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Department of Pathophysiology

CASE STUDIES

ON THE COURSE OF PATHOPHYSIOLOGY

(for self-training)

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Case Studies on the Course of Pathophysiology (for self-training).
Edited by: Professor G.V. Poryadin, Professor J.M. Salmasi 2011.

This book contains descriptions of cases which in a convenient form allow to study and analyze the most important sections of pathophysiology using typical clinico-laboratory situations. The book may be used in classes in pathophysiology as well as for independent work of students and is aimed at standartization of approaches to teaching students according to the educational standards of Higher Medical School. The tasks are composed in accordance with the requirements of the provisional Program on Pathophysiology approved by the Ministry of Education of the Russian Federation (2003).

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Contents

PREFACE

The main aim of pathophysiology is studying general laws and mechanisms of development of human diseases and forming profound knowledge of the etiology, pathogenesis, basic clinical features and principles of therapy of most common diseases.

The introduction of a continuous multi-stage system of students' training into the teaching practice of Russian medical educational institutions in order to improve and extend fundamental knowledge of future specialists requires carrying out pathophysiological analysis of real clinical situations. Analysis of typical clinical cases allows students to demonstrate and integrate their knowledge of the main concepts of pathophysiology necessary for their further medical training and practice.

The cases are grouped according to the main themes of the course based on the Program approved by the Ministry of Health and Social Development of the RF. However, many cases can be subjected to a broader pathophysiological analysis including different sections of the course.

The selection of cases (clinico-pathophysiological situations) along with the special booklets on a number of the most difficult sections of this discipline prepared by the teachers of many departments of pathophysiology will enable students to work independently, improving their basic knowledge and providing self-control of the effectiveness of their training.

List of Abbreviations.

A/G coefficient – albumin/ globulin coefficient
ABB – acid-base balance
ACE - angiotensin converting enzyme
ACTH - adrenocorticotropic hormone
AG - anion gap
AlAT – alanine-aminotransferase
AP – alkaline phosphatase
APR – acute phase response
APTT - activated partial thromboplastin time
AsAT – aspartate-aminotransferase
BB - buffer base
BE – base excess
BP – blood pressure
BR - breathing rate
BUN – blood urea nitrogen
BV - circulating blood volume
cAMP – cyclic adenosinemonophospate
CI - cardiac index; color index
CO - cardiac output
DIC-syndrome - disseminated intravascular coagulation syndrome
DLCO - diffusing lung capacity
DSV - dead space volume

EDV - end-diastolic volume
EF - ejection fraction
ESR - erythrocyte sedimentation rate
ESV - end-systolic volume
FEV_{1sec} - forced expiratory volume
FFA - free fatty acids
FVC - forced vital capacity
G-CSF – granulocyte colony-stimulating factor
GGT - gamma-glutamiltranspeptidase
GM-CSF – granulocyte macrophage colony-stimulating factor
Hb – hemoglobin
HDL – high density lipoproteids
HMG –CoA reductase - hydroxymethylglutaril-coenzyme A reductase
HR – heart rate
HSL - hormone-sensitive lipase
Ht – hematocrit
IDL – intermediate density lipoproteids
IGF-1 insulin-like growth factor-1
LDG - lactatedehydrogenase
LDL - low density lipoproteids
MAV - minute alveolar ventilation
MCH - mean corpuscular hemoglobin
MCHC - mean corpuscular hemoglobin concentration
MCV - mean corpuscular volume
MFEFR - maximum forced expiratory flow rate
MHC – major histocompatibility complex
MSH - melanocyte-stimulating hormone
MV - minute respiratory volume
MVV - maximum voluntary ventilation
NANA - N-acetylneuraminic acid
ORE - osmotic resistance of erythrocytes
PFEFR - peak forced expiratory flow rate
RI - reticulocytes index
RLV - residual lung volume
RR - respiratory reserve
$RV_{ins/exp}$ - reserve volume of inspiration / expiration
SB - standard bicarbonate
STH - somatotropic hormone
SV - stroke volume
T_3 – triiodothyronine T_4 - thyroxine
TdT - terminal desoxynucleotide-transferase
TLC - total lung capacity
TPA - tissue-type plasminogen activator
TSH - thyroid-stimulating hormone, thyrotropin
TTRF - thyrotropin-releasing factor
TV - tidal volume
VC - vital capacity of the lungs
VLDL – very low density lipoproteids

SECTION I.

General Pathophysiology.

Harmful Factors of the Environment.

Case 1.

One group of mice was exposed to X-rays at a dose of 10Gr over the period of 10 minutes, the other group was exposed to the same dose of X-rays but the period of exposure was 140 minutes.

In which group will the damaging effect of radiation be greater and why?

1) in the first group
2) in the second group
3) equal in both groups

Case 2.

In the first 30 minutes of a pilot's being at an altitude of 8,000 m his cockpit became dehermetized. The pilot developed signs of altitude decompression sickness: general weakness, dizziness, nausea, tachycardia, increased blood pressure, dyspnea, paresthesia, skin itching, muscle and joint ache, vision impairment.

Explain the mechanism of these symptoms.

The Role of Heredity in Pathology.

Case 1*.

What is the probability of a child's being born with hemophilia (%) if his father has this disease and his mother is healthy and is not a carrier of the hemophilia gene:

a) 100% b) 50% c) 25% d) 0% (all the children will be healthy)?

1. What is the type of inheritance of this disease?
2. Why doesn't the disease develop in females with the hemophilia gene?
3. What is the basis of hemophilia pathogenesis?

Case 2.

If a disease is caused by an autosomal recessive gene, and both parents are phenotypically healthy and heterozygous for this gene, what is the probability (%) that their first child will have the disease?

a) 0% b) 25% c) 50% d) 75% e) 100%

Give examples of diseases with this type of inheritance.

Case 3.

If a hereditary disease is caused by autosomal recessive gene "b", and both parents are phenotypically healthy and heterozygous for this gene, what is the probability that their first child will be healthy?

a) 25% b) 50% c) 75% d) 100%

1. What is the gene penetrance in a carrier of the dominant gene (A); in a homozygous carrier of the recessive gene (B); in a heterozygous carrier of the recessive gene (C)?

Case 4.

What is the probability of children's being born with achondroplasia if the mother is healthy and the father has this disease:

a) 25% b) 50% c) 75% d) 100%

1. What is the type of inheritance of this disease?
2. What are the main manifestations of the disease?

Reactivity, Resistance, Constitution of the Body.

Case 1.

A patient with blood type A (II) was by mistake transfused blood type B (III). As a result, a severe hemotransfusion shock developed.

1. What kinds of reactivity can be manifested in this way?
   a) group
   b) individual
   c) specific
   d) nonspecific
   e) physiological
   f) pathological

Case 2.

An attack of bronchial asthma developed in a patient after he had taken aspirin.

1. What kinds of reactivity can be manifested in this way?
   a) group
   b) individual
   c) specific
   d) nonspecific
   e) physiological
   f) pathological
2. Explain possible pathogenesis of aspirin-induced asthma.

Case 3.

Three rabbits: the first – intact, the second – after a previous subcutaneous injection of caffeine and the third – in a state of narcotic sleep (hexenal) were given subcutaneously 1%-solution of pyrogenal (1ml/ 1kg of body mass).Two hours later their rectal temperature was measured and the results were as follows: in the first rabbit the temperature rose by 1˚C, in the second – by 3˚C and in the third – by 0.2˚C.

1. Assess the form of reactivity of these animals to the administration of a pyrogenic substance.
2. What kinds of reactivity are manifested in these changes?
3. Explain the results of the experiment.

Case 4*.

Two rats: one - intact, the other – after a bilateral adrenalectomy (adrenal glands removal) were placed into a big jar filled with water. The animals began to swim, but 10 – 15 minutes later the rat with adrenalectomy started to drown and was taken out of the water, while the other continued swimming for a long time.

1. Assess the reactivity and resistance of these animals to physical load.
2. Explain the obtained results.

Case 5.

In a jar with a cubic capacity of 200 ml were placed two mice – adult and newborn – and a box with natron lime (CO_2 absorbent). The jar was tightly closed, and the mice were watched. 10-15 minutes later the breathing rate of the adult mouse sharply increased, it developed restlessness and motor activity followed by convulsions and eventually died. In the newborn mouse no visible changes were observed and by the moment of the adult mouse's death it was still alive.

1. Assess the reactivity and resistance of these animals.
2. What kinds of reactivity can we speak of?
3. Explain the obtained results.

Case 6.

The medical check-up of two young men of a military call-up age showed the following:

The first young man - height 170 cm, body mass 90 kg, the subcutaneous adipose layer is clearly manifested, the chest is broad, the epigastric angle is obtuse, the vital capacity of the lungs (VC) is 15% less than normal, horizontal position of the heart, blood pressure is 140/80 mm Hg, blood sugar level is near the upper border of the norm, basal metabolism is decreased.

The second young man – height 190 cm, body mass 70 kg, the subcutaneous adipose layer is feebly manifested, the chest is narrow, the epigastric angle is sharp, the vital capacity of the lungs (VC) is 20% more than normal, vertical position of the heart, blood pressure is 110/70 mm Hg, blood sugar level is near the lower border of the norm, basal metabolism is increased.

1. Assess the constitutional types of these young men.
2. What is the most likely explanation of the dependence of blood pressure, blood sugar level and basal metabolism on a person's constitutional type?
3. What diseases are likely to develop in the first (A) and in the second (B) young man? (tuberculosis, hypotension disease, diabetes mellitus, biliary lithiasis, hypertension, obesity, ulcer disease, generalized atherosclerosis, hyperacidic gastritis, hypoacidic gastritis).

Allergy, Immunopathology.

Case 1.

If a sensitized guinea pig is intravenously injected a colloid dye (for example, Evans blue on a protein carrier) and then is intracutaneously injected an antigen, in 3 – 4 minutes at the site of the intracutaneous injection of the antigen a blue spot appears (Ovary's phenomenon).

1. Explain the mechanism of this phenomenon.
2. Can the development of this phenomenon be suppressed:
   a) by denervation of the skin area in which the reaction occurs;
   b) by administration of antihistamine medications;
   c) by administration of blockers of cyclooxygenase ?
   Explain your answer.

Case 2.

A 10-year-old boy with a leg injury was given antitetanic serum with a prophylactic purpose. On the eighth day after the administration of the serum the child developed severe pains and swelling of the shoulder and knee joints; a generalized rash. He also had fever, acute general weakness, thudding heart sounds and a decreased blood pressure. The child was hospitalized with a diagnosis "serum disease".

1. What type of immune disorder (Gell and Coombs classification) does "serum disease" refer to?
2. Explain the pathogenesis of the disease and its main symptoms.
3. Why did the symptoms develop on the eighth day after the administration of the antitetanic serum?
4. How must the serum be administered in order to prevent the development of anaphylactic shock?

Case 3.

Patient G., 35 years old, a factory worker dealing with nickel-plating of metal articles (he puts metal things into an electrolytic bath and takes them out) applied to his physician with complaints of itching eruptions on the skin of the hands, irritability, sleeping disorders. The eruptions appeared two months ago. He treated himself with *Suprastin* and *Tavegil* (blockers of H_1-receptors) but unsuccessfully.

The examination revealed papular-vesicular rash, scratching marks, hemorrhagic crusts. An application test with nickel sulfate was positive. A macrophage migration inhibition test with a nickel preparation also gave a positive result.

1. What disease can be most likely suspected in this patient? Justify your conclusion.
2. What type of immune disorders does this disease pertain to?
3. Explain the pathogenesis of this disease.
4. What time should pass between the application test with nickel sulfate and the assessment of its result? Why?
5. Explain the inefficiency of treatment with *Suprastin* and *Tavegil.*

Case 4.

A patient applied to his physician with complaints of itching of the eyelids, lacrimation, acute rhinitis, sneezing which have been disturbing him for two years in April and May. His blood test showed large quantities of eosinophils. The patient's father suffers from bronchial asthma.

1. What disease does the patient most likely have?
2. Justify your conclusion.
3. What methods of investigation will help you to confirm your diagnosis?
4. Explain the pathogenesis of the symptoms of the disease.
5. Explain the role of eosinophils in this disease.
6. Is it expedient to administer antigen-specific immunotherapy to this patient?

Case 5.

In order to provoke an anaphylactic shock a healthy guinea pig was injected 4 ml of blood serum taken from another guinea pig previously sensitized with an antigen – horse serum. Immediately after that the animal was intravenously injected a resolving dose of the antigen – 0.2 ml of the horse serum.

1. Will the clinical picture of anaphylactic shock develop in this case?
2. Explain your answer.
3. Describe the mechanism of the development of active and passive sensitization of the guinea pig to a foreign protein.

Case 6.

A patient with atopic bronchial asthma developed an attack of asphyxia after a provocative test with an allergen. The attack was reversed within half an hour. Six hours later a bronchospasm developed again without any contact with the allergen. The X-ray film revealed the presence of an infiltrate in the patient's lungs.

1. What type of allergic reactions does the second bronchospasm pertain to?
2. Describe the mechanism of the first and the second attack of asphyxia.
3. What types of cells predominantly take part in the development of the first and the second attack of asphyxia?

Case 7.

Patient M., 32 years old, was admitted to hospital with complaints of marked weakness, dizziness, jaundice of the skin and sclera. Examination revealed a decreased level of hemoglobin and erythrocytes and an increased content of bilirubin in the blood. Coombs test was positive. From the patient's medical history it was known that she had been taking sulfonamide medications for a long time. A diagnosis was made: immune hemolytic anemia.

1. What is the role of sulfonamides in the development of this disease?
2. Explain the pathogenesis of this hemolytic anemia.
3. Can sulfonamides and other medications cause pseudoallergy?
4. What is pseudoallergy?

Case 8*.

Before administration of a resolving dose of an anaphylaxis-provoking allergen one sensitized experimental animal was injected a β-adrenoblocker, and the other – a β-adrenostimulator.

1. In which case will the pathochemical stage of the allergic reaction be more expressed and why?
2. What medications should be administered to weaken the anaphylactic reaction?
3. Explain the mechanism of their action.

Case 9.

A child, aged 10, was taken to hospital with an attack of bronchial asthma. From his medical history it is known that attacks of asthma appeared after the family had ac-

quired a dog. After a successful treatment the child was directed to an allergist who carried out diagnostic skin tests. At the site of the contact with the allergen from the dog's fur hyperemia, edema (size 2cm^2) and itching developed which quickly disappeared after this skin area was treated with 1% hydrocortisone ointment.

1. Assess the result of the skin test.
2. What time is necessary for the maximal development of skin reaction to an allergen?
3. Explain the mechanism of the skin reaction.
4. How can the effect of hydrocortisone ointment be explained?
5. What recommendations should be given to the child's parents?

Case 10.

An allergist took a portion of blood from a 5-year-old child suffering from a severe form of atopic dermatitis and injected the serum of this blood intracutaneously into the forearm of the child's father. From the child's medical history it is known that his mother suffers from pollinosis and his father is healthy. The next day the father was injected an allergen from cow's milk into that part of his forearm where the serum had been previously administered. 15 minutes later hyperemia, edema and itching appeared at the site of the allergen injection.

1. What is the name of this diagnostic test?
2. Why didn't the doctor carry out skin tests on the child' skin?
3. Explain the mechanism of the development of the positive skin test in the child's father.
4. What recommendations can you give to prevent exacerbations of this child's disease?

Case 11.

Parents and their 5-year-old son visited their friends where the child developed an attack of asphyxia after a contact with a cat. The ambulance was called in, and the doctors stopped the attack and recommended the parents to show their child to an allergist. The child's father has bronchial asthma.

1. What role does hereditary predisposition play in the development of atopic diseases? What stages of allergy pathogenesis can it influence?
2. Explain a possible mechanism of the attack of asphyxia in this child.
3. How does the content of cAMP and Ca^{2+} in mastocytes and smooth muscle cells of the airways change at the moment of the attack?
4. What medications (name the pharmacological groups) can affect the content of cAMP and Ca^{2+} in bronchial asthma?

Case 12.

A woman applied to an endocrinologist with complaints of weakness, fatigability, substantial weight gain over the previous year, persistent edemata of the face, a decrease in the body temperature to 35.6˚C and a lump on the neck. Careful examination revealed a considerable decrease in basal metabolism, goiter of

the 2-nd degree, a decreased function of the thyroid gland. She was diagnosed with Hashimoto's thyroiditis.

1. Explain possible variants of the pathogenesis of this disease.
2. Give examples of other diseases having a similar mechanism of development.

Case 13.

A group of rats were transplanted skin allografts (size 6 cm^2). The allograft rejection occurred within the first 14 days. 30 days after the rejection the skin from the same donors was once again transplanted to the same animals.

1. What is the life time of the grafts after the repeated transplantation?
2. Explain the mechanism of the allograft rejection after the first and the second transplantations.
3. What measures should be taken to prevent rejection of an organ or a tissue?

Case 14.

One drop of suspension of mast cells taken from the abdominal cavity of a guinea pig sensitized by antigen N1 (egg albumin) was placed on each of the three object glasses stained with a neutral red dye. Then the experimenters added on object glass #1 one drop of Krebs solution, on object glass #2 – one drop of antigen N2 (cow's milk protein), on object glass #3 – one drop of antigen N1. The quantity of degranulated mast cells was counted under a microscope.

The results: object glass #1 - 8% of mast cellswas degranulated, object glass# 2 – 10%, object glass #3 – 56%.

1. What is this test called?
2. Explain the obtained results.
3. Explain the mechanism of degranulation of mast cells on object glass #3.
4. What changes take place in mast cells at the moment of their degranulation?

Case 15.

Patient A., 42 years old, was admitted to hospital with complaints of general weakness, fever, itching and rash on the skin, pains in the joints.

From his medical history it is known that he was bitten by a dog which died from rabies. The patient applied to his district hospital only a week after he had been bitten. He received 30 ml of antirabic gamma-globulin in two intramuscular injections (15 ml each) with a 10-minute interval. The preliminary intracutaneous test was negative. A week and a half after the injection of antirabic gamma- globulin, the patient developed skin itching, urticaria all over the body, muscle and joint pains, headache, fever.

Examination data: submandibular and groin lymph nodes are enlarged, slightly dense, painful. Heart rate – 98/min, blood pressure – 110/70 mm Hg. Heart sounds are muffled. The knee joints are edematous and painful with a slightest movement.

Blood test: moderate leukopenia with relative lymphocytosis.

The patient was administered dexamethasone (a glucocorticoid) 4 mg intravenously twice a day. Within the next two days the rash and pains in the muscles and joints decreased, then disappeared.

1. What disease did the patient have?
2. How can you explain the development of the symptoms 10 days after the beginning of the antirabic prophylaxis?
3. Explain the pathogenesis of the skin rash and joints involvement.
4. Explain the mechanism of the positive effect of glucocorticoids.

Case 16.

In the experiments of producing *in vitro* anaphylactic contraction of isolated intestines (Schultz – Dale method) two portions of the ileum of a sensitized guinea pig were placed into two baths with Krebs solution at a temperature 37˚C and constant aeration. A specific antigen was added to the first bath after which the contracture of the ileum developed with an amplitude of 90% of the contractile reaction to a standard dose of histamine. In the second bath a blocker of H_1- histamine receptors (*tavegil*) was introduced, and 3 minutes later the same dose of the antigen was added. Then, after washing (Krebs solution was changed 3 times) the antigen was added once more.

1. Explain the mechanism of anaphylactic contraction of isolated intestines.
2. Will the amplitude of contracture of the intestines change in response to a repeated introduction of the antigen? Why?
3. Can we completely inhibit the development of contracture in response to a) histamine; b) specific antigen; by previously treating the portion of the intestines with a blocker of H_1- histamine receptors (*tavegil*)? Explain your conclusion.

Case 17.

Patient A., 23 years old, lost consciousness after a bee had stung her in the scalp and was taken to hospital. The patient developed generalized urticaria, face edema, stenotic breathing. Her BP was 70/40 mm Hg, pulse – 120/min.

From the patient's medical history it is known that her mother suffers from urticaria and Quincke's edema, her father is a bee-keeper. The patient had been repeatedly stung by bees with development of severe itching, pain, burning and edema at the site of the sting.

1. What disease does the patient have?
2. Justify your conclusion.
3. According to what type of immune disorder did the disease develop?
4. Explain the pathogenesis of the main symptoms of the disease.

Case 18.

In the experiments of producing *in vitro* anaphylactic contraction of isolated intestines according to Schultz-Dale method, two portions of the intestines of a sensitized guinea pig were placed into two baths. After a preliminary testing with a standard histamine dose, an antigen was added to one of the baths and in response to its action

anaphylactic contracture of the isolated intestines developed. A solution of salbutamol (β-adrenomimetic) in optimal concentration was added to the second bath. After a 3-minute incubation of the intestines portion with salbutamol, the same dose of the antigen was introduced into this bath.

1. Explain the mechanism of the development of anaphylactic contracture in the control experiment.
2. Will the contractile reaction of smooth-muscle organs to a specific antigen change on the background of the previous introduction of salbutamol? Justify your answer.

Case 19.

Patient R., 48 years old, a nurse. After 20 years of work in the internal disease department of a hospital she developed symptoms of allergy to penicillin in the form of allergic dermatitis of the hands, face and neck. She fell ill with left-sided pneumonia and was prescribed penicillin injections. 3-5 minutes after the first injection she lost consciousness, her blood pressure dropped sharply and stenotic breathing appeared.

1. What complication developed in this patient after the injection of penicillin?
2. According to what type of immune disorder did it develop?
3. Explain the pathogenesis of the main symptoms of the disease.

Pathophysiology of the Peripheral Circulation.

Case 1.

Several minutes after mustard plasters are put on the chest, sensation of heat, slight burning and marked reddening of the skin appear.

1. What type of hyperemia develops in this case?
2. Explain the origin of the symptoms.

Case 2.

Venous hyperemia was simulated by placing a ligature on the right femoral vein of a rabbit.

1. Name the external signs pointing to the development of venous hyperemia.
2. Explain the mechanism of its development.

Case 3*.

A 46-year-old man with severe ascites was performed a puncture of the abdominal cavity. After 5 liters of fluid was removed, the patient's condition suddenly worsened: he developed dizziness and syncope. The patient's syncope was considered to be a manifestation of insufficient blood supply of the brain due to blood redistribution.

1. What consequences for the blood supply of the abdominal organs did the ascites lead to?
2. Why did blood redistribution take place after the puncture of the abdominal cavity?

Case 4.

A frog's sciatic nerve innervating the left hind leg was cut under ester anesthesia.

1. What will happen to the blood supply of the denervated leg?
2. What is the name of this pathological process?

Case 5.

A 64-year-old patient suffering from chronic ischemic disease of the heart and marked atherosclerosis suddenly felt acute pain in his left leg, the skin of which became pale. The pulse on the back of his left foot was not palpated. The limb was cold to the touch.

1. What disturbance of the peripheral blood circulation developed in this patient?
2. Explain the mechanism of the patient's symptoms.

Pathophysiology of Hemorheology and Hemostasis.

Case 1.

Patient K., 11 years old, complains of pains in the knee after a contusion, general weakness, quick fatigability. From his medical history it is known that he often has profuse nose bleedings. Physical examination showed extended subcutaneous hematoma around the left knee joint and on the front surface of the left leg. The left joint is enlarged and its movements are painful.

Examination data: Hb – 50g/l; erythrocytes – 3.0 x 10^{12} /l; leukocytes – 9.0 x 10^{9}/l. The hemostasis system: thrombocytes – 350 x 10^{9}/l; bleeding time (Duke's test) – 3min; platelet aggregation is not disturbed; tourniquet test (-); blood clot retraction is normal; blood clotting time – 20 min; prothrombin index – 95%; thrombin time and fibrinogen content are within the norm; activity of factor VIII in the blood plasma is sharply decreased.

