CLINICAL PHARMACOLOGY AND ITS TASKS. APPLICATION OF PHARMACOKINETIC, PHARMACODINAMIC AND PHARMACOGENETIC PRINCIPLES OF RATIONAL DRUGS ADMINISTRATION. THE CONCEPT OF RATIONAL USE OF MEDICATIONS. PRINCIPLES OF RATIONAL PRESCRIBING OF MEDICINAL REMEDIES (P-DRUG AND P-TREATMENT). FORMULARY SYSTEM. DRUGS FORMULARIES. MEDICAL AND ECONOMICAL STANDARDS OF MEDICAL ASSISTANCE AND CLINICAL PROTOCOLS IN THE MOST PREVALENT DISEASES AND PATHOLOGICAL STATES.

A. Actuality

Knowing the pharmacokinetic profile, the drug distribution parameters and transformation in the body, the relationship between their plasmatic concentration and the pharmacological effect will allow the rational selection of the most appropriate way of administration and the optimal regimen of drug dosing. The application of general principles about drugs effects, location and mechanism action is important for the study of special pharmacology and promoting of rational pharmacotherapy.

B. Training aim

Learning the general principles of pharmacokinetics, pharmacogenetics and pharmacodynamics for optimizing the administration and assessing the efficacy of medicinal substances.

C. Teaching objectives

The student must have the skills to:

a) choose a minimum set of investigation methods to assess the pharmacodynamic effect of different drugs depending on their group affiliation;

b) analyze and appreciate the results of pharmacodynamic study of different drug groups;

c) predict possible complications and side effects based on the pharmacokinetics and pharmacodynamics of drugs;

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

e) apply current methods of pharmacological and non-pharmacological correction of adverse reactions, determined by the pharmacokinetic, pharmacogenetic and pharmacodynamic peculiarities of the drugs.

D. Knowledge from previously studied disciplines and related subjects

Biochemistry. Mechanisms of biochemical processes regulation (adenylate cyclase mechanism, "ion pump" etc.). The ways of metabolizing the main groups of chemical compounds. Notions: dissociation, ionization, polarity. The main types of chemical bonds in organic compounds.

Physiology, pathophysiology, histology. Absorption of chemical compounds from the digestive tract, through the skin, after intramuscular, intravenous administration and administration by inhalation. Modification of absorption of chemical compounds in functional, morphological lesions of tissues, organs and systems. The functional state of the liver and its role in the metabolism of various chemicals. The regulatory function of the vegetative nervous system. Mediators and their role in regulating biological systems.

Clinical disciplines. Etiology, pathogenesis, clinical picture, para-clinical and laboratory data, principles of diseases and pathological conditions treatment. Indications, contraindications of drug administration. Notions of the *pathogenetic and symptomatic treatment* . Main manifestations of adverse reactions. Clinical investigations performing (electrocardiography,

spirography, pneumotachometry, cycloergometry, reography, etc.) and selecting the necessary laboratory investigations to study the pharmacodynamics of drug group.

Pharmacology. Fundamental principles of pharmacokinetics (absorption, distribution and redistribution, metabolism and elimination), pharmacogenetics (enzymes and influence of drugs on the genetic apparatus) and pharmacodynamics (notion of receptor, types and subtypes, primary and secondary pharmacological effects, typical mechanisms of action, notion of dose and its types, dose-effect relations, etc.). Interaction of drugs in the body: antagonism, synergism.

E. Questions for self-training

1. Clinical pharmacology and its tasks. The correlation between pharmacokinetics, pharmacogenetics and pharmacodynamics and evolution of drug effects. Applying pharmacokinetic, pharmacogenetic and pharmacodynamic principles to the rational administration of drugs.
2. Clinical pharmacokinetics. The main pharmacokinetic parameters: bioavailability, volume of distribution, clearance, half-life, plasma concentration, elimination rate constant. Their importance to optimize dosage regimens. Factors influencing the pharmacokinetic parameters of the drug.
3. Drug absorption. Routes of administration and their peculiarities. Factors influencing absorption. The importance of liposolubility and degree of drugs electrolytic dissociation. Interaction of drugs on the level of absorption.
4. The transport of drug molecules. Particularities of drug crossing through biological barriers and membranes. Distribution and redistribution of drugs. Plasma proteins, blood cells and their importance in the transport of drugs. Factors that influence distribution. Drug interaction on the level of distribution.
5. Drugs elimination and clearance.
6. Biochemical transformation of drugs. Metabolic pathways of drugs and their clinical importance. Drug metabolism during their associated and repeated administration. Microsomal enzyme inducing and inhibiting drugs. Particularities of drug metabolism in patients with hepatic disorders.
7. Excretion of drugs. Particularities of renal elimination. Interaction of drugs on the excretion level. Particularities of drug treatment in patients with renal pathology.
8. Elimination of medicinal substances by: bile, saliva, milk, lungs, skin. The role of the enterohepatic cycle in the recirculation of drugs.
9. Particularities of the pharmacokinetics of medicinal substances according to the age (in fetus, newborn, children, old people). The notion of geriatric drugs, recommendations in their administration.
10. Pharmacogenetics and its tasks. Clinical aspects of enzymopathies, enzyme induction and suppression. Genetic polymorphism. Influence of genetic polymorphism on drugs pharmacokinetics and pharmacodynamics.
11. Clinical pharmacodynamics. Receptors and drug-receptor interaction. Types and typical mechanisms of drug action.
12. The notion of molecular pharmacology. Drug action at molecular, submolecular levels. Nonspecific action of drugs at the molecular level.
13. The action of drugs at the cellular level. The peculiarities of their action on the cell membrane. The role of second messenger systems in drugs effect developing. Drug action on the intracellular level.
14. The action of drug substances on the level of anatomical and physiological systems and of the whole body. Particularities of drug interaction in organs and anatomical and physiological systems.
15. Dose and its varieties. Dose-effect correlation. Principles of drug dosing. Age based dosage. Dosing principles in various diseases and pathological conditions.

16. Individual factors that modify the effects of drugs: weight and body surface, gender, age, health state or illness, psychological factors, etc.
17. Basic aspects of chronopharmacology, pharmacotoxicology, pharmacoepidemiology, pharmacovigilance, pharmacoeconomics.
18. The concept of rational use of medications. Principles of prescribing and rational use of drugs (P drugs and P treatment).
19. Formulary system. Drugs formularies. Medical-economic standards of healthcare and clinical protocols for the treatment of the most widespread diseases and pathological conditions.
20. Clinical pharmacology of drugs in pregnancy. Nonprescription drugs (OTC) with high risk of influencing fetus and newborn. Drugs used cautiously during breastfeeding.
21. The concept of generic, original, compensated, orphan drug. The prescription for compensated drugs. Bioequivalence of drugs.
22. Therapeutic drug monitoring (TDM): tasks, indications, pharmacokinetic and pharmacodynamic particularities, clinical interpretation of drug concentration measurements.

F. Individual Work:

1. Tests on clinical pharmacology (for faculty of medicine). Chisinau, 2014, p.21.

2. Clinical cases in clinical pharmacology. Chisinau, 2017, p.5

3. Virtual situations.