LESSON №17

IMMUNOBIOLOGICAL DRUGS

IMMUNOBIOLOGICAL DRUGS

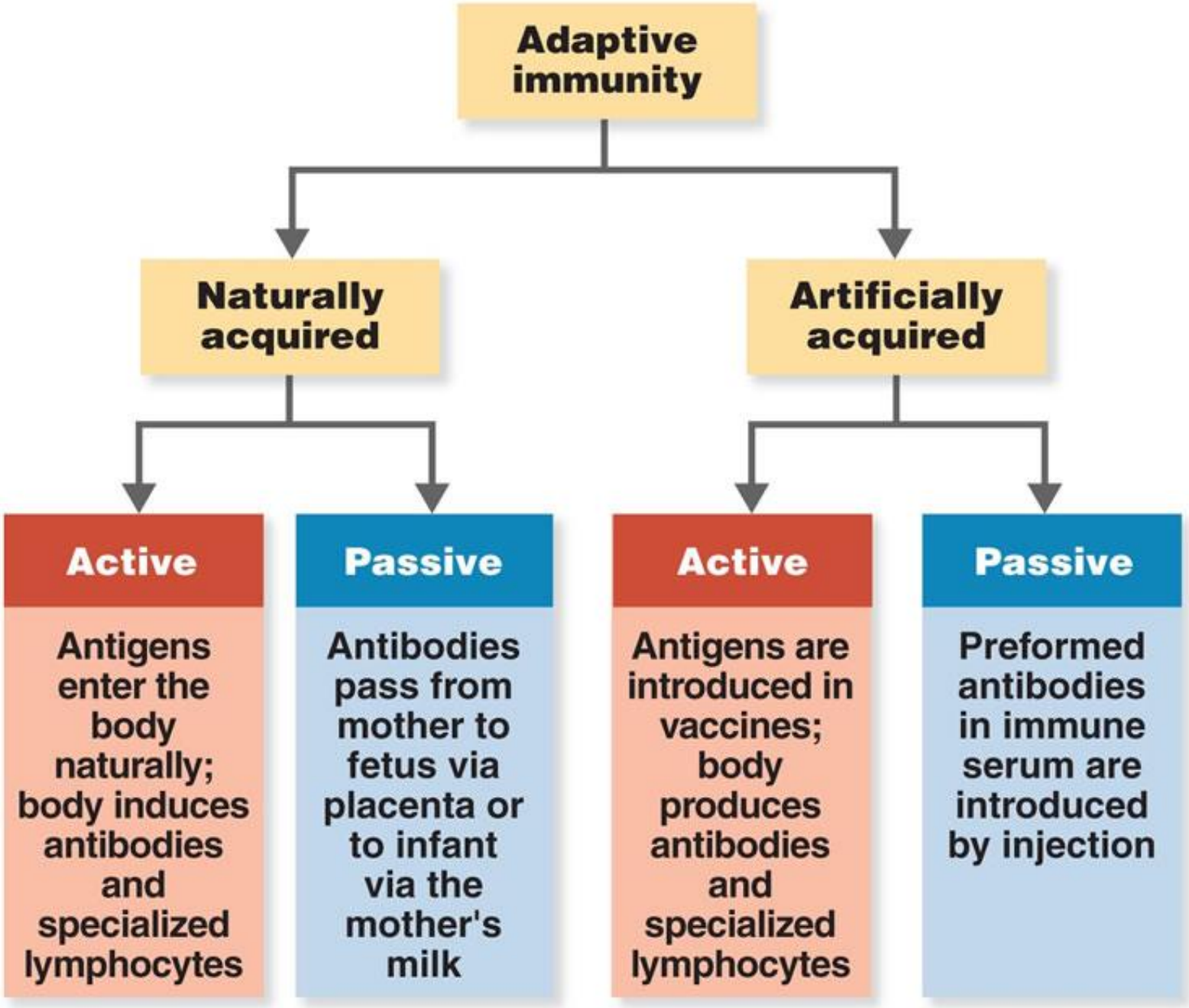
- are effective or on the immune system, or through the immune system, or the mechanism their actions are based on immunological principles
- have a complex composition, differ in nature, methods of production and use, to the left destination
- the active principle are antigens or antibodies, or microbial cells and their derivatives, or biologically active substances such as immunocytokines, immunocompetent cells and other immunoreagents

IMMUNOBIOLOGICAL DRUGS

- in addition to the active principle can include stabilizers, adjuvants, preservatives and other substances that improve its quality (vitamins, adaptogens)
- can be administered parenterally, orally, aerosolized or otherwise, so they are given the appropriate dosage form: sterile solutions and suspensions or lyophilized soluble powders for injection, tablets, aerosols, etc.
- for each drug there are strictly regulated dosages and regimens, indications and contraindications, as well as side effects

TYPES OF IMMUNOBIOLOGICAL DRUGS

1. **Preventive and medical drugs of a microbic origin** (for example, vaccines, bacteriophages, eubiotik, anatoxins)
2. **Medical immune drugs** (for example, Ig, cytokines)
3. **Diagnostic immune drugs** (for example, antiserums), and also diagnostic bacteriophages and allergens
4. **Immunomodulators** (various synthetic drugs, biostimulators of a natural origin)
5. **Adaptogens** are complex chemical substances of the vegetable, or other origin, possessing a wide range of biological including the effect on the immune system (tissue lysates, lipids, polysaccharides, vitamins, microelements, etc.).



