Odesa National Medical University

Department of Pharmacology and Pharmacognosy

PHARMACOLOGY OF ANTIBIOTIC PREPARATIONS.

SULFANILAMIDE PREPARATIONS AND

OTHER SYNTHETIC PREPARATIONS.

BASIC PRINCIPLES OF CHEMOTHERAPY

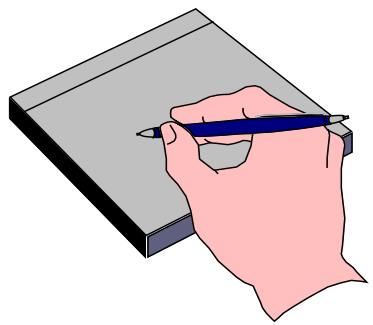
CLASSIFICATION OF CHEMOTHERAPEUTIC DRUGS

- ♦ **Antibiotics**
- ♦ **Sulfonamides**
- ♦ **Different chemical structure — derivatives of:**

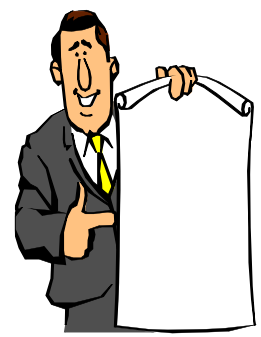
• **naphthiridin. Quinolones (nalidixic acid, etc.). Fluoroquinolones (ciprofloxacin, etc.)**
• **imidazole (metronidazol, tinidazol)**
• **8-oxyquinoline (chlorquinaldol, nitroxoline, etc.)**
• **nitrofurane (furasolidone, furadonine and etc.)**
• **quinoxaline (dioxidin, quinoxidin)**

- ♦ **By special indications:**

• **antituberculosis**
• **antisyphilytic**
• **antiprotozoal**
• **antimycotic**
• **antihelmintic**
• **antiviral**
• **antitumoural**

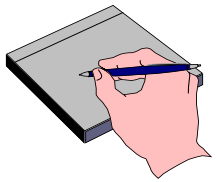


GENERAL PRINCIPLES OF CHEMOTHERAPY



Rational choice of a drug (depending on the sensitivity of disease agent, concomitant diseases, anamnesis, etc.)

- **Early beginning of treatment**
- **Way of introduction** (depending on localization, severity of a pathological process, concomitant diseases)
- **Choice of a dose** for creation of therapeutic concentration (depending on weight, age, sex, concomitant pathology, etc.)
- **Interval of introduction** (depending on the pharmacokinetic properties of preparation)
- **Duration of treatment** (“train” principle — continuation of treatment up to clinical and bacteriological recovery)
- **Combined treatment**
- **Rise of immunological reactivity** of an organism (probiotics, vitaminic drugs, immunomodulators)



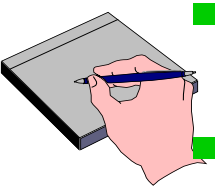
ANTIBIOTICS –

The substances of mainly biological origin (biosynthetic), their half-synthetic and synthetic analogs, causing damaging or destroying effect on the microorganisms which are sensitive to them

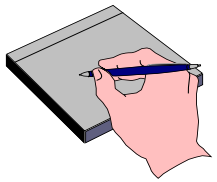
according to origin:

- **Mould fungi** — penicillins, cephalosporins, etc.
- **Radiant fungi** — streptomycin, levomicetin (chloramphnicol),tetracycline
- **Bacteria** — gramicidin
- **Synthetic analogs and derivatives** of natural antibiotics

CLASSIFICATION OF ANTIBIOTICS ACCORDING TO ANTIMICROBIAL SPECTRUM



- **With the main influence on Gr+ microbes**
  - **Beta-lactam antibiotics** ***(penicillins, cephalosporins & others beta-lactam agents)***
  - **Macrolides & azalides**
  - **Antibiotics with special indications**
- **With the main influence on Gr- microbes**
  - **Aminoglycosides**
  - **Polymyxins**
- **Influencing both on Gr+ & Gr- microbes**
  - **Tetracyclines**
  - **Levomycetin**
- **Influencing both on Gr+ & Gr- microbes and used locally: Polymyxins, Neomycin, Monomycin**
- **Antifungal**
- **Anticancer**



CLASSIFICATION OF ANTIBIOTICS

By chemical structure :

- *Beta-lactam* — beta-lactam ring (penicillins, cephalosporins, carbepenemes, monobactams)
- *Macrolides* — lactonic ring (erythromycin) and azalides (azithromycin)
- *Tetracyclines* — 4 rings (tetracycline, doxycycline, etc.)
- *Aminoglycosides* — containing aminosugars (streptomycin, gentamicin)
- *Lincosamides* (lincomycin, etc.)
- *Derivatives of dioxyaminophenilpropan* — (levomycetin)
- *Polymixins* — cyclic polypeptids (polymixin B)
- *Polyenes* (amphotericin B, nystatin, etc.) and others

