**STATE UNIVERSITY OF MEDICINE AND PHARMACY**

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**INDIVIDUAL WORKBOOK**

**Semester V**

**Student: .........................................................**

**Year: .................. Group: ..................**

**Faculty: .........................................................**

**Chișinău, 2025**

**Topic 1: Cell injuries. Necrosis. Reduced and exaggerated apoptosis. Dystrophy.**

**Clinical case 1**

Patient A., 55 years old, who suffers from atherosclerosis, was urgently admitted with the following complaints: retrosternal pain radiating to the shoulder blade and left arm (nitroglycerin administration does not alleviate the pain), general weakness, and sweating. Presumptive diagnosis – myocardial infarction.

**Objective:** pallor, cold and moist skin;
**ECG:** ST-segment elevation; pathological Q wave.
**Blood:** elevated total CK (creatine kinase), CK-MB > 190 U/L (Normal < 24 U/L), troponin I, myoglobin, LDH, AST, lactate. Hypercholesterolemia. Hyperkalemia.

**Questions:**

**1. What are the pathogenetic mechanisms of hypoxic injury? (Example of a pathogenetic chain)**

**2. What is the pathogenetic mechanism of hypoxic injury through the cessation of Na⁺/K⁺ pump activity?**

**3. What is the pathogenetic mechanism of hypoxic injury through the cessation of Ca²⁺ pump activity?**

**4. What is the pathogenetic mechanism of hypoxic injury through the activation of anaerobic glycolysis?**

**5. What is the role of oxidative stress in the pathogenesis of cellular hypoxic injury?**

**6. What indicators confirm cardiomyocyte injury in the patient?**

**7. What is the mechanism of hyperkalemia, and what electrophysiological changes are observed in the patient as a result?**

**Clinical case 2**

At the first breastfeeding, the mother noticed that the new-born was suffocating and feeding was impossible. Examination of the new-born revealed a defect of the hard palate in the form of a cavity (“cleft palate”).

**Questions:**

**1. What disorder of the apoptosis process developed in the child during the embryonic period? Definition of apoptosis. Examples of pathologies resulting from excess or deficiency of apoptosis.**

**2. The intrinsic mechanisms of apoptosis. The role of the BCL-2 family proteins, Bax, Bad, Apaf-1.**

**3. The extrinsic mechanisms of apoptosis. The role of TNF, FAS-L.**

**4. What are the criteria for differentiating apoptosis from necrosis.**

**5. What role do mitochondria play in the process of apoptosis? Argue.**

**6. What are the positive and negative signals for the initiation of the apoptosis process?**

**Clinical case 3**

Patient G., 52 years old, was admitted to the hepatology department with a preliminary diagnosis of "hepatitis." From the medical history, for 20 years he has been under the care of a narcologist with the diagnosis of "chronic alcoholism." Objective - enlarged liver with soft consistency. Liver biopsy performed for diagnostic purposes: Haematoxylin and eosin staining revealed cytoplasmic vacuolization of hepatocytes, and Sudan staining showed fat droplets.

Biochemical analysis: Moderately elevated AST and ALT, elevated triglycerides.

**Questions:**

**1. What causes contribute to fatty liver disease?**

**2. Through what mechanisms has alcohol contributed to the development of the dystrophy?**

**3. What metabolic processes have been affected and contributed to the accumulation of lipids in hepatocytes?**

**4. How does oxidative stress contribute to the damage of hepatocyte structure and to the intracellular accumulation of lipids?**

**5. What is the pathogenetic mechanism of dystrophies affecting the mitochondria?**

**6. What is the pathogenetic mechanism of dystrophies affecting the functioning of the cell membrane pumps?**

**7. What are the possible consequences of hepatic dystrophy?**

**Topic 2: Cell adaptation processes. Atrophy. Hypertrophy. Hyperplasia. Physiologic and pathologic regeneration.**

**Clinical case 1**

In patient N., 60 years old, which suffer for 30 years - arterial hypertension, the echocardiographic examination revealed an increase in myocardial mass and thickening of the left ventricular wall.
 Microscopic examination: left ventricle - diffuse proliferation of connective tissue; cardiomyocytes enlarged in volume, with a large nucleus. Electron microscopy shows an increase in the number and size of cellular organelles (mitochondria, endoplasmic reticulum, ribosomes, Golgi apparatus).

**Questions:**

1. **What are the pathogenic mechanisms of hypertrophy under conditions of cardiac overload?**
2. **What are the triggers for genome modification that activate the anabolic process at the cardiomyocyte level?**
3. **What are the common and distinctive signs of physiological and pathological hypertrophy of the myocardium?**
4. **What is the difference between hypertrophy and hyperplasia in the regenerative process?**
5. **What are the types of pathological hypertrophy? Examples.**
6. **What are the types of physiological hypertrophy? Examples.**

**Clinical case 2**

Patient R., 45 years old, was admitted to the endocrinology department with the diagnosis of "secondary hypothyroidism," presenting the following complaints: fatigue, drowsiness, memory loss, hair loss, brittle nails, and weight gain.

