REPUBLIC OF MOLDOVA
MINISTRY OF HEALTH
***NICOLAE TESTEMITANU* STATE UNIVERSITY OF MEDICINE AND PHARMACY**

PHARMACOLOGY AND CLINICAL PHARMACOLOGY DEPARTAMENT

CLINICAL CASES

in clinical pharmacology

Under the editorship of *Victor Ghicavîi* – Corresponding Member of the Academy of Sciences of the Republic of Moldova

CHISINAU
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This book is intended for the V-th -year students of general medicine to develop skills of assessment, awareness and implementation of clinical pharmacology knowledge in medical practice.

CONTENTS

INTRODUCTION

The guide is an important applicative support for students respect of theoretical knowledge consolidation, as well as abilities and practical achievements formation in the field of clinical pharmacology. Situational problems solution have as its object attraction of students attention to clinical manifestations of pharmacological effects of preparations, principles of selection, use, individualization and dosage of medicines, criteria of effectiveness and harmlessness, prevention techniques and treatment mode of adverse reactions, pharmacokinetic and pharmacogenetic particularities of preparations. The elements of pharmacotherapy with reflection of evidence based medicine principles are included in most clinical cases – that represents important part of rational use of medicines. The necessity of adequate control over prescribed treatment is emphasized by these moments, as well as information of a patient about administrated medicines and their effect upon the course of a disease.

Both simple and complex medical cases are included in this work, which were called for development of clinical thought and ability of argumentation medicines prescription in the event of diseases and pathological states. Described clinical situations are similar to those from medical practice, and are aimed at discussion and evidence of difficult problems in medical profession.

Pharmacokinetic, pharmacodynamic and pharmacogenetic principles for individualization and optimization of rational drug administration.

I. Simple clinical cases

1. Two patients with squeezing chest pain to moderate exercise consulted a GP (general practitioner). After examination the doctor diagnosed ischemic heart disease, angina pectoris functional class 2 on exertion. The doctor recommended them to take permanently nitroglycerin to relieve angina pain, but did not explain how to use it. Patient A used it orally and patient B – sublingually.

What will the effectiveness of nitroglycerin be? Explain your reasoning for your recommendations.

2. Patient M was prescribed aspirin (weak acid), and patient N quinidine (weak base). In both cases they used them immediately after meals.

Consider these recommendations. Will the effectiveness of these drugs be different? Justify your answer.

3. One patient was prescribed drugs A and B in therapeutic doses. Both are bound to serum proteins to the extent of 90%, but preparation B has a higher affinity for binding sites.

What will the effectiveness of these preparations be? Justify your answer.

4. Preparations C and D are from the same pharmacological group. Preparation C is coupled with plasma proteins to the extent of 98%, D – 20-40%. Which drug will exert a faster, more intense and shorter effect? What preparation will act more sustainably could accumulate and could cause symptoms of overdose?

What will happen if both of them are associated with other preparation that is highly protein-bound (95%)?

5. A breastfeeding mother was prescribed preparation N which is a weak base. The drug is mainly in unionized form at blood pH values of 7.4.

How do you assess doctor´s prescription? What will your recommendation be, regarding breastfeeding, if the mother´s milk pH value is 6.4. Explain your suggestions.

6. Substances M and N with supposed CNS action were studied under the experimental conditions. The research of physicochemical properties showed that the substance M is a quaternary ammonium (N4 +) compound, is water-soluble and is ionized at pH 7.4, substance N is a tertiary ammonium (N3 +) compound, it is lipid-soluble and is in unionized form at pH 7.4.

How will these substances act on the CNS? Explain their different action.

7. A 65-year old patient with chronic bronchitis was prescribed an antibacterial preparation. At the same time sputum was collected to determine the antibiotic sensitivity of bacterial pathogens. Bacteriological test results showed that the bacterial pathogen was very sensitive to antibacterial preparation, despite this, fever and symptoms of intoxication maintained on the 3rd day of treatment. After detailed discussions, the doctor found that the patient took phenobarbital to correct sleep disorders.

What will the subsequent treatment of this patient be? Explain your suggestions.

8. Two patients with leg fractures used suxamethonium for bone reposition. The drug effect lasted from 5 to 10 minutes in patient A and 90 minutes in patient B. In these patients hydrogen peroxide was used for primary wound treatment. Patient A was formed a characteristic foam, in patient B - the effect of foam was missing.

What causes the found effects? Explain the observed phenomena.

9. A patient with duodenal ulcer was prescribed cimetidine to decrease gastric secretion, also amoxicillin and metronidazole in standard doses for H. pylori eradication. 10 days later pharmacokinetic analysis found an increase in the metronidazole concentration and the amoxicillin concentration within the norm. Plasma proteins and albumin levels

are within the norm. Metronidazole and amoxicillin bind insignificantly with plasma proteins.

What are the causes of metronidazole serum level elevation?

What will the future recommendations be?

10. Two patients were hospitalized in the intensive care unit. Their condition has improved after intensive treatment. During the process of anamnesis collection the following issues were found out:

Patient A used clonidine for 2 years to treat hypertension, its effectiveness has significantly diminished in recent days. After sudden cessation of clonidine, the patient's condition worsened in a few hours with increased blood pressure over 200/100 mm Hg, substantial excitation and tachycardia.

Patient B suffers from rheumatoid arthritis and was under prednisolone treatment the last 5 years. Earlier a routine blood analysis showed increased glucose level. The doctor told him that it was a side effect of prednisolone. The patient discontinued prednisolone use without consulting a doctor. Within 24 hours the patient´s condition was worsening and he was hospitalized.

What are the causes of these phenomena?

What will your further actions be?

II. Multiple clinical cases

Clinical case 1

In experimental studies the following pharmacokinetic parameters of antimicrobial A, B, C, D, E were determined: bioavailability (Bd); volume of distribution (Vd); serum protein binding; the half-life ($T_{0,5}$).

1. **The substance could have a greater influence on the intestinal microflora if its absorption and Bd is:**
   A. 20%
   B. 80%
   C. 90%
   D. 99%
   E. 50%
2. **The substance will have a faster action if it is coupled with plasma proteins to the extent of:**
   A. 99%

B. 10%
C. 90%
D. 80%
E. 50%

3. **The substance will be effective against atypical agents (Legionella, Mycoplasma, Chlamydia) if its Vd is:**
   A. l/kg
   B. l/kg
   C. l/kg
   D. 0.05 l/kg
   E. 5 l/kg
4. **The substance will be removed faster by metabolization and/or renal elimination if its degree of coupling with plasma proteins is:**
   A. 99%
   B. 10%
   C. 90%
   D. 80%
   E. 50%
5. **Which statement about the dosing regimen will be correct for substances with T0,5 from 2.1 to 4.5 hours?**
   A. 4 times/daily (every 6 hours)
   B. 8 times/daily (every 3 hours)
   C. 1-2 times/daily (12-24 hours)
   D. 2-3 times/daily (8-12 hours)
   E. 6 times/daily (every 4 hours)

Clinical Case 2

During experimental studies of pharmacokinetics of substance A, the number of features that need to be taken into account in determining the dosage regimen were found.

1. **Why will the bioavailability be 30% in case of 90% absorption?**
   A. Increased intestinal P-glycoprotein activity
   B. reduced liver enzyme activity
   C. decreased P-glycoprotein activity
   D. decreased intestinal enzyme activity
   E. increased intestinal enzyme activity

2. **What factors will determine the distribution volume of 500 l?**
   A. penetration in all fluid body compartments
   B. distribution only in the blood
   C. distribution in the interstitial space
   D. distribution in blood and interstitial space
   E. only intracellular distribution
3. **Which kind of reaction may occur during phase I of metabolism?**
   A. sulphation
   B. oxidation
   C. methylation
   D. reduction
   E. glucuronidation
4. **Which kind of reaction may occur during phase II of metabolism?**
   A. glucuronidation
   B. oxidation
   C. reduction
   D. methylation
   E. sulphation
5. **Which statement about the dosing regimen will be correct for substances with T0,5 from 2.1 to 4.5 hours?**
   A. 4 times/daily (every 6 hours)
   B. 8 times/daily (every 3 hours)
   C. 1-2 times/daily (12-24 hours)
   D. 2-3 times/daily (8-12 hours)
   E. 6 times/daily (every 4 hours)

Clinical case 3

The study of excretion during pharmacokinetics analysis requires taking into account a number of factors that will determine the features of use, dosing regimen, treatment in case of overdose.

1. **What mechanisms will contribute to a more efficient removal depending on the physico-chemical properties of substances?**
   A. active tubular secretion of lipophilic substances
   B. active tubular secretion of ionized water soluble substances
   C. glomerular filtration of lipophilic substances

D. glomerular filtration of water-soluble substances
E. passive tubular secretion of lipophilic substances

2. What substances will be removed more quickly depending on the pH of urine?

A. weak acids at a low pH
B. weak acids at an alkaline pH
C. weak bases at a low pH
D. weak bases to an alkaline pH
E. ionized substances

3. The elimination rate will be higher in case of:

A. large volume of distribution
B. small volume of distribution
C. small degree of plasma protein and tissue binding
D. high degree of plasma protein and tissue binding
E. high degree of ionization

4. What features of substances will determine the predominance of passive reabsorption?

A. ionized form of water-soluble substances
B. unionized form of water-soluble substances
C. acid substance in alkaline environment
D. acid substance in acid environment
E. alkaline substance in alkaline environment

5. What characteristics are common for active tubular secretion and active tubular reabsorption?

A. ionized substances
B. unionized substances
C. macromolecular substances
D. it involves transporters
E. it does not require energy

Clinical case 4

During pharmacokinetic profile analysis it was found that the substance A (potassium iodide) is removed by saliva, bile, milk and lungs.

1. What is the common mechanism to eliminate substance by these ways?

A. facilitated diffusion

B. active transport
C. diffusion by change
D. passive diffusion
E. pinocytosis

2. What conditions must the substance meet in order to be eliminated by selected mechanism?

A. to be in the ionized form
B. to be in the unionized form
C. to be lipophilic
D. to bind intensively to plasma proteins
E. to bind insignificant with plasma proteins

3. What can analysing of salivary way of elimination of one substance be used for?

A. to determine the state of blood circulation
B. to determine plasma protein bound fraction
C. to determine unbound fraction
D. to determine the concentration of substance in the blood
E. to determine the volume of distribution

4. What conditions will promote the accumulation of one substance in milk?

A. acidic properties at a slight acid pH of milk
B. alkaline properties at a slight acid pH of milk
C. lipophility
D. predominance of coupled fraction with plasma proteins
E. prevalence of the free fraction in plasma

5. What may be beneficial consequences of biliary elimination pathway of one substance?

A. participation in enterohepatic circulation
B. avoidance of enterohepatic circulation
C. performing of some diagnostic tests
D. treatment of bile disorders
E. determination of the activity of liver enzymes

Clinical case 5

One of the mandatory and important requirements in a new substance research is determining of metabolic pathways, important parameters for assessing the peculiarities of clinical use (the dosing re-

gimen, the possibility of adverse reactions, including hepatotoxicity, possible drug interactions, etc). In this context, metabolism is thoroughly studied at all stages involving different enzyme systems.

1. **What can be the consequences of drug metabolism?**
   A. conversion of water-soluble substances in liposoluble
   B. conversion of liposoluble substances in water-soluble
   C. formation of more active metabolites
   D. formation of toxic compounds
   E. conversion of prodrug to drug
2. **What are the reactions of phase I metabolism?**
   A. reduction
   B. methylation
   C. hydrolysis
   D. oxidation
   E. conjugation with endogenous residue
3. **What is the main enzymatic systems participating in phase I metabolism?**
   A. cytochrome P-450 microsomal enzymes
   B. glucuronyl transferase
   C. N-acetyltransferase
   D. plasma and tissue hydrolases
   E. glutathione-S-transferase
4. **What are the reactions of phase II metabolism?**
   A. conjugation with endogenous residues
   B. oxidation
   C. hydrolysis
   D. methylation
   E. reduction
5. **What are the main enzymatic systems participating in phase II metabolism?**
   A. cytochrome P-450 microsomal enzyme
   B. glucuronyl transferase
   C. N-acetyltransferase
   D. plasma and tissue hydrolases
   E. glutathione-S-transferase

Clinical case 6

Barbiturate pharmacokinetic study showed that these drugs undergo intensive metabolism in the liver. In turn barbiturates, especially the long-acting phenobarbital, barbital, exert significant influence on the liver enzymes activity, being considered as the most powerful enzyme inducers.

1. **Which of the cytochrome P450 isoenzyme is influenced by barbiturates in a greater extent?**
   A. CYP 1A1
   B. CYP 1A2
   C. CYP 2D6
   D. CYP 3A4
   E. CYP2E1
2. **What can be the consequences of isoenzymes stimulation by barbiturates?**
   A. increase of their metabolism
   B. decrease of their metabolism
   C. formation of active intermediate compounds
   D. development of pharmacokinetic tolerance
   E. development of pharmacodynamic tolerance
3. **What phase II metabolizing enzyme is stimulated by barbiturates?**
   A. N-acetyltransferase
   B. butyryl cholinesterase
   C. glucuronyl transferase
   D. glutathion-S-transferase
   E. 6-phosphate dehydrogenase
4. **What are the consequences of isoenzyme stimulation in phase II metabolism by barbiturates?**
   A. transformation of the liposoluble compounds
   B. endogenous substances coupling with undesirable effects decreasing
   C. formation of the active compounds
   D. oxidation of increasing the water solubility
   E. formation of compounds that are eliminated by bile

5. **In which clinical cases does the phase II isoenzyme stimulation have a clinical application?**
   A. hemolytic anemia
   B. newborn hyperbilirubinemia
   C. Jilber syndrome
   D. Stivens-Johnson syndrome
   E. Krigler-Naiara syndrome

Clinical case 7

During the development of a new substance it was found that the substance has a steroidal structure similar to that of endogenous hormonal substances. Experimental models to determine mechanism of action, pharmacological effects and clinical application areas have been developed to study the pharmacodynamics of the drug.

1. **Which hypothesis of the mechanism of action can be available for this substance?**
   A. It will interact at the postsinaptic receptor level
   B. It will interact with the cytoplasmic receptors
   C. It will interact at the presinaptic receptor level
   D. It will interact with nuclear receptors
   E. It will interact directly with enzyme systems
2. **What mechanism of action will be characteristic of this substance?**
   A. allosteric
   B. mimetic
   C. lithic
   D. modifying the activity of ion channels
   E. direct influence of enzyme systems
3. **Which kind of pharmacotherapy can this substance be used for?**
   A. etiological therapy
   B. suppression therapy
   C. substitution therapy
   D. pathogenetic therapy
   E. diagnostic purposes
4. **What effects can be triggered by repeated administration of this substance?**
   A. synergism

B. tolerance
C. awareness
D. antagonism
E. aggregation

5. What effects can be triggered after an abrupt discontinuation of the given substance?

A. withdrawal syndrome
B. iatrogenic syndrome
C. drug dependence
D. rebound syndrome
E. reactivation syndrome

Clinical case 8

A pharmacokinetic study of a new liposoluble substance required the determination of pharmacokinetic parameters to establish ways of administration and development of the suitable pharmaceutical forms. Several pharmacokinetic models were developed considering the lipophilic properties of the substance.

1. What features will help to ensure good intestinal absorption after administration?

A. passive diffusion with the liver first-pass effect
B. passive diffusion without intestinal first-pass effect
C. passive diffusion with a large area of absorption
D. passive diffusion with intestinal first-pass effect
E. passive diffusion without hepatic first-pass effect

2. What ways of administration can be examined if bioavailability of the substance is 10% after enteral administration?

A. transdermal
B. intraduodenal
C. rectal
D. sublingual
E. intravenous

3. What are the causes of low bioavailability after enteral administration?

A. intestinal first-pass effect
B. avoids the vena portae
C. liver first-pass effect

D. the substance can activate intestinal P-glycoprotein
E. the substance can inhibit intestinal P-glycoprotein

4. Choose the factors that will increase the bioavailability after sublingual or rectal administration?

A. small variations in the environment pH
B. wide variations in the environment pH
C. absorption with diffusion in the vena cava
D. small absorption surface
E. long contact time

5. What are the conditions for administering the substance through a transdermal therapeutic system?

A. it occurs in the sebaceous glands
B. it occurs in the epidermis
C. the substance should be lipophilic with low molecular weight
D. the substance should be hydrophilic with low molecular weight
E. to release constantly from matrix

Clinical case 9

An important compartment is dedicated to adverse reactions during safety profile study of medicinal preparations. These can occur with abrupt discontinuation of treatment revealed by the withdrawal syndrome, functional insufficiency syndrome and rebound syndrome.

1. What are the characteristics of functional insufficiency syndrome?

A. it develops after the cessation of a pharmacological antagonist therapy
B. it develops after the cessation of treatment with natural or synthetic hormones
C. it develops after the cessation of treatment with pharmacological agonists of a modulating or inhibitory system
D. it is characterized by the symptoms of an endocrine hypofunction
E. it is characterized by returning or exaggerating symptoms of the underlying disease
F. it is characterized by symptoms due to opposite or complementary pharmacologic action

2. **What are the characteristics of rebound syndrome?**
   A. it develops after the cessation of a pharmacological antagonist therapy
   B. it develops after the cessation of treatment with natural or synthetic hormones
   C. it develops after the cessation of treatment with pharmacological agonists of a modulator or inhibitor system
   D. it is characterized by the symptoms of an endocrine hypofunction
   E. it is characterized by returning or exaggerating symptoms of the underlying disease
   F. it is characterized by symptoms due to opposite or complementary pharmacologic action
3. **What are the characteristics of withdrawal syndrome?**
   A. it develops after the cessation of a pharmacological antagonist therapy
   B. it develops after the cessation of treatment with natural or synthetic hormones
   C. it develops after the cessation of treatment with pharmacological agonists of a modulator or inhibitor system
   D. it is characterized by the symptoms of an endocrine hypofunction
   E. it is characterized by returning or exaggerating symptoms of the underlying disease
   F. it is characterized by symptoms due to opposite or complementary pharmacologic action
4. **What mechanisms promote the rebound syndrome?**
   A. it is achieved by negative feed-back mechanism
   B. it is due to high sensitivity to physiological agonist
   C. it is due to the increase in the receptors number
   D. restoring the mediator release from the activator system which was blocked earlier
   E. developing of major or exaggerated effects
5. **What mechanisms promote the withdrawal syndrome?**
   A. it is achieved by negative feed-back mechanism
   B. it is due to high sensitivity to physiological agonist
   C. it is due to the increase in the receptors number

D. restoring mediator release from the activator system previously depressed
E. developing major or exaggerated effects

Clinical case 10

Currently a pharmacokinetic study is a prerequisite for drug registration. During this study a series of pharmacokinetic parameters indispensable for assessing drug efficacy and safety are determined. The study of the drugs´ elimination from the body is an important branch of pharmacokinetics.

1. **What pharmacokinetic parameters are used to study the drugs´ elimination?**
   A. bioavailability
   B. half-life
   C. plasma clearance
   D. volume of distribution
   E. elimination rate
2. **Which of the following statements define the half-life?**
   A. it is the time in which 50% of the drug is metabolized
   B. it is the time to distribute the drug in the tissues
   C. it is the time in which the plasma concentration is reduced by 2 times
   D. it is the time in which the tissue concentration is reduced by 2 times
   E. it is the time in which 50% of the drug passes into the interstitial space from the blood
3. **What pharmacokinetic parameters will the half-life correlate with?**
   A. bioavailability
   B. volume of distribution
   C. plasma concentration
   D. plasma clearance
   E. cytochrome P450 activity
4. **What pharmacokinetic parameters can be determined based on the half-life?**
   A. time in which the plasma concentration is reduced to zero
   B. time to distribute 50% of the drug in the tissues

C. time in which an equilibrium concentration is achieved
D. time in which 50% of the drug is coupled to plasma proteins
E. time in which 50% of the drug is metabolized

5. What pharmacodynamic parameters can be determined using the half-life?

A. assessment of the rate of elimination of drugs
B. assessment of the onset of the therapeutic effect
C. assessing metabolic capacity
D. assessment of interval between doses
E. elimination pathway assessment.

Clinical pharmacology of analgesic drugs

I. Simple clinical cases

1. To relieve pain in the postoperative period patient A was prescribed preparation M and patient B was prescribed preparation N. In both cases the pain decreased, but patient B showed a better subjective state (pain no longer causes the state of suffering and a superficial sleep installed in 30 min after s/c administration), however after four hours the pain began to intensify. Patient A showed unchanged subjective state and the pain began to intensify over 8 hours.

What preparations have been prescribed? Explain the observed effects.

2. An emergency team was called for a patient with a pain syndrome. On examination a biliary colic due to cholelithiasis was found out.

What measures will be taken by the emergency team?

What measures will be taken at other stages of medical care according to the standards and clinical protocols?

Justify selected preparations.

3. The effects of an analgesic preparation were studied under experimental conditions. After 10 minutes the animals would not react to pain. To assess the analgesic dose-depending effect, the dose was doubled. A decrease in the breath frequency with its deepening was found in rabbits first of all, then it became superficial with tachypnea development, and subsequently arrhythmic breathing developed. One rabbit was administered substance M and the other was administered substance N, both substances restored the normal breathing, but the rabbit that received preparation M reacted to pain, and the one that received preparation N preserved the analgesic effect.

Which substances were administered?

What causes these disturbances?

How do you explain different effects occuring after administration of preparations M and N?

4. In intensive care unit patient A with acute myocardial infarction was administered preparation C with duration of action lasting 30-45 minutes after parenteral administration and patient B with acute myocardial infarction was administered preparation D with duration of action lasting 3-5 hours. Patient A had symptoms of cardiac failure with hypertension, and patient B – the consequences of craniocerebral trauma.

Determine the administered preparations.

Explain the pharmacodynamic features of these preparations.

What side effects may be observed in these patients?

5. A patient with inoperable cancer has moderate pain syndrome. In accordance with the clinical protocol radiotherapy and subsequent chemotherapy was performed. To control the pain syndrome it was necessary to initiate the treatment with analgesics.

Develop the symptomatic treatment of the pain syndrome for this patient.

What preparations will be selected in accordance with the principles of treatment? Justify the effectiveness of the selected drugs.

6. A neurologist examined 3 patients with pain syndrome in the lower limbs. Patient A was diagnosed type 2, subcompensated diabetes mellitus, diabetic neuropathy, patient B - soft tissue trauma, phlegmon, patient C - osteochondrosis with radicular syndrome and spasms of the skeletal muscles.

Which analgesics will be recommended for these patients? Justify your decisions.

7. Three patients with multiple traumas were hospitalized in the intensive care unit. Patient A was diagnosed open fracture of the femur (thigh-bone), traumatic hypovolemic shock; patient B - craniocerebral trauma, febrile syndrome; patient C - chest trauma with rib fractures (fifth-seventh ribs). All patients developed three groups of effects after using opioid analgesics preparations.

What can these groups of effects be?

Which of these groups can develop and will be beneficial in these patients?

8. Two patients with pain syndrome in the postoperative period were administered drug A. The pain disappeared, but the patients' general condition deteriorated by the appearance of the symptoms of psychological, neurologic, autonomic and somatic type. A doctor substituted drug A with drug B, which improved the symptoms mentioned above.

Which preparations have been used?

Explain the found manifestations and mechanisms of their development.

9. A patient with traumatic arthritis and moderate pain syndrome was prescribed diclofenac for pain treatment. The patient's state was significantly improved in 2-3 days. Which symptoms were improved in this patient?

What is the mechanism that explains the effectiveness of this drug?

What will the duration of treatment be?

10. Patients M and N with inoperable cancer with metastases and marked pain syndrome were hospitalized in the oncology clinic. The patient M was prescribed 1 ml morphine subcutaneously 3 times / daily, patient N was prescribed 1 ml morphine subcutaneously every 4 hours.

In which patients the pain will be controlled the most effective?

Justify your answer.

II. Multiple clinical cases

Clinical case 1

During pharmacodynamic studies of opioid analgesics, features of the mechanism of action, pharmacological effects and selectivity to opioid receptors were determined.

1. What analgesics are potent opioid receptor agonists?

A. methadone
B. nalorphine
C. alfentanyl
D. morphine
E. pentazocine

2. What analgesics are partial agonists of the k-opioid receptors and μ-receptors antagonists?

A. pentazocine
B. fentanyl

C. morphine
D. butorphanol
E. methadone

3. What are common pharmacological effects of opioid analgesics influencing μ- and k- opioid receptors?

A. euphoria
B. sedation
C. supraspinal and spinal analgesia
D. respiratory depression
E. drug dependence

4. The pharmacological effects of opioid analgesics on μ-opioid receptors and k receptors are:

A. supraspinal and spinal analgesia
B. peripheral analgesia
C. respiratory depression
D. euphoria
E. sedation

5. Which of the given below mechanisms of action of opioid analgesics on μ- and k-opioid receptors are correct?

A. they increase efflux of potassium ions through K^+ channels with membrane hyperpolarization
B. they inhibit influx of potassium ions into the cell membrane with hyperpolarization
C. they inhibit the adenylate cyclase and decrease cAMP
D. they activate the adenylate cyclase and increase cAMP
E. they reduce presinaptic calcium influx and block the release of neuromediators.

Clinical case 2

The analysis of pharmacodynamic effects of opioid analgesics and clinical manifestations is important for their rational and appropriate choice in different clinical cases. An important part of the efficacy and safety of opioid analgesics is the analgesic effect.

1. At which levels of pain transmission pathways do opioid analgesics act to achieve the analgesic effect?

A. cerebral cortex
B. nociceptors

C. dorsal horns of the spinal cord
D. thalamus, reticular formation, limbic system
E. peripheral nerve structures

2. What processes are influenced by opioid analgesics to achieve analgesic effect?

A. algogen mediator synthesis
B. summation of the algogen impulses
C. algogen impulses transmission
D. activation of nociception systems
E. subjective emotional feeling of pain

3. By which phenomena do opioid analgesics diminish pain?

A. they activate descending inhibitory and modulating systems
B. they block descending inhibitory and modulating systems
C. they block transmission through ascending pathways
D. they prevent perception on thalamic and cortical levels
E. they activate transmission through ascending pathways

4. Opioid analgesics will be mainly effective in:

A. neuropathic pain
B. chronic somatic and visceral pain
C. acute nociceptive pain
D. psychogenic pain
E. acute somatic and visceral pain

5. What are the most potent opioid painkillers?

A. morphine
B. buprenorphine
C. sufentanyl
D. trimeperidine
E. butorphanol

Clinical case 3

The analysis of pharmacodynamic effects of opioid analgesics and their clinical manifestations is important for their rational and appropriate choice in different clinical cases. An important part of the efficacy and safety of opioid analgesics is their sedative effect and influence on mental activity.

1. **The influence on which structures may be responsible for sedation?**
   A. ascending pathways
   B. cerebral cortex
   C. descending pathways
   D. activating reticular formation
   E. posterior spinal horn
2. **The influence on which process may be responsible for sedative effect?**
   A. algogen mediator synthesis
   B. summation of the algogen impulses
   C. algogen impulses transmission
   D. activation of nociception systems
   E. subjective emotional feeling of pain
3. **In which clinical cases is the sedative effect of opioid analgesics important?**
   A. marked painful syndrome in natural disasters
   B. trigeminal neuralgia
   C. acute pain syndrome in myocardial infarction
   D. pulmonary edema with dyspnea
   E. chronic pain syndrome
4. **What actions of opioid analgesics on the mental activity are more pronounced in those who abuse opioids?**
   A. morphine sleep
   B. euphoria
   C. dysphoria
   D. abstinence syndrome
   E. fearless, self-confidence
5. **What action of opioid analgesics on the mental activity is more pronounced in normal patients?**
   A. morphine sleep
   B. euphoria
   C. dysphoria
   D. abstinence syndrome
   E. fearless, self-confidence

Clinical case 4

The analysis of pharmacodynamic effects of opioid analgesics and their clinical manifestations is important for their rational and appropriate choice in different clinical cases. It is well known opioid analgesics influence the respiratory system.

1. **Which group of opioids does not cause inhibition of respiration?**
   A. medium opioid receptor agonists
   B. partial agonists of k-opioid receptor and μ- opioid receptor antagonists
   C. μ- opioid receptor agonists and partial antagonists of the k-receptors
   D. strong opioid receptor agonists
   E. weak opioid receptor agonists
2. **What changes in the respiration is found at therapeutic doses of opioid analgesics?**
   A. increase of respiratory rate
   B. bradypnea
   C. breath deepening
   D. decrease of the depth of breathing
   E. increase the respiratory output
3. **What are the respiration disturbances in opioid analgesics overdose?**
   A. tachypnea
   B. bradypnea
   C. arrhythmic breathing
   D. decrease of depth of breathing
   E. increase respiratory minute volume
4. **What effects on the respiratory system can occur on opioid analgesics administration?**
   A. bronchodilation of vagal origin
   B. bronchospasm of vagal origin
   C. bronchodilation of adrenergic origin
   D. bronchospasm by histamine releasing
   E. bronchospasm by direct action
5. **What effects explain the efficacy of opioid analgesics in pulmonary oedema?**
   A. afterload reduction

B. decrease of cardiac minute volume
C. decrease of preload
D. bradypnea
E. tachypnea

Clinical case 5

It is necessary to take into account the comparative activity and duration of action of analgesics according to the route of administration for proper choice and rational use of opioid analgesics in different clinical cases. These features led to the development of different pharmaceutical forms of opioid analgesic drugs.

1. **Choose the correct version (low to high potency) of the opioid analgesics activity after parenteral administration?**
   A. morphine→ fentanyl → trimeperidine
   B. fentanyl → morphine → trimeperidine
   C. trimeperidine → morphine→ fentanyl
   D. trimeperidine → fentanyl → morphine
   E. morphine→ trimeperidine → fentanyl
2. **Choose the correct version (low to high potency) of the opioid analgesics activity after enteral administration?**
   A. pentazocine→ morphine → buprenorphine
   B. buprenorphine → morphine → pentazocine
   C. pentazocine → buprenorphine→ morphine
   D. morphine →buprenorphine → pentazocine
   E. morphine → pentazocine → buprenorphine
3. **Choose the correct version of opioid analgesics according to the duration of action (from short to long) after parenteral administration?**
   A. morphine → fentanyl → buprenorphine
   B. fentanyl → morphine → buprenorphine
   C. fentanyl → buprenorphine →morphine
   D. buprenorphine→ fentanyl → morphine
   E. buprenorphine → morphine → fentanyl
4. **Choose the correct version of opioid analgesics according to the duration of action (from short to long) after enteral administration?**
   A. tramadol → morphine → buprenorphine

B. morphine → buprenorphine →tramadol
C. morphine → tramadol →buprenorphine
D. buprenorphine → tramadol → morphine
E. buprenorphine →morphine → tramadol

5. What is the optimal dosage interval for subcutaneous morphine injection?

A. every 6-8 hours
B. every 10-12 hours
C. every 3-5 hours
D. every 1-2 hours
E. every 12-24 hours

Clinical case 6

The pharmacodynamic study of morphine and metamizol showed the presence of analgesic and antipyretic effect. It was important to analyze the mechanisms of these effects and clinical manifestations and indications for their clinical use.

