

# Allergy

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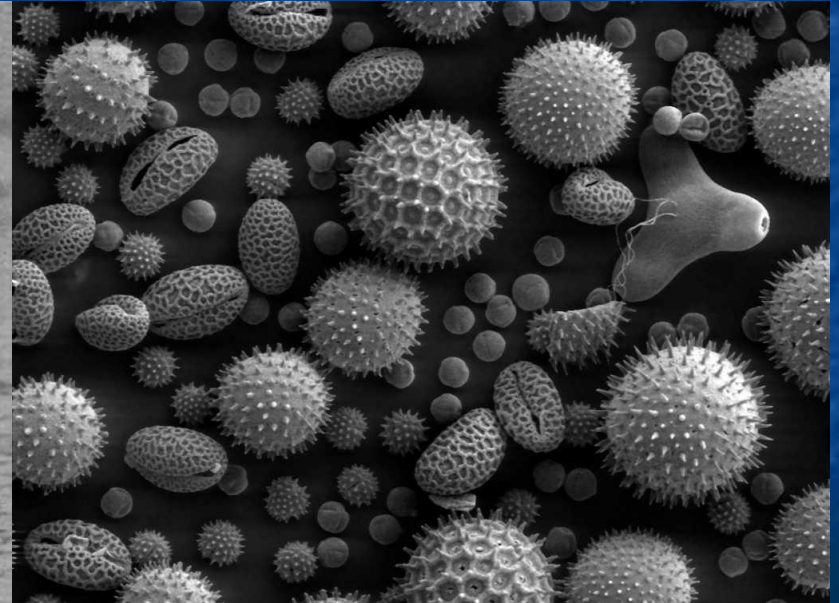
# Immune system disorders

- **Weakened immune response:**
  - Primary immunodeficiency
  - Secondary immunodeficiency
- **Excessive immune response:**
  - Allergic reactions
  - Autoimmune reactions

**Antigen** - any substance that can stimulate immune system

**Allergen** – any substance that can induce allergy

**Allergy** – excessive reaction of immune system to normally harmless substance



**House Dust Mite**

**Pollen**

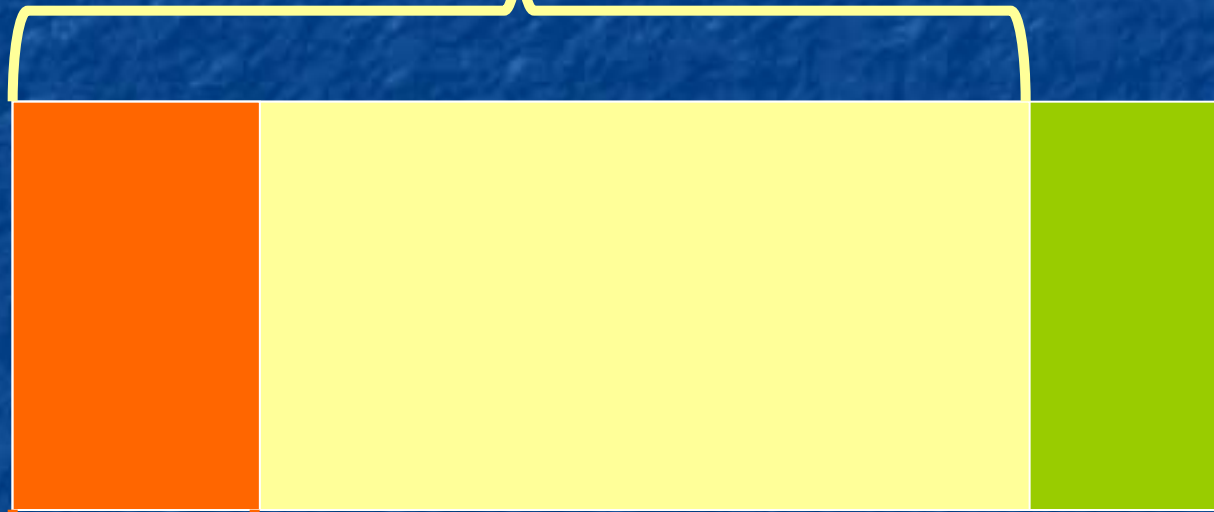
# Allergy classification

by P. G. H. Gell and R. R. A. Coombs

- Type I hypersensitivity - Anaphylactic reactions.
- Type II hypersensitivity - Cytotoxic reactions.
- Type III hypersensitivity - Reactions mediated by immune complexes.
- Type IV hypersensitivity - Cell mediated reactions.
- Type V hypersensitivity - Stimulating allergic reactions.

