Lecture IV

Fundamentals of antimicrobial therapy. Chemotherapeutic agents. Antibiotics.

Basics of chemical therapy

- Treatment of infectious diseases with chemotherapeutic drugs is called chemotherapy.
- The effect of these drugs is not against the individual symptoms of the disease, but only against the etiological factor that causes it, so they are called etiotropic drugs.

Paul Erlich is the founder of chemotherapy

- **Receptor theory of P.Erlich. In 1885, P.Erlich determined that the effect of chemicals on disease-causing microbes is due to the specific receptors in the latter.**
- **One of the main principles of chemical therapy was P.Erlich's idea of a "magic bullet". It consisted of the principle of "destroying the living in the living," that is, not harming the host organism while destroying the agent.**
- **Chemical therapeutic index is a measure of the ratio of the minimum therapeutic dose that a drug can kill to the maximum dose that the body can resist.**

Chemotherapy.

Chemotherapy is the treatment of people with infectious diseases using chemicals that act selectively on the pathogen in the human body without harming the patient's cells and organs.

Formation of Chemotherapy.

- 1885 - P. Ehrlich formulated the main idea of chemotherapy - the selectivity of the action of chemicals.
- 1886 - synthesis by P. Ehrlich and at the Pasteur Institute of antitrypanosomal drugs (trypan red and trypan blue)
- 1887-1888 - P. Ehrlich formulated the basic requirements for chemotherapeutic drugs and introduced the concept of a chemotherapeutic index

Basic requirements for chemotherapeutic drugs.

- Action specificity
- Maximum therapeutic activity
- Minimal toxicity to the body

Chemotherapy Index = Minimum therapeutic dose / Maximum Tolerated Dose

- Index must not be greater than 1

Chemotherapy Development

- 1909-1910 - the synthesis of P. Ehrlich antispirochete drugs (salvarsan and neosarvarsan)
- 1920-1930 - synthesis in Germany and France of antimalarial drugs (plasmoquine)
- 1932 - synthesis in Germany by G. Domagk of an antibacterial drug - chrysoidine sulfamide (sulfanilamide)

The range of action of chemotherapeutic drugs.

The spectrum of action distinguishes:

1. Acting on cell forms (antibacterial, antifungal, antiprotozoal)

- antibacterial can be wide and narrow spectrum of action
- 2. Acting on non-cellular forms (antiviral)
- 3. Suppressing tumor growth (antitumor)

Type of action of antimicrobial chemotherapy drugs.

- Microbicidal (bactericidal, fungicidal, etc.) chemotherapeutic agents - causing the death of microbes due to irreversible damage;
- Microbostatic chemotherapy - inhibiting the growth and reproduction of microbes

The main groups of synthetic chemotherapeutic drugs.

- Sulfanilamides - the basis of the drug is a para-amino group, which acts as an analog or antagonist of para-aminobenzoic acid, necessary for the synthesis of folic acid (co-trimoxazole, or biseptol).
- Quinolones - nalidixic acid has a limited spectrum of action.
- Fluoroquinolones - bactericidal effect, a wide range, high activity (ciprofloxacin, norfloxacin).
- Nitroimidazoles are bactericidal, especially active against anaerobic bacteria, as well as protozoa (metronidazole, trichopolum).
- Imidazoles - antifungal drugs that inhibit the synthesis of CPM (clotrimazole)
- Nitrofurans - used as uroseptics (furozalidone, furadonin, furagin)

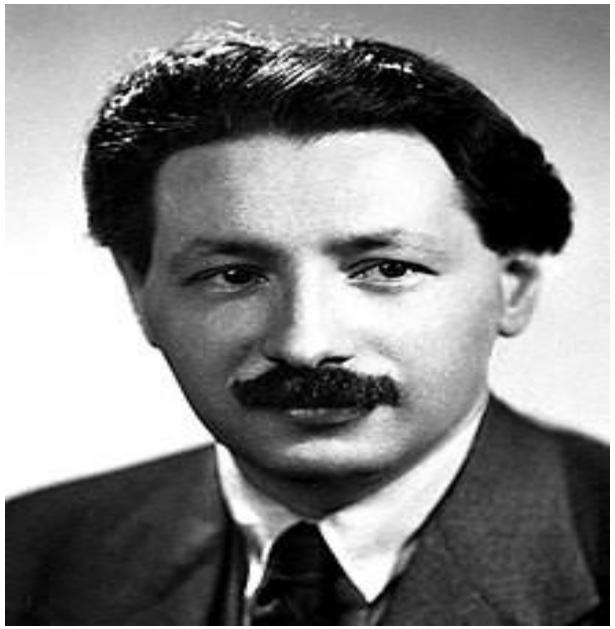
  Oxyquinolines - nitroxoline
-

Additional groups of synthetic chemotherapeutic drugs.

- Arsenic preparations - novarsenol, osarsol, etc. Bismuth
- preparations - bismoverol, xoroform, etc. Antimony
- preparations - stibenil, syurmin, etc.
- Mercury preparations - salicylic, cyanide mercury, etc.
- Acridine preparations - rivanol, flavicide, etc.
- Anti-TB drugs – PASK, ethambutol, phtivazide, etc.
- Antimalarial drugs - Akrikhin, chloroquine, etc.
- Antineoplastic drugs - sarcolysin, vinblastine, dopan, etc.

The idea of antibiotic therapy.

- 1871-1872 - V. Manassein and A. Polotebnov described the healing properties of green mold
- 1884 - L. Pasteur first observed microbial antagonism
- 1894 - I. Mechnikov discovered antagonism of lactic and putrefactive bacteria



Chain Ernst Boris (1906-1976)
English biochemical

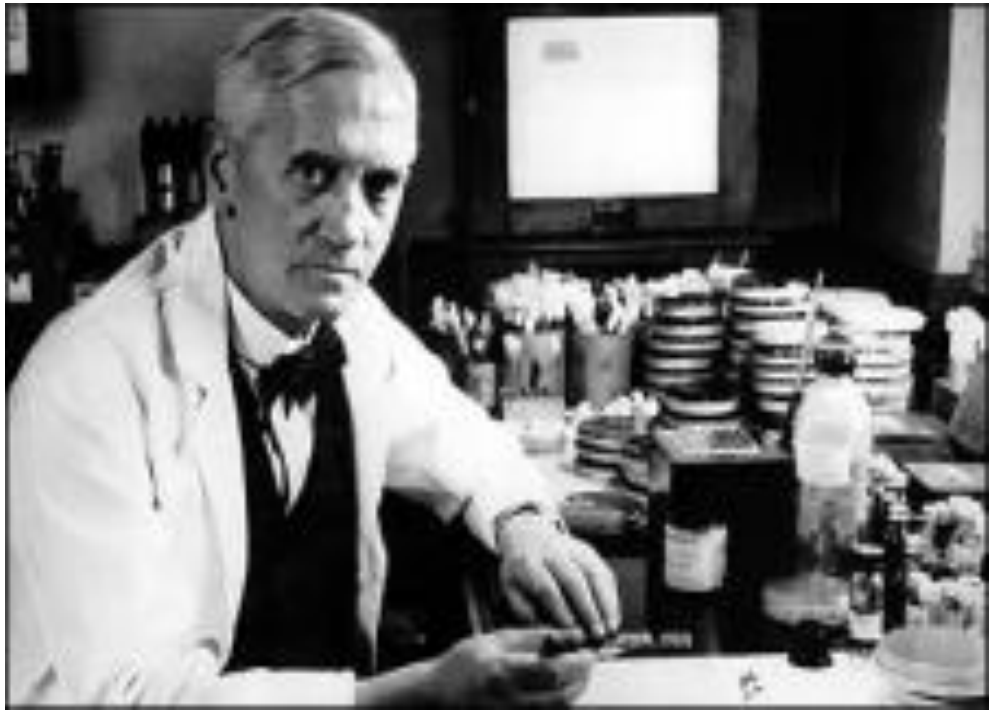
Flory Howard Wolter
(1898-1968) Pathologist
Microbiologist

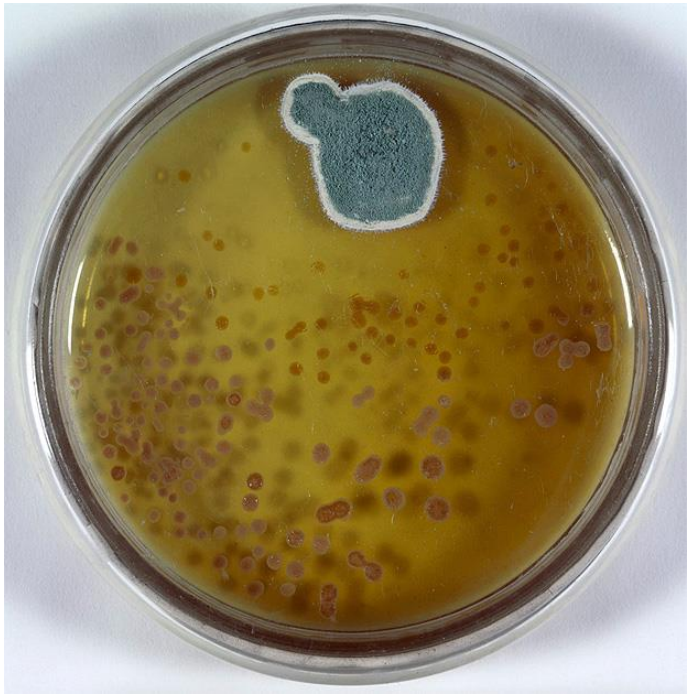
- In 1938 discovered penicillin in injection form.
- Became Nobel Laureate on physiology and medicine in 1945 along with Alexander Fleming for discovery and synthesis of penicillin.

History of antibiotics discovery.

- 1920-1929 - A. Fleming - the study of the
  - antibacterial properties of green mold and the
- discovery of penicillin
  - 1940 - G. Flory, E. Cheyne and N. Heatley -
- received purified penicillin
  - 1942 - S. Waxman coined the term antibiotic
- (Greek anti-against, bios-life)
  - 1945 - A. Fleming, G. Flory and E. Cheyne - Nobel Prize for the discovery of penicillin

Discovery of antibiotics





In 1929, when the English microbiologist Alexander Fleming was conducting an experiment, he discovered a culture of the fungus (Penicillium notatum) in the culture of the fungus (Penicillium notatum), which had grown accidentally on the surface of the nutrient medium in Petri dishes.