1. Which components of the analgesic mechanism of action characteristic of metamizol differ from that of morphine?

A. it inhibits the release of the algogenic mediators from the presynaptic membrane
B. it inhibits algogen substances synthesis
C. it blocks impulses transmission to the spinal cord
D. it blocks specific receptors in the CNS
E. it blocks impulses transmission through ascending pathways

2. What components of analgesic action of metamizol are not characteristic of morphine?

A. pain subjective-emotional assessment
B. transmission of pain
C. sedation
D. pain transmission summation in the thalamus, limbic system
E. pain perception

3. In which cases is the administration of metamizol as analgesic preferential?

A. chronic pain syndrome
B. pain syndrome in myalgia, arthralgia
C. pain syndrome in acute myocardial infarction

D. migraine
E. biliary colic

4. The hypothermic effect of metamizol differs from that of morphine by the following mechanisms:

A. it inhibits cyclooxygenase-3 in the hypothalamus
B. it inhibits cyclooxygenase in the peripheral tissues
C. it inhibits the thermoregulatory center
D. it inhibits the cerebral cortex
E. it inhibits lipoxygenase

5. What is the main difference of hypothermic action of morphine and that of metamizol?

A. it decreases the normal body temperature
B. it decreases increased body temperature
C. it decreases increased and normal temperature
D. it decreases fever in viral diseases
E. it decreases fever in bacterial diseases

Clinical case 7

In the intensive care unit opioid and non-opioid analgesics are available to physicians. Depending on the individual pharmacodynamic and pharmacokinetic properties doctor must select preparation or preparations in diseases and pathological conditions based on their pathogenesis.

1. What is the analgesic of choice in biliary colic?

A. trimeperidine
B. metamizole
C. baralgine
D. morphine
E. omnopon

2. What properties of chosen analgesic are responsible for clinical effectiveness?

A. anti-inflammatory effect
B. anticholinergic effect
C. antispasmodic effect myotropic
D. antisecretory effect
E. litholytic effect

3. **What painkillers can be used in case of failure of the analgesic administered first?**
   A. trimeperidine
   B. metamizole
   C. baralgine
   D. morphine
   E. omnopon
4. **What painkillers can be used in case of the second failure to choose an analgesic?**
   A. trimeperidine
   B. metamizole
   C. baralgine
   D. morphine
   E. omnopon
5. **What pharmacodynamic particuliarites of analgesic administered on the second stage make it a priority?**
   A. tonogen action on the smooth muscles of the digestive tract
   B. myotropic spasmolytic action
   C. cholinoblocking activity
   D. anti-inflammatory action
   E. cholecistokinetic action

Clinical case 8

According to pain pathogenesis, doctor decided to use non-opioid analgesics with central effects in following patients: A- arthralgia, myalgia and fever; B - chronic pain with depression elements; C – trigeminal neuralgia; D - pain syndrome in acute myocardial infarction with hypertension.

1. **What non-opioid analgesic with central action can be chosen for the treatment of these patients?**
   A. clonidine
   B. paracetamol
   C. carbamazepine
   D. amitriptyline
   E. tramadol

2. **What is the correct option when choosing analgesics to the mentioned patients?**
   A. clonidine for patient A; paracetamol for D; carbamazepine for C; amitriptyline for B
   B. carbamazepine for A; clonidine for B; carbamazepine for D; amitriptyline for C
   C. amitriptyline for A; carbamazepine for B, clonidine for C; paracetamol for D
   D. paracetamol for A; amitriptyline for B; carbamazepine for C; clonidine for D
   E. paracetamol for A; amitriptyline for B; clonidine for C; carbamazepine for D
3. **What mechanism of the analgesic chosen for patient B will be responsible for clinical effectiveness?**
   A. prostaglandin synthesis inhibition
   B. stimulation of opioid receptors
   C. inhibition of neuronal serotonin reuptake
   D. alpha-2-receptor stimulation
   E. GABA-A receptor stimulation
4. **What mechanism of the analgesic chosen for patient C will be responsible for clinical effectiveness?**
   A. prostaglandin synthesis inhibition
   B. stimulation of opioid receptors
   C. inhibition of neuronal serotonin reuptake
   D. alpha-2-receptor stimulation
   E. GABA-A receptor stimulation
5. **What mechanism of the analgesic chosen for patient D will be responsible for clinical effectiveness?**
   A. prostaglandin synthesis inhibition
   B. stimulation of opioid receptors
   C. inhibition of neuronal serotonin reuptake
   D. alpha-2-receptor stimulation
   E. GABA-A receptor stimulation

Clinical case 9

When studying safety of opioid analgesics, side effects, their mechanisms, the principles of treatment and prevention were determined.

It was found that opioid analgesics may cause side effects virtually on all organs and systems, and their effects may be both of central and peripheral origin.

1. **What are digestive tract side effects?**
   A. constipation
   B. diarrhea
   C. increase of intestinal smooth muscles tonus
   D. increased pressure in the biliary ducts
   E. gastric hyposecretion
2. **What mechanisms may underlie these side effects?**
   A. blockade of cholinoreceptors
   B. stimulation of the tenth cranial nerve nucleus
   C. stimulation of M-cholinoreceptors
   D. action on intramural opioid receptors
   E. decreased vagus nerve tone
3. **What side effects of opioid analgesics on the cardiovascular system may be determined by the same mechanisms?**
   A. tachycardia
   B. atrioventricular block
   C. dromotrop – positive effects
   D. bradycardia
   E. arterial hypotension
4. **Which of the urinary system side effects may be due to the same mechanisms of opioid analgesia?**
   A. urinary retention
   B. polyuria
   C. false desire to urinate
   D. increased volume of urine in the bladder
   E. urinary tract dilatation
5. **Which of the respiratory system adverse events may be caused by the same mechanisms of opioid analgesia?**
   A. bronchospasm
   B. bronchodilation
   C. bronchial hypersecretion
   D. bronchial mucosal dryness
   E. xerostomia

Clinical case 10

Opioid analgesics exhibit a wide range of CNS effects, which can be undesirable and/or desirable in certain clinical cases. Thus, opioids can inhibit the cough center, respiratory and thermoregulatory center, stimulate the III and X cranial nerves.

1. **What mechanisms underlie the antitussive effect?**
   A. reflex inhibition of the cough center
   B. direct inhibition of the cough center
   C. cortex inhibition
   D. NMDA- receptor blockade
   E. opioid receptor blockade
2. **What opioids are mainly used as antitussive?**
   A. butorphanol
   B. dextromethorphan
   C. fentanyl
   D. codeine
   E. trimeperidine
3. **Under what circumstances is antitussive effect used in the clinic?**
   A. whooping cough
   B. cough in pneumonia
   C. nocturnal cough
   D. cough in rib fractures
   E. cough in cranio-cerebral trauma
4. **What does the third cranial nerve stimulation lead to?**
   A. miosis by the cholinoblocking activity
   B. miosis by cortical stimulation
   C. miosis by M-cholinomimetic activity
   D. miosis as a diagnostic feature in opioid overdose
   E. miosis as a diagnostic criterion for the therapeutic action of opioids
5. **What characterizes the emetic effect of opioids?**
   A. direct excitation of the vomiting center
   B. they stimulate trigger zone chemoreceptors
   C. vestibular disturbancies
   D. neuroleptics diminish it
   E. it is more common in suffering patients.

Clinical pharmacology of drugs on respiratory system

I. Simple clinical cases

1. An 8-year-old girl is brought in by her mother for evaluation of allergies. Each year in spring the child develops a runny nose; itchiness, watery eyes; and sneezing. She has been treated in the last years with diphenhydramine, but the child's teacher says that she is very drowsy during school. She has no other medical problems and chronic medications. The doctor diagnosed: seasonal allergic rhinitis and prescribed clemastine.

From which group is this drug?

What is the mechanism of action of antihistamine medications?

What are the common side effects of antihistamine medications?

Prove the necessity of switching to clemastine?

2. A 9-year-old boy is brought to your office because of a chronic cough. His mother says that he coughs frequently throughout the day and might cough 2 or 3 nights a month. The boy has suffered of this illness about a year, but seems to be worse in the spring and fall. He also coughs more when he is riding his bike or playing soccer. He has been treated twice in the last year for bronchitis with antibiotics and antitussive drugs but he has never seemed to clear up completely. His examination is normal, except for his lungs, which reveal expiratory wheezing. He is diagnosed with asthma and prescribed the albuterol inhaler.

From which group is this drug?

What is the mechanism of action of the albuterol?

What are the most common side effects of the albuterol?

What medications can be used to provide long-term control of asthmatic symptoms?

3. A 45-year-old patient, who suffers from chronic obstructive bronchitis complained an increased dyspnea at efforts, it can occur night as well. He has been smoking 1 pack of cigarettes /day since 17 years. Aminophylline has been administered by 300 mg 3 times/day at 8.00, 13.00, 18.00 by him. After two days, the patient of taking this drug says that there is an improvement in breathing during the day, but the night asthma attacks have not changed.

Why haven 't the nocturnal attacks?

What is the reason of the lack of aminophylline effectiveness disappeared?

What does he need to do? Which dosage regimen of aminophylline administration will you use? Why?

4. A boy of 14 years (52 kg) has been suffering from asthma since the age of five. In his last hospitalization, he developed an asthmaticus status. After the stabilization of the child's status, it was decided to prescribe aminophylline internally. As a result of therapy, the child's condition improved at first, but then shortness of breath, dry, wheezing rales in the lungs reappeared. Doctor knows that the child has smoked 5 cigarettes /day.

Explain the ineffectiveness of aminophylline.

Find suggestions of increasing the effectiveness of aminophylline.

How do you explain to the child and his parents causes of the treatment failure?

5. A 10- year-old girl (40 kg) traveled with her parents to the countryside during the flowering of fruit trees and lilac. She soon began to choke, she started to use inhaled salbutamol every 2 hours 5 times. In the past, she suffered from bronchial asthma. After 10 hours, the girl was transported by the ambulance to the hospital with diagnosis: asthmaticus status. The patient was pale, with acrocyanosis, the skin moist. The child had expiratory dyspnea, the chest excursion was limited, the respiratory rate was 42/minute, cardiac rate - 156 beats/ minute. The size of the liver and spleen were not enlarged and there wasn’t peripheral edema.

What are the causes of salbutamol ineffectiveness?

What drugs should be preferred in this case?

What are the criteria for the therapy effectiveness?

What drugs for the prevention of asthma attacks would you recommend to parents?

6. A 12- year-old child (30 kg) was hospitalized for severe asthma attacks. Bronchospasm attack was stopped after parenteral administration of aminophylline and prednisolone, which the child received for the first time. During the treatment, the patient developed agitation, hallucinations. These symptoms were regarded as consequence of glucocorticoid therapy. To treat the agitation there was prescribed diazepam in age dosage. On the 4-th day of treatment on the background of normalization of mental status, the syndrome of bronchial obstruction reoccurred.

What side effects of aminophylline do you know?

Select the criteria for assessing the safety. Explain possible causes of the reoccurrence of bronchospasm. Offer your treatment option.

7. A 35-year-old woman, suffers from bronchial asthma, atopic form. After entering the hall of the museum, she had an attack of dyspnea. One hour later she was hospitalized.

Select the correct drugs in this case. Explain why?

A. disodium cromoglycate inhaled by 0,02 g
B. theophylline: loading dose 5,6 mg/kg, maintenance dose – 0,6 mg/kg
C. epinephrine i/m 0,3-0,5 ml of 0,1%, in 15 min - i/m 0,3-0,5 ml of 5% ephedrin
D. salbutamol, inhaler 0,0001 g
E. prednisolone i/v
F. your version.

Explain why?

8. A 32- year-old woman with bronchial asthma received aminophylline internally by 150 mg 4 times daily. On the background aminophylline therapy, asthma attacks were not repeated. Meanwhile, for the treatment of acute tonsillitis, the doctor prescribed erythromycin -250 mg 4 times per day internally. On the 3-th-day of the antimicrobial therapy the patient's state worsened: by vomit, palpitations (FCC-140 beats/min. occurring.

How do you explain the causes of the sickness appearance worsening?

A. large dose of erythromycin

B. development of the delayed allergic reactions type
C. drugs incompatibility
D. aminophylline intoxication
E. your variant

What is necessary for the liquidation of the complaints occurred?

9. A 53-year-old man had bronchial asthma attack accompanied by circulatory failure II B degree (tachycardia, epigastric pulsation, diuresis, legs edema decrease). He received i/v the following drugs: 1) aminophylline sol. 2,4% -10 ml with glucose sol. 10% - 20 ml; 2) strophanthine sol.0,05% - 0,6 ml with glucose sol. 10% - 20 ml.

Select the possible effects:

A. neutralization of the aminophylline effect and occurrence of a new asthma attack
B. the worsening of the asthma attack due to the storage of calcium in cardiomyocytes
C. disturbances of heart rhythm up to heart arrest due to the storage of calcium in cardiomyocytes, which may cause heart tetanus
D. rapid and pronounced bronchodilation

10. A 27-year-old woman suffers from bronchial asthma. She has used selective sympathomimetic drugs 4-6 doses daily for 2 years. Meanwhile, on the background of an acute infectious bronchitis she had a new asthma attack with a 6 hours' duration. The inhalation of two doses of phenoterol did not stop the exacerbation, and the doctor administered i/m epinephrine sol. 0,1%-0,8 ml. In five minutes the patient's state suddenly worsened: perioral cyanosis, vomiting, palpitations, signs of bronchial obstruction appeared.

Select adequate therapy in this case:

A. 2 ml of 4% sol. methylprednisolone acetate i / m
B. 7- 8 ml of 2,4% aminophylline in 150 ml of 0,9% sodium chlorate sol. i/v infusion
C. 1 ml of 0,1% epinephrine solution s / c
D. after emergency treatment, aminophylline therapy of 0,15 g 4 time/day internally applied.

II. Multiple clinical cases

Clinical case 1

A 32-year-old woman with bronchial asthma received aminophylline internally by 150 mg 4 times daily. On the background of aminophylline therapy asthma attacks were not repeated. Meanwhile, for the treatment of acute tonsillitis, the doctor prescribed erythromycin -250 mg 4 times per day internally. On the 3-rd day of antimicrobial therapy patient's state worsened: vomit and palpitations (FCC - 140 beats/min) occurred.

1. **How do you explain the complaints?**
   A. a low dose of erythromycin
   B. a high dose of aminophylline
   C. development of delayed allergic reaction type
   D. drugs incompatibility
   E. aminophylline intoxication
2. **What treatment measures do you propose?**
   A. treatment scheme unchanged
   B. antimicrobial drugs administration from another group
   C. aminophylline dose is increased by 20-25%
   D. aminophylline dose is reduced by 20-25%
3. **What are the symptoms of poisoning with aminophylline?**
   A. bradycardia
   B. excitement
   C. seizures
   D. nausea, vomit
   E. hypoglycemia
4. **What serum level of methylxanthine causes poisoning?**
   A. 5 mcg/ml
   B. 10 mcg/ml
   C. 15 mcg/ml
   D. 20 mcg/ml
5. **What are the contraindications of methylxanthines?**
   A. ulcer disease
   B. acute pulmonary edema
   C. epilepsy
   D. paroxysmal tachycardia
   E. migraine

Clinical case 2

A 26-year-old man, (body weight 80 kg), suffering from asthma relapsing form uses inhaler selective sympathomimetics. He did not have a corticosteroid therapy in the past. The attack duration – 8 hours. During the attack, he inhaled 6 doses of salbutamol. The last inhalation, was one hour ago, but did not have any effect. The patient is pale, dry loud crackles in lungs, expiratory dyspnea. Attenuated heart tones. Cardiac frequency=156 beats/min. The liver, spleen without changes. Intramuscular 0,5 ml of 24% aminophylline sol. and inhaled sodium cromoglicate were administered. The patient's state has not improved.

1. **Why haven't the drugs been effective?**
   A. the intramuscular utilization of drugs is not rational
   B. the dose of aminophylline is small
   C. the cromoglicate sodium dose is not sufficient in this case
   D. the administration of two drugs in the same time decreases their pharmacological effect
   E. your variant
2. **Which drugs will be effective in this case:**
   A. 2ml methylprednisolone acetate 4% i/m
   B. 7-8ml of 2.,4% aminophylline in 150ml of saline i/ v infusion
   C. 1 ml of epinephrine solution 0.1% s/c
   D. after emergency treatment, aminophylline internally in dose of 150 mg 4 time/day is indicated
   E. mucolytic
3. **In which cases the mast cell degranulation inhibitors are recommended?**
   A. stopping the exacerbation
   B. long treatment of asthma
   C. allergic rhinitis
   D. status asthmaticus
4. **Explain if the epinephrine could improve patient's state:**
   A. yes, in intravenous administration
   B. yes, in subcutaneous administration
   C. is not effective in this patient, regardless of route of administration
5. **What drugs can restore β-adrenoceptor sensitivity?**
   A. methylxanthines
   B. mast cell degranulation inhibitors

C. glucocorticoids
D. antileukotrienes
E. antispazmodics

Clinical case 3

A 29-year-old man, suffering from asthma, after some stress situation worsened a duodenal peptic ulcer. On the background of internally aminophylline treatment, the patient receives an omeprazole and clarithromycin treatment.

1. How will the clinical symptoms of both diseases develop after association of omeprazole to the treatment?

A. improvement of the symptoms of both diseases
B. signs of intoxication with aminophylline, but positive dynamics of duodenal ulcer
C. neutralization of the effects of omeprazole and aminophylline
D. worsening of ulcer disease and asthma exacerbation
E. your opinion.

2. How will you change the medication:

A. treatment of the above-mentioned
B. replacement of omeprazole with lansoprazole that does not influence the metabolism of aminophylline
C. reduction of aminophylline dose by 50%
D. increase of aminophylline dose by 50%
E. replacing omeprazole with famotidine

3. How does clarithromycin influence the effectiveness of aminophylline:

A. accelerates the aminophylline metabolism
B. inhibits the aminophylline metabolism
C. does not influence the aminophylline metabolism

4. How does omeprazole influence the effectiveness of aminophylline:

A. accelerates the aminophylline metabolism
B. inhibits the aminophylline metabolism
C. does not influence the aminophylline metabolism

5. **What will be the result of interaction between aminophylline, omeprazole, clarithromycine:**
   A. increase of the effectiveness of aminophylline
   B. decrease of the effectiveness of aminophylline
   C. decrease of the effectiveness of clarithromycine
   D. decrease of the effectiveness of omeprazole

Clinical case 4

A 25-year-old women suffering from bronchial asthma during 4 years, takes orally aminophylline in doses which were calculated according to the level of theophylline in plasma. The treatment was effective. The patient visited the neuropathologist, who prescribes treatment with fluvoxamine internally.

1. **On the 4-th day after the administration of the antidepressant drug the following symptoms appeared:**
   A. new symptoms did not appear
   B. nausea, vomiting, constipation
   C. tachycardia, palpitations
   D. seizures
2. **How do you explain these symptoms?**
   A. there are side effects of aminophylline
   B. there are side effects of fluvoxamine
   C. it is a summation of side effects of aminophylline and fluvoxamine
   D. there are signs of intoxication with aminophylline
3. **These symptoms have developed because of:**
   A. liver enzyme induction, which metabolizes aminophylline
   B. liver enzyme inhibition, which metabolizes aminophylline
   C. aminophylline elimination increase
   D. liver enzyme inhibition, which metabolizes fluvoxamine
4. **What should the doctor do in this case:**
   A. reduce the dose of fluvoxamine
   B. decrease the dose of aminophylline and control the theophylline levels in blood
   C. increase the dose of aminophylline and control the theophylline level in blood
   D. indicated therapy is appropriate
   E. your variant

5. What level of theophylline will ensure the therapeutic effect?

A. 5 mcg/ml
B. 10 mcg/ml
C. 15 mcg/ml
D. 20 mcg/ml
E. 25 mcg/ml

Clinical case *5*

A 38-year-old man was hospitalized with prolonged cough access. There were made investigations (skin tests, spirometry, etc.) He was diagnosed with bronchial asthma, infectious-allergic form. After a course of treatment with phenoxymethylpenicillin by 0,25 g 4 times/day the patient's state improved and he was sent home, where he prolonged anti-asthma treatment with aminophylline (150 mg 4 times/ day orally). After two days, the temperature increased to 39°C, catarrhal phenomena and neck pain appeared. In smear tonsils was found – Staphylococcus epidermidis pathogen, sensitive to rifampicin. Rifampicin was given by 0,3 g - 2 times/ day.

1. On the 5-th day of effective antibacterial treatment of tonsillitis appeared:

A. tachycardia, palpitations, vomit
B. dyspeptic signs, allergic reactions, leukopenia
C. improvement of the tonsillitis on the background of stable remission of asthma
D. dyspnea, dry cough on the background of normal body temperature, asthma attack

2. How do you explain these effects:

A. signs of poisoning with aminophylline
B. signs of poisoning with rifampicin
C. ineffectiveness of bronchodilator treatment
D. side effects of rifampicin

3. Explain any possible interaction between the used drugs:

A. aminophylline enhances metabolism of rifampicin
B. rifampicin enhances metabolism of aminophylline
C. rifampicin and aminophylline enhance metabolism of each other
D. rifampicin enhances its own metabolism

4. **Select rifampicin specific adverse reactions:**
   A. allergic reactions
   B. tachycardia
   C. bacterial resistance
   D. hepatotoxicity
   E. ototoxicity
5. **Select the correct therapy in this case:**
   A. reducing the aminophylline dose by 30%
   B. increasing the aminophylline dose by 50%
   C. increasing the rifampicin dose by 25%
   D. the dosage and treatment regimens are reasonable and adequate
   E. your version

Clinical case 6

A 52-year-old patient suffering from bronchial asthma recurrent form during the last three years, is taking aminophylline orally, which proves to be appropriate (the dose is calculated according to the theophylline blood level). To improve sleep there was prescribed phenobarbital by 50 mg per night.

1. **Select the clinical symptoms that may occur after one month of treatment:**
   A. tachycardia, palpitations, vomit - signs of intoxication with theophylline
   B. exacerbation of bronchial asthma
   C. dyspeptic signs, allergic skin reactions, leukopenia
   D. insomnia occurrence
   E. your variant
2. **Explain the causes of occurred symptoms:**
   A. signs of aminophylline poisoning
   B. signs of poisoning with phenobarbital
   C. reducing the duration of aminophylline action
   D. development of tolerance to phenobarbital
3. **Explain the mechanism of these symptoms:**
   A. induction of microsomal isoenzyme responsible for the metabolism of aminophylline
   B. inhibition of microsomal isoenzyme responsible for the metabolism of aminophylline

C. induction of microsomal isoenzyme responsible for the metabolism of phenobarbital
D. inhibition of microsomal isoenzyme responsible for the metabolism of phenobarbital

4. How will you change the treatment in this case:

A. increasing the dose of aminophylline by 25% and controlling blood levels of theophylline
B. reducing the aminophylline dose by 25% with controlling blood levels of theophylline
C. doubling the dose of phenobarbital
D. indicated therapy is adequate
E. replacing phenobarbital with another hypnotic from benzodiazepine group

5. Select hypnotics that are inducers of liver enzymes:

A. zolpidem
B. melatonin
C. l- tryptophan
D. diazepam
E. diphenhydramine

Clinical case 7

A 62-year-old patient suffers from atopic bronchial asthma with abundant bronchial eliminations. Cardiac frequency - 62 beats/min, blood pressure - 140/80 mm Hg

1. Choose the drugs in this case:

A. salbutamol
B. isoprenaline
C. ipratropium
D. aminophylline
E. beclometasone
F. sodium cromoglycate

2. Select the most successful combinations of bronchodilators in this patient:

A. (A)+(C)
B. (A)+(D)
C. (A)+(E)
D. (C)+(F)
E. (C)+(D)
F. (B)+(C)

3. **The doctor decided to administrate to the patient parenterally Atropine sulfate. Do you agree with the doctor's decision?**
   A. yes B. no
4. **Justify your opinion:**
   A. the drug does not reduce bronchial eliminations
   B. atropine use as broncholytic, but it increases the heart rate
   C. atropine, less than other broncholytics, produces adverse reactions on the cardiovascular system
   D. parenteral administration of atropine produces many side effects
   E. the most suitable is to use M-cholinoblockers by inhalation

1. After the administration of atropine, the patients state improved by reducing bronchial eliminations. But after 10 days of treatment, the patient's state worsened again: fever -37.8°C, cough with dense sputum, cardiac frequency = 90 beats/min. **Explain the causes of these changes in the patient?**
   A. ordinary course of the disease
   B. an overdose of atropine, which developed hyperthermia
   C. reduction of sputum drainage with her subsequent infection
   D. influence of atropine on the biosynthesis of prostaglandins stimulating the respiratory and thermoregulatory center
   E. disturbances of immune process were produced by the atropine

Clinical case 8

A 45-year-old patients with recurrent bronchial obstruction syndrome developed the reduction of susceptibility to cholinoblockers and adrenomimetics.

1. **What drug can be prescribed to reduce the number and severity of asthma attacks**:
   A. inhalation of β_2-adrenomimetics more than 6 times daily
   B. inhalation of м-cholinoblockers
   C. epinephrine s/c in big doses to stop bronchospasm
   D. aminophylline i/v
   E. systemic glucocorticoids
2. **The doctor introduced sol. Epinephrine 0.1% - 1 ml s / c. Do you agree with the drug choice?**
   A. yes B. no

3. **Explain why?**
   A. epinephrine - fast and effective bronchodilator
   B. epinephrine - increases the sensitivity of β_2-adrenoceptors
   C. if effectiveness of β_2- adrenomimetics decrease, the efficiency of epinephrine decreases too, therefore systemic glucocorticoids are recommended
   D. epinephrine causes fewer side effects
   E. aminophylline is used as broncholytic i/v
4. **After entering epinephrine the patient's state worsened. What are your actions?**
   A. to use the antagonists of epinephrine
   B. to use the β_2-adrenoblockers
   C. Bronchial lavage
   D. to use inhaler glucocorticoids
   E. to use corticosteroids i /v
5. **Select the effects of epinephrine?**
   A. excitation of CNS
   B. extrasystole
   C. toxic damage of the liver
   D. tachycardia
   E. block of conductivity

Clinical case 9

A 53-year-old patient, 70 kg, suffering from bronchial asthma non-atopic form. He has used β_2-adrenomimetic for the last 4 years inhaling by 2 sprays 3-4 times daily. In the past, he smoked (30 cigarettes/day), now he reduced to 25 cigarettes/day. During the last 3 weeks, he has administered theophylline in doses of 600 mg/24 hours. As a result, dyspnea decreased and the number of nocturnal attack reduced. But the attack in the morning hours (6.00-7.00) remained.

1. **Your opinion in choosing the drug:**
   A. to use salbutamol
   B. to use inhaled glucocorticoids
   C. to use internal prednisolone
   D. it is necessary to increase the dose and number of theophylline administration

2. **The plasma concentration of theophylline in the patient is 5 mcg/ml. Your opinion about theophylline?**
   A. indication of theophylline by 5 mg/kg, internally 800 mg/24 hours
   B. indication of theophylline by 5 mg/kg, but considering the presence of smoking
   C. daily dose must be divided in 2 administrations: 8.00 am and 8.00 pm
   D. dailyl dose must be divided: 1/3 from dose at 8.00 am and 2/3 dose in the 8.00 pm
3. **If over dosage occurs with theophylline which clinical signs can be:**
   A. tachycardia
   B. CNS inhibition
   C. seizures
4. **If the patient receives the inhaled beclomethasone, which regimen of administration would you select:**
   A. daily dose equally divided in 2 doses: in the 8.00 am and in the 8.00 pm
   B. daily dose divided: 1/3 at 8.00 and 2/3 dose in the evening
   C. daily dose divided: 2/3 at 8.00 and 1/3 dose in the evening
   D. daily dose divided: 2/3 at 8.00 and 1/3 dose at 12.00
5. **Select the side effects of beclomethasone:**
   A. tachycardia
   B. oropharyngeal candidiasis
   C. raucous voice
   D. adrenal suppression

Clinical case 10

A 67-year-old patient suffering from bronchial asthma for 3 years. In anamnesis: chronic bronchitis (contact with flour). Exacerbation of breathlessness occurs more often during the night and in conditions with high levels of dust and gas. The patient eliminates until 300-400 ml of sputum, especially at night. Attacks are accompanied by the cough with the elimination of large amounts of sputum, which can be stopped by β_2-adrenomimetics, but the patient's state worsens due to

occurrence of palpitations and tremor. Drug test results have demonstrated the effectiveness of salbutamol and ipratropium.

	maximal expiratory volum/second	**vital lung capacity**
Initial Indicators	39	75
Salbutamol	51	85
Ipratropiu bromide	59	85
Placebo	45	79

1. **Indicate the type of lung obstruction in this patient?**
   A. reversible
   B. irreversible
2. **Appreciate the drug test results:**
   A. positive pharmacological test to ipratropium and salbutmol
   B. positive pharmacological test to ipratropium
   C. positive pharmacological test to placebo
   D. no drug has priority
3. **What is the most effective drug for the patient, based on the pharmacological test?**
   A. theophylline retard
   B. β_2- adrenomimetics with short duration of action in aerosol
   C. β_2-adrenomimetics with long duration of action
   D. m-cholinoblockers in aerosol
   E. glucocorticoids in aerosol
4. **What drug is more effective and harmless for patient, avoiding the tremor?**
   A. theophylline retard
   B. β_2- adrenomimetics with short duration of action in aerosol
   C. β_2-adrenomimetics with long duration of action
   D. m-cholinoblockers in aerosol
   E. glucocorticoids in aerosol
5. **Select the most effective groups of drugs and harmless to the patient?**
   A. methyilxantines
   B. m- cholinoblockers
   C. β_2-adrenomimetics
   D. glucocorticoids;
   E. mast cell degranulation inhibitors

Clinical pharmacology of drugs used in digestive disorders

I. Simple clinic cases

1. A 75 year-old patient with acute myocardial infarction, with marked painful syndrome and sinus bradycardia was admitted to the clinic. Morphine was administered for 48 hours to relieve pain and atropine to remove bradycardia. The patient did not have stools for five days. To avoid constipation the doctor prescribed drug M - 30 ml/day in the morning during meal.

What drug did the doctor prescribe?

Explain the mechanism of drug action.

Name the indications of drug administration.

2. In the preoperative period 3 patients were prescribed drugs A, B, C. Drug A was indicated 10 mg in the evening, drug B - 10 drops before bedtime, drug C (30 capsules) 1ml 30 minutes before sleep.

Determine the drugs.

What are the mechanisms of drug action?

When will the pharmacological effect develop?

Name the indications for drug administration.

3. Two patients with absence of stools for 3 days had a visit to the pharmacy. The pharmacist in both cases dispensed drug X in packet of 30 g. Patient M took the contents of the entire packet, patient N took 5 g (after consulting the physician).

Determine the drug dispensed by the pharmacist.

Will the pharmacological effects be similar in both patients? If yes, how will they manifest?

What side effects can occur?

4. The general practitioner consulted three patients:

Patient A with mild nonspecific diarrhea;

Patient B with severe nonspecific diarrhea (6 stools for 3 hours);

Patient C with mild diarrhea and abdominal pain (symptoms of irritable colon syndrome were determined).

What drugs did the doctor prescribe?

How can the efficacy of selected drugs be explained?

What will the dosage regimen be?

5. During his working day, the doctor was asked to examine:

Patient A with vomiting after anesthesia recovery

Patient B with vomiting after radiotherapy

Patient C with vomiting and pain under the right costal margin

Patient D with vomiting caused by space sickness disorders

Patient E with gestational vomiting (in pregnancy).

What drug did the doctor administer to stop the vomiting in patients?

How can the efficacy of selected drugs be explained?

Which drugs can reduce the adverse effects of selected antiemetic drugs?

6. There were some patients admitted to the clinic:

Patient A with postoperative marked flatulence

Patient B with postoperative mild intestinal distension and flatulence

Patient C with flatulence and dyspepsia

Patient D with meteorism and steatorrhea.

What drugs will the doctor prescribe to patients?

Justify the selection of drugs.

What will the dosage regimen be?

7. A patient with duodenal ulcer associated with diabetes mellitus was prescribed an antibiotic with bacteriostatic effect for anti-Helicobacter Pylory treatment. During the treatment the patient noted an accelerated gastric and intestinal peristalsis.

What group of drugs was prescribed?

How can the beneficial effect on intestinal atony be explained?

What will the prolonged administration of these drugs lead to?

