Lecture X

Immunopathology. Immunodeficiency. Hypersensitivity reactions and their types. Autoimmune diseases. Immunodiagnostics. Immunoprevention and immunotherapy

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Immune Deficiencies

Immune deficiencies can be congenital or acquiredImmune deficiency

In any of the 4 main components that make up the immune system:

1) B-lymphocyte system (antibodies),
2) T-lymphocyte system,
3) complement system,
4) may develop as a result of disorders in phagocytes.

Clinically, opportunistic or recurrent infections are more common.

Recurrent infections of pyogenic bacterial origin, mainly B-lymphocyte deficiency,

Recurrent fungal, viral, or protozoal infections are characteristic of T-cell deficiency.

Hypersensitivity reactions

- The immune response results in unusual, dangerous reactions for the body, such as hypersensitivity, or allergy (latın, allos-alien, ergon-influence).
- The clinical manifestations of these reactions are typical in some individuals and occur in individuals who are hypersensitive to these antigens as a result of contact with a specific antigen.
- Sensitization occurs as a result of an individual's first contact with an antigen, and then repeated contact with the same antigen causes allergic reactions.

Hypersensitivity reactions

Hypersensitivity reactions are divided into 4 types.

Types I, II and III are carried out by antibodies (B-lymphocytes). Type I reactions are associated with IgE, and type II and III reactions are associated with IgG.

Type IV reactions are carried out by sensitized T-lymphocytes.

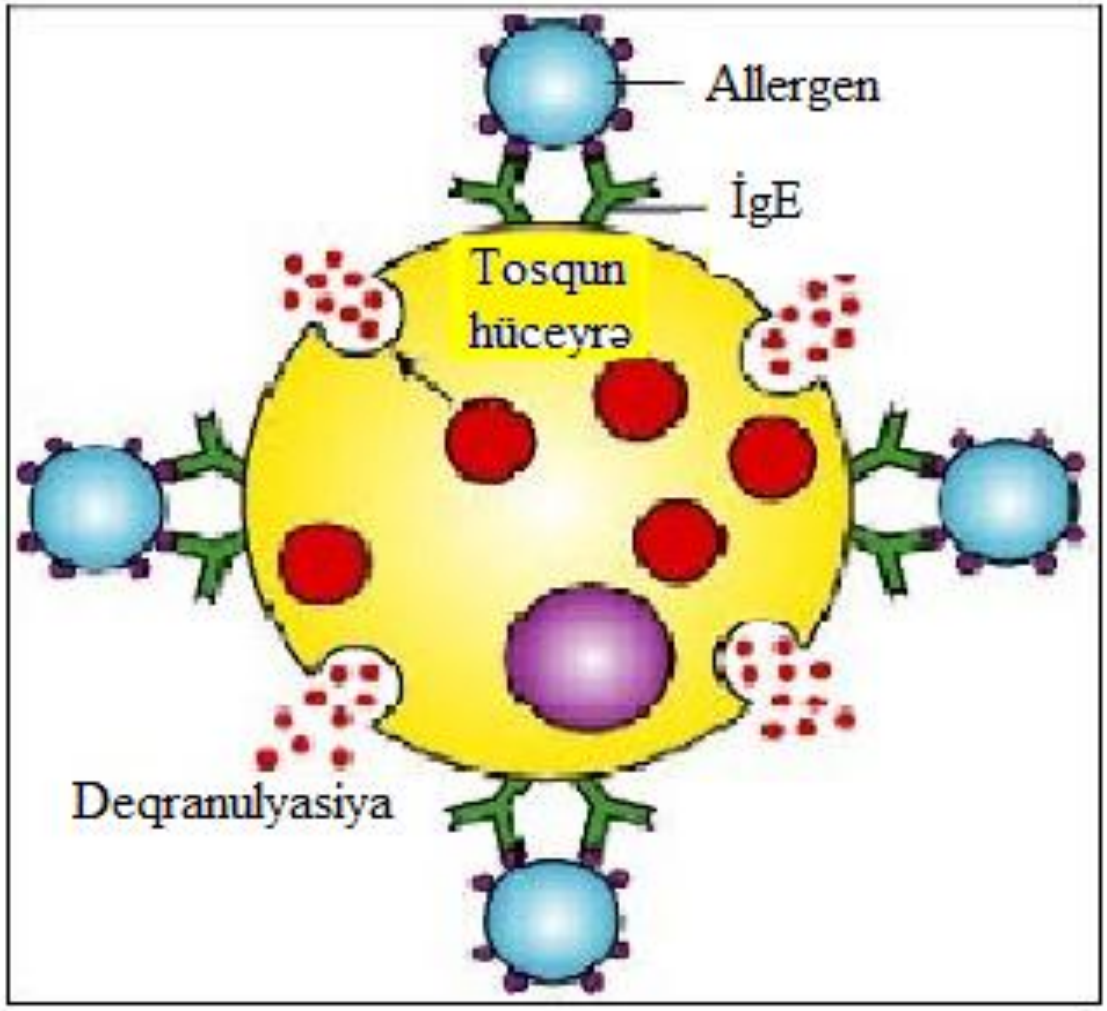
Types of hypersensitivity reactions

Mediator	Type	Reaction
Antibody (IgE)	I (immediate, yaxud anaphylactic)	IgE antibodies are induced by allergens and bind to invading cells and basophils. In repeated contact with the same allergen, it combines with IgE to cause degranulation and excretion of mediators (eg, histamine).
Antibody (IgG)	II (cytotoxic)	Antigens bind to antibodies on the cell surface and cause complement-dependent lysis, such as autoimmune hemolytic anemia.
Antibody (IgG)	III (immun complex)	Antigen-antibody complexes accumulate in tissues, complement is activated, and polymorphonuclear leukocytes migrate to these parts. They produce lysosomal enzymes and cause tissue damage.
Cell	IV (delayed)	Antigen-sensitized Th-lymphocytes produce lymphokines as a result of repeated contact with the same antigen. Lymphokines induce inflammatory reactions and activate macrophages, which in turn produce various mediators.