For diagnostic purposes, a thyroid gland biopsy was performed. Microscopic examination revealed a reduction in the number and size of follicles.

**Questions:**

1. **What typical pathological process in the thyroid gland has developed in this patient? Provide arguments.**
2. **What pathogenic factors contribute to the decrease in the number, size, and function of the thyroid gland in this patient?**
3. **What is the relationship between the intensity of the anabolic and catabolic processes in the pathogenesis of atrophy?**
4. **What is the pathogenetic role of ubiquitin-proteasome pathway activation in this pathological process?**
5. **What types of pathological atrophy do you know? Mechanisms of pathological atrophy. Examples.**
6. **What types of physiological atrophy do you know? Examples.**

**Clinical case 3**

A 55-year-old man with a 20-year history of chronic viral hepatitis C presents to the doctor with symptoms of persistent fatigue, moderate jaundice, and abdominal enlargement.

**Abdominal ultrasound:** confirms a nodular structure of the liver and ascites.
**Liver biopsy:** indicates excessive deposition of connective tissue in the liver parenchyma, macronodules, and signs of inflammation.

**Questions:**

1. **What is the typical pathological tissue process in the liver observed in this patient?**
2. **What etiological factors contribute to the development of hepatic cirrhosis?**
3. **What is the role of chronic inflammation in the pathogenesis of sclerosis?**
4. **What are the sources of sclerosis?**
5. **What is collagenogenesis and collagenolysis and what is the balance of these processes (collagenogenesis and collagenolysis) in this patient?**
6. **Which type of macrophages, M1 or M2 (classically or alternatively activated), activate fibroblasts and subsequently lead to excessive extracellular matrix deposition?**
7. **Which cytokines are important fibrogenic factors, and what is their role?**
8. **What conditions would be necessary for physiological regeneration in the liver?**

**Clinical case 4**

Patient X, 40 years old, was admitted to the gynaecology department with the following complaints: metrorrhagia lasting 8 days, moderate pain in the suprapubic region, and general weakness.

**Laboratory analysis:** hyperestrogenism.

**Physical examination:** pallor, BP = 90/60, pulse = 105, abdomen bloated, soft, painful in the suprapubic region.

**Ultrasound:** endometrium is heterogeneous in structure, thickened.

**Histological examination:** complex endometrial hyperplasia without nuclear atypia.

**Questions:**

1. **What is endometrial hyperplasia?**
2. **What is the mechanism by which estrogens induce the hyperplasia process?**
3. **Which tissues undergo exclusively hyperplastic processes and why?**
4. **Which tissues undergo exclusively hypertrophic processes and why?**
5. **What is the difference between hyperplasia and metaplasia?**

**Topic 3: Cancerogenesis. Etiology. Pathogenetic mechanisms. Carcinogenesis associated with chronic inflammation.**

**Clinical Case 1**

Patient R., 53 years old, presented to the family doctor with the following complaints: diffuse abdominal pain, flatulence, nausea, changes in bowel habits—alternating diarrhea and constipation. Over the past 3 months, the patient lost 7 kg. Recently, he developed frequent nocturnal urination with associated pain.

Following clinical and laboratory investigations, the patient was referred to an oncology center, where the presence of a malignant rectal neoplasm with metastasis to the regional lymph nodes was confirmed, as well as a second malignant tumor localized in the prostate.

**Questions:**

1. **What are the pathogenic mechanisms that contribute to the development of a malignant tumor phenotype?**
2. **What is the role of Ras protein gene mutation in the pathogenesis of colon cancer?**
3. **What role can TGF-beta mutations play in carcinogenesis?**
4. **What mechanisms could tumor cells use to evade apoptosis?**
5. **What are the pathogenic mechanisms contributing to tumor angiogenesis?**
6. **What are the steps of the metastatic cascade, particularly in the case of colon cancer metastasis to the prostate?**

**Clinical Case 2**

Patient T., 65 years old, was found to have a hard mass in the right breast during a routine examination by a mammologist. Following clinical and laboratory investigations, the patient was referred to an oncology center, where a biopsy confirmed the diagnosis of right breast cancer cT4N3(f) M0, stage III, edematous-infiltrative variant. Immunohistological conclusion: invasive cancer, HER2-positive, FISH-negative.

**Questions:**

1. **What are the phenotypic attributes of malignant neoplasms?**
2. **What pathogenic role do HER2 receptors play in breast carcinogenesis?**
3. **What are the mechanisms of immune evasion in tumorigenesis?**
4. **What is the pathogenic role of T-17 in carcinogenesis?**
5. **What is the pathogenic role of T-reg lymphocytes in carcinogenesis?**
6. **What is the FISH test?**

**Topic 4: Microcirculation disorders. Arterial hyperemia. Venous hyperemia, Ischemia, Embolism, Stasis. Disorders of blood rheology. Edema.**

**Clinical case 1**

Patient R., 48 years old, suffers from liver cirrhosis. He complains of abdominal distension, shortness of breath, and fatigue. Objective findings: pale skin, soft tissue swelling, presence of fluid in the abdominal cavity, dilation of superficial veins on the abdominal wall, hepatomegaly, and splenomegaly. Therapeutically, an abdominal puncture was performed to evacuate ascitic fluid. The puncture was conducted while the patient was seated. After the evacuation of 7 litters of fluid within 30 minutes, the patient suddenly felt dizzy and fainted. Blood pressure (BP) was 50/30 mmHg, heart rate was 160 beats per minute.