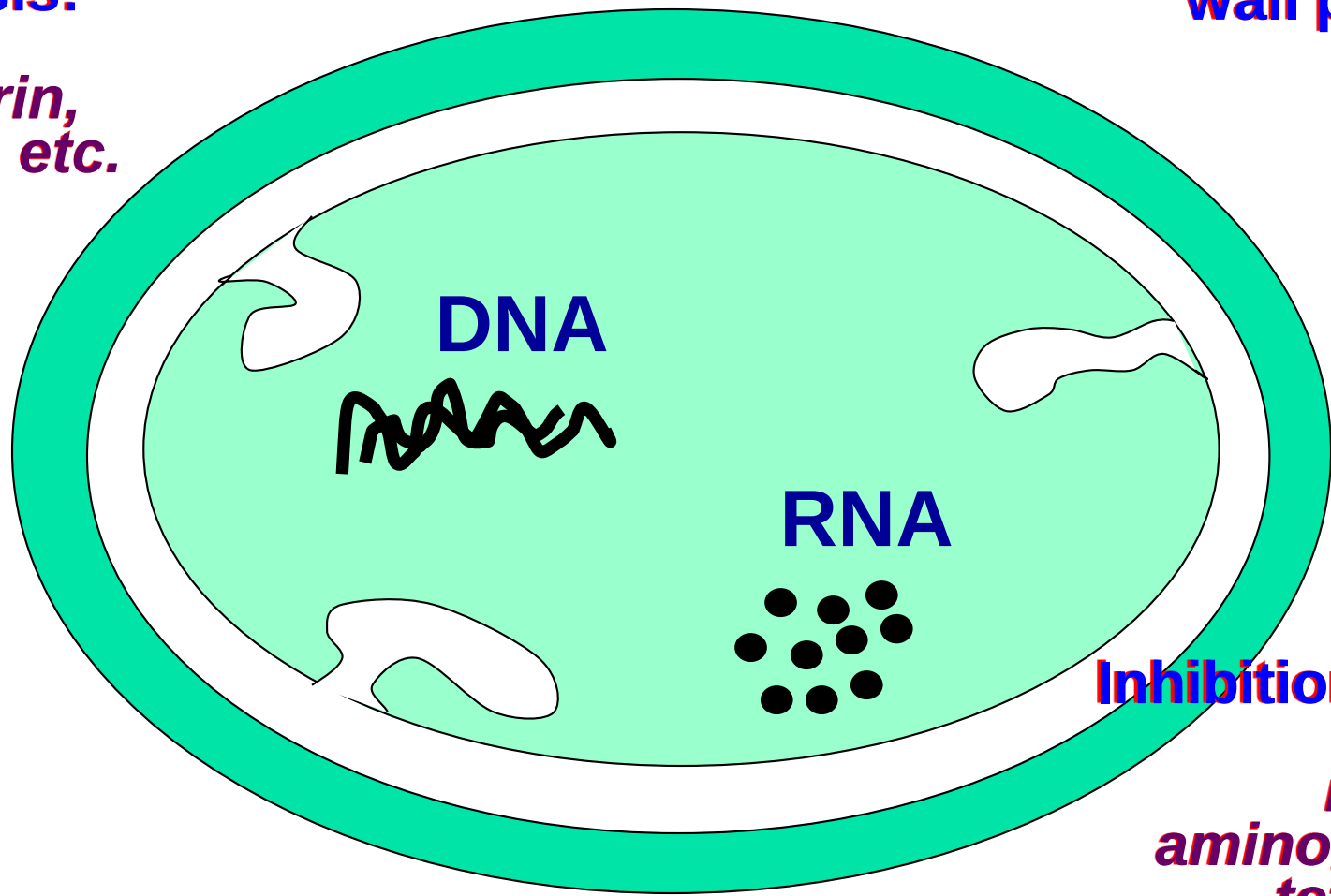
according to action:

- **Predominantly bactericidic action – penicillins, cephalosporins, aminoglycosides**
- **Predominantly bacteriostatic action – tetracyclines, levomycetin, macrolides**

CLASSIFICATION OF ANTIBIOTICS ACCORDING TO MECHANISM OF ACTION

Inhibition of cell wall synthesis: ***penicillins, cephalosporin, vancomycin etc.***

Increasing of cell wall permeability: ***polymyxins, polyene***



Inhibition of nucleic acid synthesis: ***rifampicin, griseofulvin, anticancer.***

