Allergy

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Immune system disorders

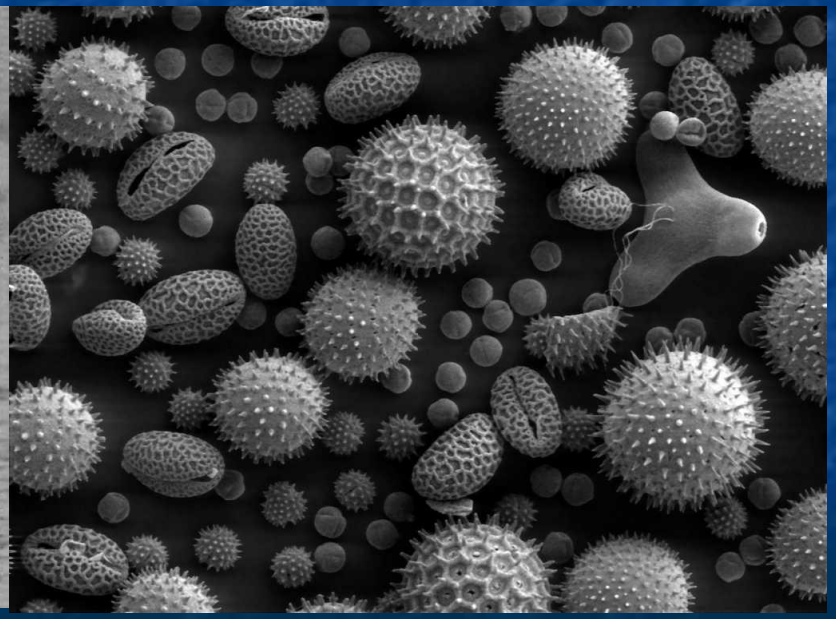
- **Weakened immune response:**
  - Primary immunodeficiency
  - Secondary immunodeficiency
- **Excessive immune response:**
  - Allergic reactions
  - Autoimmune reactions

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.

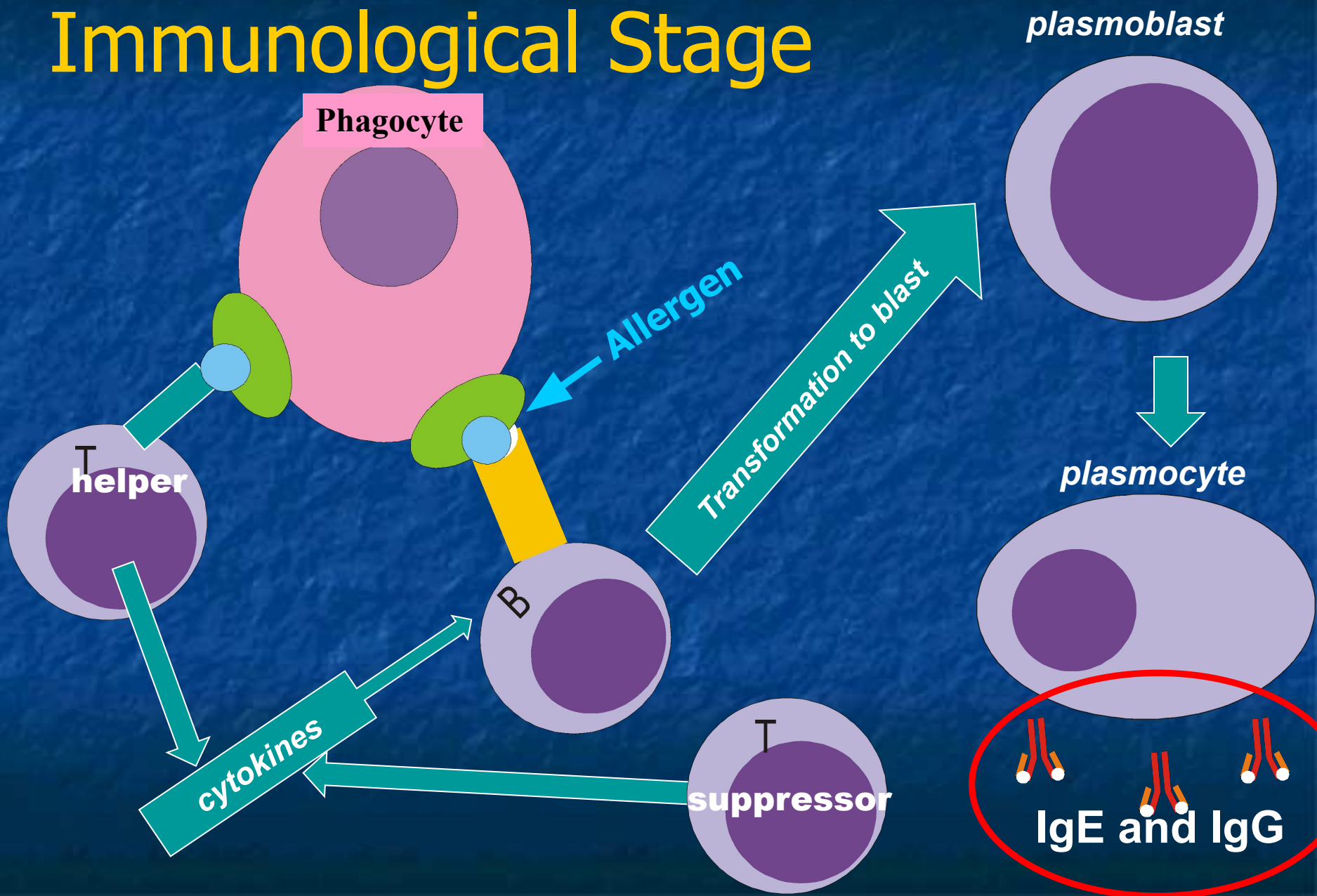
The stage of allergy clinical manifestation (type 1)

