Северный государственный медицинский университет

г. Архангельск

«СОГЛАСОВАНО»
Зав. кафедрой фармакологии,
д.м.н. И.А. Крылов

«_____»_____ 20 11 г.

«УТВЕРЖДАЮ»
Декан международного
факультета врача общей
практики, д.м.н. В.А. Болдуев

«_____»_____ 20 11 г.

WORKING PROGRAM

Pharmacology

(for general practitioners)

The international faculty (course "English Medium")

Chair of Pharmacy and Pharmacology
Years _____III_____

The terms _____5, 6_____

Lectures _____52_____ (hours)

End-of-year examination - __sixth___ term

Practical classes _____110___ (hours)

The test _____5_____ (term)

Total hours _____162_____

Arkhangelsk, 20 11 г.

The working program is arranged in accordance with:

1. State educational standard for general practitioner.
2. Pharmacology programs (2002).
3. The curriculum the North State Medical University.

Working program was confirmed on the chair conference

«___» _____ 200_11_

Head of chair

Ilya. A. Krylov

Part I

THE OBJECT AND THE TASKS OF DISCIPLINE, ITS PLACE IN CURRICULUM

1.1. The purpose of analysis of pharmacology is the acquisition by each student of a profound knowledge on pharmacology, to orient of the effects of drugs on the function of living systems; skills to use the obtained knowledge at the subsequent analysis of other fundamental and clinical disciplines, and also future practical activity of the doctor.

1.2. The students it is ground analyses of practical and idealized sections of pharmacology:

Should know:

1) Milestones of a history of pharmacology.
2) Methods of pharmacological researches and pharmacological terms (definitions).
3) Pharmaceutical classes of the drugs (pharmacologic classification).
4) Chemistry characteristics of main groups of the drugs.
5) Mechanism of action of the drugs (pharmacological actions).
6) Prevalence use of the main groups of the drugs (therapeutic applications).
7) Pharmacokinetic properties of some commonly used drugs.
8) Dosage regimen of some commonly used drugs.
9) Undesired effects of the main groups of the drugs (adverse effects, unwanted effects and dangers, toxicity) and their preventive maintenance.
10) Contraindications of some commonly used drugs.
11) Principles of drug combinations (some important interactions with other drugs).
12) Principles of the management of hypertensive emergencies.

Should know how:

1) Principles of clinical (therapeutic) efficacy.
2) Withdrawal symptoms (drug dependence).
3) Diagnosis and treatment of overdosage.
4) To use the scientific literature.

1.3. The title of disciplines interested in program division.

- The human physiology and anatomy: physiology of the autonomic nervous system, central nervous system, $GABA_A$ receptors, nociceptive and anti-nociceptive systems, electrophysiology of normal cardiac rhythm; normal regulation of blood pressure; renal tubule transport mechanisms; normal lipoprotein metabolism: synthesis and catabolism; mechanisms of blood coagulation, blood coagulation cascade (fibrin formation), initiation of clotting; hematopoiesis, the main components of the haemopoietic system; physiology and anatomy respiratory system; gastrointestinal system; the homeostatic mechanisms controlling energy balance; endocrine system; bone mineral homeostasis.
- Pathological anatomy: characteristic of inflammatory reactions, atheromatous disease, respiratory system disorders; gastrointestinal disorders; bone mineral homeostasis disorders.
- Pathological physiology: the immune response (acute or chronic), characteristic of inflammatory reactions, types of allergic or hypersensitivity reactions (immediate or anaphylactic hypersensitivity, antibody-dependent cytotoxic hypersensitivity, complex-mediated hypersensitivity, cell-mediated hypersensitivity), mediators of inflammation and immune reactions; the pathogenesis of major depression; parkinsonism pathophysiologic changes; types of heart failure; mechanisms of arrhythmias; pathophysiology of angina; systemic hypertension and regulation of blood pressure; atheromatous disease, modifiable risk factors for atheromatous disease; athophysiology of hyperlipoproteinaemia:

atherogenesis, lipoprotein transport in the blood; disorders of coagulation; types of anaemia; respiratory system disorders; gastrointestinal disorders; endocrine system disorders; bone mineral homeostasis disorders.

- Biochemistry: the cyclo-oxygenase family: tissue expression, functions; hormones; bone mineral homeostasis.
- General surgery: description of the stages of anesthesia.
- Microbiology and immunology: types of microorganisms, antibiotic resistance phenomen, the immune response (acute or chronic), characteristic of inflammatory reactions, types of allergic or hypersensitivity reactions.

Part II

VOLUME OF DISCIPLINE

The lessons	Hours
The lessons:	**162**
The lectures	52
The practical occupations	110
Laboratory work	**-**
Out-of-school work	**81**
In total	**243**

Part III

The terms.

The terms	Types of test
5	The nondifferecial test
6	Examine

Part IV

The content of discipline

4.1. The parts of discipline.

№	The section	The lectures (hours)	The practical occupations (hours)	Laboratory work (hours)
1.	**The General pharmacology**	**6**	**14**	**-**
2.	**The Private (systems) pharmacology**	**46**	**96**	**-**

4.2. Contents of the sections of discipline.

The Section I.

The General pharmacology.

Introduction to medical pharmacology. Basic principles of medical pharmacology. The history of pharmacology (pharmacology, pharmacopoeia, apothecary, materia medica). The nature of drugs. Definition of the drug, medicine, active drug, xenobiotic, poison, toxin. History of poison, uses of poison, biological poisoning, poisoning management (initial management, decontamination), specific antidotes, enhanced excretion. Characteristic (or properties) of drug mole-

cule (appropriate size, electrical charge /the degree of ionization of the drugs/, shape, and atomic composition, lipid-insoluble drugs, lipid-soluble drugs). Drug reactivity and drug-receptor bonds (covalent, electrostatic, and hydrophobic – their characteristic).

Experimental and clinical pharmacology. Clinical pharmacology: branches (pharmacodynamics, pharmacokinetics, rational prescribing, adverse drug effects, toxicology, drug interactions, drug development). Controlled clinical trial. Intercoupling between medical pharmacology and pharmaceutical industry. Pharmacogenomics (or pharmacogenetics, gene therapy), general aspects of gene therapy. Biotechnology: history, applications, pharmaceutical products, genetic testing, recombinant DNA technology. Pharmacoepidemiology (descriptive epidemiology, analytic epidemiology). Pharmacoeconomics: cost-minimization analysis, cost-effectiveness analysis, cost-benefit analysis, cost-of-illness, cost-utility analysis, disability-adjusted life year (DALY), global burden of disease, global comparative cost of pharmaceutical molecule, health utility index, health-adjusted life year (HALY), perspective (pharmacoeconomic), quality-adjusted life year (QALY), quality of life. Toxicology as a branch of medical pharmacology.The general notions of receptute.

Pharmacokinetic of the drugs (pharmacokinetic processes) (the part I): definition and uses of pharmacokinetics. Ways and means of the introduction medicine (routes of administration). The absorption (permeation): dissolution (the Noyes-Whitney equation), aqueous diffusion, lipid diffusion, special carriers (transporters), endocytosis and exocytosis, role of the ionization. Extent of absorbtion, rate of absorbtion. Transport medicinal material. Pharmacologic role of the P-glycoprotein /permeability glycoprotein/ (multidrug-resistance type 1 transporter), structure, ABCB1 transports various substrates across the cell membrane, detecting the activity of the transporter. Drug absorption from the intestine, factors affecting gastrointestinal absorption. Bioavailability and bioequivalence.

The effect (presystemic metabolism) of first-pass hepatic elimination: extraction ratio and the first-pass effect, alternative routes of administration and the first-pass effect. Prodrugs: definition, pharmacological means, classification (types and subtypes), examples. Distribution of the drugs (volume of distribution). Drug clearance principles: the ways of the elemination medicine from organism; renal excretion of drugs and drug metabolites (glomerular filtration, active tubular secretion, passive diffusion across tubular epithelium); half-life period ($t_{1/2}$) (probabilistic nature of half-life, formulae for half-life in exponential decay, half-life in non-exponential decay), drug accumulation (material and functional tapes; accumulation factors), mathematical modeling of the pharmacokinetic processes (single-compartment pharmacokinetic model, two-compartment model).

Pharmacokinetic of the drugs (pharmacokinetic processes) (the part II): metabolism of the drugs; the role of biotransformation in drug disposition. Drug biotransformation: phase I and phase II reactions. Microsomal mixed function oxidase system and phase I reactions. Human liver P_{450} enzymes and cytochrome P_{450} cycle in drug oxidations. The mechanisms of the action inductor and inhibitor ferment metabolism. Metabolism of drugs to toxic products (metabolism of acetaminophen to hepatotoxic metabolites). Clinical relevance of drug metabolism (individual differences in metabolic rate, genetic factors /slow acetylator phenotype/, diet and environmental factors, age and sex-dependent variations, drug-drug interactions during metabolism, interactions between Drugs and endogenous compounds, diseases affecting drug metabolism).

Pharmacodynamic processes and pharmacodynamic principles (drug-body interactions). The types of the action medicine. The repeated introduction of the drugs. Receptor nomenclature (International Union of Pharmacology (IUPHAR) Committee on Receptor Nomenclature and Drug Classification). Receptor hete-

rogeneity and subtypes. Macromolecular nature of drug receptors (regulatory proteins, G-proteins and second mssengers, transport proteins, structural proteins, ligand-gated channels). Types of drug-receptors: type 1 (ligand-gated ion channels), type 2 (G-protein-coupled receptors), type 3 (kinase-linked and related receptors), type 4 (nuclear receptors). Types of drug-receptor interactions: definition of pharmacologic antagonist drugs, mimic agonist drugs, receptor's affinity, drug-receptor complex, receptor-effector systems, specific macromolecules, natural ligands (hormones, neurotransmitters), drug-regulated ion channels, full agonists, partial agonists, selective agonists, functional selectivity, “spare" receptors (or a receptor reserve), definition of affinity. eceptors and inert binding sites. Relation between drug concentration and response: concentration-effect curves and receptor binding of agonists, receptor-effector coupling and spare receptors, competitive and irreversible antagonists. Drug antagonism (chemical antagonism, physiologic antagonism, pharmacokinetic antagonism, antagonism by receptor block /reversible competitive antagonism, irreversible, or non-equilibrium, competitive antagonism/, non-competitive antagonism). Relation between drug dose and clinical response. Graded dose-response relations (pharmacologic potency and maximal efficacy). Median effective dose (ED_{50}), median toxic dose (TD_{50}), median lethal dose (LD_{50}), minimum lethal dose, loading dose, "no-effect" dose, maintenance dose, course dose, dayly dose, single dose, therapeutic index, therapeutic window. The dose-concentration relationship (target concentration, maintenance dose). Beneficial or therapeutic effects. Duration of drug action: immediate effects, delayed effects, cumulative effects. Variation in drug responsiveness: unusual or idiosyncratic drug response, hyporeactive or hyperreactive, hypersensitivity, desensitization, tolerance, tachyphylaxis. Side effects of the drugs (adverse drug reactions, undesirable effects): classification (cause, seriousness and severity, overall drug risk, location), abnormal pharmacokinetics (comorbid disease states, genetic factors (phase I reactions, phase II reactions), interactions with other drugs (protein

binding, cytochrome P450), synergistic effects). Monitoring bodies. Examples of adverse effects associated with specific medications.