1. What is the pathogenesis of hemorrhagic syndrome development in this child?
2. What are the principles of pathogenetic therapy for this hemorrhagic syndrome?
3. Point out the main factors leading to the development of hemorrhagic syndromes.

Case 2.

Patient M., 52 years old, is being treated in a hematology clinic with a diagnosis: chronic lymphoblastic leukemia. He was hospitalized with complaints of easily bleeding gums, skin rash, general weakness, dark color of the feces in the last few days. *Physical examination:* numerous ecchymoses on the skin of the trunk and extremities; considerably enlarged axillary and groin lymph nodes, liver and spleen.

Laboratory findings: in the peripheral blood – hypochromic anemia, leukocytosis, 100 x 10^{9} /l with predominance of lymphocytes; thrombocytopenia (40 x 10^{9}/l); bleeding time (Duke's test) – 10 min; blood clot retraction is sharply slowed down; tourniquet test (+); platelet aggregation is not disturbed.

1. What is the pathogenesis of hemorrhagic syndrome in this patient?
2. What functions are performed by thrombocytes (platelets)?

3. Point out possible causes of disturbance of thrombocyte adhesion and aggregation.

Case 3.

Patient K., 7 years old, was hospitalized with complaints of skin rash and urine of reddish color. Physical examination showed numerous symmetric papular-hemorrhagic eruptions on the front surface of the legs and around the knee and mortise joints, macrohematuria.

Laboratory findings: circulating immune complexes in the blood; thrombocyte count, bleeding time and blood clotting time are within the norm; blood clot retraction and stimulated aggregation are not disturbed; tourniquet symptom (+).

A diagnosis was made: hemorrhagic vasculitis.

1. What is the mechanism of the hemorrhagic syndrome development?
2. How does thromboresistance of a damaged vascular wall change and why?
3. Can immune damage to a vascular wall be accompanied by thrombosis? Justify your answer.
4. What are the principles of pathogenetic therapy for this patient?

Case 4*.

Patient D., 20 years old, was admitted to hospital with profuse bleeding from the wound after a tooth extraction made 5 hours before the hospitalization. She has a history of frequent nose bleedings, prolonged bleedings after superficial injuries of the skin, profuse menstrual bleedings.

Physical examination: the skin is pale; there are petechiae on the legs. The patient often spits a mouthful of saliva with blood. Heart rate - 120/min; blood pressure – 100/60 mm Hg. The liver and spleen are not enlarged.

Laboratory findings: Hb – 80 g/l; erythrocytes – 3.6 x 10^{12} /l; color index – 0.66; thrombocytes – 40 x 10^{9}/l. Many thrombocytes have atypical shape (pear-like, caudate); their life time is decreased to several hours. Blood clotting time is 8 min; bleeding time (Duke's test) – 15 min; tourniquet symptom (+), blood clot retraction is sharply slowed down. Increased titer of IgG_3 in the blood.

On the basis of the examination a diagnosis was made: autoimmune thrombocytopenia (Werlhof disease). Administration of corticosteroids has led to a decrease in the degree of the hemorrhagic syndrome and an increase in thrombocyte count.

1. Explain the mechanism of the hemorrhagic syndrome development.
2. Point out the type of bleeding.
3. How does the production of thrombocytopoietins change in this disease?
4. What is the positive dynamics of the disease after administration of corticosteroids conditioned by?
5. What principles of pathogenetic therapy should be used in this case?

Case 5.

Patient K., 20 years old, was hospitalized to a gynecological department with uterine bleeding which developed the previous day after a criminal abortion.

Examination data: Erythrocytes- 3.6 x 10^{12}/l; Hb – 80 g/l; thrombocytes – 40 x 10^{9}/l; prothrombin index – 80%; blood clotting time – 20 min. In the peripheral blood acti-

vated forms of thrombocytes and their aggregates are detected. Besides, the content of fibrinogen/fibrin degradation products in the blood is increased and soluble fibrin-monomer complexes are found. Blood pressure – 80/60 mm Hg; heart rate – 120 /min. As a result of renal insufficiency the level of blood urea nitrogen (BUN) has increased and metabolic acidosis has developed.

1. Name the stages of thrombohemorrhagic syndrome (disseminated intravascular coagulation [DIC]-syndrome).
2. What is the pathogenesis of the patient's bleeding?
3. What stage of DIC-syndrome can be thought of in this case taking into consideration the laboratory findings?
4. Point out the principles of pathogenetic therapy of thrombohemorrhagic syndrome.

Case 6.

Patient P., 60 years old, was admitted to hospital after a hypertensive crisis with complaints of severe headache, sensation of heaviness in the occipital region, memory weakening and vision deterioration.

Laboratory findings: increased level of antihemophilic globulins (factor VIII and others) in the blood, elevated content of fibrinogen, cholesterol and β-lipoproteids; decreased activity of C-protein, decreased synthesis of prostacyclin and tissue-type plasminogen activator (TPA).

One day later the patient's condition sharply worsened, he lost consciousness, left-sided hemiparesis developed. A diagnosis was made: cerebral atherosclerosis complicated by thrombosis of the right medial cerebral artery.

1. Point out the factors contributing to thrombi formation.
2. How are rheological properties of the patient's blood changed and why?
3. List the principles of pathogenetic therapy of thromboses.

Case 7.

Patient Z., 39 years old, with postnecrotic cirrhosis of the liver after alcohol excess has uncontrollable bleeding from the alveolus of an extracted tooth.

Examination data: thrombocytes – 180 x 10^9/l; prothrombin index - 75%; fibrinogen – 3,5 g/l, bleeding time (Duke's test) – 5 min.

1. What is a possible cause of the development of this hemorrhagic syndrome?
   - thrombocytopenia
   - thrombocytopathy
   - deficiency of K-dependent blood clotting factors
   - DIC-syndrome of intoxication character
2. Explain possible mechanisms of changes in hemostasis indices.

Case 8.

Patient G., 30 years old, with massive petechial rash on the lower extremities was examined, and the following results of his hemostasis assessment were obtained: thrombocytes – 180 x 10^9/l; bleeding time – 10 min; activated partial thromboplastin time (APTT) – 30 sec; prothrombin time – 12 sec; thrombin time – 15 sec.

1. What pathological condition can be suspected in this patient?
- hemophilia
- thrombocytopathy
- hemorrhagic vasculitis
2. What additional investigations should be performed?

Inflammation, Acute Phase Response, Fever, Hyperthermia.

Case 1.

Patient C., 30 years old, is delivered to a medical aid post in a poor condition. His skin and mucosa are cyanotic, the pulse is weak,146/min; blood pressure is 90/60 mm Hg. The breathing is rapid and shallow, the temperature - 40.6˚C. The man's colleagues say that he has been working for 40 minutes at air temperature 70˚C and high humidity, liquidating an industrial accident.

1. What pathological process caused the temperature increase?
2. What is the pathogenesis of the symptoms?
3. What stage (phase) of the pathological process does the patient have?
4. Is it advisable to give the patient antipyretics? Why?

Case 2.

Patient B., 47 years old, after an operation for a thyroid gland tumor removal developed symptoms of hypothyroidism (thyroid gland insufficiency). She was prescribed thyroxin. Her condition improved, and she increased the dose of the medication without consulting her doctor. Some time later, she began to complain of insomnia and palpitations, her body temperature increased to 37.5 – 37.7˚C.

1. Can we regard the body temperature increase in this patient as a fever?
2. How can we explain an increase in body temperature in excessive intake of thyroxin?
3. Is it advisable to administer aspirin to this patient? Why?
4. What is the difference between fever and hyperthermia?

Case 3.

Patient N., 27 years old, was delivered to hospital in a condition of psychomotor excitation after an accident at the building grounds where he had fallen down from a considerable height. On examination: the patient is pale, nystagmus is present, body temperature is 37.7˚C; there are contusions of the soft parts of the body, but no fractures. A diagnosis: brain concussion.

1. Explain a possible pathogenesis of the temperature rise in this patient.
2. Is it reasonable to give aspirin to this patient? Why?
3. List the negative consequences of fever.
4. What is lytic and critical decrease of body temperature? Why is critical decrease of body temperature in the case of fever dangerous?

Case 4.

Natasha K., 6 years old, was admitted to hospital with a diagnosis "infectious inflammation of the parotid glands (mumps)". The disease began with general malaise

and gradual increase in the body temperature which reached 39˚C. The high temperature persisted for ten days. The difference between the temperature in the morning and in the evening did not exceed 1˚C. The patient developed weakness, drowsiness and poor appetite. 10 days later the temperature began to decrease gradually which was accompanied by intensive sweating.

1. What typical pathological processes were observed in this patient?
2. Explain their interrelation.
3. What type of temperature curve was found in this patient?
4. What degree of temperature rise was observed in this patient?
5. Explain the mechanism of the development of weakness, drowsiness and poor appetite.

Case 5.

Patient K., 18 years old, is admitted to an internal disease department with croupous pneumonia. His temperature is 40.5˚C, he is pale, the skin is dry. The tongue is white and coated. The patient complains of headache, complete loss of appetite, drowsiness, severe cough with sputum, dyspnea, soreness of muscles and joints. His blood pressure is 130/90 mm Hg, pulse - 98/min. The heart boundaries are normal, heart sounds are muffled. The breathing is rapid and shallow. Crepitation is heard in the lower part of the left lung. The liver is slightly enlarged.

Blood test: leukocytes – 18 x 10^9/l, neutrophil leukocytosis; erythrocyte sedimentation rate (ESR) – 22 mm/h. Blood sugar is 7mmol/l, albumin/globulin (A/G) coefficient is decreased.

1. Make a pathogenetic chain characterizing the mechanism of temperature rise in this patient.
2. What degree of temperature rise is observed in this patient?
3. Explain the connection between the inflammatory process in the lungs and general reactions of the organism.
4. What inflammatory phenomenon can crepitation be associated with?
5. Explain the mechanism of tachycardia, neutrophilia, hyperglycemia and a decrease in A/G coefficient.

Case 6.

A patient with a confirmed diagnosis of cancer disease had been running a subfebrile temperature for a year. After administration of medications suppressing protein synthesis his temperature returned to normal.

1. What pathological process caused the rise of temperature in this patient (infectious fever, noninfectious fever, endogenous hyperthermia)?
2. How can you justify your conclusion?
3. What is the mechanism of antipyretic action of medications suppressing protein synthesis? Can they normalize temperature in the case of endogenous hyperthermia?
4. Point out possible mechanisms of weight loss in this patient.

Case 7.

An ambulance was called to patient T., 43 years old, because of a renal colic. The patient complains of colicky pains in the right lumbar region radiating to the right testicle. The pain is so severe that the patient nearly faints. He has frequent micturition. In the urine newly formed erythrocytes are present; body temperature is 37.7˚C. The patient has a history of renal calculi.

The pains disappeared after an injection of morphine with atropine and a hot-water bottle on the loin. Two hours after the colic, the body temperature returned to normal.

1. Explain a possible mechanism of the temperature rise in this patient.
2. What degree of temperature rise was observed in this case?
3. What is fever?
4. What changes in the cell and protein composition o f the blood are observed in the case of acute phase response?

Case 8.

Physical examination of the patient revealed a temperature increase to 37.8 ˚C. She has a history of persistent subfebrile temperature over the last year. Taking antipyretic medications (such as aspirin) does not lead to temperature normalization.

1. What pathological process (fever or hyperthermia) takes place in this case?
2. What causes can lead to this process?
3. What additional data should be obtained to make an accurate diagnosis?
4. Name the endogenous pyrogens (3) and list their main properties.
5. Give a brief characteristic of the stages of hyperthermia.

Case 9.

A child of 8 months of age was taken to hospital with a confirmed diagnosis of an infectious disease. Physical examination revealed a temperature rise up to 39.7˚C.

1. Explain the pathogenesis of the child's temperature rise.
2. What complications associated with high temperature can develop in this case?
3. Is it advisable to use methods of physical cooling in such cases? Why?
4. What is the difference between fever and hyperthermia?
5. What changes in the protein composition of blood plasma will be observed in this child?

Case 10.

A patient, aged 20, with a confirmed diagnosis of an infectious disease at the moment of examination has a temperature 38.7 ˚C.

1. Is infectious fever an apparent indication for administration of antipyretics such as aspirin?
2. How can you justify your opinion?
3. What additional data should be obtained to decide whether administration of antipyretics is advisable in this case?
4. Is it advisable to use physical methods of cooling for treatment of infectious fever and if yes, in what cases?
5. Explain the mechanism of temperature rise in the case of fever.

Case 11.

A 42-year-old man with thyrotoxicosis has a history of constant subfebrile temperature over the last year. 5 days ago a diagnosis of pneumonia was made. The patient's temperature at the examination is 38.77 ˚C; he has neutrophil leukocytosis and increased erythrocyte sedimentation rate (ESR).

1. Can we regard a temperature increase in this case as a manifestation of infectious fever?
2. Can administration of antipyretics (aspirin) normalize temperature in cases like this?
3. Is administration of antipyretics advisable?
4. Explain the difference in the mechanisms of development of fever and endogenous hyperthermia.
5. Explain the mechanism of the development of neutrophil leukocytosis and ESR increase in this patient.

Case 12.

An experiment was done on two narcotized rats. The first rat was subcutaneously injected 0.1 ml of ***histamine*** into the left hind leg and 0.1 ml of ***histamine*** into the right hind leg on the background of previously injected ***dimedrol*** (0.1ml). The second rat was injected 0.1 ml of ***turpentine*** into the left hind leg, and 0.1 ml of ***turpentine*** into the right hind leg on the background of previously injected ***dimedrol*** (0.1 ml).

Results: The first rat: 30 minutes after the injections the left leg was 1.5 times enlarged in volume, hyperemic and warm. The right leg was insignificantly enlarged, cold and pink in color. 2 hours later all visible changes in both legs disappeared. The second rat: 30 minutes after the injections the left leg was 1.5 times enlarged in volume with accompanying redness and rise of temperature. Similar changes in the right leg were less pronounced. 2 hours later both legs enlarged in volume twice, both were hyperemic, hot and jerked periodically.

1. What pathological process developed in the first and in the second rat?
2. Explain the difference in the dynamics of the edema development in these two rats.
3. What general changes can develop in the organism of a rat on the background of turpentine injection?
4. List the mechanisms of edema development in the case of inflammation.

Case 13.

Patient B., aged 22, and patient K., aged 43, were found to have fluid accumulation in the pleural cavity. Both patients underwent a pleural puncture.

Patient B.: the punctate was cloudy, of light-yellow color with a relative density 1.029, protein content 39 g/l and high activity of lactatedehydrogenase (LDG). In the sediment there were numerous formed elements, predominantly neutrophils of degenerative forms. Microbe flora was present inside and outside the cells.

Patient K.: The punctate was transparent, of light-yellow color with a relative density 1.014, protein content 16 g/l and low activity of LDG. In the sediment there was insignificant amount of cells, mostly lymphocytes.

1. What is the character of the fluid in patient B. and in patient K.? Justify your answer.
2. Describe the main differences in the fluid composition of patient B. and patient K.
3. What are possible mechanisms of fluid accumulation in the pleural cavity of these patients?
4. Describe the mechanism of leukocytes appearance at the site of inflammation.

Case 14.

An experiment was carried out on three narcotized rats: in the hind leg of each animal 0.1 ml of turpentine (a powerful phlogogenic agent) was injected. The first rat was intact, the second was previously injected 0.1 ml of dimedrol into the same leg, the third was previously injected 0.1 ml of hydrocortisone into the same leg. The volume increase of the legs was assessed 30 minutes, 1 hour and 2 hours after the injection.

Results (volume increase)

	30 minutes	1 hour	2 hours
Rat 1 (intact)	10%	40%	90%
Rat 2 (dimedrol)	2%	35%	90%
Rat 3 (hydrocortisone)	5%	15%	40%

1. Explain the mechanism of an increase in the volume of the rats' legs.
2. Explain the difference in the dynamics of volume growth in these three rats.
3. Explain the mechanism of anti-edematous action of dimedrol.
4. Explain the mechanism of anti-edematous action of hydrocortisone.

Case 15*.

In the alteration phase in the focus of inflammation there is a marked increase in highly active enzymes: elastase, collagenase, hyaluronidase, phospholipase A_2, myeloperoxidase and others.

1. Which of these enzymes induces increased formation of prostaglandins?
2. Describe the role of prostaglandins in the focus of inflammation.
3. What other inflammation mediators are formed after activation of this enzyme? List their main properties.
4. How can increased production of this enzyme be blocked?

Case 16.

Two patients were delivered to the admitting office of a hospital with acute pain in the ileac area of the abdomen. Their blood tests were made with diagnostic purposes.

Patient A.: no deviations from the norm were found in the patient's blood. The body temperature was 36.8 ˚C. After administration of spasmolytics the pain disappeared and the patient went home.

Patient B.: neutrophil leukocytosis with the left shift and an increased erythrocyte sedimentation rate (ESR) were detected, body temperature was 38.2 ˚C. The patient was taken to the operating block for further evaluation and possible surgical intervention.

1. What pathological processes did patients A. and B. most likely have?
2. What is a possible pathogenesis of pain syndromes in patients A. and B.?
3. Explain the mechanism of leukocytosis and ESR increase in patient B.
4. Explain the mechanism of body temperature rise.

Case 17.

Two patients were delivered to the admitting office of a hospital with complaints of severe constricting pains in the chest radiating under the left scapula and to the left arm. Taking of validol was not effective. Both patients were administered analgesic and spasmolytic medications; blood tests and ECG were performed.

Patient K.: The pain disappeared within 30 minutes. His blood test was normal. ECG showed elevated symmetrical T-wave in the chest leads. The patient was allowed to go home and given a recommendation to visit a cardiologist.

Patient M.: The pain syndrome increased, body temperature rose to 37.7˚C. His blood test revealed neutrophil leukocytosis with the left shift, elevated ESR, presence of troponin in the blood. ECG showed the signs of acute myocardial infarction. The patient was hospitalized.

1. What pathological processes are most likely to be found in patients K. and M.?
2. What is the connection between patient M.'s infarction and changes in his blood?
3. Make a pathogenetic scheme of the mechanism of body temperature rise in patient M.
4. Explain the mechanism of pain syndrome in these patients.

Case 18.

Patient addressed to doctor with complaints on impairment of left eye's vision, swelling of eyelid and redness of left eye mucous, tearing, cramping of left eye. Two days ago during working in the country, foreign body got into his eye. In the morning, his eye was swollen, watery, and unable to open. During examination, eyelids are swollen, their edges were hyperemic, having purulent discharge.

1. Which typical pathological process is developed in the patient? Justify your opinion.

2. Explain the pathogenesis of mucosal redness and pus formation in the left eye.

Case 19.

A patient went to the doctor and complained that she had severe and occasionally "twitch" pain on the second finger of the right hand. Symptoms appeared on the

second day after the patient did manicure and scratched her skin around the nail meanwhile she was doing manicure.
During the examination, doctor found out that her finger was swollen, especially around the nail, it appeared to be red, and hot was felt when touching. Patient complained that it is hard to bend her finger.

1. Which typical pathological process is developed in the patient?
2. What are the classical signs for this process?
3. Specify the local pain factors and explain their appearance.

Case 20.

A child accidentally touched a hot iron at forearm and cried when he felt the pain. On the skin at the site of contact occurred rapidly reddening and bubble filled with clear liquid.

1. What is the mechanism of pain in this case?
2. What are the mechanism of occurrence of mediators in the inflammation area?
3. What are the pathological reactions which can cause release of inflammatory mediators?

Case 21.

A patient was admitted into the surgical department of hospital, with the diagnosis acute abdomen (abdominal pain). Based on the local symptoms like high temperature and neutrophilic leukocytosis, this confirms the diagnosis of acute appendicitis. The patient was sent to the operation room. As a result of appendectomy, the appendix was removed, which was then developed into purulent inflammation.

1. What is the mechanism of formation of purulent exudate?
2. How does purulent exudate fundamentally differ from serous exudate?
3. What complications can arise during the formation of purulent focus in the tissue?

Case 22.

Patient B, is diagnosed with “tuberculosis of lungs” in the lung tissue, found foci of caseous necrosis surrounded by macrophages, lymphocytes, epithelioid cells, and multinucleated cells of Pirogov-Langerhans.
Patient D, is diagnosed with “lobar pneumonia”, caused by streptococcus pneumonia, exudates are detected in alveoli of the infected lung, which contain neutrophils, isolated erythrocytes and fibrin.

1. Name the type of inflammation of lungs developed in patients B and D. Justify your answer.

2. What are the causes of this type of inflammation suffered by patient B? What are the other reasons of the inflammation that you know?

3. What kind of exudates are formed in the lungs of patient D, what is the mechanism of its formation?

Case 23.

A child accidentally touched a nettle (plants with stinging hairs that irritate the skin on contact) with his forearm and cried out in pain. On the skin at the site of contact quickly developed redness and blisters that disappeared in 25-30 mins. It is known that in the stinging hairs of the nettle contains histamine, choline, formic acid, etc. They get into the skin through the wound, which is formed by pricking the skin with sharp hairs.

1. Can the observed changes be considered as manifestations of inflammation? Why?

2. Is it possible to stop inflammation in the early stages of development?

3. What is the role of histamine in the mechanisms of cutaneous manifestations?

Pathophysiology of the Acid-Base Balance.

Case 1*.

Patient N., 62 years old, was admitted to the surgical department of a hospital with a fistula of the intestines.
Examination data: Blood pressure is 80/40 mm Hg; pulse – weak, 100/min; hematocrit – higher than the norm, plasma osmolality – 285 mOsm/kg H_2O.

The skin is flaccid, with poor turgor; the mucosa are dry, the eyeballs - soft on pressing, muscle tone – decreased. Diurnal diuresis – 600 ml. *Acid-base balance indices*: **pH = 7.26; pCO_2 = 36 mm Hg**; base excess **(BE) = – 8mmol/l;** anion gap **(AG) – 12 mEq/l.**

1. Classify the type of disturbance of acid-base balance (ABB) and fluid-electrolyte balance.
2. Explain the pathogenesis of this pathology and its symptoms.
3. What Cl^- concentration in the blood plasma must this patient have and why?
4. How do the following processes in the kidneys change: a) ammoniogenesis; b) bicarbonate reabsorption; c) sodium reabsorption: d) H^+ and K^+ secretion; e) water reabsorption?
5. How is the patient's RAAS condition changed and why?
6. Point out the principles of pathogenetic therapy for this patient.

Case 2.

Patient A., 26 years old, is being given mechanical lung ventilation during an operation. His ABB indices are: **pH = 7.26; pCO_2 = 67.5 mm Hg.**

1. Using the nomogram in your textbook (Fig.7), determine and assess the values of BB (buffer base); SB (standard bicarbonate) and BE (base excess) in this patient.
2. State the type of ABB disturbance.
3. Point out the main stages of the pathogenesis and the principles of pathogenetic therapy of this pathology.
4. What dangerous consequences can develop in this case if ABB is not normalized?

Case 3.

Patient K., 25 years old, was admitted to the traumatology department with brain concussion accompanied by incoercible vomiting, deep and rapid breathing, periodic convulsions.

On examination: Blood pressure is 90/50 mm Hg; feeble pulse 110/min; the skin and mucosa are dry, the turgor is poor. The patient is not thirsty. Plasma osmolality is 278 mOsm/kg H_2O. *ABB indices*: **pH = 7.55; pCO_2 = 30 mm Hg; HCO_3^- = 30 mmol/l.**

1. Classify the type of disturbance of ABB and fluid-electrolyte balance.
2. Explain the pathogenesis of the observed disorders and the mechanism of the symptoms.
3. What must the values of BB, BE and SB be in this patient?
4. How is water exchange between the intracellular and extracellular compartments altered in this case?
5. What are the absence of thirst and the presence of convulsions caused by?
6. List the principles of pathogenetic therapy.