# Pathogenesis of allergy

Presence of antibodies to  
hen's fluff (75 -90%)



**Allergy manifestation**  
**10-15%**

**Absence of  
antibodies**

# Immune and Allergic reactions

- **Similar features:**
  - protection of the organism from genetically foreign ones
  - similar mechanisms of reactions
  - mediated with immune cells
- **Distinctive features of allergic reactions:**
  - increased reactivity
  - transformed character of immune answer
  - **tissue injury**

# Hereditary Predisposition to Allergy

- increased permeability of barriers
- ↑ activity of T-helpers, ↑ synthesis of IgE
- ↑ synthesis of allergic mediators
- ↓ inactivation of allergic mediators
- hyperreactivity of bronchi, skin.

Allergic diseases with hereditary  
predisposition – atopic diseases – type 1  
hypersensitivity

# Immunological Stage of Allergic Reaction

- revealing the allergen
- presentation of the allergen to lymphocytes
- Ig synthesis
- immune memory cells formation
- fixation of the antibodies or T-killers in the site of allergen localization



# Biochemical Stage of Allergic Reaction

- allergen interaction with specific antibodies or sensitized lymphocytes;
- release or synthesis of biologically active substances – mediators of allergy.

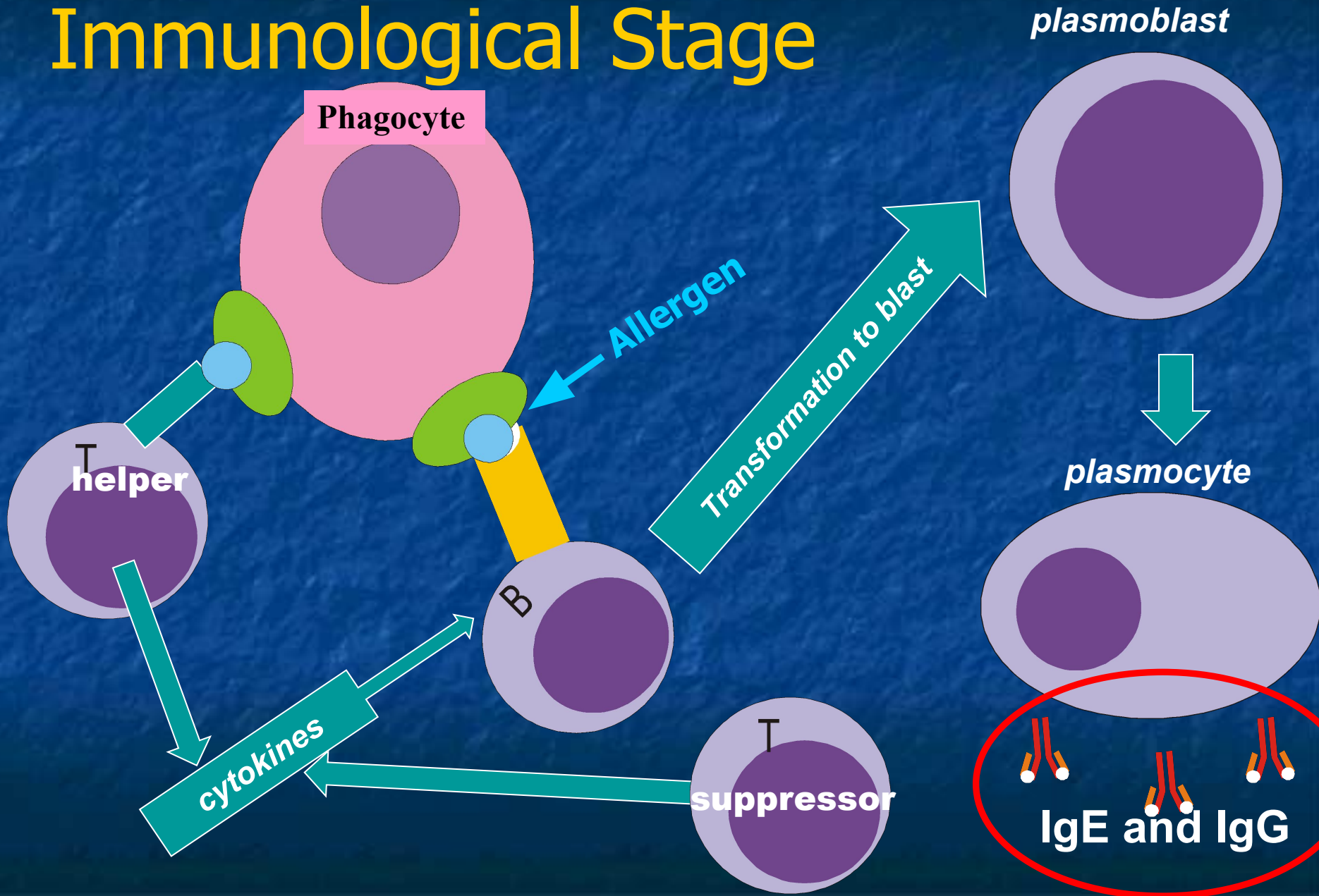
# The stage of allergy clinical manifestation (type 1)