- 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

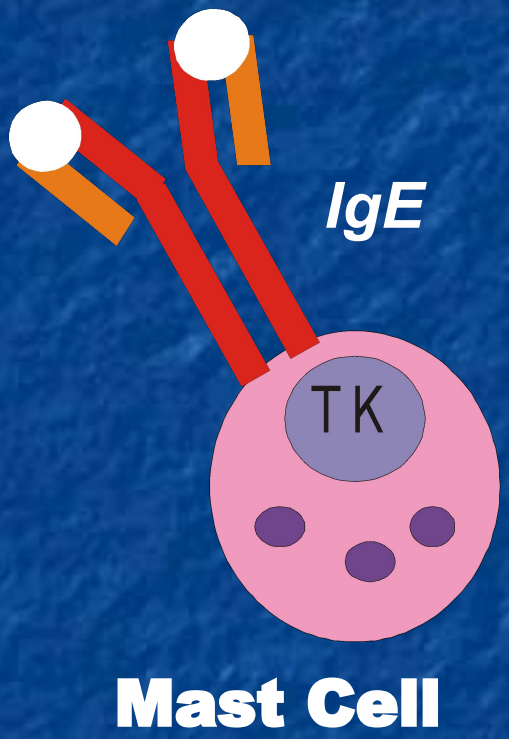
Type 1 Allergic Reactions (anaphylactic, reaginic)