**Questions:**

1. **What type of microcirculatory disorder and in which system developed in the patient after the evacuation of fluid from the abdominal cavity, based on the patient's clinical symptoms?**
2. **How does energy metabolism change at the level of the central nervous system (CNS) during ischemia? Present the causal chain that leads to fainting.**
3. **What is one of the basic pathogenetic links in the development of ascites?**
4. **Why did this patient develop tachycardia?**

**Clinical case 2**

Patient F., 52 years old, underwent surgery for the removal of a femur tumor. During the procedure, the femoral artery was injured. The artery was sutured, and the distal pulse of the artery was restored. After 24 hours, the patient complains of severe pain in the distal region of the operated leg, the pulse in the distal region (at the calf level) is not palpable, the patient cannot move the toes of the operated leg, the skin of the leg is pale, and the local temperature is reduced.

**Questions:**

1. **What type of microcirculation disorder has developed in the patient? Justify your answer.**
2. **What is the mechanism of pallor and low local temperature in the distal region of the operated leg?**
3. **What etiological factors can contribute to ischemia?**
4. **What is the pathogenetic mechanism of pain in this patient?**
5. **What types of collaterals (from a functional perspective) exist?**
6. **What is the pathogenetic mechanism of this type of microcirculation disorder?**

**Clinical case 3**

Patient H., 38 years old, was admitted to the trauma department with an open fracture of the left femur with fragment displacement. During the repositioning of the bone fragments, the patient developed shortness of breath, acrocyanosis, and a systolic blood pressure of 40 mm Hg, with diastolic pressure undetectable. After 10 minutes, the pulse in the carotid arteries disappeared, the pupils dilated, and clinical death was confirmed.

**Questions:**

1. **What type of microcirculatory disorder developed in the patient?**
2. **What is the pathophysiological mechanism of this microcirculatory disorder in this patient?**
3. **What is the path of embolus circulation, considering the patient's clinical symptoms that led to death?**
4. **What other types of embolism do you know, based on their origin (give examples)?**

**Clinical case 4**

Patient E., 43 years old, was admitted to the cardiology department with the diagnosis of "right atrioventricular orifice stenosis." She complains of fatigue, leg pain, and edema (which worsens in the evening), and cyanotic discoloration of the lips, ears, and nail beds. Objectively, acrocyanosis, hard edema localized in the calves, and hepatomegaly are observed.

Bio-microscopy of the nail bed microvessels revealed dilated venules with erythrocyte extravasation. Central venous pressure is 15 cm H₂O.

Blood biochemistry: ALAT - 80 UI/L; ASAT - 100 UI/L, Ht - 0.59. Hb - 160 g/L, Er - 5.5 x 10¹²/L.

**Questions:**

1. **What type of microcirculatory disorder do you suspect, considering the cause and clinical manifestations in the patient?**
2. **What compound causes cyanosis and acrocyanosis in venous hyperemia?**
3. **How do you explain the increased activity and levels of ALAT and ASAT in this patient?**
4. **What is the pathogenesis of stasis in right-sided heart failure?**
5. **What are the hemodynamic changes in venous hyperemia?**
6. **What are the metabolic changes in venous hyperemia?**
7. **What is the pathogenic link of hydrostatic edema in right-sided heart failure?**
8. **What is the pathogenic link of hyperosmolar edema in right-sided heart failure?**
9. **What is the pathogenic link of hypo-oncotic edema in right-sided heart failure?**
10. **What is the pathogenic link of membranous edema in right-sided heart failure?**

**Topic 5: Inflammation. Etiology. Alteration in the inflammatory focus. DAMPs, PAMPs and pattern recognition receptors. Inflammatory mediators. Vascular reactions in the inflammatory focus.**

**Clinical case 1**

Patient A., 12 years old, was admitted with a diagnosis of "acute abdomen."

Complaints: loss of appetite, persistent pain in the right iliac fossa, flatulence, general weakness; fever - 38.9°C.

Objective: Pale skin, abdomen sensitive to palpation, painful.

Complete blood count: neutrophilic leukocytosis, ESR - 40 mm/h (normal 5-15 mm/h); fibrinogen - 9 g/l (normal 2-4 g/l), C-reactive protein - 12 mg/dl (normal <0.5 mg/dl), elevated amyloid A levels.