- Local signs:
  - Itching, pain, rashes
  - Nasal congestion
  - □ Mucus secretion.
- Systemic Signs of Allergy
  - Smooth muscles constriction
    - bronchi (problems with breathing)
    - GIT (abdominal cramps)
  - Swelling of tongue, mouth
  - Vessels dilation, hypotension, shock

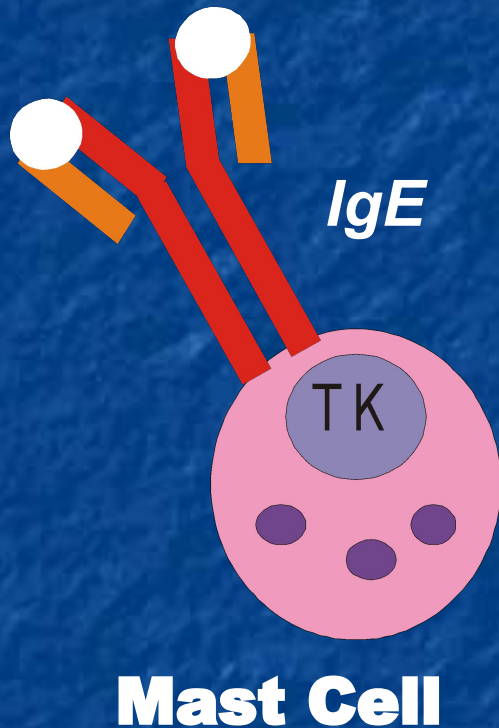
# Type 1 Allergic Reactions (anaphylactic, reaginic)

- Allergic asthma
- Conjunctivitis
- Allergic rhinitis ("hay fever")
- Anaphylactic shock
- Angionevrotic edema (**Quincke's disease**)
- Urticaria (hives).