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

Immunological Stage

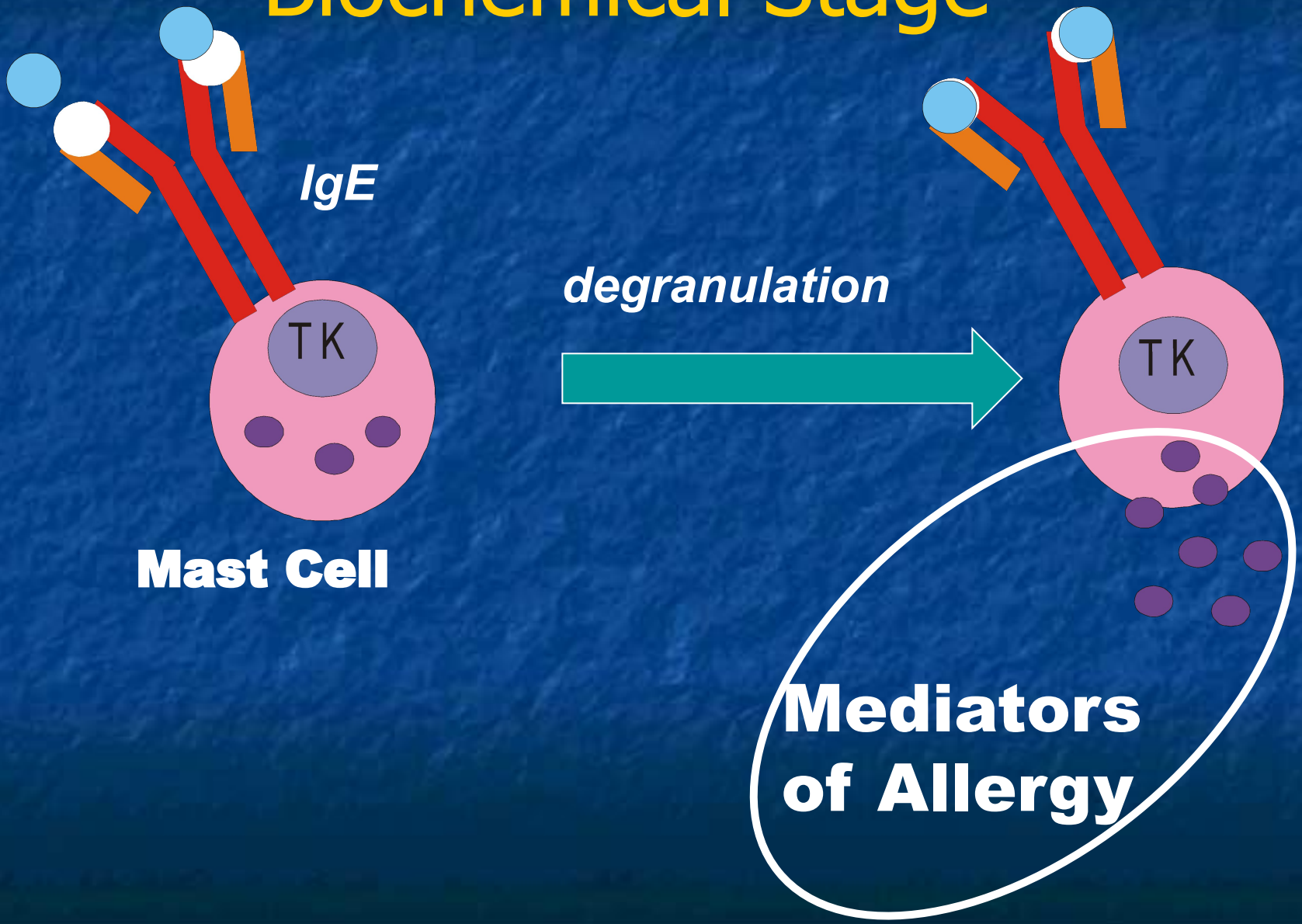


Immunological Stage Result



- 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)