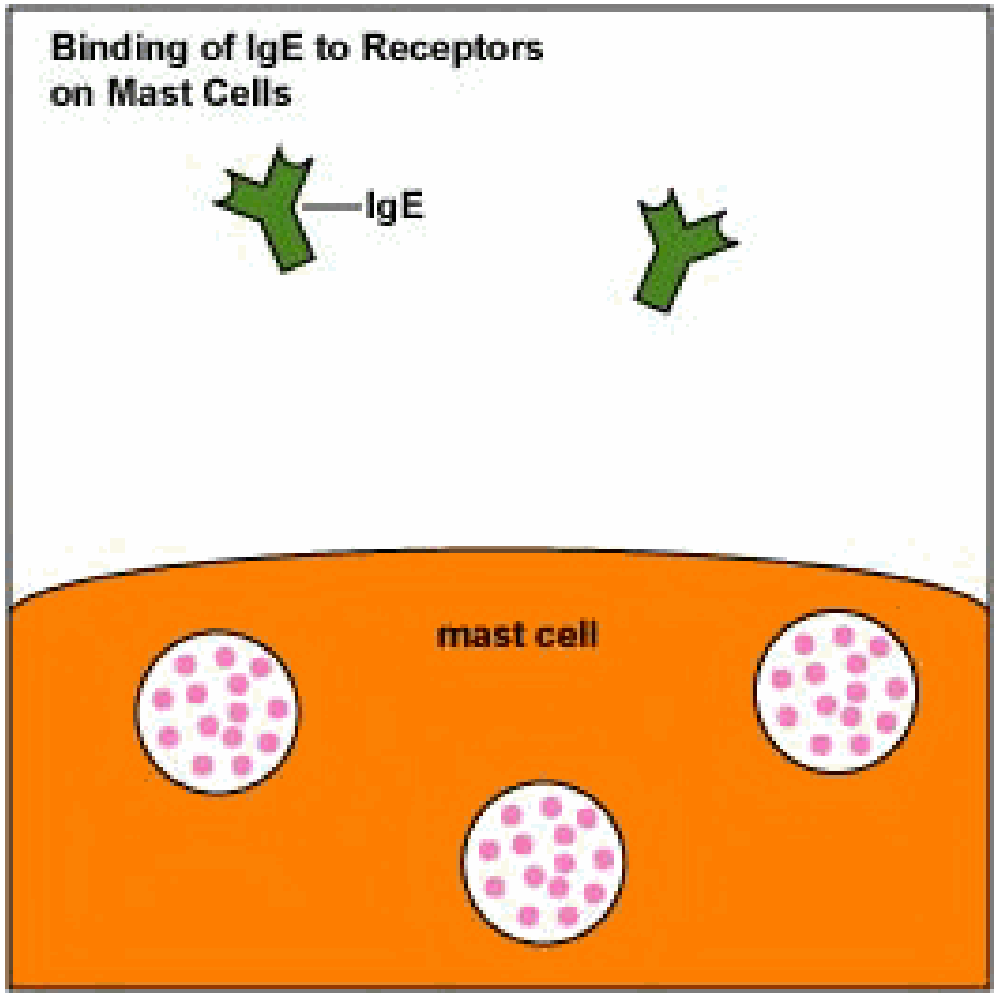
Type I (anaphylactic type) hypersensitivity reactions

- Immediate hypersensitivity reaction occurs under the influence of a number of mediators that are released as a result of the binding of antigen to IgE on the cell surface.
- The process is initially formed as a result of induction of antigen IgE antibodies and their aggregation to the surface of basophils and barrier cells through the Fc fragment. This condition is called sensitization.
- Repeated contact with the same antigen, its combination with basophil or IgE on the surface of the barrier cell, results in the release of biologically active mediators from these cells within 1 minute (immediate reaction).

Type I (anaphylactic type) hypersensitivity reactions



Type I (anaphylactic type) hypersensitivity reactions



Clinical signs of type I sensitivity

- Clinical signs of type I sensitivity include various forms, such as atopy, allergic rhinitis, or Quincke's edema, allergic eczema, allergic rhinitis, allergic conjunctivitis, or fever, allergic asthma, and so on. can manifest as.
- However, the most severe form of sudden hypersensitivity is anaphylaxis. In this case, severe bronchospasm and hypotension (shock) can be life-threatening.

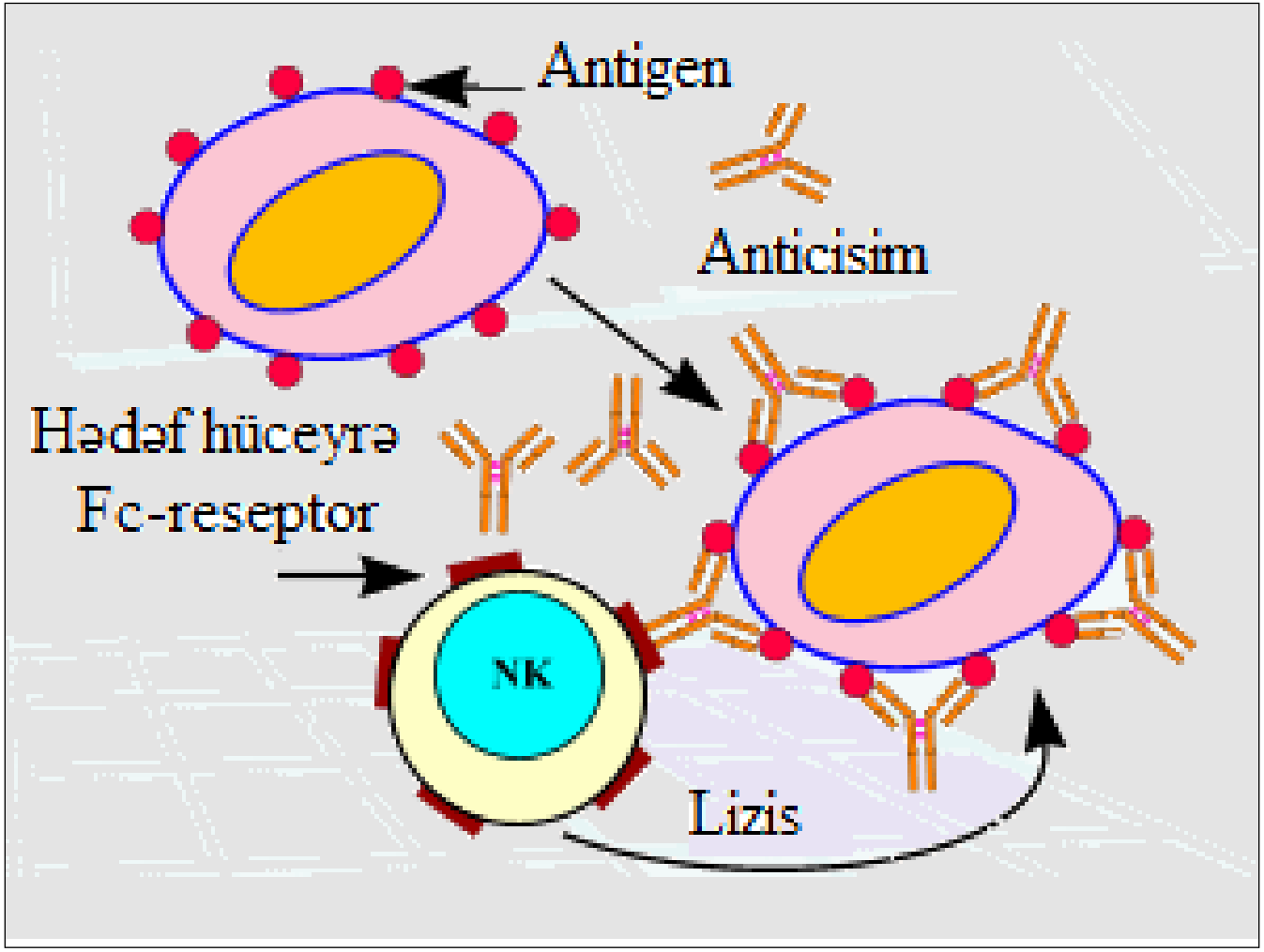
Desensitization

- It has been found that the introduction of small doses of allergens into the body results in a weakening or loss of hypersensitivity.
- In this case, due to the small amount of antigen-IgE complex formed, not enough mediators are formed for the formation of strong allergic reactions. This situation, which is the opposite of sensitization, is called desensitization. Through it, it is possible to prevent systemic anaphylaxis.
- This method (Bezredko method) allows you to prevent allergic reactions when using some drugs, especially immune serums.

