CLINICAL PHARMACOLOGY OF ANTIBIOTICS AND CHEMOTHERAPEUTICS OF DIVERSE CHEMICAL STRUCTURE. PERSONAL DRUG SELECTION.

A. Actuality

At present, with the increasing number of patients with serious infectious diseases and the emergence of multidrug-resistant microbial strains, the issue of effective and correct antibiotic therapy is very topical. Synthetic chemotherapeutics - sulfonamides, derivatives of naphthyridine and quinolones, nitroimidazole, 8-oxyquinoline, nitrofuran, chinoxaline and thiosemicarbazone - possess antibacterial, antifungal and antiprotozoal properties and are widely used in the treatment of infections caused by the pathogenic microorganisms. The understanding of their pharmacokinetics and pharmacodynamics will allow their rational selection, their combination with other preparations and the optimal dosing regimen in the treatment of infectious diseases.

B. Training aim

Acquiring clinical and pharmacological principles to justify the prescription, use, dosing regimen of drug preparations in the given antibiotics groups, and to assess their efficacy and harmlessness.

C. Teaching objectives

The student should be able to:

a) characterize antibiotics and antimicrobial synthetic chemotherapeutic agents with diverse chemical structure, according to their pharmacokinetic and pharmacodynamic characteristics

b) prescribe medicinal preparations from these groups depending on the causative pathogen, the degree of resistance, the pathological condition and the age characteristics of the patient;

c) predict the possible complications and adverse reactions of antibiotic drugs and antimicrobial synthetic chemotherapeutic agents with diverse chemical structure;

d) predict the dependence of the adverse reactions on the dosage regimen and the functional state of the organs and body systems;

e) apply methods of prophylaxis and correction of adverse reactions;

f) predict the interactions of antibiotics and antimicrobial synthetic chemotherapeutic agents with diverse chemical structure;

g) elaborate the personal form (medicines-P) of antibiotics and chemotherapeutics drudg with diverse chemical structure.

D. Knowledge from previously studied disciplines and related subjects

Histology, morphopathology, pathophysiology and microbiology

Cell structure of pathogens. Classification of pathogenic germs. Pathogenesis of septic states.

Clinical disciplines. Etiology, pathogenesis of the main nosological forms of infectious pathologies. Functional and laboratory tests applied in pulmonology, septic surgery, urology, etc. Clinical manifestations of infectious diseases.

Pharmacology. Classification of the antibiotics according to their group, spectrum and mechanism of action, antibacterial effect. Characterization of antibiotic groups by spectrum and mechanism of action, indications, side effects. Chemotherapeutics of different chemical structure: classification, spectrum and mechanism of action, indications, adverse reactions of sulfonamides, nitroimidazole derivatives, quinolones, 8-oxyquinoline, nitrofuran, oxazolididinones, thiosemicarbazone.