8. Using the principles of ulcer treatment, tailor the treatment plan for the following patients:

Patient A - duodenal ulcer and gastric hypersecretion

Patient B - Zolinger-Elisson syndrome

Patient C - gastric hyposecretion.

Justify the selected groups of drugs.
What is the optimal dosage regimen?

9. Two patients underwent self-treatment without consulting the doctor. Patient A with duodenal ulcer underwent self-treatment with sodium hydrocarbonate without medical supervision, patient B underwent self-treatment with Maalox.

Assess the self-treatment performed by the patients.
What are the differences in anti-ulcer effect of drugs?
Which complications can occur during the treatment?
What is the optimal dosage regimen?

10. Patient M with duodenal ulcer underwent self-medication, without consulting the doctor and without medical supervision, with Maalox 1 tablespoon 30 min, before meals (5 meals per day) and in the evening before sleep. Patient N with duodenal ulcer took Maalox prescribed by the doctor, 1 tablespoon 1 hour after meals (5 meals per day) and in the evening before sleep.

Which is the optimal dosage regimen?
Justify the dosage regimen.
What factors will influence the effectiveness of Maalox?
Name the causes of treatment failure.

II. Multiple clinical cases

Clinical case 1

A patient with complaints of acute pain in the epigastric region mostly at night was admitted to the Gastroenterology Department. The pain diminished with the administration of food and occured one hour after meals. The pain intensity gradually increased, reaching its peak 2-3 hours after meals. Endoscopic examination revealed: gastric hypersecretion with acidity of about 500 mecv/l; H. pylori +++. Diagnosis: acute duodenal ulcer.

1. What groups of antibacterial drugs have to be used for H. pylori eradication?

A. cephalosporins
B. macrolides
C. aminoglycosides
D. nitroimidazole derivatives

E. fluoroquinolones
F. tetracyclines

2. Which combination of antimicrobial drugs may be recommended to the patient?

A. clarithromycin + metronidazole
B. clarithromycin + gentamicin
C. amoxicillin + metronidazole
D. ceftriaxone + gentamicin
E. doxycycline + ampicillin
F. amoxicillin + clarithromycin.

3. What antimicrobial drug can manifest a prokinetic effect?

A. amoxicillin
B. metronidazole
C. doxycycline
D. clarithromycin
E. gentamicin
F. ampicillin
G. ceftriaxone
H. ciprofloxacin

4. Which drugs develop a greater resistance of H. pylori?

A. gentamicin
B. metronidazole
C. ampicillin
D. clarithromycin
E. amikacin
F. polymyxin

5. Which group of antimicrobial drugs can cause disulfiram-like reaction in case of alcohol abuse?

A. penicillins
B. macrolides
C. aminoglycosides
D. nitroimidazole derivatives
E. polymyxins
F. fluorchinolones
G. monobactams
H. carbapenems

Clinical case 2

A patient with complaints of pain in the epigastric region was admitted to the Gastroenterology Department. The pain intensified during meals. The endoscopic examination revealed: *gastric ulcer with hyposecretion, positive H. pylori*. Based on the obtained data, the diagnosis was made: *acute gastric ulcer in exacerbation*. A comprehensive etiopathogenetic treatment was initiated.

1. **Which association of anti-ulcer drug groups has to be administered?**
   A. drugs suppressing hydrochloric acid secretion + antacids
   B. antacids + anti-helicobacter drugs
   C. antacids + gastroprotectors
   D. anti-helicobacter drugs + drugs suppressing hydrochloric acid secretion +gastroprotective drugs
   E. antacids+ cytoprotector drugs + anti-helicobacter drugs.
2. **Which drugs decrease gastric secretion most effectively?**
   A. Antigastrinics
   B. H**2**- histaminoblockers
   C. M- cholinoblockers
   D. proton pump inhibitors
   E. prostaglandin analogues
3. **What combination of effects is characteristic for the antisecretory action of the most effective group?**
   A. decrease the nocturnal secretion stimulated by the vagus; the antisecretory effect lasts for 6-12 hours;
   B. decrease basal, nocturnal and stimulated secretion; the antisecretory effect lasts for 18-24 hours;
   C. decrease stimulated secretion by histamine and nocturnal one; the antisecretory effect lasts for 12-24 hours;
   D. decrease stimulated secretion by food and pentagastrin; the effect lasts for 2-11 hours;
   E. decrease stimulated secretion by gastrin, serotonin, glucagon; the effect lasts for 12-24 hours;
4. **What dosage regimen of the most effective antisecretory drugs has to recommended ?**
   A. low dose (20 mg/day) for 4-8 weeks
   B. low dose (20 mg/day) for 2 weeks

C. medium dose (40 mg/day) for 2 weeks
D. high doses (80-160 mg/day) for 4-6 weeks
E. extremely high doses (120-360 mg/day) for 2-4 weeks

5. **Which side effects can occur at uncontrolled administration of the most effective group of antisecretory drugs ?**
   A. hematological disorders
   B. malignant ulcer
   C. systemic alkalosis
   D. enzyme induction
   E. rebound phenomenon
   F. increased frequency of intestinal infections.

Clinical case 3

An out-patient with duodenal ulcer and marked hypersecretion (500 mmol/l) underwent self-treatment with sodium bicarbonate with doses determined individually depending on the intensity of the painful syndrome. After consulting the patient, the doctor made some recommendations based on the characteristics of sodium bicarbonate as antacid.

1. **Which group of antacids, according to the solubility in acid and water, does sodium bicarbonate belong to?**
   A. resorptive
   B. neutralizing
   C. adsorbent
   D. alkalizing
   E. non-systemic
2. **Describe the effectiveness of sodium bicarbonate?**
   A. fast and long-term effect
   B. slow and short-term effect, with discomfort in the epigastric region
   C. fast and short-term effect with pain relief
   D. slow and long-term effect with slow pain relief
   E. very intensive and long-term effect.
3. **How does the excessive amount of sodium bicarbonate act on ulcer?**
   A. it forms a protective layer
   B. it can cause a superficial lesion of the ulcer crater

C. it can cause deep damage of ulcer
D. it increases the prostaglandin synthesis
E. it increases the mucus formation

4. **Choose the side effects of uncontrolled administration of sodium bicarbonate?**
   A. gastric hemorrhage
   B. ulcer perforation
   C. systemic acidosis
   D. agranulocytosis
   E. pylorostenosis
5. **Sodium bicarbonate as an antacid drug differs from magnesium by:**
   A. stronger and longer effect
   B. higher incidence of systemic side effects
   C. causes constipation
   D. causes flatulence
   E. causes diarrhea

Clinical case 4

An out-patient with duodenal ulcer and moderate hypersecretion (400 mecv /l) underwent self-treatment with Maalox -15 ml 30 minutes before meals, without medical consultation and supervision. After consulting the patient, the doctor made some recommendations based on the characteristics of Maalox as antacid.

1. **Which group of antacids, according to the solubility in acid and water, does Maalox belong to?**
   A. resorptive
   B. neutralizing
   C. adsorbent
   D. alkalizing
   E. non-systemic
2. **Describe the effectiveness of Maalox?**
   A. fast and long-term effect
   B. slow and short-term effect accompanied by discomfort in the epigastric region
   C. fast effect and short pain relief
   D. slow and long-term effect with slow pain relief

E. very intense and long-term effect.

3. How does the excessive amount of Maalox act on ulcer?

A. it forms a protective film
B. it can cause a superficial lesion of the ulcer crater
C. it can cause deep damage of ulcer
D. it increases prostaglandin synthesis
E. it increases the mucus formation

4. What are the advantages of association of active compounds of Maalox compared to separate compounds?

A. reduce the incidence of constipation caused by magnesium
B. reduce the incidence of diarrhea caused by magnesium
C. reduce the incidence of constipation caused by aluminum
D. reduce the incidence of diarrhea caused by aluminum
E. increase the solubility in water
F. form insoluble salts in water

5. What is the dosage of Maalox recommended by the doctor?

A. 15 ml 1 hour after each meal (regular meals every 3-4 hours)
B. 15 ml with meals
C. 15 ml before sleep
D. 15 ml in the morning before breakfast
E. 15 ml 30 minutes before each meal

Clinical case 5

A patient with complaints of a persistent pain in the epigastric region was admitted to the the Gastroenterology Department. The pain did not decrease after prescribing Famotidine. On careful examination there was revealed a gastrointestinal tumor with marked gastrin secretion. In preoperartive period the conservative therapy was initiated.

1. Which antisecretory drugs have to be administered?

A. H2-histaminoblockers
B. proton pump inhibitors
C. M- cholinoblockers
D. somatostatin analogues
E. prostaglandin analogues

2. Choose the indications characteristic for the drug group selected for the patient?

A. duodenal ulcer with hypersecretion, Zollinger-Ellison syndrome

B. vipoma, gastrinoma, carcinoid tumors
C. gastric ulcer with hypoacidity, Zollinger-Ellison syndrome
D. duodenal ulcer with normosecretion, reflux esophagitis
E. reflux esophagitis, duodenal ulcer resistant to H**2**-histamino-blockers

3. What combination of effects is characteristic for the antisecretory action of this group?
A. decrease nocturnal secretion stimulated by vagus; the antisecretory effect lasts for 6-12 hours
B. decrease basal, nocturnal and stimulated secretion; the antisecretory effect lasts for 18-24 hours
C. decrease secretion stimulated by histamine and nocturnal secretion; the antisecretory effect lasts for 12-24 hours
D. decrease secretion stimulated by food and pentagastrin; the effect lasts for 2-11 hours
E. decrease secretion stimulated by gastrin, serotonin and glucagon; the effect lasts for 12-24 hours

4. What examinations are required to monitor the safety of the drugs taken by the patient?
A. peripheral blood
B. gallbladder ultrasonography
C. bilirubin and its fractions
D. glycemia
E. growth hormone.

5. What side effects may occur in the patient when administering the selected group of drugs?
A. hyperbilirubinemia, increased alkaline phosphatase, gamma-glutamiltranspeptidase
B. hematological disorders
C. dyspeptic disorders
D. gallstones.

Clinical case 6

A patient with acute abdomen syndrome was admitted to the Emergency Surgery Department. Preoperatively it was necessary to evacuate the intestinal contents.

1. **Which group of laxatives/purgatives can be administered in this case?**
   A. volume laxatives
   B. contact purgatives
   C. emollient laxatives
   D. osmotic purgatives
   E. laxatives for rectal use
2. **What is the mechanism of their action?**
   A. breakdown into active components under the lipase action
   B. adsorption of water with increase in volume of the drug
   C. dissociation in anions and cations with retention of water absorption and / or water attraction from the tissues
   D. irritation of the rectal mucosa
   E. inhibition of Na/K-ATPase.
3. **What therapeutic effect does it have?**
   A. it develops over 1-3 hours with the bowel contents evacuation
   B. it develops over 15-30 minutes with the rectum content evacuation
   C. it develops over 1-3 hours with the entire bowel contents evacuation
   D. it develops over 1-3 hours with the rectum contents evacuation
   E. it develops over 15-30 min with the entire bowel contents evacuation
4. **Indicate the drug form and its way of administration?**
   A. powder - 30 g, with sufficient liquid
   B. rectal clysters - 30 g
   C. enteric coated tablets - 5 g
   D. capsules - 1 ml, or bottles - 30 ml
   E. rectal suppositories.
5. **Name the indications for the selected drug as purgative?**
   A. systematic treatment of idiopathic functional constipation
   B. occasional treatment of idiopathic functional constipation
   C. acute poisoning
   D. hemorrhoids
   E. to prepare the patient for the emergency ultrasound investigation of the digestive tract

Clinical case 7

A patient with complaints of abdominal pain and stools once per 3-4 days was admitted to the Department of Internal Medicine. After examination the patient was diagnosed with *Irritable* Bowel Syndrome with constipation. The doctor decided to prescribe lactulose.

1. **Which 2 groups of laxatives and purgatives does lactulose belong to?**
   A. irritant purgatives
   B. osmotic purgatives
   C. laxatives of volume
   D. emollient laxatives
   E. laxatives for rectal use.
2. **Indicate the mechanisms of the laxative/ purgative effect:**
   A. increases in volume in the liquid medium and the bowel peristalsis increases
   B. dissociates in active components under the action of lipase
   C. enters the fecal bolus, attracts water and lubricates the intestinal contents
   D. irritates the colon mucosa through active constituents
   E. increases the osmotic pressure with retention of water and electrolyte absorption stimulating peristalsis
3. **Indicate the latency of the development of laxative and purgative effects of lactulose:**
   A. over 48-120 hours
   B. over 15-30 min
   C. over 12-24 hours
   D. over 1-3 hours
   E. over 5-10 hour
4. **Name the indications for lactulose administration as laxative:**
   A. hemorrhoids
   B. acute poisoning
   C. to avoid the effort during defecation in patients with acute myocardial infarction
   D. long-term treatment of idiopathic constipation
   E. pre-medication for emergency surgery.
5. **Select the indications for lactulose administration as laxative:**
   A. hemorrhoids

B. acute poisoning
C. to avoid the effort during defecation in patients with acute myocardial infarction
D. long-term treatment of idiopathic constipation
E. pre-medication for emergency surgery.

Clinical case 8

A patient with complaints of dyspeptic disorders (diarrhea with periodic constipation), epigastric pain, and loss of weight (5 kg over the last 2-3 months) was admitted to the Department of Internal Medicine. Based on the laboratory and instrumental investigations, the diagnosis was made: *Recurrent acute pancreatitis with painful syndrome*. *Chronic cholecystitis.*

1. Which combination of enzyme replacement drugs will you administer to the patient?
A. pancreatin + extract of the gastric mucosa
B. pancreatin + adsorbent
C. pancreatin
D. pancreatin + bile extract + hemicellulase
E. pancreatin +hemicellulase + vitamins

2. Which components of replacement drugs will be effective in the patient`s treatment?
A. hemicellulose
B. lipase
C. bile extracts
D. protease
E. amylase

3. Which drugs contain the necessary components for the above mentioned patient?
A. creon
B. panzinorm forte
C. festal
D. digestal
E. pancreoflet
F. mezim forte
G. wobenzim
H. triferment.

4. **Name the effects of the components from the selected replacement drugs that will improve the development of chronic acalculous cholecystitis:**
   A. breakdown of indigestible fiber
   B. anti-foaming action
   C. fat emulsification
   D. amylolytic action
   E. increased absorption of fat-soluble vitamins
   F. choleretic action.
5. **What effects can pancreatin action produce?**
   A. decrease of flatulence
   B. decrease of diarrhea
   C. choleretic effect
   D. decrease of pain
   E. improvement of malabsorption
   F. stabilization of body weight.

Clinical case 9

A patient with a severe pain in the epigastric region (the pain having a ring-like character) diarrhea, steatorrhea, increased elastase was admitted to the Department of Internal Medicine. Having performed the necessary investigations, the diagnosis was confirmed: *chronic pancreatitis in exacerbation with marked painful syndrome.*

1. **Which combination of enzyme substitution drugs will you administer to treat the patient?**
   A. pancreatin + bile extract + plant extract
   B. pancreatin
   C. pancreatin + extract of the gastric mucosa
   D. pancreatin + adsorbent
   E. pancreatin + bile extract + hemicellulase
2. **Which enzyme substitution drugs contain the necessary components for the patient?**
   A. mezim forte
   B. festal
   C. pangrol
   D. creon
   E. panzinorm forte

F. pancreoflet
G. wobenzim
H. triferment
I. digestal

3. Which characteristics of substitution drugs are responsible for reducing the pain in the patient?

A. increase of lipase secretion
B. decrease of cholecystokinin secretion
C. breakdown of indigestible fiber
D. use of high doses of pancreatin
E. use of low doses of pancreatin

4. Which component of substitution drugs is important for the patient with excessive loss of body mass?

A. amylase
B. protease
C. lipase
D. hemicellulose
E. bile extracts
F. dimethylpolysiloxane

5. What forms of drugs will you choose for the patient?

A. enterocapsules
B. regular tablets
C. enteric coated microspheres in capsules
D. dragées.

Clinical case 10

A patient with the diagnosis of *toxic drug hepatitis in severe evolution* was admitted to the Hematology Department. The doctor has more hepato-protective drugs.

1. Which drug is an aminoacid derivative?

A. silymarin
B. essential
C. ademethionine
D. lipoic acid
E. ursodeoxycholic acidthiotriazoline

2. **Which of the following drugs contributes to free radicals setting and lipid peroxidation inhibiting?**
   A. silymarin
   B. essential
   C. ademethionine
   D. lipoic acid
   E. ursodeoxycholic acid
   F. thiotriazoline
3. **Which of the following drugs are donors of thiol groups?**
   A. silymarin
   B. essential
   C. ademethionine
   D. lipoic acid
   E. ursodeoxycholic acid
   F. thiotriazoline
4. **Which drug contributes to the synthesis of methyl groups?**
   A. silymarin
   B. essential
   C. ademethionine
   D. lipoic acid
   E. ursodeoxycholic acid
   F. thiotriazoline
5. **What drug inhibits prostaglandin and collagen synthesis?**
   A. silymarin
   B. essential
   C. ademethionine
   D. lipoic acid
   E. ursodeoxycholic acid
   F. thiotriazoline.

Clinical pharmacology of drugs used in cardiac arrhythmias, angina pectoris and heart failure

I. Simple clinic cases

1. A 71 year-old man is seen by the doctor after being hospitalized for myocardial infarction (MI). He underwent successful angioplasty and is currently asymptomatic. Prior to his MI, he was on no medication. He is neither a smoker nor diabetic. During his hospitalization, he was noted to have persistently elevated blood pressure readings. In childhood he underwent asthma attacks, with no recent wheezing episodes reoccurring. While hospitalized, he was put on oral metoprolol.

For which adrenoceptor is metoprolol selective?

What effects do agents such as metoprolol have on the cardiovascular system?

In which organ is metoprolol primarily metabolized?

2. A 62 year-old woman with a history of two previous myocardial infarctions (MIs) comes to the emergency room with shortness of breath. During the previous 2 weeks, she has been developing dyspnea with exertion and swelling of her legs. She sleeps on three pillows because she coughs and gets short of breath if she tries to lie flat. In the emergency department, she is sitting upright, appears to be in moderate respiratory distress, tachycardia and arterial hypertension. She has jugular venous distension to the angle of her jaw. On lung auscultation, wet rales are heard bilaterally. She has pitting edema of both lower legs up to her knees. A chest X-ray confirms the diagnosis of pulmonary edema. She was placed on oxygen and i/v injection of furosemide is given immediately.

What is the mechanism of furosemide action?

What electrolyte abnormalities can be caused by furosemide?

3. A 69 year-old man sees you in the office for follow-up chronic congestive heart failure. He has a marked reduction in his ejection frac-

tion following a series of myocardial infarctions (MIs). He also has hypertension and type II diabetes mellitus. His symptoms include dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, and peripheral edema. His renal function is normal. He is put on appropriate diabetes treatment, along with angiotensin-converting enzyme (ACE) inhibitor and a loop diuretic. You decide to add digoxin to his regimen.

What is the effect of digoxin on the normal heart?

What is the effect of digoxin on the failing heart?

What neural effects does digoxin have?

What are the side effects and toxicities of digoxin?

4. A 63 year-old man is being managed in the intensive care unit following a large anterior wall myocardial infarction (MI). He has been appropriately managed with oxygen, aspirin, nitrates, and beta-adrenergic receptor blockers but has developed recurrent episodes of ventricular tachycardia. During these episodes he remains conscious but feels dizzy, and he becomes diaphoretic and hypotensive. He is given an IV bolus of lidocaine and put on an IV lidocaine infusion.

To what class of antiarrhythmics does lidocaine belong?

What is lidocaine's mechanism of action?

5. A 54 year-old patient weighing 68 kg, was admitted in the cardioreanimation department complaining of sudden palpitations, anxiety, weakness. On examination, the patient is conscious, pale, the heart rate of approximately 154/ minute, pulse 123 beats/min., cardiac arrhythmia, AP 105/70 mm Hg. On ECG - atrial fibrillation. "a paroxysm of atrial fibrillation" was diagnosed, it was decided to hold a pharmacological cardioversion by amiodarone introduction.

Which drugs can be used?

Calculate the loading dose of amiodarone.

6. A 59 year-old man was hospitalized in the reanimation department with dyspnea, anxiety. On examination there were revealed polypnea, acrocyanosis and transpiration. On auscultation: moist and crackling rales were heard over the pulmonary area. The patient was diagnosed with cardiac pulmonary edema.

What drugs will the complex treatment include?

7. Patient R. suffered from angina pectoris, IIIrd functional class. The heart rate - 90 beats per minute, blood pressure 150/80 mm Hg, conduction disturbances and cardiac contractility were not revealed. In the history of the patient chronic bronchitis with bronhoconstriction syndrome in remission and liver steatosis were registered.

Determine the objectives of pharmacotherapy (the first step of drug therapy selection).

Select the most optimal antianginal therapy scheme. Determine the dose of antianginal agents, the frequency of administration and the methods of monitoring the effectiveness and safety of the above mentioned agents.

As a result of the therapy the patient's condition improved. Frequency of angina attacks decreased from 5 to 1-2 times a day, attacks began to appear with greater exertion, attacks
completely disappeared. HR- 55 beats/ min. P-Q lengthened from 0.18 to 0.24 seconds.

Specify the changes recommended by pharmacotherapy.

8. Patient B. of 62 years old was first diagnosed with angina pectoris. Attacks occured during the physical activity on (walking and climbing stairs). In the history of the patient 5 years ago, artery occlusive disease was suspected. The blood pressure 120/60 mm Hg, the heart rate 65 beats per minute.

What antianginal drugs are indicated for the treatment of the patient?

On the background of the therapy, the patient developed acute intramural myocardial infarction.

What are the possible causes of heart attack?

9. A 56 year-old patient diagnosed with angina pectoris receives isosorbide dinitrate 10 mg 4 times /day. His heart rate is 80 beats / min, the blood pressure 140/80 mm Hg. In 1 month of therapy attacks of angina appeared again.

What are the possible causes of effectiveness failure? Why?

How would you change the antianginal therapy?

How would you change the antianginal therapy if meanwhile the therapy with nitrates would lead to cerebral stroke?

10. Patient B. of 58 years old was hospitalized being diagnosed with cardiosclerosis after myocardial infarction, atrial fibrillation, chronic circulatory failure -IIB degree. The received treatment was digoxin 0.5 mg/day, hydrochlorothiazide 100 mg/day. On the 7-th day of treatment there occurred nausea, vomiting, diarrhea and insomnia. Heart rate -54 beats/ minute. BP- 120/70 mm Hg, blood creatinine- 80 mkmol /l. In plasma: potassium 3.7 mmol, sodium 102 mmol/l. ECG: atrial fibrillation, depression of segment ST in V4-6 derivatives, ventricular extrasystoles-type trigeminy.

The doctor diagnosed a developing glycoside intoxication. What would the correct tactics be?

Against the background of ongoing activities in 3 days disappeared the phenomenon of glycoside intoxication. Electrolyte composition of blood normalized, the heart rate - 88 per minute, missing pulse deficit as well as extrasystoles disappearance. ECG revealed a dramatic expansion of cavities of the heart. Select them following the effective and safe drugs for additional treatment.

II. Multiple clinical cases

Clinical case 1

A patient was hospitalized in the cardiologic department with dyspnea on moderate physical effort, heart palpitations, edema in the region of the lower limb. The objective exam revealed, at the base of lungs, moist crackling rales, cardiomegaly, atrial fibrillation of tachysystolic form, LV ejection fraction -35%, hepatomegaly. The diagnosis was chronic congestive heart failure.

1. **Which groups of preparations can be used in the treatment of congestive heart failure?**
   A. cardiac glycosides
   B. nonglycoside cardiotonics
   C. organic nitrates
   D. angiotensin-converting enzyme inhibitors
   E. agiotenzine receptor antagonists
   F. calcium channel blockers
   G. beta-adrenoblockers

2. **Which drug from the cardiac glycoside group will represent the first choice for this patient?**
   A. strofantine
   B. corglicon
   C. digoxine
   D. lanatozide
   E. digitoxine
3. **Which dosage regimen will be recommended to the patient ?**
   A. rapid digitization
   B. slow digitization
   C. moderate digitization
   D. administration of a low dosage (example 0,125=0,25mg/day for digoxine)
4. **Which drug out of calcium channel blockers group will represent the first choice for this patient?**
   A. verapamil
   B. diltiazem
   C. nifedipine
   D. amlodipine
5. **Which diuretics may be administered to this patient and in which dosage regimen?**
   A. furosemide
   B. acetazolamide
   C. hydrochlorothiazide
   D. spironolactone
   E. triamtiren

Clinical case 2

A patient of 55 years old, during some years, has been recorded on ECG the phenomenon of WPW. Throughout the last period the patient complained of palpitations accompanied with unpleasant sensations in the heart region, vertigo, headache, nausea, fatigue. In the last 3 days, such attacks have become more frequent (up to 5-6 times a day). The patient addressed to the doctor. From the history it was found that she has been suffering from chronic heart failure II-nd degree during the last 6 years. The objective exam has revealed skin rash, the patient was

irritated. On EKG- supraventricular paroxysmal tachycardia detected on the base of WPW syndrome. Eosinophilia in the blood was spotted.

1. **Which drug must be administered to the patient for the exacerbation treatment?**
   A. amiodarone
   B. dizopiramide
   C. verapamil
   D. ajmaline
   E. izoprenaline
   F. lidocaine
   G. propranolol
   H. procainamide
2. **Determine the optimal treatment scheme for the selected preparation:**
   A. 5 mg /kg in 250 ml solution of glucoze 5% , 2-3 times per day i/v by perfusion (maximal dose 1,2 g in 24 hours)
   B. 50 mg i/v (during 3-5 min. in 10 ml solution of glucoze 5% or isotonic solution of Na Cl) or i/m.
   C. 0, 5-1, 0 i/v (each 2 min. by 0,1-0, 2) or i/m
3. **After intravenous administration of antiarrhythmic preparation, paroxysmal tachycardia was suspended.**
   What is the patient's treatment strategy next?
   A. treatment maintenance with the administration of the selected antiarrhythmic preparations
   B. surgical treatment of WPW syndrome without taking medication
   C. surgical treatment after patient stabilization through the administration of an antiarrhythmic drug
   D. dosage maintenance and drugs needed for heart failure compensation.
4. **Which drugs will you choose to continue the treatment for this patient?**
   A. digoxine
   B. verapamil
   C. amiodarone
   D. procainamide
   E. lizinopril
   F. furosemide
5. **Following the treatment during several months, there appeared other side effects: cough, dyspnea, hypotension, cheratopatia. Which drugs may cause them?**
   A. digoxine
   B. verapamil
   C. amiodarone
   D. procainamide
   E. lizinopril
   F. furosemide

Clinical case 3

Patient D, of 48 years has presented chest pain crises on moderate physical effort. The history of orthostatic hypotension was sublingual administration of nitroglicerine, the patient does not use nitroglycerin. Associated diseases: hypertension, hypofunction of the thyroid gland. The objective exam revealed BP-180/100 mmHg, HR- 62 beats /min.

1. **Which drugs are contraindicated for this patient?**
   A. beta-blockers
   B. amiodarone
   C. verapamil, ltiazem
   D. captopril
   E. nifedipine
   F. isosorbide dinitrate
2. **Select the drugs for the treatment of the patient:**
   A. atenolol
   B. amiodarone
   C. isosorbide dinitrate
   D. amlodipine
   E. verapamil
   F. enalapril
3. **The condition of the patient improved after the treatment was carried out. Chest pain crises have disappeared, BP-135/85 mmHg, HR-70/min., but in 6 months of treatment chest pain crises and hypertension have reappeared again. What is the cause?**
   A. the advancement of cardiovascular disease
   B. insufficient dosage of drugs
   C. development of medical tolerance
   D. withdrawal syndrome
4. **What changes are needed in the treatment of this patient?**
   A. increasing the dosage of administered preparations
   B. change the dosage regimen during the day without increasing the dose of administered drugs
   C. include in the treatment a selective beta-adrenoblocker
   D. changes of dosage regimen including a selective beta-blocker in the treatment
5. **What are the side effects of nitrates?**
   A. methemoglobinemia
   B. orthostatic hypotension
   C. steal coronary phenomenon
   D. headache, flushes of heat
   E. pretibial edemas
   F. bronchial spasm after large dose intake

Clinical case 4

A 62 year-old patient, was diagnosed with primary angina. Chest pain crises were triggered by physical exertion on stair lifting. From the history: five years ago the patient was suspected with endarteritis. BP-120/60 mm Hg, HR- 65 beats/ min.

1. **Which antianginal drugs are indicated for this patient?**
   A. dipyridamole
   B. trinitrolong
   C. nifedipine
   D. pentoxiphylline
   E. beta-adrenoblockers
2. **Despite the administered treatment, patient's condition worsened, the cryses have become more frequent. Which are the possible causes of myocardial infarction?**
   A. usual evolution of the disease
   B. steal coronary phenomenon
   C. increased myocardial oxygen demand
   D. insufficient action of the indicated drugs

The doctor added beta blocker-propranolol to the treatment 40 mg x 3 times each day. The patient felt well following this treatment, but the pains appeared in the lower limbs similar to those that have been experienced before. HR-65/min., cold feet, the liveliness of the vessels is weak.

3. **What is the cause of patient worsening condition?**
   A. vasodilation and arterial hypotension
   B. vasodilation, arterial hypotension and reflectory tachycardia
   C. unknown mechanism
   D. increased peripheral vascular resistance
4. **How would you proceed further?**
   A. gradually decrease the administration of propranol
   B. add calcium channel blocker to the treatment
   C. add pentoxiphylline to the treatment
   D. gradually decrease the administration of nifedipine
5. **Which are the side effects of beta-blockers?**
   A. A-V block
   B. hepatotoxicity
   C. promoting bronchoconstriction

D. worsening of peripheral microcirculation
E. hyperglycemia
F. dicrease of renal function

Clinical case 5

A 56 year-old patient has stable angina and is administered isosorbide dinitrate 10 mg 4 times a day. HR-80 beats/min., BP-140-80 mmHg.

In a month after the beginning of antianginal treatment-chest pain crises have occurred again.

1. Which are the reasons of patient's worsening condition?
A. usual evolution of the disease
B. development of tolerance to nitrates
C. steal coronary phenomenon
D. withdrawal syndrome

2. How will you change the treatment?
A. increase the dose of isosorbide dinitrate
B. add verapamil
C. stop the administration of isosorbide dinitrate
D. indicate nitrong

3. What will you change if the treatment with organic nitrates would develop acute myocardial infarction in the patient?
A. increase the dose of organic nitrates
B. decrease the dose of organic nitrates
C. stop the administration of organic nitrates and administrate drugs from other groups
D. indicate heparine
E. indicate morphine or trimeperidine
F. indicate beta-adrenoblockers

4. Which are the indications for intravenous administration?
A. vasospastic angina pectoris
B. acute left ventricle failure
C. angina pectoris ,, de novo,,
D. acute myocardial infarction
E. in the absence of a response to other treatment of angina pectoris

5. **What are the principles of nitroglycerin dosage in acute myocardial infarction?**
   A. 1% solution, intravenously
   B. before the administration, dilution with NaCl isotonic solution up to the concentration of 0,005%- 0,01% (50-100 mkg/1 ml) is necessary.
   C. initial administration speed 5-10 mkg/minute
   D. the speed will be increased if necessary within 5mkg/minute, each 3-5 minutes until 200 mkg/minute.

Clinical case 6

A patient of 63 years old, was brought to the Department of Cardiology, in an hour after developing an angina access which couldn't be suspended. Upon inspection, the patient was pale, and presented no swelling. There were rales heard in the lungs. Muffled, extrasystolic cardiac sounds. CF-58 beats per minute. BP-110/70 mmHg. The abdomen was soft and painless.