Case 4.

An inexperienced alpinist developed fatigue, apathy, nausea, dizziness, headache, tachycardia, pains in the heart, muscle weakness and muscle jerks during a mountain ascent.

Examination data: The patient is pale; BP – 80/40 mm Hg, heart rate – 100/min; irregular heart rhythm, muffled heart sounds. There are signs of intestinal paresis.
ABB indices: **pH = 7.45; pCO_2 = 23 mm Hg; HCO_3^-** concentration in the plasma = **16 mmol/l.**

1. What type of ABB disturbance does the patient have?
2. Using the nomogram, determine and assess BB, SB and BE.
3. Calculate the possible concentration of K^+ in the blood plasma.
4. What must Cl^- concentration in the plasma be and why?
5. Explain the pathogenesis of the disturbances which developed in this patient.
6. Where does the hemoglobin dissociation curve shift and what is it accompanied by?
7. What life-threatening complication can develop in this case and why?
8. Point out the principles of correction of this ABB disturbance.

Reference: normal indices in an adult person: PaO_2 = 90 – 100 mm Hg; K^+ = 4.1 – 5.2 mmol/l (4.1 – 5.2 mEq/l); Ca^{2+} = 2.25 – 2.75 mmol/l (4.5 – 5.5 mEq/l); Na^+ = 120 – 150 mmol/l (120 – 150 mEq/l); Cl^- = 98 – 105 mEq/l.

Case 5.

Patient P., 30 years old, was admitted to hospital with acute renal insufficiency.
Diurnal diuresis – 300 ml; *in the urine*: protein (8 – 10 g/l), erythrocytes, leukocytes, casts. Glomerular filtration rate and tubular reabsorption are sharply decreased. The breathing is rapid and deep, moist rales are auscultated. The heart boundaries are extended; heart rate - 120/min; arrhythmia. BP is 180/120 mm Hg. There are marked edemata, ascites. The eyeballs are firm and painful on pressing. Positive meningeal symptoms. The patient experiences agonizing thirst. *In the blood:* increased content of urea, creatinine, sulfates, phosphates and organic anions. Concentration of **K^+** in the plasma ranges from **6** to **6.5** mmol/l. *ABB indices:* **pH = 7.25; pCO_2 = 35 mm Hg; BE = - 11 mmol/l.**

1. Classify the type of disturbance of ABB and fluid-electrolyte balance. Disturbance of what processes in the renal glomerules and tubules has lead to this pathology?
2. What is the most likely value of anion gap (AG) in this patient? Why?
3. Explain the pathogenesis of the symptoms. What life-threatening complications can develop in this patient?
4. What is the treatment tactics in this case?

Case 6.

Patient S., aged 45, suffering from diabetes mellitus suddenly developed nausea, vomit, confusion, deep and noisy Kussmaul breathing and acetone odor from the mouth.
On examination: The skin and mucosa are pale and dry, decreased turgor, the tongue is red with deep wrinkles, muscles are relaxed. The eyeballs are soft, the pupil reaction to light is poor. His blood pressure is decreased. The pulse is rapid and feeble. Glucose content in the blood is 18 mmol/l.

ABB indices: **pH = 7.19; pCO_2 = 40 mm Hg; BE = - 13 mmol/l. HCO_3^- = 18 mmol/l; AG = 16 mEq/l.**

1. Characterize the disorder of acid-base and water balance in this patient. Explain the pathogenesis.
2. Explain the mechanism of the symptoms.
3. What can serve as a direct cause of the patient's death if he does not receive medical aid?
4. List the principles of pathogenetic therapy.

Case 7.

Patient O., aged 38, was admitted to the resuscitation department in a poor condition after a traffic accident. *On admission*: The patient is unconscious, the pulse is thready; marked arrhythmia; the breathing is shallow and slow.

ABB indices: **pH = 6.915; pCO_2 = 67.6 mm Hg; BE = - 19.1 mmol/l; BB = 28.8 mmol/l; HCO_3^-= 13.3 mmol/l; PaO_2 = 20 mm Hg.**

Blood test: **Hb = 55 g/l; K^+ = 7.68 mmol/l; Ca^{2+} = 1.06 mmol/l; Na^+ = 140.9 mmol/l; Cl^- = 92.6 mEq/l.**

Heart arrest occurred. 30 minutes after electrocardiostimulation and artificial lung ventilation (ALV) the patient's ABB indices are: **pH = 6.911; pCO_2 = 52.6 mm Hg; BE = - 23.2 mmol/l; BB = 24.7 mmol/l; HCO_3^-= 10.2 mmol/l; PaO_2 = 59.1 mm Hg.** *In the blood:* **Hb = 49 g/l; K^+ = 8.11 mmol/l; Ca^{2+} = 2.74 mmol/l; Na^+ = 141.3 mmol/l.** On the background of ALV, blood transfusion was begun and correction of ABB and electrolytes was carried out. 40 minutes later: **pH = 6.633; pCO_2 = 46.0 mm Hg; BE = - 34.1 mmol/l; BB = 13.8 mmol/l; HCO_3^-= 4.7 mmol/l; PaO_2 = 47.4 mm Hg; Hb = 53 g/l; K^+ = 6.14 mmol/l; Ca^{2+} = 3.15 mmol/l; Na^+ = 128.2 mmol/l.**

One hour later: **pH = 6.662; pCO_2 = 44.2 mm Hg; BE = - 32.8 mmol/l; BB = 15.1 mmol/l; HCO_3^-= 4.8 mmol/l; PaO_2 = 35.2 mm Hg; Hb = 65.3 g/l; K^+ = 6.21 mmol/l; Ca^{2+} = 1.9 mmol/l; Na^+ = 134.6 mmol/l; Cl^- = 109.8 mEq/l.**

In spite of resuscitation measures the patient died without regaining consciousness.

1. Characterize the dynamics of ABB disturbances in the patient.
2. Explain the mechanism of the observed phenomena.
3. What served as a direct cause of death?
4. What form of hypohydration was observed in this patient?
5. Calculate and assess the value of anion gap (AG) on admission and at the end of the observation.

Pathophysiology of Metabolism.

Case 1.

Patient K., 10 years old, was directed to a consultation of an endocrinologist with a 2-month history of periodic headaches and feeling of thirst. *The results of examination*

in the in-patient department: height – 200 cm, the liver and spleen are enlarged, the heart boundaries are extended. BP is 140/90 mm Hg. General content of proteins and fatty acids is increased, blood glucose level – 14 mmol/l, decreased glucose tolerance. Diurnal diuresis is 4litres. The patient drinks 4 l of liquid daily.

1. What endocrine disorders can be suspected?
2. What is the mechanism of hyperglycemia and its possible consequences?
3. Explain the mechanism of polydipsia and polyuria in this patient.

Case 2.

Three patients were admitted to the in-patient department for examination.
Patient A.: fasting hyperglycemia; decreased glucose tolerance; absence of insulin in the blood; polyuria, glucosuria, ketonuria.
Patient B. : decreased fasting glucose level; normal glucose tolerance; insulin production is not disturbed; polyuria, glucosuria.
Patient C.: fasting blood glucose level, level of insulin, glucose tolerance are normal. After consumption of 200 g of glucose, hyperglycemia and glucosuria are noted.

1. Explain possible causes and mechanisms of glucose level changes in the blood and urine of each patient.
2. Explain the mechanisms of development of hyperglycemia, polyuria and glucosuria.

Case 3.

An athlete suddenly felt bad after an intensive training. He developed general weakness, psychic excitation, tremor of extremities, pallor, profuse sweating. He complained of acute feeling of hunger, palpitation, numbness of the lips and seeing double (diplopia).

1. What metabolic change caused the patient's condition?
2. Explain the pathogenesis of the symptoms.
3. What are possible consequences of this condition?
4. Give practical recommendations to provide emergency aid to this patient and relieve his condition.

Case 4.

Does the" body mass index" correspond to the norm in a person whose weight is 75 kg and height – 175 cm?

1. What is this person's ideal weight?
2. What is obesity? Name its main causes.

Case 5.

Does the" body mass index" correspond to the norm in a person whose weight is 70 kg and height – 165 cm?

1. What is this person's ideal weight?
2. What principal mechanisms of obesity do you know?

Case 6.

If healthy pigs are fed on high cholesterol products, they develop atherosclerosis of the vessels. If pigs with experimental Willebrand's disease receive the same diet, the degree of atherosclerotic damage to the vessels is significantly lower.

1. Why is it so? Give your explanation.

Case 7*.

Patient P., a 10-year-old girl, was admitted to hospital with a diagnosis "family hypercholesterolemia type IIa, homozygous form" and multiple xanthomatosis. The patient had xanthomata on her buttocks at birth, and by the age of 3 xanthomata developed on her Achilles tendons, elbows and hands. At the age of 5 she was first diagnosed as having high blood cholesterol level (from 26 to39 mmol/l). Her parents were also found to have high blood cholesterol, and her brother has blood cholesterol level – 9.1 mmol/l. The patient complains of weakness, fatigability. Her BP is 95/60 mm Hg; pulse – 100/min. No pathology of the respiratory and abdominal organs was found. ECG monitoring revealed rare episodes of myocardial ischemia – depression of ST segment. The analysis of the lipid spectrum showed that an increase in the cholesterol level (23.5 mmol/l) was mainly due to an elevated level of low density lipoproteids (LDL) (up to 12.6 – 18 mmol/l). Prior to admission the patient was unsuccessfully treated with *Cholestiramin* and nicotinic acid and kept a diet.

1. What investigation should be done to confirm the patient's diagnosis?
2. What diet did the patient keep?
3. Why were the prescribed medications ineffective ?
4. What is a prognosis for this patient?
5. Will the administration of medications inhibiting the enzymes responsible for cholesterol synthesis in the cell (for example, *Lovastin* which blocks the activity of HMG –CoA reductase) be effective?

Case 8.

Patient K., 45 years old, and patient M., 45 years old, are found to have dyslipoproteidemia: patient K. has an increased content of total cholesterol, cholesterol of low density lipoproteids (LDL) and high density lipoproteids (HDL); patient M. has an increased content of total cholesterol, cholesterol of low density lipoproteids (LDL) and a decreased content of cholesterol of high density lipoproteids (HDL).

1. Which of the patients has a higher probability of developing atherosclerotic process? Why?
2. What role in cholesterol transport is played by LDL and HDL and their characteristic apoproteids?
3. How is cholesterol coefficient determined? What does it indicate?

Case 9**.

Petrov K., 30 years old, had a substantial meal with large amounts of fats and carbohydrates and went to sleep.

Sidorov N., 30 years old, had a 10-km run and went to take a shower.

1. What lipase will be activated in the organism of each of these men?
2. Name the types of hyperlipidemia which will develop in these men and explain the mechanism of their development.
3. Point out possible consequences of hyperlipidemia.

Case 10 *.

Patient K. was found to have a considerably increased content of chilomicrons in the blood which corresponds to hyperlipoproteidemia type I (according to Fredrickson's classification). Patient S. was found to have an increased content of LDL in the blood (hyperlipoproteidemia type IIa according to Fredrickson's classification).

1. Describe the role of chylomicrons and LDL in the lipid transport in the organism.
2. Which of these lipoproteids has a marked atherogenic effect and why?
3. Which of the patients will benefit from administration of statins? Explain the mechanism of action of these medications.

Case 11.

Two groups of patients suffering from coronary heart disease and having an increased level of cholesterol took the following medications: the first group - cholestiramin, the second - placebo, for 5 years. Before and after the investigation coronarography was performed. In the group taking cholestiramin stenosis of the coronary arteries occurred less frequently and the number of myocardial infarctions was less by 19% than in the placebo group.

1. What is the marked atherogenic effect of modified lipoproteids caused by?
2. State the sequence of events leading to formation of an atherosclerotic plaque.
3. What are "foamy cells"?
4. Explain the mechanism of action of cholestiramin which gave positive results in the experimental group of patients.

Case 12.

Patient K., aged 50, applied to his physician complaining of progressive weight gain, flaccidity, weakness and apathy. A year ago the patient underwent an operation for a thyroid tumor removal.

Investigations revealed reduced production of thyroxine and triiodothyronine (thyroid gland hormones). *Physical examination :* the patient has a hypersthenic constitution; subcutaneous adipose layer is excessively developed. Quetelet index (body mass index) – 4 (the norm is 2.4).

1. What type of obesity developed in this patient?
2. List the types of obesity and describe the mechanism of their development.
3. For what diseases is obesity a risk factor?

Case 13.

Patient M., 58 years old, is admitted to hospital in a poor condition. Her relatives report that for the last 3 days she has been complaining of weakness, flaccidity, dryness of the mouth, thirst and frequent and profuse urination.

Examination data: The patient is stupefied and confused. There are periodically repeated clonic convulsions. The skin is dry with poor turgor, the eyeballs are soft. Body temperature is 38.6 ˚C; BP – 80/50 mm Hg; the pulse is feeble, 120/min. The breathing is rapid and shallow.
Blood test: increased hematocrit, leukocytosis. Blood glucose level is 56 mmol/l; Na^+ - 156 mmol/l; increased content of chlorine and urea; pH = 7.4; plasma osmolality = 350 mOsm/kg H_2O. Diurnal diuresis is 500 ml; there is no acetone in the urine.

1. What endocrine pathology are these symptoms and laboratory findings typical of? Justify your conclusion.
2. Explain the pathogenesis of the symptoms.
3. Point out the principles of therapy of this disease.

Case 14.

Patient S., aged 45, suffering from diabetes mellitus suddenly developed nausea, vomit, confusion, deep and noisy Kussmaul breathing and acetone odor from the mouth.
On examination: The skin and mucosa are pale and dry, decreased turgor, the tongue is red with deep wrinkles, the muscles are relaxed. The eyeballs are soft, the pupil reaction to light is poor. BP is decreased, pulse – rapid and feeble. Glucose content in the blood is 18 mmol/l.
ABB indices: pH = 7.19; pCO_2 = 40 mm Hg; BE = - 13 mmol/l. HCO_3^- = 18 mmol/l; AG = 16 mEq/l.

1. What complication of diabetes mellitus developed in this patient?
2. Explain its pathogenesis.
3. Explain the mechanism of the symptoms.
4. What can serve as a direct cause of the patient's death if he does not receive medical aid?
5. List the principles of pathogenetic therapy.

Case 15.

Patient D., aged 62, was admitted to hospital with complaints of constricting pains in the heart area, pains in the legs which appeared during walking, constant torturing thirst and frequent urges to urinate, as well as sharp visual deterioration.
Her sister has diabetes mellitus.
Examination data: height – 160 cm, body mass – 110 kg; BP – 180/110 mm Hg; weak pulse in the vessels of the lower extremities. *Blood test:* fasting glucose level - 20 mmol/l; the levels of cholesterol, LDL and glycosylated hemoglobin are increased.
In the urine: presence of glucose, no acetone. Diurnal diuresis – 3 liters.

1. Calculate and assess the body mass index of the patient.
2. Explain a possible pathogenesis of the disease.
3. What is the mechanism of hyperglycemia, glucosuria, polyuria? Why is prolonged hyperglycemia dangerous?
4. Explain the mechanism of the disorders of lipid metabolism and their significance in the development of the disease complications.
5. What kind of coma is most typical of this disease?

6. List the principles of therapy.

Case 16.

Patient K., 19 years old, was admitted to hospital with complaints of frequent urges to urinate and large quantities of urine in each micturition; constant thirst (he drinks several liters of water daily). Despite normal appetite he has lost 6 kg of weight over the last year. Three years ago he suffered a severe form of rubella, in the last year he has once had tonsillitis, and twice – an acute respiratory viral infection. Recently he has begun to notice quick fatigability on exertion. The patient's grandmother suffered from diabetes mellitus from her childhood.

Examination data: height – 175 cm, body mass – 56 kg; the skin is dry, tissue turgor is decreased. Fasting blood glucose level is 15 mmol/l; increased content of glycosylated hemoglobin, fatty acids and ketone bodies. There is glucose and acetone in the urine.

1. Explain a possible etiology and pathogenesis of this disease.
2. What is the mechanism of hyperglycemia, ketonuria and clinical symptoms?
3. What long-term complications can develop in this patient? What is their mechanism?
4. List the principles of therapy.

Pathophysiology of Tissue Growth.

Case 1.

A 66-year-old woman with blood type O (I) was admitted to hospital for removal of a malignant tumor of the stomach. At laboratory investigations a moderate titer of antibodies to antigens P and P_1 (which are not normally detected) was revealed. Before the operation doctors failed to find a donor whose erythrocytes would not have P and P_1 antigens. At a tentative transfusion of 25 ml of a donor's blood having small concentration of P and P_2 antigens the patient was found to develop a marked immune reaction which was manifested in an increase of antigen titer and appearance of cytotoxic lymphocytes reacting with the donor's blood. As blood transfusion was impossible, the surgeons had to perform only a resection of the affected part of the stomach instead of a radical operation and, therefore, some quantity of malignant cells remained in the patient's organism. However, after the operation there were no tumor recurrences, and the patient lived to the age of 88 without any signs of cancer.

1. What was the cause of the patient's recovery?
2. What are the mechanisms of the tumor disappearance in this patient?

Case 2.

In an experiment on mice with melanoma which often metastasizes into the lungs, two types of tumor cells different in MHC molecules were isolated: the first type – carrying the MHC-molecules coded by genes H-2K – attracted T-lymphocytes, while the second type – carrying the MHC-molecules coded by genes H-2D – suppressed the immune recognition of tumor cells by lymphocytes. Two different clones were

grown from these two types of tumor cells, and the cells of these clones were subsequently transplanted to healthy mice, after which formation of tumor metastases in the lungs was observed.

1. Which cells (carrying H-2K or H-2D MHC molecules) did the lung metastases predominantly consist of?
2. How can this phenomenon be explained?
3. What immune antiblastoma mechanisms do you know?
4. What are current options of immunotherapy of malignant tumors?

Case 3*.

Which of the following sequences of subcutaneous introduction of three substances into experimental mice should be chosen in order to cause in the latter the most likely development of a malignant tumor?

Sequence variants:

I. DMBA (dimethylbenzanthracene) →turpentine →croton oil
II. DMBA → croton oil →turpentine
III. croton oil → DMBA → turpentine

1. Explain your choice of the sequence.
2. What stages of chemical carcinogenesis do you know?
3. What external and internal factors can play an important role at the first and second stages of carcinogenesis?

Case 4.

Patients with xeroderma pigmentosum and aplastic Fanconi's anemia are known to have an extremely high risk of developing malignant tumors.

1. How can you explain this phenomenon?

Case 5.

On hospitalization a patient with Eaton-Lambert syndrome was found to have an oat cell lung carcinoma.

1. What is the link between oat cell lung carcinoma and Eaton-Lambert syndrome?
2. List possible complications which can develop in a patient with a malignant tumor.

SECTION II

Pathophysiology of Organs and Systems.

Pathophysiology of the Nervous System.

Case 1.

Patient K., 34 years old, was admitted to hospital in a poor condition which developed 3 hours after her flat had been treated with thiophosum against domestic insects. *Neurological examination findings* : The patient is pale, confused; active movements in the lower extremities are absent; the muscle tone is decreased. Tendon reflexes are absent.

1. Explain the pathogenesis of the neurological disorders.

Case 2*.

A 28-year-old woman presented with complaints of muscle weakness, quick fatigability and diplopia (seeing double) which usually developed by the evening. A week before she had had an acute respiratory illness. The woman was hospitalized. Two days after the hospitalization she developed a left-side ptosis (dropping of an eyelid). *Neurological examination* revealed a left-side ptosis, limited up-and-down movements of the eyeball, quick fatigue of muscles on exertion – rhythmic fist clenching. The functional ability of the hand muscles restored only after a prolonged rest. Biopsy of the thymus revealed its follicular hyperplasia. Biopsy of skeletal muscles showed necrotic changes of muscle fibers with signs of focal inflammation and atrophy of some muscle fibers. Electron microscopy showed widening of the synaptic cleft, dystrophy changes of the post-synaptic membrane. In the blood serum antibodies to acetylcholine receptors were detected.

1. What disease of the nervous system is characterized by these signs?
2. Explain the pathogenesis of this disease.
3. Explain the mechanism of the symptoms.
4. Point out the principles of pathogenetic therapy.

Case 3.

A 39-year-old man applied to a clinic with complaints of involuntary movements of the hands and difficulty in walking. *Neurological examination* revealed involuntary movements of the hands and facial muscles (grimaces), bizarre “dance-like” gait, slow thinking and decreased attention. The patient had difficulty in producing voluntary movements. The muscle tone was decreased. Computerized tomography (CT) revealed widening of the brain ventricles. EEG showed diffuse changes of bioelectrical activity of the brain. The patient’s father died in a mental hospital at the age of 49.

1. Name the disease of the nervous system which is characterized by these clinical signs.
2. Explain the pathogenesis of this disease.
3. Explain the mechanism of the symptoms.
4. Point out the principles of pathogenetic therapy.

Case 4.

A family of three people (parents and a child) were taken to hospital in a poor condition with dyspeptic symptoms: nausea, vomit, acute pains in the abdomen. It is known that 8-9 hours prior to admission they ate home-made canned aubergines. *Ex-*

amination data: the patients are pale, flaccid, have swelled abdomens; the breathing is shallow and rapid; tachycardia; decreased visual acuity.
The child has a decreased muscle tone, stiff tongue, overhanging epiglottis. The parents have horse voices and hypernasal speech; they complain of dizziness.
Neurological examination revealed paresis of the epiglottis, decreased tone of the skeletal muscles, visual disorders (diplopia, poor reaction to light, dilation of the pupils). Bacteriological investigation of the vomit with culturing on a fungi medium revealed *Clostridium botulinum*, type B.

1. Name the disease characterized by these symptoms.
2. Explain the pathogenesis of this disease.
3. Explain the mechanism of the symptoms.
4. Point out the principles of pathogenetic therapy.

Case 5**.

A 65-year-old woman presented with a 3-year history of progressive memory deterioration with periodic acute episodes of disorientation in space and time. Three months prior to admission she became unable to manage her household without help, in addition, she developed urine incontinence.
Neurological examination revealed a marked disorientation in space and time, aphasia (severe speech disturbance), apraxia (inability to perform a purposeful action), pathological grasping reflex, increased tendon reflexes in the arms and legs. Computerized tomography (CT) of the brain revealed dilation of the intraventricular space and diffuse atrophy of the cortex. Five months after the hospitalization the patient died. Histological examination of the sections of the cortex and hippocampus revealed numerous foci of extracellular deposits of amyloid and intracellular neurofibrillary tangles.

1. Name the disease of the nervous system characterized by these symptoms.
2. Explain the pathogenesis of this disease.
3. Explain the mechanism of the symptoms.
4. Point out the principles of pathogenetic therapy.

Case 6.

A 32-year-old man applied to his physician with complaints of marked muscle weakness which had been disturbing him for the last two months. After the hospitalization he was found to have an oat cell lung carcinoma. *Neurological examination* revealed muscle weakness, poor tendon reflexes. Analysis of the neuromuscular junction in the biopsy material showed the following: folding of the postsynaptic membrane is not changed; reaction to acetylcholine and miniature potentials of the end plate are normal in amplitude. Potentials evoked by a single nerve irritation are small; the number of acetylcholine quanta released in response to a nerve impulse is decreased. In the blood serum antibodies to the antigens of the presynaptic membrane are found.

1. Name the disease of the nervous system characterized by these symptoms.
2. Explain the pathogenesis of this disease.
3. Explain the mechanism of the symptoms.