Antimicrobial chemotherapy.

- Antibiotics (act on the cellular forms of microbes and tumors);
- Synthetic chemotherapeutic agents (act on cellular and non-cellular forms of microbes, as well as on tumors).

Chemical therapeutic drugs

- Thousands of chemical compounds with antimicrobial activity are now known, only some of which are used as chemical therapeutic agents.
- The groups of microorganisms that can be affected by chemical therapeutic drugs determine their spectrum of activity.
- Depending on the effect of the microbe, antibacterial, antifungal, antimicrobial, antiviral, etc. antimicrobial drugs are distinguished.

Classification of antimicrobial chemotherapeutic agents according to the object of action.

- Antibacterial (most antibiotics, fluoroquinolones, nitroimidazoles, nitrofurans)
- Antifungal (nystatin, amphoterricin B, imidazoles)
- Antiparasitic (doxycycline, clindamycin, nitroimidazoles)
- Antiviral (reverse transcriptase inhibitors, protease inhibitors, fusion inhibitors, etc.
- Antineoplastic (rubomycin, olivomycin)

Antibiotics

- The most common form of antagonism is the secretion of substances by microorganisms called antibiotics (Greek, antibodies, bios-life).
- These substances stop the development of other microorganisms in very small concentrations.
- The term "antibiotic" was first coined in 1942 by S.Waxman. According to him, antibiotics are substances secreted by various microorganisms and stop the growth of certain bacteria or cause their destruction.

Classification of antibiotics by source.

- Microbial origin

 - from actinomycetes (streptomycin, tetracycline)

 - from bacteria (polymyxin, gramicidin, etc.)

- from mushrooms (penicillin, cephalosporins, etc.)

- Plant origin (volatile)
- Animal origin (interferon, ecmoline)

Classification of antibiotics by source.

- Biological synthesis (penicillin)
- Biosynthesis with subsequent chemical modifications (semi-synthetic antibiotics - benzylpenicillin, ampicillin, oxacillin)
- Chemical synthesis (synthetic analogues of natural antibiotics - chloramphenicol bicillin)

Classification of antibiotics by spectrum of activity and type of action.

- Broad spectrum (aminoglycosides and tetracyclines)
- Narrow Spectrum (Polymyxin)

•Bactericidal (fungicidal) –penicillin, cephalosporins
•Bacteriostatic (fungistatic) – tetracyclines, chloramphenicol

Classification of antibiotics by chemical structure (1)

Beta-lactams - the basis of the molecule is the beta-lactam ring They act bactericidal. These include:

- penicillins: natural - benzylpenicillin, depot preparations - bicillin, acid-resistant - phenoxymethylpenicillin, penicillin-resistant - a narrow spectrum (methicillin and oxacillin) and a wide range (ampicillin and amoxicillin), which are antisine-free, combined with bicenitazin, biceniticillin, biceniticin, (amoxicillin + clavulanic acid, amoxicillin + sulbactam).
- cephalosporins - have a wide range, but are more active against gram-negative bacteria. There are 4 generations: 1st — more active against gram-positive bacteria and sensitive to beta-lactamases (cefazolin), 2nd — more active against gram-negative bacteria and more resistant to the enzyme (cefuroxime), 3rd — more active against gram-negative bacteria and highly resistant to the enzyme (cefotaxime), 4-y - act on gram-positive bacteria, some gram-negative and Pseudomonas aeruginosa, are resistant to beta-lactamases (cefipim).
- carbopenems - have the widest spectrum of action and are resistant to beta-lactamases
- monobactams - are active against gram-negative bacteria, including Pseudomonas aeruginosa, and are resistant to beta-lactamases (aztreons).

Classification of antibiotics by chemical structure (2)

- Glycopeptides are large molecules that do not pass

  - through the pores of gram-negative bacteria, therefore they have a narrow spectrum of action (vancomycin)
- • Aminoglycosides - the molecule contains sugars, has a wide spectrum, bactericides (streptomycin, gentamicin)
- • Tetracyclines - are composed of 4 cyclic compounds, a wide spectrum (tetracycline, dioxicycline)
- • Macrolides and azolides - a family of large macrocyclic molecules with a wide spectrum of action, bacteriostatics (erythromycin, azithromycin, clarithromycin)
- • Lincosamides - bacteriostatic agents similar to macrolides are effective against anaerobes (lincomycin, clindamycin).

Classification of antibiotics by chemical structure (3)

- Chloramphenicol - have a nitrobenzene core, which gives them toxicity, bacteriostats (chloramphenicol / chloramphenicol).
- Rifampicins are broad-spectrum bactericides that are effective against mycobacterium tuberculosis (rifampicin)
- Polypeptides - narrow-spectrum bactericidal antibiotics, act only against gram-negative bacteria, toxic, applied externally (polymyxin)
- Polyenes are highly toxic antifungal drugs that are often used locally (nystatin, amphoterricin B).
- Other antibiotics (fusidic acid).

Cephalosporin's.

Cephalosporin antibiotics

1st Generation	2nd Generation	3rd Generation	4th Generation
• Cefadroxil • Cefazedone • Cefazolin • Cephalexin • Cephalothin • Cephradine • Cephaloridine • Cephapirin etc.	• Cefaclor • Cefamandole • Cefoxitin • Cefuroxime • Ceforanid • Cefonicid etc.	• cefixime • Cefoperazone • cefotaxime • cefpiramide • cefpodoxime • Ceftibuten • ceftizoxime • ceftriaxone etc.	• Cefepime • cefluprenam • Cefozopran • cefpirome • cefquinome etc.
Good against **Gram +**, Moderate against **Gram -**	**Good** against **Gram -**, Moderate against **Gram +**	**Good** against **Gram -**, Weak against **Gram +**	**Good** against **Gram -**, Extended activity against **Gram +**

Classification of antibiotics

According to the chemical composition:

- **beta-lactam antibiotics (penicillins, cephalosporins, carbapenems, monobactams)**
- **macrolides (erythromycin, spiramycin, clarithromycin, etc.)**
- **azalides (azithromycin)**
- **tetracyclines (tetracycline, doxycycline)**
- **aminoglycosides (streptomycin, kanamycin, gentamicin)**
- **levomisetin (chloramphenicol)**
- **glycopeptides (vancomycin, etc.)**
- **glycopeptides (vancomycin, etc.)**
- **rifamycins (rifampicin)**
- **cyclic polypeptides (polymyxins, basitrasins)**
- **polyenes (nystatin, levorin, amphotericin B, etc.)**

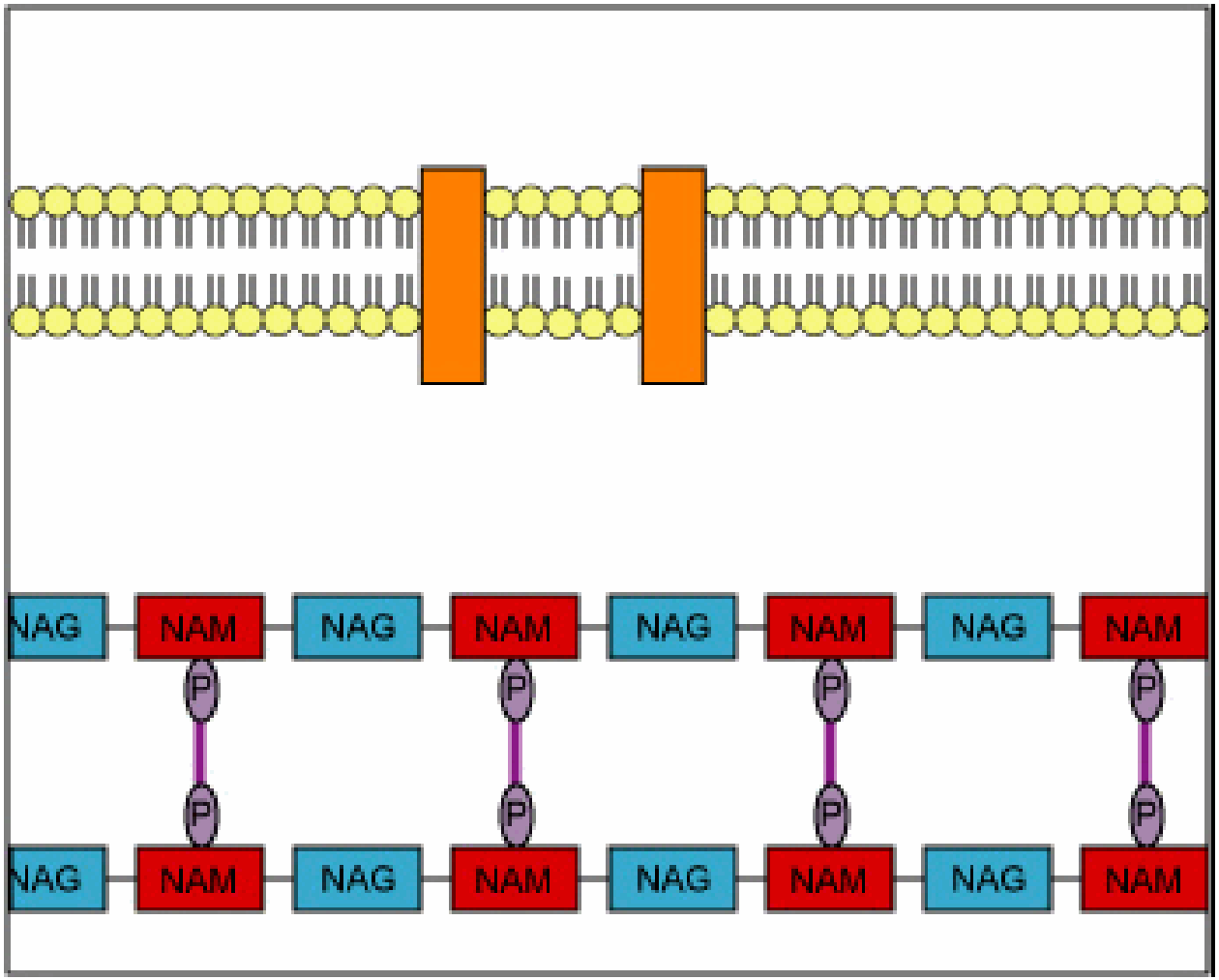
The main groups of synthetic chemical-therapeutic drugs