Special aspects of perinatal and pediatric pharmacology. Drug therapy in pregnancy: pharmacokinetics (lipid solubility, molecular weight and size, placental transporters, protein binding, placental and fetal drug metabolism), pharmacodynamics (maternal drug actions, therapeutic drug actions in the fetus, predictable toxic drug actions in the fetus, teratogenic drug actions), teratogenic agents, teratogenic mechanisms, defining a teratogen, counseling women about teratogenic risk, critical periods of human development, Wilson's 6 principles (The Six Principles of Teratology). General principles of drug therapy in infants and children: drug absorption (blood flow at the site of administration, gastrointestinal tract function), drug distribution, drug metabolism, drug excretion. Pediatric dosage forms and compliance. Drug use during lactation. Pediatric drug dosage: surface area, age and weight (calculations of dosage).

Special aspects of geriatric pharmacology. Pharmacologic changes associated with aging: effect of age on some physiologic functions, pharmacokinetic changes (absorption, distribution, metabolism, elimination), pharmacodynamic changes, behavioral and lifestyle changes. Major drug groups: sedative-hypnotics, opioid analgesics, traditional antipsychotic and antidepressant agents, drugs used in Alzheimer's disease, antihypertensive drugs, positive inotropic agents, antiarrhythmic agents, antimicrobial drugs, anti-inflammatory agents. Adverse drug reactions in the elderly.

Basic principles of drug discovery. Drug screening: the pharmacologic profile of the drug and screening procedure. Animal models of disease for the discovery of new therapeutic agents. Preclinical safety and toxicity testing (acute and chronic

toxicity of the new drugs). Evaluations in humans (clinical trials of the new drugs). The placebo response.

General principles of rational prescribing and prescription writing. Rational prescribing: rational steps. The prescription: a typical chart order, common form of outpatient prescription, elements of the prescription. Prescribing errors: omission of information, poor prescription writing, inappropriate drug prescriptions. Compliance (adherence). Labeled and unlabeled uses of drugs.

The Section II.

The Private (systems) pharmacology.

Vegetotropic drugs (autonomic pharmacology). Introduction to autonomic pharmacology: basic anatomy and physiology of the autonomic nervous system, neurotransmitter chemistry of the autonomic nervous system, general principles of chemical transmission, the main cotransmitters at postganglionic parasympathetic and sympathetic neurons. Characteristic of cholinergic transmission in the cholinergic synapses, acetylcholine metabolism (synthesis and release), types of cholinesterase enzyme, electrical events in transmission at fast cholinergic synapses. Adrenergic transmission. Autonomic receptor subtypes. Basic steps in neurochemical transmission: sites of drug action.

Cholinoceptor-activating (acetylcholine receptor stimulants, the direct-acting cholinomimetic drugs) and cholinesterase-inhibiting drugs: the major groups of cholinoceptor-activating drugs (classification), chemistry (molecular structures of choline esters and carbamic acid, structures of some cholinomimetic alkaloids, structure-activity relationships), pharmacokinetics (particularities of absorbtion, distribution, metabolism and elimination of this drugs), pharmacodynamics

(mechanism of action /the mechanism of muscarinic and nicotinic receptor activation/, organ system effects of muscarinic cholinoceptor stimulants: eye, cardiovascular system, respiratory system, gastrointestinal tract, genitourinary tract, miscellaneous secretory glands, central nervous system, peripheral nervous system, neuromuscular junction). Pharmacology of the indirect-acting cholinomimetic (cholinesterase-inhibiting drugs): pharmacologic classification (short-acting anticholinesterases, medium-duration anticholinesterases, reversible anticholinesterases, irreversible anticholinesterases), chemistry (characteristic of the three chemical groups of cholinesterase inhibitors, structure-activity relationships), structures of some organophosphate cholinesterase inhibitors and their pharmacologic characteristic, pharmacokinetics (particularities of absorbtion, distribution, metabolism and elimination of this drugs), pharmacodynamics (mechanism of action, organ system effects: eye, cardiovascular system, respiratory system, gastrointestinal tract, genitourinary tract, miscellaneous secretory glands, central nervous system, peripheral nervous system, neuromuscular junction). The major therapeutic uses of the cholinomimetic drugs, drugs that lower intraocular pressure. Said effects, acute and chronic toxicity of the cholinomimetic drugs. Contraindications to the use of muscarinic cholinoceptor stimulants drugs.

Cholinoceptor-blocking drugs (cholinoceptor antagonists). Basic pharmacology of the muscarinic receptor-blocking drugs: pharmacologic classification, source and chemistry (atropine and its naturally occurring congeners, structures of some semisynthetic and synthetic antimuscarinic drugs, structure-activity relationships), pharmacokinetics (particularities of absorbtion, distribution, metabolism and elimination of this drugs), pharmacodynamics (mechanism of action, organ system effects: eye, cardiovascular system, respiratory system, gastrointestinal tract, genitourinary tract, miscellaneous secretory glands, central nervous system), therapeutic applications (central nervous system disorders /Parkinson's disease, motion sickness/, ophthalmologic disorders, respiratory

use, cardiovascular disorders, gastrointestinal use, urinary disorders, cholinergic poisoning /antimuscarinic therapy, cholinesterase regenerator compounds/). Mushroom poisoning. Adverse effects. Contraindications to the use of antimuscarinic drugs. Drug interactions.

Basic pharmacology and characteristics of the ganglion-blocking drugs: pharmacologic classification, chemistry (structure-activity relationships), pharmacokinetics and pharmacodynamics (mechanism of action, organ system effects), therapeutic applications, adverse effects, contraindications to the use.

Basic pharmacology and characteristics of neuromuscular-blocking drugs (drugs that affect skeletal muscle function, skeletal muscle relaxants): history aspects, the mechanism of neuromuscular transmission, chemistry (structural relationship of succinylcholine, a depolarizing agent, and pancuronium, a nondepolarizing agent, to acetylcholine, the neuromuscular transmitter, structures of some isoquinoline neuromuscular blocking drugs, structures of steroid neuromuscular blocking drugs), effects and therapeutic applications of non-depolarising neuromuscular-blocking agents, effects and therapeutic applications of depolarising neuromuscular-blocking drugs. Unwanted effects and dangers of neuromuscular-blocking drugs.

Adrenoceptor-activating drugs. Adrenergic transmission, uptake and degradation of catecholamines, feedback control of noradrenaline release, metabolic degradation of catecholamines, characteristics of adrenoceptors: adrenoreceptor subtypes, receptor selectivity, molecular mechanisms of adrenoceptor-activating drugs, receptor regulation (desensitization /homologous, heterologous/, longer-term down-regulation, genetic adrenoreceptor polymorphisms). Biosynthesis of catecholamines. Chemistry: characteristic of chemical groups, structure-activity relationships, substitution on the amino group, substitution on the benzene ring, substitution on the alpha carbon, substitution on the beta carbon, chemical structure of phenylethylamine and some important catecholamines and noncatecholamine sympathomimetic drugs. Pharmacokinetics. Organ system effects: blood

vessels, heart, blood pressure, eye, respiratory system, gastrointestinal tract, genitourinary tract, metabolic effects (regulation of energy metabolism), effects on endocrine function and leukocytosis, effects on the central nervous system. Therapeutic use (cardiovascular applications, pulmonary applications, anaphylaxis, ophthalmic applications, genitourinary applications, central nervous system applications). The adverse effects of adrenoceptor agonists (toxicity of sympathomimetic drugs), drug interactions.

Alfa-adrenoceptor antagonists: the main groups of α-adrenoceptor antagonists and their pharmacologic characteristic (chemistry, pharmacokinetics, organ system effects, therapeutic applications, adverse effects and their preventive maintenance, drug interactions).

Beta-adrenoceptor antagonists: the pharmacological actions of β-receptor antagonists, and their pharmacologic characteristic (chemistry, pharmacokinetic properties, organ system effects, therapeutic applications, unwanted effects and their preventive maintenance, drug interactions).

Pharmacological control to allergies and inflammations. The immune response (acute or chronic), characteristic of inflammatory reactions, types of allergic or hypersensitivity reactions (immediate or anaphylactic hypersensitivity, antibody-dependent cytotoxic hypersensitivity, complex-mediated hypersensitivity, cell-mediated hypersensitivity). Mediators of inflammation and immune reactions: histamine (synthesis and storage, histamine release and actions, types of histamine receptors, pathophysiological roles of histamine), eicosanoids (structure and biosynthesis), prostanoids (catabolism of the prostanoids, prostanoid receptors, actions of the prostanoids, the role of the prostanoids in inflammation), leukotrienes (actions and receptors of the leukotrienes, the role of leukotrienes in inflammation), platelet-activating factor (sources of platelet-activating factor, actions and role in inflammation), bradykinin and lysyl bradykinin (source and formation of bradykinin, metabolism and inactivation of bradykinin,

actions and role of bradykinin in inflammation, bradykinin receptors). The cyclo-oxygenase family: tissue expression, functions, pharmacologic inhibitors. Therapeutic strategies (nonsteroidal anti-inflammatory drugs, glucocorticoids, disease-modifying antirheumatic drugs). Nonsteroidal anti-inflammatory drugs: pharmacologic classification (chemical classes), pharmacokinetic properties, pharmacodynamics (mechanisms of action: anti-inflammatory activity, analgesic effects, antipyretic effects, antiplatelet activity), clinical uses, dosage (optimal analgesic or antipyretic dose), adverse effects (local and systemic toxic effects) and their mechanism of the development and preventive maintenance, drug interactions. Salicylism, Reye's syndrome - mechanism of the development. Some important interactions with other drugs. Specifics of the COX-2 selective inhibitors (celecoxib, etoricoxib, valdecoxib, parecoxib).

Disease-modifyng antirheumatic drugs (antirheumatoid drugs): mechanism of antirheumatoid action, pharmacokinetic aspects, indications, adverse effects of the methotrexate, chlorambucil, cyclophosphamide, cyclosporine, azathioprine, mycophenolate mofetil, chloroquine and hydroxychloroquine, gold compounds, sulfasalazine.

Drugs used in gout: characteristic of the pathophysiologic events in a gouty joint, pharmacologic classification (inhibitors of uric acid synthesis, increasing uric acid excretion /uricosuric agents/, inhibitors of leucocyte migration into the joint, a general anti-inflammatory and analgesic effect), pharmacologic characteristic of colchicine and uricosuric drugs.

H_1-receptor antagonists (antihistamines drugs): pharmacologic classification (chemical classes), pharmacological actions, pharmacokinetic aspects, side-effects, drug interactions.

Pharmacology of central nervous system (CNS) drugs. Types of ion channels and neurotransmitter receptors in the CNS; $GABA_A$ receptor-chloride ion channel macromolecular complex, excitatory postsynaptic potential, inhibitory post-

synaptic potential, sites of drug action. Cellular organization of the brain: hierarchical systems, nonspecific or diffuse neuronal systems. Central neurotransmitters: amino acids (glutamate, glycine and GABA), acetylcholine, monoamines (dopamine and norepinephrine and 5-hydroxytryptamine /5-HT, serotonin/), CNS peptides, nitric oxide, endocannabinoids.

Basic pharmacology of sedative-hypnotic (anxiolytic) drugs: chemical classification and characteristic (benzodiazepines, barbiturates, chemical structures of newer hypnotics), pharmacokinetics (absorption and distribution, metabolic transformation, excretion, factors affecting biodisposition), pharmacodynamics of benzodiazepines, barbiturates and newer hypnotics (molecular components of the $GABA_A$ receptor, types of ligand-benzodia-zepine receptor interactions, organ level effects /sedation, hypnosis, anesthesia, anticonvulsant effects, muscle relaxation, effects on respiration and cardiovascular function/), tolerance; psychologic and physiologic dependence; adverse effects (direct toxic actions); benzodiazepine antagonists (flumazenil), drug interactions. Pharmacologic principles of treatment of anxiety states, sleep disorders, psychiatric and other therapeutic uses of sedative-hypnotic (anxiolytic) drugs.