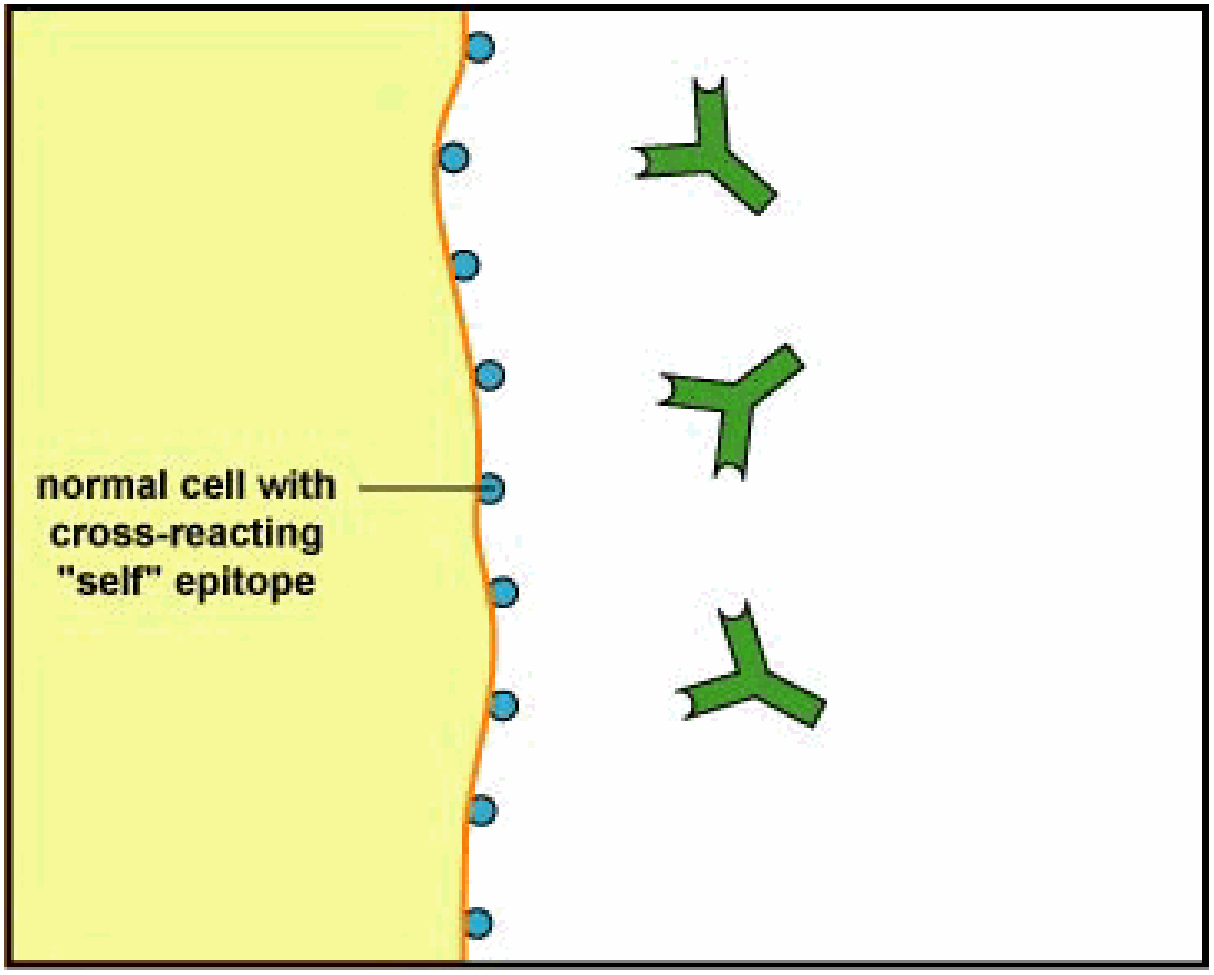
Type II (cytotoxic type) hypersensitivity reactions

- Hypersensitivity of the cytotoxic type occurs as a result of the combination of antibodies against the cell membrane antigen with this antigen and the activation of the complement.
- The antibody (IgG) binds to the antigen through the Fab fragment and to the complement through the Fc fragment. This results in the formation of a complement membrane-invading complex and damage to the cell membrane.
- As a result, complement-mediated lysis of the type of hemolytic anemia occurs, as in the case of incompatible blood transfusion reactions due to the ABO system or Rhesus factor.

Type II (cytotoxic type) hypersensitivity reactions



Type II (cytotoxic type) hypersensitivity reactions



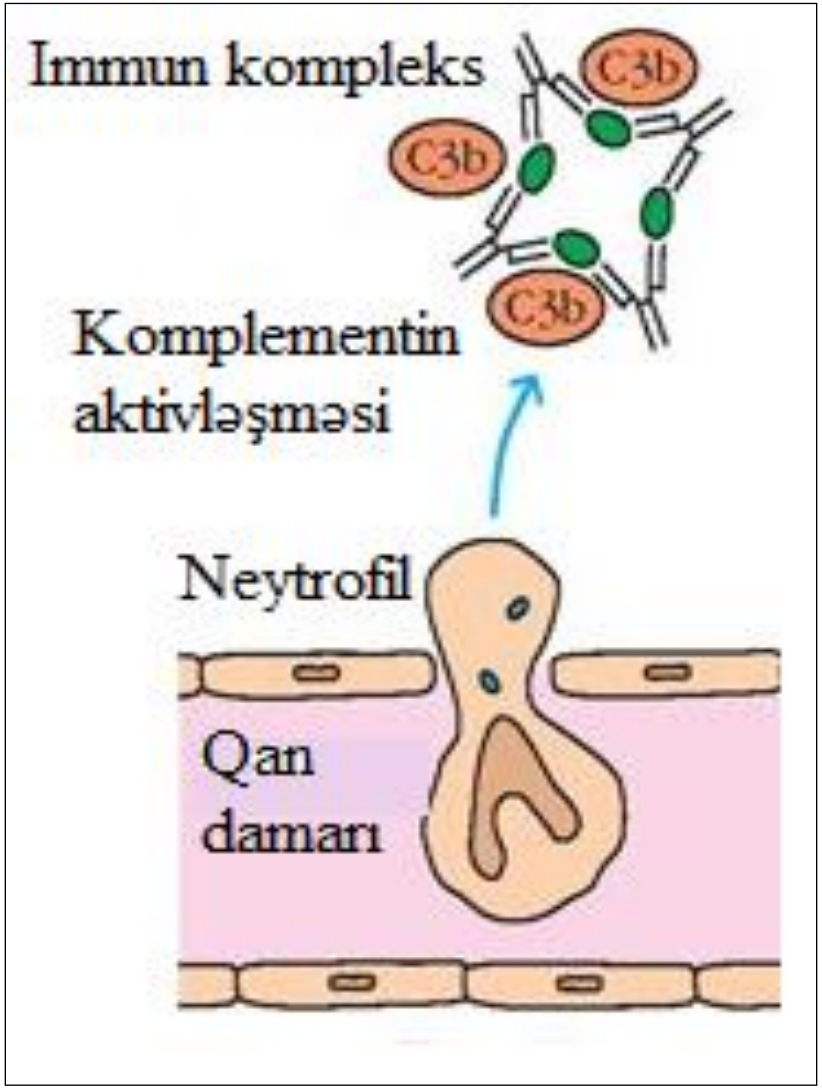
Type III (immune complex type) hypersensitivity reactions