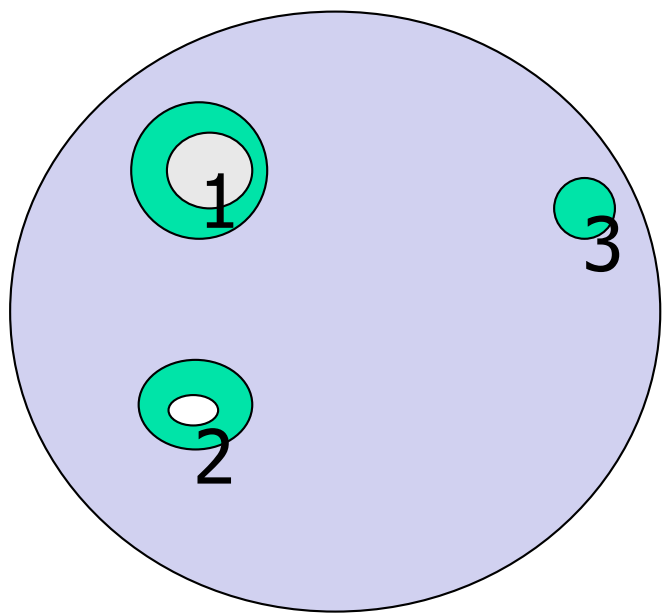
Inhibition of protein synthesis: ***macrolides, aminoglycosides, tetracyclines, levomycetin, lincomycin etc.***

GENERAL PRINCIPLES OF ANTIBIOTIC THERAPY

Rational choice of antibiotic (depending on disease causative agent sensitivity, concomitant diseases, allergologic, medicinal anamnesis, etc.)

disk-diffuse method

A zone of microorganism growth depression around the disk with antibiotic (1 — the microorganisms are resistant to antibiotic or 2 — the microorganisms are moderately resistant to antibiotic)



There is no zone of microorganism growth depression around the disk with antibiotic (3 — microorganisms are resistant to antibiotic)

GENERAL PRINCIPLES OF ANTIBIOTIC THERAPY

Rational choice of antibiotic

Category of sensitivity	*Clinical characteristics*
Sensitive	Therapy is successful in usual doses
With intermediate	Therapy is successful with resistance maximal doses or localization of infection in antibiotic accumulated tissues
Resistant	Maximal doses are ineffective

GENERAL PRINCIPLES OF ANTIBIOTIC THERAPY

- **Early onset of treatment**
- **Way of introduction** (depending on localization and severity of process, concomitant diseases)
- **Choice of dose for creation of therapeutic concentration** (depending on the body weight, age, concomitant diseases)
- **Interval of introduction** (depending on pharmacokinetic parameters)

GENERAL PRINCIPLES OF ANTIBIOTIC THERAPY

- **Duration of treatment:**

In accordance with recommendations of the World Health Organization (WHO), 1 drug for no more than 5–7 days long; the “train” principle

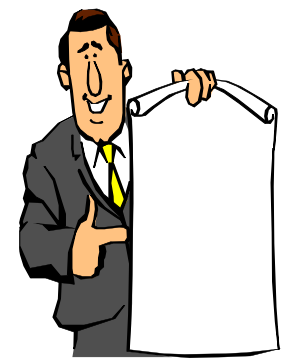
Postantibiotic effect (PAE) — depression of vital function of microorganisms, proceeding after stopping a contact with antibiotic (minutes, hours)

- **Combined treatment:**

Makes sense with mixed infection, threat to life more frequent — bactericidal with bactericidal, bacteriostatic with bacteriostatic

- **Rise of immunological reactivity of an organism**

(probiotics, vitaminic drugs, immunomodulators)

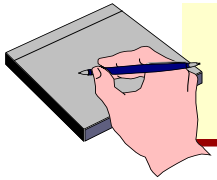


ADVERSE EFFECTS OF ANTIBIOTIC THERAPY

- **Development of polyresistance in microorganisms** (biological, specific, secondary, persistent, cross)
- **Development of allergic reactions** (immediate type — betalactam, etc.; delayed type)
- **Direct organotoxic effects** (neuro-, hepato-, myelo-, nephrotoxicity, gastrointestinal disturbances, etc.)
- **Development of exacerbation reaction** (endotoxic)
- **Development of superinfection** (candidomycosis, staphylococcosis, hypovitaminosis)
- **Mutagenic, teratogenic, embryo- and fetotoxic action**

GENERAL DEMANDS AND CRITERIA OF ANTIBIOTICS DISTINCTION

- **Resistance to microorganisms**, mutated during the process of antibacterial drugs application
- Range of **antibacterial action spectrum**
- The **minimal toxicity** for macroorganism
- **Prolongation** of action
- **Acid stability**
- **If necessary — penetration through** the blood brain barrier



КЛАССИФИКАЦИЯ ПЕНИЦИЛЛИНОВ

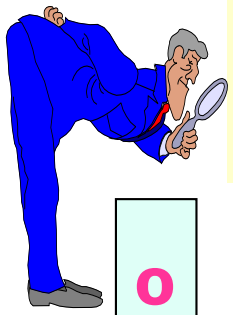
- **Biosynthetic:** ***short action*** — benzylpenicillin sodium and potassium salts, phenoxymethylpenicillin; ***depo-preparations*** — benzathine benzylpenicillin (extencillin), bicillin-1), bicillin-5
- **Semi-synthetic:**
  - ***izoxazolilpenicillins*** — oxacillin, cloxacillin, flucloxacillin
  - ***aminopenicillins*** — ampicillin, amoxicillin
  - ***antipyocyanic*** — carboxypenicillins (carbenicillin, ticarcillin) and ureidopenicillins (azlocillin, piperacillin)
  - ***combined and inhibitor-protected*** — ampiox, helicocide (amoxicillin + metronidazol), amoxiclav (amoxicillin + clavulanate), ampicillin + sulbactam, ticarcillin+ clavulanate, piperacillin + tazobactam, etc.

