

**CLINICAL PHARMACOLOGY AND ITS TASKS. APPLICATION OF  
PHARMACOKINETIC, PHARMACODYNAMIC AND PHARMACOGENETIC  
PRINCIPLES OF DRUGS ADMINISTRATION.  
THE CONCEPT OF RATIONAL USE AND RATIONAL PRESCRIBING OF MEDICINES  
(P-DRUG AND P-TREATMENT).  
FORMULARY SYSTEM. MEDICAL AND ECONOMICAL STANDARDS, 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, and 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 drug effects, location and mechanism action is essential for studying special pharmacology and promoting rational pharmacotherapy.

**B. Training aim**

To learn 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) to appreciate and use pharmacokinetic parameters in the study of preparations;
- b) to implement reforms in the field of medicine and the concept of rational use of medicines;
- c) to apply pharmacogenetic and pharmacogenomic aspects in treatment individualization;
- d) to use clinical standards and protocols in clinical activity;
- e) to elucidate and predict the effects of repeated and associated use of 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.** Aetiology, pathogenesis, clinical picture, paraclinical 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 performed (electrocardiography, spirometry, 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. Drug regulation.
2. The concept of rational use of medications. Principles of prescribing and rational use of drugs (P drugs and P treatment). Self-treatment (self-medication).
3. Formulary system. Medical-economic standards, clinical protocols for the treatment of the most widespread diseases and pathological conditions.
4. The concept of essential and vital medicines, original and generic drug, biosimilars, Over-the-Counter (OTC) medications, orphan drugs. Bioequivalence of drugs.
5. Personalized Medicine: its purpose and clinical importance. The role of Clinical Pharmacologists in Precision Medicine.
6. Complications of drug treatment. Classification of adverse reactions. Pharmacovigilance activity.
7. Basic aspects of pharmacoepidemiology, pharmacotoxicology and pharmacoeconomics.
8. Clinical pharmacokinetics. The main pharmacokinetic parameters: bioavailability, volume of distribution, clearance, half-life, plasma concentration and *elimination* rate constant. Their importance to optimize dosage regimens. Factors influencing the pharmacokinetic parameters of the drug.
9. 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.
10. 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.
11. Biochemical transformation of drugs. Metabolic pathways of drugs and their clinical importance. Drug metabolism during their associated and repeated administration. Phase I (Cytochrome P450) and phase II of hepatic drug metabolism, microsomal enzyme inducing and inhibiting drugs. Particularities of drug metabolism in patients with hepatic disorders.
12. Microsomal enzyme (Cytochrome P450) inducing and inhibiting drugs, substrates. Drug transporters and influence on drug pharmacokinetics.
13. Excretion of drugs. Particularities of renal elimination. Interaction of drugs on the excretion level. Particularities of drug treatment in patients with renal pathology. Elimination of medicinal substances by: bile, saliva, milk, lungs, skin. The role of the enterohepatic cycle in the recirculation of drugs.
14. Pharmacogenetics and its tasks. Clinical aspects of enzymopathies, enzyme induction and suppression. Genetic polymorphism. Influence of genetic polymorphism on drugs pharmacokinetics and pharmacodynamics.
15. The goal of Pharmacogenomics, its impact in personalized medicine.
16. Clinical pharmacodynamics. Receptors and drug-receptor interaction. Types and typical mechanisms of drug action.
17. The notion of molecular pharmacology. Drug action at molecular level. Nonspecific action of drugs at the molecular level.
18. The action of drugs at the cellular level. The peculiarities of their action on the cell membrane. The role of second messenger systems in drug effect development. Drug action on the intracellular level.
19. 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.

20. Dose and its varieties. Dose-effect correlation. Principles of drug dosing. Age based dosage. Dosing principles in various diseases and pathological conditions.
21. Individual factors that modify the effects of drugs: weight and body surface, gender, age, health state or illness, psychological factors, etc.
22. Particularities of the pharmacokinetics of medicinal substances according to the age (in fetus, newborn, children, old people). Principles of geriatric pharmacotherapy.
23. Pharmacotherapeutic aspects during pregnancy and breastfeeding (classification of drugs used in pregnancy (FDA classification system)). Information sources on the safety of medicines during pregnancy and breastfeeding (SmPC, databases, specialized books and journals, clinical guidelines).
24. The correlation between pharmacokinetics, pharmacogenetics and pharmacodynamics and evolution of drug effects. Applying pharmacokinetic, pharmacogenetic and pharmacodynamic principles to the rational administration of drugs.
25. Therapeutic drug monitoring (TDM): tasks, indications, pharmacokinetic and pharmacodynamic particularities, clinical interpretation of drug concentration measurements.

#### **F. Individual Work:**

1. **Tests.** *Tests on Clinical Pharmacology* (for faculty of medicine). Chisinau, 2014, p.21.

#### **G. Interactive activity**

1. **Clinical cases.** *Clinical cases in Clinical Pharmacology*, Chisinau, 2017, p.34.