- Hypersensitivity of the immune complex type is characterized by the formation of inflammatory processes in tissues by antigen-antibody complexes.
- Normally, immune complexes are eliminated from the body through the reticuloendothelial system, but sometimes they remain in the body and cause a number of diseases in the tissues.
- In persistent bacterial and viral infections, immune complexes can accumulate in organs, such as the adrenal glands, causing damage. In autoimmune disorders, "native" antigens (autoantigens) can induce the synthesis of autoantibodies.

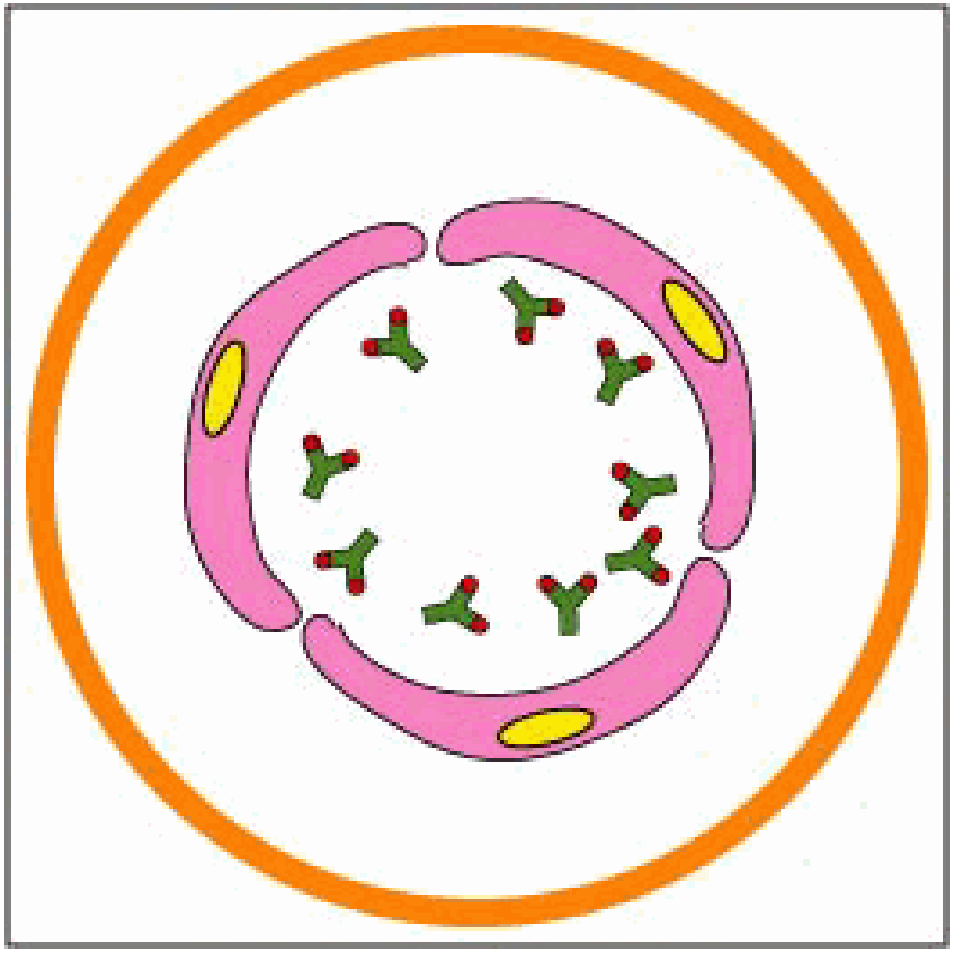
Type III (immune complex type) hypersensitivity reactions

- The latter combine with relevant antigens or form deposits in organs such as complexes, especially in the joints (arthritis), kidneys (nephritis) or blood vessels (vasculitis).
- The deposition of immune complexes in tissues, such as blood vessel walls, is accompanied by activation of the complement system and chemotaxis of neutrophils to these parts, leading to inflammation and tissue damage (eg, vasculitis).
- Type III hypersensitivity reactions include Arthus phenomenon and serum sickness.

Type III (immune complex type) hypersensitivity reactions



Type III (immune complex type) hypersensitivity reactions



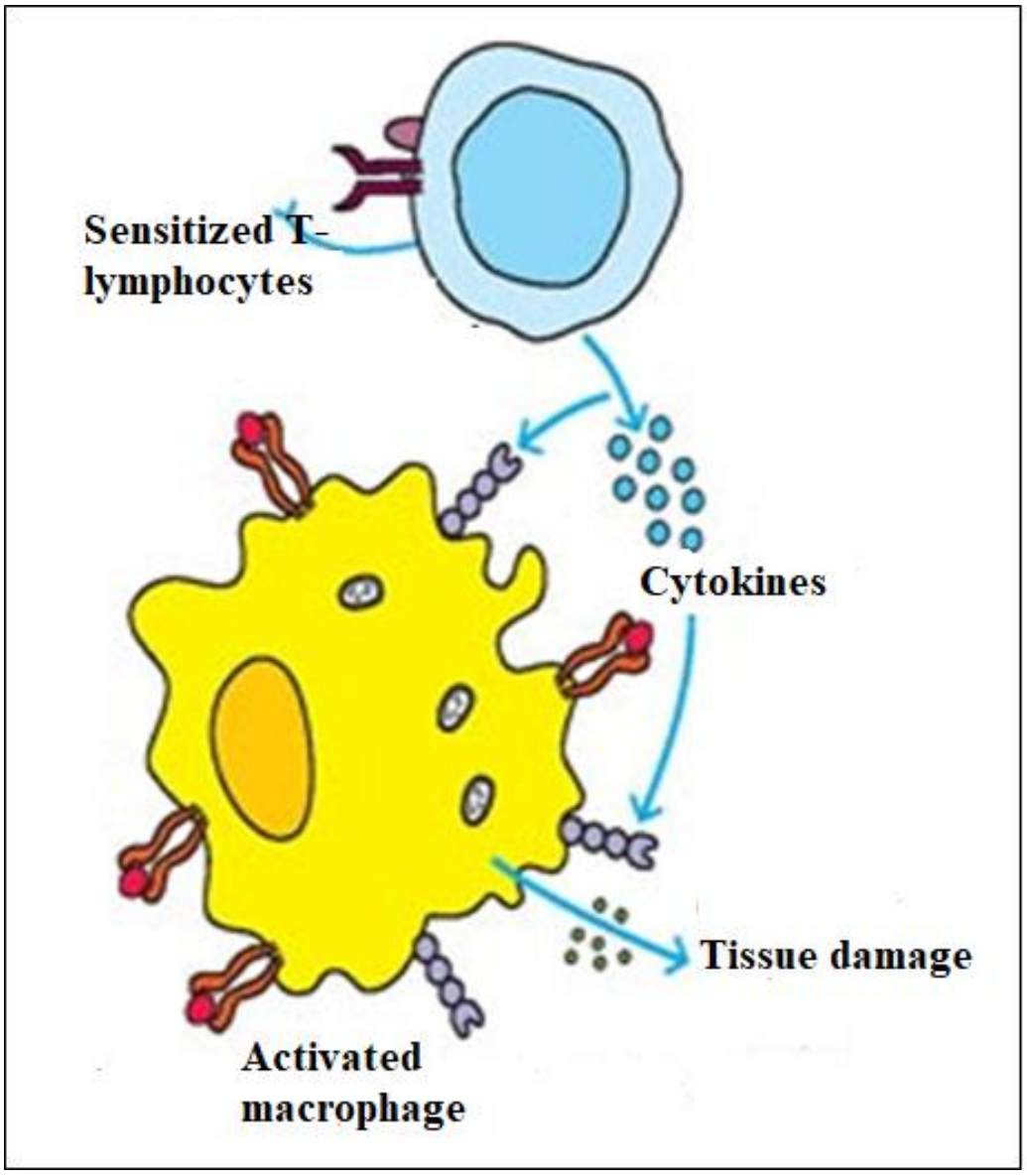
Type IV (delayed type) hypersensitivity reactions