4. Point out the principles of pathogenetic therapy.

Case 7.

A 50-year-old man applied to his physician with complaints of difficulty in writing in a straight line and tremor of the right hand. The symptoms appeared a month after he had had tick-borne encephalitis in a non-evident form. After his hospitalization a *neurological examination* revealed involuntary tremor of the right hand at rest and tremor of the left hand on slight exertion. The muscle tone was normal; the rate of the voluntary movements was preserved. He had a festinating gait with the trunk bent forward. His speech was quiet and monotonous; the face was amimic and looked like a mask. A pathological eye-movement reflex was observed - fixation of the look upwards for some minutes. Hyperfunction of the thyroid gland was not found.

1. Name the disease of the nervous system characterized by these symptoms.
2. Explain the pathogenesis of this disease.
3. Explain the mechanism of the symptoms.
4. Point out the principles of pathogenetic therapy.

Pathophysiology of the Endocrine System.

Case 1*.

Patient D., 48 years old, has been suffering from bronchial asthma for 30 years. In the last 10 years asthma attacks have become more frequent and the patient was prescribed glucocorticoids. Later, the patient began to take these preparations without consulting his doctor to relieve asthma attacks. Over the last year he has become obese (with predominant fat deposits on his cheeks and abdomen), his blood pressure has become higher (180/100 – 190/110 mm Hg). Asthma attacks ceased, and the patient stopped taking the hormonal medications. Several days after the medication had been discontinued, dizziness, acute muscle weakness, anorexia and diarrhea developed. The symptoms worsened, and the patient was hospitalized.

Examination data: The patient is of medium height, with signs of upper-body obesity. There are purple striae on his abdomen, numerous acnes on the face. BP is 70/50 mm Hg; pulse – slow and feeble. Blood glucose level is 2.7 mmol/l; obvious hyponatremia.

1. What syndrome developed in this patient due to long-term treatment with glucocorticoids? What syndrome developed after he had stopped taking these medications?
2. What is “upper-body obesity”?
3. What is the mechanism of obesity, striae formation and hypertension in the long-term use of glucocorticoids?
4. Why did hypotension, hyponatremia and hypoglycemia develop after withdrawal of the medications?
5. Point out the principles of treatment and prevention.

Case 2.

Patient R., a 35-year-old woman, presents with complaints of attacks of pulsating headaches, palpitations, pallor, profuse sweating, visual impairment, tremor of the limbs, pains in the chest and abdomen. These attacks have occurred for the last two years several times a week, sometimes several times daily; they develop after emotional excitement or physical exercise and usually last about 30 minutes (sometimes several hours). At the end of the attack the patient has a slow pulse, her face reddens, she voids large quantities of light urine; sometimes there is nausea, vomiting and hypersalivation. She has considerably lost weight.

Examination data at the moment of the attack: BP – 210/180 mm Hg; the pulse is 120/min; arrhythmia. Blood glucose level is 14 mmol/l; increased content of fatty acids and lactate. X-ray examination revealed a tumor of the left adrenal gland.

1. What pathology of the endocrine system can be suspected in this patient?
2. Explain the pathogenesis of the observed disorders.
3. What complications can lead to the lethal outcome?

Case 3.

Patient F., 47 years old, is being treated by an endocrinologist for a severe form of obesity, arterial hypertension, coronary heart disease, diabetes mellitus type 2, dysmenorrhea. Some years ago she was treated for multiple fractures of the limbs, concussion and contusion of the brain after a car accident.

Examination data: height – 167 cm, body mass – 110 kg. Fat deposits are mainly on the face (moon-like face), breasts, hips and abdomen, around the 7^{th} cervical vertebra. On the extremities the subcutaneous adipose layer is not expressed. There are purple and cyanotic striae on the thin ("parchment") skin of the hips and abdomen. The scars at the sites of injuries and appendectomy are hyperpigmented. Hirsutism of the male type; mild degree of virilization. BP is 210/120 mm Hg; heart boundaries are expanded, on ECG – signs of myocardial ischemia. *In the blood:* erythrocytosis, neutrophil leukocytosis, eosinophilia and lymphocytopenia, hypernatremia, hypokalemia, pH = 7.52. Blood glucose is 11 mmol/l; cholesterol – 9 mmol/l; HDL/LDL ratio is decreased. Diurnal diuresis is increased. *In the urine:* moderate proteinuria, glucosuria, increased content of 17-OKS (oxyketosteroids). Ketonuria is absent.

1. What disease of the endocrine system is characterized by this clinical picture?
2. Explain the etiology and pathogenesis of the disease and its complications in this patient.
3. What additional investigations can help to make a differential diagnostics with other disorders?
4. Explain the mechanism of lipid, protein, carbohydrate and fluid-electrolyte metabolism disturbances in this patient. Assess the acid-base balance.
5. What complications can be life-threatening for this patient?

Case 4.

A 31-year-old woman is being treated at the endocrinology department.

Examination data: The patient is of medium height and normal build, but extremely exhausted (looks like a skeleton). She moves with difficulty, quickly gets tired,

speaks slowly, with long pauses and in a very low voice (almost whisper). The skin is dry, flaccid, hyperpigmented, especially at the sites where it is rubbed by clothes. The turgor is decreased. There are white depigmented spots on the skin of the chest and arms (vitiligo). Appetite is absent, but there is an increased need in table salt. The patient has frequent vomiting and diarrhea. BP is 80/50 mm Hg, pulse – slow and weak. Circulating blood volume (BV), stroke volume (SV) and cardiac output (CO) are decreased. *In the blood:* decreased count of erythrocytes and neutrophils, lower glucose level and Na^+ and Cl^- concentration, but increased content of K^+ and H^+ as well as ACTH (adrenocorticotropic hormone).

Antibodies to ACTH and MSH (melanocyte-stimulating hormone) are revealed.

1. What disease is characterized by this clinical picture? Give all the names of the disease.
2. Explain the etiology of this disease and point out other possible causes if its development.
3. Explain the pathogenesis of the disease and its main clinical features.
4. List the principles of treatment of this disease.

Case 5.

Patient A., aged 62, presented with complaints of severe palpitations and pains in the heart, profuse sweating, tremor of hands, irritability, constant feeling of heat, lacrimation and photophobia. Over the last three months he lost 10 kg of body weight in spite of increased appetite.

Examination data: The patient is of normal build, deficient nutrition. The thyroid gland is slightly enlarged (diffuse goiter of the 1-st degree). Exophthalmos of medium degree, brightness of the eyes, impaired convergence. Body temperature is 37.4˚C; BP – 160/80 mm Hg; heart rate - 120/min. On ECG – atrial flutter and polytopic extrasystoles, signs of myocardial changes. Basal metabolism is increased by 40%. *In the blood*: LATS-factor and antibodies to periorbital tissues are detected.

1. List all the names of this disease.
2. What is LATS-factor and what role does it play in the disease pathogenesis?
3. What levels of TTRF (thyrotropin-releasing factor), TSH (thyroid-stimulating hormone, thyrotropin), T_4, and T_3 are likely to be found in this patient?
4. Explain the mechanism of the development of goiter, increase in basal metabolism and body temperature, disturbance of heart activity and ocular symptoms.
5. What are the principles of treatment of this disease?

Case 6.

Patient L., 54 years old, presented with agonizing pains in the epigastrium. The skin is dry; the pulse is weak and rhythmic, 84/min; BP – 100/60 mmHg; muffled heart sounds. Body temperature is 37.5˚C. Erythrocytes – 3.6 x $10^{12/}$ /l; leukocytes - 12 x 10^9/l; ESR – 10 mm/h.

Because of suspected perforated stomach ulcer a laparotomy was performed, but no pathology of the abdominal organs was found. Two days after the operation the patient was in a condition of moderate severity. BP was 110/70 mm Hg, the pulse

– weak, 80/min; abdomen – painful on palpation; dry and moist rales in the lungs; body temperature – 38.9˚C.

On the 3-rd day after the operation the patient's condition suddenly worsened: stupefied consciousness, cyanosis, involuntary defecation and urination, signs of dehydration were noted. BP dropped to 80/60 mm Hg and some hours later became undetectable. The pulse was not palpable and the heart sounds could not be auscultated. Deep, noisy intermittent breathing changed into agonal. The pupils were dilated, reaction to light – absent. Despite closed-chest cardiac massage and injection of epinephrine and strophantine the patient died. A presumptive clinical diagnosis was made – myocardial infarction.

The postmortem examination revealed massive petechiasis on the lateral surface of the chest, acute venous hyperemia of the lungs, myocardium, liver and kidneys. Both adrenal glands were enlarged (the size of a big plum); their sections had an appearance of a blood clot. Histological examination showed total infiltration of the adrenal glands by fresh depigmented erythrocytes and leukocytes and destruction of the stroma cells.

1. What is this syndrome called?
2. What was the cause of its development?
3. Point out other possible causes of this syndrome.
4. Explain the pathogenesis of the observed disorders.
5. What was the direct cause of the patient's death?
6. Why were treatment measures ineffective?

Case 7.

Patient A., 19 years old, complains of severe headaches which are not relieved by analgesics and hypotensive drugs, fatigability on exertion, pains in the muscles and joints. By the age of 10 years his height was 200cm. Recently, he has noticed changes in the face: enlargement of the low jaw, nose and ears, widening of the interdental gaps, as well as deterioration of vision and hearing, permanent thirst and frequent urination.

Examination data: height – 230 cm, body mass – 125 kg, rough voice ("as if from a depth"); the skin is moist and greasy with numerous acnes and hypertrichosis. BP is 180/110 mm Hg; the heart, kidneys, spleen and other organs are enlarged. *In the blood*: increased content of erythrocytes, STH (somatotropic hormone), IGF-1 (insulin-like growth factor-1), insulin, glucose (up to 10 – 11 mmol/l), ketone bodies, free fatty acids (FFA) and LDL (low-density lipoproteids). There are signs of lung ventilation disturbance of obstructive type, colon polyps. X-ray film of the brain shows a tumor in area of the Turkish saddle.

1. What pathology of the endocrine system does the patient have?
2. What is the name of this tumor and what cells does it consist of?
3. Explain the pathogenesis of this syndrome, its clinical symptoms and metabolic disturbances.
4. What syndrome develops if a similar tumor arises in people over 20 years old?
5. What complication has developed in this patient? Explain its pathogenesis.

6. What is a probable prognosis of the disease? What are the principles of its treatment?

Case 8.

Two patients are observed by an endocrinologist.

Patient K., 15 years old, has a height of 95 cm, disproportional build, increased body mass. The skin is pale, dry and cold. He has a marked periorbital edema and edema of the lips and tongue. There are signs of hypogonadism and oligophrenia (stage of imbecility). Body temperature is 35.2˚C. Basal metabolism is decreased. The pulse is rare, soft and weak. Heart boundaries are expanded, cardiac output is reduced. The patient is prone to hypoglycemia.

Patient D., 18 years old, has a height of 82 cm, proportional build, thin subcutaneous adipose layer, splanchnomicria. The skin is dry, pale and flaccid (geroderma) with an icteric tint. There are no edemata. Body temperature is 36.2˚C; basal metabolism is not disturbed. BP is 90/50 mm Hg; heart sounds are muffled; there is a systolic murmur over the apex. Infantilism is present, but intelligence is preserved. The patient is known to have had a delayed replacement of deciduous teeth.

1. What are the names of the endocrinological syndromes in patient K. and in patient D.?
2. What additional investigations must be carried out?
3. State possible causes of the development of these syndromes.
4. Explain the pathogenesis of the clinical symptoms and metabolic disorders.
5. Point out the principles of therapy for these patients.

Case 9.

Patient N., a 19-year-old woman, applied to her physician with complaints of an increasing goiter. Lately she has begun to experience a sensation of a foreign body in the esophagus and difficulty in swallowing. She lives in an area where 32% of adult population have goiter of various degrees; 6% of children are mentally and physically retarded.

Examination data: proportional build, height – 156 cm, body mass – 78 kg, goiter of considerable size partly located behind the sternum. Body temperature is 36.0 ˚C; BP - 100/60 mm Hg, pulse - 58/min, weak. Basal metabolism is decreased by 15 %. Uptake of iodine by the thyroid gland is accelerated.

1. What is the name of this syndrome?
2. Explain the mechanism of goiter formation.
3. Explain the functional state of the thyroid gland in the patient basing on the clinical manifestation of the disease. Explain their mechanism.
4. What types of goiter do you know?
5. What endocrine syndrome develops in children of this region?
6. Explain the mechanism of their physical and mental retardation.

Case 10.

Patient Z., 54 years old, underwent a resection of the thyroid gland for euthyroid goiter of the 4-th degree predominantly located behind the sternum. A year after the

strumectomy she applied to an endocrinologist with complaints of a considerable weight gain (she put on "three sizes" in spite of bad appetite), increased fatigability, weakness and chronic fatigue even in the morning, as well as worsening of memory, apathy, drowsiness. She permanently feels cold. Her voice has become horse, especially in the morning.

Examination data: height – 164 cm, body mass – 90 kg, t˚ - 35.4 ˚C. The face is pale, edematous (edemata of the eyelids, lips and tongue – teeth prints are seen). The pulse is 56/min, soft and weak. Heart boundaries are expanded, stroke volume and cardiac output are decreased. ECG shows a very low voltage and signs of pericarditis. Basal metabolism is decreased by 28%. Content of sodium, cholesterol and LDL is increased, glucose level is 3.6 mmol/l.

1. What is "euthyroid goiter"?
2. What syndrome developed in the patient after the operation? Why is it called so?
3. Explain the pathogenesis of this syndrome and its manifestations.
4. What TSH (thyroid- stimulating hormone) production must the patient have and why?
5. Give examples of diseases when this syndrome develops on the background of enlarged thyroid gland (goiter).

Case 11.

Patient V., a 39-year-old man, presented with complaints of severe headaches which were not relieved by analgesics, pains in the heart area, frequent micturition, permanent torturing thirst.

Examination data: medium height, proportional build, body mass – within the norm; poor tissue turgor, dry skin and mucosa. BP – 180/110 mm Hg. *In the blood:* hypernatremia, hypochloremia, hypokalemia, pH = 7.53; glucose – 5.2 mmol/l; diurnal diuresis – up to 10 liters. A tumor of the left adrenal gland is revealed.

1. What is this syndrome and this tumor called?
2. From what similar syndrome should it be distinguished? What is the principal difference between these syndromes?
3. Classify the type of fluid-electrolyte and acid-base balance disturbances and explain the mechanism of their development.
4. Why is hypernatremia accompanied by polyuria?
5. Explain the mechanism of the development of hypertension and torturing thirst.

Case 12.

Patient D., 50 years old, was admitted to hospital two weeks after a strumectomy with complaints of periodic convulsions in the muscles of the extremities, constricting pains in the epigastrium, attacks of asphyxia (she does not have bronchial asthma). She complains of numbness and tingling in the extremities, feeling creepy and increased sensitivity of the teeth.

Examination revealed hypocalcaemia and hyperphosphatemia; Chvostek's and Trousseau's signs, as well as lung hyperventilation test are positive.

1. What complications developed in the patient after strumectomy?
2. List other possible causes of this pathology.
3. Explain the pathogenesis of the observed disorders.
4. List the principles of treatment.

Case 13.

Patient G., 35 years old, complains of appetite loss, nausea, constipations, pains in the abdomen, muscle and bone aches (especially during movement), muscle weakness, loosening of healthy teeth. Over the previous year he has had two fractures of the forearm bones and one attack of a renal colic.

Examination data: increased content of calcium and alkaline phosphatase and decreased content of phosphorus in the blood. *In the urine*: increased content of calcium and oxyprolin. X-ray examination showed signs of fractures of the forearm bones, deformation of the phalanges of both hands, signs of osteoporosis. Ultrasound investigation of the kidneys revealed nephrocalcinosis and calculi in the renal pelvis.

1. What endocrine pathology can be suspected in this case?
2. What investigation should be done and what are its presumptive results?
3. If you presumption is correct, explain the pathogenesis of the observed disorders.

Pathophysiology of the Cardiovascular System.

Case 1.

A disabled woman, aged 36, was admitted to hospital with complaints of dyspnea, tachycardia, edemata of the legs, abdominal distension, quick fatigability and muscle weakness. From her medical history it is known that she has had repeated rheumocarditis, suffers from a heart disease (combined mitral valve defect with prevalence of stenosis). *Examination data*: The patient is exhausted and pale; the skin is cyanotic, cold at touch; there is apparent jaundice of the sclera. There are edemata on the legs and loin, ascites, bilateral hydrothorax. The liver projects from the costal arch by 8cm. The heart is sharply enlarged (both right and left parts). The patient has ciliary arrhythmia; heart rate is 110 – 120/min. The ejection fraction of the left ventricle is 29%. "Wedge" pressure of the pulmonary capillaries is 25 mm Hg. *In the blood:* albumin content – 29 g/l. globulin content – 30 g/l. Norepinephrine level is 3 times as high as normal. End-systolic volume (ESV) is 179 ml; end-diastolic volume (EDV) – 254 ml. Diurnal diuresis is 700 ml.

1. What is this form of cardiac insufficiency called? Confirm your diagnosis by the examination findings.
2. Explain the change in the "wedge" pressure of the pulmonary capillaries in this patient.

3. What is the prognosis of maximum life expectancy of patients with this disease?
4. What pathogenetic therapy is used for this form of cardiac insufficiency?
5. Explain the mechanism of dyspnea, tachycardia, muscle weakness and exhaustion in this patient.
6. Explain the mechanism of edemata and arrhythmia.
7. What signs are suggestive of remodeling of the patient's myocardium? What is its pathogenesis?
8. Explain the mechanism of diuresis reduction in this patient.

Case 2.

A 68-year-old man suffering from stable effort angina has been noting attacks of the disease 1 – 2 times a day during walking. Over the last week the number of attacks has increased up to 10 – 15 a day, but their severity has not changed: they ceased after a rest and, sometimes, after taking nitroglycerin. He did not apply to a physician and did not take anti-anginal medications. On the day of hospitalization, when the patient was outside his home, a severe attack of angina developed which was not relieved by nitroglycerin.

On admission: The patient is pale, scared, complains of severe chest pain. BP is 90/60 mm Hg, pulse – 100/min. *On ECG* : in leads I, aVL, V_1-V_6 - marked elevation of ST segment (monophase curve). *Echography* shows thinning of the left ventricle wall with an area of akinesia. There are increased levels of myoglobin and troponin in the blood, neutrophil leukocytosis, accelerated ESR. Body temperature is 38.4 ˚C.

1. What disease can be suspected in this patient? Confirm your diagnosis by the examination findings. What can the disease be caused by?
2. What do leukocytosis, increase in the body temperature, acceleration of ESR and results of the biochemical blood test indicate?
3. What is the mechanism of the patient's severe pain attack?
4. What is the pathogenetic therapy in this case?

Case 3.

A 68-year-old man suffering from stable effort angina has been noting attacks of the disease 1 – 2 times a day during walking. Over the last week the number of attacks has increased up to 10 – 15 a day, but their severity has not changed: they ceased after a rest and, sometimes, after taking nitroglycerin. He did not apply to a physician and did not take anti-anginal medications regularly. On the day of hospitalization, when the patient was outside his home, a severe attack of angina developed which was relieved only in the in-patient department. *On ECG:* in leads II, III, aVF,V_5,V_6 - tall widened peaked T-wave. Blood levels of myoglobin, troponin, creatinephosphokinase and aspartate-aminotranspherase are normal.

1. What pathological process in the patient's myocardium can be thought of? Confirm your supposition by the examination findings.
2. What additional investigation should be carried out to administer a proper treatment?
3. Point out the principles of prevention of myocardial infarction.

Case 4.

A 84-year-old man was admitted to hospital in an extremely severe condition with a paroxysm of ciliary tachyarrhythmia and quickly progressing pulmonary edema, tachyarrhythmia - 130 per minute on ECG, arterial hypotension – 85/60 mm Hg. ECG showed atrial fibrillation, scar changes in the posterodiaphragmal wall of the left ventricle, signs of acute myocardial infarction of the anterior wall of the left ventricle and interventricular septum. Anti-arrhythmic therapy was not effective.

10 minutes after the admission transthoracal defibrillation was performed on vital indications; sinus rhythm (94/min) was restored. Over the following 15 minutes acute left-ventricular insufficiency sharply decreased. Blood pressure became 120/70 mm Hg.

1. Why did the paroxysm of ciliary tachyarrhythmia sharply worsen the patient's condition?
2. How and why could the end-diastolic volume change at the moment of tachyarrhythmia?
3. What factors contributing to arrhythmia development arise in myocardial infarction?
4. Why did the provided treatment quickly improve the patient's condition?

Case 5.

A 75-year-old man was admitted to hospital in an extremely severe condition with a paroxysm of ciliary tachyarrhythmia (about 130 per minute), quickly progressing pulmonary edema and arterial hypertension (185/120 mm Hg). *On ECG:* frequent polytopic and group ventricular extrasystoles, scar changes in the posterodiaphragmal wall of the left ventricle, signs of myocardial infarction of the anterior wall of the left ventricle and interventricular septum. Anti-arrhythmic therapy was not effective.10 minutes after the admission transthoracal defibrillation was performed on vital indications; sinus rhythm (94/min) was restored; a diuretic and a vasodilator were introduced intravenously. Over the following 30 minutes acute left-ventricular insufficiency sharply decreased; blood pressure reduced to 120/70 mm Hg.

1. What factors provoked the development of acute left-ventricular insufficiency in this patient?
2. How did the contractile function of the left ventricle myocardium change and why?
3. How could the indices of intracardiac hemodynamics change and why?
4. Why did the provided treatment quickly improve the patient's condition?

Case 6.

A 35-year-old woman presented with persistent recurrent headaches and attacks of palpitations which at times interfere with her sleep and moving. She sometimes complains of dizziness, tingling in the ears, burning sensation in her arms and legs, white or black "floaters" in the eyes. She has a 9-year history of these symptoms. 12 years ago the patient's blood pressure measurement in an out-patient clinic showed 160/80

mm Hg. She was periodically treated with various hypotensive drugs. *On examination:* the heart is moderately enlarged to the left; pulse – 72 – 96/min, slightly tense. While the patient was staying in hospital her blood pressure varied: 170/100; 160/100, 145/90 and even 125/80 mm Hg. The patient's mood is very unstable. *ECG* reveals signs of left ventricle hypertrophy; PQ interval – 0.22 sec. Examination of the eye fundus indicates narrowing of the arteries due to organic changes in them. The patient's diagnosis – arterial hypertension.

1. Calculate the variants of the patient's mean blood pressure.
2. Classify this hypertension according to BP level.
3. What stage of arterial hypertension does this patient have? Justify your conclusion.
4. What types of arterial hypertension do you know? What type may this patient have? What investigations should be performed to specify the diagnosis?
5. Explain the mechanism of the left ventricle hypertrophy.

Case 7.

A disabled woman, 38 years old, was admitted to hospital with complaints of dyspnea, tachycardia, leg edemata and abdomen distension. From her medical history it is known that she has had repeated rheumocarditis, suffers from a heart disease (combined mitral valve defect with prevalence of stenosis). *Examination data*: The patient is exhausted; her skin is pale and cold at touch; she has acrocyanosis, jaundice of the sclera. There are edemata on the legs and loin, ascites, bilateral hydrothorax. The liver projects from the costal arch by 8cm. The heart is sharply enlarged (both right and left parts). The patient has ciliary arrhythmia, heart rate is 110 – 120/min. Diurnal diuresis is 700 ml.