- Sulfanilamides (streptocide, sulfadimesine, sulfadimethoxine, etc.)
- Antimetabolites - nicotinic acid hydrazides (isoniazid, ftivazid, tubazid, etc.)
- Preparations from the quinolone group - nalidixic acid (nevigramon), ofloxacin, ciprofloxacin, norfloxacin, etc.
- Nitroimidazole derivatives (metronidazole, ornidazole, etc.)
- Derivatives of 8-oxyquinoline (5-nitroxoline, quinazole, intesopan, etc.)
- Nitrofuran derivatives (furacilin, furazolidone, furagin, etc.)
- Imidazole derivatives (ketoconazole, miconazole, clotrimazole, etc.)
- Triazole derivatives (fluconazole)

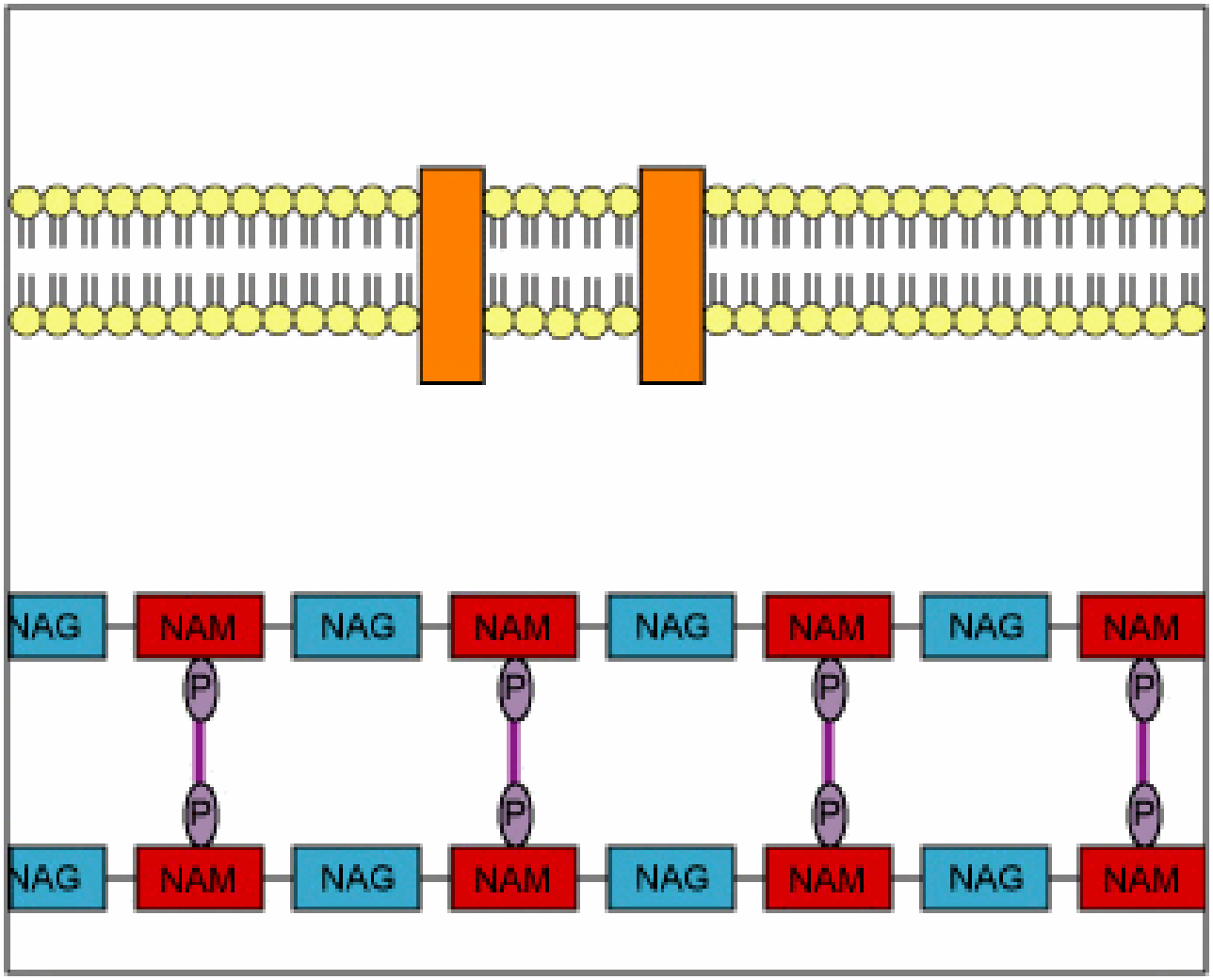
Mechanisms of antimicrobial action of antibiotics

- **Inhibitors of cell wall synthesis (antipeptidoglycan antibiotics). Beta-lactam antibiotics (penicillins and cephalosporins), glycopeptide antibiotics (vancomycin and teicoplanin)**
- **Inhibitors of protein synthesis (antiribosomal antibiotics) Aminoglycosides and tetracyclines with 30S-subcomponents of ribosomes, macrolides, chloramphenicol in the macrolides, chloramphenicol and lincoids.**
- **Inhibitors of nucleic acid synthesis - rifamycins (rifampicin) bind to RNA polymerase and block the transcription process, ie the information stops the synthesis of RNA.**
- **Antibiotics that affect the permeability of the cytoplasmic membrane (membrane-anthropic antibiotics) - polypeptides (polymyxins), polyene antibiotics (nystatin, levorin, amorphous).**

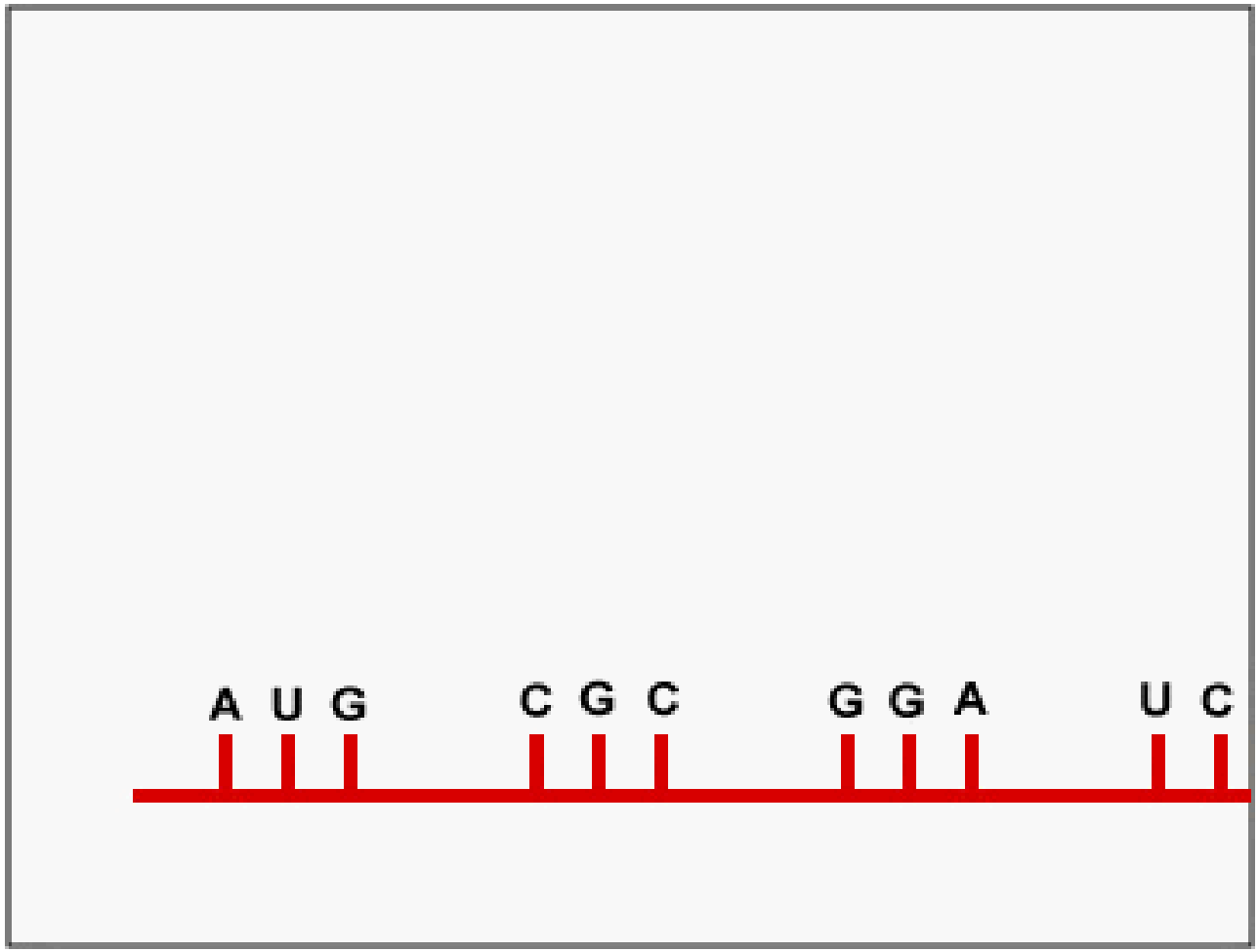
Synthesis of peptidoglycan in the cell wall