On the ECG characteristic for signs of acute myocardial infarction of anterior wall of left ventricle common extrasystoles. PQ-2 sec., QRS-0.1 seC, QT-0, 42 sec.

1. **Select the antiarrhythmic drug of choice for this patient:**
   A. metoprolol
   B. moracizine
   C. lidocaine
   D. disopyramide
   E. verapamil
   F. amiodarone
2. **What are the typical side effects for the selected drug?**
   A. hypotension
   B. decrease of conduction
   C. decrease of heart contractility
   D. neurotoxicity- dizziness, drowsiness, tremor, paresthesia
   E. none of the above
3. **Which route of administration for the selected drug must be used?**
   A. intramuscular
   B. intravenous in jet

C. internal
D. intravenos perfusion
E. intravenous in jet in association with intravenos perfusion

4. What drug will be more effective and harmless for the patient in the future?

A. metoprolol
B. lidocaine
C. moracizine
D. disopyramide
E. amiodarone

5. What side effects would be characteristic for the second drug selected by you?

A. diminishing of hearing
B. bronchospasm
C. confusion
D. hypoglycemia
E. I-st degree A-V blockage
F. acute urinary retention

6. What will your tactics be to the appearance of side effects:

A. decrease the dose
B. continue the treatment with the same dose
C. administration suspension
D. replacement by another drug

Clinical case 7

Patient M, of 52 years old was hospitalized presenting charges: rhythm disorders, heart palpitations caused by physical exertion. From the history it is known that the patient suffered the last 3 years of chest pain crises in the resting period and on effort. Objective examination revealed muffled heart sounds, arrithymics 10 extrasystoles/minute-HR 72/min., BP-140/80 mmHg. ECG-sinus rhythm, HR-74 beats/min., PQ-0.18; QT-4 sec., frequent ventricular extrasystoles, were identified 2 paroxisms of atrial fibrillation.

1. Select the antiarrhythmic drug for this patient:

A. verapamil
B. disopyramide
C. ajmaline
D. amiodarone
E. quinidine
F. lidocaine

G. moracizine
H. propafenone

2. The selected antiarrhythmic drug is considered the first choice because:

A. depresses the ectopic foci in the atriums and ventricles
B. depresses the ectopic foci only in the atriums
C. depresses the ectopic foci only in the ventricles
D. no influence on the myocardial contractility
E. improves conduction through all paths leading to heart

3. Dosage regimen of the selected drug may be:

A. initially 200 mg 3 times daily with gradually decreasing the dose to 200 mg daily
B. initial dose 150 mg at each 8 hours with increasing it up to 900 mg daily
C. nictemerael dose de 600 mg
D. starting with 150 mg 3 times daily up to 200 mg daily

4. What may the side effects of the selected drug be?

A. hypotension
B. decompensation of heart activity
C. sinusal tachycardia
D. sinusal bradycardia
E. nausea, decrease of appetite
F. increase of liver enzymes
G. lupoid syndrome
H. skin photosensitivity
I. hypo or, more rarely- hyperthyroidism
J. drug storage in the cornea
K. pulmonary fibrosis

5. What methods of drug safety monitoring you know?

A. hemogram
B. liver enzymes control
C. chest X-ray
D. determination of serum concentration of the antiarrhythmic drug
E. ophtalmologyc control

Clinical case 8

A 35 year-old man after suffering an acute viral infection, blaming it on heart palpitations, which got worse on physical exertion, general weakness, shortness of breath were stated as a result of exercising.

1. **The objective exam detected atrial fibrillation which was also confirmed on ECG.**
   A. atrial extrasistolia
   B. paroxysmal supraventricular tachycardia
   C. atrial fibrillation
   D. paroxysmal ventricular tachycardia
2. **Select the antiarrhythmic drug for the treatment of paroxysmal atrial fibrillation:**
   A. quinidine
   B. propafenone
   C. propranolol
   D. verapamil
   E. procainamyde
   F. amiodarone
3. **How will you administrate procainamide in emergencies?**
   A. intravenously through perfusion
   B. orally - 0,5 g 4 times daily
   C. orally - 1 g 3 times daily
   D. intravenously through jet - 50 mg/min., up to 1000 mg
4. **How will you administrate quinidine?**
   A. 1 tablet (0.2) 3 times daily
   B. 0,2 each hour, until 1 gr., than the maintenance dose
   C. intravenously through perfusion 16 mg/min
   D. orally: first day – 1 gram, second day – 1,5 grams, third day – 2 grams
5. **How will you administrate propafenone ?**
   A. initially 1,5-3 mg/ kg i /v by perfusion in 1– 3 hours, the infusion may be repeated in 2 – 3 hours
   B. internally by 0, 15 3 times daily, then, in 3 days increasing the dose up to 0,3 3 times daily
   C. internally fixed dose 450 mg/daily (0.15 3 times daily)
   D. intravenously - 10 mg/ minute

Clinical case 9

A 58 year-old man over the past 5 years, regularly accuses retrosternal pain. After some negative emotions he felt intense pain and nau-

sea in the epigastric region. He is pale and accuses dyspnea at rest. The exam revealed extrasystoles, tachycardia, reduction of I apex sound, AP-110/80 mm Hg, supple painless belly. Non-ST elevation on ECG and pathological Q wave.

1. **What is the presumptive diagnosis?**
   A. biliary colic
   B. acute cholecystitis
   C. acute pancreatitis
   D. perforated ulcer
   E. myocardial infarction
2. **What drugs does the patient need immediately?**
   A. opioid analgesic
   B. antipyretic analgesic
   C. spasmolithycs
   D. antianginal drugs
   E. antiarrhythmics
   F. anticoagulants
3. **Which of antianginal drugs represent the first choice in this case?**
   A. nifedipine
   B. verapamil
   C. metoprolol
   D. nitroglicerine
   E. dipyridamole
   F. amlodipine
4. **Which route of administration is more suitable in this case?**
   A. oral
   B. sublingual
   C. ointment
   D. intravenous perfusion
   E. retard plaster
   F. intramuscular
5. **What antithrombotics represent the first choice in this case?**
   A. heparine
   B. nadroparine
   C. warfarine
   D. ethyl biscumacetate
   E. streptokinase
   F. acetylsalicylic acid

Clinical case 10

A 40 year-old man is stressed out due to problems at work. He has unpleasant dreams at night, retrosternal pain that stops under sublingual nitroglycerin administration. The ECG, performed in the clinic revealed no pathological changes.

1. **What is the presumptive diagnosis for this patient?**
   A. neuro-circulatory dystonia, cardia type
   B. angina rest
   C. neurasthenia
   D. prinzmetal angina
   E. insomnia
2. **What medical treatment will you prescribe to this patient?**
   A. neuroleptics
   B. hypnotice
   C. sedatives
   D. antianginals
   E. anxiolytics
   F. antiaplatelets
3. **In case of antianginal drug prescription, which one will represent the first choice?**
   A. nitroglycerin
   B. bisoprolol
   C. isosorbide dinitrate
   D. nifedipine
   E. verapamil
   F. amiodarone
4. **What are the mechanisms by which the calcium channel blockers from the dihydropyridines group manifest their effect?**
   A. decreasing the left ventricular afterload due to smooth muscle relaxation of arteries
   B. reduction of preload due to expansion of capacitance vessels
   C. coronarodilation
   D. reduction of cardiac inotropism and, as a result, reduction of oxygen demand
   E. decrease of simpato-adrenergic influences on the heart
   F. increasing of myocardium resistance to hypoxia
5. **What are the side effects of calcium channel blockers?**
   A. hypotension
   B. excessive heart depression with bradycardia, A-V blocks, heart failure worsening
   C. tachycardia, heart palpitations, nausea and vomiting, elevation of liver enzymes
   D. interstitial alveolitis, pulmonary fibrosis
   E. allergic reactions, bronchial spasm.

Clinical pharmacology of antihypertensive drugs, antihypotensive drugs and diuretics

I. Simple clinical cases

1. A 65-year-old woman is admitted to the intensive care unit (ICU) of the hospital with sepsis caused by a urinary tract infection. She is hypotensive, the blood pressure 80/40 mmHg and has an elevated heart rate (tachycardia) and decreased urine output (oliguria). Along with the institution of appropriate antibiotic therapy and i/v fluids, a decision is made to start with an intravenous infusion of dopamine to attempt to raise her blood pressure.

What effects can be expected with low-dose dopamine?

Which receptors mediate these effects?

What effects occur with higher doses of dopamine and which receptors mediate these?

2. A 72-year-old man comes for a routine follow up. He is treated for hypertension and congestive heart failure with enalapril and a diuretic. His blood pressure is under the acceptable control and he has no symptoms of heart failure now. He complained of frequent and prolonged cough in the past few months. History and exam revealed no other causes of a chronic cough. So was decided to discontinue enalapril treatment and start treating with losartan.

What is the mechanism of action of enalapril?

What is the mechanism of enalapril conversion to its active form enalaprilat?

What is the likely cause of cough?

What is losartan mechanism of action?

3. A 50-year-old man comes for a follow-up of his hypertension. He is maintaining a low-sodium diet, exercising regularly, and taking metoprolol at maximum dosage. He uses no other medications. His blood pressure remains elevated at 150/100 mmHg. His examination is

otherwise unremarkable. You decide to add a thiazide diuretic to his regimen.

What is the mechanism of action of metoprolol?

What is the mechanism of action of thiazide diuretics?

What electrolyte abnormalities commonly occur with thiazide diuretics?

4. A 60-year-old man with hypertension and type II diabetes mellitus came for a follow-up. Along with an appropriate diet and lifestyle changes, he is taking an angiotensin-converting enzyme (ACE) inhibitor-thiazide diuretic combination for his hypertension and metformin for his diabetes mellitus. His blood pressure and diabetes mellitus are under acceptable control. Routine blood work revealed normal electrolytes, renal function, and liver enzymes. He is noted to have elevated total cholesterol and low-density lipoprotein (LDL) levels, which have remained high despite of his lifestyle changes. Besides his efforts to reduce the risk of developing coronary artery disease, he started to take a 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor.

What is the mechanism of action of HMG-CoA reductase inhibitors?

What effect do they have on total and LDL cholesterol levels?

What are the common adverse effects of HMG-CoA reductase inhibitors?

5. A 40-year-old woman complains of chronic migraine headaches. She reports that approximately once a month she has a severe, unilateral headache associated with nausea and extreme photophobia. The headache will last for a full day if not treated. She had success in reducing the severity of the headaches with opioid medications, but usually she is too nauseous to take them. When she is able to tolerate them, she will have to sleep for several hours afterwards. She is missing about a day of work a month because of the headaches. She has no other significant medical history and takes no medications on a regular basis. Her examination today is normal. You decide to prescribe sumatriptan and try to relieve next migraine headache.

What receptor is the site of action of sumatriptan?

What is the mechanism of action of sumatriptan?

6. You are called to see a 23-year-old woman who approximately 1 hour ago underwent a vaginal delivery of an 8 lb infant. The nurse was concerned that the patient is continuing to bleed more than it would be expected, and that her uterine fundus isn't firm at palpation. Her placenta went out spontaneously and intact. She has no significant evidences. Examination of the patient feels comfortable and is cooperative but she has mild tachycardia. Vaginal examination shows no cervical or vaginal lacerations, but there is a steady flow of blood from the still-dilated cervix. You diagnose the patient as having a postpartum hemorrhage secondary to uterine atony and order an immediate IM injection of methylergometrine.

What is the mechanism of action of methylergometrine?

What are the common adverse effects of methylergometrine?

7. A 35-year-old man, 3 years suffered from hypertension. He complained of the stabbing pain in the heart, pulsating feeling in his head, sweating. Heart beats 100 /min, but BP 189/100 mm Hg.

What are the drugs to use from the following drugs and why?

A. isosorbide dinitrate
B. dipyridamole
C. atenolol
D. enalapril
E. nifedipine
F. furosemide

8. Patient M, 38 with II degree arterial hypertension was rescribed clonidine in doses of 0,075 - 2 times/day. After 2 hours from the first dose, the blood pressure decreased from 180/100 to 140/80 mm Hg. On the 4-th day in the evening was registered a higher level of BP up to 200/100 mm Hg. After that the dose was regarded as inadequate and increased to 0.15 mg - 2 times/day.

Is the prescribed treatment regimen correct?

What are the indications for clonidine indications?

What are the side effects due to clonidine administration?

9. Which of the following antiangina drugs is best to administer to patients with stable II nd degree angina II functional class with a concomitant hypertension disease?

A. nifedipine
B. methyldopa
C. isosorbide dinitrate
D. diltiazem

10. Patient D, suffers from vegetative vascular dystonia manifested by fluid retention. The periodical examination detected symptoms of subcompensated and uncompensated alkalosis, therefore she was administered acetazolamide per 0.25 1-2 times/day. Sometimes she used other diuretics. Now due to pregnancy (6 weeks), tries not to take any drugs. However, diuretics refuse has led to marked oedema and signs of toxicosis. BP was higher than normal (170/95 mm Hg).

What medicines from the following can be administered to the patient?

Triamterene, amiloride, theophylline, furosemide, spironolactone, hydrochlorothiazide, nifedipine, magnezium sulphate, methyldopa, atenolol, enalapril.

Can she take acetazolamide?

What hypertensive drugs can be administered to the patient?

II. Multiple clinical cases

Clinical case 1

Patient H, 63 years old, suffers from essential hypertension gr. III. He was hospitalized in connection with the worsening of his condition after a psychoemotional stress. Objective examination -patient's condition-relatively satisfactory, accuses of headache. BP-180/100 mmHg. HR -90/minute. He was prescriber atenolol 50 mg 2 times per day.

1. Do you agree with the indicated treatment?

A. yes
B. no, there are no indications for atenolol treatment
C. no, there are more efficient drugs
D. no, because atenolol is useful in I-II degree hypertension

In 5 days of treatment, blood pressure wasn't normal (BP-170/100 mm Hg), HR-80/min.

2. What is your tactics?

A. increase the dose of atenolol
B. add a diuretic (exemple-hydroclorothiazide)
C. add verapamil
D. monitor the patient during the following 5-7 days

3. What changes can occur if you add verapamil?

A. GIT stimulation intensification
B. hypertensive crisis development

C. inotropic negative effect intensification
D. chronotropic positive effect intensification
E. chronotropic negative effect intensification

4. Glycaemia a jeun- 8mmol/l was revealed at laboratory investigations. What changes of the treatment will you make?

A. stop atenolol administration
B. stop hydrochlorthyaside administration
C. add a beta-blocker of higher for beta 1 receptors selectivity – e.g. bisoprolol
D. add a diuretic from thiazide group of a higher potency – e.g. indapamid
E. prescribe another antihypertensive drug
F. if yes, than what drugs? (your opinion)

5. What are hydrochlorothiazide side effects?

A. electrolytic disturbances: hypocalciemia, hypermagneziemia
B. dyspeptic disturbances: nausea, vomiting
C. metabolic disturbances: hyperazotemia, hyperglycemia
D. additional basic disturbances: metabolic acidosis
E. hematopoetic disturbances: thrombocytopenia, leucopoenia, agranulocytosis

Clinical case 2

Patient N, 62-years-old, suffers from second degree arterial hypertension. The condition worsened as a result of a psychoemotional stress. He accuses of moderate headache, vertigo.

At objective examination: BP-170/110 mmHg. HR-90 beats/ min. The doctor indicated propranolol 20 mg 3 times daily.

1. What is your opinion towards the indicated treatment?

A. it is correct
B. there is no need for medical treatment
C. there are some more effective drugs than propranolol
D. there is no need to prescribe the drug, because it is useful only in first degree hypertension.

2. After 5 days of treatment BP- 160/100 mmHg, HR-80 /min. The patient accuses of „cold limbs". How do you act further?

A. to increase the dose of propranolol
B. to add a diuretic to the treatment

C. to add amlodipine
D. to replace the proprandol with another beta-blocker
E. to continue the treatment 5-7 days more

3. What kind of patient's behavioural changes can occur if you add verapamil to proprandol?

A. GIT stimulation intensification
B. hypertensive crysis development
C. inotropic negative effect intensification
D. chronotropic negative effect intensification
E. chronotropic positive effect intensification

4. **What is the cause of,, cold limbs feeling,,?**

A. atherosclerosis of lower limbs vessels
B. obliterant endarteritis
C. Raynaud syndrome
D. vessel spasm due to vessels beta- receptors blocking
E. inhibition of nitricoxidsynthetase

5. What are the peculiarities of administration of antihypertensive drugs in old patients?

A. the treatment should be correlated with the risk factors, and the associated diseases
B. it is necessary to take in account the damage of the target organs
C. blood pressure must be measured in orthostatic position also
D. target blood pressure is >140/90 mm Hg
E. drugs doses are less than in young patients.

Clinical case 3

Patient D, 52-years-old, suffers from hypertension II-nd degree. 2 years ago he had transmural myocardial infarction. He came to the doctor in connection with the appearance of jaundice of skin and mucous membranes. The additional investigations, revealed the diagnosis of viral B hepatitis. Objective examination: BP- 180/120 mmHg. HR-58 beats/min. ECG- changes of myocardium cicatrix in V3-V6, the interval PQ-0.23 sec.

1. What drugs are contraindicated?

A. beta-adrenoblockers
B. sympatholythics
C. verapamil

D. metildopa
E. diuretics
F. myotropic vasodilators
G. alpha-adrenoblockers
H. nifedipine

2. Explain why are the selected drugs contraindicated?

A. A-V node conduction disturbance
B. cholestasis
C. viral C hepatitis
D. scarred changes in myocardium
E. bradychardia

3. What medicines can be administered to patients with hypertension and ischemic heart disease in case of congestive heart failure?

A. beta-adrenoblockers
B. calcium channel blockers (phenilalchilamines)
C. calcium channel blockers (dihydroperidines)
D. conversion enzyme inhibitors
E. angiotensin receptors antagonits
F. diuretics

4. Which of the following drugs are preferred to prevent sudden death for patients with transmural myocardial infarction?

A. calcium channel blockers
B. beta-adrenoblockers
C. alpha-adrenoblockers
D. metabolic drugs (inosine, trimetazidine)
E. conversion enzyme inhibitors

5. What are the pharmacologic effects of beta-adrenoblockers?

A. antihypertensive effect
B. antianginal effect
C. prevent and diminish the pathological remodelling of the myocardium
D. antiaterogenic effect
E. inhibits apoptosis of cardiomyocytes

Clinical case 4

Patient M 55-years-old, suffers from chronic obstructive bronchitis, pulmonary emphysema, arterial hypertension II- nd degree, heart failure II-nd degree. Worsening of the disease 2-4 times a year, is mostly in spring and autumn. Administered theophylline 2-5 tablets a day, the access of bronchial spasm, by increasing the dose of theophylline and using inhaled adrenomimetics (up to 10). From antihypertensive preparations was irregularly administered captopril, nifedipine. In the last 2 years the patient's condition has worsened, crises of breathlessness have become longer and more frequent, BP- basically does not descend below the 170-100 mmHg, often has heart palpitations, pain in the region of the heart. Heart rate remains 90 beats/minute. On ECG-signs of hypertrophy of both ventricles, ventricular extrasystoles, sinus tachycardia (100/min), metabolic alterations in the myocardium.

1. **What is the cause of patient's condition worsening? What is the correct treatment?**
   A. the treatment is correct
   B. antihypertensive drugs are incorrectly chosen
   C. the patient's condition worsening cause is the irregular regimen drug administration
   D. the patient's condition worsening cause in the evolution of chronic bronchitis in bronchial asthma
   E. the patient's condition worsening cause is tolerance to adrenomimetics appearance
2. **Select the necessary drugs for the patient taking into account his individual peculiarities.**
   A. may be administered to the patient a selective beta-adrenoblocker
   B. it is rational to replace captopril with another conversion enzyme inhibitor
   C. it is rational to replace nifedipine with another calcium channel blocker
   D. it is necessary to supplement the treatment with a diuretic
   E. it is necessary to supplement the treatment with an inhaled glucocorticoid
   F. it is necessary to supplement the treatment with an antagonist of angiotensin receptors

3. **What are the contraindications of beta-blockers administration?**
   A. bronchial asthma
   B. chronic obstructive brochopneumopathy
   C. A-V block II-III-rd degree
   D. tachyarrithmias
   E. hypo-, hyperkaliemia
   F. metabolic syndrome
4. **What are adrenomimetics side effects?**
   A. tachycardia and arrhythmias
   B. headache, dizziness
   C. hyperglycemia
   D. tolerance
   E. fingers tremor
   F. rebound syndrome
5. **What are the possible side effects of inhaled glucocorticoids administration?**
   A. Cushing syndrome
   B. xerostomia, dysphonia
   C. atrophic rhinitis, nasal bleeding
   D. oral candidosis
   E. diminish of mucocilliary clearance
   F. bronchial infection aggravation

Clinical case 5

Patient P. 77-years-old, with arterial hypertension III-rd degree, is administered clonidine per 0,075mg 4 times/daily. In connection with depression appearance, the psychiatrist recommended melipramine to the patient. In 3 days after the beginning of the administration of melipramine, the patient developed a hypretensive relapse. On the eve he didn't take clonidine.

1. **What are the causes of patient's worsening condition?**
   A. the possible evolution of the disease
   B. the hypertensive effect of melipramine
   C. rebound syndrome development
   D. nitrates tolerance appearance
2. **What measures must be takenin the created situation?**
   A. to decrease gradually clonidine administration

B. to stop immediately the administration of melipramine
C. to indicate a beta-adrenergic blocker
D. to replace clonidine with nifedipine
E. to stop hypertensive crisis administer urapidil

In order to stop hypertensive crisis, the patient was administered sodium nitroprusside intravenously, the speed dose of 8 mcg per minute. Dyspnoea, acrocyanosis, retrosternal pains, muscle fasciculations appeared.

3. What is the cause of patient's worsening condition?
A. sodium nitroprussiatic toxic action
B. sodium nitroprusside inotropic negativ effect
C. bronchial obstruction increase
D. stasis phenomena in small circuit

4. What are the side effects in case of sodium nitroprusside overdosage and rapid administration?
A. BP abrupt decrease
B. symptoms characteristic to cyanides poison
C. bradycardia
D. dyspeptic disturbances: nausea, vomiting
E. drug hypersensitivity reactions

5. What drugs may be used in case of sodium nitroprusside overdose?
A. blue methylene
B. cyanocobalamin
C. oxycobolamin
D. sodium thiosulphate
E. unithiol

Clinical case 6

A 52-year old patient, suffering from diabetes mellitus came to the doctor with the next complaints: headache, dizziness and heart palpitations. The objective examination revealed BP–160/95 mmHg, HR–80/min.
ECG - frequent atrial extrasystoles.

1. Is it necessary to start antihypertensive treatment? If yes- what antihypertensive drugs can be indicated?
A. beta – adrenoblockers
B. diuretics

C. calcium channel blockers
D. conversion enzyme inhibitors
E. angiotensin receptors antagonists
F. sympatholythic

2. The patient was prescribed bisoprolol 10 mg and hydrochlorothiazide 50 mg daily, an antihypertensive treatment. BP decreased to140/ 90 mm Hg, but such symptoms as hypoglycemia, general weakness, cardiac palpitation appeared during the treatment. What is the cause of hypoglycemia?

A. incorrect alimentation
B. antidiabetics overdosage
C. inhibition of glucose formation from glycogen
D. bisoprolol increased the effect of antidiabetics action

3. What are the side effects of beta-adrenoblockers?

A. bradycardia or tachycardia
B. atrioventricular blockings
C. hypoglycaemic reaction in diabetics
D. tolerance
E. increase level of lipoproteins with high density

4. Laboratory investigation revealed total cholesterol, LDL, triglycerides increase and decreased potassium level in plasma. What are the patient's treatment necessary changes?

A. stop bisoprolol administration
B. decrease the dose of antidiabetic drugs
C. to replace hydrochlorothiazide with econometric potassium
D. add a statin group drug to the treatment

5. What antihypertensive drugs would be administered to this patient?

A. verapamil
B. enalapril
C. nebivolol
D. methyldopa
E. indapamid
F. amlodipine

Clinical case 7

At a routine examination a pregnant woman (24 weeks gestation period) was diagnosed with arterial hypertension-160/100 mmHg. At ECG: left ventricular hypertrophy signs.

1. **What antihypertensive drugs may be administered during pregnancy?**
   A. conversion of enzyme inhibitors
   B. beta – adrenoblockers
   C. diuretics
   D. angiotensine receptors antagonists
   E. calcium channel blockers
   F. central alpha-adrenomimetics
2. **Methyldopa preparation was indicated, but the patient has not complied with the prescribed dosage regimen and hypertensive crises occurred BP- 180/110 mm Hg.**
   What crisis stoppage drug would be chosen?
   A. captopril sublingually
   B. nifedipine sublingually
   C. magnezium sulphate i/v
   D. labetalol i/v
   E. bendazol i/v
3. **Hypertensive urgency was stopped, the patient continues the treatment at home with methyldopa, but periodically she observes high BP indices.**
   What are your actions?
   A. increase the dose of methyldopa
   B. passing to a calcium channel blocker
   C. passing to a beta-adrenoblocker
   D. association between methyldopa and a calcium channel blocker
4. **Three weeks before giving birth, the patient is admitted to the emergency clinic unit in preeclampsia with BP- 210/115 mm Hg. and with pulmonary oedema.**

   What drugs should be administered to help the patient overcome preeclampsia?
   A. sodium nitroprusside i/v
   B. hydralysine i/v
   C. furosemid i/v

D. nitroglycerin i/v
E. labetalol i/v

5. The patient overcame preeclampsia, BP-140/90 mm Hg, high glycemia index- 9 mmol/l.
What antidiabetic drug should be administered in this case?
A. glypisid
B. metphormin
C. repaglynide
D. pioglytasone
E. insulin

Clinical case 8

A young woman of 26 years addressed to the family doctor, complaining of symptoms of throbbing headache, vertigo. The objective exam revealed tha tthe patient is overweight. HR 80/min; BP-160/95 mm Hg. On the ECG- without any pathological changes.

1. What will be the correct therapeutic management of the patient?
A. to lose weight
B. hypotensive diet rich in fruits, vegetables with a low amount of saturated fats
C. decrease the salt intake
D. daily phisycal effort (30min/24 hours)
E. medical treatment

2. The patient respected doctor's recommendations and in 6 months, the patient lost 10 kg, but body's weight index didn't return to the normal figures, (18,5−24,9 kg) BP indices maintained at a high level (155/95 mm Hg)
What drugs should be administered to this patient?
A. Indapamide
B. Hydrochlorothiazide
C. Enalapril
D. Metoprolol
E. Bisoprolol
F. Amlodipine

3. **The patient stated, at o more detailed anamnesis, that is administered hormonal contraceptives over the past 5 years.**
   What would be the recommendations for the patient?
   A. to stop the use of hormonal contraceptives which contain estrogens
   B. to chose the anticontraceptives which do not contain estrogens
   C. to continue the antihypertensive treatment
   D. in case of estrogens contraceptives discard, to stop the antihypertensive treatment and to follow up the patient
4. **What drugs groups may induce arterial hypertension?**
   A. NSAI
   B. glucocorticoids and other steroids
   C. amphetamine
   D. cyclosporin
   E. tacrolimus
5. **In pheocrocytoma the diagnosis is based on stable or paroxystic character of arterial hypertension and on catecholamines increased plasmatic level detection.**
   What drugs shoul be administered in hypertensive crisis from pheocromocytoma?
   A. beta-adrenoblockers
   B. alpha-nonselective adrenoblockers (phentolamine)
   C. alpha-beta-adrenoblockers (labetalol)
   D. calcium canals bockers (amlodipine)
   E. sodium nitroprusside
   F. nitroglycerin

Clinical case 9

A person was involved in a car accident. The urgent medical assistance, at the accident's place, noticed poly traumatism, anaphylactic shock. The patient was unconscious BP-60/40 mm Hg, HR-100 beats/ min.

1. **What drugs are firstly chosen to stabilize urgently the blood pressure that will allow patient's transportation to the hospital?**
   A. plasmatic colloidal substituents
   B. plasmatic crystalloid substituents
   C. glucocorticoids
   D. alpha-beta-adrenomimetics

E. alpha-adrenomimetics
F. isothyoureic derivates

2. **The doctor from ambulance administered to the patient 1 ml sol of 10 % of an antihypertensive drug which reestablished BP up to 120/75 mm Hg, HR -decreased to 80 per min. The antihypotensive effect lasted during 1 hour and a half, allowing the transportation of the patient to the hospital in the intensive care unit. What drug was administered to the patient?**
   A. epinephrine
   B. norepinephrine
   C. prednisolone
   D. isothoron
   E. raviten
3. **After hospitalization the patient was conscious but his general condition remained grave, the blood pressure collapsed again (80/50 mm col. Hg.) the patient was repeatedly administered the same drug intramuscularly, which reestablished and maintained BP at the normal level (125/80 mm HG) during four hours, meanwhile blood transfusions and surgical interventions were made. What is the mechanism of action of isothyoureic derivates?**
   A. stimulation of alpha− adrenoreceptors
   B. stimulationof alpha and beta−adrenoreceptors
   C. direct miotropic action on vessel wall smooth muscle
   D. CNS vasomotor centre stimulation
4. **What are the antihypotensive effect peculiarities of the drugs from this group?**
   A. the antihypotensive effect is caused by sympaphatic tone increase
   B. the antihypotensive effect is caused by arterio- and veno constriction
   C. increase hypertensive action of adrenomimetics
   D. the antihypotensive effect is not decreased by alpha-adrenoblockers, ganglioblockers
   E. decrease cardiac volume, increase heart rate

5. **What other pharmacodynamic peculiarities are typical for isothiouretic derivatives?**
   A. increase tonus and intestinal motility
   B. possess tocolytic action
   C. increase uterus contraction capacity
   D. increase tissue oxygen consumption
   E. possess radioprotection actions

Clinical case 10

A patient with jaundice caused by acute viral hepatitis, with high level of liver enzymes and bilirubin, in the first day of treatment, in hospital, he was prescribed infusions with electrolytic solutions (Sol. NaCl 0,9%, Sol. Ringher, Sol. Ringher-Loc). The treatment response was good. In the second day, after intravenous infusion of 200 ml Ringher sol., followed by an infusion of 400 ml Dextran 40. Instantly after the infusion the patient's condition suddenly worsened: he accused of: dyspnoea, dizziness, general weakness, numbness, cold perspiration, hypotension with loss of consciousness, HR-100/ min. BP can't be determined. The patient was diagnosed with anaphylactic shock.

1. **What are the medicines groups which must be in the antishock set in case of anaphylactic shock urgent help?**
   A. alpha-adrenomimetics
   B. alpha-beta-adrenomimetics
   C. dopaminomimetics
   D. beta 2-adrenonomimetics
   E. direct anticoagulants
   F. isothyoureic derivates
   G. methylxantins
   H. glucocorticoids
2. **What are the first aid drugs chosen in order to help this patient?**
   A. phenylephrine
   B. isoturon
   C. epinephrine
   D. aminophylline
   E. salbutamol
   F. dopamine
   G. prednisolone

3. **What are the mechanisms of action and the effects of epinephrine:**
   A. cardiostimulator effect through beta 1 receptors excitation from heart
   B. vasoconstrictive effect through stimulation of alfa–receptors from blood vessels
   C. vasodilatators effect through stimulation of beta 2 receptors from blood vessels
   D. bronchodilator effect through stimulation of M cholinoreceptors from bronchi
   E. hypoglycaemia effect by the decrease of glucose level in blood
4. **What are the action mechanisms and efects of glucocorticoids in shock conditions?**
   A. antihypotensive effect through the mineralocorticoid action
   B. hypertensive effect through permissive mechanism with vessels sensibility increase to adrenaline and angiotensin
   C. inotropic–positive and chronotropic–positive effect on heart
   D. decrease membrane permeability inhibiting hyaluronidase
   E. block histamine receptors with a marked antiallergic effect
5. **What is the dosage regimen of glucucorticoids in anaphylactic shock?**
   A. prednisolone hemisuccinate i/v per 25–150 mg, up to 400 mg
   B. prednisolone hemisuccinate per 1000–1200 (pulse therapy)
   C. triamcinolone intramuscularly per 40–80 mg
   D. cortisone acetate orally 100–200 mg

Clinical pharmacology of antithrombotic and hemostatic drugs

I Simple clinical cases

1. A patient underwent 1/3 pulmonary resection. Thrombin was used to stop local capillary bleeding. The formed thrombi were unstable and quickly dissolving, along with restoring of the capillary bleeding.