Opioid analgesics and antagonists. Source. Pharmacological classification, chemistry characteristic. Endogenous opioid peptides. Pharmacokinetic properties: absorbtion, distribution, metabolism, excretion. Pharmacodynamics. Mechanism of action: receptor types, cellular actions, relation of physiologic effects to receptor type, receptor distribution and neural mechanisms of analgesia /spinal action, supraspinal actions/, tolerance and physical dependence /withdrawal or abstinence syndrome, the concept of receptor uncoupling/. Organ system effects of morphine and its surrogates: central nervous system effects (analgesia, euphoria, sedation, respiratory depression, cough suppression, miosis, truncal rigidity, nausea and vomiting, temperature), peripheral effects (cardiovascular system,

gastrointestinal tract, biliary tract, renal function, uterus, neuroendocrine, pruritus, miscellaneous). Effects of opioids with both agonist and antagonist actions. Clinical use of opioid analgesics: analgesia, acute pulmonary edema, cough, diarrhea, shivering, applications in anesthesia. Alternative routes of administrations. Toxicity. Undesired effects. Drug dependence: physical dependence, psychologic dependence. Tolerance. Cross-tolerance. Diagnosis and treatment of opioid overdosage. Contraindications and cautions in therapy. Use of pure agonists with weak partial agonists. Use in patients with head injuries. Use in patients with impaired pulmonary function. Use in patients with impaired hepatic or renal function. Use in patients with endocrine disease. Drug interactions. Specific agents: pharmacologic characteristic of strong agonists (phenanthrenes /morphine, hydromorphone, and oxymorphone, heroin/, phenylheptylamines /methadone/, phenylpiperidines / Fentanyl, sufentanil, alfentanil, remifentanil and meperidine/, morphinans /levorphanol/), mild to moderate agonists (phenanthrenes /codeine, oxycodone, dihydrocodeine and hydrocodone/, phenylheptylamines /propoxyphene/, phenylpiperidines /loperamide, diphenoxylate and its metabolite, difenoxin/), opioids with mixed receptor actions (phenanthrenes /nalbuphine, buprenorphine/, morphinans /butorphanol/, benzomorphans /pentazocine/), miscellaneous (tramadol), antitussives agents (dextromethorphan, codeine, levopropoxyphene), the pure opioid antagonist drugs (naloxone, naltrexone and nalmefene).

Drugs of abuse. Dependence versus addiction. Addictive drugs increase the level of dopamine: reinforcement. The dopamine hypothesis of addiction. Nonaddictive drugs of abuse. Opioids. Cannabinoids (endogenous cannabinoids and exogenous cannabinoids). Gamma-hydroxybutyric acid. Hallucinogens (LSD, mescaline and psilocybin). Drugs that mediate their effects via ionotropic receptors: nicotine, benzodiazepines (barbiturates), alcohol (ethanol), ketamine and

phencyclidine. Drugs that bind to transponters of biogenic amines: cocaine, amphetamines, ecstasy (methylenedioxymethamphetamine).

Antipsychotic (neuroleptic) agents. History aspects, terminology. Nature of psychosis and schizophrenia. Dopamine hypothesis for schizophrenia. Chemical types of antipsychotic (neuroleptic) drugs. First generation antipsychotics: butyrophenones (haloperidol, droperidol), phenothiazine derivatives (chlorpromazine, fluphenazine, perphenazine, prochlorperazine, thioridazine, trifluoperazine, mesoridazine, promazine, triflupromazine, levomepromazine, promethazine, pimozide), thioxanthenes (chlorprothixene, flupenthixol, thiothixene, zuclopenthixol). Second generation antipsychotics: clozapine (clozaril), olanzapine (zyprexa), risperidone (risperdal), quetiapine (seroquel), ziprasidone (geodon), amisulpride (solian), asenapine, paliperidone (invega). Third generation antipsychotics: aripiprazole (abilify), bifeprunox, norclozapine. Other options: tetrabenazine, cannabidiol.
Drug action. Structural formulas of some older antipsychotic drugs. Structural formulas of some newer antipsychotic drugs. Structural effects. Pharmacodynamics and central effects. Peripheral effects. Efficacy. Prevalence of use. Dosage and administration. Off-label and controversial uses. Side effects. Overdoses. Typical versus atypical. Drug interactions. Drug combinations. Tolerance and withdrawal.

Lithium carbonate and other mood-stabilizing drugs. Nature of bipolar affective (manic-depressive) disorder. Pharmacologic characteristic of lithium carbonate: mechanism of action, pharmacokinetic properties, pharmacodynamics (effects on electrolytes and ion transport, effects on neurotransmitters, effects on second messengers /effect of lithium on the IP_3 and DAG second-messenger system/). Clinical use: bipolar affective disorder, other applications (recurrent endogenous depression). Monitoring treatment. Maintenance treatment. Drug interactions.

Harmful effects of lithium and complications: neurologic and psychiatric adverse effects, decreased thyroid function, nephrogenic diabetes insipidus and other renal adverse effects, edema, cardiac adverse effects, use during pregnancy, miscellaneous adverse effects. Therapeutic overdoses. Other drugs: valproic acid (valproate), carbamazepine.

Antidepressant agents. The pathogenesis of major depression: the amine hypothesis and subsequent developments. Chemical structure. Structural relationships between various tricyclic antidepressants. Pharmacologic classification and characteristic (types of antidepressants). Selective serotonin reuptake inhibitors (SSRIs): citalopram, escitalopram, fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft). Serotonin-norepinephrine reuptake inhibitors (SNRIs): desvenlafaxine, duloxetine, milnacipram, venlafaxine. Noradrenergic and specific serotonergic antidepressants (NaSSAs): mianserin, mirtazapine. Norepinephrine (noradrenaline) reuptake inhibitors (NRIs): atomoxetine, mazindol, reboxetine, viloxazine. Norepinephrine-dopamine reuptake inhibitors (NDRIs): bupropion. Tricyclic antidepressants (TCAs): tertiary amine tricyclic antidepressants (amitriptyline, clomipramine, doxepin, imipramine, trimipramine), secondary amine tricyclic antidepressants (desipramine, nortriptyline, protriptyline). Monoamine oxidase inhibitor (MAOIs): isocarboxazid (Marplan), moclobemide, phenelzine, selegiline, tranylcypromine. Augmenter drugs: buspirone, gepirone, nefazodone, tandospirone, trazodone. Mechanisms of antidepressive pharmacologic action, anti-inflammatory and immunomodulation, clinical indications, therapeutic efficacy, long-term use, medication failure, withdrawal symptoms, side effects (general, sexual dysfunction, weight gain, thymoanesthesia, effects on REM sleep), overdoses, unresponsive patients, controversy, drug interactions.

Basic pharmacology of alcohol. Ethanol. Pharmacokinetics (alcohol absorbtion, metabolism /metabolism of ethanol by alcohol dehydrogenase and the microsomal ethanol-oxidizing system/, elimination), pharmacodynamics of acute ethanol consumption (central nervous system effects, heart effects and other system effects). Consequences of chronic alcohol consumption: liver and gastrointestinal tract (pathogenesis of alcoholic liver disease), nervous system (tolerance and physical dependence, neurotoxicity), cardiovascular system (cardiomyopathy and heart failure, arrhythmias, hypertension, coronary heart disease), blood changes, endocrine system and electrolyte balance, fetal alcohol syndrome, effects of alcohol on the immune system, increased risk of cancer. Alcohol-drug interactions (interactions between ethanol and other drugs, pharmacokinetic and pharmacodynamic alcohol interactions). Management of acute alcohol intoxication. Management of alcohol withdrawal syndrome. Treatment of alcoholism (treatment of alcohol dependence). Basic pharmacology of other alcohols: methanol (methyl alcohol, wood alcohol), ethylene glycol.

Antiseizure drugs (anticonvulsant, antiepileptic drugs). International classification of epileptic seizures. Chemistry (barbiturates, hydantoins, oxazolidinediones, succinimides and acetylureas), pharmacokinetic properties. Drugs used in partial seizures: phenytoin, carbamazepine, oxcarbazepine, phenobarbital, primidone (2-desoxyphenobarbital), vigabatrin, lamotrigine, felbamate, gabapentin, pregabalin, levetiracetam, tiagabine, topiramate, zonisamide. Drugs used in generalized seizures: ethosuximide, phensuximide and methsuximide, valproic acid and sodium valproate, oxazolidinediones. Treatment of infantile spasms. Management of status epilepticus.

Pharmacology of general anesthetics. Description of the stages of anesthesia. Classification of general anesthetics (intravenous anesthetics, inhaled anesthetics

- mode of administration). Method of action: lipid theory (Overton and Meyer), ion channels and other.

Pharmacology of inhaled anesthetics: pharmacokinetics (solubility, anesthetic concentration in the inspired air, pulmonary ventilation, pulmonary blood flow, anesthetic concentration gradient between arterial and mixed venous blood, elimination /clearance of inhaled anesthetics via the lungs/), pharmacodynamics (mechanism of action, dose-response characteristics: the concept of minimum alveolar anesthetic concentration; organ system effects of inhaled anesthetics: effects on the cardiovascular system, effects on the respiratory system, effects on the brain, effects on the kidney, effects on the liver, effect on uterine musculature), toxicity (hepatotoxicity, nephrotoxicity, malignant hyperthermia), chronic toxicity (mutagenicity, carcinogenicity, effects on reproductive organs, hematotoxicity), clinical use of inhaled anesthetics. Pharmacologic characteristic of ethers class (diethyl ether, methoxypropane, vinyl ether, halogenated ethers (desflurane, enflurane, isoflurane, methoxyflurane, sevoflurane), haloalkanes (chloroform, halothane, trichloroethylene), others (cyclopropane, ethylene, nitrous oxide, xenon).

Intravenous anesthetics: pharmacology of the barbiturates (hexobarbital, methohexital, narcobarbital, thiopental), benzodiazepines (diazepam, lorazepam and midazolam), opioid analgesics – neuroleptanesthesia (alfentanil, anileridine, fentanyl, phenoperidine, remifentanil, sufentanil), propofol (2,6-diisopropylphenol), group of neuroactive steroids (alfaxalone, minaxolone). Conscious sedation, dissociative anesthetic state, deep sedation.

Pharmacologic management of parkinsonism (paralysis agitans) and other movement disorders. Classification of parkinsonism, main signs and symptoms, pathophysiologic changes. Pharmacologic characteristic of L-dopa (levodopa), dopa decarboxylase inhibitors (carbidopa and benserazide), COMT enzyme inhibitors (tolcapone, entacapone), dopamine agonists (bromocriptine, pergolide,

pramipexole, ropinirole, cabergoline, apomorphine, and lisuride). Neurorehabilitation, prognosis. Research directions: gene therapy, neuroprotective treatments, complementary therapies.

Nootropic drugs. Availability and prevalence. Hazards. Nootropics and racetams. Piracetam group: pharmacologic effects, mechanisms of action, approval and usage, dosage, side effects, contraindications. Pharmacology of vinpocetine (cavinton): mechanism of action, possible nootropic properties, use as a vasodilator, negative effects, dosage.
Pharmacology of stimulants: amphetamines (amphetamine, methamphetamine, methylphenidate, pemoline), eugeroics /"wakefulness enhancers"/ (adrafinil, armodafinil, modafinil), xanthines (caffeine, theophylline).