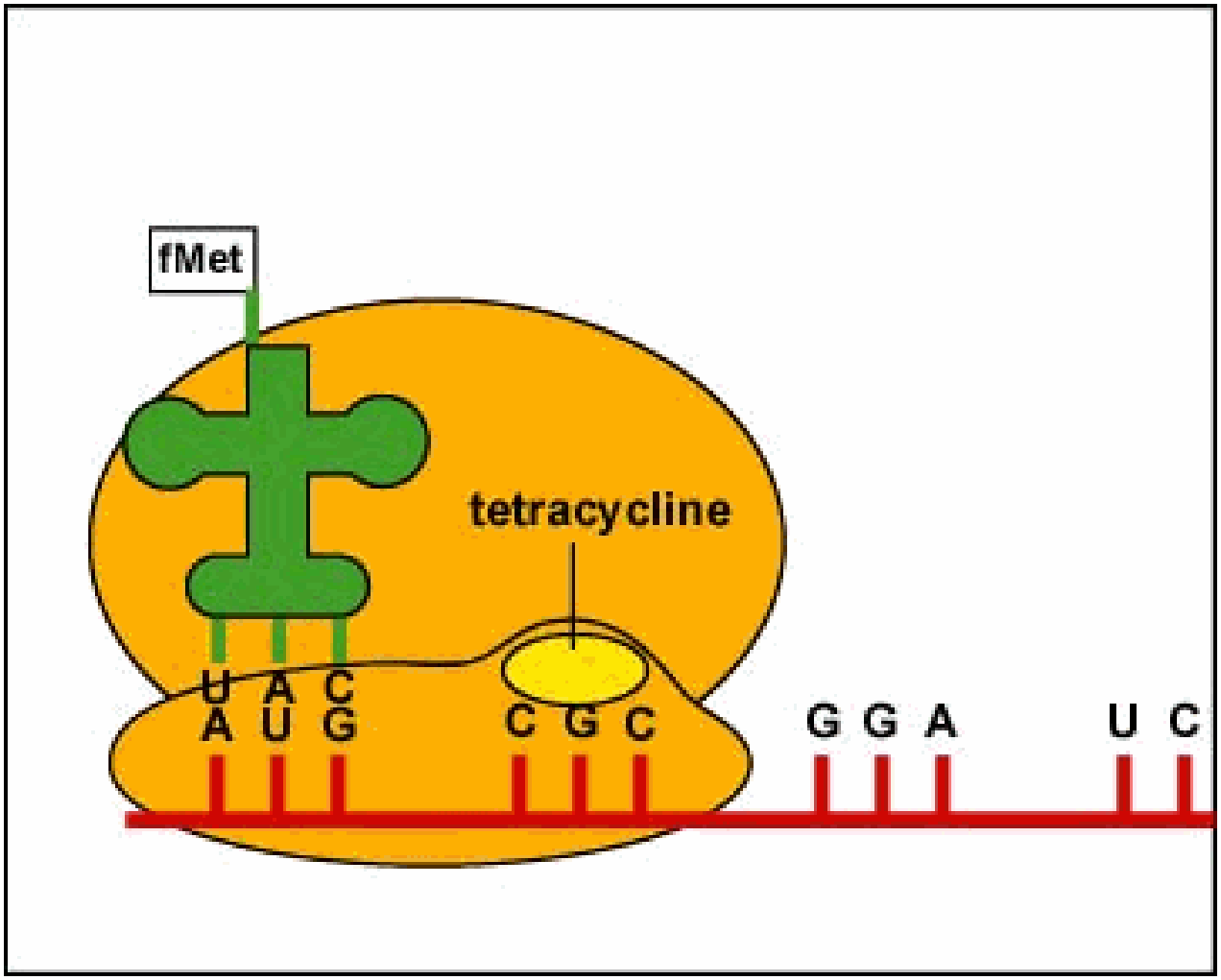
Inhibition of peptidoglycan synthesis in the cell wall with penicillin



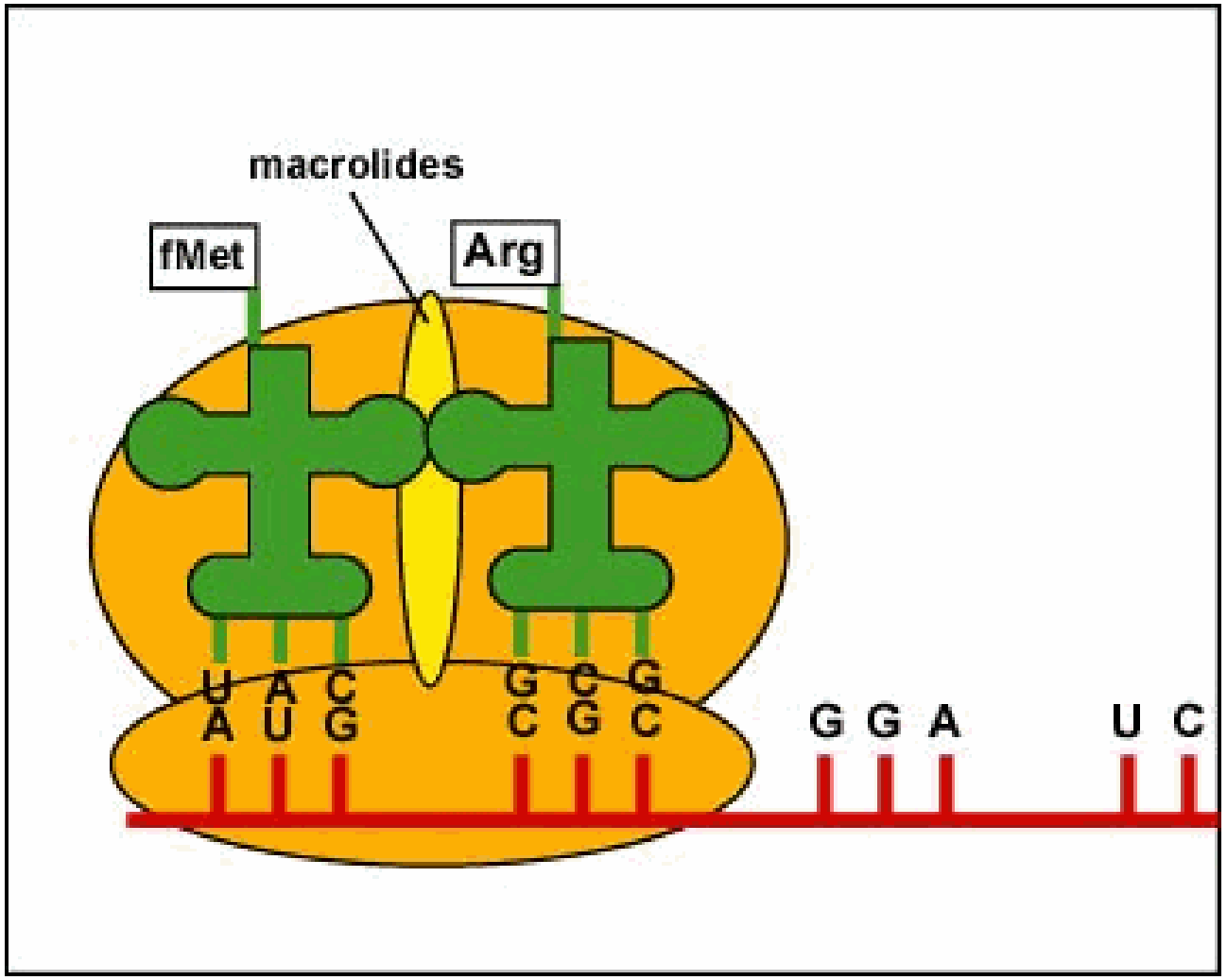
Aminoglycosides combine with 30S subcomponents of ribosomes to stop protein synthesis in bacterial cells



Tetracyclines combine with 30S subcomponents of ribosomes to stop protein synthesis in bacterial cells



Macrolides combine with 50S-subcomponents of ribosomes to stop protein synthesis in bacterial cells



The mechanism action of antimicrobial agents.

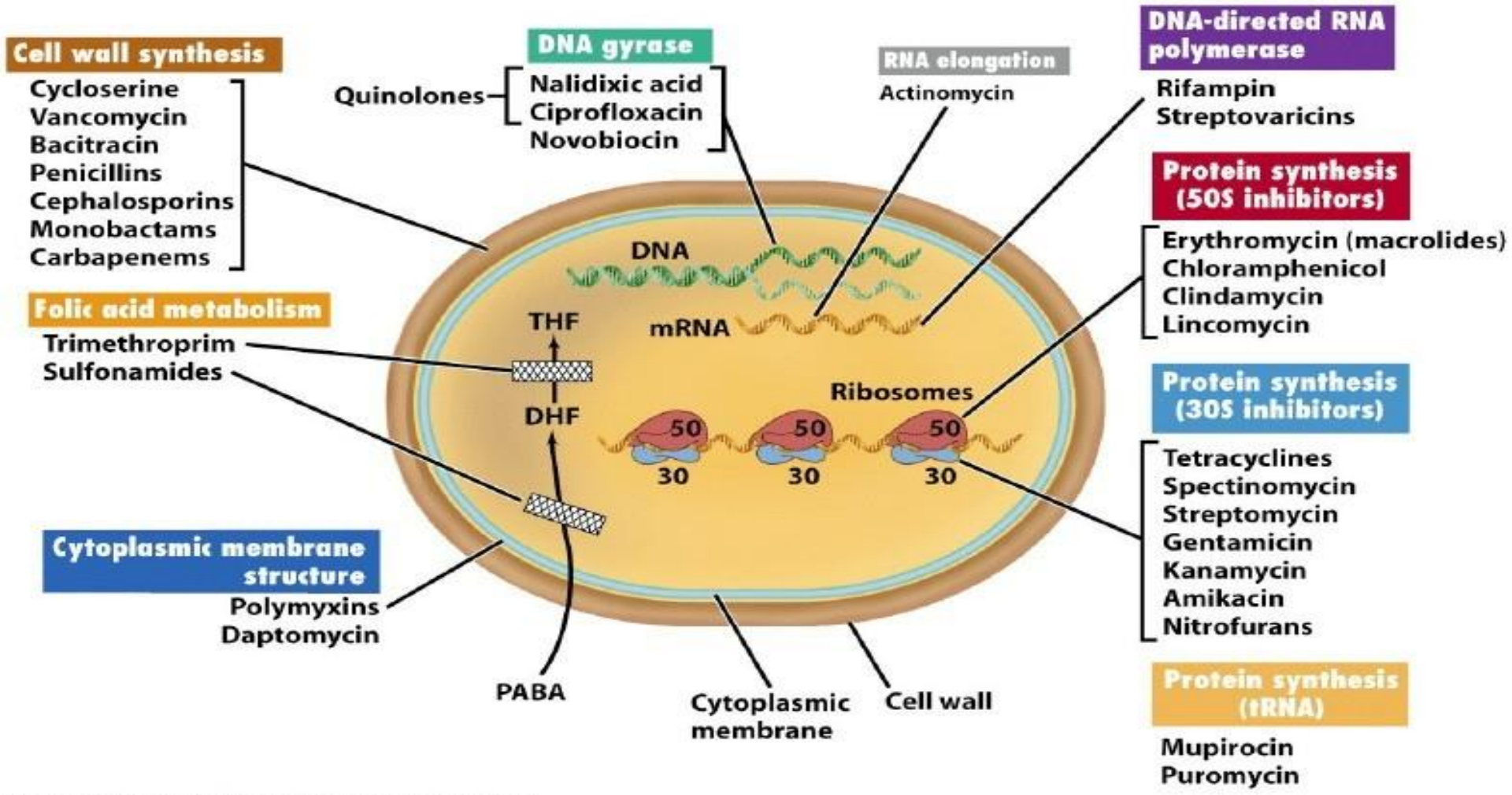


Figure 20-14 Brock Biology of Microorganisms 11/e

© 2006 Pearson Prentice Hall, Inc.