What is the possible cause of the observed phenomenon?

What group of drugs would you use to cease bleeding?

How will you explain the efficacy of using these drugs?

2. Patients A and B were admitted to the clinic. Patient A, who suffered from endarteritis obliterans, presented a decreasing peripheral flow within the limbs and a high risk of thrombus formation. Patient B, who suffered from varicose veins in the lower limbs, presented an increased level of prothrombin, fibrinogen, as well as elevated blood viscosity.

What groups of drugs would you use to prevent the formation and / or dissolution of thrombus?

Explain the principles of drug group selection.

3. Patient C. aged 67 years old was hospitalized for acute myocardial infarction. On the 4th day of treatment, the patient presented epigastric pain, which was considered as manifestation of myocardial infarction. Bloody vomit appeared 3 days later. The fibrogastroscopic examination identified multiple erosions of the gastric mucosa.

Which drug would you prescribe?

Explain why.

A. epsilon- aminocaproic acid i/v
B. epsilon- aminocaproic acid and etamsylate, both orally
C. crioplasmă, heparin and pentoxiphylline
D. phytomenadione, i/m, i/v
E. surgical treatment

4. A 4-month-old baby D. was diagnosed with hemorrhagic (bleeding) syndrome.

What drug would you select in this case? Explain your choice:

A. menadion 0,3 mg/kg
B. phytomenadion 0,3 mg/kg
C. etamsilate 0,5 mg/kg
D. aminocaproic acid 2g i/v

What is the cause of the hemorrhagic syndrome?

What are the preventive measures of this syndrome?

5. 2 patients with ischemic stroke were admitted to the neurology department, 6 hours after its onset. Patient A. was administered X drug, 0.6 ml/2 times/day subcutaneously; whereas patient B –Y drug, initially 10,000 IU in bolus, then 5000 IU/4 times/daily, subcutaneously. Both cases proved their efficacy according to clinical parameters of coagulogramma.

What drugs were the patients prescribed?

What are the pharmacodynamic and pharmacokinetic peculiarities of the prescribed drugs?

6. A 27-year-old woman who presented pain and swelling in her right leg was admitted to the emergency room. An ultrasound study showed thrombosis in the poplitea vein. The patient, who was in the third trimester of pregnancy, was treated for 7 days with intravenous unfractionated (standard) heparin. The pain resolved during the course of therapy, and the patient was discharged on the 8^{th} day.

Which of the following drugs would be the most appropriate to an out-patient follow-up therapy for this patient?

A. warfarin
B. acetylsalicylic acid
C. alteplase
D. unfractionated heparin
E. low-molecular-weight heparin (LMWH).

7. Patient F. suffered from deep vein thrombophlebitis on the left leg and was treated with indirect anticoagulants. Prothrombinic index remained within the range of 64-70%. Simultaneously, the patient received a sedative and hypnotic drug, viz. phenobarbital for 6 days.

How will the prothrombinic index (PI) change on a phenobarbital background and how will the dosing of indirect anticoagulants be further administered?

A. PI does not change, therefore the indirect anticoagulant is recommended to keep in the same dose.
B. PI increases, because the barbiturates accelerate metabolism of indirect anticoagulants, so the indication of barbiturates needs an increased dose of anticoagulants.
C. PI will increase, as barbiturates squeezed indirect anticoagulants from binding with plasma proteins, so the dose of anticoagulants should be reduced.
D. PI increase, because barbiturates slow down the metabolism of indirect anticoagulants, so it is necessary to decrease the dose of indirect anticoagulants.
E. PI will decrease, as barbiturates potentiate the pharmacological effect of indirect anticoagulants, so there is a need to decrease the dose of the indirect anticoagulants.

8. Patient J., aged 45 years old was diagnosed with gastric cancer and underwent a radical surgery. On the 4-th day after surgery the investigations showed hypercoagulation and reduced fibrinolytic activity of blood.

What is the appropriate therapy of administration of anticoagulants?

A. anticoagulants are necessary
B. anticoagulants are optional
C. anticoagulants are indicated, but they should be carefully monitored in order to prevent hemorrhagic syndrome
D. anticoagulants are not applied after surgery
E. antifibrinolytic therapy is necessary

9. A 65-year-old man was diagnosed with deep-vein thrombosis. The patient was treated with heparin in bolus. One hour later, a profuse bleeding developed on the intravenous site. The heparin therapy was suspended, but the bleeding continued.

What drug would you administer? Why?

A. phytomenadion
B. aminocapronic acid

C. protamine sulphate
D. epinephrine
E. hemostatic sponge

Explain the mechanisms of this drug action.

10. A 14-day-old child (4.5 kg.) was hospitalized with complaints of weakness and breast refusal. Examination: the child's condition is severe; pale skin; bleeding on the injection site. The clinical analysis of blood: hemoglobin = 80 g/l; erythrocytes = I,8 $xI0^{12}$; coagulation index = 0,6; prothrombinic index = 50%. The feces tests showed a positive reaction to occult blood. Cerebrospinal fluid : modified and unchanged erythrocytes. Anamnesis: the child was maturely born by a woman with epilepsy, who had constantly been receiving anticonvulsants. After the birth, the baby presented prolonged bleeding from the umbilical stump.

Explain the cause of bleeding in newborns.

Which drugs would you administer?

Explain whether this hemorrhage could be avoided.

II. Multiple clinical cases

Clinical case 1

Patient L. diagnosed with deep venous thrombosis underwent a treatment with heparin at 10 000 IU/ 2 times /day for a week, then the treatment was changed with warfarin at 15 mg /day. On the 24-th day of treatment, the patient manifested pain in epigastric and lumbar region, micro hematuria and hematemesis. It was established that Quick time was 3 times increased, while INR was 5. There were detected 75 erythrocytes in urine.

1. How do you comment the appearance of these symptoms?

A. it is the summation of the heparin and warfarin effects
B. it is a heparin overdose
C. it is a warfarin overdose

2. What is the follow-up strategy of treatment?

A. 0.6 g routine vitamin and ascorbic acid 1g/day is added to the treatment
B. the dose of warfarin is reduced till the normalization of Quick time

C. warfarin is cancelled and crioplasma, heparin and phytomenadione-20 mg i/v is prescribed

3. What are the criteria for determining the effectiveness of indirect anticoagulants?

A. protrombinic index >40 %
B. protrombinic index 50-70%
C. protrombinic index <70-100%
D. international normalized index >2
E. international normalized index 2-3,5
F. international normalized index >4

4. What is the latency of the warfarin effects?

A. 24 hours
B. 24-36 hours
C. 36-48 hours
D. 48-72 hours

5. What is the duration of warfarin action?

A. 3 days
B. 5-7 days
C. 8-10 days
D. 20 days

Clinical case 2

Patient M. 65 year-old was admitted to emergency department, complaining of weakness and limitation of movements in his hand and right foot, speech disorders, (couldn't name the objects). The results of the computerized tomography excluded an intracerebral hemorrhage, and the patient was diagnosed with acute tromboembolic cerebrovascular stroke.

1. Which of these drugs have to be selected in 1,5 hour after the onset of the accident?

A. abciximab
B. alteplase
C. VIII factor
D. phytomenadione
E. standard heparin

2. **After a prompt intervention of doctors, the symptoms regressed for 2 days. Justify your choice of drugs .**

   What are the criteria of effectiveness for heparin therapy?

   A. cuagulation time according to Li-Wait
   B. international normalizing index
   C. time of partially activated thromboplastine
   D. number of thrombocytes
   E. recalcification time

3. **Which index confirms the effectiveness of heparin therapy?**

   A. cuagulation time according to Li-Wait must last for 7-10 minutes
   B. cuagulation time according to Li-Wait must last for 10-15 minute
   C. cuagulation time according to Li-Wait must last for 20-25 minute

4. **Name the side effects of heparin:**

Clinical case 3

A 58 year-old man complaining of chest pain during the last five years, experienced some negative emotions, followed by intensive pain in the epigastric area and nausea. He presented pale skin, cold sweat, and slight dyspnea at rest. Physical examination: tachycardia, extra systoles, reduction of the I-st heart tone at apex, BP-110/80mm Hg, painless and flat abdomen.

1. **What is the presumptive diagnosis?**

   A. biliary colics
   B. acute cholecystitis
   C. acute pancreatitis
   D. perforated ulcer
   E. myocardial infarction

2. **What emergent treatment does the patient require?**

   A. opioid analgesics
   B. antipyretic analgesics
   C. antispasmodics
   D. antianginal drugs
   E. antiarrhythmics
   F. antithrombotics

3. **What groups of antithrombotics would be selected in this case? Justify your answer.**
   A. direct anticoagulants
   B. indirect anticoagulants
   C. antiaggregants
   D. fibrinolytics
   E. dextran – 40
4. **If the patient received streptokinase 6 months ago, it is recommended:**
   A. to repeatedly administer the drug, since its effectiveness has already been demonstrated;
   B. to change drug because, since it has developed a drug tolerance
   C. to change the drug in order to avoid anaphylactic shock
5. **Select the side effects of the fibrinolytics:**
   A. systemic hemorrhages
   B. thrombocytopenia
   C. anaphylactic shock
   D. alopecia
   E. myocardial rupture

Clinical case 4

A woman of 29 year-old, 25-weeks pregnancy, addressed to the doctor with aggravation of deep vein thrombosis on her right leg. Protrombinic index was 60 %. Warfarin 10 mg/day for a 3 weeks period was prescribed.

1. **Appreciate the choice of treatment:**
   A. incorrect treatment
   B. correct treatment
2. **Justify your answer for the 1st point.**
   A. oral anticoagulants cross the placental barrier
   B. oral anticoagulants do not pass the placental barrier
   C. the drug is contraindicated in pregnancy
   D. prothrombinic index allows oral anticoagulants
   E. prothrombinic index does not allow oral anticoagulants
   F. the drug is contraindicated in pregnancy

3. **What group of drugs is recommended during pregnancy?**
   A. direct anticoagulants
   B. indirect anticoagulants
   C. antiaggregants
   D. dextrans
4. **Select the drug that can be administered:**
   A. melagatran
   B. nadroparin
   C. bivaluridine
   D. danaparoide
5. **What is the dose of the drug?**
   A. nadroparin s/c 0,2 - 0,4 ml/day
   B. acetylsalicylic acid 75- 100 mg/day
   C. ticlopidine oral 250 mg /2 times/day
   D. clopidogrel , internal ,75 mg/day

Clinical case 5

Patient P, diagnosed with insulin-dependent type II diabetes, diabetic angiopathy with microcirculatory disorders and atherosclerosis, coronary and cerebral atherosclerotic angiopathy, obesity III degree, follows the following treatment:

   A. glibenclamide - 0.015g /2 times/day;
   B. clofibrate - 0.25 g /3 times /day;
   C. acetylsalicylic acid 325 mg/day;
   D. etilbiscumacetate - 0,6g /day.

1. **Appreciate the prescribed treatment:**
   A. correct, the doses are appropriate and effective, harmless drug interactions;
   B. not correct, because of dangerous drug interactions;
   C. improper, because of low doses; harmless drug interactions;
   D. improper, because of high doses; harmless drug interactions.
2. **What complications may occur in case of dangerous drug interactions?**
   A. hyperglycemia and hyperglycemic coma
   B. hypoglycemia and hypoglycemic coma
   C. hemorrhages

D. exacerbations of angiopathies due to thrombosis; worsening of microcirculatory disorders
E. hepatic or renal failure

3. Justify the choice of answer:

A. internal hypoglycemic effect of oral anticoagulants increases, moving them from the albumin
B. internal hypoglycemic agents decreases the effect of anticoagulants
C. clofibrate increases the effect of indirect anticoagulants, moving them from the albumin
D. clofibrate decreases the effect of indirect anticoagulants
E. antiplatelets enhances the effect of anticoagulants
F. antiplatelets decreases the action of anticoagulants, increasing the risk of hemorrhages

Clinical case 6

A 46 year-old patient was hospitalized at emergency unit with acute transmural myocardial infarction, which occurred about 5 hours ago. Prescriptions: propranolol 20 mg 4 times/day orally, heparin 10 000 IU i/v every 4 hours. The clotting time according to Lee-White lasted 28-30 minutes. On the 4-th day of treatment, the patient presented microhematuria (22 erythrocytes in the field -of -view).

1. What is the treatment strategy?

A. A. heparin is immediately cancelled
B. the dose of heparin is reduced until the Lee-White clotting time is 10-12 minutes
C. phytomenadione s/c is administered, whereas heparin is kept at the same dose
D. intravenous administration of heparin is immediately substituted with subcutaneous one
E. the dose of heparin is reduced until the Lee-White clotting time is 20-25 minutes

2. The next day, the patient was diagnosed with right lobar pneumonia. Sodium benzylpenicillin (500000 units every 4 hours) was indicated to. After 4 hours of administration, the Lee-White clotting time was 8 min. What is the cause of clotting time change?

A. random result
B. physicochemical incompatibility between heparin and penicillin
C. activation of prothrombin complex factors synthesis by the penicillin
D. activation of platelet aggregation by the penicillin

3. What is your treatment strategy?
A. to replace penicillin with ampicillin, keep the same regimen of administration
B. to replace heparin with indirect anticoagulants
C. to increase the dose of heparin
D. to change the administration way of penicillin

4. On the 2nd day of treatment with penicillin skin rash, pruritus, eosinophylia (8%) appeared. What are the causes of these symptoms?
A. delayed allergic reaction to heparin
B. allergic reaction to penicillin
C. allergic reaction to combination of heparin with penicillin

5. How will you proceed after the appearance of adverse reactions?
A. immediately cancel of all drugs;
B. to cancel the antibiotic and prescribe antihistamines;
C. cancel the antibiotics and heparin; prescribe antihistamines;
D. to combine 15 mg prednizolone/day to the therapy;
E. to administer direct anticoagulants for 2-3 days and cancel heparin

Clinical case 7

Patient S., 65 year-old was diagnosed with a deep vein thrombosis of the leg. The patient received heparin in 20000 IU dose in bolus. In an hour, patient presented nose bleeding. The doctor indicated emergency treatment to stop the bleeding.

1. What drugs are recommended to be used?
A. phytomenadione
B. aminocaproic acid
C. protamine sulfate

2. What is the ratio of protamine sulfate and heparin?
A. 0,5 ml of protamine sulphate for 1000 units of heparin
B. 1 ml protamine sulphate for 1000 units of heparin

C. 1,2 ml protamine for 1000 units of heparin

3. **Calculate the quantity of protamine required to neutralize 20,000 IU of heparin:**
   A. 10 ml
   B. 15 ml
   C. 20 ml
   D. 25 ml
4. **Calculate the quantity of protamine required to neutralize 20,000 IU of heparin 1 hour after its administration:**
   A. 10 ml
   B. 15 ml
   C. 20 ml
   D. 25 ml
5. **Name the mechanisms of protamine action**
   A. inactivates heparin;
   B. inactivates antithrombin;
   C. activates the coagulation cascade.

Clinical case 8

Patient T., 39 year-old suffered from dilated varicose veins of the left leg for last 7 years. As a result of patient's health aggravation, he/she experienced pulmonary thromboembolism of small arteries, 5 years ago. Accompanying diseases: Urolithiasis (kidney stones), chronic pyelonephritis in remission, hypercholesterolemia. He was admitted to hospital with deep vein thrombophlebitis of the left calf. Health condition was relatively satisfied. There was determined a mild pain in the region of the left leg, which was hot, edematous and increased in diameter, compared to the right one. Lee-White clotting time was 4 minutes. After administering 5000 IU of heparin intravenously, the Lee-White clotting time became-7 minutes over an hour.

1. **Determine patient's susceptibility to heparin:**
   A. high
   B. low
   C. normal
2. **Determine the cause of sensitiveness to heparin:**
   A. chronic pyelonephritis increases the susceptibility to heparin
   B. chronic pyelonephritis decreases the susceptibility to heparin

C. hypercholesterolemia increases the susceptibility to heparin
D. hypercholesterolemia diminishes the susceptibility to heparin

3. Based on type of susceptibility, select the required dose of Heparin:
A. 5000 IU
B. 10000 IU
C. 15000 IU
D. 20000 IU

4. Select the way of heparin administration:
A. A. Intravenously
B. Intramuscular
C. subcutaneous.

5. The Lee-White clotting time on the heparin therapy background must be*:*
A. 10-15 minutes
B. 15-20 minutes
C. 20- 25 minutes
D. 25-30 minutes

Clinical case 9

A 52 year-old patient was hospitalized at the resuscitation department and diagnosed with transmural myocardial infarction, pulmonary thromboembolism of small arteries. The complex treatment included heparin 10,000 IU i/v for every 4 hours ,under the control of Lee-White clotting time, that ranged between 20-23 min. At the 7-th day of treatment the patient was transferred gradually from heparin to ethyl biscumacetate, which is administered as supportive dose 0.1- 0.15/24 hours. Prothrombinic index was 35-45%. Over 35 days of treatment, the patient complained of pain in the right calf; he/she was diagnosed with thrombophlebitis of superficial veins. Considering that, ethyl was replaced with biscumacetate, while the coagulogram test was not performed; the time of recalcification was determined and coagulation index =1,2 ; prothrombinic index = 30%; single erythrocytes in the urine; Lee-White clotting time = 6 minutes.

1. How do you explain the prothrombin index?
A. high dosage of ethyl biscumacetate and risk of hemorrhage
B. shows a good efficacy of ethyl biscumacetate
C. indicates a risk of thrombosis

2. **How do you explain the coagulation index?**
   A. indicates a hypercoagulation
   B. indicates a hypocoagulation
   C. indicates physiological data
3. **How do you explain Lee-White coagulation time:**
   A. indicates a hypercoagulation
   B. indicates a hypocoagulation
   C. no informative data in this case
4. **Explain the cause of thrombosis on the background of optimal prothrombin index:**
   A. the diagnosis was incorrect
   B. laboratory investigations are not correct
   C. compensatory reaction of the organism, manifested by producing other coagulation factors are not influenced by indirect anticoagulants
   D. thrombophlebitis of superficial veins is a possible manifestation of an older process developed before the treatment onset
5. **Choose the ccorrective strategy in this case:**
   A. to suspend the administration of ethyl biscumacetate
   B. to suspend the administration of ethyl biscumacetate, and initiate the prophylactic treatment with heparin
   C. to decrease the dose of ethyl biscumacetate in order to avoid hemorrhage
   D. to decrease the dose of ethyl biscumacetate and add supplementing antiplatelet drugs

Clinical case 10

A child of 4 year-old (15 kg) after a severe pneumonia and a long-term intravenous catheterization, experienced acute pain along the ulnar vein; local hyperemia; edemas; subfebrile temperature. In 3 days after the initiation of antithrombotic therapy, there was observed that the urine coloured into a slight reddish tint.

1. **Explain the appearance of such an effect:**
   A. it is an usual response to subfebrility
   B. renal impairment
   C. overdose of antithrombotic drugs

2. **What antithrombotic drug was administrated to the child?**
   A. direct anticoagulants
   B. indirect anticoagulants
   C. antiplatelet
   D. fibrinolytic
3. **What antithrombotic drugs are recommended?**
   A. direct anticoagulants
   B. indirect anticoagulants
   C. antiplatelets
   D. fibrinolytics
4. **If you use heparin which form and route of administration will you choose?**
   A. subcutaneous
   B. intravenously
   C. intramuscular
   D. local ointment
5. **Choose the rational drugs combination:**
   A. heparin and fibrinoliytic, intravenously
   B. heparin subcutaneously, antiplatelets prescribed
   C. heparin and coloids drugs, intravenously

Clinical pharmacology of psychotropic, hypnotic and anticonvulsive drugs

I. Simple Clinical Cases

1. Two patients were admitted to the hospital department. Patient A was diagnosis with instability, psychomotor agitation and aggressiveness. Patient B was diagnosed with behaviour disorders, hallucinations and persecutory delusion.

What drugs will you prescribe to these patients?

Give the reasons for the choice of the drugs.

What side effects and manifestations thereof are possible?

2. Patient A's schizophrenia with agitated-aggressive syndrome was associated with arterial hypertension. The intake of captopril and nifedipine gave no positive effects in case of the development of a hypertension attack. He was prescribed drug B that, besides the decrease of arterial tension, also caused somnolence, apathy, inhibition and annoying xerostomia.

What drug was administered?

What effects serve the basis for efficiency in case of a hypertension attack and the effects mentioned?

3. What groups and P (Personal) drugs will you recommend to the patients, who have to undergo complicated diagnostic procedures and dental surgeries?

What effects will serve the basis for drug intake?

4. In order to manage a heavier workload, two persons took: parient A – caffeine, patient B – amphetamine.

What will be the effects that may be identified?

How is the efficiency of the drugs explained?

What will the recommendations on repeated intake be?

5. Two persons drank a cup of coffee (150 mg) each. Person A takes it permanently, person B – from time to time.

Will there be any difference in the appeared effects?

How will the arterial tension and heart rate change?

6. There were hospitalized patients with:

Anxiety with paresis of the lower limb after a cranio-cerebral injury;

Anxiety with epileptiform syndrome;

Anxiety with depressive syndrome;

Anxiety with sleep onset disorder.

Choose the drugs prescribed to these patients.

Give the reasons for selection of the drugs and their efficiency.

7. Piracetam was prescribed to patient A having hypertensive encephalopathy and to patient B with consequences of ischemic ictus.

Give the reasons for the prescription of the drug to the patients.

What will be the dosage regimen?

What will further recommendations be?

8. There were hospitalized the patients with: depression with suppression of initiative and will, melancholy, gitated depression, depression with anxiety

Choose the drugs for each of these patients.

Give the reasons for the choice of the drugs and their efficiency.

9. Patient A was administered diphenhydramine by the emergency team and patient B was administered diazepam.

What effects may be identified in the patients?

How will their sleep change?

10. Patients A and B, who had schizophrenia, were prescribed haloperidol. Motor disorders were noted in patient A some days later but in patient B – several years later.

What are the manifestations of motor disorders and the mechanisms they are based on?

II. Multiple clinical cases

Clinical case 1

During the experimental research of a substance with supposed antipsychotic (neuroleptic) properties, there was developed a range of pathological patterns, allowing to demonstrate the mechanism of action and eventual pharmacological effects.

1. **The arterial hypertension pattern showed the capacity of this substance to lower arterial tension, determined by the following mechanism:**
   A. dopamine receptor blockade
   B. M-choline receptor blockade
   C. serotonin receptor blockade
   D. histamine receptor blockade
   E. alfa-adrenal receptor blockade
2. **Later it was shown that this mechanism was the main one in realisation of one of the principal effects of antipsychotics:**
   A. antiemetic
   B. muscle relaxing
   C. psycho-sedative
   D. anxiolytic
   E. antipsychotic
3. **Clinical manifestations of this effect are:**
   A. elimination of psychomotor agitation
   B. elimination of delirium and hallucinations
   C. apathy and somnolence
   D. suppression of the interest in the enviroment
   E. reactivation with return to activities
4. **This mechanism may also serve the basis for other effects of antipsychotics:**
   A. antiemetic
   B. hypothermic
   C. anxiolytic
   D. potentiating the analgesics
   E. antipsychotic
5. **This mechanism may also respond to the following side effects:**
   A. extrapyramidal disorders
   B. depression

C. xerostomia and bradycardia
D. arterial hypotension
E. hypothermia

Clinical case 2

During an experimental and clinical research, it was proved that antipsychotics (neuroleptics) manifested 2 main effects: psycho-sedative and antipsychotic ones. Predomination or correlation thereof determines, to a greater extent, the choice of the drug in different clinical cases.

1. **The antipsychotic effect serves the basis for the administration in case of the following mental diseases:**
   A. manic - depressive disorders
   B. psychomotor agitations in exacerbation of psychical diseases
   C. endogenous psychoses with hallucinations
   D. abstinence syndrome in alcoholics
   E. psychomotor agitations in psychopathic situations
2. **The antipsychotic effect shall serve the basis for the administration in case of the following somatic diseases:**
   A. central vomit in origin
   B. chronic arterial hypotension
   C. postoperative vomits
   D. complex treatment of traumatic shock
   E. vomit produced by pharmaceutical drugs
3. **The psycho-sedative effect shall serve the basis for the administration in case of the following mental diseases:**
   A. manic- depressive disorders
   B. psychomotor agitations in exacerbation of psychical diseases
   C. endogenous psychoses with hallucinations
   D. abstinence syndrome in alcoholics
   E. psychomotor agitations in psychopathic situations
4. **The psycho-sedative effect shall serve the basis for administration in case of the following somatic diseases:**
   A. spastic states after ictus and traumas
   B. vegetative neuroses in ischemic cardiomyopathy
   C. chronic arterial hypotension
   D. postoperative vomits
   E. complex treatment of traumatic shock

5. **The psycho-sedative effect shall be useful in the following emergency states:**
   A. collapse
   B. convulsions of various geneses
   C. hypertensive emergencies
   D. critical febrile states
   E. severe hypothermia

Clinical case 3

During the experimental research of a substance having the supposed antipsychotic (neuroleptic) properties, there was developed a range of pathological models, allowing the demonstration of the mechanism of action and eventual pharmacological effects.

1. **The anti-vomiting effect is determined by the following mechanism:**
   A. dopamine receptor blockade
   B. M-choline receptor blockade
   C. serotonin receptor blockade
   D. histamine receptor blockade
   E. alfa-adrenal receptor blockade
2. **It was demonstrated later that the main mechanism in realization of one of the principal effects of antipsychotics is:**
   A. antiemetic
   B. muscle relaxing
   C. psycho-sedative
   D. anxiolytic
   E. antipsychotic
3. **Clinical manifestations of this effect are:**
   A. elimination of psychomotor agitation
   B. elimination of delirium and hallucinations
   C. apathy and somnolence
   D. suppression of the interest in the world around
   E. reactivation and resumption of activities
4. **The mechanism may also produce other effects of antipsychotics, like:**
   A. antiemetic
   B. hypothermic

C. anxiolytic
D. potentiation of analgesics
E. antipsychotic

5. This mechanism responds for the following side effects:

A. parkinsonian syndrome
B. depression
C. tardive dyskinesia
D. arterial hypotension
E. ” malignant” syndrome.

Clinical case 4

During the experimental research a substance with supposed antidepressive properties, a range of pathological patterns, allowing to demonstrate the mechanism of action and the eventual pharmacological effects, was modelled.

1. Based on the experimental pattern, there was demonstrated the substance capacity to increase noradrenaline, serotonin and dopamine levels determined by the following mechanism:

A. increase in mediator synthesis
B. increase in neuronal recapture
C. serotonin receptor blockade
D. histamine receptor blockade
E. mediator recapture blockade

2. It was demonstrated later that the main mechanism in the realization of one of the principal effects of antipsychotics is:

A. thymoleptic
B. muscle relaxing
C. psycho-sedative
D. anxiolytic
E. antipsychotic

3. The clinical manifestations of this effect are:

A. elimination of sadness and melancholy
B. elimination of delirium and hallucinations
C. apathy and somnolence
D. recovered of interest in the enviroment
E. strengthening of concentration and thinking capacities

4. **This effect may be also determined by other actions of antidepressants:**
   A. m-choline blocking
   B. dopamine blocking
   C. alfa-adrenal blocking
   D. histamine blocking
   E. serotonin blocking
5. **Supplementary actions of the main mechanism determine the following effects of antidepressants:**
   A. antiemetic
   B. vasodilating
   C. sedative and anxiolytic
   D. analgesic and potentiating the analgesics
   E. antipsychotic.

Clinical case 5

During the clinical studies of some pharmaceutical drugs belonging to the group of antipsychotics (chlorpromazine), anxiolytics (diazepam) and antidepressants (amitriptyline), a series of common clinical effects, distinguished by the mechanisms of their action and by their clinical manifestations were determined.

1. **Which variant characteriz the psycho-sedative effect of these pharmaceutical drugs in the ascending order?**
   A. chlorpromazine → diazepam → amitriptyline
   B. diazepam → amitriptyline → chlorpromazine
   C. amitriptyline → diazepam → chlorpromazine
   D. diazepam → amitriptyline → chlorpromazine
   E. diazepam → chlorpromazine → amitriptyline
2. **What actions are the basis for the psycho-sedative effect of antipsychotics and antidepressants?**
   A. alfa-adrenomimetic
   B. m-choline blocking
   C. serotonin blocking
   D. alfa-adrenal blocking
   E. GABA-ergic

3. **What effects are characteristic of anxiolytics and antipsychotics?**
   A. antiemetic
   B. muscle relaxing
   C. antipsychotic
   D. anticonvulsive
   E. antidepressive
4. **What effects are characteristic of antidepressants and antipsychotics?**
   A. antidepressive
   B. antipsychotic
   C. potentiation of analgesics, alcohol
   D. psycho-sedative
   E. orexigenic
5. **What effects may be identified in anxiolytics, antidepressants and antipsychotics?**
   A. hypnotic
   B. antidepressive
   C. psycho-sedative
   D. hypotensive
   E. relief of motor retardation

Clinical case 6

A patient complaining of sleep disorders consulted a neurologist. When taking the history, it was stated that the patient had disorders caused by slow falling asleep (more than an hour after going to bed). The general practitioner prescribed diazepam, which the patient took right before going to bed. Sleep disorders were partially corrected. The state of somnolence began developing in 30-40 minutes. Based on pharmacodynamical and pharmacotherapeutic principles, the physician decided to prescribe a drug belonging to the group of hypnotic inductors.

1. **What groups of drugs belong to hypnotic inductors?**
   A. barbiturates
   B. nonbenzodiazepines
   C. antidepressants
   D. h1-antihistamines
   E. benzodiazepines

2. **What pharmacodynamic features are characteristic of hypnotic inductors?**
   A. they show mainly selective action on the central nervous system
   B. they produce the dose-dependent inhibition of the central nervous system
   C. the inhibition of the central nervous system is not dose-dependent
   D. they show mainly unselective action on the central nervous system
   E. they slightly influence on the vital areas
3. **What are the effects of hypnotic inductors on the sleep structure?**
   A. they produce deep sleep
   B. they produce more superficial sleep
   C. they reduce duration of rapid eye movement
   D. they do not modify the correlation between sleep phases
   E. they reduce the slow-wave sleep phase
4. **What side effects are characteristic of hypnotic inductors?**
   A. pronounced post-action effect
   B. slightly manifested rebound effect
   C. low post-action effect
   D. major risk of drug dependence
   E. minor risk of drug dependence
5. **What hypnotic inductors could the physician choose for this patient?**
   A. diazepam
   B. zolpidem
   C. zopiclone
   D. oxazepam
   E. midazolam.

Clinical case 7

A patient having sleep disorders consulted the physician-neurologist. When taking the history, it was stated that patient well asleep, but used to wake up in 3.5 to 4 hours. In this patient the normal duration of sleep is 6-7 hours. The general physician prescribed phenobarbital earlier. The sleep duration became 8-10 hours, however, the patient did not

get enough sleep and experienced an unpleasant state of morning somnolence and impaired concentration.