Pharmacology of local anesthetics. Pharmacology of topical anesthesia (surface), infiltration, plexus block, epidural (extradural) block, spinal anesthesia (subarachnoid block). Chemistry characteristic, classification. Pharmacokinetic properties (local and systemic absorption, distribution, metabolism and elimination), pharmacodynamics (primary mechanism of action of local anesthetics, pharmacologic effects), undesired effects - toxicity (systemic effects following absorption /general adverse effects/, direct neurotoxicity, hypersensitivity and allergy, localized adverse effects, causes of localized symptoms), therapeutic applications, unwanted effects and their preventive maintenance, drug interactions.
Private pharmacology of local anesthetics. Local anesthetics in clinical use: esters (benzocaine, chloroprocaine, cocaine, cyclomethycaine, dimethocaine /larocaine/, propoxycaine, procaine /novocaine/, proparacaine, tetracaine /amethocaine/), amides group (articaine, bupivacaine, carticaine, cinchocaine /dibucaine/, etidocaine, levobupivacaine, lidocaine /lignocaine/, mepivacaine,

piperocaine, prilocaine, ropivacaine, trimecaine), combinations (lidocaine / prilocaine), natural local anesthetics (saxitoxin, tetrodotoxin).

Drugs used in heart failure. Types of heart failure (systolic failure, diastolic failure) and their characteristic. Control of normal cardiac contractility (sensitivity of the contractile proteins to calcium, the amount of calcium released from the sarcoplasmic reticulum, the amount of calcium stored in the sarcoplasmic reticulum, the amount of trigger calcium, activity of the sodium-calcium exchanger, intracellular sodium concentration and activity of Na^+/K^+ ATPase). Pathophysiology of heart failure. Compensatory responses that occur during congestive heart failure. Basic pharmacology of drugs used in heart failure. Cardiac glycosides group. Chemistry, pharmacokinetics (absorbtion and distribution, metabolism and excretion). Pharmacodynamics (molecular mechanisms of action; cardiac effects (mechanical effects, electrical effects), effects on other organs; side-effects and their prevention and treatment, drug interactions. Other positive inotropic drugs used in heart failure (general pharmacology): inhibitors of phosphodiesterases (bipyridines inamrinone and milrinone), group of beta-adrenoceptor stimulants (the selective β_1-agonists - dobutamine). Drugs without positive inotropic effect used in heart failure: diuretics, angiotensin-converting enzyme inhibitors, angiotensin AT_1-receptor-blockers drugs, vasodilators (hydralazine, isosorbide dinitrate, synthetic form of the endogenous peptide brain natriuretic peptide – nesiritide, inhibitor of endothelin - bosentan), beta-adrenoblockers drugs. Principles of management of acute heart failure.

Antiarrhythmic drugs - agents used in cardiac arrhythmias. Electrophysiology of normal cardiac rhythm, phases of the cardiac action, potential ionic basis of membrane electrical activity, mechanisms of arrhythmias, disturbances of impulse formation (ectopic pacemaker activity), disturbances of impulse conduction (block, reentry /"circus movement"/). Antiarrhythmic drugs. Pharmacologic

classification and characteristic (the Vaughan Williams classification (Vaughan Williams' Oxford group), introduced in 1970): class I agents interfere with the sodium channel (IA - Na^+ channel block (intermediate association/dissociation), IB - Na^+ channel block (fast association/dissociation), IC - Na^+ channel block (slow association/dissociation)), class II agents are anti-sympathetic nervous system agents, class III agents affect potassium (K^+) efflux, class IV agents affect calcium channels and the AV node (but not dihydropyridines). Cardiac effects, extracardiac effects, toxicity, drug interactions. Medicine applicable under atrial fibrillation, atrial flutter, ventricular tachycardia, and ventricular fibrillation.

Antianginal drugs. Pathophysiology of angina, causes of angina pectoris, determinants of myocardial oxygen demand, determinants of coronary blood flow and myocardial oxygen supply, determinants of vascular tone. Classification of IHD: myocardial ischemia: myocardial infarction, classic angina (atherosclerotic angina), vasospastic angina (variant angina or Prinzmetal's angina), acute coronary syndrome (unstable angina, myocardial infarction). Basic pharmacology of drugs used to treat angina and myocardial infarction. Drug groups use in angina (organic nitrates, calcium channel blockers, and beta-adrenoblockers drugs). Pharmacologic characteristic of organic nitrates: classifications, pharmacological actions, their pharmacologic characteristic (chemistry, pharmacokinetic properties, organ system effects /cardiac and peripheral/, therapeutic applications, unwanted effects /acute toxicities, tolerance, tachyphylaxis/ and their preventive maintenance), drug interactions. Pharmacologic characteristic of calcium channel-blocking drugs: classifications (chemical groups), mechanisms of the action, pharmacologic characteristic (chemistry, pharmacokinetic properties, organ system effects /cardiac and peripheral/, therapeutic applications, unwanted effects and their preventive maintenance), drug interactions. Pharmacologic characteristic of beta-adrenoblockers drugs: classifications (selective and nonselec-

tive), mechanisms of the action, pharmacologic characteristic (chemistry, pharmacokinetic properties, organ system effects /cardiac and peripheral/, therapeutic applications, unwanted effects and their preventive maintenance), drug interactions. Management of the myocardial infarction: thrombolytic and antiplatelet drugs, opioids, beta-adrenoceptor antagonists, angiotensin-converting enzyme inhibitors. Pharmacologic characteristic of cardioprotective drugs (trimetazidine).

Antihypertensive drugs. Systemic hypertension and regulation of blood pressure. Etiology of hypertension. Normal regulation of blood pressure. Basic pharmacology of antihypertensive drugs.

Diuretics as a antihypertensive agents: their pharmacologic characteristic. Sympathoplegic agents: their pharmacologic characteristic.

Agents that block production or action of angiotensin (angiotensin-converting enzyme inhibitors). Physiologic characteristic of renin-angiotensin-aldosterone system. Classification of angiotensin-converting enzyme inhibitors: sulfhydryl-containing agents (captopril, zofenopril), dicarboxylate-containing agents (enalapril, ramipril, quinapril, perindopril, lisinopril, benazepril), phosphonate-containing agents (fosinopril) and their pharmacologic characteristic.

Angiotensin II receptor antagonists: losartan, valsartan, candesartan, eprosartan, irbesartan, telmisartan.

Ganglion blockers: their pharmacologic characteristic.

Adrenergic neuron-blocking drugs (guanethidine, guanadrel, bethanidine, debrisoquin, reserpine) their pharmacologic characteristic.

Centrally acting sympathoplegic drugs (methyldopa, clonidine, guanabenz and guanfacine): mechanisms and sites of action, pharmacokinetic characteristics, dosage, undesirable effects, contraindications to use, drug interactions.

Adrenoceptor antagonists: α- and β-adrenoceptor blockers drugs as a antihypertensive agents.

Calcium channel blockers drugs as a antihypertensive agents: pharmacologic classification (chemical classes), pharmacological actions, pharmacokinetic aspects and side-effects, contraindications to use, drug interactions.
Principles of the management of hypertensive emergencies.
Drugs used in pulmonary hypertension: oral anticoagulants, diuretics, calcium channel blockers, epoprostenol, prostanoid analogues (iloprost, treprostinil, beraprost), phosphodiesterase V inhibitor (sildenafil), cardiac glycosides, activators of soluble guanylate cyclase (cinaciguat and riociguat).

Diuretic agents. Renal tubule transport mechanisms: proximal tubule (proximal convoluted tubule), loop of henle, distal convoluted tubule, collecting tubule. Basic pharmacology of diuretic agents. Carbonic anhydrase inhibitors (acetazolamide): pharmacokinetics, pharmacodynamics, clinical Indications (reduction of aqueous humor formation, urinary alkalization, metabolic alkalosis, acute mountain sickness) and dosage, toxicity (hyperchloremic metabolic acidosis, renal stones, renal potassium wasting), contraindications. Group of loop diuretics (furosemide and ethacrynic acid): chemistry characteristic, pharmacokinetic properties, aspects of pharmacodynamic, clinical Indications and dosage, toxicity, contraindications. Thiazide diuretics: pharmacologic characteristic of hydrochlorothiazide (chemistry, pharmacokinetics, mechanism of the action, pharmacologic effects, clinical efficacy, therapeutic applications, unwanted effects and dangers, contraindications). Group of potassium-sparing diuretics: spironolactone, eplerenone, amiloride, triamterene (chemical structures, pharmacokinetics, mechanism of the action, pharmacodynamic effects, clinical indications and dosage, side effects, contraindications. Agents that alter water excretion. Group of osmotic diuretics: pharmacologic characteristic of mannitol. Antidiuretic hormone (ADH) agonists: pharmacologic characteristic of vasopressin and desmopressin. Antidiuretic hormone antagonists: pharmacology of conivaptan (pharmacokinetics, mechanism of the action, pharmacodynamic effects, clin-

ical indications and dosage, side effects, contraindications). Diuretic combinations.

Atherosclerosis and lipoprotein metabolism. Normal lipoprotein metabolism: synthesis and catabolism. Atheromatous disease, modifiable risk factors for atheromatous disease. Pathophysiology of hyperlipoproteinaemia: atherogenesis, lipoprotein transport in the blood. Dyslipidaemia, Frederickson / World Health Organization classification of hyperlipoproteinaemia. The main agents used clinically: statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors - lovastatin, atorvastatin, fluvastatin, pravastatin, simvastatin, rosuvastatin), fibric acid derivatives (gemfibrozil, fenofibrate, bezafibrate), inhibitors of cholesterol absorption /bile acid-binding resins/ (colestyramine, colestipol, colesevelam), inhibitors of intestinal sretol absorption (ezetimibe), nicotinic acid or its derivatives, fish oil derivatives: pharmacological actions, pharmacokinetic aspects and side-effects, contraindications to use. Principals of combined drug therapy of hyperlipoproteinaemia (fibric acid derivatives and bile acid-binding resins, HMG-CoA reductase inhibitors and bile acid-binding resins, niacin and bile acid-binding resins, niacin and reductase inhibitors, reductase inhibitors and ezetimibe, reductase inhibitors and fibrates). Dietary management of hyperlipoproteinaemia (general principals).

Drugs used in disorders of coagulation. Mechanisms of blood coagulation, blood coagulation cascade (fibrin formation), initiation of clotting: the tissue factor-VIIa complex. Fibrinolysis. Characteristic of the fibrinolytic system. Pharmacologic classification of the drugs used in disorders of coagulation. Pharmacology of the anticoagulant drugs. The indirect thrombin inhibitors (heparin and low-molecular-weight heparins /enoxaparin, dalteparin, fondaparinux/): chemistry (subunit structure of heparin) and mechanism of action, administration, dosage, drug interactions, laboratory monitoring of heparin effect, toxicity, contraindica-

tions. The direct thrombin inhibitors: chemistry, mechanism of action, administration, dosage, drug interactions, laboratory monitoring, toxicity, contraindications. Pharmacology of the fibrinolytic drugs (streptokinase, urokinase, anistreplase, alteplase, reteplase, tenecteplase, duteplase): chemistry, mechanism of action, administration, dosage, drug interactions, laboratory monitoring, toxicity, contraindications. Pharmacology of the antiplatelet drugs (clopidogrel, ticlopidine, aspirin, dipyridamole): chemistry, mechanism of action, administration, dosage, drug interactions, laboratory monitoring, adverse effects, contraindications. Pharmacology of the platelet glycoprotein IIb/IIIa receptors inhibitors (abciximab, eptifibatide, tirofiban): mechanism of action, administration, dosage, drug interactions, negative effects, contraindications. Pharmacology of the drugs used in bleeding disorders. vitamin K: sources and preparations, administration and pharmacokinetic aspects, clinical uses. Pharmacology of the inhibitors of fibrinolysis - aminocaproic acid. Pharmacologic characteristic of the serine protease inhibitors – aprotinin.