# Immunological Stage

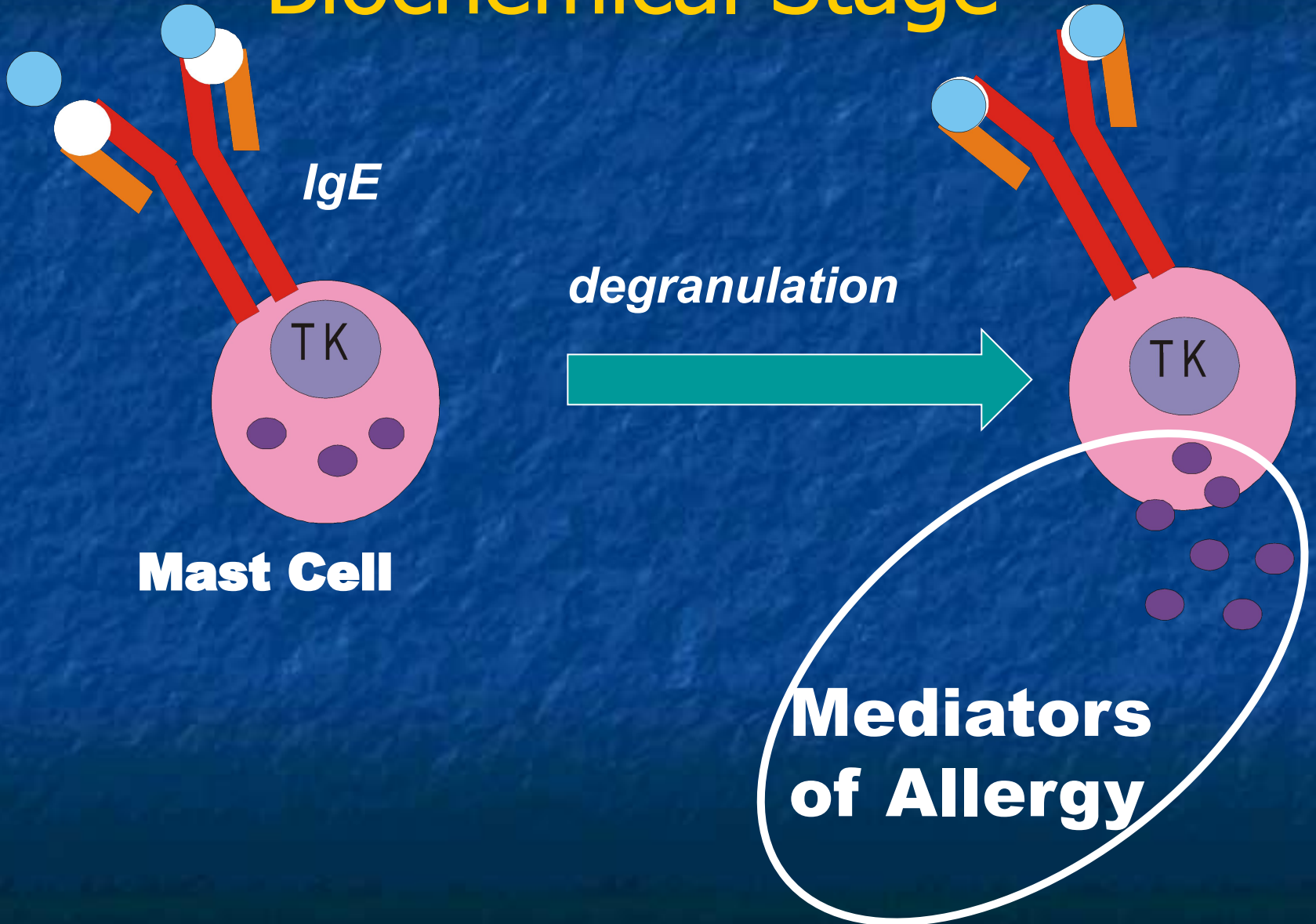


# Immunological Stage Result



- Fixation of antibodies on the mast cells and basophils
- Its possible to detect IgE in blood serum (diagnosis of type 1 hypersensitivity)

# Biochemical Stage



# Classification of Allergy Mediators

## **Primary (pre-stored)**

**Histamine  
Heparine  
Serotonine**

## **Secondary (new synthesis)**

**Prostaglandins  
Leukotrienes  
Cytokines**

# Primary Mediators Effects

- **Histamine & Serotonin** – vasodilation, □ vascular permeability, □ tone of smooth muscle cells
  - **Histamine** + pain, itching
  - **Serotonin** + □ secretion of mucus.
- **Heparin** decreases blood clotting
- **Chemotaxins** for neutrophils and eosinophils – provide the movement of the neutrophils and eosinophils



# Secondary Mediators

- **Leukotrienes** - ↑ vessels permeability, spasm of smooth muscles, chemotactic factors.
- **Prostaglandins** – bronchospasm, ↑ mucus secretion.
- **Platelet-activating factor** - platelet aggregation, bronchospasm, release of histamine.
- **Cytokines** – interleukins, tumor necrosis factor

# Type 2 allergic reactions (antibody-dependent cytotoxicity)

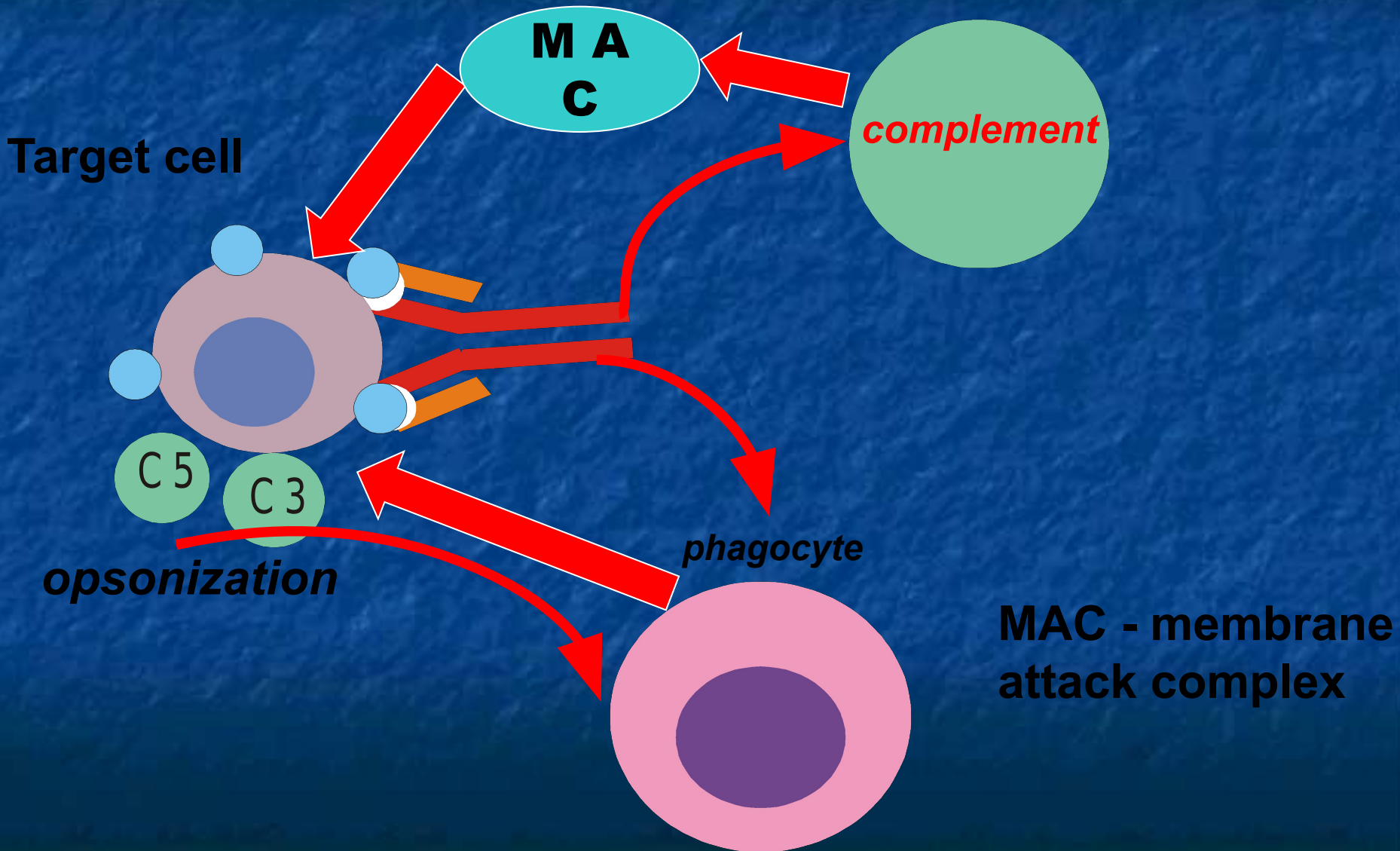
Transfusion reactions, autoimmune anemia, leukopenia, thrombocytopenia, thyroiditis.