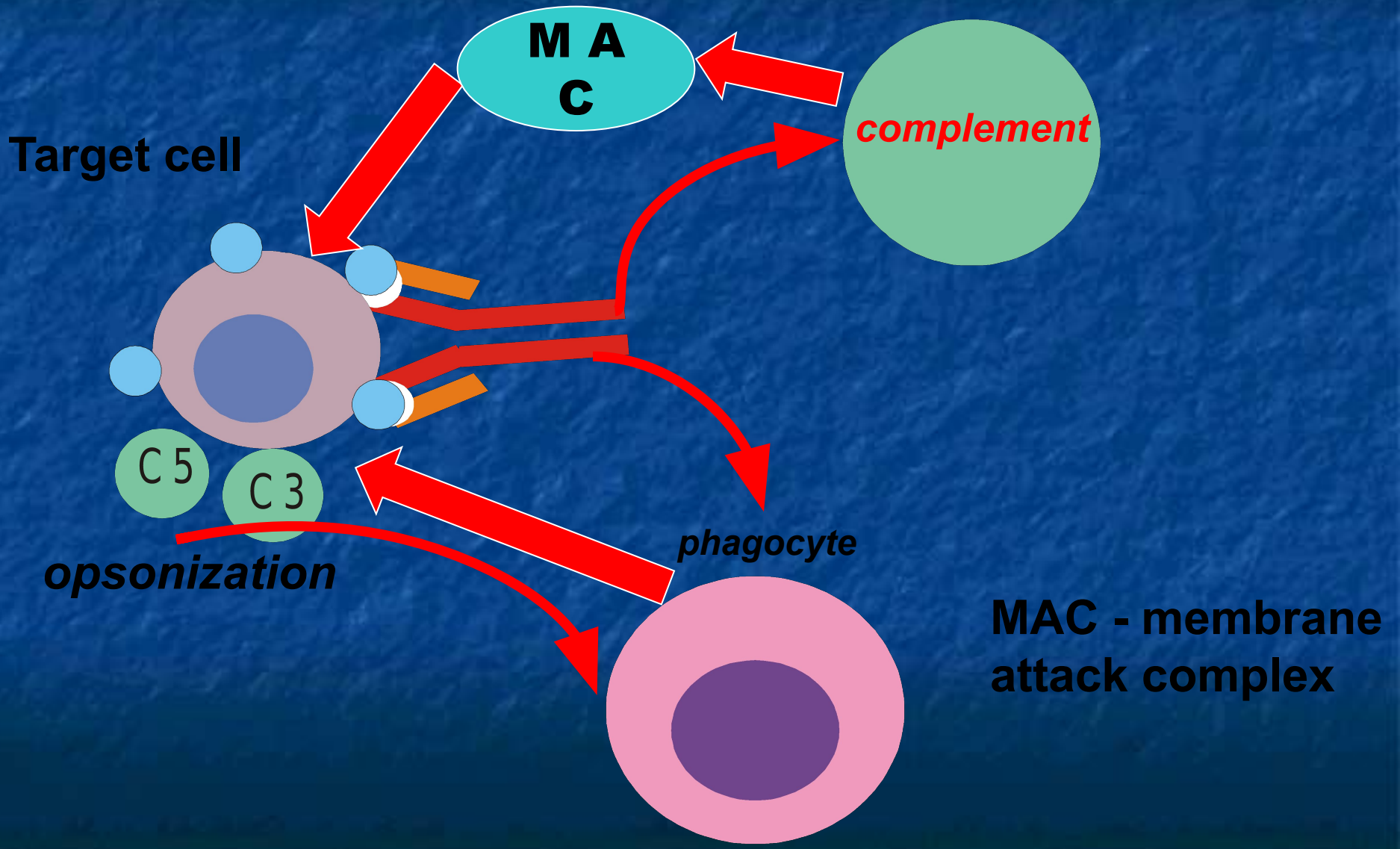
Transfusion reactions, autoimmune anemia, leukopenia, thrombocytopenia, thyroiditis.