E. Questions for self-training

1. Classification of antibiotics according to spectrum and mechanism of action, antibacterial effect.

2. Clinical pharmacology of penicillins: classification, spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
3. Cephalosporins: classification according to generations and mode of administration, spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
4. Carbapenems: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
5. Monobactams: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
6. Aminoglycosides: classification, spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
7. Tetracyclines: classification, spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
8. Amphenicols: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
9. Macrolides: classification, spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
10. Lincosamides: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
11. Ansamycins: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
12. Glycopeptides: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
13. Polypeptides: spectrum and mechanism of actions, peculiarities, indications and principles of selection, typical side effects and their prophylaxis, pharmacokinetics.
14. Indications and principles of antibiotics association (according to mechanism, spectrum of actions, and side effects).
15. Bacterial resistance to antibiotics (forms, development mechanisms, causes, ways of fighting).
16. Pharmacokinetic and pharmacodynamic peculiarities of antibiotics in children. Dosing principles. Side effects of antibiotics in children.
17. Peculiarities of antibiotic administration during pregnancy and lactation period.
18. Clinical pharmacology of sulfamides. Classification of sulfonamides by route of administration. Classification of systemic sulfonamides by duration of action. The particularities of the spectrum and the mechanism of action. Indications and principles of dosage and choice depending on the mode of administration. Pharmacokinetics. Combined sulfamides: spectrum and mechanism of action, indications. Adverse reactions - clinical manifestations, methods of prophylaxis and treatment. Contraindications. Drug interactions. Resistance and ways to fight. Peculiarities of sulfonamide administration during pregnancy and breastfeeding.
19. Naphthyridine derivatives and quinolones. Fluoroquinolones: classification. Non-fluorinated quinolones: action spectrum, indications. Fluorquinolones: classification, spectrum features and mechanism of action of fluorquinolones from different generations. Pharmacokinetic aspects. Indications and principles of selection and use. Absolute and relative contraindications. Adverse reactions - prophylaxis and their treatment. Drug interactions.
20. Derivatives of nitroimidazole: classification. Spectrum peculiarities and mechanism of action. Pharmacokinetic aspects. Indications and principles of selection and use. Contraindications. Side effects, their prophylaxis and treatment. Drug interactions.
21. Derivatives of 8-oxyquinoline. Spectrum peculiarities and mechanism of action of systemic and topical drugs. Pharmacokinetic aspects. Indications and principles of

selection and use. Contraindications. Side effects, their prophylaxis and treatment. Drug interactions.

22. Derivates of nitrofuran: classification. Spectrum peculiarities and mechanism of action of systemic, intestinal and topical drugs. Pharmacokinetic aspects. Indications and principles of selection and use. Contraindications. Side effects, their prophylaxis and combating. Drug interactions.
23. Oxazolidinediones. Spectrum peculiarities and mechanism of action, pharmacokinetic aspects. Indications and principles of selection and use. Contraindications. Side effects.
24. Pharmacokinetic and pharmacodynamics aspects of synthetic chemotherapeutic drugs in children. Peculiarities of synthetic chemotherapeutic drugs administration in pregnancy and lactation.

F. Individual Individual work (p. 1.1 and 1.2. are done in writing during the preparation process):

1.1. Indicate the pharmacological groups and drugs used in (for):

pneumonias caused by benzilpenicillin-resistant staphylococci; methicillin-resistant staphylococcal infections; follicular angina; acute pyelonephritis; antibacterial treatment in gastric and duodenal ulcers; nosocomial infections caused by Bac. fragilis; nosocomial infections caused by piocyanic bacillus (Ps.aeruginosa); oral cavity infections; infections of the skin and soft tissues; bone infections; urinary tract infections; infections caused by chlamydias, mycoplasmas; meningitis caused by H. influenzae; pseudomembranous colitis (Clostridium dificile); bacterial dysentery; tetanus; cholera; typhus abdominal; exanthematous typhus; prophylaxis of anaerobic infections in surgical interventions; intestinal infections; topical treatment of wounds, burns, trophic ulcers, bacterial dysentery; amebian dysentery; trichomonadosis, urinary infections; intestinal infections; infections caused by atypical germs (legionella, mycoplasmas, chlamydias); oral anaerobic infections; protozoal infections; pulmonary tuberculosis; nonspecific ulcerative enterocolitis; conjunctivitis; respiratory infections; systemic staphylococcal infections with poly-resistance.

1.2.For each indication, write the prescription(s) for the drug(s) of choice (from the list of mandatory drugs); the form of delivery and the dosage regimen should be appropriate for the respective pathology:

sodium benzylpenicillin, benzatinbenzylpenicillin, ampicillin, amoxicillin, carbenicillin, augmentin, imipenem, meropenem, cefuroxim, cefixim, cefotaxim, ceftriaxon, cefepim, ceftobiprol, gentamicin, sisomicin, amikacin, azitromicin, claritromicin, lincomycin, clindamicin, doxiciclin, cloramfenicol, rifampicin, vancomycin, colistin, fuzidin, sulfadimetoxim, sulfalen, ftalilsulfatiazol, sulfasalazin, co-trimoxazol, nalidixic acid, ciprofloxacin, lomefloxacin, moxifloxacin, norfloxacin, metronidazol, linesolid, tinezolid, nitroxolin, furazolidon, nifuroxazid.