PHARMACOKINETICS OF PENICILLINS

- **Absorption:** parenterally and per oral (on an empty stomach orin an **hour after the meal!);** bioavailability 30–50%
- **Binding with proteins: different** (biosynthetic — about 80%,oxacillin — 90%, ampicillin — 20%)
- **Distribution:** high concentration in the **liver, lungs, kidneys,**reproductive organs, lower in tissues of the eyes, prostate gland, CNS, penetrate well to the mucous membranes, badly to the bone tissue
- **Time of therapeutic concentration (ThC) is different:**

benzypenicillin — 3–4 hrs, depo preparations — up to 2–4 weeks, semi-synthetic — 6–8 hrs

- **Biotransformation:** in the liver practically does not metabolize, except for oxacillin, etc.
- **Excretion:** excrete mainly by the kidneys, and also by the liver,saliva, breast milk



ANTIMICROBIAL SPECTRUM OF PENICILLINS

oxacillin

benzylpenicillin

ampicillin

Staphylococci, penicillinase producing
Gr^+ & Gr^- cocci (streptococci, pneumococci, staphylococci, meningococci, gonococci, not producing penicillinase)
Gr^+ rods (corynebacteria diphtheria)
Anaerobes (clostridium)
Spirocheta (Treponema pallidum)
Actinomycets
Other rods (E.coli, Ps. aeruginosa)
Enterobacteria (Esherichia, Shigella, Salmonella, Proteus)

CHEMOTHERAPEUTIC SPECTRUM OF PENICILLINS

- **Benzyl penicillin sodium & potassium salts – respiratory system infection, rheumatic fever, syphilis, endocarditis, meningitis, anthrax, gas gangrene, infection of female reproductive organs;**
- **Bicillin-5 – rheumatic fever, syphilis, scarlet fever;**
- **Oxacillin sodium - respiratory system infection, gas gangrene, purulent infection of skin and soft tissues;**
- **Ampicillin - respiratory system infection, endocarditis, bacterial meningitis, gas gangrene, intestinal infection;**
- **Carbenicillin - endocarditis, bacterial meningitis, infection of skin, joints and soft tissues, urinary tract infection, prostatitis**

ADVERSE EFFECTS OF PENICILLINS

- **Allergic reactions (immediate! & delayed type).** ***Cross-hypersensitivity with cephalosporins!***
- **Endotoxic reaction (reaction of aggravation) – benzyl penicillin at syphilis**
- **Superinfection**
- **Neurotoxicity**
- **Gastrointestinal upset (ampicillin, oxacillin)**

CLASSIFICATION OF CEPHALOSPORINS

- **first-generation:**
  - ***for parenteral administration*** **– cephaloridine, cefazolin, cephalothin;**
  - ***for oral intake*** **– cephalexin;**
- **second-generation :**
  - ***for parenteral administration*****– cefuroxime, cefoxitin, cefamandole;**
  - ***for oral intake*****– cefaclor;**

  third generation :
  - ***for parenteral administration*****– cefotaxime, ceftriaxone, cefoperazone;**
  - ***for oral intake*****– cefixime;**
- **fourth generation** ***(parenteral administration only):*** **cefepime, cefpirome**

ANTIMICROBIAL SPECTRUM OF CEPHALOSPORINS

- **First-generation –** Gr$^+$ rods & cocci (N. gonorrhoeae, E.coli, Kl. pneumoniae, and Proteus mirabilis).
- **Second-generation –** see first-generation plus extended Gr- coverage, e.g., Proteus vulgaris, Enterobacter, Haemophilus influenzae.
- **Third-generation –** less active against gram-positive cocci, active against Serratia, Enterobacter as well as β-lactamase-producing strains of Haemophilus and Neisseria.

- **Fourth-generation –** similar to third-generation agents, but it is more resistant to hydrolysis by chromosomal beta-lactamases (e.g., those produced by Enterobacter).

CHEMOTHERAPUTIC SPECTRUM OF CEPHALOSPORINS

- Infection of respiratory system
- Infection of urinary tract,
- Infection of skin, bone and soft tissues;
- Infection of reproductive system (i.e., gonorrhea);
- Postoperation infection;
- Endocarditis;
- ENT-pathology;
- Peritonitis.