Agents used in anemias. Hematopoiesis, the main components of the haemopoietic system, types of anaemia. Iron (iron salts): pharmacokinetics (absorbtion, transport, distribution of iron in the body, storage, elimination, iron turnover and balance), indications for the use of iron, treatment (oral iron therapy, parenteral iron therapy), clinical toxicity (acute and chronic iron toxicity), drug interactions, contraindications. The treatment of acute and chronic iron toxicity. Vitamin B_{12}: their biochemical actions, the role of vitamin B_{12} in the synthesis of folate polyglutamate, chemistry, pharmacokinetics, pharmacodynamics, clinical uses (megaloblastic anemia, pernicious anemia). Pharmacologic characteristic of the folic acid (pteroylglutamic acid): chemistry, pharmacokinetics, pharmacodynamics, clinical applications. Pharmacology of the hematopoietic growth factors and colony-stimulating factors: erythropoietin (epoetin alfa), granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating fac-

tor (GM-CSF), and interleukin-11 (IL-11), pegfilgrastim, sargramostim, darbopoietin, lenograstim.

Pharmacology of respiratory system disorders. Basic aspects of the physiology of the respiratory system. Pathogenesis of the bronchial asthma and "aspirin-sensitive" asthma, chronic obstructive pulmonary disease. Categories of anti-asthma drugs: bronchodilators (β_2-adrenoceptor agonists, methylxanthines, muscarinic receptor antagonists /ipratropium, thiotropium/) /short- and long-acting inhaled bronchodilators/ and anti-inflammatory (cysteinyl leukotriene receptor antagonists, glucocorticoids, cromoglicate and nedocromil, anti-IgE - monoclonal antibodies treatment /omalizumab/) agents their pharmacological characteristic. Management of the severe acute asthma (status asthmaticus). Chronic obstructive pulmonary disease: pathogenesis, principles of treatment, specific aspects of treatment. Pulmonary surfactants drugs their pharmacological characteristic.

Drugs used in the treatment of gastrointestinal diseases. Drugs used in the acid-peptic diseases. Agents that reduce intragastric activity. Physiology of acid secretion (physiologic control of hydrogen ion secretion by the gastric parietal cell. ECL cell, enterochromaffin-like cell; G (CCK-B), gastrin-cholecystokinin-B receptor; H, histamine; H_2, histamine H_2 receptor; M_1, M_3, muscarinic receptors; ST_2, somatostatin-2 receptor; ATPase, H^+/K^+ ATPase proton pump). Role of *H. pylori* in ulcer disease. Antacids: chemistry, pharmacokinetic properties, effects, therapeutic applications, unwanted effects and their preventive maintenance, drug interactions. H_2-receptor antagonists (H_2-receptor-blocking drugs): chemistry, pharmacokinetics, effects, clinical uses, unwanted effects (mental status changes, endocrine effects, pregnancy and nursing mothers) and their preventive maintenance, drug interactions. Group of the proton pump inhibitors: chemistry (molecular structure of the proton pump inhibitors), pharmacokinetic

properties, effects, therapeutic applications, unwanted effects and their preventive maintenance, drug interactions. Mucosal protective agents: mucosal prostaglandin analogs (misoprostol), sucralfate, colloidal bismuth compounds (bismuth subsalicylate, bismuth subcitrate and bismuth dinitrate). Drugs stimulating gastrointestinal motility - drugs that selectively stimulate gut motor function (prokinetic agents): physiology of the enteric nervous system; 5-HT_3-receptor antagonists and 5-HT_4-receptor agonists, cholinomimetic agonists (bethanechol, neostigmine), D_2 receptor antagonists (metoclopramide and domperidone). Laxatives: classification (bulk-forming laxatives, stool surfactant agents /softeners/, osmotic laxatives, stimulant laxatives /cathartics/, serotonin 5-HT_4 receptors agonists), chemistry, pharmacokinetic properties, effects, therapeutic applications, unwanted effects and their preventive maintenance, drug interactions. Pharmacology of the antidiarrheal agents: opioid agonists, colloidal bismuth compounds, bile salt-binding resins (cholestyramine, colestipol), octreotide (somatostatin). Drugs used in the treatment of irritable bowel syndrome (directions of the pharmacologic therapies for irritable bowel syndrome): antispasmodics (anticholinergics), serotonin 5-HT_3 receptors antagonists (blockers of central 5-HT_3 receptors)/ ondansetron, granisetron, dolasetron, and alosetron; and the 5-HT_4 partial agonist tegaserod/, serotonin 5-HT_4 receptors antagonists. Antiemetic agents: selective serotonin 5-HT_3-receptor antagonists, neurokinin 1 (NK_1) receptor antagonists, phenothiazines, butyrophenones, substituted benzamides (metoclopramide and trimethobenzamide), anticholinergic agents, H_1-receptor antagonists, benzodiazepines, cannabinoids (dronabinol, nabilone). Drugs used to treat inflammatory bowel disease: Drugs that contain 5-aminosalicylic acid - aminosalicylates - (sulfasalazine, olsalazine, balsalazide, and various forms of mesalamine), glucocorticoids, purine analogs (azathioprine and 6-mercaptopurine), methotrexate, anti-tumor necrosis factor therapy (infliximab, adalimumab, certolizumab). Pancreatic enzyme supplements. Pharmacologic

characteristic of the creon, pancrease, ultrase. Bile acid therapy for gallstones: pharmacologic characteristic of the ursodiol (ursodeoxycholic acid).

Obesity treatment. The homeostatic mechanisms controlling energy balance: the role of leptin, insulin and hypothalamic peptides in the regulation of energy balance and fat stores, integration of information and effect on energy balance, regulation of food intake and energy expenditure. The pathophysiology of human obesity: obesity as a disorder of homeostatic control of energy balance, genetic factors and obesity, food intake and obesity, physical exercise and obesity. Pharmacological approaches to the problem of obesity. Pharmacologic characteristic of 'anorectic' (e.g. appetite suppressant) agents: amphetamines, fenfluramine, sibutramine and orlistat (mechanism of action, pharmacologic effects, pharmacokinetic aspects, clinical efficacy, unwanted effects).

Pharmacology of hypothalamic and pituitary hormones. Physiology of hypothalamic-pituitary endocrine system. Anterior pituitary hormones and their hypothalamic regulators. Growth hormone (somatotropin): chemistry and pharmacokinetics, pharmacodynamics, uses of growth hormone, toxicity and contraindications. Growth hormone antagonists: pharmacologic characteristic of somatostatin, octreotide and pegvisomant. The gonadotropins (follicle-stimulating hormone, luteinizing hormone and human chorionic gonadotropin): chemistry and pharmacokinetics, pharmacodynamics, therapeutic applications, unwanted effects and their preventive maintenance, drug interactions. Gonadotropin-releasing hormone and its synthetic analogs (goserelin, histrelin, leuprolide, nafarelin, and triptorelin): chemistry, pharmacokinetics, pharmacodynamics, therapeutic applications, unwanted effects. GnRH (gonadotropin-releasing hormone) receptor antagonists (ganirelix and cetrorelix): pharmacologic characteristic. Pharmacologic characteristic of prolactin. Dopamine agonists (bromocriptine, cabergoline, pergolide and quinagolide): chemistry, pharmacokinetics,

pharmacodynamics, clinical uses, clinical toxicity, contraindications. Pharmacologic characteristic of posterior pituitary hormones: vasopressin and oxytocin (antidiuretic hormon). Vasopressin antagonists: conivaptan and tolvaptan.

Pharmacology of pancreatic hormones and antidiabetic drugs. The endocrine pancreas; categories of diabetes mellitus (the current classification of diabetes mellitus): type 1, insulin-dependent diabetes; type 2, noninsulin-dependent diabetes; type 3, other; and type 4, gestational diabetes mellitus (Expert Committee, 2003). Insulin: chemistry, insulin secretion, insulin degradation, circulating insulin, the insulin receptor, effects of insulin on its targets. Characteristics of available insulin preparations (commercial insulin preparations): rapid-acting, with very fast onset and short duration; short-acting, with rapid onset of action; intermediate-acting; and long-acting, with slow onset of action. Insulin analogs by recombinant DNA techniques. Insulin delivery systems: portable pen-sized injectors, continuous subcutaneous insulin infusion devices, inhaled insulin preparation. Treatment with insulin, benefit of glycemic control in diabetes mellitus. Complications of insulin therapy: hypoglycemic reactions (mechanisms and diagnosis, treatment of hypoglycemia), immunopathology of insulin therapy (insulin allergy, immune insulin resistance), lipodystrophy at injection sites. The oral antidiabetic agents. Insulin secretagogues. Sulfonylureas: mechanism of action, efficacy and safety of the sulfonylureas, first-generation sulfonylureas (tolbutamide, chlorpropamide, tolazamide), second-generation sulfonylureas (glyburide, glipizide, and glimepiride), secondary failure and tachyphylaxis to sulfonylureas. Meglitinides: mechanism of action, efficacy and safety. D-phenylalanine derivative: mechanism of action, efficacy and safety of the nateglinide. Biguanides: mechanisms of action, metabolism and excretion, clinical use, toxic effects, contraindications. Thiazolidinediones: mechanisms of action, pharmacologic characteristic of the pioglitazone and rosiglitazone. Alpha-glucosidase inhibitors: pharmacologic characteristic of the acarbose and migli-

tol. Pharmacologic characteristic of the pramlintide, exenatide, sitagliptin. Principles of the combination therapy with oral antidiabetic agents and injectable medication. Pharmacology of glucagon: chemistry characteristic and metabolism, "Gut Glucagon", pharmacologic effects of glucagon (metabolic effects, cardiac effects, effects on smooth muscle), therapeutic applications (severe hypoglycemic reactions, diagnose endocrine disorders, beta-blocker poisoning, radiology of the bowel), adverse reactions.