1	**Name of the drug**	**Medicinal form/dose**
1	Benzathinbenzylpenicillin	Powder 1500000 IU; 1200000 IU; 600000 IU
2	Ampicillin	Capsules 0,25; 0,5 Powder 0,5; 1,0 in vials
3	Amoxicillin	Capsules 0,25; 0,5 Powder 0,5; 1,0 in vials
4	Amoxicillin + clavulanic acid	Tablets 0,5/0,125; 0,875/0,125 Powder for oral suspension 0,2/0,028/5ml; 0,4/0,057/5ml
5	Imipenem	Powder 0,5 in vials
6	Meropenem	Powder 0,5; 1,0 in vials
7	Cefuroxim	Tablets 0,25; 0,5 Granules for suspension 125/5ml-100ml;50ml Powder 0,75; 1,5 in vials
8	Cefixim	Tablets 0,4

		Capsules 0,2
9	Cefotaxim	Powder 1,0 in vials
10	Ceftriaxon	Powder 0,5; 1,0; 2,0 in vials
11	Cefepime	Powder 1,0 in vials
12	Gentamycin	Sol. 4%-2ml in ampoules
13	Amikacin	Powder 0,5; 1,0 in vials Sol. 25%-2ml in ampoules
14	Azithromycin	Tablets 0,5 Capsules 0,25 Powder 0,5 in vials Powder for suspension 0,2/5ml-15ml; 20ml;30ml
15	Clarithromycin	Tablets 0,25; 0,5 Granules for suspension 0,125/5ml-100ml; 0,25/5ml-100ml Powder 0,5 in vials
16	Lincomycin	Capsules 0,25 Sol.for injection 30%-1ml; 2ml in ampoules
17	Clindamycin	Capsules 0,15; 0,3
18	Doxycycline	Capsules 0,1
19	Chloramphenicol	Powder 1,0 in vials
20	Rifampicin+Izoniazid	Tablets 0,15/0,075
21	Vancomycin	Powder 1,0 in vials
22	Colistin	Powder1000000UI in vials
23	Sulfasalazine	Tablets 0,5
24	Ciprofloxacin	Tablets 0,25; 0,5; 0,75 Sol. 0,2%-100ml; 200ml in vials Sol.1%-10ml in ampoules
25	Norfloxacin	Tablets 0,4
26	Moxifloxacin	Tablets 0,4 Sol. 0,16%-250ml in vials
27	Metronidazole	Sol. for injection 0,5%-100ml in vials Tablets 0,25; 0,5
28	Nifuroxazide	Tablets 0,1 Capsules 0,1; 0,2 Oral suspension 4,4% - 90ml

2. Tests on Clinical Pharmacology (for faculty of medicine), Chisinau-2004, page 103.

G. Interactive activity

1. The didactic instructional work and the patient's discussion.

2. Clinical and pharmacological selection and use of drugs in some pathological conditions and diseases:

Principles of antibiotic selection and use in staphylococcal infections.

Principles of antibiotic selection and use in infections with gram-negative bacteria (Ps. Aeruginosae, Klebsiella pneumoniae, etc.).

Principles of antibiotic selection and use in anaerobic infections.

Principles of antibiotic selection and use in difficult Clostridium infections

Principles of antibiotic selection and use in infections with atypical agents.
Principles of rational use of antibiotics and antimicrobial synthetic chemotherapeutic agents with diverse chemical structure (empirical and targeted selection).

3. Clinical cases in Clinical Pharmacology (Clinical Cases Guide), Chisinau-2017, page 141.

4. Personal Drug (P-Drug) Selection and P-Treatment (Personal Treatment) according to the criteria of effectacy, safety, acceptability and cost for inclusion in the personal form (P drugs).