ADVERSE EFFECTS OF CEPHALOSPORINS

- Allergic reactions (including cross-hypersensitivity with penicillins);
- Superinfection;
- Dyspepsia;
- Phlebitis;
- Hepatotoxicity;
- Leucopenia, agranulocytosis;
- Neurotoxicity.

OTHER BETA-LACTAM ANTIBIOTICS

MONOBACTAMS (Aztreonam)

- **Spectrum activity** – Gr- rods (including Pseudomonas, Klebsiella, Serratia, and Proteus mirabilis), Gr+ rods, anaerobes.
- **Uses** bacterial pneumonia, skin and soft tissue infections, urinary tract infections, gynecologic and intra-abdominal infections, septicemia ;
- **Adverse effects** – allergic reactions, phlebitis, dyspepsia, diarrhea etc

CARBAPENEMS (Tienam, Meropenem)

- **Spectrum activity** – Gr- rods (Pseudomonas, Enterobacter, Serratia), gram-positive organisms, and anaerobes .
- **Uses** the treatment of intra-abdominal infections, skin and soft tissue infections caused by susceptible organisms;
- **Adverse effects** – nausea, vomiting, diarrhea, skin rashes, and reactions at the infusion sites.

MACROLIDES & AZALIDES

	Erythromycin	Azithromycin
Anti-microbial spectrum activity	Cocci Gr+ & Gr-, spirocheta, Rickettsia sp., corynebacteria, Chlamidia, Mycoplasma, Legionella, Helicobacter species.	Slightly less active against staphylo- & streptococci and slightly more active against H.influenzae & Chlamydia.
Pharmaco kinetics	Badly absorbed in GIT; don't cross BBB; $T_{1/2}$ – 2-5 hrs	Badly absorbed in GIT; don't cross BBB; $T_{1/2}$ (tissue) – 2-5 hrs; store in tissues
Adverse effects	Hepatotoxicity, allergic reactions, superinfection	Nausea, vomiting, diarrhea

AMINOGLYCOSIDES

Streptomycin, Kanamycin, Gentamicin, Amikacin, Sisomicin, Tobramycin.

Spectrum	Streptomycin	Gentamicin
Antimicrobial	Majority of Gr- rods like, E.coli, Kl. pneumonia, Shigella dysentery, brucella, Francisella tularensis, Yersinia pestis, M.tuberculosis.	Gr+ & Gr- bacteria; Proteus, E.coli, Salmonella.
Chemotherapeutic	Tuberulosis, endocarditis, peritonitis, urinary tract and GI-tract infections, brucella, tularemia, plague	Pneumonia, pleuritis, empiema, peritonitis, meningitis, sepsis, urinary tract infection, prostatitis.

ADVERSE EFFECTS OF AMINOGLYCOSIDES

- Ototoxicity;
- Allergic reactions;
- Superinfection;
- Nephrotoxicity;
- Neuroxicity;
- Curare-like effect;
- Fetotoxic and embryotoxic effect.

POLYMIXINS B and E

Mechanism of action — bactericidal; disturb permeability of cellular wall and transport mechanisms, binding with the bacteria's cell membrane

Antimicrobial spectrum — Gr– microflora

Pharmacokinetics — do not absorb into the GIT, with parenteral introduction badly penetrate the tissues, do not get to alive cells; excretion by kidneys

Adverse effects — high nephro- and neurotoxicity (parestesia, dizziness, discoordination of movements), respiratory paralysis, etc.

The usage — locally (the skin, mucosa, in the pleura, joint cavity, etc.)

BROAD-SPECTRUM ANTIBIOTICS

- **Tetracyclines:**
  1) ***biosynthetic*** **– tetracycline, oxytetracycline;**
  2) ***semisynthetic*** **- methacycline, doxycycline);**
  3) ***combines*** **– oletetrine;**
- **Levomycetin – levomycetin (chloramphenicol), synthomycin.**

TETRACYCLINES

- *Biosynthetic* — tetracycline, oxytetracycline
- *Semi-synthetic* — metacycline, doxycycline (vibramycin)
- *Combined* — oletetrine, ericycline

Mechanism of action — bacteriostatic; disturbance of synthesis of bacterial cell's protein — binding with 30S-subunit of ribosomeses results in disturbance of peptide chain; the formation of the chelate compounds with metals causes depression of the enzymic systems

Antimicrobial spectrum — broad: Gr+ and Gr- microflora, causative agents of plague, cholera, dysenteries, brucellosis, tularemia, malarias, rickettsial infection, spirochetes, actinomycetes, some protozoa, etc.