Obtaining of antibiotics

- During the cultivation of microorganisms, they are excreted in the nutrient medium and obtained by chemical separation from the nutrient medium.
- In some cases, antibiotics are obtained by semi-synthesis and synthesis. Thus, there are three main methods of obtaining antibiotics:
- Biosynthesis method
- Semi-synthesis method
- Method of chemical synthesis

Modification of the target of antimicrobial action

- Methylation of RNA (ribosomal RNA) in the 50S subcomponent of ribosomes is one of the main mechanisms of resistance to macrolides and linosamides.
- Metallization of the nucleotide of only two adenes prevents the combination of these antibiotics with the 50S-components. The synthesis of the enzyme that catalyzes this process - methylase - is encoded in the R-plasmid.

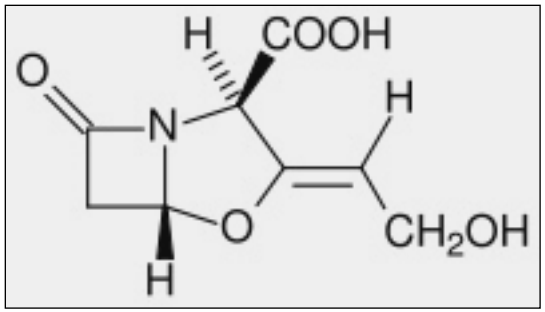
Inactivation of an antimicrobial agent

- It is one of the main mechanisms of drug resistance of microorganisms.
- Some bacteria have the ability to synthesize special enzymes that inactivate antibiotics.
- Beta-lactamase (penicillin), a beta-lactamase (penicillin) that breaks down the beta-lactam ring in penicillins and cephalosporins to form inactive compounds between these enzymes.
- Synthesis of beta-lactamases is encoded in R-plasmid.

Ways to prevent resistance to antibiotics

- Rational use of antimicrobials
- synthesis of new antibiotics
- Combination of some antibiotics with beta-lactamase enzyme inhibitors (sulbactam and clavulanic acid):

- The beta-lactam ring in these substances combines with beta-lactamases to neutralize them, thereby counteracting the effect of these enzymes on beta-lactam antibiotics.
- Preparations of ampicillin combined with sulbactam (ampicid, etc.) and amoxicillin with clavulanic acid (augmentin, amoxiclav, etc.) are widely used in medical practice.



Principles of rational antibiotic therapy.

- The microbiological principle is to establish the causative agent of the disease and determine its individual sensitivity to the antibiotic.
- Pharmacological principle - consider pharmacokinetics and pharmacodynamics.
- The clinical principle is to take into account the individual characteristics of the patient's condition.
- The epidemiological principle is to take into account the state of resistance of microbial strains circulating in a given region
- The pharmaceutical principle is to take into account the expiration date and follow the storage rules of the drug.

Complications during antimicrobial therapy.

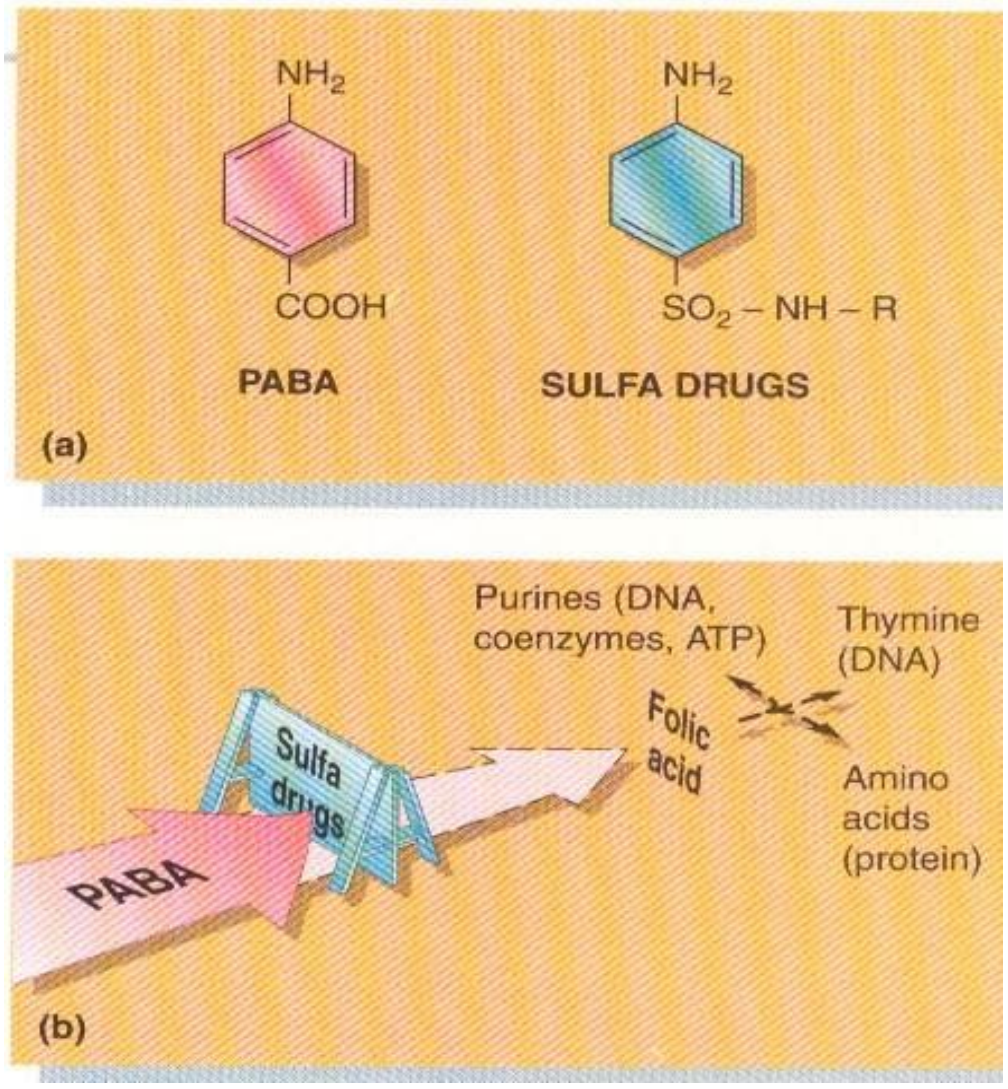
1. From the macroorganism:

- Toxic effect of drugs Dysbiosis (dysbiosis)
- Immune system dysfunctions (allergies, depression)
- Endotoxic shock
- Negative interactions when combining drugs.
-

2. On the part of microorganisms:

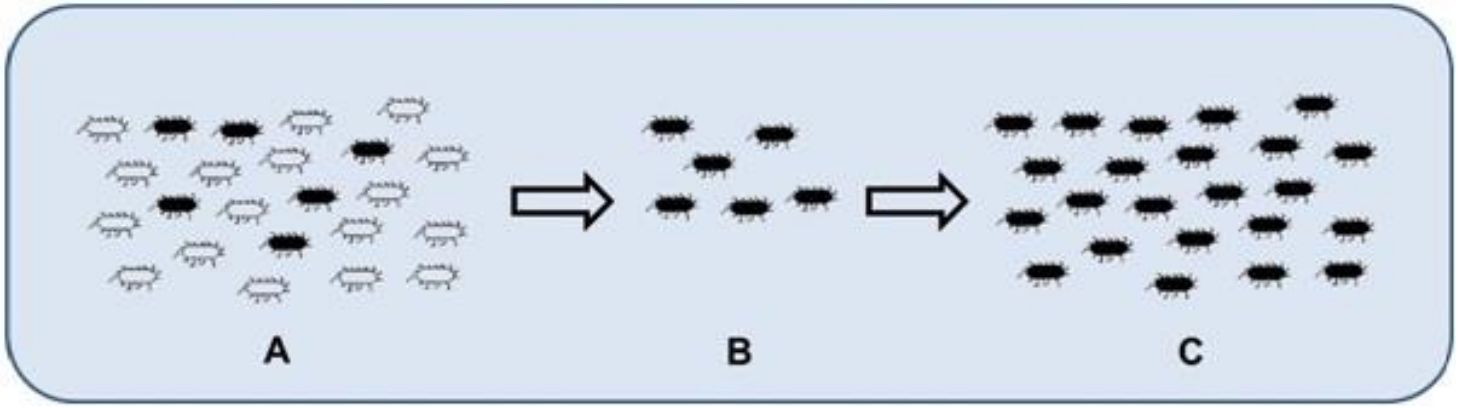
- The formation of L-forms and persistent forms of microbes The
- formation of antibiotic dependence
- The formation of drug resistance, including antibiotic resistance

The mechanism of action of sulfa drugs.



Genetic basis of antibiotic resistance

- Resistance to antibiotics is mainly provided by resistance genes (r-genes). Plasmids that have resistance genes are called R-plasmids, or R-factor. Resistance genes primarily encode the synthesis of enzymes (eg, beta-lactamase, etc.) that ensure the drug resistance of microorganisms.
- Antibiotics do not induce the formation of r-genes, but only cause the selection of microbial populations that possess these genes.