Pharmacology of thyroid and antithyroid drugs. Basic thyroid physiology: iodide metabolism, biosynthesis of thyroid hormones, peripheral metabolism of thyroxine, transport of thyroid hormones, evaluation of thyroid function (thyroid-pituitary relationships, autoregulation of the thyroid gland, abnormal thyroid stimulators). Pharmacology of thyroid drugs. Thyroid hormones: chemistry (the structural formulas of thyroxine and triiodothyronine), pharmacokinetic properties, mechanism of action, model of the interaction of T3 with the T3 receptor, pharmacologic effects of thyroid hormones, thyroid preparations, drug interactions, laboratory monitoring, adverse effects, contraindications. Pharmacology of antithyroid drugs. Thioamides (methimazole and propylthiouracil): chemical structures, pharmacokinetics, mechanisms, pharmacodynamics, adverse reactions to the thioamides. Anion inhibitors: pharmacologic characteristic. Iodides: pharmacodynamics, clinical use of iodide, adverse reactions to iodine (iodism). Radioactive iodine, adrenoceptor-blocking agents. Principles of the management of hypothyroidism: special problems in management of hypothyroidism (myxedema coma, hypothyroidism and pregnamcy, subclinical hypothyroidism, drug-induced hypothyroidism). Principles of the management of hyperthyroidism: Graves' disease (antithyroid drug therapy, radioiodine therapy, adjuncts to atntithyroid therapy). Toxic uninodular goiter and toxic multinodular goiter, subacute thyroiditis, special problems (thyroid storm, ophthalmopathy, dermopathy or pretibial myxedema, thyrotoxicosis during pregnancy, neonatal Graves' dis-

ease, subclinical hyperthyroidism, amiodarone-induced thyrotoxicosis, nontoxic goiter, thyroid neoplasms). Preparations available: thyroid agents (Levothyroxine [T4], Liothyronine [T3], Liotrix, Thyroid desiccated [USP]), antithyroid drugs (Diatrizoate sodium, Iodide (131I) sodium, Iohexol, Methimazole, Potassium iodide, Propylthiouracil, Thyrotropin; recombinant human TSH).

Pharmacology of adrenocorticosteroids and adrenocortical antagonists. Pharmacologic classification. The naturally occurring glucocorticoids, cortisol (hydrocotisone): pharmacokinetic characteristics, pharmacodynamic properties (mechanism of glucocorticoid action, basic pharmacologic effects, metabolic effects, catabolic and antianabolic effects, anti-inflammatory and immunosuppressive effects). Synthetic corticosteroids: pharmacokinetics (source, disposition), pharmacodynamic properties (the actions of the synthetic steroids, glucocorticoid to mineralocorticoid potency). Therapeutic applications: adrenocortical insufficiency (chronic (Addison's disease), acute adrenocortical insufficiency), adrenocortical hypo- and hyperfunction (congenital adrenal hyperplasia, Cushing's syndrome, primary aldosteronism, secondary aldosteronism), use of glucocorticoids for diagnostic purposes (dexamethasone suppression test), toxicity (metabolic effects, peptic ulcers, growth-suppressing potency, adrenal suppression), contraindications and cautions (special precautions, contraindications), selection of drug and dosage schedule (acth versus adrenocortical steroids, dosage regimen, special dosage forms /topical preparations for skin disease, ophthalmic forms for eye disease, intra-articular injections for joint disease, inhaled steroids for asthma/). Pharmacology of mineralocorticoid (aldosterone, deoxycorticosterone, fludrocortisone): physiologic and pharmacologic effects, metabolism (pharmacokinetic properties). Antagonists of adrenocortical agents. Synthesis inhibitors and glucocorticoid antagonists (metyrapone, aminoglutethimide, ketoconazole, mifepristone, mitotane, trilostane). Mineralocorticoid antagonists: spironolactone, eplerenone, drospirenone (pharmacologic characteristic). Prepara-

tions available. Glucocorticoids: betamethasone, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, methylprednisolone, methylprednisolone acetate, prednisolone, prednisolone sodium phosphate, triamcinolone. Mineralocorticoids: fludrocortisone acetate. Mineralocorticoid antagonists: aminoglutethimide, ketoconazole, mifepristone, mitotane.

Pharmacology of gonadal hormones and inhibitors. The ovary (estrogens, progestins, other ovarian hormones, oral contraceptives, inhibitors and antagonists, ovulation-inducing agents). The menstrual cycle, plasma levels of pituitary and ovarian hormones and histologic changes, disturbances in ovarian function. The estrogens. Natural Estrogens: estradiol (estradiol-17b, E2), estrone (E1), and estriol (E3), biosynthesis and metabolism. Synthetic estrogens: chemical compounds with estrogenic activity, pharmacokinetics, mechanism of action, female maturation, endometrial effects, metabolic and cardiovascular effects, effects on blood coagulation, clinical uses (primary hypogonadism, postmenopausal hormonal therapy, intractable dysmenorrhea, hirsutism and amenorrhea), unwanted effects and dangers (postmenopausal uterine bleeding, cancer), contraindications, preparations and dosages (diethylstilbestrol diphosphate, estradiol cypionate in oil, estradiol, estradiol valerate in oil, estrone). The progestins. Natural progestins: progesterone (its characteristis). Synthetic progestins: chemistry characteristics, pharmacokinetic properties, mechanism of action, spectrum of pharmacologic effects, clinical uses of progestins (hormone replacement therapy, hormonal contraception, diagnostic uses), contraindications, cautions and adverse effects. Hormonal contraception (oral, parenteral and implanted contraceptives). Pharmacologic classification (monophasic, biphasic and triphasic forms), mechanism of action, spectrum of pharmacologic effects (effects on the ovary, effects on the uterus, effects on the breast, effects on the central nervous system, effects on endocrine function, effects on blood, effects on the liver,

effects on lipid metabolism, effects on carbohydrate metabolism, effects on the cardiovascular system, effects on the skin), therapeutic applications (oral contraception, treatment of endometriosis, prevents the periodic breakdown of the endometrial tissue, endometrial fibrosis), adverse effects (mild, moderate adverse effects, severe adverse effects), contraindications and cautions, contraception with progestins alone, postcoital contraceptives, beneficial effects of oral contraceptives, hormonal preparations (hydroxyprogesterone caproate, levonorgestrel, medroxyprogesterone acetate, megestrol acetate, norethindrone acetate, norgestrel, progesterone). Estrogen and progesterone inhibitors and antagonists. Tamoxifen and related partial agonist estrogens its pharmacologic characteristic. Pharmacology of mifepristone, danazol. Ovulation-inducing drugs (clomiphene citrate): mechanism of action, pharmacologic effects, clinical use, side-effects, contraindications and cautions. Androgens and anabolic steroids: metabolism, synthetic steroids with androgenic and anabolic action, mechanisms of action, pharmacologic effects, clinical uses (androgen replacement therapy in men, gynecologic disorders, use as protein anabolic agents, anemias, osteoporosis, stimulate growth, anabolic steroid and androgen abuse in sports, aging), adverse effects of these compounds, contraindications. Pharmacology of antiandrogens: steroid synthesis inhibitors, conversion of steroid precursors to androgens, receptor inhibitors. Oral contraceptive for men (Gossypol).

Agents that affect bone mineral homeostasis. Mechanisms contributing to bone mineral homeostasis. The hormonal interactions controlling bone mineral homeostasis. Principal hormonal regulators of bone mineral homeostasis (parathyroid hormone, vitamin D, glucocorticoid hormones, estrogens). Pharmacologic characteristic of vitamin D, metabolites and analogs (calcitriol, cholecalciferol [D3], doxercalciferol, ergocalciferol [D2] (vitamin D2, calciferol), paricalcitol), calcium preparations, phosphate.

Chemotherapeutic drugs. Pharmacology of antimicrobial agents. General principles of antimicrobial therapy. Antibiotic: definition, main characteristics (properties), pharmacologic groups. Gram-positive and Gram-negative bacteria: biological organization. Minimum inhibitory concentration (definition). History of antibiotics: role of Louis Pasteur, Robert Koch, Alexander Fleming, Ernst Chain, Howard Florey and Paul Ehrlich. Characteristic of bactericidal or bacteriostatic effects. "Narrow-spectrum" and broad-spectrum antibiotics: definition, examples. Classification of antibiotics (mechanism of action, production (sources). Negative effects of antibiotic drugs and their prophylactic. Antibiotic resistance: definition, tapes, molecular mechanisms. Empiric antimicrobial therapy, approach to empiric therapy, choice of antimicrobial agent, principles of antimicrobial therapy of infections with known etiology, interpretation of culture results, guiding antimicrobial therapy of established infections, susceptibility testing, definition of minimal inhibitory concentration and minimal bactericidal concentration, specialized assay methods, monitoring therapeutic response, clinical failure of antimicrobial therapy, bacteriostatic versus bactericidal activity (concentration-dependent killing, time-dependent killing), postantibiotic effect, pharmacokinetic considerations (route of administration, conditions that alter antimicrobial pharmacokinetics, drug concentrations in body fluids, monitoring serum concentrations of antimicrobial agents), management of antimicrobial drug toxicity, antimicrobial drug combinations (rationale for combination antimicrobial therapy, synergism and antagonism, mechanisms of synergistic action, mechanisms of antagonistic action), antimicrobial prophylaxis (surgical prophylaxis).

Beta-lactam and other cell wall- and membrane-active antibiotics. Chemical characteristic of beta-lactam compounds. Pharmacologic characteristic of penicillins. Basic chemical structure, classifications, mechanism of action, resistance to penicillins and other β-lactams (general mechanisms). The private pharmacology of penicillins: Benzylpenicillin, Procaine benzylpenicillin, Phenoxyme-

thylpenicillin, Oxacillin sodium, Cloxacillin, Dicloxacillin, Flucloxacillin, Meticillin, Nafcillin sodium, aminopenicillins, carboxypenicillins, ureidopenicillins. Beta-lactamase inhibitors: examples, chemical structure, pharmacologic role. Group of cephalosporin: history, chemical structure, mode of action, clinical indications, adverse effects, pharmacologic classification (generation and their characteristic – spectrum of antibiotic activities). Monobactams: chemical structure, mechanism of action, spectrum of activities, common adverse effects. Carbapenem class: chemical structure, examples of the preparations (drugs), spectrum of antibacterial activities, clinical uses.

Pharmacology of aminoglycosides: generic names, common uses, possible side effects, mechanism of action. The private pharmacology of aminoglycosides: amikacin, gentamicin.

Glycopeptide antibiotic: mechanism, therapeutic applications, administration. Pharmacologic characteristic of vancomycin, teicoplanin.

Pharmacology of tetracycline antibiotics: mechanism of action, mechanism and resistance, indication, administration, cautions, contraindications, side effects, pharmacologic classification (according to source, according to duration of action).

Macrolides: definition (chemical characteristic), common antibiotic macrolides, uses (spectrum of antibacterial activity), mechanism of action, pharmacodynamics, resistance, unwanted effects.

Lincosamides class: definition, history and uses, resistance, formulation.

Streptogramins group: general pharmacologic characteristic, examples.

Oxazolidinone (initiation inhibitors) class: pharmacology of linezolid.

Steroid antibacterials (prokaryotic elongation factors): pharmacology of fusidic acid.

Polypeptide antibiotics: pharmacologic characteristic of polymyxin B and actinomycin.

Quinolones group: history, pharmacology, mechanism of the action, adverse effects, contraindications, scripting abuse and bacterial resistance, generations.
Chloramphenicol: dosage, dose monitoring, chloramphenicol and the liver, chloramphenicol and the kidneys, uses (spectrum of antibacterial activity), adverse effects, mechanism and resistance.
Dihydropteroate synthetase inhibitors (group sulfonamide): chemistry, classification and characteristic.

Antifungal drugs. Classification of human fungal infections. Classes: polyene antifungals, imidazole, triazole and thiazole antifungals, imidazoles, triazoles, thiazoles, allylamines, echinocandins, others.
Systemic antifungal drugs for systemic infections. Pharmacologic characteristic of Amphotericin B: chemistry properties, pharmacokinetics, mechanism of action, resistance to amphotericin B, antifungal activity, clinical use (for treatment of systemic fungal disease, local administration), adverse reactions (infusion-related reactions, cumulative toxicity). Pharmacology of flucytosine. Azoles class (ketoconazole, itraconazole, fluconazole, voriconazole): antifungal activity (mechanism of action), the spectrum of action of azole, resistance to azoles, adverse effects, drug interactions. Pharmacology of group echinocandins (caspofungin, micafungin and anidulafungin): pharmacologic properties, pharmacological actions, unwanted effects and dangers. Systemic antifungal drugs for mucocutaneous infections: pharmacologic characteristic of griseofulvin and terbinafine. Topical antifungal drugs: nystatin, topical azoles.