1. What is this form of cardiac insufficiency called?
2. Confirm your diagnosis by examination findings.
3. What could hemodynamic indices in this patient be (cardiac output, cardiac index, arterio-venous (A-V) oxygen difference, oxygen utilization coefficient, peripheral vascular resistance, central venous pressure, cathecholamine level)?
4. Explain your answer.

Case 8.

A disabled woman, 39 years old, was admitted to hospital with complaints of dyspnea, tachycardia, leg edemata, abdomen distention, increased fatigability and muscle weakness. From her medical history it is known that she has had repeated rheumocarditis, suffers from a heart disease (combined mitral valve defect with prevalence of stenosis). *Examination data*: The patient is exhausted; her skin is pale with a cyanotic tint, jaundice of the sclera is noted. There are edemata on the legs and loin, ascites, bilateral hydrothorax. The liver projects from the costal arch by 8cm. The heart is sharply enlarged (both right and left parts). The patient has ciliary arrhythmia, heart rate is 110 – 120/min. Left ventricle indices: stroke volume – 77 ml, end-systolic volume – 179 ml, end-diastolic volume – 254 ml. Diurnal diuresis – 800 ml.

1. What is this form of cardiac insufficiency called?

2. Confirm your diagnosis by the examination findings.
3. What hemodynamic index can confirm a decrease in left ventricle myocardium contractility in this patient?
4. How and why could the indices of compliance and relaxation of the patient's myocardium change?

Case 9.

A disabled woman, 42 years old, was admitted to hospital with complaints of dyspnea, tachycardia, leg edemata, abdomen distention, increased fatigability and muscle weakness. From her medical history it is known that she has had repeated rheumocarditis, suffers from a heart disease (combined mitral valve defect with prevalence of stenosis). *Examination data*: The patient is exhausted; her skin is pale with a cyanotic tint, jaundice of the sclera is noted. There are edemata on the legs and loin, ascites, bilateral hydrothorax. The liver projects from the costal arch by 8cm. The heart is sharply enlarged (both right and left parts). The patient has ciliary arrhythmia, heart rate is 110 – 120/min. Diurnal diuresis – 400 ml.

1. What is this form of cardiac insufficiency called?
2. Confirm your diagnosis by the examination findings.
3. What changes of the intracardiac hemodynamic indices are most likely to be found in this patient (stroke volume [SV], cardiac index [CI], ejection fraction [EF], end-diastolic volume [EDV], end-systolic volume [ESV], filling pressure in the left and right heart)? Compare these results with the norm (higher, lower or within the norm).
4. Explain the pathogenesis of the skin symptoms and myocardium hypertrophy.

Case 10

A disabled man, 58 years old, only recently worked as an engineer. He presented with complaints of periodic palpitations, seeing a "net" in front of the eyes, severe headaches sometimes accompanied by vomiting. 9 years ago the patient was first noticed to have blood pressure of 180-190/100 mm Hg. He periodically took hypotensive drugs. Over the last 3 years he had been having nocturnal attacks of asphyxia. Half a year ago he had right-sided hemiparesis. *Examination data*: The patient is edematous, pale, a little euphoric, talkative; his memory is markedly decreased. Heart boundaries are expanded both to the left and to the right. The pulse is 64-68 per minute, tense; blood pressure – from 200/120 to 180/90 mm Hg. *On ECG:* hypertrophy of the left ventricle and slowing down of the intraventricular conductivity. Eye fundus examination revealed sharp narrowing of the retinal arteries, sometimes with thickening of their walls, pinpoint hemorrhages. The kidneys are almost unchanged; slight albuminuria – 0.06 %.

1. Calculate fluctuations of the patient's mean BP.
2. Classify this hypertension according to the level of BP.

3. What stage of arterial hypertension does the patient have? Justify your conclusion.
4. Point out the target organs of the arterial hypertension in this patient.
5. Explain the pathogenesis of the patient's symptoms associated with his main disease.
6. What are pathogenetically-grounded recommendations for treatment of this patient?

Case 11.

Patient K., 53 years old, was hospitalized with a diagnosis: acute anteroseptal myocardial infarction of the left ventricle. He was given standard therapy but his condition suddenly deteriorated: he developed dyspnea with respiratory frequency of 40/min, cough with foamy pink sputum. Moist rales were auscultated all over the lungs, heart sounds were muffled with an accent of sound II over the pulmonary artery.

1. What complication of myocardial infarction developed in this patient? Justify your answer. Describe the pathogenesis of this complication.
2. What ECG sign indicates the development of an ischemic lesion of the myocardium? Describe its mechanism.
3. Point out the principles of pathogenetic therapy for this patient.

Case 12.

Patient N., 56 years old, was hospitalized with a diagnosis: hypertensive crisis.
History data: The patient has been suffering from arterial hypertension for 10 years. When her blood pressure rose up to 240/130 mm Hg, she developed asphyxia, gurgling rales all over the lungs, cardialgia, tachycardia. At the moment of the attack ECG showed a negative symmetrical T-wave in leads V_2 - V_5.

1. What complication of hypertensive crisis developed in this patient? Justify your answer.
2. What does a negative symmetrical T-wave in the chest leads indicate? Explain the mechanism of its formation.
3. Explain the pathogenesis of this complication.
4. Point out the principles of pathogenetic therapy for this patient.

Pathophysiology of Breathing.

Case 1*.

Patient V., 60 years old, height -160 cm, body mass – 80 kg, was admitted to hospital with complaints of acute weakness, dyspnea, palpitations, cough with "rusty" sputum, headache, drowsiness, decreased appetite, temperature rise up to 38 – 39˚C with marked chills. She became ill several days ago.
Examination findings: body temperature – 38.5˚C; leukocyte count – 13 x 10^9 /l; ESR – 20 mm/h. On auscultation in the left lung crepitation and pleural friction murmur

are heard. Pa O_2 – 60 mm Hg, Pa CO_2 – 50 mm Hg; diffusing lung capacity (DLCO) – 10 ml/ 1 mm Hg/min.

Ventilation indices: breathing rate (BR) – 30/min; tidal volume (TV) – 0.25liters; reserve volume of inspiration (RV_{ins}) -1 liter; vital capacity of lungs (VC) –
2.5 litres; forced vital capacity (FVC) – 2.3 liters ; forced expiratory volume (FEV_{1sec}) – 2 liters; total lung capacity (TLC) – 3.7 liters, dead space volume (DSV) – 150 ml.

1. Calculate and assess minute respiratory volume (MV), minute alveolar ventilation (MAV) and Tiffeneau index.
2. What type of respiration does the patient have?
3. What is the type of lung ventilation disturbance?
4. Is gas diffusion in the patient's lungs disturbed? Confirm your viewpoint.
5. What disease can be thought of?
6. Explain the pathogenesis of the symptoms.

Reference (predictive values): ***Pred***MV = 6.7 l/min; ***Pred***VC = 3.2 l; ***Pred***MAV = 4.3 – 4.5 l/min

Case 2.

Patient K., 45 years old, height – 175 cm, complains of cough with sputum which has been disturbing him for the last three years, expiratory dyspnea, palpitations, increased fatigability, headache. He has been smoking since the age of 15, smokes 2 packs of cigarettes a day.

Examination findings: body temperature is 36.7˚C; ESR – 7 mm/h; barrel chest; bandbox sound on percussion. Diffusing lung capacity (DLCO) is 12 ml/1mm Hg/ min. Forced expiratory flow rate: peak forced expiratory flow rate (PFEFR), maximum forced expiratory flow rate - $MFEFR_{25}$, $MFEFR_{50}$, $MFEFR_{75}$ are less than predictive values.

Ventilation indices: BR – 30/min; VC – 3.8 liters; FVC – 3.3 liters; FEV_{1sec} – 1.4 liters; TLC – 6.6 liters; RV_{ins} – 1litre.

1. Calculate and assess Tiffeneau index and residual lung volume (RLV).
2. Determine the type of lung ventilation disturbance.
3. Determine the type of respiratory insufficiency according to its pathogenesis.
4. What disease can be thought of?
5. Explain the pathogenesis of this disease.
6. What are the symptoms of the disease conditioned by?

Reference (predictive values): ***Pred***VC = 4.65 l; ***Pred***RLV = 1.5 l

Case 3.

Patient N., a 20-years-old woman, height – 164 cm, body mass – 65 kg; complains of periodic attacks of asphyxia with difficulty in expiration which are accompanied by excretion of viscous glassy sputum. The attacks began two years ago after the family had acquired a dog. The attacks are often triggered by inhaling cold air or strong emotions. Her mother suffers from urticaria, her brother has pollinosis.

Examination findings: Diffusing lung capacity (DLCO) – 20 ml/ 1 mm Hg/ min. The results of the test "flow/ volume curve": peak forced expiratory flow rate (PFEFR) and maximum forced expiratory flow rate $MFEFR_{25}$ are not changed, $MFEFR_{50}$ and $MFEFR_{75}$ are less than the predictive values.
Ventilation indices: BR – 20/min; tidal volume (TV) – 0.4 liters; maximum voluntary ventilation (MVV) – 60 l/min; vital capacity of the lungs (VL) –
3.7 liters; forced vital capacity (FVC) – 3.4 liters; forced expiratory volume (FEV_{1sec}) – 2 liters; residual lung volume (RLV) – 1.8 liters; inspiration/ expiration ratio – 1: 1.5.

1. Calculate and assess respiratory reserve (RR), Tiffeneau index and total lung capacity (TLC).
2. What type of lung ventilation disturbance does the patient have?
3. What is the type of respiratory insufficiency according to its pathogenesis?
4. What is this disease called?
5. What long-term consequence can develop in this patient if the disease is progressing? What is the mechanism of its development?
6. Is it reasonable to use M-cholinoblockers in the complex treatment of this patient? Why?

Reference (predictive values): PredMV= 6.3 l/min; ***Pred***VC= 3.7 l; ***Pred***RR = 81.4 l/min; ***Pred***TLC = 5.2 l.

Case 4.

Patient M., 32 years old, height 175 cm, body mass – 80 kg, complains of dyspnea, palpitations, weakness, increased fatigability. On X-ray examination of the chest a large amount of fluid in the pleural cavity is detected. In the pleural puncture transparent fluid with the density of 1.012 and protein content of 12 g/l was obtained. Diffusing lung capacity (DLCO) is 10 ml/ 1 mm Hg/ min.
Ventilation indices: breathing rate (BR) – 35/min; tidal volume (TV) – 0.25 liters; maximum voluntary ventilation (MVV) – 50 l/min; reserve volume of inspiration (RV_{ins}) – 1.2 liters; reserve volume of expiration (RV_{exp}) – 1 liter; vital capacity of the lungs (VC) – 2.5 liters; total lung capacity (TLC) – 3.5 liters; dead space volume (DSV) – 150 ml.

1. Calculate and assess minute alveolar ventilation (MAV), respiratory reserve (RR) and residual lung volume (RLV).
2. What type of lung ventilation disturbance does the patient have?
3. What is the type of respiratory insufficiency according to its pathogenesis?
4. What Tiffeneau index is typical of this pathology?
5. What peculiarities does the test "flow/ volume curve" have in this pathology?
6. What are the patient's complaints mainly conditioned by?

Reference (predictive values): PredVC = 5.0 l; ***Pred***MV = 6.2 l/min; ***Pred***MVV = 110 l/min; ***Pred***RR = 103.8 l/min; ***Pred***RLV = 1.5 l.

Pathophysiology of the Blood System.

Case 1.

A 36-year-old woman was admitted to hospital with complaints of acute weakness, increased body temperature, chills, pains in the loin, dyspnea at rest, pains in the heart area and palpitations. *On examination:* The patient is pale, the skin has a lemon-yellow tint; the spleen is enlarged and painful on palpation.

Blood test: hemoglobin (Hb) – 60 g/l; erythrocytes – 1.8 x 10^{12}/l; hematocrit (Ht) – 0.16 l/l; reticulocytes – 28%; reticulocytes index (RI) – 5.3; thrombocytes – 180 x 10^9 /l; leukocytes – 14.5 x 10^9/l. Leukocyte formula (%): basophils – 1; eosinophils – 4; neutrophils: metamyelocytes -2, band neutrophils – 11, segmented neutrophils – 62; lymphocytes – 17; monocytes – 3. *In the blood smear*: anisocytosis, poikilocytosis, polychromasia, single oxyphilic and polychromatophilic normocytes. Erythrocyte sedimentation rate – 40 mm/h. Iron level in the blood serum – 45 mCmol/l, bilirubin – 85 mCmol/l. Osmotic resistance of erythrocytes (ORE): minimal – 0.56%, maximal – 0.32% NaCl. Coombs test is positive. MCV (mean corpuscular volume), MCH (mean corpuscular hemoglobin), MCHC (mean corpuscular hemoglobin concentration) are normal.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is characterized by this hemogram?
3. Explain the pathogenesis of this pathology and classify it according to its main features (pathogenesis, functional state of the bone marrow, type of hemopoiesis, erythrocyte size and hemoglobin content in the erythrocytes).
4. Explain the mechanism of the symptoms and hemogram changes.
5. What does Coombs test mean?

Case 2.

A 19-year-old woman was admitted to hospital with complaints of attacks of sneezing with profuse watery discharges from the nose, congestion and itching of the nasal sinuses, itching of the eyelids, lacrimation, photophobia, stabbing pain in the eyes. This condition has been observed for the last three years from the beginning of May till June. The patient also complained of weakness, fatigability, decreased appetite, dryness of the skin, brittleness of the nails, hair loss, dyspepsia.

Blood test: Hb – 70 g/l; erythrocytes – 3.5 x 10^{12} /l; Ht – 0.31 l/l; reticulocytes – 3%; reticulocytes index (RI) -1.1; thrombocytes – 280 x 10^9/l; leukocytes – 8.0 x 10^9/l. Leukocyte formula (%): basophils – 0, eosinophils – 13, neutrophils: metamyelocytes – 0, band neutrophils – 4, segmented neutrophils – 56, lymphocytes – 24, monocytes – 4.

In the blood smear: anisocytosis, poikilocytosis, anisochromasia. MCV, MCH, MCHC are decreased, erythrocyte sedimentation rate (ESR) – 20 mm/h. Serum iron level – 5.1.mCmol, bilirubin – 12 mCmol/l.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is characterized by this hemogram? Classify it according to its main features.
3. Explain the pathogenesis of the patient's complaints and possible causes of the disease.

4. What additional investigations must be done to specify the diagnosis?
5. State the main principles of treatment of this disease.

Case 3.

A 59-year-old woman was admitted to hospital with complaints of general weakness, fatigability, severe headaches, dizziness, palpitations, lancinating pains in the chest.
Blood test: Hb – 135g/l; erythrocytes – 4.5 x 10^{12}/l; Ht – 0.40 l/l; reticulocytes – 0.8 %; thrombocytes – 245 x 10^9/l; leukocytes – 5.2 x 10^9 /l; leukocyte formula (%): basophils – 0, eosinophils – 4, neutrophils: metamyelocytes – 0, bands – 3, segmented neutrophils – 59, lymphocytes – 30, monocytes – 4.
In the blood smear: single polychromatophilic erythrocytes. ESR – 9 mm/h. Serum iron level – 17 mCmol/l; bilirubin – 18.55 mCmol/l. Osmotic resistance of erythrocytes (ORE): minimal – 0.44%, maximal – 0.32% NaCl. MCV, MCH, MCHC are within the norm.

1. Determine the color index and the functional state of the bone marrow.
2. Determine the absolute count of neutrophils and lymphocytes in the blood and assess these values.
3. What are the patient's complaints conditioned by?

Case 4.

Patient K., 20 years old, was admitted to hospital with complaints of weakness, increased fatigability, headaches, dyspnea and palpitation on slight exertion. He is known to have been having these symptoms since his childhood. His mother's father suffered from anemia.
Blood test: Hb – 70g/l; erythrocytes – 3.5 x 10^{12}/l; Ht – 0.32 l/l; reticulocytes – 0.4 %; RI – 0.13; thrombocytes – 295 x 10^9/l; leukocytes – 3.9 x 10^9/l; ESR – 38 mm/h. Leukocyte formula (%): basophils – 0, eosinophils – 1, neutrophils: metamyelocytes – 0, bands – 4, segmented neutrophils – 44, lymphocytes – 46, monocytes – 5. *In the blood smear:* anisocytosis, poikilocytosis, microcytosis, anisochromasia. There is an increased content of sideroblasts (ring-form) in the bone marrow. Serum iron content – 64 mCmol/l; latent iron-binding capacity is decreased; serum bilirubin – 14 mCmol/l. MCV, MCH, MCHC are decreased.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is characterized by these symptoms and hemogram? Classify it according to its main features.
3. Explain the etiology and pathogenesis of this disease.
4. What complications can this pathology lead to? What measures should be taken for their prevention?

Case 5.

Patient D., 30 years old, presented with complaints of weakness, dizziness, palpitations, recurrent hepatic colics. She has been ill since her childhood. Her father and sister have a similar disease. On examination pallor of the skin with an icteric tint and enlarged painful spleen were noted.

Blood test: Hb -90 g/l; erythrocytes – 3.2 x 10^{12}/l; Ht – 0.32 l/l; reticulocytes – 20%; reticulocytes index (RI) – 7.1; thrombocytes – 240 x 10^9/l; leukocytes – 14 x 10^9/l; ESR – 28 mm/h. Leukocyte formula (%): basophils – 1, eosinophils – 3, neutrophils: myelocytes – 1, metamyelocytes – 6, bands – 11, segmented – 60, lymphocytes – 15, monocytes – 3. *In the blood smear:* anisocytosis, poikilocytosis, polychromasia, single oxyphilic normocytes. Price – Jones curve is shifted to the left. MCV is normal, MCH is higher than the norm. ORE: minimal – 0.70%, maximal – 0.36% NaCl. Serum iron content – 40 mCmol/l; bilirubin – 46 mCmol/l. Coombs test is negative.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is characterized by these symptoms and hemogram? Classify it according to its main features.
3. Explain the pathogenesis of this pathology and its symptoms.
4. Can you explain the changes in ORE, reticulocyte and leukocyte count, iron and bilirubin content?

Case 6.

Patient S., 16 years old, was admitted to hospital with complaints of weakness, dizziness, increased body temperature, painful swallowing. From his history it is known that he has inhaled benzene vapor for three months with narcotic purposes. On examination he was found to have pale skin, numerous pinpoint and spot hemorrhages, necrotic ulcers of the faucial and oral mucosa. The liver and spleen are not enlarged.
Blood test: hemoglobin – 60 g/l; erythrocytes – 2.0 x 10^{12}/l; reticulocytes – 0.1%; RI – 0; Ht – 18.4 l/l; thrombocytes – 30 x 10^9/l; leukocytes – 2.5 x 10^9/l; ESR –
44 mm/h. Leukocyte formula (%): basophils – 0, eosinophils – 2, neutrophils: metamyelocytes – 0, bands – 1, segmented neutrophils – 25, lymphocytes – 69, monocytes – 3. *In the blood smear:* anisocytosis, poikilocytosis, MCV, MCH, MCHC are within the norm. Bone marrow puncture does not show any signs of hemoblastosis. Serum iron content – 40 mCmol/l; bilirubin – 10 mCmol/l.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is characterized by these symptoms and hemogram? Classify this pathology according to its main features.
3. Determine the absolute neutrophil and lymphocyte count in the blood and assess these values.
4. Explain the etiology and pathogenesis of the disease and the mechanism of the symptoms.

Case 7.

A child, 1 year old, was referred to the in-patient department with a diagnosis: anemia. *History data:* the child is preterm; since the age of 3 weeks he has been on artificial feeding; has had frequent colds. The child has a body mass deficit, decreased appetite, dryness of the skin, hair loss, angular stomatitis, pallor of the skin and mucosa.
Blood test: Hb – 60 g/l; erythrocytes – 3 x 10^{12}/l; hematocrit – 0.3 l/l; thrombocytes – 170 x 10^9/l; leukocytes – 6.4 x 10^9/l; reticulocytes – 2.5%; RI – 0.9; ESR – 22 mm/h.

Leukocyte formula (%): basophils – 0, eosinophils – 2, neutrophils: metamyelocytes – 0, bands – 4, segmented – 32, lymphocytes – 53, monocytes – 9. *In the blood smear:* anisocytosis (microcytosis), poikilocytosis, anisochromasia. MCV, MCH, MCHC are decreased. Serum iron content –
5.8 mCmol/l; bilirubin – 15 mCmol/l.

1. Determine the color index and the functional state of the bone marrow.
2. What type of anemia are these symptoms and this hemogram typical of? Justify your conclusion.
3. Classify this anemia according to its main features.
4. Explain the pathogenesis of anemia and the symptoms of the disease.
5. How do total iron-binding capacity and latent iron-binding capacity of blood serum, coefficient of transferrin saturation by iron and content of sideroblasts in the red bone marrow change in this anemia?

Case 8.

Patient U., 49 years old was admitted to hospital with complaints of progressing weakness, palpitations, dizziness, dyspnea at rest, pain and burning sensation in the tongue, dyspepsia, numbness of the limbs, derangement of motor coordination.
Examination revealed pallor of the skin with a lemon-yellow tint, bright-crimson tongue with flattened papillae. Fibrogastroduodenoscopy showed signs of atrophy gastritis.
Blood test: hemoglobin – 60 g/l; erythrocytes – 1.5 x 10^{12}/l; hematocrit – 0.14 l/l; reticulocytes – 0.4%; RI – 0.05; thrombocytes – 110 x 10^{9}/ l; leukocytes – 3.8 x 10^{9}/l. Leukocyte formula (%): basophils -0, eosinophils -1, neutrophils: metamyelocytes – 0, bands – 1, segmented – 40, lymphocytes – 53, monocytes -5.
In the blood smear: anisocytosis, poikilocytosis, anisochromasia, megalocytes; erythrocytes with Jolly's bodies and Cabot's rings – single ones in the visual field; polysegmented neutrophils – single ones in the visual field. Price – Jones curve is shifted to the right. MCV and MCH are higher than the norm. Serum iron content – 41 mCmol/l; bilirubin – 43 mCmol/h; osmotic resistance of erythrocytes (ORE): min. – 0.54%, max. – 0.34% NaCl. ESR – 28 mm/h.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology are these symptoms and this hemogram typical of?
3. Classify this pathology according to its main features.
4. What main syndromes are typical of this disease? Explain their pathogenesis.
5. How can you explain the changes in iron and bilirubin content in the blood serum and in ORE?

Case 9.

Patient M., aged 39, was admitted to hospital with complaints of weakness, increased fatigability, dizziness, hair loss, brittleness and stratification of the nails, derangement of taste, decreased appetite, pains in the epigastrium exacerbated by fasting, especially in spring and autumn. He suffers from a duodenal ulcer.

Blood test: hemoglobin –70 g/l; erythrocytes – 3.5 x 10^{12}/l; hematocrit – 0.32 l/l; reticulocytes – 1.2%; RI – 0.35; thrombocytes – 360 x 10^{9}/ l; leukocytes – 4.4 x 10^{9}/l. Leukocyte formula (%): basophils -0, eosinophils -3, neutrophils: metamyelocytes – 0, bands – 2, segmented – 65, lymphocytes – 26, monocytes -4.
In the blood smear: anisocytosis, poikilocytosis; Price – Jones curve is shifted to the left. ESR – 19 mm/h. MCV, MCH, MCHC are decreased. Serum iron content – 5.8 mCmol/l; bilirubin – 18 mCmol/l.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology are these symptoms and this hemogram typical of?
3. Classify this pathology according to its main features.
4. Explain the etiology and pathogenesis of this pathology and its main symptoms.
5. Point out possible changes in total iron-binding capacity and latent iron-binding capacity of the blood serum and sideroblast content in the red bone marrow in this pathology.

Case 10.