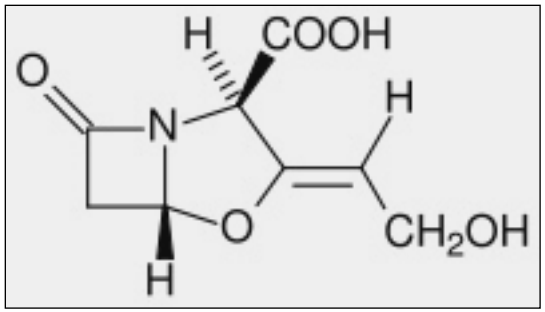
Genetic basis of antibiotic resistance

- Mutations in the microbial population also play a role in ensuring the resistance of microorganisms to antibiotics.
- For example, the persistence of some S. aureus strains to methylcellulose is due to gene mutations in them that result in penicillin binding proteins, which is unable to bind to beta-lactam antibiotics. For this reason, methicillin-resistant S. aureus (MRCA) strains are resistant to all beta-lactam antibiotics.

Ways to prevent resistance to antibiotics

- Rational use of antimicrobials
- synthesis of new antibiotics
- Combination of some antibiotics with beta-lactamase enzyme inhibitors (sulbactam and clavulanic acid):

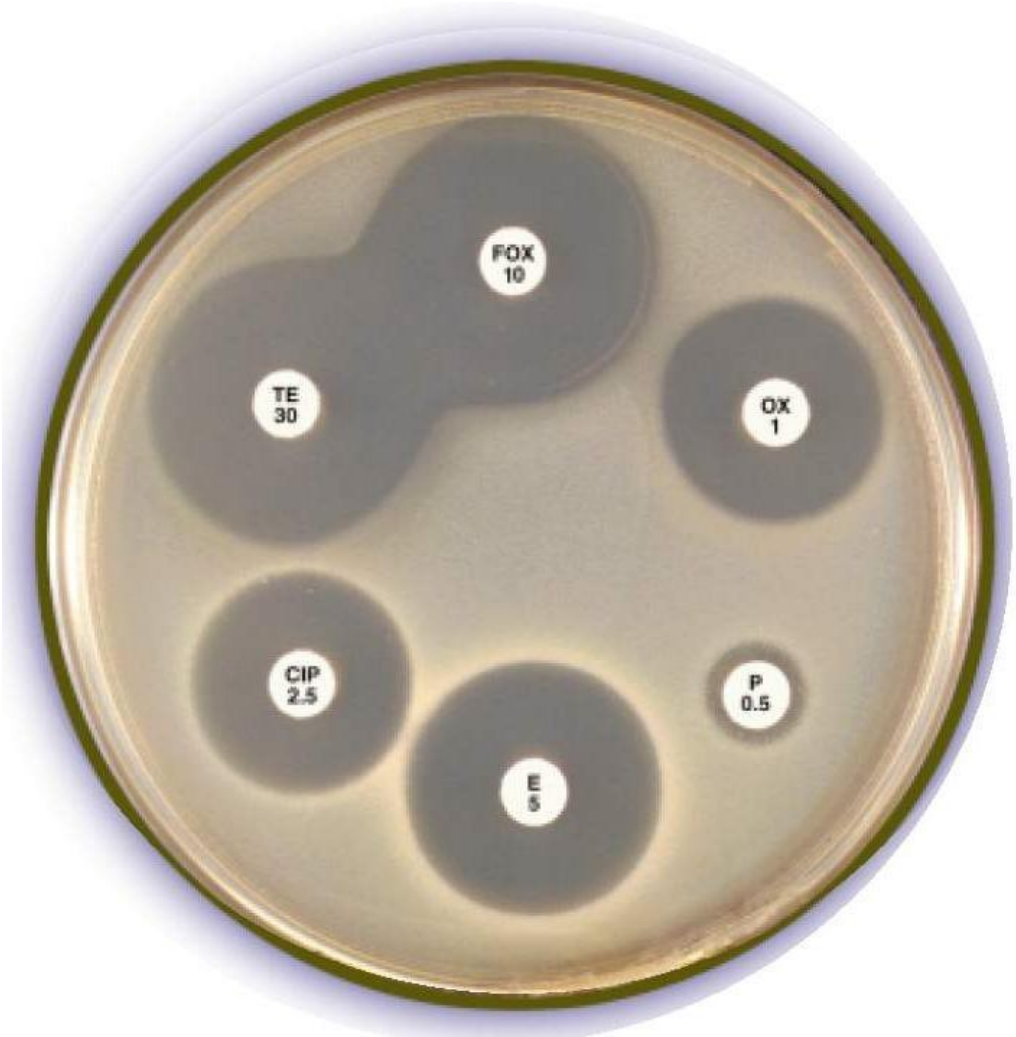
- The beta-lactam ring in these substances combines with beta-lactamases to neutralize them, thereby counteracting the effect of these enzymes on beta-lactam antibiotics.
- Preparations of ampicillin combined with sulbactam (ampicid, etc.) and amoxicillin with clavulanic acid (augmentin, amoxiclav, etc.) are widely used in medical practice.



Ways to prevent resistance to antibiotics

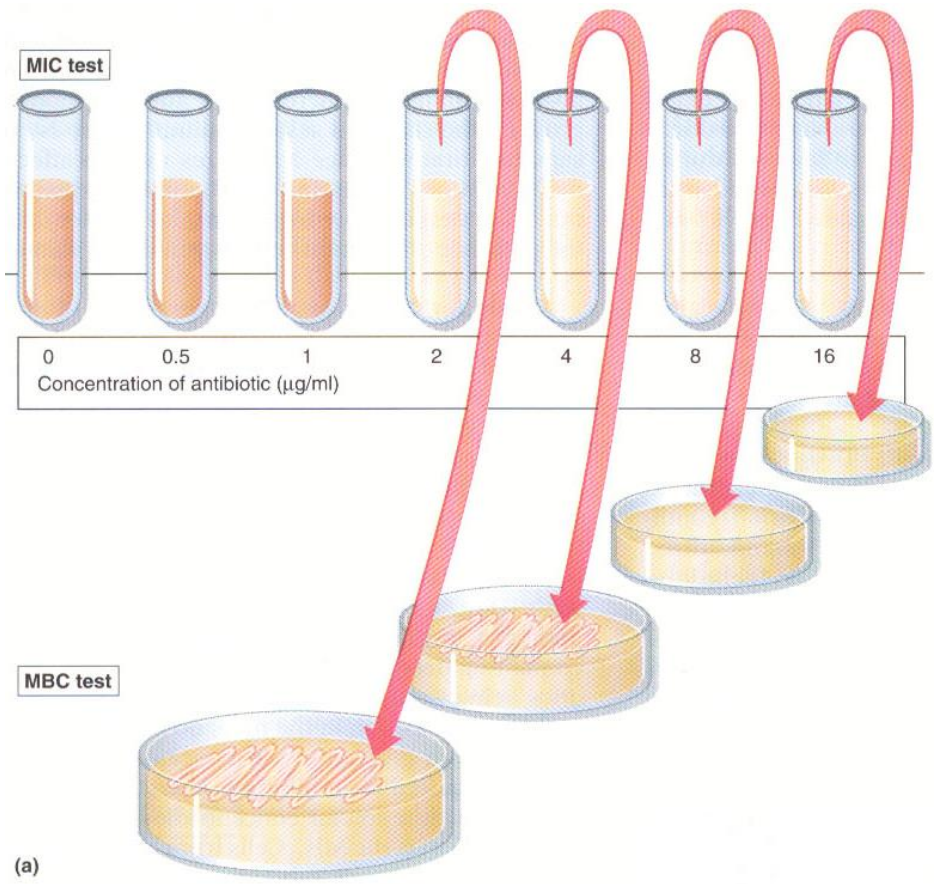
- One of the ways to prevent the resistance of microorganisms to antibiotics is to take into account the sensitivity to antibiotics during treatment.
- Qualitative and quantitative methods are used to determine the susceptibility of bacteria to antibiotics.
- Quality method. The disk-diffusion method (Kirby-Bauer method) is more widely used.
- The quantitative method allows to determine the minimum inhibition of antibiotics and bactericidal concentrations.

Disc-diffusion method



Determination of the minimum inhibitory concentration by the method of sequential dilution.

The principle of the method is based on the cessation of the growth of microorganisms in a nutrient medium to which certain concentrations of antibiotics are added.



Determination of minimum inhibitory concentration by agar diffusion method (E-test)

Complications that can occur under the influence of antibiotics and ways to prevent them

- **Hypersensitivity reactions - allergic reactions- consideration of hypersensitivity reactions**
- **Dysbiosis and dysbacteriosis**
- **Combination of antibiotics with antifungal drugs during long-term use- use of eubiotics**
- **representatives of normal microflora during long-term use**

Toxic effects

- consideration of contraindications and side effects

Antiviral drugs.

- Interferons
- Inductors of endogenous interforons
- Synthetic chemotherapeutic drugs
- Immunomodulators

- Interferon – related to major defending proteins of immune system. Discovered in 1957 by A.Aiseek and J. Lindemaan by studying interference of viruses (lat. Inter- between and ferens-carrier) phenomenon, when animals and cell culture infected by one virus, they become insensitive to other viruses. It became known that interference is due to creation of protein, consisting of defensive antiviral features. This protein was called interferon. In nowadays interferon is studied good enough, structure and features, it is widely used in medicine as preventive, healing and therapeutic agent.

Interferon represents itself the family of glycoprotein proteins with the molecular mass from 15 till 70 kda, which synthesize with the cells of immune system and connecting tissues.

Depending on which cells interferon synthesize, they create 3 main types: alfa, beta, y-interferons.

Types of interferons.