**Questions**:

1. **What molecular pattern contributed to the onset and development of appendix inflammation? Which components are related to the exogenous molecular pattern?**
2. **What molecular pattern contributed to the onset and development of inflammation caused by cellular damage induced by physical, chemical, and mechanical factors?**
3. **What types of PRRs (Pattern Recognition Receptors) and with what cellular localization interact with PAMPs and DAMPs?**
4. **What type of inflammation (acute or chronic) has developed in the patient, and what biochemical changes confirm the type of inflammation?**
5. **Deduce the pathogenetic chain of proinflammatory cytokine synthesis initiated by PAMPs.**
6. **What are the pathogenetic factors that contribute to the development of inflammatory edema in the patient?**
7. **What type of exudate forms in this patient? What is the biological significance of exudation in acute inflammation?**
8. **What is C-reactive protein, and what is its role in inflammation?**
9. **What is the role of serum amyloid in inflammation?**
10. **Which cytokines induce the general clinical manifestations (loss of appetite, general weakness; fever - 38.9°C) in the acute phase reaction?**
11. **What types of macrophages do you know? Which type predominates in acute inflammation, and what is their pathogenetic role?**
12. **Which type of macrophages predominates in chronic inflammation, and what is their pathogenetic role?**

**Topic 6: Hypersensitivity reactions. Classification. General pathogenesis. Allergic reaction type I, II, III and IV.**

**Clinical case 1**

Patient N., a 32-year-old, complains of intense nose itching, violent sneezing, excessive tearing, watery nasal discharge, sore throat, cough and headache. According to the medical history, these symptoms have appeared every spring for the past three years. The patient’s condition worsens when in the forest or public gardens.

**Examination Findings**: The sclera is hyperaemic, with eyelid erythema and edema, tearing, seromucous nasal discharge, and laboured breathing. Swelling of the nasopharyngeal mucosa with abundant mucus secretion is noted.

**Hemogramm**: Leukocytes - 10.5 × 10⁹/L (N= 4.8–10.8 × 10⁹/L); Lymphocytes - 22% (N= 25–33%); Neutrophils: band - 2% (N=1-5%), segmented - 56% (N=40–70%); Monocytes - 7% (N= 3–7%); Eosinophils - 10% (N= 0–6%)

**Immunogram**: CD4+ T-cells - 1400/mm³ (N= 500–1200/mm³); T-helper cells - 58.5%; B-lymphocytes: 62%; IgA - 2.00 g/L (N= 0.70–3.50 g/L); IgM- 2.1 g/L (N= 0.50–3.0 g/L); IgG - 13.0 mg/dL (N= 7.0–17.0 g/L); Serum IgE level - 500 IU/mL (N= 0–100 IU/mL)

During a **percutaneous test** with plant allergens (flower pollen), a papule surrounded by erythema without induration formed in response to maple pollen.

**Questions:**

1. **What type of allergic reaction has developed in the patient? Explain using the medical history, clinical signs, and laboratory data.**
2. **Deduce the pathogenic chain of active sensitization in Type I (Anaphylactic) allergic reaction. Describe the role of B and T lymphocytes.**
3. **Which pre-synthesized cellular mediators (and their sources) contribute to the development of erythema, edema, tearing, and mucus secretion?**
4. **Which de novo synthesized mediators contribute to the clinical signs of an anaphylactic reaction? Outline the synthesis pathway of prostaglandins and leukotrienes.**
5. **What is the pathogenesis of blood pressure reduction in anaphylactic shock? What are the mechanisms of bronchial obstruction in anaphylactic shock?**
6. **Interpret the pathogenic increase in the percentage of B and T lymphocytes in an anaphylactic reaction. Explain the prevalence of B lymphocytes in the immunogram.**
7. **Explain the increase in eosinophil percentage in the complete blood count. List the mediators and their functions synthesized by eosinophils.**

**Clinical case 2**

Patient G, 48 years old, presents with asthenia, vertigo, nausea, and drowsiness. From the medical history: the patient had salmonellosis and was treated with levomycetin for three months.

**Objective:** The skin appears pale, cold, and dry. Respiratory rate is 20 breaths per minute, vesicular breath sounds on auscultation, pulse rate is 86 beats per minute, blood pressure is 110/65 mm Hg.

**In the hemogram**: Erythrocytes - 2.4 × 1012/L (N= 4.0 - 5.2 × 1012/L); Hemoglobin - 110 g/L (N= 120–158 g/L); Hematocrit - 30% (N= 35.4–44.4%); Leukocytes - 10.5 × 10⁹/L (N= 4.8 – 10.8 × 10⁹/L); Lymphocytes - 25% (N= 25–33%); non-segmented neutrophils - 4% (N= 0-5%); Segmented neutrophils - 58% (N= 40–70%); Monocytes - 4% (N= 3-7%); Eosinophils - 12% (N= 0–6%); ESR - 15 mm/hour (N= 2-15 mm/hour)

**Immunogram:** CD4+ - 1400/mm³ (N= 500 to 1200/mm³)**;** CD8+ - 300/mm³ (N= 150 to 1000/mm³)**;** T-helper - 58.5%**;** B lymphocytes - 62%**;** IgA - 1.0 g/L (N= 0.70–3.50 g/L)**;** IgM - 3.4 g/L (N= 0.50–3.0 g/L)**;** IgG - 28.1 g/L (N= 7.0–17.0 g/L)