- Delayed-type hypersensitivity (DTH) reactions are associated with T-helpers (CD4) and cytotoxic T-lymphocytes. DTH is a lymphoid-macrophage reaction that develops as a result of immune activation of macrophages under the influence of allergen-sensitized lymphocytes.
- Immune-inflammatory mechanisms are based on DTH: the antigen enters the body, is phagocytosed by macrophages, is broken down into small pieces, and its class is divided into fragments. Antigen-II class MHC complex interacts with antigen-specific receptors on the surface of Th-lymphocytes. Activation and clonal proliferation of Th-lymphocytes occur under the influence of IL1 produced by macrophages and IL2 synthesized by lymphocytes.

Type IV (delayed type) hypersensitivity reactions

- Sensitization - the body produces sensitized T-lymphocytes against allergens
- The allergen is recognized by sensitized T-lymphocytes upon re-entry.
- This causes the synthesis of cytokines by sensitized T-lymphocytes.
- Cytokines activate macrophages and migrate to the area where the antigen is located.
- Destruction and elimination of allergens by macrophages
- Infiltration and granuloma of lymphocytes and macrophages form in the allergen area.

Type IV (delayed type) hypersensitivity reactions



Autoimmune diseases

- Tolerance to tissue antigens in adults is usually observed against antigens that came into contact during the embryonic period and are known as "native".
- In some cases, tolerance is lost and the immune system develops an immune response against its own antigens, in other words, an autoimmune disease develops. In this regard, various bacteria, viruses, as well as drug-induced cross-reactive antigens, such as autoreactive T- or B-lymphocytes, are activated.
- In the pathogenesis of autoimmune diseases, the interaction of the components of the immune system with their own healthy cells and tissues stops. Autoimmune diseases are sometimes referred to as immune complex diseases.

Features of immunity in some infections

Features of antiviral immunity

- Non-specific immunity is mainly determined by interferon and NK cells
- Specific antibodies can only act on extracellular viruses and not on intracellular viruses.
- Infected cells express viral proteins in a cytoplasmic membrane containing class I MHC antigens. Such target cells carrying foreign information are destroyed by T-killers through antigen-independent cell cytotoxicity, resulting in limited viral replication.

Features of immunity against fungi

- Fungal antigens have a relatively weak immunogenicity and induce antibody production poorly, but they stimulate cellular immunity to a sufficient extent.
- Cellular immunity plays a leading role in fungal immunity
- Delayed-type hypersensitivity (DTH) is observed as a rule in skin mycoses and visceral mycoses

Features of antiparasitic immunity

- Specific antibodies cause the destruction of parasites, especially helminths, by antigen-dependent cellular cytotoxicity.
- Specific antibodies (IgE or IgA) combined with parasites are recognized by eosinophils. Activated eosinophils secrete a number of toxic substances that have a lethal effect on helminths as a result of degranulation.
- Eosinophilia (increased number of eosinophils) observed in parasitic infections is related to this. In most cases, DTH is formed against the microorganisms.
- Many parasites (eg, malaria plasmodium, toxoplasmosis) are multi-stage developmental cycles in the body, which are accompanied by changes in the antigenic structure of the immune system, which in turn affects the immune system.

Immunodiagnosis

- Diagnosis of diseases by means of immune reactions is widely used in practical medicine. The most commonly used reactions in immunodiagnostics are based on the specific interaction of antibodies and antigens.
- It is known that specific antibodies are formed in the blood serum against antigens that enter the body. These antibodies have the ability to bind specifically to antigens not only in the body (in vivo) but also outside the body (in vitro).
- Because the interaction between antibodies and antigens is so specific, it is possible to identify an unknown antibody based on a known antigen, or vice versa.
- These reactions are called serological reactions because of the use of blood serum containing antibodies.

Serological reactions

Serological reactions can be carried out in two directions:

Known serologic reactions use known antibodies to identify unknown antigens or microorganisms and their toxins.

These antibodies are present in diagnostic immune serums. Recognition of microorganisms by appropriate immune serums is called serological identification.