TETRACYCLINES

Chemotherapeutic spectrum

Preparations of choice with infections caused by *Mycoplasmae, Chlamydia, Ricketsia,* some *Spirochetes*

- **They are effective with dysentery, brucellosis, tularemia,plague, cholera, meningitis, malaria, intestinal infections and biliary ducts**

Pharmacokinetics

Absorption in the small intestine — from 30 to 100%; binding with proteins — 40–80%; **well penetrate** (except for the cerebrospinal fluid), **can deposit** in the osteal and dental tissues, easily penetrate through the placenta; T1/2 — 6–12 hrs and more, **excretion** by the kidneys, intestine, milk, saliva. The **enterohepatic cycle of metabolism** is peculiar to semi-synthetic ones

ADVERSE EFFECTS OF TETRACYCLINES

- **Superinfection**
- **Gastrointestinal disorders** (glossitis, stomatitis, diarrhea, proctitis, etc.)
- **Hepato- and nephrotoxicity**
- **Haematological deviations** (trombocyto-, neutropenia, eosinophilia)
- **Catabolic effect on macroorganism**
- **Allergic reactions**
- **Disturbance of the osteal and dental tissue formation** (chelate compounds).

Contraindicated before 12 years old!

- **Teratogenicity**
- **Photosensitization**
- **Cross resistance**

LEVOMYCETINE (CHLORAMPHENICOL)

Mechanism of action — bacteriostatic; disturbance of bacterial cell's protein synthesis — binding with 50S-subunit of ribosomes and the blockade of peptidyltransferase results in peptide chain disturbance

Antimicrobial spectrum — broad: Gr+ and Gr - microflora, rickettsia, spirochetes, large viruses, bacteroids, etc. Resistance arises seldom

The usage — with the threat of life and severe conditions at salmonellosis infections (typhoid fever), meningitis, sepsis, microflora resistance to other antibiotics

Pharmacokinetics — is well absorbed, binding with proteins — 30%, well penetrates all the tissues, T1/2 — 6–8 hrs; biotransformation — conjugation and reduction;excretion by kidneys

ADVERSE EFFECTS OF LEVOMYCETIN

- **Myelotoxicity** (leukopenia, agranulocytosis, reticulocytopenia, aplastic anaemia up to the lethal outcome!).
Control of blood on every 2nd day!

- **"Grey baby syndrome"**
- **Superinfection**
- **Gastrointestinal disorders** (glossitis, stomatitis, diarrhea, etc.)
- **Hepato- and nephrotoxicity**
- **Reaction of exacerbation** (with typhoid fever)
- **Allergic reactions**
- **Neurotoxicity** (ophthalmic nerve neuritis)

SULFANILAMIDES.

ANTIMICROBIAL AGENTS

OF DIFFERENT ORIGIN

HISTORY

Klarer & Mietz in 1932 year

in Germany it was synthesized and studied *in vitro* antibacterial activity of prontosile (red streptocidum)

G. Domagc in 1935 year

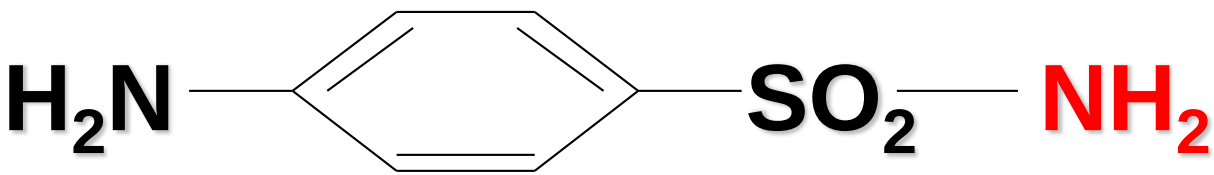
at first it was shown *in vivo* its activity against hemolytic streptococcus and other bacteria

RINCLES OF RATIONAL CHEMOTHERAPY

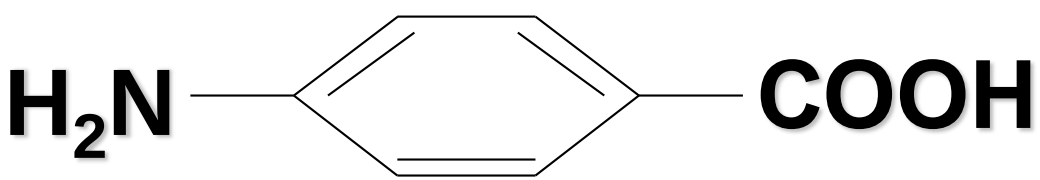
- **Rational choice of agent** ***(depending on sensitivity of infectional agent, concomitant diseases, anamnesis etc);***
- **Early onset of treatment;**
- **Route of administration;**
- **Choice of dose for achievement of therapeutic concentration** ***(depending on weight, age, sex, concomitant diseases etc.);***
- **Intervel of administration** ***(depending on pharmacokinetic properties of agent);***
- **Duration of therapy** ***(principle of train);***
- **Combined therapy;**
- **Improvement of immunologic reactivity of organism** ***(vitamins, immunostimulators).***