A 24-year-old woman was admitted to hospital with complaints of weakness, increased fatigability, dizziness, palpitations, dyspnea at rest, hemorrhages on the skin. Examination revealed pallor of the skin, edematous face and numerous pinpoint and spot hemorrhages on the skin. The liver, spleen and lymph nodes are not enlarged.
Blood test: hemoglobin –70 g/l; erythrocytes – 2.1 x 10^{12}/l; hematocrit – 0.21 l/l; reticulocytes – 0.1%; RI – 0.03; thrombocytes – 29 x 10^{9}/ l; leukocytes – 3.0 x 10^{9}/l. ESR – 41 mm/h. Leukocyte formula (%): basophils -0, eosinophils -2, neutrophils: metamyelocytes – 0, bands – 1, segmented – 28, lymphocytes – 63, monocytes - 6.
In the blood smear: anisocytosis, poikilocytosis, toxic stippling of neutrophils. Iron content in the blood serum – 43 mCmol/l, bilirubin – 30 mCmol/l. MCV, MCH, MCHC are within the norm. No signs of hemoblastosis were found at bone marrow investigation.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology are these symptoms and this hemogram typical of?
3. State possible causes of the disease.
4. Explain the mechanism of the symptoms and changes in the hemogram.
5. What complication can develop in this patient and why?

Case 11.

Patient V., 47 years old, a worker at an accumulator factory, was admitted to hospital with complaints of weakness, quick fatigability, frequent headaches, memory worsening, dyspnea and pains in the abdomen and lower limbs. Examination showed ashen pallor of her skin, a grey-lilac border of the gums. Neurological examination revealed symptoms of polyneuritis.
Blood test: hemoglobin –70 g/l; erythrocytes – 3.5 x 10^{12}/l; hematocrit – 0.32 l/l; reticulocytes – 6 %; RI – 2.4; thrombocytes – 210 x 10^{9}/ l; leukocytes – 6.8 x 10^{9}/l. ESR – 18 mm/h. Leukocyte formula (%): basophils -0, eosinophils -3, neutrophils:

metamyelocytes – 0, bands – 4, segmented – 56, lymphocytes – 30, monocytes -7. *In the blood smear:* anisocytosis, poikilocytosis, anisochromasia, basophilic stippling of erythrocytes. MCV, MCH, MCHC are decreased. Serum iron content – 56 mCmol/l, bilirubin – 26 mCmol/l. In the bone marrow there are numerous sideroblasts (ring-form). *In the urine*: the content of aminolevulinic acid is 30 times as high as the upper border of the norm, increased content of coproporphyrin and free protoporphyrin.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology are these symptoms and this hemogram typical of?
3. Classify the disease according to its main features.
4. Explain the pathogenesis of the disease and its main symptoms.
5. What are sideroblasts?

Case 12.

A 53-year-old woman was admitted to hospital with complaints of progressive weakness, palpitations, dyspnea at rest, dizziness, decreased appetite, pain and burning sensation in the tongue when eating spicy and sour food. Examination showed marked pallor of the skin and icteric sclera. Neurological examination did not reveal any pathology. Two years prior to this hospitalization the patient underwent a jejunectomy.

Blood test: hemoglobin –70 g/l; erythrocytes – 1.75 x 10^{12}/l; thrombocytes – 140 x 10^9/ l; reticulocytes – 1 %; RI – 0.23; leukocytes – 3.9 x 10^9/l. ESR – 27 mm/h. Leukocyte formula (%): basophils -0, eosinophils -2, neutrophils: metamyelocytes – 0, bands – 1, segmented – 43, lymphocytes – 50, monocytes – 4. *In the blood smear:* anisocytosis, poikilocytosis, anisochromasia, megalocytes, single oxyphilic megaloblasts and polysegmented neutrophils. MCV, MCH are increased. Serum iron – 46 mCmol/l, indirect bilirubin – 39 mCmol/l. Osmotic resistance of erythrocytes (ORE): min. – 0.58%, max. – 0.34% NaCl.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology are these symptoms and this hemogram typical of?
3. Classify this pathology according to its main features.
4. Explain the pathogenesis of the disease and its main clinical syndromes.
5. What other pathology of the blood system should this disease be distinguished from? Justify your answer.

Case 13.

Patient G., 34 years old, was admitted to hospital in a poor condition after a car accident. On admission: the patient is stuporous, indifferent to his surroundings; the skin is pale, the pulse is thready, BP – 65/30 mm Hg. After an anti-shock therapy the patient's condition improved; BP rose up to 115/70 mm Hg. The treatment was given under a constant control of his blood system condition.

Results of one of the blood tests in the process of treatment: hemoglobin –66 g/l; erythrocytes – 2.5 x 10^{12}/l; hematocrit – 0.23 l/l; reticulocytes – 8.5 %; RI – 2.12; thrombocytes – 380 x 10^9/ l leukocytes – 14 x 10^9/l. ESR – 20 mm/h. Leukocyte formula (%): basophils -0, eosinophils -2, neutrophils: metamyelocytes – 2, bands – 12,

segmented – 60, lymphocytes – 20, monocytes – 4. *In the blood smear:* polychromasia, single oxyphilic normocytes. Serum iron – 12.5 mCmol/l; bilirubin – 19 mCmol/l. Osmotic resistance of erythrocytes: min. – 0.44%, max. – 0.32% NaCl.

1. Determine the color index.
2. What blood pathology are these symptoms and hemogram typical of?
3. Classify the disease according to its main features.
4. Explain the pathogenesis of the disease and stages of its development.
5. Point out (approximately) on what day after hospitalization the repeated blood test was made.

Case 14.

Student U., 18 years old, at a medical check-up complained of increased fatigability, irritability, sleepiness, worsening of memory. She had her blood test made the day before an examination in normal anatomy.

Blood test: hemoglobin –135 g/l; erythrocytes – 4.5 x 10^{12}/l; hematocrit – 0.40 l/l reticulocytes – 0.8 %; thrombocytes – 200 x 10^9/ l; leukocytes – 8 x 10^9/l. ESR – 10 mm/h. Leukocyte formula (%): basophils -0, eosinophils -0, neutrophils: metamyelocytes – 0, bands – 6, segmented – 78, lymphocytes – 10, monocytes – 6.

In the blood smear: single polychromatophilic erythrocytes. MCV, MCH, MCHC are within the norm. Serum iron content – 14 mCmol/l; bilirubin – 14 mCmol/l. ORE: min. – 0.44%, max. – 0.34% of NaCl solution.

1. Determine the color index and absolute neutrophil and lymphocyte count.
2. Assess these values.
3. Explain a possible mechanism of the changes in the hemogram.

Case 15.

Patient G., aged 44, was admitted to hospital with a diagnosis: trichinellosis.

Blood test: hemoglobin –135 g/l; erythrocytes – 4.5 x 10^{12}/l; hematocrit – 0.4 l/l reticulocytes – 0.5 %; thrombocytes – 230 x 10^9/ l; leukocytes – 11 x 10^9/l. ESR – 18 mm/h. Leukocyte formula (%): basophils -0, eosinophils -18, neutrophils: metamyelocytes – 1, bands – 7, segmented – 47, lymphocytes – 21, monocytes – 6.

MCV, MCH, MCHC are within the norm. Serum iron content – 15 mCmol/l; bilirubin – 18 mCmol/l. ESR – 24 mm/h. ORE: min. – 0.46%, max – 0.34% of NaCl solution.

1. Determine the color index and the functional state of the bone marrow.
2. Characterize the changes in the hemogram. Justify your conclusion.
3. Calculate the absolute neutrophil and eosinophil count in the patient's blood.
4. Explain the role of leukocytes in the realization of anti-parasite immunity.

Case 16.

Patient U., 60 years old, was admitted to hospital with complaints of general weakness, excessive sweating, body temperature increase up to 37 -38 ˚C, dyspnea, abdominal pains, dyspepsia. Physical examination revealed pallor of the skin with a lemon-yellow tint, icteric sclera, considerable enlargement of peripheral lymph nodes and the spleen, moderate enlargement of the liver.

Blood test: hemoglobin –80 g/l; erythrocytes – 2.4 x 10^{12}/l; hematocrit – 0.22 l/l; reticulocytes – 3 %; RI – 0.7; thrombocytes – 104 x 10^9/ l leukocytes – 80 x 10^9/l. ESR – 27 mm/h. Leukocyte formula (%): basophils -0, eosinophils -0, neutrophils: metamyelocytes – 0, bands – 1, segmented – 6, lymphocytes – 92, monocytes – 1. *In the blood smear:* anisocytosis, poikilocytosis, single prolymphocytes and Botkin-Gumprecht shadows. On the myelogram – 37% of lymphocytes. Serum iron content – 40 mCmol/l; bilirubin – 68.4 mCmol/l. Coombs reaction is positive. Phenotyping of lymphoid cells with monoclonal antibodies revealed markers CD19, CD20. Cytogenetic investigation revealed trisomy of chromosome 12.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is this hemogram typical of? Justify your answer.
3. Determine the absolute neutrophil and lymphocyte count in the blood and assess these values.
4. Explain the mechanism of the symptoms and changes in the hemogram.
5. Assess a prognosis for this patient.

Case 17.

Patient E., 5 years old, complains of weakness, dizziness, pains in the lower limbs, mild abdominal pain, dry cough. On examination: multiple pinpoint and spot hemorrhages on the skin. The liver, spleen and lymph nodes are enlarged.

Blood test: hemoglobin –90 g/l; erythrocytes – 3.0 x 10^{12}/l; hematocrit – 0.27 l/l; reticulocytes – 0.6 %; RI – 0.2; thrombocytes – 30 x 10^9/ l leukocytes – 17 x 10^9/l. Leukocyte formula (%): blast cells – 75, basophils -0, eosinophils -2, neutrophils: metamyelocytes – 0, bands – 1, segmented – 5, lymphocytes – 15, monocytes – 2.

ESR – 25 mm/h. *Histochemical analysis* of blast cells showed negative reaction to myeloperoxidase and lipids, positive PAS-reaction (periodic acid – Schiff reaction) (polysaccharides in the form of separate granules), positive reaction to TdT (terminal desoxynucleotidiltransferase). Immunophenotyping revealed markers CD10 and CD19.

1. Determine the color index, the functional state of the bone marrow and assess the absolute lymphocyte count in the blood.
2. What blood pathology is characterized by this hemogram? Justify your answer.
3. Explain the pathogenesis of this pathology.
4. Explain the pathogenesis of the symptoms, changes in the hemogram and hemorrhagic syndrome.

Case 18.

Patient M., 45 years old, was admitted to hospital with complaints of weakness, excessive sweating, pains in the left side of the abdomen, palpitations, dyspnea, periodic rise of temperature to 37.5 – 39 ˚C, pain in the bones, easy bruising.

Examination revealed hepatomegaly, splenomegaly, enlarged painful lymph nodes.

Blood test: hemoglobin –70 g/l; erythrocytes – 3.0 x 10^{12}/l; hematocrit – 0.28 l/l; reticulocytes – 0.4 %; RI – 0.1; thrombocytes – 80 x 10^9/ l leukocytes – 450 x 10^9/l. *In the blood smear*: anisocytosis, poikilocytosis, anisochromasia.

Leukocyte formula (%): basophils -7, eosinophils -8, myeloblasts – 4, promyelocytes – 7, myelocytes – 17, metamyelocytes – 24, band neutrophils – 19, segmented neutrophils– 13, lymphocytes – 1, monocytes – 0.

1. Determine the color index and assess the absolute neutrophil, basophile, eosinophil and lymphocyte count in the blood.
2. What blood pathology is characterized by this hemogram? Justify your answer.
3. Explain the mechanism of the symptoms and changed in the hemogram.
4. Name possible etiological factors of this disease.
5. What chromosome abnormality can be found in the majority of patients with this disease?

Case 19.

Patient A., 28 years old, was admitted to hospital with complaints of weakness, increase in body temperature, chills and painful swallowing. She fell ill suddenly. Examination revealed signs of ulcerous necrotic tonsillitis and stomatitis, enlargement and tenderness of the submandibular lymph nodes. From the patient's history it is known that she often takes biceptol.

Blood test: hemoglobin –126 g/l; erythrocytes – 4.2 x 10^{12}/l; hematocrit – 0.39 l/l; reticulocytes – 0.6 %; thrombocytes – 195 x 10^{9}/ l leukocytes – 1.3 x 10^{9}/l. Leukocyte formula (%): basophils -0, eosinophils -0, neutrophils: metamyelocytes – 0, bands – 2, segmented – 13, lymphocytes – 80, monocytes – 5. The proportion of fat and cell elements in the bone marrow is normal.

1. Determine the color index and assess the absolute neutrophil and lymphocyte count in the blood.
2. What blood pathology is characterized by this hemogram? Explain its pathogenesis.
3. What is the origin of the symptoms?
4. What similar pathology should this hematological disorder be distinguished from?

Case 20.

Patient O., a 27-year-old woman, was admitted to hospital with complaints of weakness, dyspnea, dry cough, rise of temperature, chills, pain in the oral cavity, ulceration of the oral mucosa. Examination revealed ulcerous stomatitis and pneumonia which was almost asymptomatic. The liver and the spleen are not enlarged.

Blood test: hemoglobin –96 g/l; erythrocytes – 3.2 x 10^{12}/l; hematocrit – 0.29 l/l; reticulocytes – 0.3 %; RI – 0.1 thrombocytes – 49 x 10^{9}/ l leukocytes – 1.5 x 10^{9}/l. Leukocyte formula (%): basophils -0, eosinophils -0, neutrophils: metamyelocytes – 0, bands – 0, segmented – 22, lymphocytes – 75, monocytes – 3. ESR – 28 mm/h.

In the blood smear: moderate anisocytosis, poikilocytosis, neutrophils with pycnosis of the nuclei and toxic stippling of the cytoplasm. There are no signs of lymphoid metaplasia in the bone marrow punctate. Serum iron – 41 mCmol/l.

1. Determine the color index and the functional state of the bone marrow.
2. What blood pathology is this hemogram typical of?

3. State possible causes of the disease. Explain the mechanism of the symptoms and changes in the patient's hemogram.
4. What complication can develop in this patient and why?

Case 20.

Patient X., 58 years old, was admitted to hospital with complaints of increased fatigability, headaches, vision deterioration, pain in the heart area, nasal bleedings, pains in the bones of the lower extremities, skin itching which exacerbated after exposure to hot water. On examination: cherry-colored skin, hyperemia of the conjunctiva, enlargement of the liver and spleen, arterial hypertension, myocardium hypertrophy.

Blood test: hemoglobin –216 g/l; erythrocytes – 7.2 x 10^{12}/l; reticulocytes – 2.6 %; thrombocytes – 785 x 10^{9}/ l; leukocytes – 12.5 x 10^{9}/l. ESR – 1 mm/h; hematocrit index – 69%. Leukocyte formula (%): basophils -2, eosinophils -8, neutrophils: metamyelocytes – 1, bands – 10, segmented – 67, lymphocytes – 6, monocytes – 6.

In the blood smear: anisocytosis, anisochromasia, polychromasia, single oxyphilic normocytes.

1. Determine the color index and assess the absolute count of basophils and neutrophils in the blood.
2. What blood pathology is characterized by this hemogram?
3. Explain the pathogenesis of the disease and the mechanism of the symptoms.
4. What complications are typical of this pathology and why?

Case 22.

Patient A., 60 years old, was referred to hospital with a diagnosis: pneumonia.

In his history: frequent colds; over the last year he has had pneumonia twice but was treated on an out-patient basis. Examination revealed enlarged neck and axillary lymph nodes of elastic pasty consistency painless on palpation. The liver and the spleen are enlarged. Body temperature at the moment of examination is increased.

Blood test: hemoglobin –100 g/l; erythrocytes – 4.0 x 10^{12}/l; hematocrit – 0.37 l/l; reticulocytes – 0.5 %; RI – 0.2; thrombocytes – 145 x 10^{9}/ l; leukocytes – 53 x 10^{9}/l. Leukocyte formula (%): basophils -0, eosinophils -0, neutrophils: metamyelocytes – 0, bands – 0, segmented – 4, prolymphocytes – 5, lymphocytes – 86, monocytes – 1. ESR – 25 mm/h.

In the blood smear: moderate anisocytosis, Botkin-Gumprecht shadows. In the bone marrow punctate – 30% of lymphocytic elements. Phenotyping of the lymphoid elements revealed antigen markers CD19, CD20.

1. Determine the color index and assess the absolute lymphocyte count in the blood.
2. What blood pathology and what stage of this pathology is this hemogram typical of? Justify your answer.
3. Explain the pathogenesis of the main clinical features and changes in the hemogram. Assess a prognosis for this patient.
4. How can you explain the patient's susceptibility to colds and pneumonias?

Case 23.

Patient B., 23 years old, was admitted to hospital with complains of weakness, increased fatigability, pains in the bones, dyspnea, increased temperature and chills, painful swallowing. Examination revealed signs of ulcerous necrotic tonsillitis, enlargement of the liver, spleen and regional lymph nodes.

Blood test: hemoglobin – 70 g/l; erythrocytes – 2.6 x 10^{12}/l; hematocrit – 0.24 l/l; reticulocytes – 0.4 %; RI – 0.1; thrombocytes – 40 x 10^{9}/ l; leukocytes – 25 x 10^{9}/l. ESR – 34 mm/h. Leukocyte formula (%): blast cells – 78, basophils -0, eosinophils – 1, neutrophils: myelocytes – 0, metamyelocytes – 0, bands – 0, segmented – 10, lymphocytes – 10, monocytes – 1.

In the blood smear: anisocytosis, poikilocytosis. Cytochemical analysis of blast cells revealed: positive reaction to myeloperoxidase and lipids; negative reaction to TdT (terminal desoxynucleotide-transferase). Immunophenotyping revealed antigen markers CD33, CD13. In the bone marrow punctate > 30% of blast cells.

1. Determine the color index and assess the absolute neutrophil and lymphocyte count in the blood.
2. What disease is characterized by these clinical features and this hemogram? Justify your answer.
3. Explain the pathogenesis of the disease, its main symptoms and changes in the hemogram.
4. Point out the principles of treatment.

Case 24.

Patient E., 24 years old, was admitted to an in-patient department with complaints of weakness, increased body temperature, chills, massive sweating, painful swallowing. On examination: the skin is pale with an ashen tint, multiple bruises and hemorrhages, necrotic ulcers of the faucial and oral mucosa. The liver, spleen and some groups of lymph nodes are enlarged and painless on palpation.

Blood test: hemoglobin –60 g/l; erythrocytes – 2.0 x 10^{12}/l; thrombocytes – 28 x 10^{9}/ l; reticulocytes – 0.1 %; leukocytes – 30 x 10^{9}/l. ESR – 51 mm/h. Leukocyte formula (%): blast cells – 86, basophils -0, eosinophils -0, neutrophils: myelocytes – 0, metamyelocytes – 0, bands – 0, segmented neutrophils – 8, lymphocytes – 5, monocytes – 1. *In the blood smear:* anisocytosis, poikilocytosis. Cytochemical analysis of blast cells revealed negative reaction to myeloperoxidase, lipids and polysaccharides (PAS-reaction). Immunophenotyping revealed markers CD7, CD38, CD34.

1. Determine the color index and assess the absolute neutrophil and lymphocyte count in the blood.
2. What disease of the blood system is characterized by this hemogram?
3. Explain the pathogenesis of the symptoms. Assess a prognosis for this patient.
4. Describe a possible etiology and pathogenesis of this pathology.

Case 25**.

Patient G., a 17-year- old girl, presented with complaints of general weakness, malaise, increased body temperature, chills, muscle and joint aches, painful swallowing. Examination revealed enlargement and hyperemia of the tonsils, presence of purulent exudates in the tonsil lacunae. The neck lymph nodes are moderately enlarged, painful on palpation.

Blood test: hemoglobin –150 g/l; erythrocytes – 4.5 x 10^{12}/l; reticulocytes – 0.7 %; thrombocytes – 245 x 10^{9}/ l; leukocytes – 16 x 10^{9}/l. ESR – 24 mm/h. Leukocyte formula (%): basophils -0, eosinophils -2, neutrophils: metamyelocytes – 8, bands – 20, segmented – 56, lymphocytes – 11, monocytes – 3.

1. Determine the color index and assess the absolute neutrophil and lymphocyte count in the blood.
2. Write a conclusion about changes in the hemogram.
3. Explain the pathogenesis of the disease symptoms and changes in the hemogram.

Pathophysiology of Digestion.

Case 1*.

For experimental simulation of stomach ulcers a ligature is placed on the pyloric region of the stomach preserving its passability (Shay's method).

1. Explain the mechanism of ulcer formation in this case.
2. How do secretory and motor functions of the stomach change in this case and why?

Case 2.

Two groups of rats were exposed to immobilization stress. During the experiment one group of rats received natural feeding, the other – parenteral feeding.

1. Explain the mechanism of stress ulcer formation.
2. In which of the two groups are the conditions for ulcer development more favorable and why?
3. What is the difference between stress ulcers and ulcer disease?

Case 3.

Rats with body mass 160 – 180 g were given daily intramuscular injections of 0.5 – 1.0 mg of hydrocortisone per 100g of body mass. After 10 – 15 injections all animals developed erosions and ulcers in the secretory region of the stomach.

1. Explain the mechanism of ulcer formation in this case.

Case 4.

Immunocytochemical investigation of the bioptate taken from the antral mucosa of the stomach of the patient suffering from a duodenal ulcer revealed a sharp increase in G-cell count and a decrease in D-cell count.

1. How can these changes be associated with the development of peptic ulcer disease?

2. What is the name of this syndrome?

Case 5.

A 21-year-old man with an asthenic constitution and blood type O (I) (Rh-) was taken to hospital in a poor condition: his consciousness was confused, BP – 60/30 mm Hg, thready pulse with a rate of 120/min, breathing rate – 20/min. Hb – 40 g/l, erythrocyte count – 2.1 x 10^{12}/l; incoercible coffee-ground vomiting, diurnal diuresis – 200 ml. His relatives reported that the man had been following a course of "remedial fasting" without consulting a doctor for the last 2 weeks to treat his chronic bronchitis with a slight asthmatic component. During this period he did not eat anything and only drank fruit juices. Despite all treatment measures the doctors were not able to stop profuse bleeding and save the patient's life. The post mortem examination showed two large "kissing" ulcers of the pyloric region of the stomach.

1. Explain possible pathogenesis of gastric ulcer formation.
2. What are the clinical manifestations of the disease caused by?

Case 6.

Patient D., 42 years old, a locomotive-driver, in March applied to his physician with complaints of intensive dull pains in the epigastrium radiating to the lumbar region and appearing 1.5 – 2 hours after meals and at night which disappeared after consuming a small amount of food. The patient had similar symptoms the previous autumn but he did not go to a doctor and treated himself with a diet. All the winter he did not have any symptoms. In the spring, however, his pains renewed, became more intensive, heartburns appeared. Twice the patient had nausea and vomiting, constipations became more frequent, once he noticed a tarry stool. Over the last 2 months he has lost 2 kg of weight in spite of a good appetite. The patient smokes a lot (up to 2 packs a day), has a cough with sputum (especially in mornings). He also complains of bad sleep, increased fatigability, irritability, unstable mood, increased sweating.

Examination data: The patient has an asthenic constitution, low body mass; hand type is radial, foot type is intermediate, blood type – O(I). The skin is pale with marked nasolabial folds. The tongue is white and coated, filiform and fungiform papillae are hypertrophic. The abdomen is painful and resistant on palpation, especially in the epigastric region. Mendel's syndrome is positive (tenderness in the epigastrium on percussion). BP – 110/60 mm Hg; heart rate – 60/min; Hb – 105 g/l; erythrocytes – 4.5 x 10^{12}/l; leukocytes – 9 x 10^{9}/l. Urine test is normal. Feces analysis showed creatorrhea and steatorrhea, fecal occult blood test is positive. Basal and stimulated HCl secretion is higher than the norm. Coefficient of gastric juice aggression approaches 1. X-ray examination detected a "niche" symptom in the duodenal bulb area.