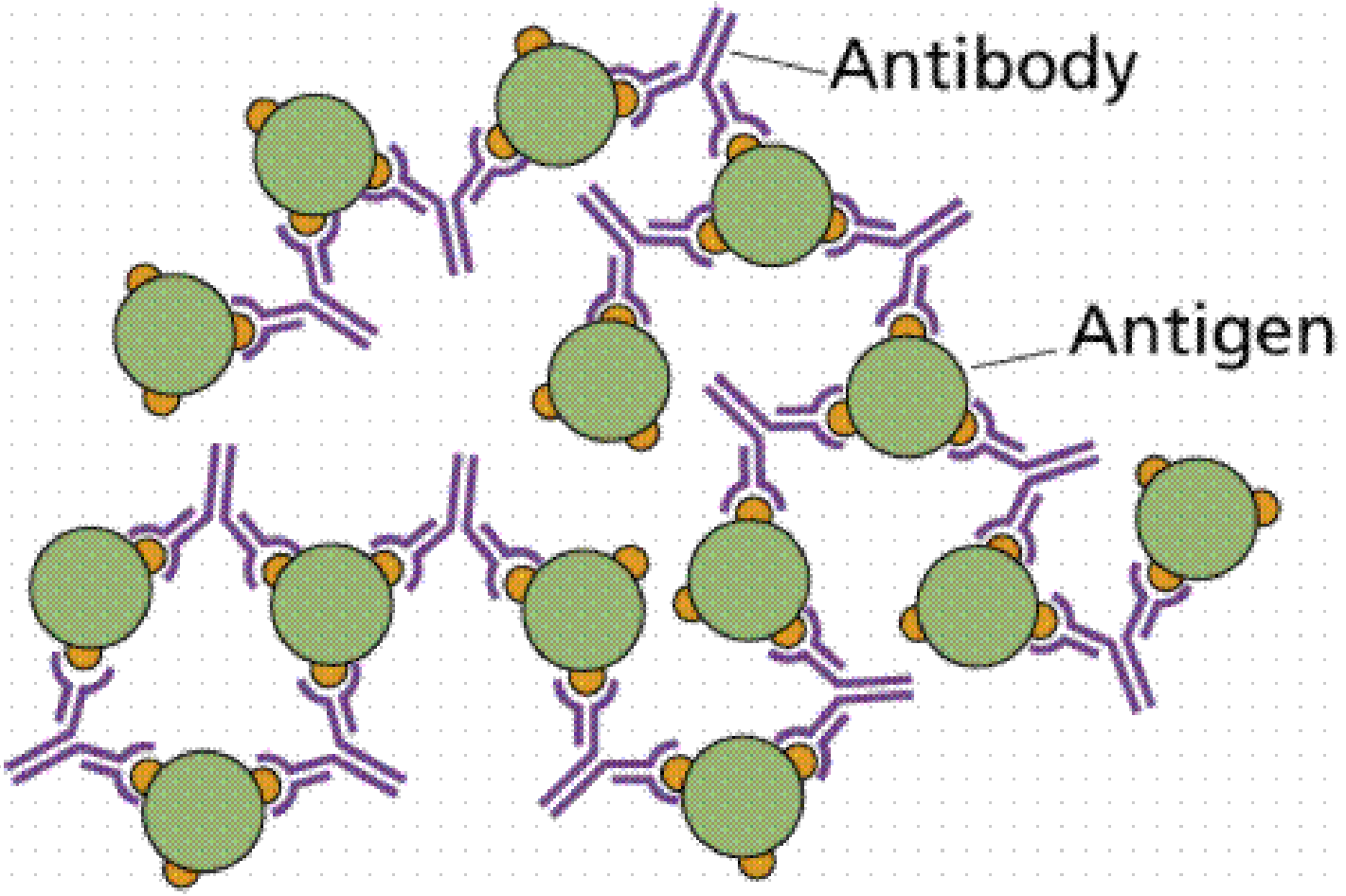
Serological reactions

- Serological reactions used to identify unknown antibodies use known antigens or microorganisms - diagnostic cumulators.
- More commonly used strains of microorganisms, or antigens derived from them, are used as diagnostics. Unknown antibodies are often detected in the blood serum of patients.
- This is called a serological diagnostic test because the presence of antibodies in the serum against the causative agent often indicates disease.

Serological reactions

- The results of serological reactions are evaluated based on the formation of the antigen-antibody complex.
- As a rule, a positive serological reaction is accompanied by the formation of this complex.
- Mechanisms, participating ingredients, the nature of the formed antigen-antibody complex, etc. Depending on the serological reactions are different.
- Agglutination, precipitation, neutralization, complement fixation reaction, labeled antibody and reaction with antigens for immunodiagnostic purposes.

The phenomenon of agglutination



Immunoprophylaxis and immunotherapy

- Immunoprophylaxis and immunotherapy are active and passive immunoassays against the causative agent by forming insensitivity to their causative agents in order to prevent infectious diseases.
- Active or passive immunity is induced in the body as a result of immunization carried out to protect against infectious diseases.

Vaccines

- Active immunity is formed as a result of immunization with vaccines.
- Vaccines are preparations made from microorganisms or their antigens, the introduction of which into the body forms an artificially acquired immunity against the relevant disease.

Inactivated (killed) vaccines

- Chemicals (eg phenol, formaldehyde), high temperature, etc. consists of killed microorganisms that have lost their viability under the influence of
- In order to obtain inactivated vaccines, pathogenic microorganisms are cultured in artificial nutrient media, then inactivated, purified, and obtained in liquid or lyophilized form.

Live (weakened virulence, attenuated) vaccines

- It is prepared from appropriate strains of microorganisms with weakened virulence.
- These vaccines are microorganisms that have lost their ability to cause disease, but have been acquired, retained the ability to develop specific anti-infective immunity, and have undergone genetic modification (BGG vaccine, rabies, measles vaccine, etc.).
- Recombinant DNA technology is currently being used to obtain attenuated vaccine strains. In order to prepare viral vaccines, the genes responsible for the synthesis of their antigens are transferred to vectors, such as large DNA-containing flower viruses. Such vaccines are called vector vaccines.