There are several types of interferons:

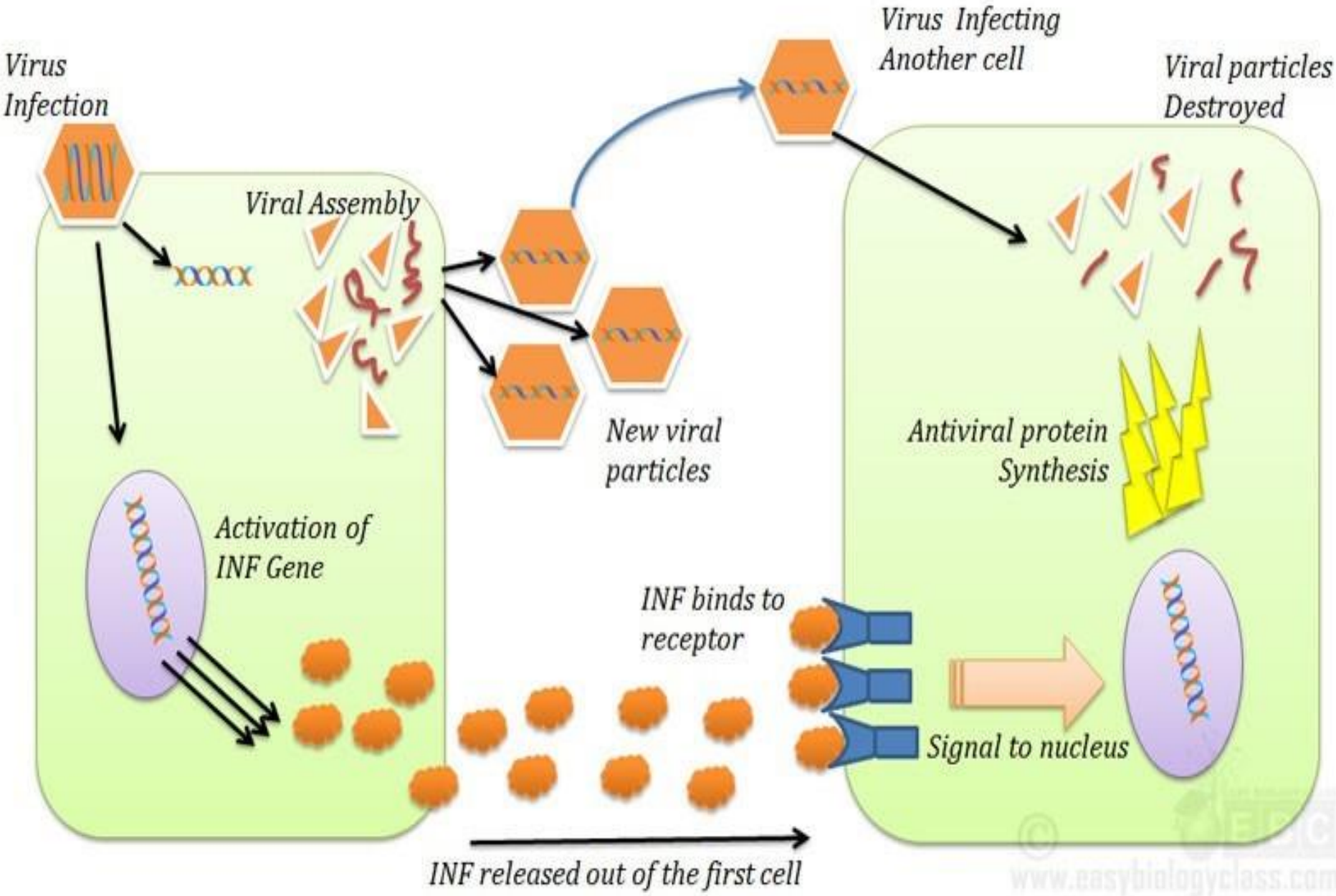
- - alpha-IFN - leukocyte (B-lymphocytes, macrophages);
- - beta IFN - fibroblast (fibroblasts, macrophages, endotheliocytes);
- gamma IFN - immune (T-lymphocytes, production is enhanced with the participation of macrophages and NK cells);

- - omega-IFN - has common features with alpha-IFN;
- - tau-IFN - found in sheep, cows and birds;
- - lambda-IFN - discovered in 2003 and originally assigned to interleukins. They have their own receptor and are classified as type III interferons. Appointment - protection of the skin, lungs and gastrointestinal tract from the action of viruses (rotaviruses).

Interferon actions.

- Antiviral effect (inhibits the process of reproduction of the virus at the stage of protein synthesis)
- Antiproliferative effect (delays the growth of tumor cells
- Immunoregulatory effect (stimulation of macrophage, EKK, antibody production, complement formation, IL-1 and IL-2, expression of MHC class II antigens)

ANTIVIRAL ACTION OF INTERFERON (INF)



© www.easybiologyclass.com

Synthetic antiviral drugs.

- Drugs that inhibit the adsorption of the virus on the cell and its deproteinization inside the cell (amantadine and remantadine)
- Inhibitors of virus-specific DNA polymerase (iodoxyuridine)
- Nucleoside analogues (acyclovir, ribavirin)
- Reverse transcriptase inhibitors (azidothymidine)
- Viral protease inhibitors (saquinavir)

Obtaining of antibiotics

- During the cultivation of microorganisms, they are excreted in the nutrient medium and obtained by chemical separation from the nutrient medium.
- In some cases, antibiotics are obtained by semi-synthesis and synthesis. Thus, there are three main methods of obtaining antibiotics:
- Biosynthesis method
- Semi-synthesis method
- Method of chemical synthesis

Modification of the target of antimicrobial action

- Methylation of RNA (ribosomal RNA) in the 50S subcomponent of ribosomes is one of the main mechanisms of resistance to macrolides and linosamides.
- Metallization of the nucleotide of only two adenes prevents the combination of these antibiotics with the 50S-components. The synthesis of the enzyme that catalyzes this process - methylase - is encoded in the R-plasmid.

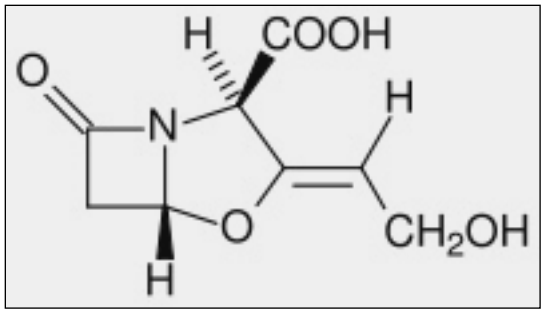
Inactivation of an antimicrobial agent

- It is one of the main mechanisms of drug resistance of microorganisms.
- Some bacteria have the ability to synthesize special enzymes that inactivate antibiotics.
- Beta-lactamase (penicillin), a beta-lactamase (penicillin) that breaks down the beta-lactam ring in penicillins and cephalosporins to form inactive compounds between these enzymes.
- Synthesis of beta-lactamases is encoded in R-plasmid.

Ways to prevent resistance to antibiotics

- Rational use of antimicrobials
- synthesis of new antibiotics
- Combination of some antibiotics with beta-lactamase enzyme inhibitors (sulbactam and clavulanic acid):

- The beta-lactam ring in these substances combines with beta-lactamases to neutralize them, thereby counteracting the effect of these enzymes on beta-lactam antibiotics.
- Preparations of ampicillin combined with sulbactam (ampicid, etc.) and amoxicillin with clavulanic acid (augmentin, amoxiclav, etc.) are widely used in medical practice.



Ways to prevent resistance to antibiotics

- One of the ways to prevent the resistance of microorganisms to antibiotics is to take into account the sensitivity to antibiotics during treatment.
- Qualitative and quantitative methods are used to determine the susceptibility of bacteria to antibiotics.
- Quality method. The disk-diffusion method (Kirby-Bauer method) is more widely used.
- The quantitative method allows to determine the minimum inhibition of antibiotics and bactericidal concentrations.

Complications that can occur under the influence of antibiotics and ways to prevent them

- **Hypersensitivity reactions - allergic reactions- consideration of hypersensitivity reactions**
- **Dysbiosis and dysbacteriosis**
- **Combination of antibiotics with antifungal drugs during long-term use- use of eubiotics**
- **representatives of normal microflora during long-term use**

Toxic effects

- consideration of contraindications and side effects

Principles of chemical therapy of viral infections

- Due to the nature of action and clinical significance, drugs used to treat viral infections can be divided into the following groups:
- Etiotropic (antivirus) drugs;
- Pathogenetic drugs (drugs that affect the development of the disease);
- Symptomatic (drugs that eliminate the symptoms of the disease).

Etiotropic drugs

- Etiotropic drugs used in the treatment of viral diseases can be divided into several groups:
- chemical preparations
- interferons and their inductors

Antiviral chemicals

Antiviral drugs selectively slow down the individual stages of virus reproduction without causing significant damage to macroorganism cells. Based on this, synthetic antiviral drugs can be divided into the following groups:

Inhibitors of adsorption of viruses into the host cell

Inhibitors of viral degradation in host cells (amantadine and rementadine)

Inhibitors of viral DNA polymerase enzyme

- Analogues of nucleosides (purine and primidine bases) (idoxyuridine, vidarbin, etc.)
- those that selectively act within the infected cell (acyclovir, gansiclovir, famsyclovir, ribavirin, foscarnet, etc.)

Inhibitors of the reverse transcriptase enzyme - azidothymidine (zidovudine), zalcitabine, lamivudine, etc.

Inhibitors of viral proteases (saquinavir, ritonavir, etc.)

Inhibitors of the synthesis of the latest viral proteins (methicone and marboran)

Inhibitors of adsorption of viruses into the host cell

- Analogues of immunoglobulins (anti-gp120) and recombinant CD4 molecules against the surface glycoproteins (gp120) of the human immunodeficiency virus (HIV) in the cell culture of the virus.
- Both drugs bind to gp120, a surface glycoprotein of the virus, thereby preventing the virus from being adsorbed into the host cell. The possibility of using these drugs for treatment is currently being studied.

Inhibitors of viral deproteinization in the host cell

- Due to their chemical nature, amantadine and remantadine, which are human derivatives, have antiviral activity against influenza A virus.
- These drugs interact with the matrix protein (M2-protein) involved in the deproteinization of the virus. This protein ensures the transport of protons into the virion by forming an ion channel in the lipid membrane of the virus, thus deproteinization the virus.