CHEMICAL STRUCTURE

Derivetive of sulfanyl acid (usually, white, has no smell, bitter, weak acids, badly dissolved in water)



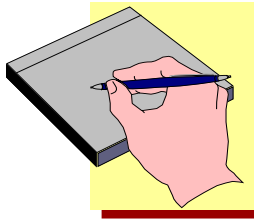
sulfanilamide (streptocide)



para-aminobenzoic acid (PABA)

Modification of aminogroup leads to physical, chemical, pharmacological properties;

majority available as sodium salts



CLASSIFICATION OF SULFANILAMIDE AGENTS

- **Well-absorbed in gastro-intestinal tract for resorptive action:**
  - **short-acting ($T_{1/2}$ < 10 hrs) – streptocide, ethazole, norsulfazole, sulfadimezine;**
  - **long-acting ($T_{1/2}$< 24-28 hrs) – sulfapyridazine, sulfadimethoxine**
  - **ultralong ($T_{1/2}$ < 65 hrs) – sulfalen**
- ***Badly absorbed* in gastro-intestinal tract: phthalazole**
- ***Combined:***
  - **with salicylic acid – salazopyridazine, salazosulfapyridine;**
  - **with thimethaprim – co-trimoxazole (bactrim, biseptol), sulfatone**
- ***For local use* – streptocide, sulfacyl sodium & other sodium salts**

PHARMACOKINETICS

Absorption **(well-absorbed agents): mainly, in small intestine.**

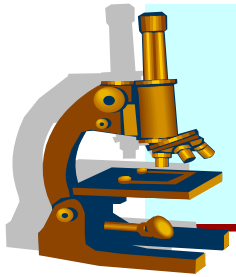
Binding with plasma proteins: **20-90 %.**

Distribution: **highest concentration – in liver, kidn lungs, skin; less – in fat tissues. Readily cross in liqu compartments of organism, including BBB, placenta.**

Biotransformation: **Acetylation, oxidation, glucuronidation or unchanged.** ***Acetylated forms (especially in acidic medium!) precipitate in urine, leads to crystalluria.***

Excretion: **via kidneys, mainly, through glomerular filtration. Long-acting agents undergo reabsorption.**

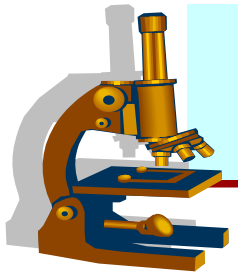
In children and aged people can be changed!



CONDITIONS, DETERMINING ANTIMICROBIAL ACTIVITY

The concentration of sulfonamides in 100-1000 times should overcome PABA concentration in substrate

Antibacterial activity drop at presence of pus, blood, products of tissue degradation, where PABA present in large amount

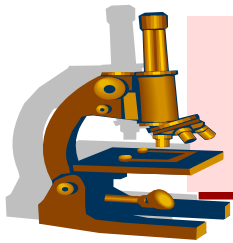


ANTIMICROBIAL SPECTRUM

Action is bacteriostatic

- **Highly susceptible microorganisms: cocci (pneumococci, gonococci, meningococci, streptococci), intestinal (E.coli, Salmonella, Vibrio cholera), large viruses (trachoma), Protozoal (Plasmodium, Toxoplasma gondii), Chlamydia, Cl. perfringens, Corynebacteria etc**
- **Moderately susceptible: staphylococci, enterococci, Kl. pneumonia, Mycobacterium, Yersinia pestis, Actinomycets.**

In combination with trimethaprim - bactericidic, antibacterial spectrum is more wide



RESISTANCE

Only those microorganisms are sensitive that essentially need PABA

In result of often and unwise use of drugs staphylococci, meningococci, streptococci, gonococci, Enterobacter became resistant to sulfonamides

There is cross-resistance among sulfonamides.

GENERAL PRINCIPLES OF SULFONAMIDES THERAPY

- Rational choice of sulfanilamide
- Early beginning of treatment
- Route of administration
- Principle of loading dose
- Intervals of administration
- Duration of treatment
- Combined therapy *(sulfanilamides should not be combined with!)*, interaction with other agents *(novocain, diphenin, NSAIDs, synthetic hypoglycemic agents, diuretics, anticoagulants etc.)*
- Increasing of immune resistance of organism *(vitamins, immunomodulators).*