Antiviral drugs. Classification of viral infections, virus life cycle. Inadequacy of vaccines. Anti-viral targeting technique. Approaches by life cycle stage: before cell entry, entry inhibitor, uncoating inhibitor, during viral synthesis, reverse transcription, integrase, transcription, translation / antisense, translation / ribozymes, protease inhibitors, assembly, release phase.

Agents to treat herpes simplex virus and varicella-zoster virus infections: acyclovir, valacyclovir, famciclovir, penciclovir, docosanol, trifluridine (trifluorothymidine). Agents to treat cytomegalovirus infections: ganciclovir, valganciclovir, foscarnet (phosphonoformic acid), cidofovir. Antiretroviral therapy: treatment of HIV-infected individuals, nucleoside and nucleotide reverse transcriptase inhibitors (life cycle of HIV, pharmacologic characteristic of abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir, zalcitabine, zidovudine (azidothymidine; AZT), nonnucleoside reverse transcriptase inhibitors (delavirdine, efavirenz, nevirapine), protease inhibitors (amprenavir, atazanavir, fosamprenavir, indinavir, lopinavir-100 / ritonavir-400, nelfinavir, ritonavir, saquinavir, tipranavir), fusion inhibitors (enfuvirtide). Antihepatitis drugs: pharmacologic characteristic of group interferons, treatment of hepatitis B virus infection (lamivudine, adefovir dipivoxil, entecavir), treatment of hepatitis C virus infection (ribavirin). Anti-influenza drugs: pharmacology of amantadine, rimantadine, zanamivir and oseltamivir.

Miscellaneous antimicrobial agents; disinfectants, antiseptics and sterilants. Pharmacologic characteristic of metronidazole, mupirocin (pseudomonic acid), group of polymyxins (polymyxin B and polymyxin E (colistin)), urinary antiseptics (nitrofurantoin, methenamine mandelate). Disinfectants: alcohols, chlorhexidine, halogens (iodine, iodophors, chlorine), phenolics, quaternary ammonium compounds ("quats"), aldehydes (formaldehyde and glutaraldehyde), superoxidized water, peroxygen compounds (hydrogen peroxide and peracetic acid), heavy metals (thimerosal, silver nitrate, silver sulfadiazine), boric acid, calcium hypochlorite.

Antiparasitic chemotherapy. Targets of chemotherapy. Antiprotozoal drugs. Treatment of malaria. Species of plasmodium cause human malaria, parasite life cycle, drug classification, pharmacologic characteristic of Cchloroquine, amo-

diaquine, quinine and quinidine, mefloquine, primaquine, atovaquone (chemistry and pharmacokinetics, antimalarial action, pharmacological actions, resistance, therapeutic applications, unwanted effects and dangers, contraindications and cautions), inhibitors of folate synthesis (pyrimethamine, proguanil, fansidar), antibiotics (halofantrine hydrochloride, lumefantrine, artemisinin (qinghaosu)). Treatment of amebiasis: pharmacologic classification of the drugs, pharmacologic characteristic of metronidazole, iodoquinol (diiodohydroxyquin), paromomycin sulfate, emetine and dehydroemetine. Other antiprotozoal drugs: pentamidine, sodium stibogluconate, nitazoxanide, suramin, melarsoprol, eflornithine (difluoromethylornithine), nifurtimox, benznidazole, miltefosine.

Pharmacology of the anthelmintic drugs. Chemotherapy of helminthic infections: pharmaceutical classes, anthelmintic resistance, development of resistance. Pharmacologic characteristic of albendazole, bithionol, diethylcarbamazine citrate, doxycycline, ivermectin, mebendazole, metrifonate, niclosamide, oxamniquine, piperazine, praziquantel, pyrantel pamoate, thiabendazole (anthelmintic actions, clinical uses, adverse reactions, contraindications, cautions).

Cancer chemotherapy. Causes of cancer, history of cancer chemotherapy, cancer therapeutic modalities, anticancer drug development, importance of neoplastic cell burden, importance of cell cycle kinetics (cell cycle-specific and cell cycle-nonspecific drugs), resistance to cytotoxic drugs (P-glycoprotein, multidrug resistance protein 1). Combination chemotherapy. Adjuvant therapy. Supportive care during chemotherapy. The private pharmacology. Polyfunctional alkylating agents: chemical structures of major classes of alkylating agents, mechanism of action (mechanism of alkylation of DNA guanine), mechanism of acquired resistance, pharmacologic effects. The nitrosoureas group. Related drugs acting as alkylating agents: procarbazine, dacarbazine, altretamine (hexamethylmelamine), platinum analogs. Antimetabolites: mechanisms of action, pharmacology

of methotrexate (action, uses, dosage and toxicity, resistance to methotrexate), pemetrexed. Pharmacologic characteristic of purine antagonists: 6-Thiopurines (6-Mercaptopurine, 6-Thioguanine), fludarabine, cladribine (2-chlorodeoxyadenosine). Pyrimidine antagonists group: 5-Fluorouracil, capecitabine, cytarabine (cytosine arabinoside, ara-C), gemcitabine. Plant alcaloids group: vinblastine, vincristine, vinorelbine. Epipodophyllotoxins: etoposide, teniposide. Camptothecins: topotecan, irinotecan. Taxanes: paclitaxel, docetaxel. Antitumor antibiotics: anthracycline antibiotics (doxorubicin, daunorubicin, idarubicin, epirubicin), mitoxantrone (dihydroxyanthracenedione), dactinomycin, mitomycin (mitomycin C), bleomycin. Hormonal agents: estrogen and androgen inhibitors (tamoxifen, flutamide and bicalutamide). Gonadotropin-releasing hormone antagonists: leuprolide and goserelin. Aromatase inhibitors: aminoglutethimide, anastrozole, letrozole, exemestane. Miscellaneous anticancer drugs: imatinib, dasatinib (sprycel), growth factor receptor inhibitors (cetuximab, gefitinib and erlotinib). Asparaginase (L-asparagine amidohydrolase). Hydroxyurea. All-trans-retinoic acid (tretinoin). Arsenic trioxide (AS_2O_3). Monoclonal antibodies (rituximab).

Immunopharmacology. Normal immune responses. The innate immune system, Role of complement in innate immunity. The adaptive immune system. Abnormal immune responses: classification of hypersensitivity (types), autoimmunity, immunodeficiency diseases. Pharmacology of immunosuppressive agents (immunodepressants): glucocorticoids (corticosteroids), immunophilin ligands (cyclosporine (cyclosporin A), tacrolimus, sirolimus (rapamycin)). Cytotoxic drugs: azathioprine, cyclophosphamide, leflunomide, hydroxychloroquine, other cytotoxic agents (vincristine, methotrexate, and cytarabine). Immunosuppressive antibodies: pharmacology of antilymphocyte and antithymocyte antibodies, muromonab-CD3, immune globulin intravenous (IGIV), Rho(D) immune globulin micro-dose, hyperimmune immunoglobulins. Monoclonal antibodies: antitumor

monoclonal antibodies (alemtuzumab, bevacizumab, cetuximab, gemtuzumab, rituximab, trastuzumab), antitumor monoclonal antibodies used to deliver isotopes to tumors (arcitumomab, capromab pendetide, ibritumomab tiuxetan, nofetumomab, tositumomab), monoclonal antibodies used as immunosuppressants and anti-inflammatory agents (pharmacologic characteristic of adalimumab, etanercept, infliximab, abatacept, alefacept, basiliximab, daclizumab, efalizumab, omalizumab), other monoclonal antibodies (abciximab, palivizumab).
Immunologic reactions to drugs and drug allergy. Immediate type I drug allergy. Drug treatment of immediate allergy. Desensitization to drugs. Autoimmune (type II) reactions to drugs. Serum sickness and vasculitic (type III) reactions.
Drugs acting on immunophilins: ciclosporin, tacrolimus, sirolimus, interferons, TNF binding proteins, mycophenolic acid.

Introduction to toxicology: occupational and environmental. Occupational toxicology. Environmental toxicology. Ecotoxicology. Carbon monoxide: mechanism of action, clinical effects (CO intoxication), treatment. Sulfur dioxide (SO_2): mechanism of action, clinical effects and treatment. Nitrogen dioxide (NO_2): mechanism of action, clinical effects and treatment. Ozone (O_3): mechanism of action, clinical effects and treatment. Solvents: halogenated aliphatic hydrocarbons (mechanism of action, clinical effects and treatment), aromatic hydrocarbons (benzene, toluene (methylbenzene)). Insecticides: organochlorine insecticides (human toxicology /the acute toxic properties of the organochlorine insecticides/, environmental toxicology), organophosphorus insecticides (human toxicology, environmental toxicology), carbamate insecticides, botanical insecticides (nicotine, rotenone, and pyrethrum). Herbicides: chlorophenoxy herbicides (dioxins), bipyridyl herbicides (paraquat).

Pharmacology of vaccines, immune globulins and other complex biologic products. Principles of active immunization, passive immunization. Legal liability for untoward reactions.

Pharmacology of botanicals (herbal medications) and nutritional supplements. Clinical aspects of the use of botanicals. Botanical substances. Echinacea (Echinacea purpurea): chemistry characteristic, pharmacologic effects, clinical trials, adverse effects, drug interactions and precautions, dosage. Garlic (Allium sativum): chemistry, pharmacologic effects, adverse effects, drug interactions and precautions, dosage. Ginkgo (Ginkgo biloba): chemistry, pharmacologic effects, adverse effects, drug interactions and precautions, dosage. Ginseng: chemistry characteristic, pharmacologic effects, clinical trials, adverse effects, drug interactions and precautions, dosage. Milk thistle (Silybum marianum): chemistry characteristic, pharmacologic effects, clinical trials, adverse effects, drug interactions and precautions, dosage. St. John's wort (hypericum): chemistry characteristic, pharmacologic effects, clinical trials, adverse effects, drug interactions and precautions, dosage. Saw palmetto: chemistry characteristic, pharmacologic effects, clinical trials, adverse effects, drug interactions and precautions, dosage. Pharmacology of purified nutritional supplements (chemistry characteristic, pharmacologic effects, clinical trials, adverse effects, drug interactions and precautions, dosage): coenzyme Q10, glucosamine, melatonin.