Preparation of vector vaccines

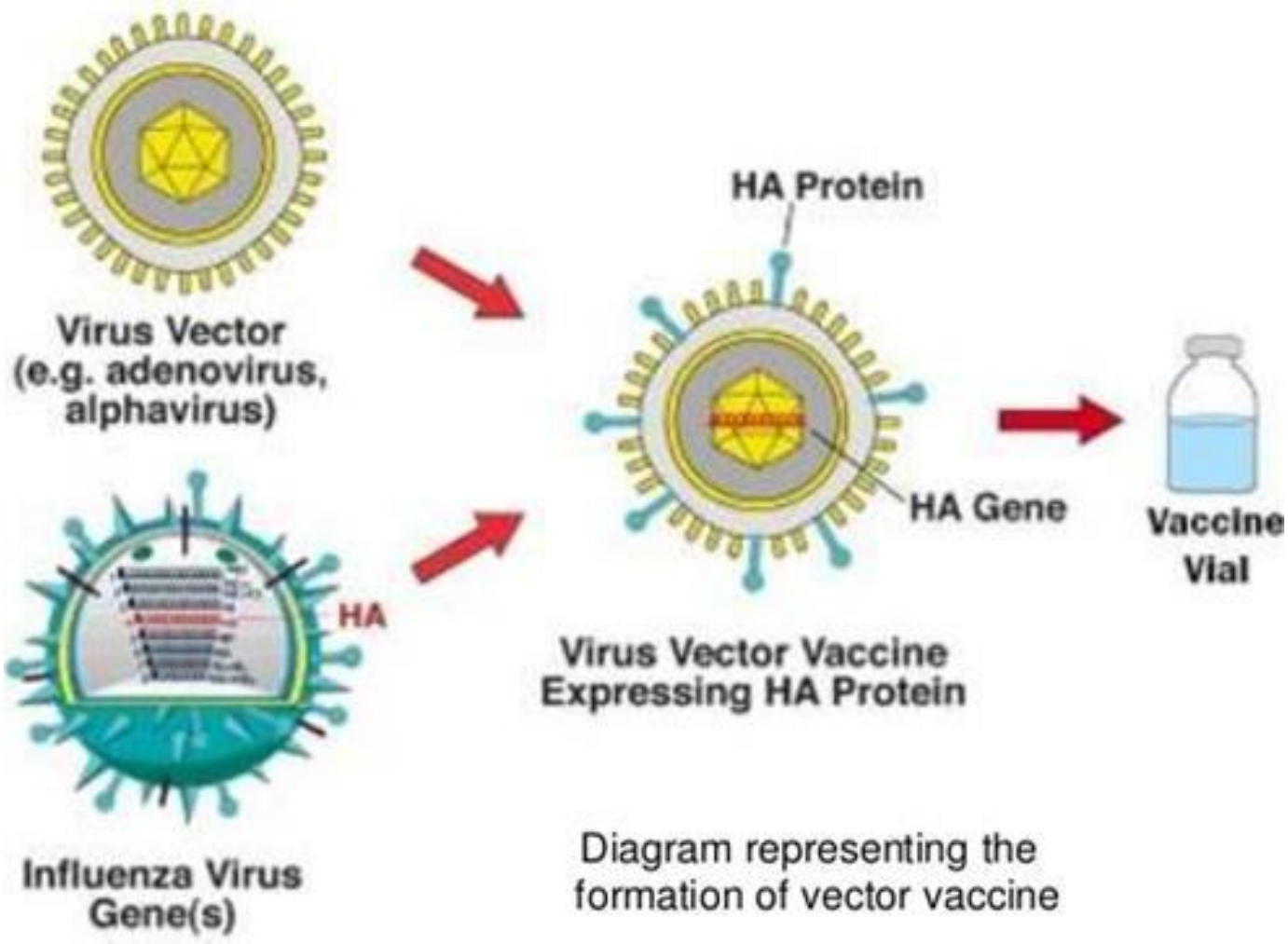
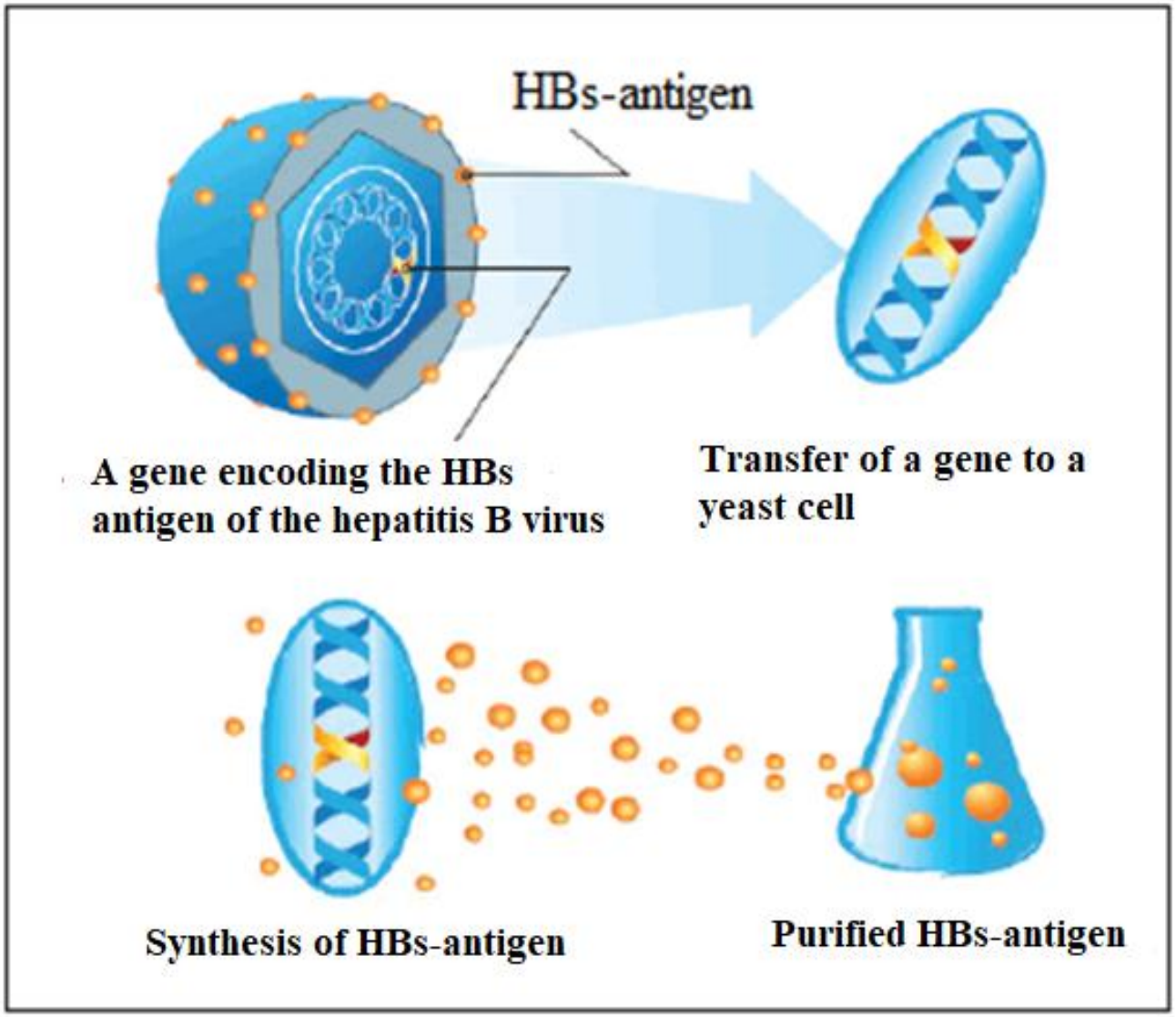


Diagram representing the formation of vector vaccine

Chemical vaccines

- It is obtained by disintegration of microbial cells, consisting of individual components (antigens) of microbial cells.
- Recently, these vaccines are obtained by genetic engineering, they are called recombinant vaccines.
- To do this, recombinant yeast strains are created by transferring genes that enable the synthesis of immunodominal antigen of any microorganism to producer cells, such as yeast fungal cells.
- As a result, the recombinant leukocytes synthesize the appropriate antigen because they have genes that will allow them to synthesize a specific antigen.
- At present, a vaccine prepared from viral antigen (HBs-antigen) synthesized by recombinant yeast strains is used in the specific prophylaxis of hepatitis B.