THERAPEUTIC USES

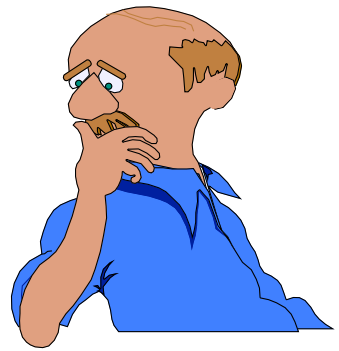
- **Acute coccal infections** ***(pneumonia, tonsillitis, bronchitis, sinusitis, otitis, cholecystitis, meningitis etc.)*** **– resorptive long- and ultra-long-acting (sulfadimethoxine, sulfalen), co-trimoxazol;**
- **Acute infections of bile & urinary ducts** ***(cystitis, pyelonephritis etc.)*** **– resorptive short acting (urosulfan), co-trimoxazol;**
- **Acute intestinal infections** ***(dysentery, enterocolitis, colitis etc.)*** **– badly absorbed (phthalazol);** ***nonspecific ulcerative colitis*** **– salazosulfanilamides;**
- **Ophthalmic infections** ***(conjuctivitis)*** **– sulfacyl-sodium;**
- **For the treatment of trachoma, malaria, chlamydiasis, toxoplasmosis, actinomycosis, lepra etc.**

ADVERSE EFFECTS

- **Renal damage : crystalluria, hematuria, urine retention**
- **Inhibition of bone marrow: leucopenia, agranulocytosis, anemias**
- **Hepatotoxicity: hepatitis, in children – jaundice (insufficiency of glucuronyl transferase)**
- **Allergic reactions: dermatitis, синдром Stevens-Johnson syndrom etc**
- **Dysbacteriosis (hypovitaminosis B, K).**
- **Neurotoxicity (dizziness, headache, mental depression)**

CONDITIONS OF RATIONAL SULFANILAMIDE THERAPY

- Patient's anamnesis (did he/she take sulfanilamides before, disease)
- Loading dose!
- Alkaline drinking!
- Duration 6-8 days (at acute infections and especially in children and aged people)
- Control of urine and blood!
- For prevention of complications – vitamins group B, probiotics, immuno-, biostimulators etc; пат complications – discontinuation of the drug, vitamins B, C.



MISCELLENOUS CHEMOTHERAPEUTIC AGENTS

- Fluoroquinolones
- Naftiridine derivatives
- 8-oxyquinolines
- Nitrofurane derivatives
- Imidazole derivatives
- Quinoxolone derivatives

FLUOROQUINOLONES

1 generation – ciprofloxacine, ofloxacine, pefloxacine, norfloxacine etc;
2 generation – lomefloxacine, sparfloxacine;
3 generation – flerofloxacine, trovafloxacine

Mechanism of action: **Bactericidic – inhibit DNA-gyrase. Also possess immunomodulative activity.**

Bacterial spectrum: **Ultra-broad. Gr^+ & Gr^- bacteria, Proteus, Pseudomonas, Chlamydia, Mycoplasma, Ureaplasma, Rickketsia, Legionella, Mycobacterium etc. Active against bacteria, resistant to other antimicrobial agents**

Uses: **infections of different localization**

Adverse effects: **in children – dysplasia of cartilage tissue (banned before 18 years and for pregnant!), dysbacteriosis and dyspepsia, allergic reactions, photosensibilization, hypercoagulation.**

8-OXYQUINOLINES DERIVATIVES

Nitroxoline (5-NOK), chlorquinaldol, intetrix, oxolinic acid

Mechanism of action: **Bactericidic – inhibit protein synthesis, chelate-formation, induction of oxidative process in protoplasma.**

Bacterial spectrum activity: **Broad. Gr^+ & Gr^- bacteria (staphyloccoci, enterobacteria), Protozoal (amoeba, gardia), fungi.**

Uses: **Effective at resistance to other antibacterial agents.**

- **intestinal infection and dysbacteriosis (chlorquinaldol, intetrix);**
- **urinary tract infection (nitroxoline).**

Adverse effects: **subacute myelo-optic neuropathy (SMON), allergic reactions, abdominal cramps, nausea.**

NITROFURANE DERIVATIVE

Furadonine, furazolidone, furagin; locally – furacillin.

Mechanism of action: **Bacteriostatic & bacteriocidic(depending on concentration). Nitrogroup reduce to aminogroup, that inhibit synthesis of DNA, tissue respiration, Creb's cycle. pH < 5,5 increases action!**

Bacterial spectrum: **Gr^+ & Gr^- bacteria, Protozoal (Amoeba, Gardia, trichomonada), large viruses, fungi.**

Uses: **Effective at resistance to antibiotics & sulfanilamides.**
- **intestinal infection (furazolidone);**
- **infection of urinary tract (furadonine, furagin).**

Adverse effects: **allergic reactions, neuritis, bleeding, methemoglobinemia, nephrotoxicity, dyspepsia, embryotoxicity.**

QUINOXOLINES

Dioxydinum, chinoxydinum

Mechanism of action: **Bactericidic – block of DNA synthesis**

Bacterial spectrum: **Gr^+ & Gr^- bacteria, Proteus vulgaris, Pseudomonas, anaerobs. Active against bacteria resistant to other chemotherapeutic agents**

Uses: **arthritis, severe purulent-visceral processes, sepsis etc.**

Adverse effects: **mutagenic, teratogenic, embryotoxic, seizures, allergic reactions, hyperthermia**

Only for adults under restrict doctor supervision !