

- **A first exposure** to an allergen activates a strong Th2 cell response.
- Cytokines interleukin IL-4 and IL-13 from the Th2 cells activate B cells specific to the same allergen, differentiate into plasma cells, and **antibody-class switch from production of IgM to production of IgE**.
- **The (Fc) regions of the IgE antibodies bind to specific receptors on the surface of mast cells** throughout the body. It is estimated that each mast cell can bind up to 500,000 IgE molecules, which have antigen-binding (Fab) sites available for binding **allergen** on subsequent exposures.
- **On subsequent exposure, allergens bind to multiple IgE molecules on mast cells, cross-linking the IgE molecules.**
- Within minutes, **this cross-linking of IgE activates the mast cells and triggers degranulation and release the mast cell content** from granules such **histamine, serotonin, and bradykinin**.
- **Histamine** stimulates mucus secretion in nasal passages and tear formation from lacrimal glands, promoting the runny nose and watery eyes of allergies.



# Type I hypersensitivity mechanism

- 1 Upon first exposure to allergen, APC processes antigen and presents it to  $T_H2$  cell.





# Type II hypersensitivity

- ▶ **Type II hypersensitivities, or cytotoxic hypersensitivities, are mediated by IgG and IgM antibodies binding to cell-surface antigens**
- ▶ These antibodies can either activate **complement**, resulting in an **inflammatory response and lysis of the targeted cells**, or they can be involved in **antibody-dependent cell-mediated cytotoxicity (ADCC)** with **cytotoxic T cells**.
- ▶ In some cases, the antigen may be a self-antigen, in which case the reaction would also be described as an **autoimmune disease**.
- ▶ In other cases, antibodies may bind to naturally occurring, but **exogenous**, cell-surface molecules such as **antigens associated with blood typing found on red blood cells (RBCs)**. This leads to the coating of the RBCs by antibodies, activation of the complement cascade, and **complement-mediated lysis of RBCs**, as well as **opsonization** of RBCs for phagocytosis.
- ▶ Two examples of type II hypersensitivity reactions involving RBCs are **hemolytic transfusion reaction (HTR)** and **hemolytic disease of the newborn (HDN)**.

# Common Type II Hypersensitivities

## Common Name

## Cause

## Signs and Symptoms

**Hemolytic disease of the newborn (HDN)**

IgG from mother crosses the placenta, targeting the fetus' RBCs for destruction

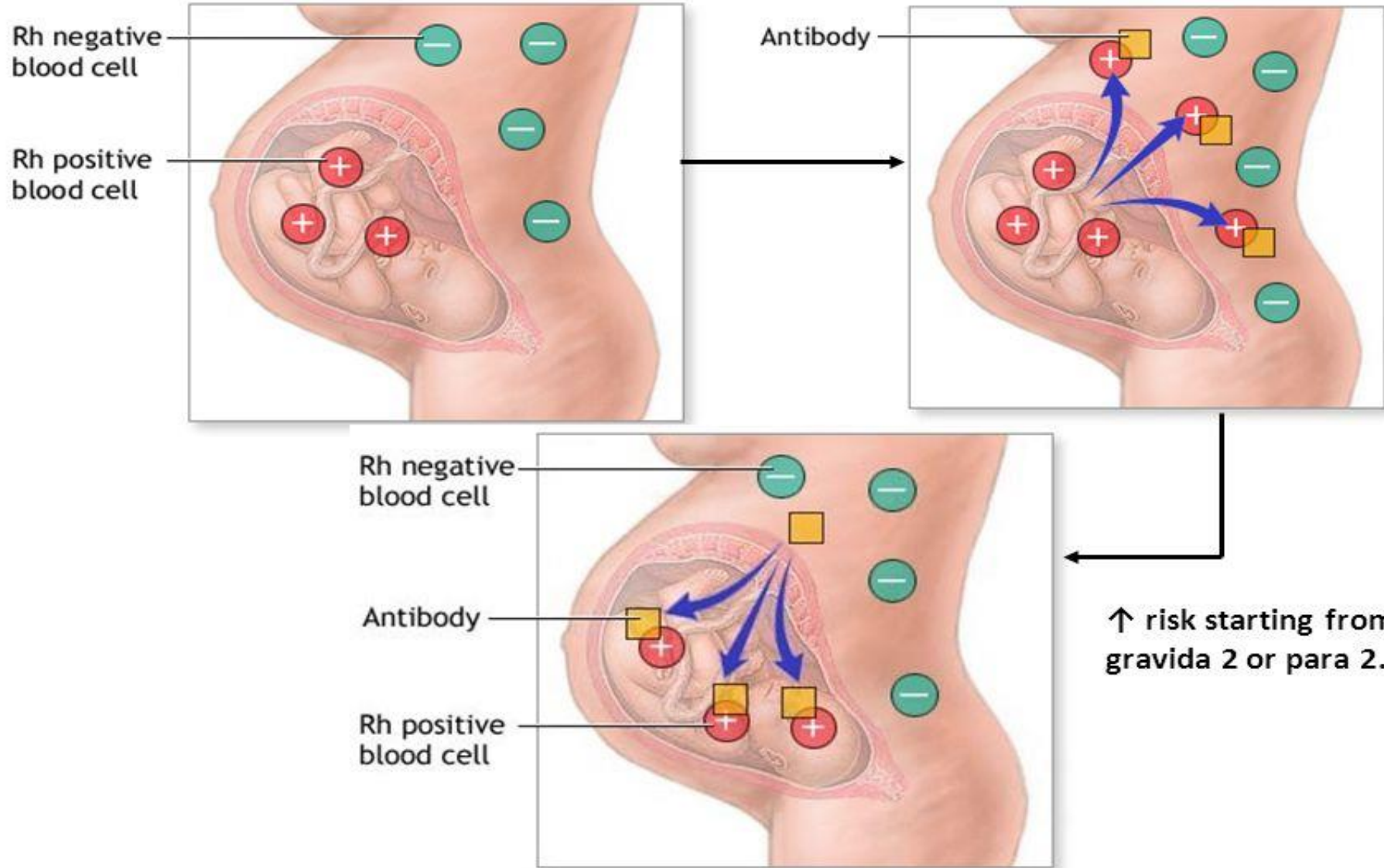
Anemia, edema, enlarged liver or spleen, hydrops (fluid in body cavity), leading to death of newborn in severe cases