Scheme of preparation of recombinant vaccine from HBs-antigen of hepatitis B virus



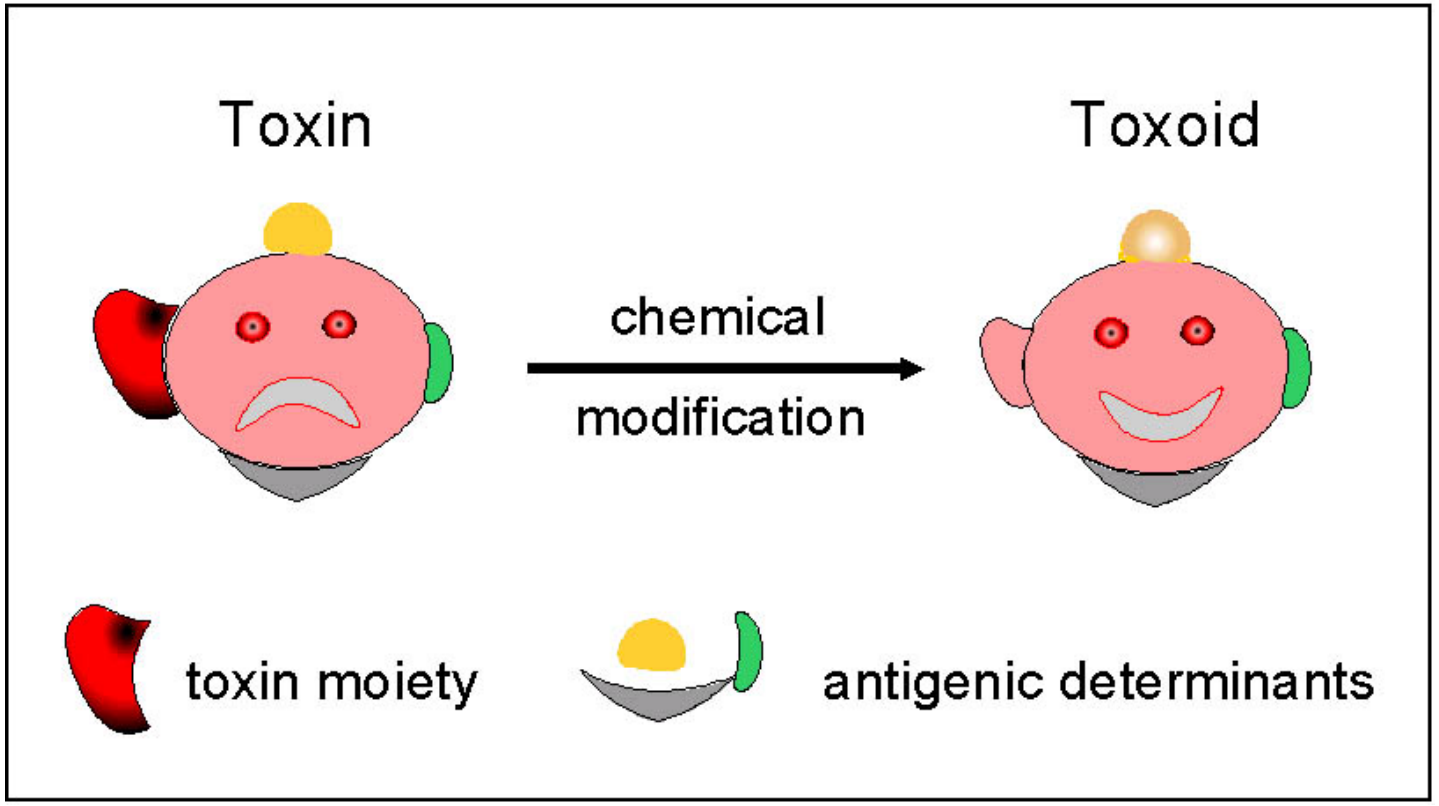
Synthetic vaccines

- The production of synthetic vaccines is based on the use of artificially synthesized immunodominant antigen (protective antigen) of the pathogen. To do this, the amino acid sequence of the immunodominant antigen is studied and synthesized, so that the resulting protective antigen can theoretically be used as a vaccine.
- However, synthetic peptides are weak antigens and must be combined with a carrier protein or synthetic biopolymer (muramil peptide, D-glutamine copolymers, etc.) to increase immunogenicity. Automatic synthesizers are used to produce such vaccines
- So far, attempts to use synthetic vaccines against mumps have been unsuccessful. The vaccine has been tested in guinea pigs, pigs and cattle. Although the vaccine protects against the disease, the antibody response caused by it is 10-100 times weaker than immunization with complete virions. This vaccine is not widely used.

Anatoxins or toxoid vaccines

- Some vaccines contain anatoxins that do not cause disease but have the ability to induce an immune response instead of microorganisms.
- Exotoxins lose their toxicity under the influence of 0.4% formaldehyde at 37°C for 3-4 weeks, but are converted to anatoxin (toxoid) while maintaining specific antigenicity.

Anatoxins or toxoid vaccines



Widely used toxoid vaccines

Adjuvants

- Adjuvant (auxiliary) - a complex or complex substance used to enhance the immune response when administered simultaneously with an immunogen.
- Unlike immunomodulators, they are used to increase a certain immune response in the body (for example, during vaccination) and to normalize a weakened immune response.
- Most adjuvants adsorb antigens on their surface, creating a depot that allows them to be stored in the body for a long time, which increases the duration of action on the immune system.

The most commonly used adjuvants

- Adjuvants can be inorganic (aluminum and calcium phosphates, calcium chloride, etc.) and organic (agar, glycerol, protamines, etc.). Currently, the following adjuvants are more commonly used.
- Freund's incomplete adjuvant. It is an aqueous-oily emulsion containing Vaseline oil, lanolin and emulsifier. Enhances phagocyte retention by antigen storage
- Freund's full adjuvant. In addition to the above components, BCG or muramyl dipeptide is added. This allows macrophages to be activated and T-cells to be stimulated.
- Aluminum hydroxide - Al (OH) 3 stores antigens due to its high sorption capacity and enhances phagocytosis.

Vaccination

- It is carried out according to planned and epidemiological instructions.
- Each country has a prophylactic vaccination schedule and control over the planned preventive vaccinations.
- Mandatory conduct of such vaccinations is regulated by law.

Immune serums

- In immunoprophylaxis and immunotherapy, immunosuppressants are used in immunosuppressants - preparations containing antibodies to the appropriate agent or its toxin to create passive immunity.
- The mechanism of action of immune serums used for these purposes is related to the neutralization of the relevant microorganisms and their toxins by specific antibodies.

Immune serums used for seroprophylaxis and serotherapy

- Immune serums and immunoglobulins are used for two purposes: prophylaxis (seroprophylaxis) and treatment (serotherapy).
- In order to obtain immune serums, large animals, such as horses, are hyperimmunized with microorganisms or their antigens. It is then used as an immune serum after purifying the blood serum of such animals from ballast substances.
- In some cases, the serum of people infected with the disease, such as immune serum, or the blood serum of specifically immunized donors, as well as the placenta.

Application of immune serums

- Immune serums are particularly effective against toxinemic infections (tetanus, botulism, diphtheria, gas gangrene), as well as some bacterial and viral infections (measles, mumps, rubella, plague, plague, plague).
- The prophylactic dose of these drugs is significantly less than the therapeutic dose.
- To create passive immunity, the drug is usually given intramuscularly to people who have been in contact with patients or other sources of infection. Immunity is formed quickly and usually lasts up to a month. After this period, with the removal of antibodies from the body, the immunity disappears.

Diagnostic immune serums

- Diagnostic immune serums are used to identify microorganisms in various serological reactions.
- These serums are usually obtained by hyperimmunizing small animals, such as wasps, with microorganisms or their antigens.
- Diagnostic immune serum is used in the blood serum of laboratory animals (mainly rabbits) hyperimmunized with appropriate antigens.