ARTIFICIALLY ACQUIRED IMMUNITY

Artificially acquired immunity is the immunity obtained through the administration of a vaccine or immune serum.

1. Artificially acquired active immunity - the antigen is introduced into the vaccine (immunization), the body generates an immune response to the antigen. Immunity can be lifelong (oral polio vaccine) or temporary (tetanus).
2. Artificially acquired passive immunity: ready antibodies (antisera) are injected into the body. Immune serum of horses or rabbits with snake bites. Immunity is short-lived, determined by the half-life of IgG (three weeks). The human immune system does not respond to the antigen.

VACCINES

- are preparations used to create active artificial immunity against certain pathogens and their toxins
- are used mainly for prevention, but are sometimes used to treat infectious diseases
- are obtained from bacteria, viruses, fungi, protozoa, and also from products of their vital activity

ACTIVE PRINCIPLE OF VACCINE

- live or inactivated microorganisms (bacteria, viruses)
- antigens possessing pronounced immunogenic properties, so-called protective antigens
- the products of vital activity of microorganisms (toxins)
- antigens obtained by chemical synthesis of antigens obtained with using methods of genetic engineering.

TYPES OF VACCINES ACCORDING ANTIGEN TYPES

- monovaccines containing the antigen of a single serovar
- polivaccines, containing antigens of several serovars
- complex, combined or associated vaccines that contain antigens of several types of microorganisms, or one and the other the same species, but in different versions (for example, corpuscular and molecular antigens)

TYPES OF VACCINES ACCORDING ITS NATURE AND WAY OF OBTAINING

- Live
- Inactivated
- Recombinant

REQUIREMENTS FOR VACCINES

- cause the formation of a lasting and, as far as possible, long-term immunity
- be absolutely safe for the body
- have low reactogenicity
- no pyrogenicity
- do not cause undesirable side reactions
- be stable when stored

LIVE VACCINES

1. Attenuated: the active principle – strains of pathogenic microorganisms (bacteria, viruses) which were weakened by one way or another, have lost virulence, but have retained specific antigenicity

LIVE VACCINES

2. Divergent: the active principle – non-pathogenic strains of microorganisms having common protective antigens with pathogens for human infectious agents of infectious diseases (vaccine against human smallpox - cow cowpox vaccine, BCG vaccine - bovine mycobacteria are used)

LIVE VACCINES

3. Recombinant non-pathogenic for human recombinant strains carrying the genes of protective antigens of pathogenic microbes and capable of multiplying in the human body, synthesizing a specific antigen and creating immunity to the pathogen

INACTIVATED (NON-LIVE) VACCINES

1. Corpuscular:

- whole cell - the active ingredient is killed by chemical or by the physical method of culture of pathogenic bacteria
- whole-virion - the active principle is killed by chemical or the physical method of culture of pathogenic viruses
- subunit:

  a) *subcellular* - the active principle are pathogens derived from pathogenic bacteria contain, in their composition protective antigens

  b) *subvirion* - the active principle are complexes extracted from pathogenic viruses contain, in their composition protective antigens

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INACTIVATED (NON-LIVE) VACCINES

2. **Molecular – antigen is in molecular form or fragments of its molecules, which determine the specificity of antigenicity:**

- biosynthetically natural – anatoxins – non-toxic derivatives of toxins, preserving specific antigenicity and immunogenicity (diphtheria, tetanus, botulism, gas gangrene)
- genetically engineered biosynthetic - production of recombinant strains capable of synthesizing molecules of antigens that are not characteristic of them (eg, it is possible to obtain antigens of HIV, viral hepatitis, tularemy, brucellosis, syphilis, etc.)
- chemically synthesized - antigen in molecular form or its determinants are obtained by chemical synthesis, after decoding it structure

ANATOXINS

- Anatoxins (toxois) are bacterial exotoxins that have lost their toxic, but retained antigenic and immunogenic properties

PRODUCTION OF ANATOXINS

1. Exotoxin synthesis by bacteria and removal of the microbial bodies by filtration.
2. The preparation of the native toxoid is carried out according to the Ramon scheme: 0.3-1.4% formalin is added to the filtrate and kept in a thermostat at 37-40^{0}C for 4 weeks until the toxic properties completely disappear. The native toxoid is tested for sterility, harmlessness and immunogenicity.
3. Purification and concentration of the native toxoid.
4. Adsorption of anatoxin on adjuvants, mineral sorbents.
5. Determination of antigenic activity of anatoxin.
6. Determination of the immunogenic properties of an anatoxin by immunizing animals and expressed in immunizing units.