**Anti-erythrocytes antibodies were detected in the blood.**

**Questions:**

1. **What type of allergic reaction has developed in the patient? Justify based on the medical history, clinical signs, and laboratory data.**
2. **What does haptens represent? What is their role in the etiology of allergic reactions? Differentiate between a complete allergen and a hapten.**
3. **Deduce the pathogenic chain of active sensitization in the type II cytotoxic allergic reaction. What is the role of B and T lymphocytes?**
4. **What pathogenetic mechanisms contribute to the hemolysis of erythrocytes in this patient?**
5. **Which components of the complement system induce hemolysis of erythrocytes, and through what mechanisms?**
6. **Deduce the pathogenetic chain of complement activation via the classical and alternative pathways.**
7. **Interpret the pathogenic increase in the percentage of B lymphocytes and T lymphocytes in the cytotoxic reaction. Justify the prevalence of B lymphocytes in the immunogram.**

**Clinical case 3**

Patient D, 9 years old, received 3000 IU of hyperimmune horse antitoxin serum prophylactically due to a leg injury. On the 9th day after the serum was administered, the child developed severe pain and swelling in the brachial and knee joints, generalized skin rashes, and general weakness.

**Objective:** The injection site of the serum is swollen and painful, the morning body temperature is 38.8 °C, and the heart sounds are muffled with blood pressure at 80/50 mm Hg. The child was hospitalized.

**Immunogram:** CD4+ - 1300/mm³ (N= 500 to 1200/mm³), T-helper - 52%, B lymphocytes - 56%, IgA - 1.8 g/L (N= 0.70–3.50 g/L), IgM - 3.2 g/L (N= 0.50–3.0 g/L), IgG - 31.3 g/L (N= 7.0–17.0 g/L).

**The complement fractions in the blood serum are decreased.**

**Questions:**

1. **What type of allergic reaction has developed in the patient? Justify your answer based on the medical history, clinical signs, and laboratory test results.**
2. **Deduce the pathogenic chain of active sensitization in the context of a type III allergic reaction. The role of B and T lymphocytes.**
3. **What mediators contributed to the injury and inflammation of the brachial and knee joints in the patient?**
4. **Explain the mechanism of circulation and sedimentation of circulating immune complexes in the context of a type III allergic reaction.**
5. **What plasma mediators are involved in the pathogenesis of type III allergic reactions? Justify your answer based on the effects of these mediators.**
6. **Interpret the pathogenic increase in the percentage of B and T lymphocytes in the context of a type III allergic reaction. Justify the prevalence of B lymphocytes in the immunogram.**
7. **Explain the essence of the decrease in complement system fractions in the blood serum in the context of a type III allergic reaction.**

**Clinical case 4**

Patient R, 18 years old, presented to the family doctor with the following complaints: itching, redness, rashes, and ulcers on the skin in the area of the left arm.

From the medical history: one month ago, she purchased a yellow metal alloy bracelet, and regular wearing of it, over two weeks, caused the aforementioned manifestations.

**Hemogram:** leukocytes - 9.5 × 10^9/L (N = 4.8 – 10.8 × 10^9/L), lymphocytes - 40% (N = 25–33%), bend neutrophils - 3% (N = 0-5%), segmented neutrophils - 46% (N = 40–70%), monocytes - 7% (N = 3-7%), eosinophils - 4% (N = 0–6%).

**Immunogram:** CD4+ - 1600/mm³ (N = 500 to 1200/mm³), CD8+ - 1300/mm³ (N = 150 to 1000/mm³), T-lymphocytes - 68%, B-lymphocytes - 32%. IgA - 1.4 g/L (N = 0.70–3.50 g/L), IgM - 1.8 g/L (N = 0.50–3.0 g/L), IgG - 12.5 g/L (N = 7.0–17.0 g/L).

**Questions:**

1. **What type of allergic reaction has developed in the patient? Justify your answer based on the medical history, clinical signs, and laboratory test results.**
2. **Deduce the pathogenic chain of active sensitization in the context of type IV allergic reaction. What is the pathogenic role of T lymphocytes?**
3. **What mediators contributed to the injury and inflammation associated with contact dermatitis?**
4. **What cellular mediators are involved in the pathogenesis of type IV allergic reactions? Justify your answer by discussing the effects of these mediators.**
5. **Interpret the pathogenic increase in the percentage of T lymphocytes in the context of type IV allergic reaction. Justify the prevalence of T lymphocytes in the immunogram.**
6. **Explain the functions of CD4+ and CD8+ lymphocytes in the pathogenesis of type IV allergic reaction.**
7. **What types of cytokines mediate type IV allergic reactions? What are their effects in the context of type IV allergic reaction?**

**Topic 7: Carbohydrate dyshomeostasis. Hyperglycemia. Hypoglycemia. Etiology. Pathogenesis. Lipid and protein dyshomeostasis. Hypoproteinemia. Dyslipidemia. Etiology. Pathogenesis.**

**Clinical case 1**

Patient B., 32 years old, was brought to the emergency medicine ward with the following complaints: confusion, general weakness, sweating, tachycardia, palpitations, excessive feeling of hunger and episodes of loss of consciousness.