1. Make a conclusion about the nature of the patient's main disease. Justify your conclusion.
2. Explain the etiology and pathogenesis of the disease.
3. What additional investigations would you carry out?
4. Point out the principles of pathogenetic therapy for this disease.

Case 7**.

Patient N., 52 years old, a gastroenterologist, often performs endoscopic investigations. Recently she has begun to note gnawing pains in the left epigastric region radiating to the xiphisternum region and left part of the chest. She believed the pains to be caused by angina pectoris and took validol, but unsuccessfully. The patient has paid attention to the fact that pains appear 30 minutes – 1 hour after meals. She has also noted bitter eructation and meteorism, unstable stools, frequent diarrhea. She sleeps badly, her working ability has decreased. She gets tired quickly and has become irritable; her mood is often bad, sometimes depressive.

Examination data: normosthenic body type, subcutaneous adipose layer is within the norm. The tongue is coated and white, the papillae are flattened. Bad smell from the mouth (halitosis); on palpation – tenderness in the left epigastric region. Blood pressure – 140/80 mm Hg, heart rate – 70/min; breathing rate – 16. Hemoglobin – 115 g/l, leukocytes – 8 x 10^9/l. Urine and feces tests are normal. Basal and stimulated secretion of gastric juice is sharply decreased. A test for urease presence in the gastric juice is positive. Proteolytic activity of the gastric juice is increased. Fucose and N-acetylneuraminic acid (NANA) content in the gastric juice is decreased. X-ray examination reveals a "niche" symptom in the upper part of the cardial region of the stomach.

1. Make a conclusion about the nature of the patient's main disease. Justify your conclusion.
2. Explain possible pathogenesis of the disease and the mechanism of the symptoms.
3. Point out the principles of pathogenetic therapy.
4. What complications can this disease lead to?

Case 8.

Patient K., 48 years old, applied to his physician with the following complaints: 20 – 30 minutes after a meal (especially after eating sweet or milk products) he develops an attack of general weakness, dizziness (he has to lie down), sleepiness; his face becomes hot, he sweats, feels palpitation and pain in the heart area, headache, colicky pains in the abdomen and diarrhea. A year ago he underwent a resection of the stomach (Billroth's operation II) for a perforated gastric ulcer.

1. What complication developed in this patient after the operation?
2. Explain possible pathogenesis of this syndrome.
3. How do blood pressure and blood sugar level change in this syndrome?
4. What recommendations should be given to this patient?

Pathophysiology of the Liver.

Case 1.

Patient Sh., a 48-year-old nurse at a TB dispensary, had been having general weakness, ache in the muscles and joints of the extremities, skin itching, continuous nau-

sea (once she vomited) and a decreased appetite for a week before hospitalization. For four days she had been also having a fever (37.5 – 37.7˚C) and taking an anti-flu medicine on her doctor's advice. She was admitted to a hepatology center after having developed jaundice. Her condition was of moderate severity, but persistent skin itching, bad sleep and headaches added to the previous symptoms.

Physical examination findings: marked jaundice of the skin, sclera and mucosa; single hemorrhages on the skin; coated white tongue. The liver is 3 cm lower than the costal arch, soft, tender on palpation and percussion. The spleen is not enlarged.

Blood test: Hb -120 g/l, erythrocytes – 4.5 x 10^{12}/l, leukocytes – 4.7 x 10^{9}/l, erythrocyte sedimentation rate (ESR) – 27 mm/h. AlAT activity - 4 times as high as normal, increased alkaline phosphatase (AP) activity. Total bilirubin – 156.9 mCmol/l, bilirubin index – 81%. "Australian" antigen and increased IgG are detected. Prothrombin index - 73%; decreased content of proaccelerin and proconvertin; decreased albumin/ globulin coefficient. Fasting glucose level ranges from 2 to 4.5 mmol/l.

The jaundice and itching persisted for 45 days. The patient was discharged after two months of treatment with AlAT twice as high as normal.

1. What type of jaundice did the patient have? What are possible causes of its development?
2. Justify your conclusion.
3. Explain the mechanism of the symptoms and changes in the laboratory data.
4. What syndromes are observed in this patient?
5. What changes can be found in the patient's urine?

Case 2.

Patient S., a 32-year-old woman, was admitted to hospital with complaints of acute weakness, dizziness, dyspnea at rest, pain in the heart area and palpitations, headache.

Examination findings: the skin is pale with a lemon-yellow tint, the sclera – icteric, the spleen is slightly enlarged and painful on palpation. BP -140/80 mm Hg, HR – 90 – 100/min.

Blood test: Hb – 40g/l, erythrocytes – 1.5 x 10^{12}/l, reticulocytes – 28%, platelets – 240 x 10^{9}/l, leukocytes – 14.5 x 10^{9}/l. Coombs test is positive. Total bilirubin – 80 mCmol/l, bilirubin index – 20%, serum iron – 45 mCmol/l, total protein level and albumin/globulin index are normal, activity of alanine-aminotransferase (AlAT), aspartate-aminotransferase (AsAT), alkaline phosphatase (AP) and gamma-glutamyltranspeptidase (GGT) – within the norm; the level of LDG is increased, prothrombin index – 95%, ESR – 38 mm/h.

The feces are hypercholic, the urine – dark. The patient is known to have been taking sulfonamide medications for a long time.

1. What type of jaundice does the patient have? Justify your conclusion.
2. Explain the pathogenesis of jaundice in this patient.
3. Name the main features distinguishing this type of jaundice from the others.
4. Explain the mechanism of the symptoms and changes in the laboratory data.

Case 3.

Patient T., a 55-year-old man, was admitted to hospital with complaints of jaundice of the skin and sclera, skin itching, feeling of heaviness in the right infracostal and epigastric area, weakness, dark urine. He became ill three days ago, when he suddenly felt a severe pain in the right infracostal and epigastric area radiating to the right shoulder and lumbar region. The attack had lasted for about two hours and was stopped with an intravenous administration of spasmolytic drugs. A similar attack occurred two days after the first one and was accompanied by nausea, vomit, chills, and temperature rise (up to 38˚C). The next day jaundice, skin itching and colorless feces appeared.

Physical examination findings: The condition is satisfactory, the skin and the sclera are icteric with a greenish tint. BP – 100/60 mm Hg, HR – 54/min, the tongue is moist, the abdomen – soft and tender in the right infracostal area. The liver and gall bladder are not palpated.

Blood test: Hb – 130 g/l, erythrocytes – 4.3 x 10^{12}/ l, reticulocytes – 0.5%, leukocytes – 11.5 x 10^{9}/ l, ESR – 20 mm/h. Total bilirubin is 149 mCmol/l, conjugated bilirubin (CB) – 97 mCmol/l. Activity of alkaline phosphatase (AP) and gamma-glutamiltranspeptidase (GGT) is elevated. AlAT and AsAT are normal. Albumin/globulin index is unchanged; prothrombin index – 95%.

The feces are colorless and contain free fats and fatty acids. The urine is dark and foamy when shaken.

1. What type of jaundice does the patient have? Justify your opinion.
2. Explain the pathogenesis of jaundice in this patient.
3. Make a differential diagnostics with other types of jaundice.
4. Explain the mechanism of the symptoms and changes in the laboratory data.
5. What tactics should a physician choose?

Case 4.

Patient D., 23 years old, applied to an out-patient department because of icteric sclera and dark urine. She had become ill five days before: she was feeling general weakness, nausea, loss of appetite; for three days she had been running a temperature (37.8˚C) with chills. A month before her younger sister had had jaundice.

Examination findings: jaundice of the skin and sclera is not strongly marked. The urine has a color of strong tea, when it is shaken orange foam appears. The feces are of light color. The liver is 1.5 cm below the edge of the costal arch, soft and tender on palpation. The spleen is slightly enlarged.

Blood test: Hb – 140 g/l, erythrocytes – 4.5 x 10^{12}/l, leukocytes – 5.0 x 10^{9}/l, ESR – 9 mm/h. AlAT activity is increased. Total bilirubin is 66 mCmol/l, bilirubin index – 73%. Thymol test is strongly positive, the content of IgM is increased, “Australian” antigen (HbsAg) is absent. Prothrombin index is 85%. The content of urea, ammonium and amino acids is normal. Fasting glucose level – 3- 4 mmol/l.

The icteric period lasted 4 days. The patient was discharged on the 30th day of the disease in a satisfactory condition with normal AlAT.

1. What type of jaundice did the patient have? Justify your conclusion.
2. Explain the pathogenesis of jaundice in this patient.

3. Explain the mechanism of the symptoms and changes in the laboratory data.
4. Assess the functional state of the liver using the data of the laboratory tests.

Case 5.

Patient K., 45 years old, after drinking alcohol and eating fat food felt a girdle pain in the left infracostal region; he vomited; his temperature rose up to 38˚C; chills and acute weakness appeared; BP fell to 70/40 mm Hg. The next three days he was observed by a surgeon because of suspected cholecystitis. On the third day jaundice of the skin developed and the feces became colorless. For the preceding 9 years the patient had been consuming large amounts of alcohol.

Physical examination findings: strongly marked jaundice of the skin and sclera; the hard palate is of saffron color; the subcutaneous veins of the front abdominal wall and chest are distended, the abdomen circumference is enlarged and free fluid is detected in the abdominal cavity. On palpation the pancreatic area is painful; the liver margin is 10 cm below the costal arch; the liver is moderately dense, painless; its margin is sharp. The spleen is dense, its margin projecting 7 cm out of the costal arch. The body temperature is 37.6 ˚C.

Blood test: Hb – 125 g/l; erythrocytes – 4.2 x 10^{12}/l; leukocytes – 4.0 x 10^{9}/l; platelets – 129 x 10^{9}/l. ESR – 24 mm/h. Fasting glucose level – 11.8 mmol/l. Total bilirubin – 599 mCmol/l, conjugated bilirubin – 462 mCmol/l; AP – 1.5 times as high as normal; GGT – 20 times as high as normal; AlAT 3 times exceeds the norm, AsAT - 7 times the norm (AsAT/ AlAT coefficient > 1.33). Total protein – 68 g/l, albumin/globulin coefficient is decreased. “Australian” antigen and alpha- fetoprotein are not detected. Prothrombin index – 75%. Blood amylase content twice exceeds the norm.

The feces are colorless and contain indigested fats and striated muscle fibers. The urine is dark and becomes very foamy when shaken. Echography of the pancreas reveals enlargement of the pancreatic head up to 12 cm with edema and periprocess. Angiogram shows a diffuse lesion of the liver.

1. Make a conclusion about the character of the patient’s disease and its complication. Justify your conclusion.
2. Name the syndromes found in this patient.
3. Explain the mechanism of these syndromes.
4. Determine the type of the patient’s jaundice. Explain its pathogenesis.
5. Explain the mechanism of the changes in the laboratory data.
6. Assess the functional state of the liver and the pancreas.

Case 6.

Patient B., 38 years old, two years ago had a cold after which fever and the symptoms of polyneuritis developed (she could not hold a spoon); the patient lost weight. On examination she was found to have anemia, thrombocytopenia, increased ESR, enlarged liver. A diagnosis “nodular periarteriitis” was made, and the patient was treated with glucocorticoids. Half a year after the treatment with prednisolone had been discontinued, she developed weakness, pains in the right infracostal area and in the

epigastrium, dyspepsia, meteorism, skin itching, subfebrile temperature. Physical examination showed jaundice of the sclera, vascular "spiders" on the chest and shoulders, hyperemia of the face and palms. The liver projected 9 cm out of the costal arch, the spleen was near the edge of the costal arch. Some symptoms of polyradiculoneuritis were still present.

Blood test: Hb – 80g/l; leukocytes – 10 x 10^9/l; ESR – 57 mm/h; total protein – 67 g/l, A/G coefficient is decreased. Conjugated bilirubin – 40 mCmol/l, bilirubin index – 70%. AlAT activity 4 times as high as normal; there is a two-fold increase in AP and GGT. Scanning of the liver revealed its marked enlargement with a diffuse-focal decrease in the accumulation of the preparation in all parts.

The patient's relatives reported that she had been abusing alcohol for 10 years. A considerable improvement of the patient's condition was achieved by administering *Essentiale* intravenously and orally.

1. What liver pathology can be most likely suspected in this patient?
2. What symptoms and syndromes can be found in this pathology?
3. Explain their mechanism.
4. Determine the type of jaundice.

Case 7.

Patient G., 23 years old, suffers from chronic alcoholism; for the last two months he has been taking illegal drugs instead of alcohol. He has not been working for a year and a half. In the last ten days he has been ill, having nausea and vomiting; he has not eaten anything for 4 days. He was taken to hospital by an ambulance in a poor condition after having developed jaundice: he was conscious, but confused and disoriented.

Complaints on admission: nausea, vomiting, headache, dizziness, complete loss of appetite, floaters in the eyes.

Physical examination findings: Body temperature is 36.7˚C. Subcutaneous adipose layer is almost absent; there are marks of injections on the veins of the arms. The patient presents with intensive jaundice, obvious hemorrhages on the skin and mucosa, multiple vascular "spiders", marks of scratching, "hepatic palms" with Dupuytren's contracture and tremor of hands. The liver projects 5 cm out of the costal arch, slightly dense, tender on palpation; the spleen is not enlarged.

Blood test: Hb – 164 g/l; erythrocytes – 4.5 x 10^{12}/l; leukocytes – 12.8 x 10^9/l (neutrophils – 72%); ESR – 2 mm/h. Total bilirubin – 232 mCmol/l, bilirubin index – 52.5%; a six-fold increase in AlAT activity; alkaline phosphatase is within the norm. A high concentration of HbsAg ("Australian" antigen) is detected. Prothrombin index – 45%; decreased content of proaccelirin and proconvertin, A/G coefficient is decreased, increased content of tyrosine and alanine.

The urine is dark and produces orange foam when shaken: the feces are colorless. Aminoaciduria.

A day after hospitalization the patient's condition got worse, he lost consciousness; hepatic smell from the mouth appeared; there were convulsions and vomit. BP decreased; bradycardia developed; there was profuse bleeding from the nose. *Examination data:* total bilirubin – 435 mCmol/l, bilirubin index – 30%; blood pH –

7.75. Prothrombin index – 35%. Decreased blood urea, high blood level of ammonium, hypocalcaemia.
The patient died without regaining consciousness.

1. Make a conclusion about the nature of the patient's disease and type of jaundice.
2. What complication caused the lethal outcome?
3. Explain the pathogenesis of this complication.
4. How was the functional state of the liver changing as the disease progressed?
5. Confirm your conclusions by the objective findings.
6. Explain the mechanism of the observed syndromes and symptoms.

Pathophysiology of the Kidneys.

Case 1.

Patient B., 39 years old, was admitted to an internal disease department with complaints of persistent headaches, impaired vision, fatigability, pains in the heart, nausea, continuous thirst, skin itching, face edemata in the morning. The patient is known to have frequent anginas (tonsillitis). He has been having these symptoms for more than a year.
Examination findings: The patient is pale, the skin is dry. The heart boundaries are extended to the left. BP is 190/100 mm Hg, breathing rate – 25/min.
Blood test: Hb – 90 g/l; erythrocytes – 3.2 x 10^{12} /l; leukocytes – 6.2 x 10^{9}/l, plasma osmolality is > 290 mOsm/l; blood pH – 7.3. Diurnal diuresis is 4 liters, nocturia. In Zimnitsky test the relative urine density in all portions is 1010 – 1012, concentration index – 1.2; creatinine clearance - 40 ml/min; blood urea – 17 mmol/l, creatinine – 0.5 mmol/l.
Urine test: protein 1 – 1.92 g/l (molecular mass >70, 000); leached erythrocytes – 5 – 6 in the vision field, casts – 2 – 4 in the vision field. Selectivity index (ratio of IgG and transferrin) is > 0.1.

1. Assess the functional state of the renal glomerules and renal tubules. Justify your conclusion.
2. Make a preliminary conclusion about the patient's renal pathology and determine the stage of the disease.
3. Explain the etiology and pathogenesis of this disease.
4. Explain the pathogenesis of the main renal and extrarenal syndromes.
5. List the principles of pathogenetic therapy for this patient.

Case 2*.

Patient K., 28 years old, was admitted to hospital 3 weeks after having tonsilitis, with complaints of dull pain in the loin, headache, frequent urination, face edemata (especially in the morning), dyspnea, thirst.
Examination findings: The patient is pale, with edemata on the legs and especially on the face. BP is 180/100 mm Hg; HR – 100; on ECG – signs of diffuse lesion of the myocardium.

Blood test: Hb – 100 g/l; ESR – 26 mm/h; BUN (blood urea nitrogen) – 70-85 mmol/l; increased level of globulin fractions in the blood. Diurnal diuresis is 1litre; relative urine density – 1029; concentration index – 3.3. The urine is cloudy, looks like "meat slops" and contains large quantities of erythrocytes as "shadows"; leukocytes - 6-8 in the vision field, hyaline casts – 3 – 4 in the vision field; protein – 1.5 – 2 g/l (molecular mass < 70, 000). Creatinine clearance is less than 50% of the norm. In the needle bioptate of the kidneys deposits of immune complexes are detected.

1. What disease are these clinical features and laboratory findings typical of? Justify your conclusion.
2. Explain the etiology and pathogenesis of this nephropathy.
3. Assess the filtration and concentration function of the kidneys.
4. Explain the mechanism of the patient's symptoms and syndromes.

Case 3.

Patient N., a 20- year-old woman, was admitted to hospital with signs of sepsis in an extremely severe condition.

Examination findings: The patient is pale with a cyanotic tint and jaundice of the sclera; the body temperature is 36 – 37˚C in the morning and 41 – 42˚C in the evening. She has chills, confused consciousness, nausea, vomit (with the smell of ammonium), edemata all over the body, convulsions and meningeal symptoms. The heart rate is 110/min; the heart boundaries are extended to the left; the tones are muffled; there is a pericardial friction murmur. ECG shows decreased voltage, extrasystoles. The patient has Kussmaul breathing and unstable blood pressure. Diurnal diuresis is about 100 ml, the urine is dark and cloudy; hemoglobinuria, nonselective proteinuria (up to 5 g/l), leukocyturia, large amounts of casts. Concentration index is 0.9.

Blood test: Hb – 60 g/l; pH – 7.0; BUN – 290 mmol/l; creatinine – 0.9 mmol/l; urea – 29 mmol/l; potassium– 7 mmol/l.

1. Assess the functional state of the kidneys.
2. What nephropathy are these clinical features and laboratory findings typical of? Determine the form and stage of this nephropathy. Justify your conclusion.
3. What renal and extrarenal syndromes are characteristic of this pathology? Explain their pathogenesis.
4. Point out the principles of treatment of this pathology.

Case 4.

Patient A., 48 years old, is being treated in the internal disease department for chronic glomerulonephritis. Recently his condition has become worse: he is suffering from persistent distending headaches, night insomnia and daytime sleepiness, dyspnea, vomiting with admixture of blood, diarrhea, skin itching, thirst and bone pain.

Examination findings: the patient is exhausted, torpid and apathetic; his face is edematous with sallow complexion; the skin is dry with scratching marks and hemorrhagic eruptions. BP is 210/120 mm Hg; HR – 100/min, pericardial friction murmur. On ECG there are signs of the left ventricle hypertrophy, impairment of conductivity, ex-

trasystoles. The breathing is noisy and deep; there are signs of congestive phenomena in the lungs.
Blood test: Hb – 80 g/l; erythrocytes – 4 x 10^{12}/ l; creatinine – 0.9 mmol/l; blood urea – 22 mmol/l; pH – 7.25. Diurnal diuresis is 300 ml, isosthenuria.
In the urine there are proteins, casts and erythrocytes (3 – 6 in the vision field).

1. Name the type and the stage of renal insufficiency in this patient. Justify your opinion.
2. What values of BUN and glomerular filtration rate are likely to be found in this patient?
3. Name the main syndromes characteristic of the patient's stage of renal insufficiency and explain their pathogenesis.
4. List the principles of this patient's treatment.

Case 5.

A 46-year-old woman suffering from lipoid nephrosis was admitted to an internal disease department with complaints of marked edemata, weakness, bad appetite.
Examination findings: The patient is extremely pale, edematous, having ascites. The heart sounds are muffled. HR is 96; the heart boundaries are extended.
Blood test: albumins – 15g/l; dysproteinemia, hyperlipidemia, hypercholesterolemia.
In the urine: protein – 20g/l daily (protein molecular mass > 70, 000); hyaline, waxy and granular casts – up to 10 in the vision field.

1. What is this syndrome called?
2. Explain the mechanism of the edemata, presence of casts in the urine and proteinuria.
3. What type of proteinuria is typical of this syndrome? Justify your answer.
4. State the most likely cause of antithrombin III, transferrin and γ-globulin deficiency in this patient. What are the consequences of this condition?

Case 6.

Patient D., a 12-year-old girl, was admitted to hospital with complaints of headache, chills, temperature rise to 39 – 40˚C, pains in the loin and abdomen, frequent and painful urination.
Examination findings: the tongue is dry and coated; BP – 100/60 mm Hg; kidney area is painful on palpation.
In the blood: Hb – 120 g/l; neutrophil leukocytosis with the left shift, BUN (blood urea nitrogen) – 11 mmol/l, ESR – 35 mm/h.
In the urine: protein < 1 g/l (albumins and β- microglobulins); erythrocytes – 3-5 in the vision field (of irregular form < 15%); leukocytes – 25-30 in the vision field; bacteriuria > 150, 000/ml. Diurnal diuresis is 2 – 2.5 liters, hyposthenuria. Creatinine clearance – 100 ml/min.

1. What renal disease are these clinical features and laboratory findings typical of?
2. Assess the function of the renal glomerules and tubules in this patient.

3. Explain the etiology and pathogenesis of this disease and the mechanism of the symptoms.
4. List the principles of therapy of the disease.

Case 7.

Patient K., 43 years old, suffering from urolithiasis, was undergoing a scheduled examination without exacerbation of the disease. In the last months he began to experience more frequent micturition urges, he consumed more water and sometimes had increased temperature (37.2 – 37.6 ˚C). He also developed allergy to certain foods.
Examination findings: blood test without marked changes; ESR – 15 mm/h. Diurnal diuresis - 2 – 2.3 liters.
In the urine: protein < 1g/l; erythrocytes – 2 – 4 in the vision field; leukocytes – 5 -8 in the vision field. Urine density in the morning portion is 1015. Creatinine clearance – 110 ml/min. After a test with an 18-hour liquid-restriction diet the urine density is 1017. Additional investigations are administered: blood glucose test, urine glucose test, ultrasound investigation of the kidneys and urography.

1. What kidney disease has developed in the patient on the background of urolithiasis?
2. Explain the pathogenesis of this disease and its symptoms.
3. Assess the test with a liquid-restriction diet.
4. What is the aim of the additional investigations?
5. State the principles of treatment for this patient.

Examples of Case Analysis.

The Role of Heredity in Pathology.

Case 1*.

- d)

1. recessive, sex-linked
2. because the other X-chromosome has the normal allele suppressing the hemophilia gene
3. deficit of anti-hemophilic globulins – blood clotting factors VIII, IX, XI and, as a result, secondary hemostasis disturbance.

Reactivity, Resistance, Constitution of the Body.

Case 4*.