**Hemolytic transfusion reactions (HTR)**

IgG and IgM bind to antigens on transfused RBCs, targeting donor RBCs for destruction

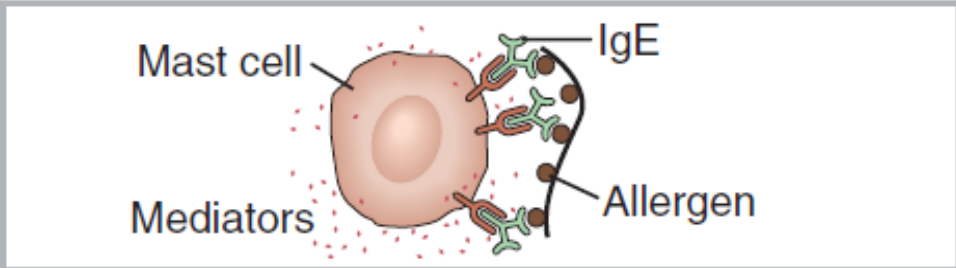
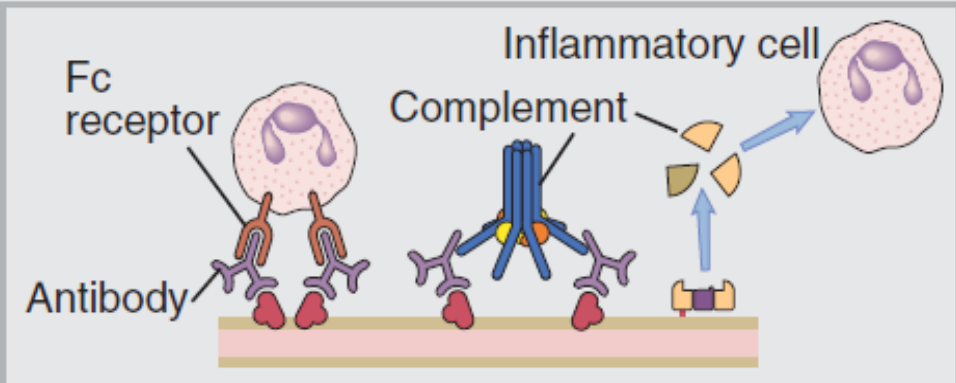
Fever, jaundice, hypotension, disseminated intravascular coagulation, possibly leading to kidney failure and death

# ERYTHROBLASTOSIS FETALIS





# Mechanism of type I and type II hypersensitivity

| Type of hypersensitivity             | Pathologic immune mechanisms   | Mechanisms of tissue injury and disease   |
|--------------------------------------|--|---|
| Immediate hypersensitivity (Type I)  | <p><math>T_H2</math> cells, IgE antibody, mast cells, eosinophils</p>              | <p>Mast cell-derived mediators (vasoactive amines, lipid mediators, cytokines)</p> <p>Cytokine-mediated inflammation (eosinophils, neutrophils)</p>   |
| Antibody-mediated diseases (Type II) | <p>IgM, IgG antibodies against cell surface or extracellular matrix antigens</p>  | <p>Complement and Fc receptor-mediated recruitment and activation of leukocytes (neutrophils, macrophages)</p> <p>Opsonization and phagocytosis of cells</p> <p>Abnormalities in cellular function, e.g. hormone receptor signaling</p> |



**Thank you**