1. **What group of hypnotics does phenobarbital belong to, according to the pharmacodynamical and pharmacotherapeutic properties?**
   A. hypnotic inductors
   B. psychodisleptics
   C. psychoanaleptics
   D. hypnotic coercives
   E. analeptics
2. **What pharmacodynamics features are characteristic of phenobarbital?**
   A. it shows mainly selective action on the central nervous system
   B. it causes the dose-dependent inhibition of the central nervous system
   C. the inhibition of the central nervous system is not dose-dependent
   D. it shows mainly unselective action on the central nervous system
   E. it slightly influences on the vital areas
3. **What are the specific effects of phenobarbital on the sleep structure?**
   A. it produces moderately deep sleep
   B. it produces more superficial sleep
   C. it reduces duration of rapid eye movement
   D. it does not modify the correlation between sleep phases
   E. it reduces the slow-wave sleep phase
4. **What side effects are characteristic of hypnotic phenobarbital?**
   A. pronounced post-action effect
   B. slightly manifested rebound effect
   C. low post-action effect
   D. major risk of drug dependence
   E. minor risk of drug dependence
5. **What hypnotics could the physician choose for this patient?**
   A. nitrazepam
   B. barbital
   C. flunitrazepam

D. pentobarbital
E. zolpidem

Clinical case 8

During the clinical studies of a new pharmaceutical drug from the group of benzodiazepine tranquilisers (anxiolytics), there were assessed clinical manifestations of pharmacological effects (anxiolytic, psycho-sedative, hypnotic, muscle relaxing, anticonvulsive, general anaesthetic ones) in patients with relevant pathologies, in order to determine and give the reasons for their administration.

1. **What are clinical manifestations of the anxiolytic effect, that may be identified in patients?**
   A. elimination of hallucinations
   B. elimination of dismay and feat
   C. elimination of rage
   D. elimination of psycho-emotional tension
   E. attenuation of the reaction to exogenous stimuli
2. **The anxiolytic effect stands for clinical efficiency in case of:**
   A. psychoses
   B. neuroses
   C. depressions
   D. premedication
   E. psychomotor agitation
3. **What are clinical manifestations of anxiolytic effect, which might be identified in patients?**
   A. it does not modify the correlation between the sleep phases
   B. it reduces the phase of rapid eye movement
   C. it contributes to sleep onset
   D. it increases the total duration of sleep
   E. it reduces the slow-wave sleep phase
4. **What group of action duration does the drug belong to, if it is mainly prescribed in case of terminal insomnias?**
   A. 10 to 15 minutes latency; 2 to 3 hours duration
   B. 40 to 60 minutes latency; 8 to 12 hours duration
   C. 90 minutes latency; 12 to 24 hours duration
   D. 20 to 40 minutes latency; 4 to 6 hours duration
   E. 2 to 5 minutes latency; 1 to 2hours duration

5. **In case of what indications, will the drug be used as a central muscle relaxant?**
   A. biliary colic
   B. paresis after craniocerebral injuries
   C. paresis after ischemic ictus
   D. intestinal colic
   E. paresis in medullary lesions.

Clinical case 9

In the psychiatry department, a long-time treatment of a patient suffering from schizophrenia stated a range of adverse effects caused by the administration of antipsychotic alongside with improvement of clinical symptoms. It was stated that some adverse effects were caused by the pharmacological effects and others were caused by the chemical structure of the drug.

1. **What adverse effects may be caused by the central and peripheral alfa-adrenal blocking action?**
   A. somnolence and sedation
   B. extrapyramidal disorders
   C. collapse and tachycardia
   D. depression and deep apathy
   E. psychomotor agitation
2. **What adverse effects may be caused by the dopamine blocking action?**
   A. manic-depressive disorders
   B. malignant syndrome
   C. parkinsonian syndrome
   D. nausea and vomit
   E. tardive dyskinesia
3. **What adverse effects may be caused by the central and peripheral M-choline blocking action?**
   A. sedation and somnolence
   B. galactorrhea and amenorrhea
   C. xerostomia and constipations
   D. difficult urination and urinary retention
   E. intestinal colic

4. **Hyperprolactinemia induced by antipsychotics may cause the following adverse endocrine effects:**
   A. cushing's syndrome
   B. gynaecomastia
   C. amenorrhea
   D. priapism
   E. false pregnancy tests
5. **The toxic action of antipsychotics may cause the following adverse effects:**
   A. haemolytic anaemia
   B. leucocytosis
   C. hepatitis with icterus
   D. agranulocytosis
   E. erythropenia

Clinical case 10

The study of pharmacokinetic parameters of benzodiazepines showed a great variety of thier pharmacological effects, including side effects, and the both depend on the dosage regimen.

1. **Choose the right variant (short → mean → long) of the relevant pharmaceutical drugs, according to their duration of action**
   A. diazepam → oxazepam → alprazolam
   B. alprazolam → diazepam → oxazepam
   C. oxazepam → alprazolam → diazepam
   D. alprazolam → oxazepam → diazepam
   E. oxazepam → diazepam → alprazolam
2. **Which of the following statements about benzodiazepine absorption is true?**
   A. they are absorbed well, however, subject to a varied rate
   B. they are absorbed well and rapidly in case of intramuscular injection
   C. they are absorbed rapidly in case of administration per anum, in the form of a solution
   D. they are absorbed slowly and variedly in case of intramuscular administration
   E. they are absorbed slightly in case of administration per anum.

3. **Which of the following statements about benzodiazepine distribution is true?**
   A. it has a big volume of distribution
   B. it has a small volume of distribution
   C. it coupled intensely to plasma proteins
   D. it is characterized by redistribution process due to high lipophilicity
   E. it does not penetrate into the placenta and epithelium of the mammary glands
4. **Which of the following statements about benzodiazepine metabolism is true?**
   A. it is subject exclusively to conjugation processes
   B. it is metabolised through biotransformation and conjugation
   C. it forms active metabolites
   D. it produces a slight induction of microsomal liver enzymes
   E. liver diseases influence mainly on microsomal oxidation but not on conjugation.
5. **Choose the right variant (short → mean → long) of the relevant drugs, according to their half-life**
   A. oxazepam → alprazolam → diazepam
   B. alprazolam → diazepam → oxazepam
   C. diazepam → oxazepam → alprazolam
   D. oxazepam → diazepam → alprazolam
   E. alprazolam → oxazepam → diazepam.

Anti-inflammatory and antirheumatic medication

I. Simple clinical cases

1. A 45-year-old man suffering from rheumatoid arthritis for many years, was prescribed treatment with sodium aurothiomalate 50 mg/week. During the treatment the patient's condition improved, but after 4 months of administration the therapy was discontinued because of an outbreak of proteinuriea. The patient was recommended sulfasalazine administration which was also discontinued after three months because of an outbreak of thrombocytopenia.

What is the cause of the outbreak of thrombocytopenia?

What other side effects occur at the administration of gold salts?

Which drug can be used as an antidote in serious complications?

2. A 54-year-old patient was hospitalized with symptoms of intermittent pain in the joints of the knees and small joints of the hands. These symptoms persisted for 5 years.

The patient received aurotiomalat 50 mg/week, acetylsalicylic acid 4 g/day, over the past four months. The patient's condition improved, but pain in the abdomen occurrred and pronounced diarrhea developed.

What is the cause of the occurrence of pain in the abdomen and diarrhea?

Is the choise of drugs for the treatment of the patient correct?

What drugs are included in ,,the gold standard,, according to the criteria of efficacy and safety?

3. A 62-year-old man presented the following symptoms: astenia, fatigability during 5 weeks. The onset of the disease was manifested by subfebrility, 110 g/l hemoglobin, VSH-30 mm/HR. Clinical examination did not detect any pathology.

Is the treatment with any NSAI drugs necessary?

Is it necessary to initiate the treatment with antibacterial drugs?

Is further patient supervision necessary?

4. A 40-year-old patient suffering from rheumatoid arthritis for years consulted a doctor for an outbreak of a generalized skin pruritis. The patient undrewent a treatment with sodium aurothiomalate 50 mg/week (intramuscular administration). Objective examination of the thorax and upper limb showed erythematous rash. The results of laboratory investigations showed all indices within the normal range.

What is the cause of the occurrence of erythematous eruption?

What changes are needed in the treatment of the patient?

What are the side effects of sodium aurothiomalate?

5. A 66-year-old patient suffering from Horton disease over the last year was administered treatment with prednisolone in a dose of 10 mg/day. After the decrease of the dose up to 7.5 mg/day, pain and stiffness occurred in coxo-femoral joints of the shoulder on motion, VSH increased up to 34 mm/HR.

What is the cause of the patient's condition worsening?

What measures should be taken to improve the patient's condition?

What are the side effects of glucocorticoids?

6. A 48-year-old patient suffering from rheumatoid arthritis over a period of 10 years. Treatment with steroidal anti-inflammatory medicines and derivatives of 4-aminoquinolines did not produce the expected effect. The patient's condition worsened and destructive modifications increased in the joints. There were pathological changes in the kidneys accompanied by moderate proteinuria. The patient was administered methotrexate 7.5 mg/week increasing the dose up to 2.5 mg/week in association with meloxicam 15 mg/day. Methotrexate 17.5 mg/week caused anemia and thrombocytopenia.

What is the cause of the occurrence of blood disturbences?

What changes are needed in the treatment of the patient to improve his condition?

What drugs does methotrexate have to be associated with?

7. A 54-year-old patient with the complains of swelling in the region of the lower limbs and face edema was consulted by the family doctor. He was considered to be ill over the past two years and his condition was getting worse, progressively. He was treated with diuretics and antihypertensive drugs, but the treatment did not result in complete disappearance of edema and normal blood pressure. In the patient his-

tory it was noted that he suffered from rheumatoid arthritis, and he had been administered chloroquine, indometacine, and meloxicam for a long period of time. Respiratory system and gastrointestinal tract pathologies were not detected, HR-80 min.; BP /170/100 mm Hg. There were revealed swelling in the region of the lower legs, soles; face pastosity and urinary incontinence. Creatinine clearance constituted 75 ml/min.

What is the cause of the current state of the patient and antihypertensive and diuretics treatment's inefficiency?

What changes in the treatment of this paient are necessary?

What are the side effects of nonsteroidal anti-inflammatory drugs?

8. A 10-year-old patient, 32 kg, was diagnosed with chronic glomerulonephritis, nephrotic form. Over the last two days, his face, hands and lower legs considerably increased in size due to edema. He put on 1,2 kg daily and diuresis accounted 200 ml. In the analysis of urine proteins 7 g/l, single, altered erythrocytes. Biochemical analysis of blood showed 38-g/l of total protein, 31% globulin, 69% globulin and urea 9 mmol/l.

To remove edema the patient was administered 2 ml of furosemide. After 3 hours the patient excreted 80 ml of urine.

Explain the cause of diuretic refractoriness.

Recommend your own version of the treatment.

What are the criteria for the assessment of treatment effectiveness?

9. A 48-year-old patient, with rheumatoid arthritis was administered methotrexate 15 mg/week. On the background of the treatment, disease symptoms decreased in intensity, but after 5 months of treatment the patient again went to the doctor with complaints of dyspnea.

Radiological examination detected pneumonic pulmonary infiltration – pneumonitis, which was considered by the physician as a manifestation of methotrexate toxicity as a result of high plasma concentration (0.04 mcml/l norma being 0,02 mcml/l). In order to determine the cause of increased plasma concentration of methotrexate genetic investigation was peformed which found that patient had polymorphism gene encoding the enzyme responsible for the organic anions transport in the renal tubule.

Why did plasma methotrexate concentration increase in the patient?

What dose does the effectiveness of methotrexate vary in?

What investigations may monitor methotrexate treatment safety?

10. A 48-year-old patient, with rheumatoid arthritis, high blood pressure and depression in the history is admitted to the hospital with complaints: dyspnea and dry cough. The treatment of the patient until the admission included: azathioprine (50 mg/day), olanzapine (10 mg/day) and valsartan (160 mg/day).

The auscultation showed bilateral wet rales in the lungs. ECG showed Hiss left bundle-branch block. QT-interval was normal. EcoCG revealed local areas of hypokinezia with ejection fraction-35%.

The x-ray of the lungs discovered bilateral pulmonary infiltrates suggesting pneumonia. Blood count showed moderate leukocytosis. The patient, in addition to the treatment received previously ciprofloxac in 800/mg/day intravenously and furosemide 40 mg/day. The patient's condition improved gradually, but on the third day ECG showed QT enlargement up to 610 ms.

Ciprofloxacin was replaced with cefotaxime. The patient was transferred to the intensive care unit for permanent monitoring of ECG. During the treatment within 10 days, QT gradually reduced until the initial values. As the patient refused to undergo further investigation, including coronarography, she was discharged from the hospital with recommendation to continue the treatment she had been administered before the hospitalization and take a diuretic drug.

What is the cause of an outbreak of pneumonia in the patient?

What caused the elongation of QT interval?

Why did Q T return to the norm after discontinuation of ciproflaxine?

II. Multiple clinical cases

Clinic case 1

A 43-year-old man suddenly, during night, experienced signs of acute arthritis of metatarso-phalangian joint. Medical history: abuse of alcohol, meat products and fats.

1. What is the presumptive diagnosis?

A. reiter's syndrome

B. septic arthritis
C. onset of osteoarthroses
D. onset of rheumatoid arthritis
E. gout

2. In order to establish the right diagnosis what drugs are necessary for the treatment of arthritis symptoms?

A. allopurinol
B. indometacine
C. glucocorticoids
D. colchicine
E. gold compounds
F. acetylsalicylic acid 2 g/day

3. The effect of allopurinol administered in patients with hyperuricemia is due to:

A. phagocytosis of urate crystals deposited in joints
B. blocking of uric acid formation
C. interaction with anions transporting mechanism in contort proximal tubule
D. inhibition of xanthinoxidase which participates in transformation of hypoxanthine in xanthine
E. facilitation of the release of hypoxanthine and xanthine through urine

4. What is the mechanism of antigout effect of colchicine?

A. blocks amyloid precurssors production
B. blocks the synthesis of amiloidoaccelerator factor
C. inhibits transformation of hypoxantyine in xanthine and xanthine in uric acid
D. prevents amyloid fibers formation
E. uricozuric effect is due to the antimitotic action

5. In what dose can calcitonin be administered in acute gout?

A. 1 mg twice a day (morning and evening) until the crises stopes
B. maximum total dose 10 mg
C. 1-3 mg a day for a long period
D. 0.5 mg 2 times/day for 5 days

Clinical case 2

Patient C, aged 54-year-old, was suffering from lower limb deformity osteoarthrosis with marked synovites for the last 5 years. Medical history showed the presence of allergic reaction to many medical substances (phenylbutazone, indometacine, theophylline). In the hospital

she underwent a treatment with reopirine 5 ml/m (once per day), 100 mg of prednisolone intra-articularly (in the joints of the knees) and clemastine. An erythematous rash accompanied by pruritis occurred 3 days later.

1. **What is the cause of patient's condition worsening?**
   A. progression of the basic disease
   B. cutaneous manifestations of a systemic vasculitis which was undiagnosed previously
   C. drug allergy
   D. candida of the tegument

Additionally, the patient was administered indovasin (topical gel) in the region of joints. Within 2 days, erythematous rash became confluent and spread on the limbs. The dermatologist suspected drug allergic dermatitis.

2. **Your recommendations:**
   A. to change the ways of drug administration -reopirine internally
   B. replacement of all drugs with diphenhydramine ointment
   C. to cease methindol administration and to replace indometacine with prednisolone 20 mg/day orally.
   D. to cease indovasin-gel administration
3. **The patient's condition improved and skin eruption reduced. What are your steps for further treatment?**
   A. to cease drugs administration and to follow up the patient's condition
   B. to cease prednisolone administration and to continue the treatment with other nonsteroidal anti-inflammatory drugs
   C. to cease the administration of all drugs except prednisolon and clemastine
   D. to cease the administration of all drugs and initiate a pathogenetic treatment with a combined drug containing glucosamine and condroitine
4. **Treatment with teraflex (one capsule 3times/day) was initiated. Administration of the drug for one week did not show any evident therapeutic effects.**
   What is the management of further pharmacoterapy?
   A. to cease the administration of teraflex and to administer dexamethasone

B. to cease the administration of teraflex and administer nonsteroidal anti-inflammatory drugs from the aril-propionic group
C. to continue the treatment with teraflex and add of ibuprofen 600 mg/day

5. **After 10 days of therapy the patient's condition improved considerably. The inflammatory symptoms in the knee joints were diminished; the functional ability of the joints improved but occurred some problems with the digestive tract as nausea, vomiting, diarrhea and pain in the epigastric region.**
   What do you do in this situation?
   A. continue the treatment with teraflex in the same dose and decrease the dose of ibuprofen by 50%
   B. decrease by half the dose of teraflex and continue the administration of ibuprofen in the same dose
   C. continue the treatment with both drugs in the same dose and ad to the treatment with Almagel
   D. continue the treatment with teraflex 1 capsule 2 times/day and ibuprofen 300 mg/day.

Clinical case 3

Patient G, aged 35-year-old, with presumptive diagnosis of rheumatoid arthritis and high activity of articular syndrome resistant to the monotherapy with anti-inflammatory drugs, was administered methotrexate 2.5 mg 3 times/day and 0.025 mg diclofenac 3 times/day. The knee joints were injected with 125 mg of hydrocortisone.

1. **How do you evaluate the drugs selection and their dosage regimen?**
   A. drugs selection and the dosage regimen are correct
   B. dosage regimen of methotrexate is incorrect- the dose is too high
   C. association of diclofenac with methotrexate is not reasonable
   D. methotrexate should be administered 7.5 to 20 mg/week in combination with folic acid
   E. methotrexate can be associated with a nonsteroidal anti-inflammatory drug except for sacetylsalicylic acid and diclofenac

2. **The diagnosis of rheumatoid arthritis was confirmed in the patient. How quickly will the "specific" action of methotrexate occurred from the beginning of its administration?**
   A. A.2 hours after first administration
   B. one week later
   C. over one month
   D. over several months
   E. more than a year
3. **What measures would you undertake to ensure a harmless pharmacotherapy with methotrexate in this patient?**
   A. weekly control of hemogram (more than 2 times per week)
   B. blood analysis with assessment of platelets count
   C. urine analysis
   D. assessment of uric acid level
   E. assessment of fecal occult blood
   F. assessment of transaminase and total bilirubin
4. **The patient, after the treatment with methotrexate, complains of massive nasal hemorrhage. What is the cause of bleeding?**
   A. damage of the nasal vessels by rheumatoid arthritis
   B. diminution of prothrombin index as a result of toxic hepatitis caused by methotrexate
   C. decrease of platelet aggregation under the influence of methotrexate
   D. thrombocytopenia induced by drug administration
   E. toxic action of methotrexate on nasal vessels
5. **What drugs with "specific" (basic) action on the treatment of rheumatoid arthritis do you know?**
   A. amino-quinoline derivatives
   B. cytostatic preparations (methotrexate, azathioprine, cyclophosphamide, etc.)
   C. glucocorticoids (prednisolone etc.)
   D. nonsteroidal drugs
   E. gold compounds (auranofin etc.)
   F. sulfasalzine
   G. antibiotics (tetracyclines etc.)

Clinical case 4

Patient B, aged 25-year-old, suffering from rheumatism in active phase, II stage, was administered the treatment with chloroquine 0,25 g in the evening, indometacine 0,025 g 4 times/day, and 1500000 IU i/m of benzathine benzylpenicillin once every 4 weeks. The patient complained of moderate pain in epigastric area, after two weeks. The patient was diagnosed with gastritis after fibrogastroscopy.

1. **How would you change the antirheumatic treatment in case that no other disorders will be reveled?**
   A. cease the administration of chloroquine
   B. cease the administration of indometacine
   C. rectal administration of indometacine
   D. cease the administration of indometacine and prescribe intramuscular administration of diclofenac
   E. start antiulcer prophylactic treatment
   F. decrease twice the dose of indomethacin
   G. additionally prescribe misoprostol
2. **Will you change the antirheumatic treatment in case that peptic ulcer is diagnosed?**
   A. stop the administration of indometacine
   B. administer diclofenac intramusculary
   C. prescribe anti-ulcer treatment
   D. cease the administration of chloroquine
   E. prescribe non-selective, non-steroidal anti-inflammatory drugs
3. **What recommendations would you give to the patient about the administration of indomethacine and food ingestion?**
   A. 30 min before meal
   B. right before meal
   C. during meal
   D. right after meal
   E. 10 min after meal
4. **How will chloroquine be administered according to food ingestion?**
   Use the variants of answers from the previous question.
5. **How will you perform the safety control of medication with chloroquine in case of prolonged use of this drug?**
   A. hemogramma

B. urine analysis
C. ECG
D. eye back examination
E. examination of the vision fields
F. radiography of the chest organs
G. assessment of the number of platelets
H. examination of cornea

Clinical case 5

Patient K, aged 44-year-old, suffering from rheumatoid arthritis, predominantly articular form, III stage, was prescribed the following medicamentous treatment:

1. internal administration of prednisolone 5 mg 3 times/day
2. administration of sodium aurothiomalate 50 mg per week i/m
3. internal administration of diclofenac 25 mg 4 times/day
4. internal administration of ibuprofen 0,2 de 3 times/day

1. What is your opinion concerning this treatment?

A. association of glucocorticoids with NSAI is not correct
B. association of glucocorticoids with gold preparations is not correct
C. administration of two nonsteroidal anti-inflammatory drugs is not correct
D. dosage regimen is incorrect (doses are insufficient)
E. drugs choise is correct and the dosage regimen is correct

2. What are efficacy criteria of this treatment?

A. positive clinic development of articular syndrome
B. positive evolution of articular manifestations at X-ray
C. lack of articular manifestations progress at X-ray
D. positive development of rheumatic manifestations
E. decrease of titres of rheumatoid factor
F. absence of LE cells

3. When will the effect of sodium aurothiomalate appear?

A. after one week of administration
B. after 3-4 weeks of administration
C. after 3-4 months of administration
D. after 6 months of administration

4. **How will you check the safety of antirheumatic treatment at this patient?**
   A. hemogramma
   B. urine analysis
   C. assessment of C-reactive protein
   D. assessment of transaminase level, general bilirubine
   E. X-ray of the thoracic cavity
   F. assessment of fecal occult blood
   G. ureea, creatinine
5. **What pharmacotherapy complications may appear?**
   A. hypertension
   B. skin eruptions, stomatitis, conjunctivitis
   C. proteinuria
   D. alergic dermatitis
   E. anemia, thrombocytopenia
   F. peptic ulcer
   G. hypoglycemia
   H. toxic hepatitis

Clinical case 6

A 51-year-old woman suffering from rheumatoid arthritis was hospitalized in the rheumatologic department. Clinic and laboratory investigations revealed seropositive rheumatoid arthritis, III stage, IFA functional class III.

1. **What is the drug you have to start the treatment with?**
   A. nonsteroidal anti-inflammatory drugs
   B. glucocorticoids
   C. sulfasalazine
   D. immunosuppressive cytotoxic drugs
   E. biologic drugs
2. **What is the eficacy of nonsteroidal anti-inflammatory drugs in rheumatoid arthritis?**
   A. reduce pain and inflammation in the joints
   B. prevent the progression of joint erosions
   C. prevent the occurrence of extraarticular manifestations

D. have only symptomatic effect which lasts only during the treatment
E. reduce the risk of development of peripheral erosions in the insertion of synovitis on the bone

3. What is the role of systemic corticotherapy in rheumatoid arthritis?

A. can be prescribed in a monotherapy or in combination with NSAIDs for the treatment of mild forms of the disease
B. is prescribed for severe attacks or in forms with severe clinic evolution of rheumatoid arthritis
C. may be prescribed in small doses, during a short period of time, at the beginning of remission therapy (Bridge therapy)
D. in case of vasculitis or other systemic manifestations of rheumatoid arthritis is preferable the administration of glucocorticoizilor in pulse therapy

4. What are the contraindications for performing pulse therapy with corticosteroids?

A. diabetes mellitus type II
B. uncontrolled hypertension
C. endogenous psychosis
D. peptic ulcer
E. simultaneous infection

5. What are the main mechanisms determining the anti-inflammatory effect of sulfasalazine in rheumatoid arthritis?

A. anti-inflammatory effect of sulfasalazineis due to acid 5 aminosalicilyc
B. sulfasalazine inhibits NFKB transcription factor, which plays an important role in regulation of the synthesis of proinflammatory cytokines
C. efficacy of sulfasalazine in rheumatoid arthritis is compaired with the efficacy of methotrexate
D. sulfasalazine inhibits the synthesis of TNF alpha (tumor necrosis factor alpha)
E. efficacy of sulfasalazine in rheumatoid arthritis is comparable to the one of gold salts

Clinical case 7

A 30-year-old pregnant woman (9 weeks) was diagnosed with seropositive rheumatoid arthritis, II stage, phase II, IFA class II.

1. **What drugs with minimal risk for the fetus can be indicated to the patient?**
   A. ibuprofen
   B. diclofenac
   C. celecoxib
   D. prednisolone
   E. hydroxiclorochine
   F. sulfasalazine
2. **The patient was prescribed the treatment with diclofenac and prednisolone, her condition improved partially (pain in joints was diminished but fully functional capacity of joints and laboratory indexes did not restore). What is the further pharmacotherapeutic management of the patient?**
   A. addition of hydroxiclorochine to the treatment
   B. addition of sulfasalazine
   C. cease of the administration of diclofenac, prednisolonei and administrate cyclosporine
   D. cease of the administration of nonsteroidal anti-inflammatory, glucocorticoids and indication of a biologic treatment with infliximab or etanercept
3. **What of the following drugs are contraindicated in pregnancy?**
   A. rituximab
   B. azathyoprine
   C. leflunomid
   D. metotrexat
   E. adalimab
   F. micofenolat
   G. cyclofosfamide
4. **At what period (until conception) the administration of metotrexat in pregnant women should be suspended?**
   A. 5-10 days
   B. 2-3 weaks
   C. 2 -3 months
   D. 4-6 months
   E. one day before conception
5. **At what period (until conception) the administration of metotrexat in men should be suspended?**
   A. 5- 10 days
   B. 2 -3weeks
   C. 3 months
   D. 4-6 months
   E. one day before conception

Clinical case 8

A 46-year-old patient was hospitalized with fever, gastrocnemius myalgia, pain in the talocrural joints and skin rash.

Examination revealed vascular purpura in the region of lower limb; swelling of talocrural joints with limitation of their functional capacity; proteinuria and microhematuria. Diagnosis of nodular periarteritis was confirmed by angiography of vessels of the lower limbs. There were revealed additional stenosis and aneurysms of medium size in the lower limbs.

1. **What drugs are needed to start the treatment?**
   A. nonsteroidal anti-inflammatory
   B. anti TNF alfa drugs
   C. aminoquinoline derivatives
   D. glucocorticoids
   E. nonsteroidal anti-inflammatory in association with glucocorticoids
2. **What is the dosage regimen of glucocorticoids at the onset of the disease?**
   A. 15-20 mg prednisolone in 24 hours/3 times
   B. 30-40 mg prednisolone in 24 hours/3 times
   C. 1-2 mg kg prednisolon in some intakes
   D. after obtaining the desired effect to decrease the nictimerale dose by 5 mg per week
   E. puls therapy 1000 mg in 24 hours for 3days with subsequent administration of a dose of 10 mg/day.
3. **What cytotoxic immunosuppresive drug is used in the treatment of nodular periarteritis?**
   A. azathyoprine
   B. metotrexat
   C. cyclofosfamide
   D. mercaptopurine
   E. clorambucil
4. **The patient was prescribed cytotoxic immunosuppresive drug in nictameral dose 2 mg/kg for one month due to the high level of creatinine.**
   What are the monitoring parameters in this case?
   A. blood count is performed after one day

B. number of leukocytes 3000, 3500
C. serum creatinine 200mmol /l
D. leukocyte number 5000
E. number of neutrophils 500- 800
F. number of neutrophils 1000 -1500
G. blood count is performed once in two weeks

5. Severe adverse effects established after administration of citotoxic drug. What is further treatment of the patient in this case?

A. decrease the dose of cytotoxic immunosuppresive drug
B. puls therapy with methyilprednisolone 15/mg kg/24 hours, for 3 days
C. prednisolone in dose of 1 mg/kg/24 hours
D. 7 to 10 plasmopheresis procedures with removal of plasma volume of 60 m/kg and its substitution with equal amounts of human albumin 5%

Clinic case 9

A patient suffering from systemic lupus erythematosus was administered treatment with corticosteroids (prednisolone 5 mg/day) over the last 5 years. She was admitted to hospital after the exacerbation of her condition due to an acute viral respiratory infection. Clinical and laboratory examination revealed pulmonary fibrosis, pleural effusion of both sides and persistent proteinuria-1 gr/24 hour.

1. What is the cause of aggravation of the patient's condition?

A. insufficient nictameral dose of the drug
B. acute viral respiratory infection
C. incorrect treatment of systemic lupus erythematosus

The prednisolone dose was increased up to 50 mg/day in hospital. Initially, the patient's condition improved, but after 4 weeks of treatment black stools occurred. Fibrogastroduodenoscopy detected duodenal ulcer of 1 cm.

2. What drugs should be indicated for further treatment of this patient?

A. association of prednisolone with famotidine, almagel, misoprostol
B. addition of omeprasol, maalox, bismuth coliodal subcitrate

C. decrease of the dose of prednisolone with 1 mg/week
D. cease the administration of prednisolon and start the treatment with metotrexat 7,5/mg/week

3. What are the contraindications for methotrexate administration?
A. bronchial asthma and obstructive bronhopneumopathy
B. leukopenia, thrombocytopenia
C. liver diseases
D. rheumatoid arthritis
E. renal diseases

4. Repeated fibrogastroduodenoscopy reveled scarring of duodenal ulcer after 4 weeks of anti-ulcerous treatment; but the proteinuria grew up to 5 g in /24 hours. What are the indications for performing pulsotherapy in systemic lupus erythematosus?
A. old-aged people
B. fulminant progressive nephritis
C. polyserositis, exudative pleuritis, pericarditis
D. high immunologic impairment
E. impairment of the nervous system

5. What are the dosage principles of the pulsotherapy?
A. i /v 500-1000 mg methyilprednisolone for 3-5 days
B. oral administration of prednisolone 300 mg 1, 10 and 20/month
C. association of 1000 mg methylprednisolon with 1000 mg cyclofosfamide from the first day
D. i/v cyclofosfamide 1000 mg with further increase from 200 mg up to 5000 mg

Clinical case 10

A 40-year-old man suffering from seropositive rheumatoid arthritis, second stage, was prescribed the treatment with indometacine 75 mg/day and chloroquine 250 mg/day in the outpatient condition. Dyspeptic disorders as nausea, vomiting, headaches, visual disturbances and epigastric pain occurred after 6 months of treatment. Ophthalmologic examination revealed deposition of chloroquine in the retina. The administration of drug was suspended, but patient's condition worsened. Suddenly, pains in joint became marked. Radiologic examination detected osteoporosis and cartilage injuries.

1. **What is the cause of the aggravation of patient's condition?**
   A. incorrect selection of drugs
   B. pharmacodynamic features in rheumatoid arthritis of indometacine and chloroquine
   C. inadequate doses of drugs for patient's condition
   D. common development of the disease
2. **What nonsteroidal anti-inflammatory drugs connstitute the first choice in the treatment of rheumatoid arthritis?**
   A. acetylsalicylic acid
   B. diclofenac
   C. mefenamic acid
   D. piroxicam
   E. meloxicamul
   F. celecoxib
3. **What drug is considered the gold standard in the treatment of rheumatoid seropositive arthritis, having the best efficacy/toxicity correlation?**
   A. acetylsalicylic acid
   B. diclofenac
   C. metotrexat
   D. piroxicam
   E. meloxicam
   F. celecoxib
4. **The patient was prescribed leflunomid 100 mg/day for 3 days with the subsequent administration of 20 mg/day.**
   What are the pharmacodynamic properties of the drug?
   A. inhibits NF kb transcription factor that regulates synthesis of inflammatory mediators
   B. inhibits the synthesis of pirimidinic nucleotids and activates T-limfocitele
   C. inhibits the expression of genes that code the synthesis of inflammatory mediators
   D. inhibits the metaloproteinases which causes joint damage
   E. inhibits osteoblasts which cause bone destruction
5. **In case that leflunomid monotherapy is inefficient. What drug can be associated with leflunomid?**
   A. sulfasalazine
   B. metotrexate
   C. NSAI
   D. aminoquinoline derivatives
   E. penicillamine
   F. biologic drugs – infliximab, rituximab

Clinical pharmacology of antibacterial, anti-fungal and antiviral drugs

I. Simple clinical cases

1. A 19-year-old young girl underwent a 'criminal' abortion. She was hospitalised in a very severe state in 4 days: semicoma, hyperthermia (t – 40°C). Blood pressure 80/50 mm Hg, rhythmic pulse from 120 to 130 beats per minute (septic shock), hepatic, renal and respiratory failure. Eventual infection: *Escherichia coli, Klebsiella.*

What antibacterial drugs are elective?