The patient reported a constant sensation of vertigo for the last 2-3 months, which improved after taking the sweetened drinks. From past history the patient did not suffer from any chronic disease or previous surgeries. The patient is a non-smoker and does not consume alcohol.

*Objective:* cold, moist skin. BP - 140/90 mm Hg; pulse - 112 per minute; FCC - 100 b/min; FR - 20/min.

Laboratory data: glucose - 40 mg/dl; serum insulin - 50.8 μU/ml (6 - 35 μU/ml), C-peptide - 10.6 ng/ml (0.9-4 ng/ml); Na+ - 160 mEq/l; K+ - 3.0 mEq/l.

On CT scan was found a tumor in the pancreas - insulinoma.

**Questions:**

1. **What change in carbohydrate metabolism is seen in this patient and what is the pathogenetic mechanism? Argument answer.**
2. **What is the mechanism of tachycardia in this patient (replay by pathogenetic chain)?**
3. **What is the mechanism of the elevated blood pressure in this patient (replayed by pathogenetic chain)?**
4. **How do glucagon and epinephrine compensate for hypoglycemia?**
5. **How does cortisol compensate for hypoglycemia?**
6. **What explains the electrolyte changes in this patient?**
7. **Insulin is an anabolic hormone; how do carbohydrate metabolic processes change with insulin hypersecretion? (Glycolysis, glycogenolysis, glycogenogenesis, gluconeogenesis) (indicate by increase or decrease arrows)**

**Clinical case 2**

Patient A., 13 years old, was brought in by her parents with the following complaints general weakness, vomiting, obtundation, deep and noisy breathing.

According to the parents, a few months ago they noticed a decrease in the child's body mass, although he was eating quite frequently, intense thirst, frequent urination. Following further investigations, the endocrinologist diagnosed type 1 diabetes mellitus.

 *Objective:* cold, clammy skin. BP - 90/60 mm Hg; RF - 30/min; FCC - 100 b/min; pulse - 110/min; acetone odor.

Laboratory data: Glucose - 200 mg/dL; Na+ - 125 mEq/L; K+ - 5.9 mEq/L; Bicarbonates - 10 mEq/L; Urea - 18 mmol/L; Creatinine -140 mmol/L; Hb - 14 g/dL (12.0-15.5 g/dL); Ht - 49% (35-45%); ketone bodies - +++; osmolarity - 330 mOsm/l.

Urine: glucose - +++, ketone bodies - +++

Blood gas: pH - 7.2; PaO2 - 107 mm Hg; PaCO2 - 20 mm Hg.

**Questions:**

1. **What is the mechanism of hyperglycemia in this patient? Argument answer.**
2. **What is the mechanism of polyuria? (Replay by pathogenetic chain)**
3. **What is the mechanism of polydipsia? (Replay by pathogenetic chain)**
4. **How do carbohydrate metabolic processes change in insulin hyposecretion? (Glycolysis, glycogenolysis, glycogenogenesis, gluconeogenesis) (indicate by increase or decrease arrows)**
5. **Which laboratory and blood gas data indicate an acid-base imbalance and which imbalance is present in this patient?**
6. **What is the mechanism of diabetic ketoacidosis?**
7. **What is the type of breathing and how does it work?**
8. **What are the mechanisms of reduced lipogenesis and enhanced peripheral lipolysis?**

**Clinical case 3**

Patient P., 49 years old, suffering from chronic alcoholism, was admitted with the following complaints: general weakness, lack of appetite, vomiting, diarrhea, edema, epistaxis and gingival bleeding.

***Objective:*** cachexia, pale and dry skin with ecchymosis, generalized edema, hepatomegaly. Body mass index - 16.5 (norm 18.5 - 24)

**Laboratory data:** Plasma protein - 40 g/dL, albumin - 2.5 g/dL (norm 3.4-4.7 g/dL); transferrin - 1.0 (norm 2.0-3.6 g/L); Glucose - 60 mg/dL; Na+ - 155 mEq/L; K+ - 2.9 mEq/L; Creatinine -0.3 mg/dL (norm 0.6-1.2 mg/dL); Hb - 11.5 g/dL (13.6-17.5 g/dL); ALAT - 85 IU/L (norm 7-56 IU/L); ASAT - 55 IU/L (norm 0-35 IU/L); polyuria.

MRI (nuclear magnetic resonance) - liver steatosis was detected.

**Questions:**

1. **What is the mechanism of protein maldigestion and malabsorbtion?**
2. **What is the pathogenetic mechanism of fatty liver dystrophy due to hypoproteinemia?**
3. **What is the mechanism of generalized edema in this patient? (Explain by pathogenetic chain)**
4. **The patient with hypoproteinemia shows clinical signs suggestive of haemorrhagic syndrome (epistaxis, gingival bleeding and ecchymoses on the skin surface). What is the pathogenetic mechanism of haemorrhagic syndrome?**
5. **How does the immune status change in patients with hypoproteinemia? Argument.**

**Clinical case 4**

 Patient X, a 60 years old man, addresses to the family doctor with complaints of periodic pain in the precordial region.