Transformation of own antigens to “non-self” antigens by chemicals, viruses.

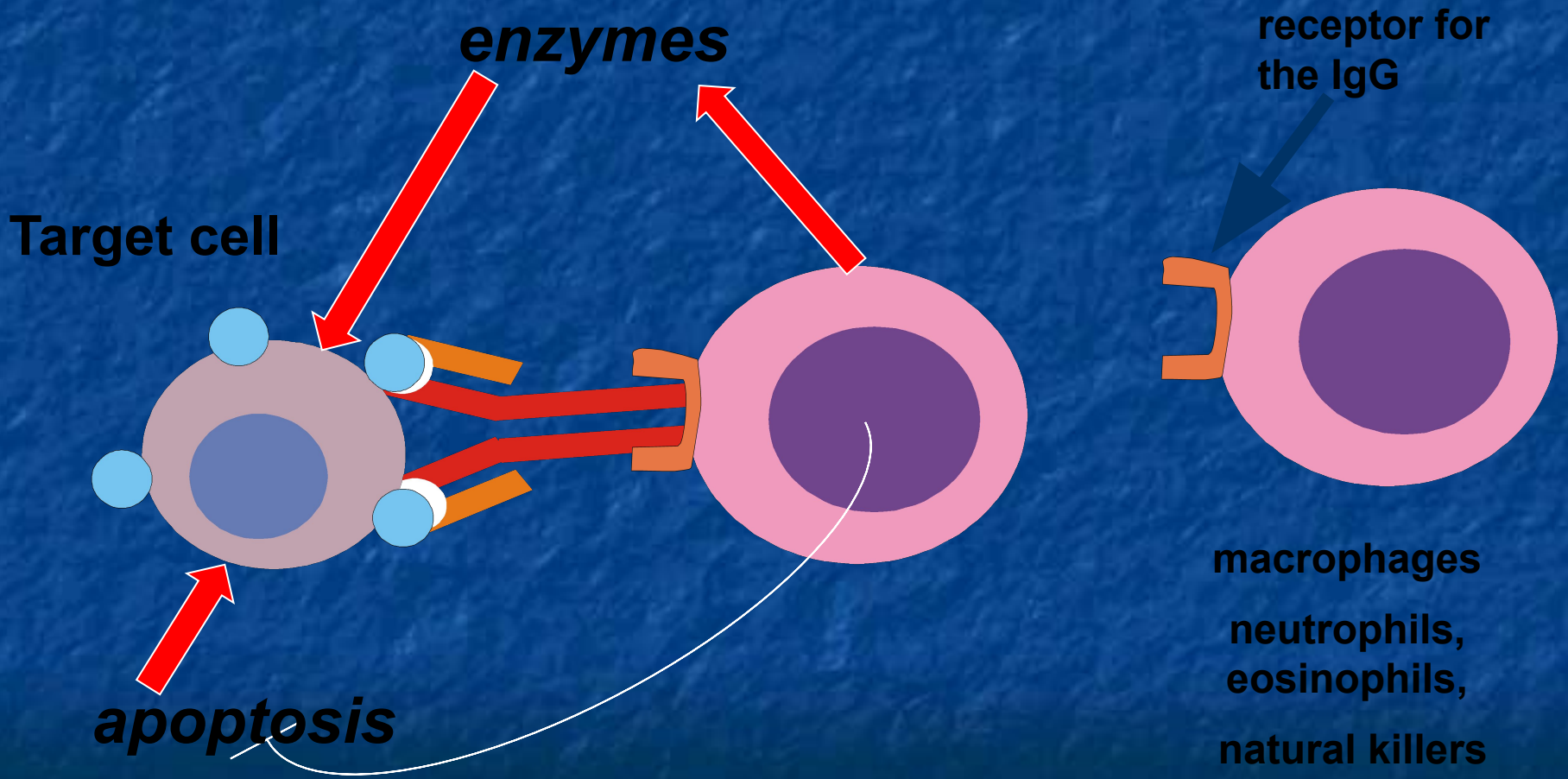
The cell with transformed antigen – **target cell**

Synthesis of **IgG and IgM** against target cell antigens

# Antibody-dependent mechanisms of cell damage



# Antibody-dependent cell-mediated cytotoxicity



# Type 5 allergic reactions (stimulating reactions)

## **Autoimmune thyroiditis**

- Antibodies bind to TSH receptor on thyroid epithelial cells and **STIMULATE** them
  - Thyroid gland hyperplasia
  - Excessive secretion of thyroid hormones.