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

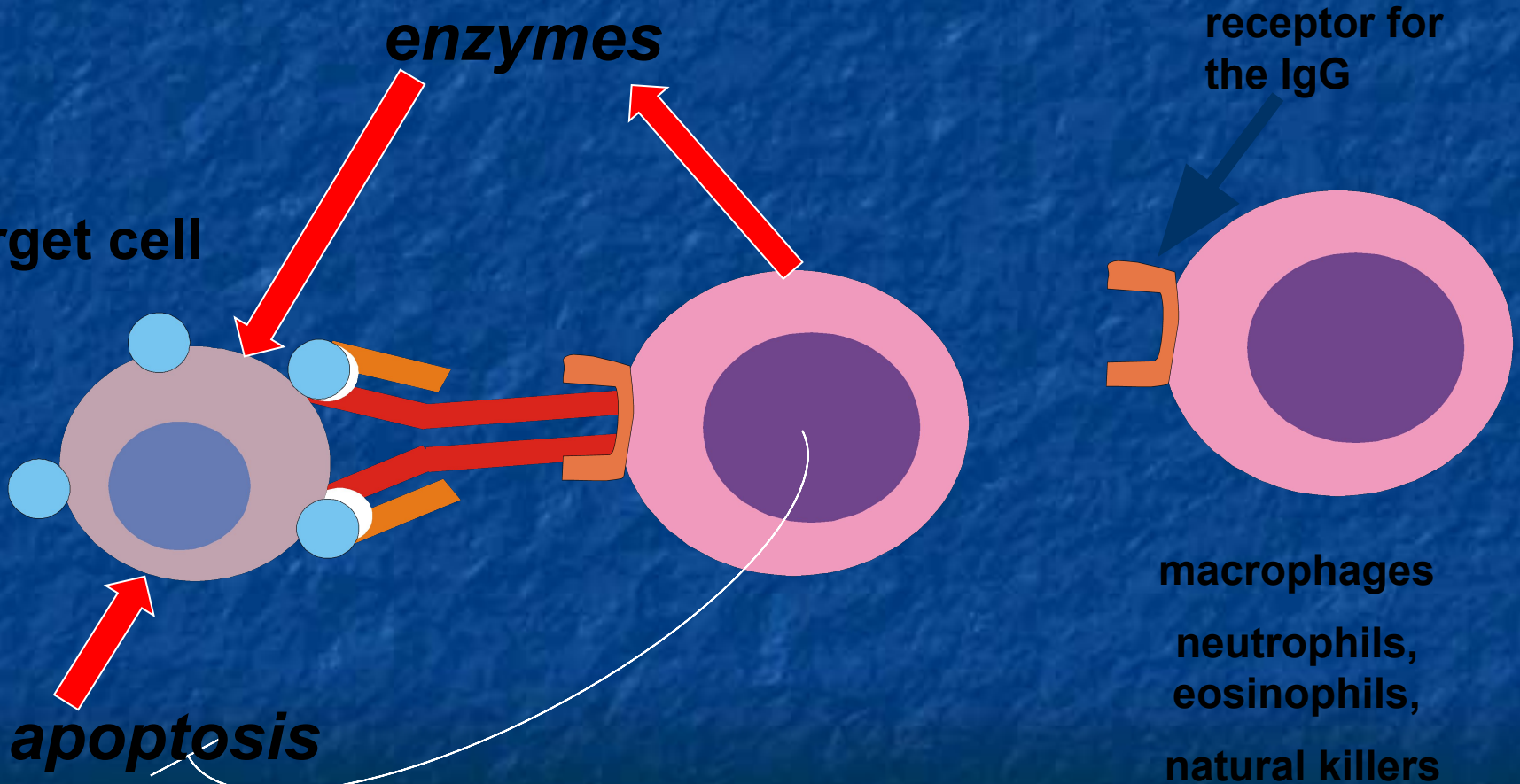
The cell with transformed antigen – target cell