 **From the anamnesis**: The job involves constant emotional stress, working as a lawyer and consumes a lot of animal fat. 2 years ago he suffered a myocardial infarction. For 1 year he is taking statins.

 **Objective**: Mass=115 kg, Height=170 cm. BP=150/105 mmHg. Ps=90.

 Paraclinically, the patient's lipid profile was of interest:

|  |  |  |
| --- | --- | --- |
| Walk | Patient value | Standard |
| Total cholesterol | 450 | <200 mg/dl |
| HDL-cholesterol | 25 | >40 mg/dl |
| LDL-cholesterol | 300 | <100 mg/dl |
| Triglyceride | 400 | <150 mg/dl |

**It has been established:** Absolute coronary insufficiency was established on the basis of atherosclerosis of the coronary arteries. Secondary hypercholesterolemia. Obesity gr. II.

1. **What changes in lipid metabolism are seen in the patient? Argue from the data of the problem.**
2. **What are the types of hyperlipidemia? Pathogenesis of transport hyperlipidemia.**
3. **What are the types of hyperlipidemia? Pathogenesis of retention hyperlipidemia.**
4. **Which lipoprotein fractions are atherogenic? Argue from the data of the problem.**
5. What is the role of emotional stress in the pathogenesis of atherogenesis?

**Topic 8: Dysregulation of hydroelectrolytic homeostasis. Hyperhydration, dehydration. Dyshomeostasis of sodium, potassium and calcium. Etiology. Pathogenesis. Compensatory reactions.**

**Clinical case 1**

Patient, M, 54 years old was admitted with complaints of abdominal pain, diarrhea for 4 days, dizziness, muscle weakness. On objective examination dry skin, reduced cutaneous turgor, dry mucosa of the oral cavity, dental impressions on the sides of the tongue. Diuresis for 24 hours approximately 500 ml. Blood pressure reduced - 75/ 45 mmHg, FCC - 118/min.

**Blood biochemical analysis:** serum sodium - 143 mEq/L (N: 135 - 145 mEq/L), serum potassium - 4.9 mEq/L (N: 3.5 - 5.5 mEqL), serum osmolarity 305 mOsm/L.

**Questions:**

**1. What water dyshomeostasis is present in this patient and what is the pathogenetic mechanism?**

1. **How is the extracellular water compartment affected in this water dyshomeostasis?**
2. **How is the intracellular water compartment affected in this water dyshomeostasis?**
3. **How is the intravascular water compartment affected in this water dyshomeostasis? What clinical manifestations are reflective of this change?**
4. **What changes in the general blood analysis (erythrocytes, hemoglobin, hematocrit) are expected to be present in this hydric dyshomeostasis?**
5. **What compensatory reactions are triggered in this hydrate dyshomeostasis?**
6. **What are the pathogenetic mechanisms that explain the reduction in diuresis in this patient?**

**Clinical case 2**

The patient, M, 64 years old was hospitalized with complaints of headache, tinnitus, muscle weakness, heart palpitations.

**On objective examination** icteric and dry skin, reduced cutaneous turgor, dry mucosa of the oral cavity, dental impressions on the sides of the tongue. Diuresis for 24 hours approximately 3500 ml. Blood pressure reduced - 60/ 40 mmHg, FCC - 128/min.

**Blood electrolytes:** Serum sodium - 123 mEq/L (N: 135 - 145 mEq/L), serum potassium - 6.4 mEq/L (N: 3.5 - 5.5 mEqL), Serum osmolarity 265 mOsm/L.

**From the anamnesis**, the patient is known to have ovarian tumor, and at the last examination, about 10 months ago, multiple metastases in the adrenal cortex were detected.

**Questions:**

* 1. **What water dyshomeostasis is present in this patient and what is the pathogenetic mechanism?**
1. **How is the extracellular hydric compartment affected in this hydric dyshomeostasis?**
2. **How is the intracellular water compartment affected in this water dyshomeostasis?**
3. **How is the intravascular water compartment affected in this water dyshomeostasis? What clinical manifestations are reflective of this change?**
4. **What changes in the general blood analysis (erythrocytes, hemoglobin, hematocrit) are expected to be present in this hydric dyshomeostasis?**
5. **How can the presence of hyperkalemia in this water dyshomeostasis be explained?**
6. **What sodium dyshomeostasis is present in this patient and explain the pathogenetic mechanism?**
7. **What compensatory reactions are triggered in this hydrate dyshomeostasis?**

**Clinical case 3**

Patient P, 72 years old was hospitalized in an unconscious state. According to his son he was found at home by neighbours. He is presumed to have been in this unconscious state for approximately 72 hours.

**On objective examination** dry skin, reduced cutaneous turgor, dry mucosa of the oral cavity, dental impressions on the sides of the tongue. Blood pressure low - 60/40 mmHg, C.B.C. 125/min. Respiration rate 36/min.

**Blood Electrolytes:** Serum Sodium - 163 mEq/L (N: 135 - 145 mEq/L), Serum Potassium - 4.4 mEq/L (N: 3.5 - 5.5 mEqL), Serum Osmolarity 365 mOsm/L.