UNITS OF ANATOXIN ACTIVITY

- international unit IU / ml: a unit for measuring the dose of a substance based on its biological activity (is used for specific (immunogenic) activity of anatoxins in the composition of adsorbed vaccines)

UNITS OF ANATOXIN ACTIVITY

- units of flocculation Lf:

  Titration of toxoids in a flocculation reaction (according to Ramon's method) is performed using standard flocculating antitoxic serum, in which the amount of International Antitoxic Units (IU) is known in 1 ml. One antigenic unit of an anatoxin is designated Limes flocculationis (Lf is the flocculation threshold); this is the amount of anatoxin, which is completely associated with one antitoxic unit of the antitoxin.

  Flocculation is the type of coagulation, in which fine particles, suspended in a liquid or gaseous medium, form loose flocculent clusters, so-called, floccula.

UNITS OF ANATOXIN ACTIVITY

- units of binding UB / ml:

  The amount of anatoxin that binds 1 IU of the corresponding antitoxin is taken as 1 unit of binding (UB). The specific activity of anatoxins determined in the antitoxin binding reaction is expressed in UB / ml.

ASSOCIATED VACCINES (LIVE + INACTIVE)

- polyvaccines contain homogeneous antigens (poliomyelitis – types I, II, III; polyanatoxins)
- combined vaccines consist of dissimilar antigens (DTP vaccine protects against 3 infectious diseases, namely diphtheria, tetanus and pertussis)

SERUM IMMUNE PREPARATIONS

1. Therapeutic and preventive sera:

- Immune sera and Ig
- active principles are specific antibodies
- provide passive immunity to infectious agents (antibacterial, antiviral and antifungal)
- are usually administered parenterally
- while the state of immunity develops rapidly, but does not last long (within 2-6 weeks)

SERUM IMMUNE PREPARATIONS

2. Diagnostic sera:

- Immune sera and Ig
- active principles are specific antibodies
- can have agglutinating, precipitating, complement-binding, neutralizing, and other effects

SERUM IMMUNE PREPARATIONS

- are obtained from the blood of artificially immunized animals and human donors (peripheral, placental and abortion blood is used for this purpose)
- to obtain high titers horses and rabbits are immunized with fractional administration of corresponding antigens at high doses

SERUM IMMUNE PREPARATIONS

- Serum titre is the minimum serum concentration (greatest dilution) containing antibodies, sufficient to neutralize the virus, to prevent its cytopathic effect; is usually determined by the plaque method
- The titre of the diagnostic serum is considered to be its greatest dilution, which results in an agglutination / precipitation / hemolysis reaction with the corresponding antigen

SERUM IMMUNE PREPARATIONS

- heterologous (foreign) sera are made from animal blood contain heterologous antibodies (administered to a person under precautionary measures – preliminary sensitivity skin test, Bezredki method, use of desensitizing agents)

  horse serum against botulism, gas gangrene, diphtheria, tetanus

- homologous sera are made from the blood of immunized donors contain homologous antibodies; are devoid of many side effects of heterologous sera

  prevention and treatment of viral hepatitis, measles, for the treatment of botulism, tetanus, staphylococcal infections, tick-borne encephalitis, hepatitis B

  After the introduction of heterologous sera, the immunity state lasts 2-3 weeks, the effect of homologous Ab persists for 4-6 weeks.

BEZREDKI METHOD

- is the method of desensitization, which is necessarily used to prevent anaphylactic reactions
- injecting antibacterial and antitoxic therapeutic and prophylactic sera: first 0.1-0.3 ml of serum is injected subcutaneously, and after 1-2 hours the rest of the dose

SERUM IMMUNE PREPARATIONS

- are clear liquids, pale yellow in color
- in ampoules
- are administered subcutaneously, intramuscularly, less commonly - intravenously or into the spinal canal
- after production pass state control in accordance with the instructions of the Ministry of Health – monitoring for:
  - sterility
  - harmlessness
  - amount of protein
  - transparency and activity (antibody titer)

From the sera, immunoglobulins are obtained by water-alcohol extraction (purification). Immunoglobulins are purified and concentrated immune sera.

IMMUNOGLOBULINS

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horse immunoglobulins against rabies (rabies anti-rabies), tick-borne encephalitis, Ebola fever, Japanese encephalitis, anthrax; immunoglobulins from blood serum of oxen for the treatment of leptospirosis

IMMUNOMODULATORS

Immunomodulators are used for immunocorrection, treatment and prevention of infectious and non-infectious diseases, immunodeficiencies:

- exogenous immunomodulators – substances of different chemical origin which have nonspecific activating or suppressive effect on the immune system, but being foreign to the organism (adjuvants, some antibiotics, antimetabolites, hormones)
- endogenous immunomodulators – a large group of oligosaccharides synthesized by the body itself, its immunocompetent and other cells, and capable of activating the immune system by enhancing the proliferation and function of immunomethient accessory cells (interleukins, interferons, thymus peptides, myelopeptides, etc.)