# Type 3 allergic reactions (immune complexes)

- Immune complex glomerulonephritis
- Serum sickness
- Arthus reaction (local reaction)

Antigens – antibiotics, Ig (serum as medicine), bacteria, viruses

# Features of type 3 hypersensitivity

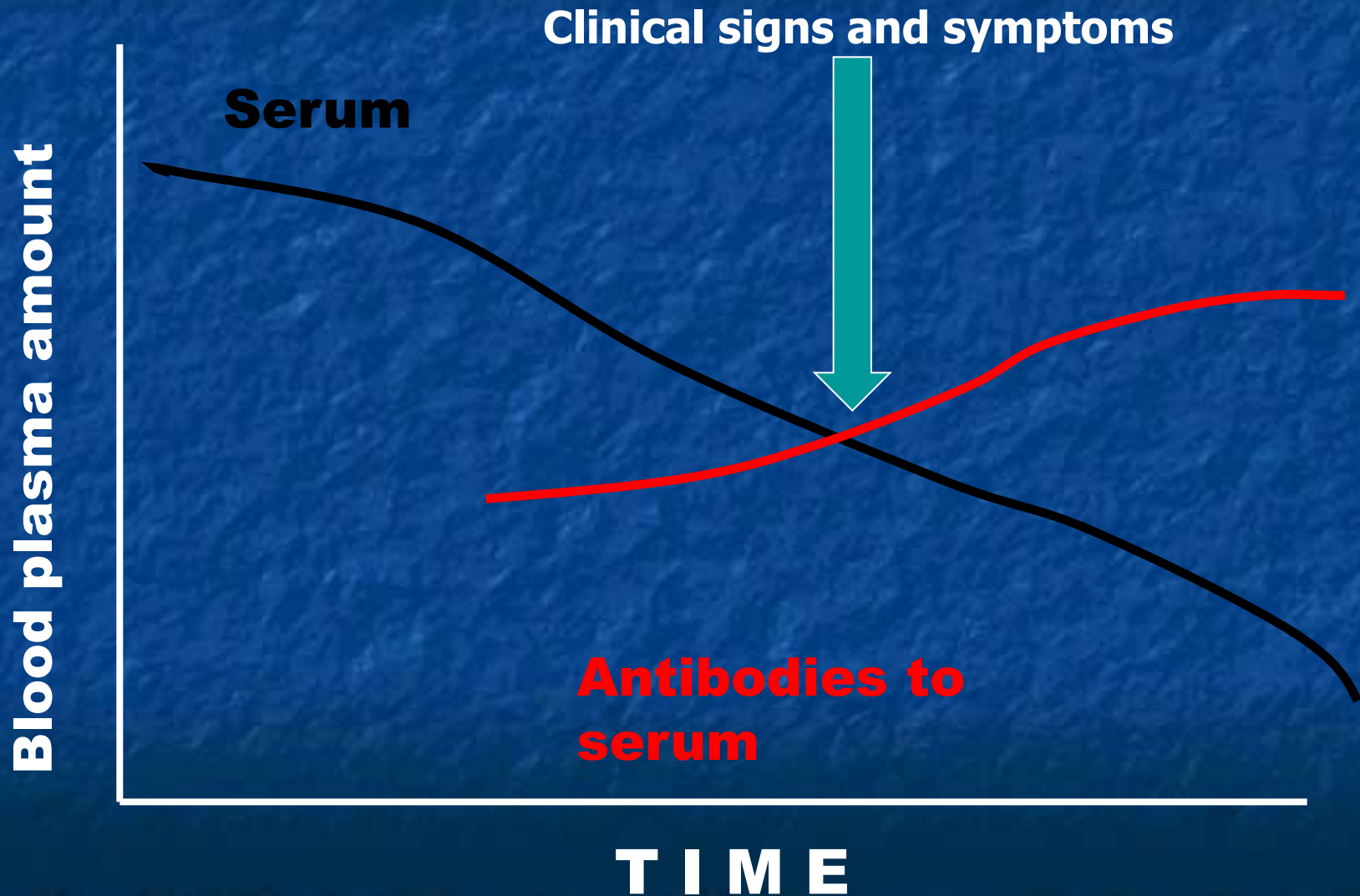
- Circulation of immune complexes in blood (systemic diseases)
- IgG and IgM
- Involvement of complement and phagocytes in tissue injury
- Low blood complement level

# Phases of the systemic immune-complex disease

- formation of antigen-antibody complexes in circulation;
- deposition of the immune complexes in various tissues;
- inflammatory reaction in the site of immune complexes deposition.