1. The rat with adrenalectomy has a decreased reactivity (hypoergy) and resistance to physical load as compared with the intact rat.
2. After adrenalectomy a rat develops deficit of most essential adaptive hormones – glucocorticoids, mineralocorticoids and catecholamines – which results in

hyponatremia, hypoglycemia, a sharp decrease in the circulating blood volume, weakening of the influence of the sympathetic nervous system on the heart and vessels. As a consequence, cardiac output and blood pressure decrease, hypoxia and severe muscle weakness develop which reduces reactivity and resistance to physical load.

Allergy, Immunopathology.

Case 8*.

1. The pathochemical stage of the allergic reaction will be more expressed in the animal which received a β-adrenoblocker. B-adrenoblockers decrease, while β-adrenostimulators increase the intracellular content of the secondary messenger – cAMP changing the activity of adenylatcyclase. Persistent increase in cAMP concentration inhibits the input of calcium ions into the cytoplasm of cells, including that of mast cells. This, in turn, inhibits degranulation of mast cells and synthesis of allergy mediators (decrease in phospholipase activation, suppressing myofibril contraction and other calcium-dependent reactions).
2. In order to weaken an anaphylactic reaction the following medications should be given: 1) blockers of allergy mediators' receptors; 2) blockers of allergy mediators' synthesis; 3) stabilizers of mast cell membrane; 4) preparations increasing cAMP concentration in cells.
3. The blockers of allergy mediators' receptors (antihistaminic medications, blockers of leukotriene receptors) prevent stimulation of the corresponding receptors and, thus, inhibit the development of clinical manifestations of allergy (edema, skin itching, rhinorrhea, etc). Blockers of mediator synthesis exert a similar action by inhibiting the synthesis of the corresponding mediators (for example, synthesis of leukotrienes in mast cells). Stabilizers of mast cell membranes are not able to inhibit an anaphylactic reaction once it has developed but they can prevent it if given prophylactically.

Pathophysiology of the Peripheral Circulation.

Case 3*.

Accumulation of a large amount of fluid in the abdominal cavity led to compression of the arterial vessels of the mesentery, a decrease in the blood supply and development of ischemia. In the ischemic area the content of H^+ cations, organic acids, ADP, adenosine, histamine, kinins, prostaglandins and other active substances which decrease the tone of the smooth- muscular cells of the vessel wall became higher. After a quick removal of the ascitic fluid the pressure in the abdominal cavity sharply decreased and blood rushed to the dilated mesenterial vessels which led to the development of regional post-ischemic arterial hyperemia. As a result, blood redistribution in the body occurred and the symptoms of brain ischemia developed.

Pathophysiology of Hemorheology and Hemostasis.

Case 4*.

1. Hemorrhagic syndrome is caused by the disturbance of the primary (vascular-thrombocytic) hemostasis due to thrombocytopenia. A decrease in the throm-

bocyte count occurs as a result of their destruction in the blood via a cytotoxic mechanism by means of IgG_3 –antibodies and activated complement proteins. Thrombocytopenia is associated with petechial hemorrhages.

2. Production of thrombocytopoietins is increased which leads to an increased production of thrombocytes in the bone marrow. Despite this fact, the normal thrombocyte count is not restored because of their intensive destruction.
3. Positive dynamics after the administration of corticosteroids is connected with their anti-inflammatory and immunodepressive effect.
4. The pathogenetic therapy includes: immunodepressants, plasmapheresis, splenectomy, local and general hemostatic medications.

Inflammation, Acute Phase Response, Fever, Hyperthermia.

Case 15.

Increased production of prostaglandins is associated with activation of phospholipase A_2. Phospholipase A_2 breaks down phospholipids of the cell membrane allowing a release of acids, including polyunsaturated arachidonic acid which has 20 carbon atoms and 4 double bonds.

Arachidonic acid is a substrate for the synthesis of many mediators of inflammation: prostaglandins, thromboxan A_2, leukotrienes and lipoxins. Prostaglandins dilate microcirculatory vessels, increase vascular permeability, contribute to the development of inflammatory hyperemia and edema, increase sensitivity of the nerve endings to various pain stimuli (histamine, bradykinin, serotonin, etc). Thromboxan A_2 participates in platelet activation; platelet-activating factor (PAF) causes platelet activation and aggregation and bronchial muscle spasm. Leukotrienes increase vascular permeability, cause contraction of smooth muscles of the vessels, intestines and bronchi. Leukotriene B_4 is a powerful chemoattractant for leukocytes. Lipoxins exert an anti-inflammatory action.

Besides, phospholipase A_2 participates in the initial stage of formation of one more inflammatory mediator which has a lipid nature – platelet activating factor (PAF) (see above).

Phospholipase A_2 activity can be reduced by using glucocorticoids.

Pathophysiology of Acid-Base Balance.

Case 1*.

Patient N., 62 years old, has **uncompensated metabolic (non-gaseous) acidosis without an increase in AG. Isoosmolalic hypohydration.**

Loss of water, bicarbonate and electrolytes occurs via the fistula of the intestines. Diurnal production of the gastric juice is 65% of the extracellular fluid volume and its osmolality is equal to that of the blood plasma, that is why isoosmolalic hypohydration develops. Bicarbonate deficiency causes acidosis. The value of BE (- 8 mmol/l) points to base deficiency. Normal pCO_2 indicates the absence of respiratory compensation. The symptoms are mainly caused by dehydration, decrease in circulating blood volume (BV) and BP, thickening of the blood, derangement of the central and peripheral circulation, hypoxia.

Cl^- concentration in the plasma must be increased because the value of AG is normal. It means that in order to preserve electroneutrality the decreased HCO_3^- concentration is compensated for by an increase in the concentration of Cl^- ions, which come to the plasma from erythrocytes.

To compensate for acidosis (to excrete H^+ and return bicarbonate) and hypohydration (to decrease diuresis) the kidneys: a) increase ammoniogenesis;
b) increase reabsorption of bicarbonate; c) increase sodium reabsorption; d) increase secretion of H^+ and K^+; e) increase reabsorption of water.

The activity of RAAS is compensatorily increased, because when BV, renal blood flow and activation of the sympathetic nervous system are reduced, the output of renin from the juxtaglomerular apparatus rises. RAAS provides the retention of water and sodium in the organism and increases the vascular tone.

For correction of acidosis sodium bicarbonate or trisamine solution is infused which binds H^+ and increases HCO_3^- . Hypohydration is removed by administration of isotonic NaCl solution, 2.5 – 5% solution of glucose with insulin. It is essential to remove the cause which has led to the acid-base imbalance.

Pathophysiology of Metabolism.

Case 7*.

1. It is necessary to determine the quantity of receptors to LDL on the patient's cells (culture of fibroblasts, thrombocytes, lymphocytes). The borderline with pathology – 70% of the norm.
2. Hypocholesterol diet – moderate restriction of product energy value, decreased amount of easily available carbohydrates, restriction of animal fats (recommended products – "lean" meat [veal, chicken], curds, skim milk) and eggs, greater consumption of vegetable oil, fish, vegetables and fruit, restriction of salt.
3. Cholestiramin binds bile acids in the intestines. Thus, the amount of bile acids which return from the intestines to the liver is reduced. Their synthesis in the liver from the cholesterol depot increases and the number of receptors to LDL on the liver cells becomes greater in order to take cholesterol from the blood. → The level of cholesterol in the blood becomes lower. A preparation of nicotinic acid – for example, niacin - reduces production of LDL in the liver and elevates production of HDL. Inhibitors of hydroxymethylglutaril –coenzyme A –reductase suppress the synthesis of cholesterol in the liver. In all situations a decrease in cholesterol in the cell is a signal determining the number of LDL receptors on hepatocytes. The cells take more cholesterol from the blood and its blood level drops. But in the homozygous form of hypercholesterolemia type IIa non-functioning receptors to LDL are formed: they penetrate the cell membrane but cannot bind LDL because they have lost affinity to these lipoproteids. Such receptors do not bind blood cholesterol despite any changes in the cholesterol content in hepatocytes.
4. Without treatment the prognosis is unfavorable. As a rule, such patients die early from myocardial infarction.
5. The most promising current treatment is immunosorption of LDL on sorption columns with monoclonal antibodies against LDL.

Case 9**.

1. Petrov: an increased activity of lipoproteidlipase which catalyzes hydrolysis of chylomicrons' triglycerides (the content of which increases after consumption of fat food) to free fatty acids and glycerin. FFA are absorbed by cells of the extrahepatic organs, including adipose tissue, where resynthesis of triglycerides from FFA and fat deposition occur.
   Sidorov : activation of hormone-sensitive lipase (HSL) which causes lipolysis of triglycerides of fat depots and release of NEFA (non-esterified fatty acids) which are used as a source of energy in considerable physical exertion.
2. Petrov will develop alimentary hyperlipidemia which is characterized by elevated blood content of chylomicrons - carriers of exogenous triglycerides to the sites of their utilization and deposition.
   Sidorov will develop transport hyperlipidemia which results from enhanced lipolysis of triglycerides by HSL. Considerable physical exertion is a stress leading to a release of epinephrine and glucocorticoids which activate HSL.
3. Consequences of hyperlipidemia:

- Fat infiltration of the liver
- Obesity (alimentary)
- Atherosclerosis

Case 10.***

1. Chylomicrons are synthesized in the enterocytes of the small intestines from the products of hydrolysis of alimentary fats. They get into the blood via the lymphatic ducts and transport exogenous triglycerides to the sites of their utilization and deposition. LDLs are formed from IDL (intermediate density lipoproteids) under the influence of hepatic triglyceridelipase. The main function of these lipoproteids is to transport cholesterol to peripheral cells.
2. LDLs possess a marked atherogenic effect. Due to their small size they can penetrate into the extravascular space and via the ligand-receptor interaction (apo-B_{100}- LDL receptor) deliver cholesterol to cells, including the cells of the vascular wall.
3. Statins are inhibitors of HMG -CoA- reductase, an enzyme which takes part in the synthesis of cholesterol. A decrease in the enzyme activity leads to a lower cholesterol synthesis. Thus, administration of statins is indicated to patient S. Decreased synthesis of cholesterol in the cell requires its increased uptake from the blood. As a result, the number of receptors to LDL increases which leads to enhanced removal of LDL from the blood and a reduction in total cholesterol content.

Pathophysiology of Tissue Growth.

Case 3*.

1. The second sequence.

2. Stages of initiation and promotion. DMBA is a powerful carcinogen, it causes irreversible changes in cells, actually turning some tissue cells into cancerous. The initiator is followed by a promoter. The promoter enhances proliferative processes in the tissue and contributes to the tumor cell selection. Turpentine kills cells and its action can be allowed only after the effects of the initiator and the promoter (turpentine itself is neither initiator nor promoter).
3. Initiating agents can be chemical carcinogens, viruses, ionizing radiation. Promotion effect is caused by hormones of steroid nature, secondary bile acids, metabolites of some aminoacids. The role of promoters can be played by alimentary fats (linoleic acid and prostaglandins which are formed from it). Antipromotion effect is exerted by oleic acid, alimentary fibers, vitamin A. Chronic mechanical irritation of a tissue (chronic inflammation) can also play a role of promoter.

Pathophysiology of the Nervous System.

Case 2*.

1. Myasthenia gravis.
2. Appearance of autoantibodies to acetylcholine receptors on the postsynaptic membrane of the skeletal muscle fibers.
3. A decrease in the number of acetylcholine receptors on the postsynaptic membrane, weakening of excitatory action of acetylcholine on a muscle.
4. Use of cholinesterase blockers to increase the concentration of acetylcholine in the synaptic cleft and facilitate a neuromuscular transmission (eserine, neostigmin, tensilon). Thymectomy. Plasmapheresis to reduce the concentration of autoantibodies in the blood. Immunodepressants, corticosteroids. Antilymphocytic globulin.

Case 5**.

1. Alzheimer's disease.
2. Disturbance of cholinergic communications between the neurons of the basal ganglia (Meynert's nucleus) and the hippocampus cortex.
3. Higher nervous activity disorders.
4. Use of central blockers of cholinesterase: acridine, physostigmin.

Pathophysiology of the Endocrine System.

Case 1*.

1. (I) Itsenko-Cushing's syndrome, iatrogenic form; (II) withdrawal syndrome, acute adrenal insufficiency.
2. Excessive fat deposits mainly on the face (moon-like face), in the shoulder girdle area, chest, abdomen and in the area of the 7^{th} cervical vertebra ("climacteric hump"). The extremities become thinner or preserve their usual size.
3. Different tissues have different quantity of receptors to glucocorticoids, epinephrine, insulin and androgens. Thus, in hypercortisolism some tissues can have predominant catabolism of proteins (skin, striated muscles) or fats (adipose tissue of

the extremities). In the blood there are increased levels of FFA, VLDL, LDL and glucose which is released by the liver due to enhanced gluconeogenesis. In response to this, hyperinsulinism develops. Insulin contributes to conversion of glucose and FFA into triglycerides which are deposited as fat at the sites characteristic of this syndrome. Purple striae are noted at the sites of fat deposition because the thinned skin stretches and subcutaneous hyperemic capillaries (hypervolemia + erythrocytosis) become visible.

Hypertension develops as a result of 1) increased heart work in response to increased blood volume and permissive effect of glucocorticoids on catecholamines; 2) vascular spasm due to hypernatremia, permissive effect of glucocorticoids, increased synthesis of endothelins and a decrease in nitrogen oxide; 3) increased synthesis of angiotensin and angiotensin converting enzyme (ACE).

4. The basis of acute adrenal insufficiency is the atrophy of the adrenal cortex which developed via a feedback mechanism as a result of prolonged treatment with glucocorticoids: increase in exogenous glucocorticoids → decrease in corticotrophin-releasing factor synthesis in the hypothalamus → decrease in ACTH synthesis in the pituitary gland → atrophy of the adrenal cortex. This led to a decreased production of glucocorticoids as well as mineralocorticoids which resulted in sodium loss with urine, hypovolemia, absence of permissive effect of glucocorticoids on catecholamines and hypotension, as well as hypoglycemia.
5. The principle of therapy is replacement: administration of glucocorticoids, sodium, water and glucose. The principle of prevention: gradual withdrawal of the preparation; gradually decreasing dose of glucocorticoids; possibly, additional administration of ACTH.

Pathophysiology of the Cardiovascular System.

Case 2*.

1. Myocardial infarction affecting the anterior wall of the left ventricle. Possible cause – thrombosis of the stenotic left coronary artery with its total obstruction (probably with a plaque destruction).
2. Acute phase response and development of resorptive-necrotic syndrome.
3. Release of alenosine, the degree of the myocardium stretching and quantity of dead cells are of importance.
4. Administration of thrombolytics, analgesics, use of nitrates, anti-aggregation preparations; later administration of ACE inhibitors to prevent the myocardium remodeling.

Pathophysiology of Breathing.

Case 1*.

1. V., aged 60, MV = 7.5 l/min; *P*MV = 1.81 x 3.7=6.7 l/min; *P*VC = 3.2 liters, MAV = 3.0 l/min; Tiffeneau index – 80%.
2. Polypnoea. 3. Restrictive.
4. Yes, because DLCO is < than normal.
5. Pneumonia.

6. The symptoms are due to exudative inflammation in the lungs, hypoxia and APR.

Pathophysiology of the Blood System.

Case 9*.

1. Color index – 0.85. Classification: CI –normochromic; mean erythrocyte diameter – normocytic; type of hemopoiesis – normoblastic; functional state of the bone marrow – hyperregenerative; pathogenesis – due to increased erythrocyte destruction.
2. Autoimmune hemolytic anemia.
3. Explanation: typical clinical features of a hemolytic crisis, hyperregenerative course (increased content of reticulocytes – up to 28%, increased RI – up to 5.3%, polychromasia, presence of single oxyphilic and polychromatophilic normocytes, neutrophil leukocytosis with the left nuclear shift). Increased content of bilirubin and iron in the blood serum and decreased minimal ORE; positive direct Coombs test. Pathogenesis of this anemia is associated with autoimmune damage to erythrocytes which develops according to cytotoxic type of immune reactions. The basic mechanisms: 1) complement –dependent lysis of erythrocytes with participation of the large membrane attack complex C5b,C6,C7,C8,C9; 2) antibody-dependent cytotoxicity with perforine mechanism; 3) phagocytosis.
4. Increased body temperature and chills are manifestations of APR. Weakness, pains in the heart area, palpitations and dyspnea at rest are connected with heme-type hypoxia. Enlargement and tenderness of the spleen are conditioned by massive hemolysis of opsonized erythrocytes in this organ. High content of reticulocytes and appearance of single normocytes is conditioned by sharp activation of erythropoiesis. Decreased content of oxygen in the blood stimulates production of erythropoietins in the juxtaglomerular apparatus of the kidneys. Action of cytokines (IL-1, IL-3, GM –CSF) secreted by activated macrophages and other cells increases proliferation of early and late precursors of erythrocytes. A decrease in the minimal ORE is explained by damage to the membrane, swelling and increased spherical index of erythrocytes.
5. Direct Coombs' test using ass's and rabbit's antisera to human IgG and IgM reveals the presence of anti-erythrocyte antibodies.

Case 25**.

1. Absolute neutrophil count 13.44 x 10^9 /l is higher than the upper limit of the norm and indicates absolute neutrophilia. Absolute lymphocyte count 1.76 x 10^9 /l is within the norm, percentage of lymphocytes is decreased which indicates relative lymphocytopenia.
2. An increase in the absolute neutrophil count, presence of metamyelocytes in the peripheral blood, increased content of bands and a higher index of the nuclear shift – all indicate neutrophil leukocytosis with the left shift.

3. Neutrophil leukocytosis in bacterial infection develops by stages. Increased activity of the sympatho-adrenal system and an increase in cardiac output (as a manifestation of stress reaction in APR) cause mobilization of the marginal pool of leukocytes. Elevated production of IL-1, IL-6, GM-CSF and G-CSF in APR as well as increased production of glucocorticoids by the adrenal cortex causes an accelerated release of bands and segmented neutrophils into the peripheral blood from the bone marrow reserve. An increase in IL-1, IL-6, GM-CSF and G-CSF content in the blood stimulates proliferation and differentiation of early and late precursors of neutrophils in the red bone marrow.
4. Weakness, anorexia, fever, pain in the muscles and joints are manifestations of CNS reaction to the action of APR mediators. Hyperemia, edema of the tonsils, accumulation of pus in the lacunae, painful swallowing and swelling of the neck lymph nodes are manifestations of acute streptococcal infection.

Pathophysiology of Digestion.

Case 1*.

Formation of erosions and ulcers on the gastric mucosa is caused by an increase in the secretory function of the stomach, derangement of the motor-evacuation function, damage to the mucous barrier due to an increase of the vagus tone, activation of the sympatho-adrenal system, enhanced release of glucocorticoids by the adrenal glands. Besides the direct effect of the surgical trauma and artificial stenosis of the pylorus and the absence of buffer action of food (the rats only receive water), the animals develop stress accompanied by disorders of the neuro-endocrine regulation of the gastrointestinal tract.

Case 7**.

1. Ulcer disease of the cardial region of the stomach ("niche" symptom).
2. Possible pathogenetic mechanisms: 1) helicobacteriosis (presence of urease in the gastric juice, bad smell from the mouth can be caused by release of ammonium, meteorism – by excessive formation of CO_2 under the influence of *Helicobacter pylori*); 2) disturbance of the mucus composition (decrease of sialic acids – fucose and NANA - in the gastric juice is a marker of the mucus condition); 3) increase in proteolytic activity of the gastric juice despite hypoacidic condition. One should pay attention to the peculiar features of the pain syndrome (early in ulcers of the cardial region versus late in ulcers of the pyloric region and duodenal ulcers; peculiarities of irradiation). Bitter eructation can be a sign of the presence of duodeno-gastral reflux. Diarrhea is a result of hyposecretion of the gastric juice. Endoscopy is a risk factor for infection with *Helicobacter pylori*. Flattening of the papillae is characteristic of atrophy gastritis with a decreased secretion in contrast to their hypertrophy in an increased secretion of the gastric juice.
3. Possible complications of ulcer disease: stomach cancer (especially in achylia), bleeding, perforation, penetration.

Pathophysiology of the Liver.

Case 1*.

1. Hepatic (parenchymatous) jaundice in the patient with viral hepatitis B of moderate severity.
2. Viral hepatitis is characterized by signs of APR from the onset of the disease and detection of "Australian" antigen (antigen of virus B). The jaundice is hepatic, because on the background of high hyperbilirubinemia there are signs of a marked decrease in the hepatic function: disturbance of the synthesis of albumins (decreased A/G coefficient) and procoagulants (prothrombin, proaccelerin, proconvertin), derangement of carbohydrate metabolism (hypoglycemia). An increase in AlAT (a cytolytic enzyme) indicates hepatocyte damage. The patient is discharged in a state of incomplete recovery (increased AlAT).
3. The symptoms (weakness, muscle and joint aches, dyspepsia, fever, accelerated ESR) are manifestations of APR conditioned by inflammatory process in the liver and intoxication. Viruses in conjunction with autoimmune mechanisms damage hepatocytes, causing disturbance of excretion and, later, entrapment and conjugation of UB. The content of CB and, to a lesser degree, UB in the blood increases. Since total bilirubin is >>35 mCmol/l, jaundice develops. The inflammatory process in the liver is accompanied by edema and infiltration, the liver becomes enlarged. The content of fatty acids and, possibly, other toxic metabolites in the blood increases which leads to skin itching, sleep disorders and headaches. The synthesis of procoagulants in the damaged liver is impaired and, thus, hemorrhagic syndrome develops due to disturbance of the secondary hemostasis. Hypoalbuminemia and hypoglycemia result from disturbance of the metabolic function of the liver.
4. The following syndromes are present: jaundice, cholestasis (its marker is an increased content of AP in the blood), cholemia (skin itching is associated with elevated content of fatty acids), syndrome of hepatocellular insufficiency. Typical pathological processes – acute phase response and inflammation are noted.
5. The patient's urine must be dark because of the presence of CB (its content in the blood is > 34 mCmol/l and it easily passes through the renal filter) and must foam when shaken due to the presence of fatty acids which decrease its surface tension.

Pathophysiology of the Kidneys.

Case 2*.

1. Acute glomerulonephritis. There is a characteristic association with an infectious disease, signs of predominant damage to the glomerular apparatus while the normal functioning of the tubules is preserved. The symptom of "humps" in the bioptate, presence of antistreptolysin-O and decreased fraction of the complement confirm the immune character of the nephropathy.
2. Glomerulonephritis is an immune nephropathy which usually develops 10-20 days after an infectious disease. In the process of infection large quantities of immune complexes (antigen + antibody) activating the system of complement accumulate in the glomerular apparatus. Thus, immune inflammation develops which attracts neutrophils, macrophages, thrombocytes and other cells. Under the

influence of the mediators thrombosis of the glomerular capillaries occurs which leads to a decrease of the filtration area, lower renal bloodflow; effective filtration pressure drops, permeability of the renal vessels increases.

3. Creatinine clearance in the patient shows a sharp decrease in the filtration and excretory function of the kidneys. Instead of 100 ml/min only 50 ml of primary urine is filtered, and hence, only 50 ml of blood instead of 100 is cleared from the toxic substances. Concentration index and relative density of the urine are normal which points to the normal function of the renal tubules.
4. Oliguria (diuresis 1 liter) is caused by decreased glomerular filtration. "Urine" syndrome – selective proteinuria, hematuria, leukocyturia, presence of casts in the urine – is a consequence of inflammation and increased vascular permeability.

Hyperhydration and edema result from oliguria and RAAS activation.

Arterial hypertension is caused by increased blood volume and increased tone of the arterioles under the influence of AT-II, vasopressin and sodium retention due to RAAS activation.

Anemia (low Hb) can be a result of hematuria.

Azotemia (BUN >30 mmol/l) is caused by weakening of the excretory function of the glomerules.