4.3. Thematic plane of the lectures and practical lessons.

<table>
<tr><td colspan="2">The Section I.
The General pharmacology.</td></tr>
<tr><td>Lectures</td><td>Practical occupations</td></tr>
<tr><td>1. Pharmacology as a science, the methods of pharmacological investigations.
2. Drug receptors and pharmacodynamics.
3. General principles of rational prescribing and prescription writing.</td><td>Module I
BASIC PRINCIPLES OF PHARMACOLOGY
1. Basic principles. Introduction.
2. Drug receptors (part I).
3. Drug receptors (drug-receptor bonds) (part II).
4. Pharmacokinetics.
5. Pharmacodynamics.
6. Individual variation and drug interaction. Harmful effects of drugs.
7. General principles of rational prescribing and prescription writing. The total test.</td></tr>
<tr><td colspan="2">The Section II.
The Private (systems) pharmacology.</td></tr>
<tr><td>1. Cholinoceptor-activating (cholinomimetic drugs) and cholinesterase-inhibiting drugs.
2. Cholinoceptor-blocking drugs.
3. Adrenoceptor-activating and other sympathomimetic drugs. Adrenoceptor antagonist drugs.
4. Sedative-hypnotic drugs.
5. Opioid analgesics and</td><td>Module II
AUTONOMIC DRUGS
1. Cholinoceptor-activating (cholinomimetic drugs) and cholinesterase-inhibiting agents.
2. Cholinoceptor-blocking drugs.
3. Adrenoceptor-activating drugs.
4. Adrenoceptor antagonist drugs.
5. The total test.
Module III
DRUGS USED TO TREAT INFLAMMATION</td></tr>
</table>

antagonists.
6. Antihypertensive agents.
7. Agents used in cardiac arrhythmias.
8. Agents used in anemias.
9. Anti-inflammatory drugs (part I).
10. Anti-inflammatory drugs (part II).
11. Drugs used in disorders of coagulation.
12. Pharmacology of the anti-platelet drugs.
13. Agents used in anemias.
14. Pharmacology of respiratory system disorders.
15. Drugs used in the treatment of gastrointestinal diseases (part I).
16. Drugs used in the treatment of gastrointestinal diseases (part II).
17. Antifungal drugs.
18. Antiviral drugs.
19. Immunopharmacology.
20. Special aspects of perinatal and pediatric pharmacology.
21. Special aspects of geriatric pharmacology.
22. Introduction to toxicology.
23. Basic principles of drug discovery. Pharmacology of botanicals (herbal medications) and nutritional supplements.

6. Introduction. Histamine, serotonin. The eicosanoids: prostaglandins, thromboxanes, leukotrienes and related compounds.
7. Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, non-opioid analgesics (part I).
8. Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, non-opioid analgesics (part II).
9. Steroidal anti-inflammatory drugs.
10. The total test.

Module IV

DRUGS THAT ACT IN THE CENTRAL NERVOUS SYSTEM

11. General anesthetics.
12. Sedative-hypnotic drugs.
13. Antipsychotic agents and lithium.
14. Pharmacologic management of parkinsonism.
15. Opioid analgesics and antagonists.
16. Drugs of abuse.
17. The total test.

Module V

CARDIOVASCULAR-RENAL DRUGS

18. Drugs used in heart failure.
19. Antihypertensive agents (part I).
20. Antihypertensive agents (part II).
21. Treatment of angina pectoris.
22. Agents used in cardiac arrhythmias (part I).
23. Agents used in cardiac arrhythmias (part II).
24. Agents used in hyperlipidemia.
25. Diuretic agents.
26. The total test.

Module VI

DRUGS USED TO TREAT DISEASES OF THE BLOOD

27. Agents used in anemias.
28. Hematopoietic growth factors.
29. Drugs used in disorders of coagulation (part I).
30. Drugs used in disorders of coagulation (part II).

	31. Final occupation. The total test. **Module VII** **ENDOCRINE DRUGS** 32. Hypothalamic and pituitary hormones. 33. Thyroid and antithyroid drugs. 34. Adrenocorticosteroids and adrenocortical antagonists. 35. The gonadal hormones and inhibitors. 36. Pancreatic hormones and antidiabetic drugs. 37. Agents that affect bone mineral homeostasis. The total test. **Module VIII** **CHEMOTHERAPEUTIC DRUGS** 38. Beta-lactam, other cell wall- and membrane-active antibiotics (part I). 39. Beta-lactam, other cell wall- and membrane-active antibiotics (part II). 40. Tetracyclines, macrolides, clindamycin, chloramphenicol and streptogramins antibiotics (part I). 41. Tetracyclines, macrolides, clindamycin, chloramphenicol and streptogramins antibiotics (part II). 42. Aminoglycosides and spectinomycin. 43. Sulfonamides, trimethoprim and quinolones. 44. Antimycobacterial drugs. 45. Antifungal agents. 46. Antiviral agents. 47. Clinical use of antimicrobial agents. 48. The total test.

Part V

Methodical literature and protection

5.1. Methodical literature.

5.1.1. Basic literature.

1) Rang and Dales, Pharmacology, 2008.

2) BASIC AND CLINICAL PHARMACOLOGY - 11th Ed. (2008), Bertram G. Katzung.

5.1.2. Additional literature.

1) Kaplan Notes Pharmacology, 2002.

2) Color Atlas of Pharmacology, Thyeme, 2005.

3) Drug Today, INDIA, Ready reckoner of current medical formulations, 2009.

Part VI

Materials

Computers and audio-visual technices of studies.

1) Computer «SAMSUNG X05».
2) RGB (multimedia) – projector.
3) Multimedia-presentations (topics): 1) Pharmacology as a science, the methods of pharmacological investigations. 2) Drug receptors (part I). 3) Drug receptors (part II). 4) General principles of rational prescribing and prescription writing. 5) Pharmacokinetics. 6) Pharmacodynamics. 7) Individual variation and drug interaction. Harmful effects of drugs. 8) Cholinoceptor-activating (cholinomimetic drugs) and cholinesterase-inhibiting agents. 9) Cholinoceptor-blocking drugs. 10) Adrenoceptor-activating drugs. 11) Adrenoceptor antagonist drugs. 12) Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, nonopioid analgesics (part I). 13) Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, nonopioid analgesics (part II). 14) Steroidal anti-inflammatory drugs. 15) General anesthetics. 16) Sedative-hypnotic drugs. 17) Antipsychotic agents and lithium. 18) Pharmacologic management of parkinsonism. 19) Opioid analgesics and antagonists. 20) Drugs of abuse. 21) Drugs used in heart failure. 22) Antihypertensive agents (part I). 23) Antihypertensive agents (part II). 24) Treatment of angina pectoris. 25) Agents used in cardiac arrhythmias (part I). 26) Agents used in cardiac arrhythmias (part II). 27) Agents used in

hyperlipidemia. 28) Diuretic agents. 29) Agents used in anemias, hematopoietic growth factors. 30) Drugs used in disorders of coagulation (part I). 31) Drugs used in disorders of coagulation (part II). 32) Hypothalamic and pituitary hormones. 33) Thyroid and antithyroid drugs. 34) Adrenocorticosteroids and adrenocortical antagonists. 35) The gonadal hormones and inhibitors. 36) Pancreatic hormones and antidiabetic drugs. 37) Agents that affect bone mineral homeostasis. 38) Beta-lactam, other cell wall- and membrane-active antibiotics (part I). 39) Beta-lactam, other cell wall- and membrane-active antibiotics (part II). 40) Tetracyclines, macrolides, clindamycin, chloramphenicol and streptogramins antibiotics (part I). 41) Tetracyclines, macrolides, clindamycin, chloramphenicol and streptogramins antibiotics (part II). 42) Aminoglycosides and spectinomycin. 43) Sulfonamides, trimethoprim and quinolones. 44) Antimycobacterial drugs. 45) Antifungal agents. 46) Antiviral agents. 47) Clinical use of antimicrobial agents. 48) Immunopharmacology. 49) Special aspects of perinatal and pediatric pharmacology. 50) Special aspects of geriatric pharmacology. 51) Introduction to toxicology. 52) Basic principles of drug discovery. Pharmacology of botanicals (herbal medications) and nutritional supplements.

Part VII

Contents of the tests and examine

The examination is carried out in one stage - interview (3 problems) under the question card.

The questions for examine:

1) Introduction to medical pharmacology. Basic principles of medical pharmacology. The history of pharmacology (pharmacology, pharmacopoeia, apothecary, materia medica). The nature of drugs. Definition of the drug, medicine, active drug, xenobiotic, poison, toxin.
2) Ways and means of the introduction medicine (routes of administration).

3) The absorption (permeation): dissolution (the Noyes-Whitney equation), aqueous diffusion, lipid diffusion, special carriers (transporters), endocytosis and exocytosis, role of the ionization.
4) Transport medicinal material.
5) Bioavailability, bioequivalence, the effect of first-pass hepatic elimination, prodrugs, distribution of the drugs.
6) Drug clearance principles.
7) Metabolism of the drugs; the role of biotransformation in drug disposition.
8) Pharmacodynamic processes and pharmacodynamic principles (drug-body interactions). The types of the action medicine. Types of drug-receptors.
9) Drug agonism and antagonism. Types of the doses.
10) Side effects of the drugs: definition, classification, abnormal pharmacokinetics, examples of adverse effects associated with specific medications.
11) Drug therapy in pregnancy, in infants and children, special aspects of geriatric pharmacology. Basic principles of drug discovery.
12) General principles of rational prescribing and prescription writing.
13) Cholinoceptor-activating and cholinesterase-inhibiting drugs.
14) Cholinoceptor-blocking drugs (cholinoceptor antagonists).
15) Adrenoceptor-activating drugs.
16) Adrenoceptor antagonists.
17) Nonsteroidal anti-inflammatory drugs, disease-modifyng antirheumatic drugs (antirheumatoid drugs), drugs used in gout.
18) H_1-receptor antagonists (antihistamines drugs).
19) Sedative-hypnotic (anxiolytic) drugs.
20) Opioid analgesics and antagonists. Drugs of abuse, dependence.
21) Antipsychotic (neuroleptic) agents, lithium carbonate and other mood-stabilizing drugs.
22) Antidepressant agents.
23) Basic pharmacology of alcohol.

24) Antiseizure drugs (anticonvulsant, antiepileptic drugs).
25) General anesthetics.
26) Pharmacologic management of parkinsonism (paralysis agitans) and other movement disorders.
27) Nootropic drugs. Pharmacology of stimulants.
28) Pharmacology of local anesthetics.
29) Drugs used in heart failure.
30) Antiarrhythmic drugs - agents used in cardiac arrhythmias.
31) Antianginal drugs.
32) Antihypertensive drugs.
33) Diuretic agents.
34) Anti-atherosclerotic and anti-dislipidemic drugs.
35) Drugs used in disorders of coagulation.
36) Agents used in anemias.
37) Pharmacology of respiratory system disorders (bronchodilatators).
38) Anti-ulcer drugs.
39) Drugs stimulating gastrointestinal motility.
40) Laxatives.
41) Antidiarrheal drugs.
42) Antiemetic agents.
43) Pancreatic enzyme supplements. Obesity treatment.
44) Pharmacology of hypothalamic and pituitary hormones.
45) Pharmacology of pancreatic hormones and antidiabetic drugs.
46) Pharmacology of thyroid and antithyroid drugs.
47) Pharmacology of adrenocorticosteroids and adrenocortical antagonists.
48) Pharmacology of gonadal hormones and inhibitors.
49) Agents that affect bone mineral homeostasis.
50) Beta-lactam and other cell wall- and membrane-active antibiotics.
51) Aminoglycosides.

52) Macrolides, lincosamides class, streptogramins group.

53) Oxazolidinone (initiation inhibitors) class, ppolypeptide antibiotics, quinolones group, chloramphenicol.

54) Dihydropteroate synthetase inhibitors (group sulfonamide).

55) Antifungal drugs.

56) Antiviral drugs.

57) Disinfectants, antiseptics and sterilants.

58) Antiparasitic chemotherapy.

59) Pharmacology of the anthelmintic drugs.

60) Cancer chemotherapy.

61) Immunopharmacology.

62) Pharmacologic toxicology.

63) Pharmacology of vaccines, immune globulins and other complex biologic products. Probiotics.

64) Pharmacology of botanicals (herbal medications) and nutritional supplements.