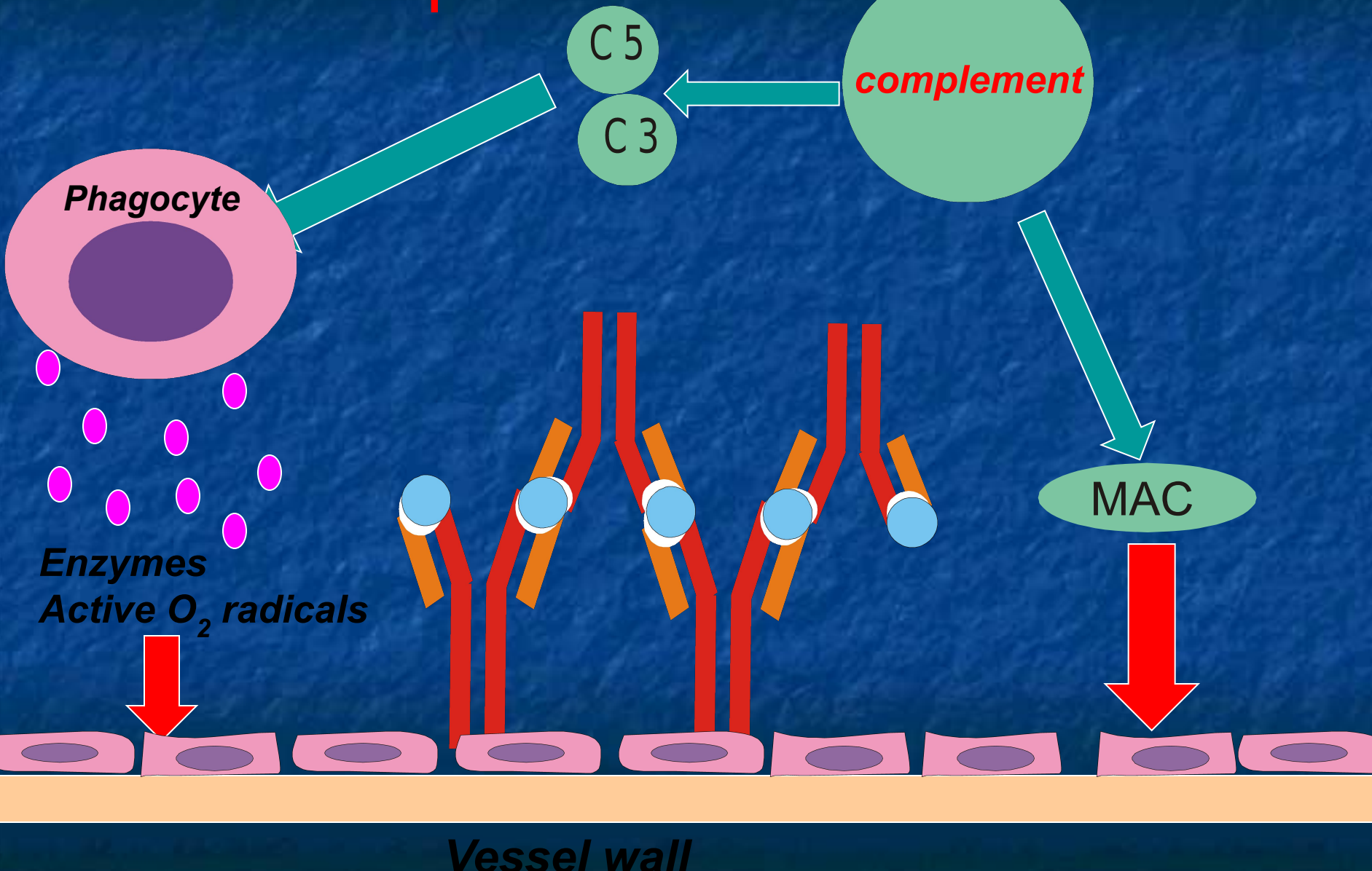
# Serum Sickness



# Pathogenic properties of immune complexes

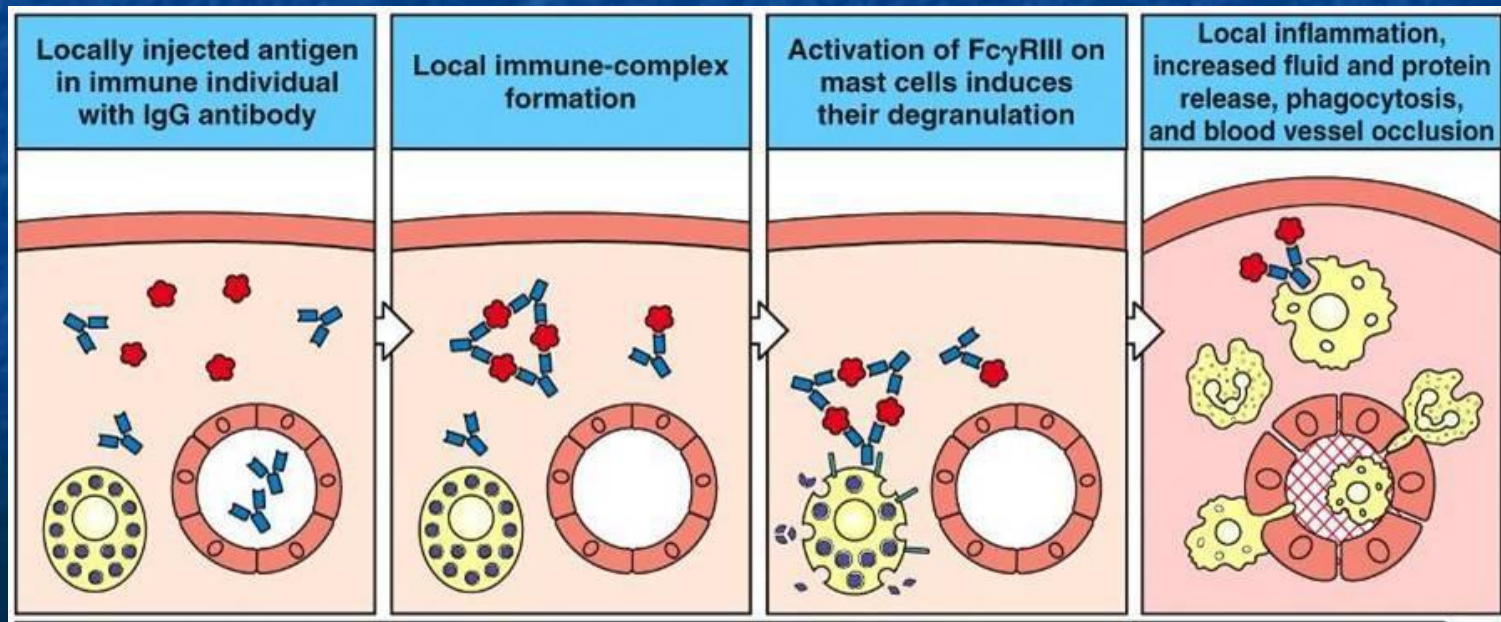
- The amount of antigen - large enough to form immune complexes.
- The size of the complexes - intermediate or small.
- The dysfunction or overloading of phagocyte system.
- Deposition of immune complexes: kidneys, joints, skin, heart, lungs, arterioles.

# Mechanism of tissue injury by immune complexes



# Local Manifestation of Immunocomplex Reaction

- Arthus reaction - local area of tissue necrosis.
- Cause - frequent injections of antigen into the fixed site of skin.



# Type 4 allergic reactions (cell-mediated, delayed)

- Tuberculin test (Mantoux reaction )
- Tuberculosis and leprosy
- Transplant rejection
- Viral infection
- Tumor cells

# Type 4 hypersensitivity

- Immunological stage - production of sensitized T-lymphocytes
- Cell injury is mediated by phagocytes and cytokines.
- Cytokines function:
  - Organization and regulation of immune response and inflammation
  - Cell injury (perforation of membranes, induction of apoptosis)

# Mechanisms of tissue injury

- T-killers (perforins, granzymes)
- phagocytes (active oxygen radicals)
- lysosomal enzymes
- granulomatous (specific) inflammation

# Pseudoallergy distinctive features

- Sensitization (immunologic) phase is absent
- Symptoms can occur at the first exposure.
- The symptoms are directly depend on the dose of the substance