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

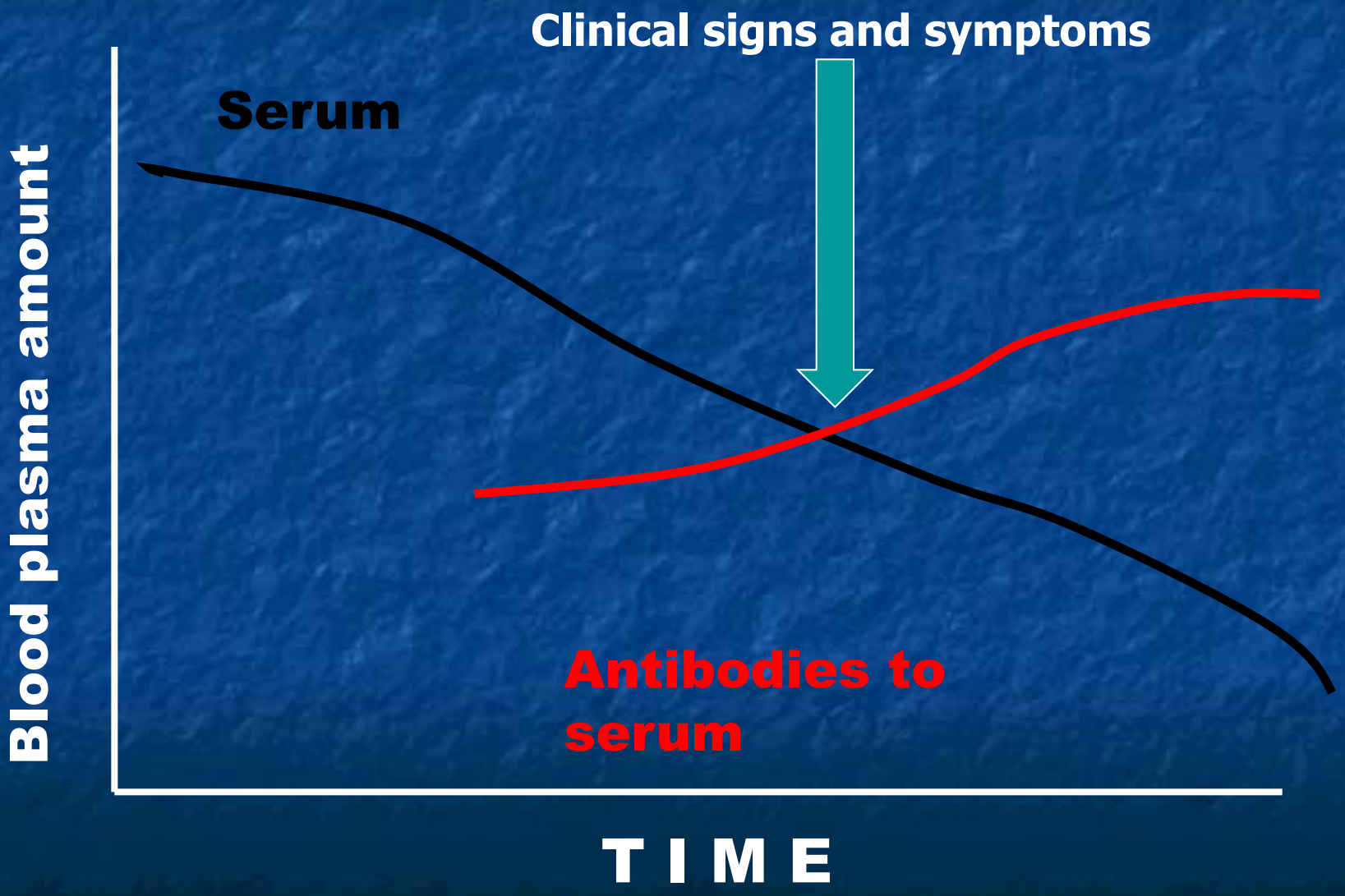
Features of type 3 hypersensitivity

- 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.