What drugs are alternative in case of contraindications to those elective ones?

What are the principles of intake and dosage of the drugs used?

2. A 40-year-old man had a perforation of duodenal ulcer. He was admitted in a severe state to the surgical department in 8 hours: t 39^0C, blood pressure 110/70 mm Hg, rhythmic pulse 100 beats per minute. Generalized peritonitis. Eventual infection: *Pseudomonas aeruginosae, Proteus mirabilis, Escherichia coli.*

What antibiotic therapy principles shall be adhered to in this clinical case?

What are the groups of drugs that may be used?

What drugs are elective for this patient?

3. A 45-year-old man had mitral valve implantation. The patient was admitted to the hospital with septic endocarditis with Staphylococcus *aureus*, in three days. The patient's state was very severe: hyperthermia, toxaemia, CHF (Congestive heart failure) NYHA class II.

What drugs will you choose for intensive therapy of the patient?

What drugs are elective in case of infections caused by Staphylococcus *aureus*?

What antibiotics are alternative in case of inefficiency of the drugs administered initially?

4. A young boy aged 17 is suffering from rheumatism and pyelonephritis for 5 years. He was admitted to the rheumatology department of with the diagnosis of rheumatism with activity II degree and septic endocarditis provoked by gram-negative bacilli. The patient's state was severe: hyperthermia, grade 2 heart failure.

What antibacterial drugs may be prescribed for the etiopathogenetic purposes in case of rheumatism?

What antibiotics have precedence over gram-negative microflora?

What personal drugs will be selected to treat this patient?

5. A young girl was hospitalized in a severe state and was diagnosed with acute gangrenous perforated appendicitis and purulent generalised peritonitis. She is in the intensive care unit after the surgical intervention.

What antibacterial drugs will you administer to treat this patient, taking into account the fact that peritonitis is caused by associated microflora?

What drugs will you choose to detoxify the patient and to maintain the function of vital organs?

What is the patient's dosage regimen of the administered drugs?

6. A 20-year-old young boy was hospitalized in a severe state with bilateral pneumonia occurred after influenza. He had hyperthermia (t 40°C) and severe cardiorespiratory failure on the admission. Eventual infection: influenza virus, *Haemophilus influensae*.

Is it necessary to administer antiviral drugs and if yes, namely what drugs?

Is it necessary to administer antibiotics and if yes, namely what drugs?

What are eventual side effects of the chosen drugs?

7. A group of tourists is going on trip to a region, where multiple cases of encephalitis caused by *Rickettsii* were recorded.

May these tourists use antibiotics for prophylactic purposes?

What antibiotics may be used for prophylactic purposes in this case?

What is the dosage regimen of the administered antibiotics?

8. Patient A., aged 20, is treated for bacterial pneumonia. She has hyperthermia of up to 39.9°. She takes benzylpenicillin intramuscularly in the dose of 1 g every 6 hours. Her state slightly improved on the 4th day, however, hyperthermia remained at the level of 37.8 to 38.5°C and haemoptysis also developd. Enterococci and staphylococci were identified in sputum.

Will you continue treatment with the same drug, having increased its dose?

What drugs are elective in case of infections caused by enterococci?

What drugs are elective in case of infections caused by staphylococci?

9. A pregnant (trimester I) woman aged 23 complains of dysuria. The urinealysis showed leukocyturia. The germ of E. coli was identified in the urine culture and the antibiogram determined sensitivity to the following chemotherapeutical drugs: nalidixic acid, co-trimoxazole, nitrofurantoin.

Which of the listed drugs may be used in the I trimester of pregnancy?

What antibiotics are elective in case of infections caused by E. coli?

What antibiotics may be used in the course of pregnancy?

10. A 28-year-old woman complains of fever, frissons and bilateral pains in the lumbar region, shooting pain in urinary bladder, in 3 weeks after child birth. The general state is altered. The haematological investigation identified leukocytosis with neutrophilia and increased erythrocyte sedimentation rate. The urinalysis identified pyuria and bacteriuria. The Proteus germ was identified in the urine culture:

What drugs may be used in case of pyelonephritis gravidarum?

What drugs are elective in case of infections caused by Proteus?

What drugs may be used in case of patient's urinary infection, taking into account the fact that she is breastfeeding?

II. Multiple clinical cases

Clinical case 1

A patient was hospitalized with community-acquired pneumonia and administeted amoxicillin during 5 days, however, this treatment

proved to be ineffective. The sputum was collected for bacteriological test and the patient was prescribed antibacterial therapy with cefotaxime intramuscularly, in a daily dose of 2 g (in the morning and in the evening). Despite the prescribed treatment, cough and fever persisted.

1. **What is the cause of treatment failure?**
   A. narrow spectrum of the antibiotic
   B. compromised immunity of the patient
   C. insufficient drug dose
   D. wrong regimen of administration
   E. absence of sensitivity of the pathogenic agent to the antibiotic
   F. the principle of antibiotic therapy is to know pharmacokinetics of administered antibiotic.
2. **What are pharmacokinetic features of cefotaxime?**
   A. it is absorbed rapidly in case of ingestion
   B. half-life is from 4 to 5 hours
   C. C max is 1.5 hours
   D. the bactericide blood concentration is maintained more than 12 hours
   E. about 30 to 60% of the drug is excreted with urine in the unchanged form and in the form of active metabolites.

The repeated radiological investigation showed destruction foci in the lower right lobe. Staphylococcus aureus resistant to methicillin was identified in the bacteriological sputum test.

3. **What is the mechanism of the development of antibiotic resistance of staphylococcus?**
   A. permeability disorder of the external membranes of bacterial cells
   B. modification of the target action
   C. enzymatic inactivation of antibiotic
   D. active elimination of antibiotic from a cell
   E. protection of the target action
4. **What are elective antibiotics in the treatment of infections caused by staphylococci resistant methicillin?**
   A. oxacillin
   B. dicloxacillin
   C. vancomycin
   D. clarithromycin
   E. teicoplanin
   F. cefepime

5. **What pathogenic microorganisms, except for staphylococci, are comprised in the spectrum of action of these antibiotics?**
   A. gram-negative cocci (gonococci, meningococci)
   B. streptococci
   C. pneumococci (including the strains resistant to penicillin)
   D. mycoplasma
   E. clostridia
   F. peptostreptococci

Clinical case 2

A 44-year-old patient, a veterinarian by profession, consulted a physician complaining of: moderate intermittent fever, cephalgia, abundant night sweats, arthralgia and myalgia.

The patient was admitted to the infectious disease hospital and after clinical and laboratory investigations, he was diagnosed with brucellosis.

The patient was prescribed the treatment: tetracycline at a dose of 3 gr per day, in combination with streptomycin at a dose 1 g of per day intramuscularly.

After a week of treatment, the patient developed nauseas, vomit and pains in the epigastrium.

1. **What are adverse reactions to tetracycline administration?**
   A. phenomena of gastric irritation – pirosis, nausea, vomit, epigastric pains, diarrhoea
   B. toxic action on haematopoiesis with leucopoenia and thrombocytopenia
   C. hepatotoxic action
   D. neurotoxic action (dizziness, vertigoes, somnolence)
   E. photosensitivity to sun rays

Fibrogastroduodenoscopy detected gastric ulcer 1 cm in diameter.

2. **What antiulcer drugs will you prescribe to the patient?**
   A. famotidine, maalox, sucralfate
   B. omeprazole, almagel, misoprostol
   C. pantoprazole, phosphalugel, sea-buckthorn oil
   D. ranitidine, colloidal bismuth subcitrate, vicalin

During the antiulcer treatment, the pains in the epigastrium reduced, however, cough, dyspnoea and asthenia developed. The radiolo-

gical investigation identified pneumonia with peribronchovascular infiltrates and brucellosis granulomas, pleurisy on the right.

3. What is the cause of the patient's state aggravation?

A. resistance of the pathogenic agent to administered antibiotics
B. disorder of tetracycline absorption in the digestive duct
C. liver failure symptoms
D. incapacity of antibiotics to influence intracellular bacteria

4. What kind of alternative treatment may be administered to this patient?

A. benzylpenicillin intramuscularly
B. co-trimoxazole per os
C. cephalexin per os
D. polymyxin B intramuscularly

5. What are contraindications to the administration of tetracycline?

A. hepatic and renal diseases
B. gastric and duodenal ulcer
C. fungal diseases
D. breast-feeding period and children up to 8 years
E. heart arrhythmias.

Clinical case 3

A 56-year-old female patient suffering from type I diabetes mellitus developed abscess of soft tissues because of non-compliance with antiseptic rules at the place of insulin administration. The abscess was opened, bacteriological test was made and Staphylococcus aureus was detected.

1. What antibiotic is elective?

A. benzylpenicillin
B. oxacillin
C. erythromycin
D. lincomycin
E. doxycycline
F. chloramphenicol

The patient was prescribed elective antibiotic at a dose of 2 gr per day, nevertheless, despite the antibacterial treatment, multiple furuncles developd.

2. **What antibiotic is alternative?**
   A. ampiox (ampicillin/oxacillin)
   B. amoxicillin/clavulanate
   C. meropenem
   D. ristotycine
   E. cefazolin
3. **The patient developed urticaria and pruritus on the second day of administration of an alternative antibiotic. She was prescribed 1 pill of 0.01 loratadine per day and cutaneous eruptions disappeared in 2 days.**

   What antibacterial drug of the reserve group may be prescribed to the patient?
   A. ceftriaxone
   B. amoxicillin/sulbactam
   C. co-trimoxazole
   D. clarithromycin
   E. vancomycin
4. **What are pharmacokinetic properties of the prescribed reserve drug?**
   A. high bioavailability in case of intake thereof
   B. the therapeutic concentration is maintained for 8 to10 hours after intravenous administration
   C. about 60% of drug is metabolised in the liver
   D. it is excreted via the kidneys, mainly in the unchanged form.
5. **What side effects may occur in case of intravenous administration of the drug?**
   A. oto- and nephrotoxic actions
   B. thrombophlebitis and vasculitis
   C. dyspeptic disorders (nausea, vomit)
   D. arterial hypotension
   E. hyperaemia of the upper part of the body

Clinical case 4

A 21-year-old female patient was hospitalized with mastitis and hyperthermia (t 39.5°C). She was hospitalized on the 10^{th} day after child birth and was sick for 3 days. She underwent a surgical intervention.

1. **Choose an elective antibiotic for this case:**
   A. cefazolin
   B. benzylpenicillin
   C. tetracycline
   D. gentamicin
2. **The patient developed cepahlgia, vertigo, abdominal pains and arterial hypotension after the 2nd antibiotic injection. What complication occurred?**
   A. anaphylaxis
   B. aggravation of the disease
   C. bacterial shock
   D. acute abdomen
   E. toxic effect
3. **What shall you undertake?**
   A. immediate discontinuation of antibiotic, intravenous administration of glucocorticoids and adrenomimetic drugs
   B. administration of detoxifiers (dextran 40, neopolyvidone), associated with administration of the increased antibiotic doses
   C. reduction of the antibiotic dose
   D. transfer of the patient to the surgical department
   E. administration of glucocorticoids and antihistaminic drugs
4. **What reserve antibiotic will you choose in this case?**
   A. cephalothine
   B. tetracycline
   C. ampicillin
   D. clarithromycin
5. **Penicillin-resistant staphylococcus was detected in the lesion. Choose the antibiotic, taking into account its pharmacokinetic properties:**
   A. oxacyclin
   B. gentamicin
   C. cefoperazone
   D. chloramphenicol
   E. vancomycin

Clinical case 5

A 53-year-old patient was hospitalized with the diagnosis: ischemic cardiomyopathy, functional class III stable angina pectoris of CF III, postinfarction cardiosclerosis, atrial fibrillation, CHF NYHA Class III. He was treated with isosorbide dinitrate, lisinopril, digoxin, morphine, furosemide, warfarin and panangin in medium therapeutic doses. Fever - 38°C, cough, dyspnoea, crepitation in the right lung were recorded. Radiologically: infiltrate in the lower right lobe. The treatment was complemented by cefoperazone, bromhexine, aminophylline and chloropyramine.

1. **What drug interactions may occur in this patient in the course of intensive therapy?**
   A. cefoperazone and furosemide combination may cause a nephrotoxic effect
   B. cefoperazone and warfarin combination increases the risk of haemorrhages
   C. chloropyramine and furosemide combination may cause a nephrotoxic effect
2. **Klebsiella was detected in the bacteriological sputum test. What antibiotic is elective, taking into account its pharmacokinetics, mechanism of action and spectrum of action?**
   A. ampicillin
   B. tetracycline
   C. erythromycin
   D. cefoperazone
   E. ciprofloxacin
3. **Patient broke the hospital regime and consumed some amount of alcohol, because of his birthday. The reaction of disulfiram type developed. What treatment does the patient need?**
   A. administration of dextran 40 and neopolyvidone for the purpose of detoxication
   B. increase of furosemide dose
   C. suspension of antibiotic administration
   D. suspension of administration of all pharmaceutical drugs
4. **What is the adequate dosage regimen of cefoperazone for the patient?**
   A. 1 - 2 g once daily

B. 4 g within 24 hours (in the morning and in the evening), depending on the severity of the disease
C. 6 g within 24 hours (in the morning and in the evening), depending on severity of the disease
D. up to 12 g in (2 to 3 intakes) in case of piocyanic-bacillus infections

5. What are eventual side effects of cefoperazone administration?

A. hypoprothrombinemia with clotting reduction
B. neutropenia, anaemia, eosinophilia
C. neurotoxic action
D. hepatorenal function disorder.

Clinical case 6

A 23-year-old man complains of purulent discharges from the urethra in the morning, pollakiuria and pains in the perineum. He was considered ill for 6 months. Antibiotic therapy (rifampicin, chloramphenicol, benzylpenicillin) gave no positive results. Endourethral instillations of different antiseptics were ineffective. Rectal examination is non-conclusive (microscopy) and the cultures of urethral and prostatic discharge did not identify any pathogenic microorganisms in the purulence. *Chlamydia trachomatis* was identified through special techniques.

1. What is the first-line drug in chronic prostatitis caused by *Chlamydia trachomatis?*

A. rifampicin
B. sulphamide
C. chloramphenicol
D. ampicillin
E. azithromycin

2. Choose the dose, dosage regimen and therapy duration:

A. 0.5 g 4 times per day, for 7 -14 days
B. 0.3 g 3 times per day, for 7 -10 days
C. 1.0 g once daily
D. 1^{st} day – 1.0 g once per day, 2^{nd} day – 0.5 g once per day
E. 1^{st} day – 1.0 g once per day, 2^{nd}-5^{th} day – 0.5 g once per day

3. **In case of ineffectiveness of the applied treatment (persisting infection), the following therapy is administered:**
   A. tetracycline
   B. cephalosporin of the 1st and 2nd generation
   C. cephalosporin of the 3rd generation
   D. metronidazole
   E. trimethoprim
   F. immune-stimulating remedies (methyluracil, thymalin, sodium nucleinate, etc.)
4. **Allergic cutaneous eruptions developed after 3 days of treatment. Choose an adequate chemotherapeutic, in order to continue the treatment.**
   A. doxycycline
   B. minocycline
   C. metacycline
   D. ofloxacin
   E. ciprofloxacin
   F. pefloxacin
5. **When assessing the renal function, the decrease of creatinine clearance to 35 ml/min was revealed.**
   What are the dose and adequate dosage regimen of chosen drug ?
   A. 0.1 g 2 times per day, for 10 days
   B. 0.2 g 2 times per day, for 10 days
   C. 0.3 g 2 times per day, for 10 days
   D. 0.4 g 2 times per day, for 10 days
   E. 0.2 g once daily, for 7 to 10 days
   F. 0.2 g once daily, then 0.1 g once daily, for 7 to 10 days
   G. immediate suspension of chemotherapeutic

Clinical case 7

A pregnant 28-year-old woman (trimester I), complains of dysuria. The urinealysis showed leukocyturia and a pathogenic germ sensitive to the listed below chemotherapeutics were detected in the urine culture.

1. **Choose effective and inoffensive drugs for this case of cystitis:**
   A. penicillin
   B. cephalosporin
   C. lincomycin
   D. fucidin
   E. nitroxoline
   F. itrofurantoin
2. **When the patient was in the 7 - 8 months of pregnancy, cystitis aggravated. Which of the following chemotherapeutics (used prudently) may this recurrence be treated with?**

A. sulphamide
B. tetracycline
C. pipemidic acid
D. nalidixic acid
E. carbenicillin
F. piperacillin

3. Pyelonephritis aggravated during the first week after child birth. Which of these chemotherapeutics may be used (prudently) during breast-feeding?

A. sulphamide
B. chloramphenicol
C. norfloxacin
D. nalidixic acid
E. nitrofurantoin

4. In two years after the child birth, the urine test showed leukocyturia and a pathogenic germ sensitive to nitrofurantoin was identified in the urine culture. The assessment of the renal function showed the decrease of creatinine clearance up to 40 ml/minute.

Choose the doses, dosage regimen and therapy duration of the administered drug:

A. 8 to 10 mg/kg 4 times per day, for 10 days
B. 7.5 mg/kg 2 times per day, for 10 days
C. 5 to 6 mg/kg 4 times per day, for 10 days
D. 5 to 6 mg/kg 2 times per day, for 7 days
E. 7.5 mg/kg 4 times per day, for 10 days
F. this chemotherapeutic is contraindicated

5. Contraindications to nitrofurantoin administration are:

A. pregnancy
B. gastric and duodenal ulcer
C. hepatorenal function disorder
D. severe heart diseases
E. acute porphyria

Clinical case 8

A 67-year-old patient was hospitalised urgently with clinical signs characteristic of acute pyelonephritis on the right. The clinical investi-

gation showed on enlarged right kidney and Giordano's signs. The laboratory investigation revealed: leukocytosis, azotemia, bacteriuria and pyuria. The echography showed a renal calculus and dilatation of the renal collecting system on the right. The radioisotope renography showed a curve of 'obstructive' type on the right. The intravenous urinography confirmed the existence of a calculus enclosed in the pyeloureteral junction (PUJ) stenosis, grade II hydronephrosis and lower lumbar renal ectopy. The urine culture and blood culture showed the presence of a gram-negative germ *Pseudomonas aeruginosa*. Polymixin, gentamicin, cefazolin and penicillin G caused allergic reactions. An attempt of retrograde urethral catheterisation failed. It was decided to carry on antiinfectious treatment without unblocking of the malformed kidney through percutaneous nephrostomy.

1. **Choose the chemotherapeutics suitable for this case of septic syndrome:**
   A. polypeptides
   B. fluorocinolone
   C. aminoglycosides
   D. cephalosporin
   E. penicillin
2. **After the 2nd intake of the chosen chemotherapeutics, the patient's state deteriorated and was characterised by: agitation, fever, repeated frissons, warm and dry teguments of normal colour, tachypnoea, followed by a long-term drop of arterial pressure.**
   What complication developed?
   A. anaphylaxis
   B. pulmonary embolism
   C. toxic and septic shock
   D. myocardial infarction
   E. cerebral ictus
3. **During the hyperdynamic phase of warm shock, the following treatment indicated:**
   A. parenteral antibacterial therapy with broad-spectrum bactericide drugs, then a targeted chemotherapeutic, depending on the results of the urinary antibiogram and/or of the blood culture

B. abolition of hypovolemia by the administration of colloidal solutions (dextran 70), subject to control of the central venous pressure (CVP)
C. cardiotonic therapy with inotrope substances, vasoconstrictors and vasoactive remedies (dopamine, etc.), after adjustment of hypovolemia, subject to repeated CVP control
D. antihypotensive agents with a permissive action (hydrocortisone, prednisolone, dexamethasone, etc.).
E. administration of hepatoprotectors, diuretics and oxygen therapy.

4. In case of the development of the DIC (disseminated intravascular coagulation) syndrome in the phase of hypercoagulation with hypofibrinolysis, the following treatment is administered:
A. direct anticoagulants (heparin)
B. substitution therapy (platelet concentrate, quarantine fresh-frozen plasma)
C. antiaggregants (pentoxifylline, prostacyclin)
D. haemostatics (fibrinogen, etc.)
E. fibrinolytic remedies (fibrinolysin, streptokinase)
F. fibrinolysis inhibitors (aprotinin, aminocaproic acid, ambene)

5. In case of the development of the DIC syndrome in the phase of hypercoagulation with secondary hyperfibrinolysis, the following treatment is administered:
A. direct anticoagulants (heparin)
B. substitution therapy (platelet concentrate, quarantine fresh-frozen plasma)
C. antiaggregants (pentoxifylline, prostacyclin)
D. haemostatics (fibrinogen, etc.)
E. fibrinolytic remedies (fibrinolysin, streptokinase)
F. fibrinolysis inhibitors (aprotinin, aminocaproic acid, ambene)

Clinical case 9

A 59-year-old patient with pulmonary abscess was admitted to the thoracic surgery department for surgical treatment. Since the surgical intervention assumes the risk of complications, the decision was made to administer antibiotics for prophylactic purposes.

1. **In surgical interventions antibiotic prophylaxis is characterized by:**
   A. the spectrum of action shall include the most possible pathogenic agents of postoperative infections
   B. the dose of antibiotic administered for antibiotic prophylaxis shall be doubled in comparison to common therapeutic dose
   C. the optimal time of administration is 30 to 40 minutes before the operation
   D. the administration shall be realized at the beginning of the operation
   E. in case of long-lasting surgical interventions, the repeated administration shall be realized at an interval comprising the half-lives of the drug from the moment of the first administration
   F. the administration of antibiotics for the purpose of prophylaxis of postoperative infection is ineffective and unreasonable, after the operation is ended
   G. intramuscular administration is preferable
   H. intravenous administration is preferable
2. **What is the elective drug for antibiotic prophylaxis in the patient, from the point of view of efficiency and inoffensiveness, taking into account the most probable pathogenic agent?**
   A. cefuroxime
   B. amoxicillin/clavulanate
   C. vancomycin
   D. ampicillin/sulbactam
   E. ciprofloxacin
3. **During the postoperative period, the patient developed pneumonia in the lower right lobe. The laboratory investigation of sputum identified the pathogenic agent Klebsiella peumoniae. What pharmaceutical drugs are elective for the treatment of the patient?**
   A. teicoplanin
   B. clarithromycin
   C. ceftriaxone
   D. ciprofloxacin
   E. cefotaxime
   F. amoxicillin/clavulanate
   G. ampicillin/subactam

4. **What pharmaceutical drugs are alternative in case of contraindications to the elective pharmaceutical drugs?**
   A. cefepim
   B. gentamicin
   C. amikacin
   D. meropenem
   E. aztreonam
   F. azithromycin
5. **What are the most common side effects in case of aztreonam administration ?**
   A. local irritant action in the area of administration
   B. neurotoxic action
   C. temporary increase of transaminases
   D. dyspeptic disorders – nausea, vomit, diarrhoea
   E. increase of prothrombin time
   F. agranulocytosis and leucopoenia

Clinical case 10

A 58-year-old female patient has type I diabetes mellitus associated with atherosclerotic occlusion of the peripheral arteries, developed infected trophic ulcer in the plantar area of the lower right limb. The bacteriological investigation detected aerobic gram-positive cocci (streptococci, staphylococci).

1. **What antibacterial drugs are elective for this patient?**
   A. cephalexin
   B. amoxicillin
   C. clindamycin
   D. lincomycin
   E. gentamicin
   F. doxycillin
2. **Initially, the patient's state ameliorated, however, her state aggravated again in a month. What pharmaceutical drugs are alternative in case of severe septic evolution of the infectious process?**
   A. amoxicillin/clavulanate
   B. ampicillin/sulbactam
   C. carumonam

D. ticarcillin/clavulanate
E. clarithromycin

3. The patient developed papular cutaneous eruptions associated with pruritus, on the background of therapy with penicillins in combination with ß-lactamase inhibitors. What is the tactics of further treatment?

A. an antihistaminic drug (terfenadine) as an adjuvant to antibacterial treatment
B. glucocorticoid (dexamethasone) as an adjuvant to antibacterial treatment
C. antibacterial treatment is suspended, and terfenadine and dexamethasone is administered

4. Select the pharmaceutical drugs that might be prescribed to the patient, taking into account the severity of her state.

A. tigemonam
B. cefepime
C. meropenem
D. vancomycin
E. ristomycin
F. biapenem

5. Select the dosage regimen in case of prescription of meropenem to this patient.

A. 0.5 g every 6 hours, intravenously
B. 1 g every 8 hours, intravenously
C. 1 g every 8 hours, intramuscularly
D. 120 mg/kg once per day
E. 2 g every 8 hours, intramuscularly

Hormonal drugs

I. Simple Clinical Cases

1. Following investigations, a 37-year-old patient was diagnosed with Type 2 diabetes mellitus, 13-14 weeks pregnancy.

What drugs will you recommend?

Justify your choice and determine the dosage regimen.

2. A 55-year-old patient was diagnosed with medium severity toxic goiter.

What preparations will be prescribed?

Determine principles and dosing regimen.

What can be side effects and principles of their prevention?

3. A patient, diagnosed with moderate hypothyroidism, was admitted to the endocrinology department. He also suffered from ischemic heart disease, functional class III stable angina.

What preparations are prescribed?

Determine principles and dose regimen.

What are the criteria for determining the efficacy and safety of treatment?

4. A 29-year-old patient was primary diagnosed with type 1 diabetes mellitus.

What drugs will be prescribed?

Determine the dose regimen.

5. Patient A was diagnosed with primary acute adrenal insufficiency, based on objective information and investigations.

What drugs will be prescribed?

What are the dosage and management of the patient?

What are possible side effects?

6. Two patients were admitted to the intensive care unit. Patient A was diagnosed with anaphylactic shock after dextrans administration, and patient B - worsening of bronchial asthma and developing status asthmaticus.

What hormonal drugs will be prescribed?

What will the dosage and further management be?

7. A patient with type 2 diabetes mellitus was admitted to the endocrinology department. He also has diabetic angiopathy and left second toe gangrene.

What drugs will be prescribed?

What will the dosage be?

What metabolic effects will the administered preparations trigger?

8. A patient with lupus erythematosus was admitted to the rheumatology clinic.

What hormonal drugs will be prescribed?

What will the dosage and further patient management be?

What side effects can occur after a long-term treatment?

9. A patient with type 2 diabetes mellitus was admitted to the endocrinology department, he was administered preparation A for 2 years. He was overweight (III degree obesity) when he began the treatment with the drug two years ago. The dose regimen was – 1 g twice per day. Last week he developed muscle pain, along with dyspeptic disorders. Blood analysis showed megaloblastic anemia and lactate level of 7 mmol/l.

What preparation was prescribed?

What causes these symptoms?

What are the characteristics of antidiabetic effect?

10. Two pregnant women were admitted to obstetrics and gynecology department in serious condition. One of them, suffering from asthma, developed asthmatic status. The examination of the fetus in pregnant B found a risk of development of respiratory distress syndrome. It was decided to use glucocorticoids.

What preparations will be prescribed in these cases?

Justify the choice of those preparations.

II. Multiple clinical cases

Clinical case 1

A 29-year-old patient with type 1 subcompensated diabetes mellitus was admitted to the endocrinology unit for treatment correction and compensation. The doctor decided to use human insulin preparations.

1. **Which of the listed preparations is ultra-fast and ultra-rapid acting human insulin?**
   A. insulin aspart
   B. insulin glargine
   C. insulin lispro
   D. insulin determir
   E. regular human insulin
2. **Which of the human insulin preparations listed below is slow-acting and long-lasting?**
   A. insulin aspart
   B. insulin glargine
   C. insulin lispro
   D. insulin determir
   E. regular human insulin
3. **What are pharmacodynamic characteristics of human ultra-fast and ultra-rapid acting insulins?**
   A. they prevent more effective nocturnal hyperglycaemia
   B. they control more effective postprandial hyperglycemia
   C. they reduce more significantly glycosylated hemoglobin
   D. they have similar affinity to insulin receptors as short acting insulin
   E. they increase the patient's compliance
4. **What are pharmacokinetic characteristics of human ultra-fast and ultra-rapid acting insulins?**
   A. they form hexamers at the injection site
   B. they mimic endogenous insulin properties
   C. they dissociate to insulin monomers
   D. they ensure a higher maximum concentration and faster elimination
   E. they ensure a gradual concentration with a slower elimination

5. **What are the indications for human ultra-fast and ultra-rapid acting insulins?**
   A. type 1 and 2 diabetes mellitus with insufficiently controlled post-prandial hyperglycaemia
   B. diabetes mellitus associated with obesity
   C. type 1 diabetes mellitus with acute insulin resistance
   D. type 1 and 2 diabetes mellitus in children
   E. type 2 diabetes mellitus in case of surgery, severe trauma

Clinical case 2

Developing strategies for providing patients with type 2 diabetes with antidiabetic drugs by the National Pharmacotherapeutical Formulary Committee, the list of oral antidiabetic drugs which should be submitted for purchase was discussed. In this context, decisions were made based on the principles of treatment and rational choice and use of the preparations.

1. **Which groups of oral antidiabetic agents act by influencing the release of endogenous insulin?**
   A. biguanides
   B. sulfonylureas
   C. tetrasaccharides
   D. meglitinides
   E. incretins
   F. thiazolidinediones
2. **Which groups of oral antidiabetic work by increasing glucose utilization?**
   A. sulfonylureas
   B. tetrasaccharides
   C. biguanides
   D. amylin derivatives
   E. incretins
   F. meglitinides
3. **Which group of oral antidiabetic acts by increasing the sensitivity of target cells to insulin?**
   A. biguanides
   B. sulfonylureas
   C. tetrasaccharides

D. meglitinides
E. incretins
F. thiazolidinediones

4. Which group of oral antidiabetic agents acts by reducing absorption of glucose from the gut?

A. biguanides
B. tetrasaccharides
C. sulfonylureas
D. meglitinides
E. incretins
F. thiazolidinediones

5. Which group of oral antidiabetic agents acts by disrupting metabolism of glucose to sorbitol?

A. alpha-glucosidase inhibitors
B. dipeptidyl peptidase-4 inhibitors
C. aldose reductase inhibitors
D. amylin analogs
E. thiazolidinediones
F. biguanides

Clinical case 3

Doctors recommended to include the following glucocorticoids: dexamethasone, hydrocortisone, prednisolone in the Institutional Pharmacotherapeutical Formulary. The inclusion of these drugs was reasoned by answering the following questions:

1. Which of the following options of action potency (from the lowest to highest) is correct?

A. hydrocortisone → dexamethasone → prednisolone
B. prednisolone → hydrocortisone → dexamethasone
C. dexamethasone → hydrocortisone → prednisolone
D. hydrocortisone → prednisolone → dexamethasone
E. dexamethasone → prednisolone → hydrocortisone

2. Which variant of the duration of action (from short to long) is correct?

A. hydrocortisone → dexamethasone → prednisolone
B. prednisolone → hydrocortisone → dexamethasone

C. dexamethasone → hydrocortisone → prednisolone
D. hydrocortisone → prednisolone → dexamethasone
E. dexamethasone → prednisolone → hydrocortisone

3. Which option of the expression of mineralocorticoid effect in decreasing order is correct?

A. hydrocortisone → dexamethasone → prednisolone
B. prednisolone → hydrocortisone → dexamethasone
C. dexamethasone → hydrocortisone → prednisolone
D. hydrocortisone → prednisolone → dexamethasone
E. dexamethasone → prednisolone → hydrocortisone

4. What option of the degree of inhibition of the hypothalamic-pituitary-adrenal axis in decreasing order is correct?

A. hydrocortisone → dexamethasone → prednisolone
B. prednisolone → hydrocortisone → dexamethasone
C. dexamethasone → hydrocortisone → prednisolone
D. hydrocortisone → prednisolone → dexamethasone
E. dexamethasone → prednisolone → hydrocortisone

5. Which of the following arguments to recommend prednisolone therapy as the reference drug in guides is true?

A. it has the most marked anti-inflammatory effect
B. it has a lower mineralocorticoid effect than hydrocortisone
C. it has a lower mineralocorticoid effect than dexamethasone
D. it has a lower degree of developing adrenal insufficiency than dexamethasone
E. it has a greater duration of action than dexamethasone
F. it has a plasmatic half-life less than dexamethasone

Clinical case 4

Glucocorticoids are drugs widely used by doctors of different specialities due to various pharmacological effects, beneficial in states of emergency and systematic treatment of diseases and pathological conditions. In these cases rational use of glucocorticoids is determined by certain pharmacological features.