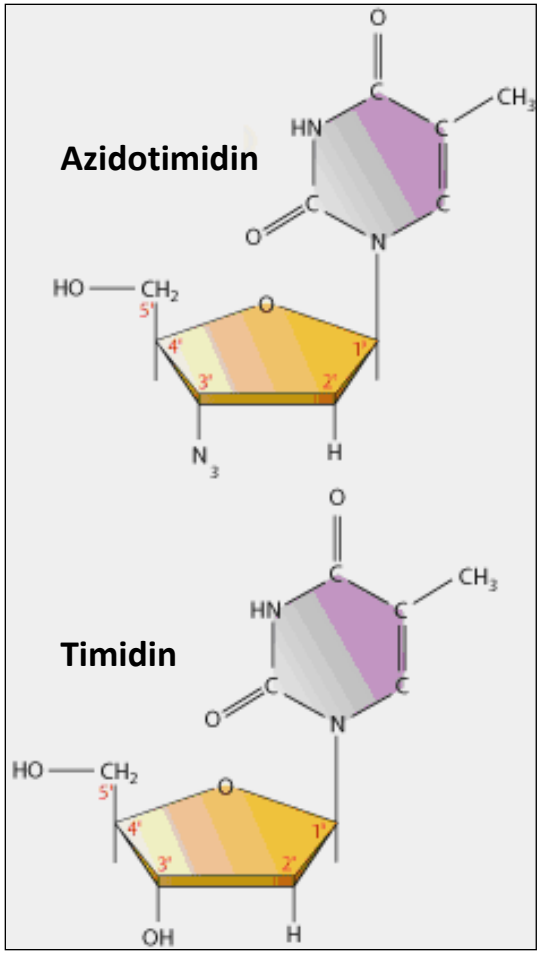
Inhibitors of viral DNA polymerase enzyme

- These drugs (idoxyuridine, vidarbin, etc.), which are mainly used in the treatment of herpesvirus infections, do not contain radicals that can form chemical bonds. Thus, they cannot bind to other nucleotides and stop their synthesis when they enter the DNA chain. These drugs have serious side effects because they inhibit the synthesis of not only viral DNA, but also cellular DNA.
- Some of them are even used as a cytostatic drug, for example, in the treatment of tumors.Some of the nucleoside analogues (acyclovir, gancyclovir, famciclovir, etc.) selectively act within the infected cell. The virus-specific enzyme thymidine kinase activates (phosphorylates) these drugs, so these drugs can not affect the synthesis of DNA in non-virus-infected cells. It is mainly used in the treatment of herpesvirus infections. Recently, nucleoside analogues (ribavirin, foscarnet, etc.) with a wide range of effects are also applied.

Inhibitors of reverse transcriptase enzymes

Drugs from this group interact with retroviruses, including MIA reverse transcriptase enzymes. It is reminiscent of thymidine due to its chemical structure.

The drug inhibits the reverse transcriptase enzyme by competitively inhibiting it, as well as binding it instead of thymidine in the nucleic acid chain. Azidothymidine (zidovudine), as well as zalsitabine, lamivudine, etc. It is used in the treatment of HIV infection



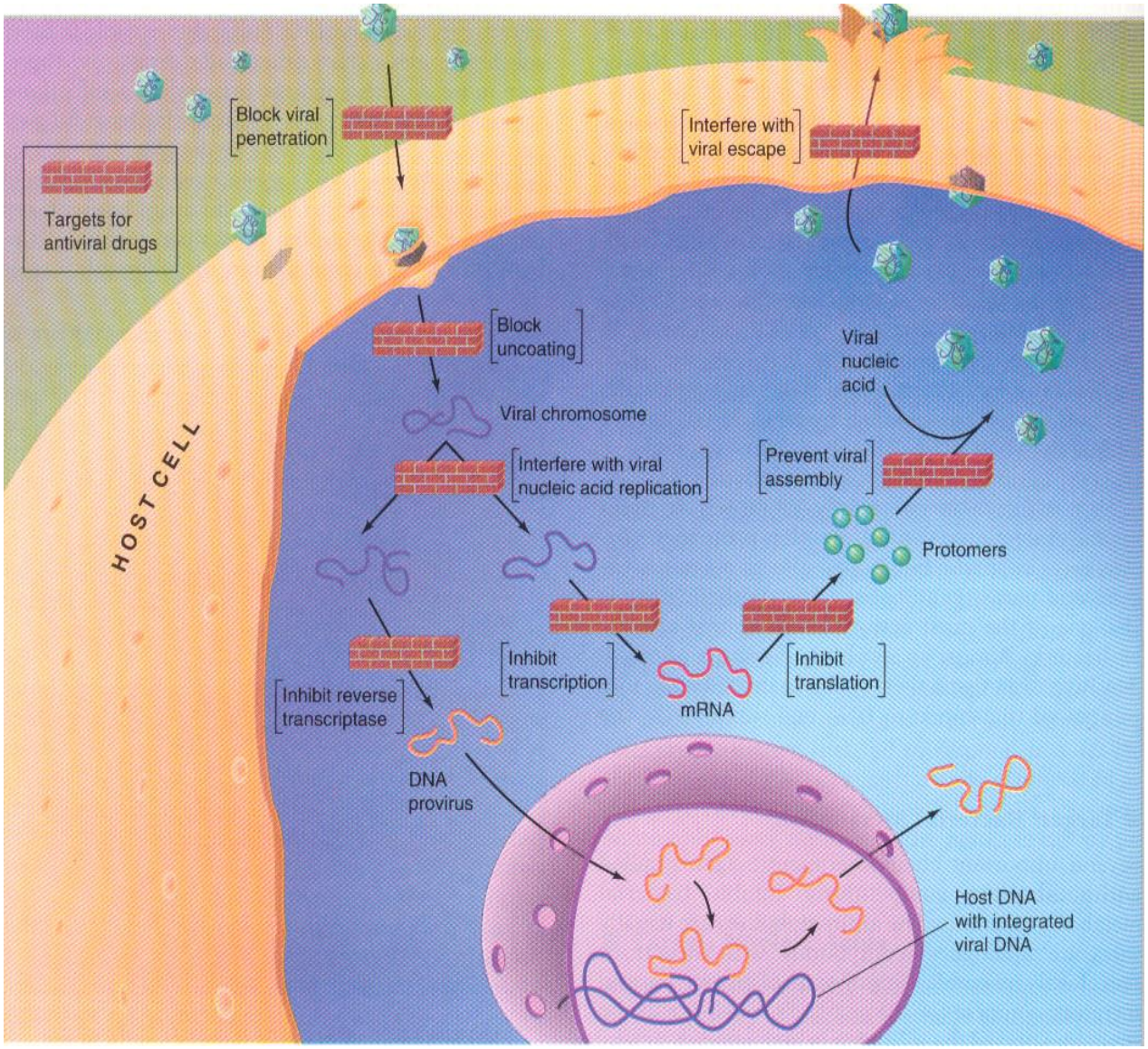
Inhibitors of viral proteases

- Non-hydrolyzed synthetic peptides (saquinavir, ritonavir, etc.) have antiviral effects by competitively inhibiting viral proteases.
- It is mainly used in the treatment of HIV infection

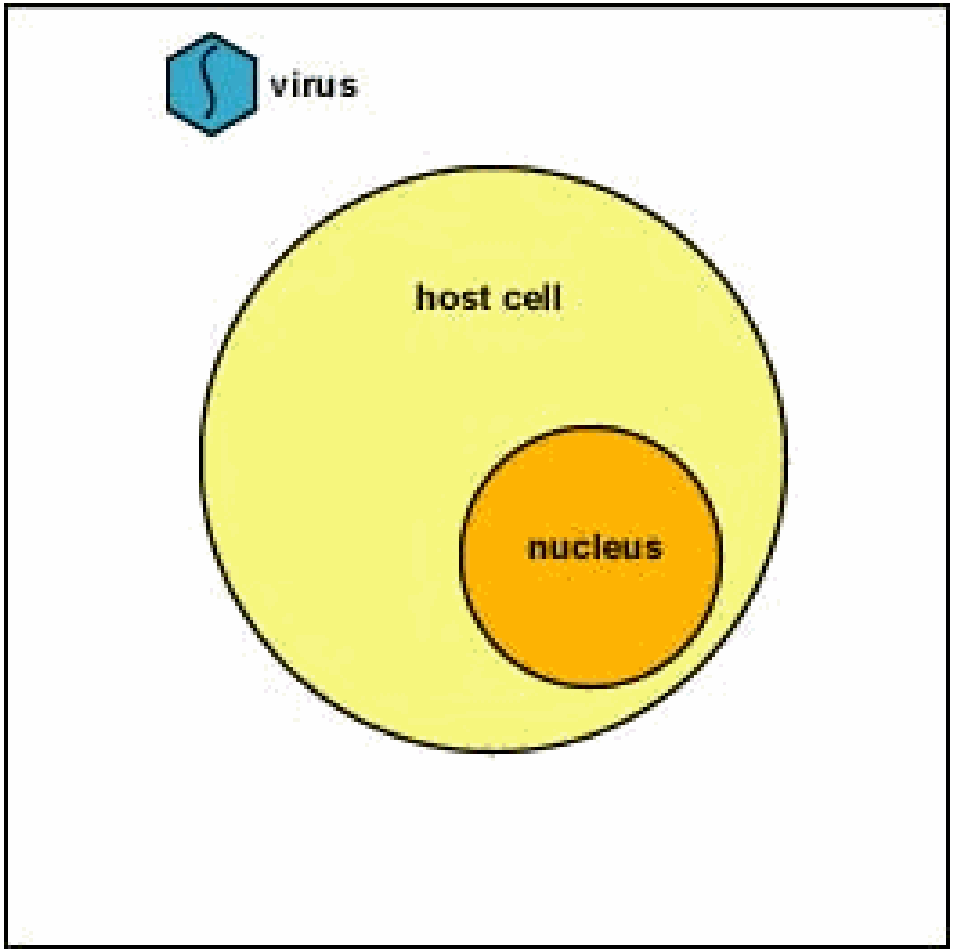
Inhibitors of the synthesis of the latest viral proteins

- They have active antiviral activity, mainly against viruses of the genus Poxviridae (natural flower virus).
- Due to its chemical nature, metisasone and marboran, which are derivatives of thiosemcarbazone, are highly effective in natural flower disease.
- These drugs are also effective in the treatment of recurrent genital herpes and herpes zoster.

Targets of antiviral drugs



The mechanism of action of interferons



Inductors of interferon **- interferonogens**

- Infection of cells with viruses dramatically increases the production of interferon.
- Interferon yields also depend on interferon inducers, such as RNA, DNA, complex polymers, and so on. is also observed during the impact.
- Such inductors of interferon are called interferonogens. At present, synthetic interferonogens (cycloferon, etc.) are widely used in medical practice.