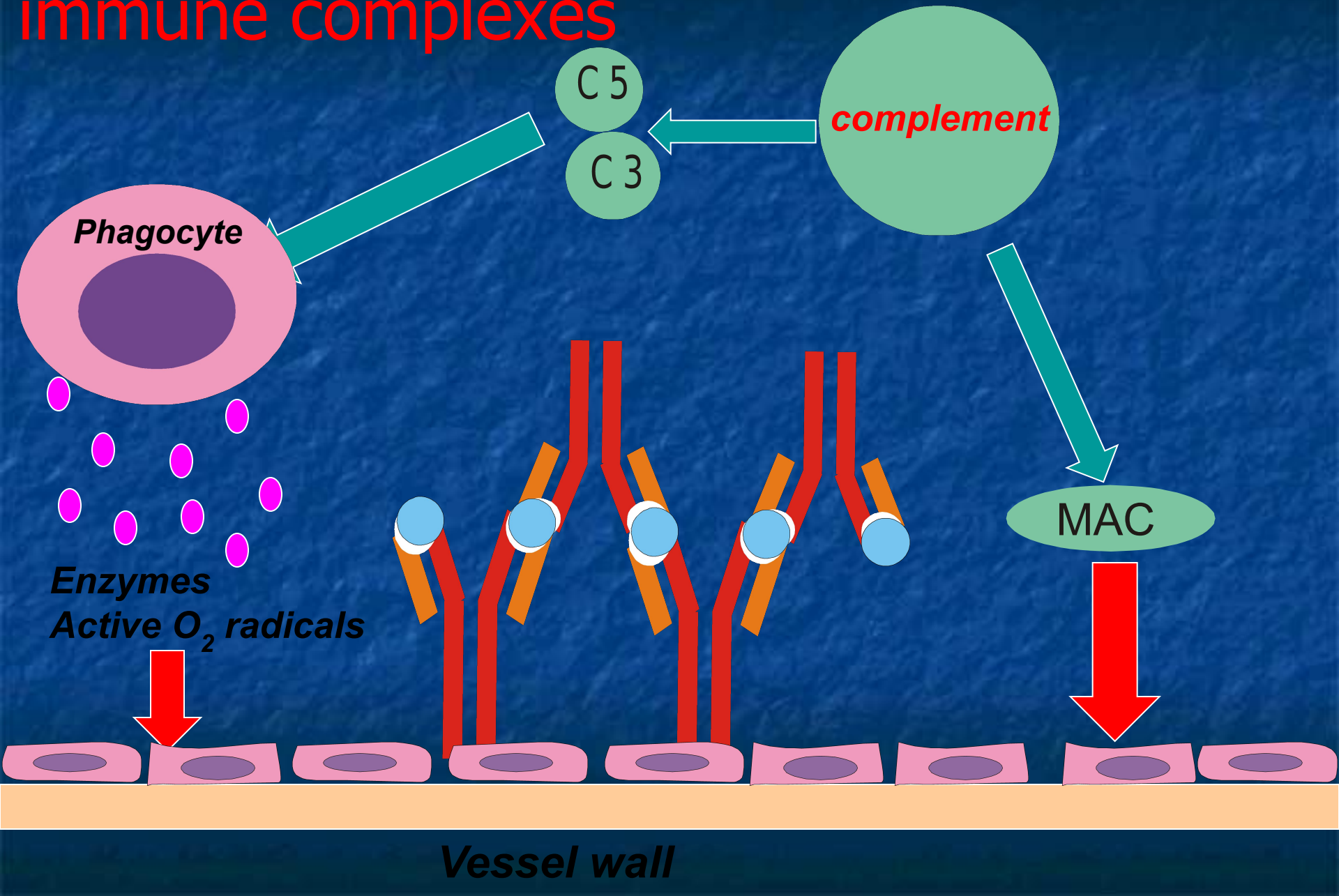
Serum Sickness



Pathogenic properties of immune complexes

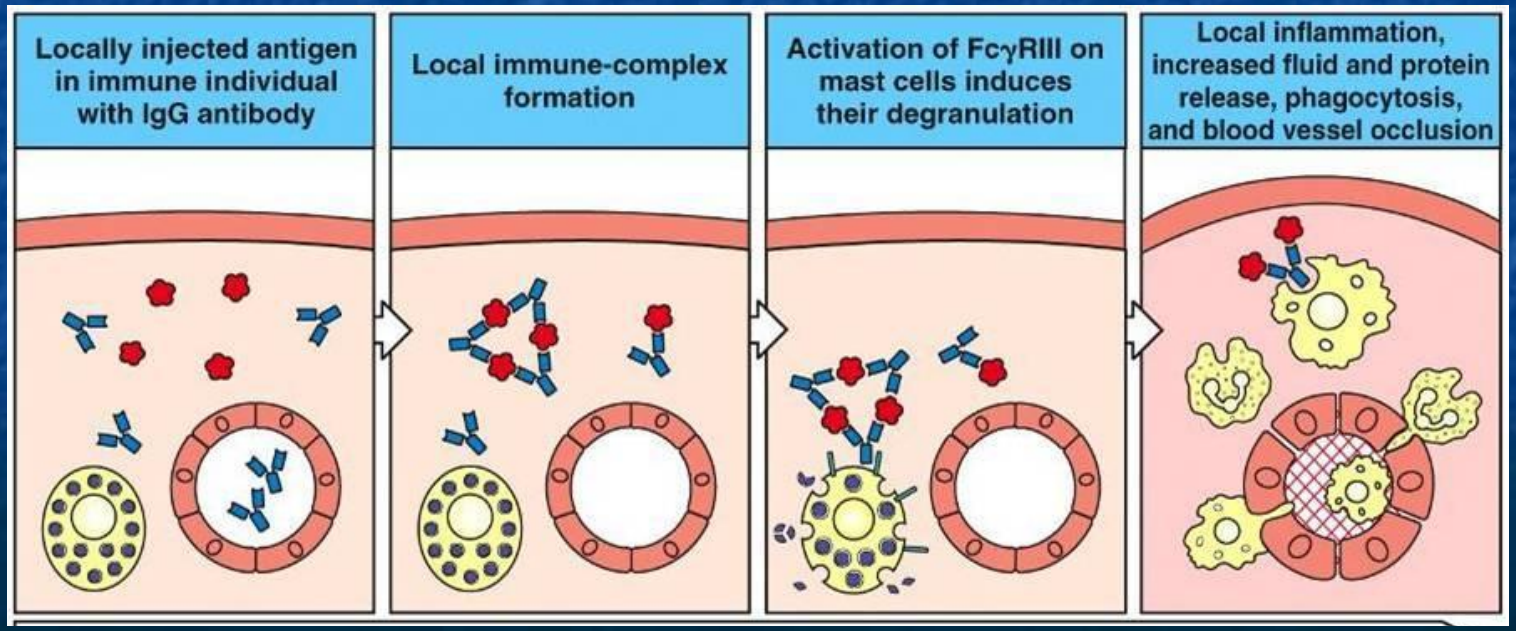
- The amount of antigen - large enough to form immune complexes.
- The size of the complexes - intermediate or small.
- The dysfunction or overloading of phagocyte system.
- Deposition of immune complexes: kidneys, joints, skin, heart, lungs, arterioles.

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 artritis)

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