1. In medical practice glucocorticoids are administered for the purpose of:

A. suppression
B. substitution treatment
C. ethiologic treatment
D. pharmacodynamic treatment
E. diagnosis

2. Very high doses of corticosteroids (5-30 mg/kg prednisolone) are administered for a short time (24-48 hours) in the following pathological conditions:

A. a myocardial infarction with hypertension
B. status asthmaticus
C. anaphylactic shock
D. gout attack
E. hemolytic anemia

3. Which of the following is the preferred glucocorticoid for pulse therapy?

A. fluticasone
B. hydrocortisone
C. prednisolone
D. dexamethasone
E. methylprednisolone
F. triamcinolone

4. What effects of glucocorticoids are responsible for pharmacodynamic activity?

A. antiinflammatory
B. hypoglycemic
C. anti-shock
D. antihypertensive
E. anti-allergic
F. immunostimulatory

5. What dosage regimens can be used for a long-term treatment of rheumatoid arthritis?

A. alternate-day
B. intensive
C. limited
D. intermittent
E. classical

Clinical case 5

The Institutional Pharmacotherapeutical Formulary Committee establishes the criteria for procurement of insulin preparations of animal and human origin for the next year, based on the specific indications for treatment of patients with type 1 and 2 diabetes. An approximate need of insulin products was estimated, according to dosing principles.

1. **What are the absolute indications for insulin preparations?**
   A. type 2 diabetes mellitus with cachexia
   B. type 2 diabetes in pregnant women
   C. type 1 diabetes mellitus
   D. type 2 diabetes with complications
   E. diabetic pre-coma and coma
   F. type 2 diabetes in case of surgery, trauma, infections
2. **What are the relative indications for insulin preparations?**
   A. type 2 diabetes mellitus with cachexia
   B. type 2 diabetes in pregnant women
   C. type 1 diabetes mellitus
   D. type 2 diabetes with complications
   E. diabetic pre-coma and coma
   F. type 2 diabetes in case of surgery, trauma, infections
3. **What are the indications for human insulin preparations?**
   A. primary discovered diabetes mellitus
   B. gestational diabetes
   C. type 2 diabetes with obesity
   D. labile diabetes mellitus
   E. diabetes in the elderly
4. **What are the dosage criteria for an adult patient treatment with an insulin?**
   A. 0.7-0.8 IU/kg
   B. 0.2-0.6 IU/kg
   C. 0.7-1 IU/kg
   D. 0.1 IU/kg
   E. 1 IU/kg
5. **What are the dosage criteria for insulin treatment in diabetic coma?**
   A. 0.7-0.8 IU/kg
   B. 0.2-0.6 IU/kg

C. 0.7-1 IU/kg
D. 0.1 IU/kg
E. 1 IU/kg

Clinical Case 6

A patient with hypothyroidism was prescribed levothyroxine. To ensure the effectiveness and safety of the treatment, the doctor explained the need to follow some strict recommendations, based on the pharmacokinetic features of levothyroxine.

1. **Which of the following statements is characteristic of levothyroxine absorption?**
   A. food increases the bioavailability
   B. absorption is different (from 35 to 80%)
   C. it is better absorbed after administration on an empty stomach
   D. absorption is increased in myxedema
   E. abosrbtion is lower in the begining of treatment
2. **Which of the following statements is characteristic of levothyroxine distribution?**
   A. it has a low affinity to serum albumin
   B. it has a high affinity for serum albumin
   C. it is bound intensively with a high affinity globulin
   D. it is coupled with transferrin
   E. it is bound intensively with serum albumins
3. **What is the half-life of levothyroxine in hypothyroidism?**
   A. 6-8 hours
   B. 7 days
   C. 3 days
   D. 14 days
   E. 12 to 24 hours
4. **Which of the following statements is characteristic of levothyroxine metabolism?**
   A. it is subjected to oxidative deamination
   B. it is subjected to conjugation
   C. it is subject to iodination with the formation of mono- and diiodtirozine
   D. it is eliminated by bile
   E. conjugates are hydrolyzed and involved in the enterohepatic cycle

5. **Levothyroxine deiodination, involving deiodinases, is characterized by the following features:**
   A. type 1 deiodinase from the liver, kidney, thyroid gland is increased in hypothyroidism and is decreased in hyperthyroidism
   B. type 1 deiodinase from the brain, myocardium is increased in hypothyroidism
   C. type 2 deiodinase from the brain, myocardium is increased in hypothyroidism
   D. type 2 deiodinase from the brain, myocardium is decreased in hypothyroidism
   E. type 2 deiodinase is the main enzyme that forms T3

Clinical case 7

A patient with moderate hyperthyroidism was admitted to the endocrinology clinic. Tiamazol was prescribed and to monitor the effectiveness it is necessary to take into account a number of its pharmacological features.

1. **What is the main mechanism that provides the therapeutic effect of tiamazol?**
   A. it inhibits deiodinase
   B. it increases coupling of thyroxine with serum albumin
   C. it inhibits thyroxine synthesis
   D. it inhibits thyroxine metabolism
   E. it inhibits the storage of thyroxine
2. **A stable clinical effect of tiamazol occurs in?**
   A. 24 hours
   B. 3-5 days
   C. 6-8 weeks
   D. 1-2 weeks
   E. 6-12 hours
3. **The therapeutic effect of tiamazol is influenced by:**
   A. thyroxine coupling with serum albumins
   B. the half-life of thyroxine
   C. liver enzyme activities
   D. renal function
   E. degree of thiroid gland distruction

4. **The initial effect of tiamazol is:**
   A. slower because thyroxine acts slower
   B. faster because thyroxine has a lower half-life
   C. faster because thyroxine has a greater half-life
   D. slower because thyroxine has a greater half-life
   E. very fast because thyroxine is not synthesize
5. **Thyroxine level is decreased by half over:**
   A. 12 hours
   B. 24 hours
   C. 3 days
   D. 14 days
   E. 7 days

Clinical case 8

A patient with hypothyroidism started the treatment with levothyroxine. To assess the efficacy of treatment it is necessary to monitor the evolution of some clinical symptoms.

1. **What are the effects of levothyroxine on the cardiovascular system?**
   A. chronotropic negative effect
   B. positive inotropic effect
   C. negative inotropic effect
   D. positive chronotropic effect
   E. positive bathmotropic effect
2. **What are the effects of levothyroxine on the central nervous system?**
   A. it diminishes apathy
   B. it reduces excitability
   C. excitability to insomnia
   D. slow speech
   E. drowsiness
3. **What are the effects of levothyroxine on the digestive tract?**
   A. constipation
   B. it restores intestinal transit
   C. it restores gastric acidity
   D. it reduces metabolic processes in the liver
   E. it intensifies metabolic processes in the liver

4. **What are the effects of levothyroxine on lipid metabolism?**
   A. it reduces hypercholesterolemia
   B. it does not reduce hypercholesterolemia
   C. it reduces the level of low density lipoproteins
   D. it increases the level of low density lipoproteins
   E. it diminishes the sensitivity of adipose tissue with lipolysis inhibition
5. **What are the effects of levothyroxine on carbohydrate and protein metabolism?**
   A. it causes hypoglycemia
   B. it increases blood glucose level
   C. it enhances protein synthesis
   D. it increases protein utilization
   E. it enhances gluconeogenesis

Clinical case 9

Currently biguanides are the most common group of oral agents used to treat diabetes. Its priority is determined by a number of pharmacological features.

1. **What are the main indications for biguanides?**
   A. primary diagnosed type 1 diabetes
   B. diabetes with obesity
   C. diabetes in adolescents and children
   D. metabolic syndrome
   E. diabetes with cachexia
2. **What metabolic effects make biguanides useful in these indications?**
   A. they inhibit lipolysis in adipose tissue and muscles
   B. they cause hypercholesterolemia
   C. they decrease triglyceride levels with reducing the very low density lipoproteins
   D. they increase the level of high-density lipoproteins
   E. they reduce the level of high-density lipoproteins
3. **What other effects make the biguanides use advantageous in these indications?**
   A. antiplatelet effect
   B. hemostatic effect

C. cardioprotector effect
D. fibrinolytic effect
E. antifibrinolytic effect

4. What pathogenetic links are influenced beneficialy by biguanides in diabetes?

A. they reduce hypoinsulinemia
B. they impair glucose tolerance
C. they reduce hyperinsulinemia
D. they stimulate endocrine function of the pancreas
E. they reduce insulin resistance

5. What are the particularities of the biguanides hypoglycemic effect?

A. it decreases hyperglycemia with subsequent hypoglycemia
B. it reduces hyperinsulinemia
C. it increases body weight
D. it normalizes increased glucose level
E. it increases insulin secretion

Clinical case 10

During a long-term treatment with systemic corticosteroids, first it is necessary to examine thoroughly patients and to monitor clinical symptoms and laboratory parameters for timely detection and prevention of characteristic adverse reactions.

1. Why is it necessary to monitor blood pressure?

A. corticosteroids exhibit mineralocorticoid action
B. corticosteroids manifest hypertensive permissive action
C. corticosteroids exhibit hypotensive action
D. corticosteroids increase vascular permeability
E. corticosteroids inhibit vasomotor center

2. Why is it necessary to monitor blood glucose levels?

A. corticosteroids cause hypoglycemia through increased glycolysis
B. corticosteroids cause hyperglycemia through antagonizing insulin effect
C. corticosteroids reduce glucose use by peripheral tissues
D. corticosteroids increase the utilization of glucose by peripheral tissues
E. corticosteroids stimulate gluconeogenesis in the liver

3. **Why is it necessary to monitor electrolyte level?**
   A. corticosteroids exhibit mineralocorticoid action
   B. corticosteroids enhance bone mineralization
   C. corticosteroids produce hipocalcemia by reducing the absorption and accelerated elimination of calcium
   D. corticosteroids enhance potassium elimination
   E. corticosteroids enhance sodium elimination
4. **Why is it necessary to monitor the levels of fatty acids and cholesterol?**
   A. corticosteroids produce hypocholesterolemia
   B. corticosteroids increase the level of fatty acids in the plasma
   C. corticosteroids decrease the plasma fatty acids
   D. corticosteroids amplify the lipolytic action of catecholamines, thyroid hormones
   E. corticosteroids cause redistribution of body fat on limbs
5. **Why is it necessary to monitor coagulation tests and general blood analysis?**
   A. corticosteroids increase red blood cells number and hemoglobin
   B. corticosteroids decrease red blood cells number and hemoglobin
   C. corticosteroids produce blood hypercoagulation state
   D. corticosteroids reduce the number of monocytes, basophils
   E. corticosteroids increase number of lymphocytes, monocytes, basophils

Drug interactions

Simple Clinical Cases:

1. A 60-year-old patient with 3-rd degree HTN receives combined antihypertensive pharmaceutical treatment.

What is the goal of the adjuvant treatment?

What drug interactions does this goal ensure?

What rational combinations can you recommend to this patient?

2. A patient with rheumatoid arthitis was administered a nonsteroidal anti-inflammatory drug, which couples to plasma proteins by more than 90%. At the same time, this patient also takes a medicine with low therapeutic index and coupling to plasma proteins higher than 90%.

What types of drug interactions may develop in this case?

What are the consequences of such an interaction?

What preventive measures may be undertaken in order to avoid the consequences of such an interaction?

3. The physician prescribed cimetidine to a patient with duodenal ulcer, in order to reduce gastric secretion, and amoxicillin and metronidazole in standard doses for antihelicobacterial treatment. On the 10^{th} day, pharmacokinetic tests stated the increase in metronidazole concentration with amoxicillin concentration being within the normal limits. The level of plasma proteins is within normal limits. Metronidazole and amoxicillin couple insignificantly to plasma proteins.

What are the possible reasons for the increase of metronidazole concentration in plasma?

What is the physician's tactics in this case?

4. Pharmaceutical drugs A and B belong to the same pharmacological group. Drug A couples to plasma proteins by 98% and pharmaceutical drug B couples to plasma proteins by 20 - 40%. When monitoring a patient with congestive heart failure, who was treated with cardiac

glycosides and prescribed pharmaceutical drugs A and B, the initial symptoms of intoxication were identified.

What is the reason of the appearance of intoxication symptoms?

Which of these pharmaceutical drugs will have a faster, more intense and shorter effect?

What phenomena will occur if both of these drugs are combined with another pharmaceutical drug that couples to plasma proteins by up to 95%?

5. A general practitioner prescribed ampicillin to a 65-year-old patient, in order to treat chronic bronchitis. At the same time, a sample of sputum was taken from him, in order to identify a pathogenic agent and antibiotic sensitivity. The results of bacteriological investigation showed that the pathogenic agent was sensitive to the administered pharmaceutical drug. Meanwhile, the patient's state did not improve on the 3rd day of treatment: fever and intoxication symptoms persisted. After a more rigorous history taking, the physician stated that the patient was taking phenobarbital to improve sleeping.

What is the reason of inefficiency of antibacterial treatment?

What will the tactics of further treatment of this patient be?

Give the reason for your suggestions.

6. After acute appendicitis operation, the physician prescribed galantamine to a patient during the postoperative period, in order to restore the peristalsis. The patient was also administered amitriptyline, propranolol, baralgin and furosemide.

Which of the pharmaceutical drugs used by the patient will have the interactions of pharmacodynamical type, when taking galantamine?

Explain this drug interaction.

7. A patient with peptic ulcer disease was administered the following combinations of drugs:

A. Cimetidine + pirenzepine

B. Colloidal bismuth subcitrate + solcoseryl

C. Cimetidine + solcoseryl

D. Pirenzepine + antacid

E. Colloidal bismuth subcitrate + antacid

Which of these combinations will be more effective from the point of view of pharmacodynamical interactions? Justify the answer.

What is your treatment tactics in this case?

8. A patient with pneumonia was prescribed an antibiotic of the penicillin group at a dose of 1 pill thrice a day on an outpatient basis. The patient suffers from gout and was continuously administered probenecid.

What types of drug interaction may occur as a result of such combination?

What will the consequences of probenecid-antibiotic interaction be?

What is your tactics in such a case?

9. A patient with acute peritonitis was administered heparin treatment in standard doses, in order to avoid postoperative thromboembolic complications. The patient takes simultaneously diclofenac, ciprofloxacin and ceftriaxone. Nasal haemorrhage, haemoptysis and macrohaematuria developed in the patient on the 2nd day of treatment. The laboratory investigation stated the increase of coagulation time.

What is the ground for such a complication?

What types of drug interactions may occur in this case?

What will your tactics be?

10. A female patient suffering from II degree rheumatism in active phase, activity, was taking chloroquine, metamizole and indomethacin per os, and benzylpenicillin intramuscularly. After 2 weeks of treatment, intermittent pains in the epigastrium developed.

What pharmacotherapeutic complication occurred?

What additional investigations will you order to confirm the diagnosis?

What pharmaceutical drug or drugs stand by this complication?

What will be your tactics?

II. Multiple clinical cases

Clinical case 1

A patient suffering from rheumatoid arthitis (RA) was prescribed nonsteroidal anti-inflammatory drugs and penicillin. It is known that these drugs are secreted at the level of renal tubes but nonsteroidal anti-inflammatory drugs have a greater affinity to transport systems.

1. **How will such features of the pharmaceutical drugs impact on the kinetics thereof?**
   A. the clearance of both pharmaceutical drugs will increase
   B. the clearance of penicillin will increase
   C. the clearance of NSAID will decrease
   D. the clearance of penicillin will decrease
   E. they will have no influence on the clearance of any of these pharmaceutical drugs
2. **How will the concentration of the pharmaceutical drugs in plasma be modified?**
   A. the concentration of penicillin in plasma will increase
   B. the concentration of nonsteroidal anti-inflammatory drugs in plasma will decrease
   C. the concentration in plasma of both pharmaceutical drugs will increase
   D. the concentration of both pharmaceutical drugs in plasma will decrease
   E. the concentration of nonsteroidal anti-inflammatory drugs in plasma will increase.
3. **How will the half-life ($T_{1/2}$) of the pharmaceutical drugs be modified?**
   A. the half-life of penicillin will increase
   B. the half-life of both pharmaceutical drugs will increase
   C. the half-life of NSAID will decrease
   D. the half-life of penicillin will decrease
   E. the half-life of none of the pharmaceutical drugs will be modified
4. **How will the therapeutic benefit of the pharmaceutical drugs be modified?**
   A. the therapeutic benefit of NSAID will increase
   B. the therapeutic benefit of NSAID will decrease
   C. the therapeutic benefit of NSAID will not be modified
   D. the therapeutic benefit of penicillin will increase
   E. the therapeutic benefit of penicillin will decrease
5. **How will the safety profile of the administered pharmaceutical drugs be modified?**
   A. the incidence of RA will increase for NSAID

B. the incidence of RA will decrease for NSAID
C. the NSAID safety profile will not be modified
D. the incidence of RA will increase for penicillin
E. the incidence of RA will decrease for penicillin

Clinical case 2

After examining a patient, the physician prescribed the treatment with a pharmaceutical drug belonging to antibacterial sulphonamides, and penicillin. **What adverse effects may occur during the treatment with such pharmaceutical drugs?**

1. Adverse effects of anaphylactic type:
A. anaphylaxis
B. Quincke's oedema
C. bronchial asthma
D. allergic rhinitis
E. urticaria

2. Immune complexes mediated allergy:
A. serum sickness
B. Stevens – Johnson syndrome
C. Lyell's syndrome
D. urticaria
E. vasculitis

3. Allergy of cytotoxic type:
A. immune and autoimmune haemolytic anaemia
B. anaphylaxis
C. contact dermatitis
D. immune agranulocytosis
E. lupus erythematosus

4. Allergy of toxic type (organ affection):
A. ulcerogenic
B. nephrotoxic
C. ototoxic
D. neonatal icterus
E. neurotoxic

5. Adverse effects caused by the pharmacotherapeutic effect:
A. haemolytic anaemia
B. superinfection

C. dysbiosis
D. crystalluria
E. contact dermatitis

Clinical case 3

A man with the signs of intoxication caused by a toxic belonging to the heavy metal group, was admitted to the Reception Department.

What pharmaceutical drugs will you choose to:

1. Avoid absorption:
A. apomorphine
B. tannin
C. dimercaprol
D. atropine
E. naloxone

2. Neutralise the absorbed toxic:
A. activated carbon
B. apomorphine
C. dimercaprol
D. atropine
E. succimer

3. Accelerate release:
A. respiratory analeptics
B. atropine
C. phenylephrine
D. furosemide
E. furosemide + electronic solutions

4. What pharmaceutical drugs will form chelates with metal ions (cuprum, plumb, mercury, zinc, aurum)?
A. activated carbon
B. apomorphine
C. dimercaprol
D. penicillamine
E. naloxone

5. What antidotes will you recommend in case of acute intoxication with iron compounds?
A. activated carbon
B. methylene blue

C. deferoxamine methansulfonate
D. penicillamine
E. naloxone

Clinical case 4

What are the possible consequences of a long-term administration of acetylsalicylic acid and phenobarbital?

1. At the level of absorption:
A. the absorption thereof will increase
B. the absorption of acetylsalicylic acid will decrease
C. the absorption of acetylsalicylic acid will increase
D. the absorption thereof will not be modified
E. the absorption of phenobarbital will decrease

2. At the level of distribution:
A. the concentration of acetylsalicylic acid in plasma will increase
B. the concentration of acetylsalicylic acid in plasma will decrease
C. the concentration of phenobarbital in plasma will decrease
D. the concentration of phenobarbital in plasma will increase
E. the concentration of these drugs in plasma will not be modified

3. At the level of metabolism:
A. the metabolism of phenobarbital will increase
B. the metabolism of acetylsalicylic acid will increase
C. the metabolism of acetylsalicylic acid will decrease
D. the metabolism of phenobarbital will decrease
E. the metabolism of both pharmaceutical drugs will not be modified

4. Therapeutic benefit:
A. it will decrease in case of phenobarbital
B. it will decrease in case of acetylsalicylic acid
C. it will increase in case of acetylsalicylic acid
D. it will increase in case of phenobarbital
E. the therapeutic benefit of both pharmaceutical drugs will not be modified

5. Adverse effects:
A. they will reduce in case of phenobarbital
B. they will reduce in case of acetylsalicylic acid
C. the incidence thereof will increase in case of acetylsalicylic acid

D. the incidence and severity thereof will increase in case of phenobarbital
E. the safety profile of both pharmaceutical drugs will not be modified

Clinical case 5

A physician prescribed 5 mg of warfarin per day to a 52-year-old female patient with deep vein thrombosis, for the purpose of prophylaxis of thromboembolic complications. In 2 weeks after the warfarin therapy started, a bacterial infection of the respiratory tract developed in the patient and the antibacterial therapy with erythromycin started. In 3 days, the patient noticed the appearance of cutaneous eruptions in the form of petechiae, nasal haemorrhage, haemoptysis and macrohaematuria. The INR was 8 (International Normalised Ratio, norm – 2 to 3), but at the beginning of warfarin therapy, the INR was 1.2. The concentration of warfarin in plasma was 12.2 ng/ml (the therapeutic range from 2 to 6 ng/ml).

1. How do you diagnose such manifestations?
A. adverse reaction to warfarin
B. adverse reaction to erythromycin
C. pharmacotherapeutic complication due to drug interaction
D. overdose of warfarin
E. overdose of erythromycin

2. Why did the concentration of warfarin in plasma increase in this patient?
A. erythromycin activated (induced) liver enzymes
B. erythromycin supressed (inhibited) liver enzymes
C. warfarin activated (induced) liver enzymes
D. warfarin supressed (inhibited) liver enzymes
E. the genotypic assay showed the presence of a mutant allele codifying CYP2C9

3. What type of drug interaction occurred in this case?
A. pharmaceutical interaction
B. pharmacodynamical interaction
C. pharmacokinetic interaction
D. pharmaceutical incompatibility
E. pharmacological incompatibility

4. **Choose the side effects of warfarin**
   A. haemorrhages
   B. necrosis of soft tissues
   C. teratogenicity
   D. rethrombosis
   E. all above mentioned
5. **Physician's tactics in this case:**
   A. suspension of warfarin
   B. correction of warfarin dose
   C. suspension of erythromycin
   D. suspension of both pharmaceutical drugs and antibiotic substitution
   E. local anti-haemorrhagic treatment

Clinical case 6

A female patient was hospitalized with the diagnosis of acute myocardial infarction accompanied by arterial hypotension and breathing disorder.

1. **What adjuvant treatment is recommended in this case?**
   A. neuroleptanalgesia
   B. ataralgesia
   C. antidepranalgesia
   D. pharmacokinetic combination
   E. all above mentioned
2. **What is the purpose for prescription of such a combination?**
   A. elimination of dismay
   B. combating the pain
   C. reduction of arterial pressure
   D. antiplatelet effect
   E. potentiation of desired effects
3. **Which of the following interactions is based on this combination?**
   A. pharmaceutical interaction
   B. pharmacokinetic interaction
   C. pharmacodynamical interaction
   D. pharmacological incompatibility

4. **How will this combination impact on the therapeutic benefit?**
   A. the benefit of analgesic will decrease
   B. the analgesic action will be potentiated
   C. it will remain unchanged
   D. the neuroleptic effect will increase
   E. the neuroleptic effect will decrease
5. **How will the safety profile be influenced in this case?**
   A. it will decrease in case of analgesic
   B. it will decrease in case of neuroleptic
   C. the incidence thereof will increase for both pharmaceutical drugs
   D. the incidence and severity thereof will decrease for both pharmaceutical drugs
   E. the safety profile of both pharmaceutical drugs will not be significantly modified

Clinical case 7

A 40-year-old patient with tuberculosis, who was taking the elective (first-line) antituberculosis therapy, was diagnosed with type II diabetes mellitus and started tolbutamide therapy.

1. **Drug interactions (DI) that may occur in this case are:**
   A. DI through enzymatic induction
   B. DI through enzymatic suspension
   C. IM at the level of distribution
   D. pharmacodynamical DI potentiating antituberculosis actions
   E. pharmacodynamical DI antagonising anticonvulsive action
2. **The most comman prescribed combined antituberculosis pharmaceutical drugs are:**
   A. rifampicin + isoniazid
   B. rifampicin + isoniazid + pyridoxine
   C. rifampicin + isoniazid + pyrazinamide + ethambutol + pyridoxine
   D. rifampicin + isoniazid + ethambutol
   E. All abovementioned
3. **What are the consequences of combination of the antituberculosis pharmaceutical drug rifampicin with tolbutamide?**
   A. increase of antituberculosis therapy efficiency

B. decrease of antituberculosis therapy efficiency
C. induction of liver enzymes by tolbutamide
D. Increase of microbial resistance to antituberculosis therapy
E. decrease of microbial tuberculosis resistance

4. What are the most common adverse effects produced by antituberculosis pharmaceutical drugs?

A. hepatotoxicity
B. nephrotoxicity
C. GIT disorders
D. allergic reactions
E. neurological

5. What adverse effects of isoniazid does pyridoxine combat?

A. hepatotoxicity
B. red colouration of urine, tears and sweat
C. endocrine disorders
D. allergic reaction
E. neurological

Clinical case 8

A 24-year-old female patient with epilepsy takes carbamazepine as antiepileptic therapy. She has been taking oral contraceptive pills for the last 3 years. She had bilateral pneumonia not long ago and was prescribed antimicrobial therapy with erythromycin.

In several days, the patient developed the signs of carbamazepine overdose (tachycardia, arterial hypertension, ataxia, tremor and hypoventilation).

1. What are the possible reasons of the development of carbamazepine overdose signs?

A. development of hepatic failure
B. drug interaction of pharmacodynamical type
C. hypertensive effect of oral contraceptive pills
D. erythromycin inhibited hepatic metabolism of carbamazepine
E. carbamazepine reduced the concentration of oral contraceptive pills in plasma

2. What is necessary to undertake in this case?

A. to suspend administration of carbamazepine
B. to suspend administration of erythromycin

C. to suspend oral contraceptive pills
D. to substitute carbamazepine with valproate
E. to reduce the dose of carbamazepine

The patient consulted a physician-gynaecologist in 2 months, complaining of supressed menstruation. She was diagnosed with 4 weeks gestation

3. What is the reason of oral contraceptive pills failure?

A. increase in the concentration of carbamazepine in plasma
B. induction of liver enzymes by carbamazepine
C. reduction of efficiency of oral contraceptive pills by carbamazepine
D. reduction in the concentration of carbamazepine in plasma
E. increase of the concentration of oral contraceptive pills in plasma

4. In what pharmaceutical drugs will carbamazepine reduce the concentration thereof in plasma and, respectively, diminish their efficiency?

A. glucocorticoids
B. indirect anticoagulants
C. MAOIs
D. furazolidone
E. methylxanthines

5. Choose the tactics in this case

A. increase of carbamazepine dose
B. reduction of carbamazepine dose
C. termination of pregnancy
D. suspension of carbamazepine and prescription of other antiepileptic drugs
E. the administered therapy is the adequate one
F. your variant

Clinical case 9

A 22-year-old female patient suffering from recidivating bronchial asthma for 3 years, was diagnosed with epilepsy and prescribed antiepileptic treatment with carbamazepine. Until antiepileptic therapy started, antiasthmatic therapy was adequate, since aminophylline dose per os was calculated according to the blood level of aminophylline.

1. **The following clinical symptoms developed after a month of treatment:**
   A. tachycardia, palpitations, vomit – signs of intoxication with theophylline
   B. dyspnoea, dry cough without fervescence, asthma attacks
   C. signs of dyspepsia, cutaneous allergic reactions, leukopenia
   D. somnolence, apathy, adynamia, bradycardia, constipations
   E. your variant
2. **What is the reason of occurrence of such manifestations?**
   A. aggravation of bronchial asthma
   B. adverse effects of aminophylline
   C. adverse effects of carbamazepine
   D. relevant clinical drug interaction
   E. all abovementioned
3. **What type of drug interactions (DI) could such phenomena develop?**
   A. DI at the level of excretion
   B. DI through enzymatic induction
   C. DI through enzymatic inhibition
   D. DI at the level of distribution
   E. DI at the level of the absorption process
4. **Choose pharmacodynamical DIs:**
   A. antagonism
   B. synergism
   C. potentiation of therapeutic benefit
   D. diminution of adverse effects
   E. all above mentioned
5. **In this case the correct treatment is:**
   A. increase of aminophylline dose by 25%, subject to monitoring the blood level of theophylline
   B. reduction of aminophylline dose by 25%, subject to monitoring the blood level of theophylline
   C. suspension of carbamazepine and prescription of other antiepileptic drugs
   D. the administered therapy is the adequate one
   E. your variant

Clinical case 10

A 61-year-old patient was hospitalised with the diagnosis of pulmonary tuberculosis, and the therapy with isoniazid, rifampicin and pyrazinamide was started. The patient had been taking warfarin because of mechanical prosthetic valves and had been subject to therapeutic INR monitoring for 4 years. After 3 weeks of antituberculosis therapy and the therapy with warfarin, the INR index was within normal limits and warfarin dose was increased. In 3 weeks after rifampicin was discontinued, this patient was hospitalized again, complaining of severe cephalgia, somnolence and eye pupils of different dimensions. The INR value was 7.0. He was refered to a neurosurgeon to be consulted.

1. Why did this complication occur?

A. suspension of rifampicin
B. adverse reaction to warfarin
C. warfarin dose was not modified after rifampicin was suspended
D. induction of liver enzymes by rifampicin
E. inhibition of liver enzymes by rifampicin

2. Such clinical manifestations are specific for:

A. subarachnoid haemorrhage
B. neurological disorders
C. cardiac failure
D. arterial hypotension
E. systemic haemorrhages

3. What measures should be undertaken, in order to avoid this complication?

A. continuation of therapy with rifampicin
B. suspension of warfarin administration
C. increase of warfarin dose
D. reduction of the warfarin dose, after rifampicin is suspended
E. physician's tactics was right

4. What type of drug interaction developed in this patient?

A. pharmacokinetic interaction at the level of absorption
B. pharmacokinetic interaction at the level of distribution
C. pharmacokinetic interaction at the level of hepatic metabolism
D. pharmacodynamical interaction
E. drug indifference

5. Side effects of warfarin are:

A. intracranial haemorrhages
B. systemic haemorrhages
C. arterial hypotension
D. cutaneous eruptions
E. all above mentioned