# Pseudo-allergy mechanisms

- Non-immune degranulation of mast cells (histamine – liberating substances).
- The alternative pathway of complement activation (without action of specific IgG and M antibodies).
- Disturbances of arachidonic acid metabolism – aspirin asthma

# The mechanisms of self reactivity prevention

- Selection and deletion of self-reactive T-cells and B-cells.
- Peripheral suppression by T-suppressor cells.

# Mechanisms of autoimmune diseases

- Damage of physiological isolation (nervous system, a crystalline lens, thyroid gland).
- Altering of self-antigens (burns, medicines, chemicals).
- Similarity of exogenous antigen to self antigen:
  - (streptococci antigens are similar to myocardial and kidneys antigens).
- Primary changes of immune system.

# General mechanisms of autoimmune pathology

- Direct **antibody** mediated effects (diabetes mellitus, autoimmune hemolytic anemia)
- **T cell** mediated effects (psoriasis)
- **Immune complex** mediated effects (lupus erythematosus, rheumatoid arthritis)

# Hyposensitization

The patient is gradually vaccinated with progressively larger doses of the allergen.

## Mechanism:

Increase of IgG synthesis  
(blocking antibodies)

# Allergy testing

Intradermal allergy test reactions



The blood test measures the levels of allergy antibody, or IgE, produced when your blood is mixed with a series of allergens in a laboratory