**Questions:**

1. **What water dyshomeostasis is present in this patient and what is the pathogenetic mechanism?**
2. **How is the extracellular water compartment affected in this water dyshomeostasis?**
3. **How is the intracellular water compartment affected in this water dyshomeostasis?**
4. **How is the intravascular water compartment affected in this water dyshomeostasis? What clinical manifestations are reflective of this change?**
5. **What changes in the general blood analysis (erythrocytes, hemoglobin, hematocrit) are expected to be present in this hydric dyshomeostasis?**
6. **What sodium dyshomeostasis is present in this patient and explain the pathogenetic mechanism?**
7. **What compensatory reactions are triggered in this hydrate dyshomeostasis?**

**Clinical case 4**

The patient, D, 54 years old was admitted with complaints of headache, generalized peripheral edema. On objective examination edema in both legs and on the sides of the abdomen. Diuresis for 24 hours about 800 ml. Blood pressure - 180/115 mmHg, CBC - 67/min.

**Blood electrolytes:** Serum sodium - 158 mEq/L (N: 135 - 145 mEq/L), serum potassium - 3.2 mEq/L (N: 3.5 - 5.5 mEqL), serum osmolarity 365 mOsm/L, pH = 7.3 (N: 7.35 - 7.45)

From the history, the patient is known to have active secreting tumor in the glomerular area of the left adrenal gland.

**Questions:**

**1. What water dyshomeostasis is present in this patient and what is the pathogenetic mechanism?**

1. **How is the extracellular hydric compartment affected in this hydric dyshomeostasis?**
2. **How is the intracellular water compartment affected in this water dyshomeostasis?**
3. **How is the intravascular water compartment affected in this water dyshomeostasis? What clinical manifestations are reflective of this change?**
4. **What changes in the general blood analysis (erythrocytes, hemoglobin, hematocrit) are expected to be present in this hydric dyshomeostasis?**
5. **How can the presence of hypokalemia in this hydric dyshomeostasis be explained?**
6. **What sodium dyshomeostasis is present in this patient and explain the pathogenetic mechanism?**
7. **What are the pathophysiologic mechanisms of edema associated with this hydric dyshomeostasis?**
8. **What compensatory reactions are triggered in this hydric dyshomeostasis?**

**Clinical case 5**

The patient, G, 64 years old, was admitted with complaints of headache, generalized peripheral edema, muscle weakness, heart palpitations.

**On objective examination** jaundiced skin, edema on both legs and sides of the abdomen. Diuresis for 24 hours about 500 ml. Blood pressure - 175/110 mmHg, CBC - 68/min.

**Blood electrolytes:** Serum sodium - 128 mEq/L (N: 135 - 145 mEq/L), serum potassium - 5.9 mEq/L (N: 3.5 - 5.5 mEqL), serum osmolarity 265 mOsm/L.

From history, the patient is known to have ADH-secreting bronchial carcinoma.

**Questions:**

**1. What water dyshomeostasis is present in this patient and what is the pathogenetic mechanism?**

1. **How is the extracellular hydric compartment affected in this hydric dyshomeostasis?**
2. **How is the intracellular water compartment affected in this water dyshomeostasis?**
3. **How is the intravascular water compartment affected in this water dyshomeostasis? What clinical manifestations are reflective of this change?**
4. **What changes in the general blood analysis (erythrocytes, hemoglobin, hematocrit) are expected to be present in this hydric dyshomeostasis?**
5. **How can the presence of hyperkalemia in this hydric dyshomeostasis be explained?**
6. **What sodium dyshomeostasis is present in this patient and explain the pathogenetic mechanism?**
7. **What are the pathophysiologic mechanisms of edema associated with this hydric dyshomeostasis?**
8. **What compensatory reactions are triggered in this hydric dyshomeostasis?**

**Topic 9: Dysregulation of acid-base balance. Metabolic and respiratory**

**acidosis. Metabolic and respiratory alkalosis. Etiology. Pathogenesis. Compensatory reactions**

**Clinical case 1**

Patient B, 56 years old, known to have diabetes mellitus, insulin-dependent, was admitted urgently with the following manifestations: confusion, feeling nauseous and vomiting, dizziness.

**On objective examination**: deep and accelerated breathing, low blood pressure, hot, sweaty skin.

**Blood biochemistry reveals**: Glucose - 206 mg/dL (norm 60 - 110 mg/dL), free fatty acids - 2.3 mmol/L (norm 0 - 0.70 mmol/L), Sodium - 158 mEqL (norm 135 - 145 mEq/L), Potassium - 6.1 mEq/L (norm 3.5 - 5,5 mEq/L), Calcium - 2,9 mmol/L (norm 2,1 - 2,6 mmol/L), Chloride - 90 mmol/L (norm 98 - 106 mmol/L), ketone bodies 3,8 mg/dL (norm below 1,0 mg/dL), lactic acid 0,6 mmol/L (norm < 2,0 mmol/L).

**Analysis of acid-base balance** reveals: pH - 7.31 (norm 7.35 - 7.45), Plasma bicarbonate - 18 mEq/L (norm 24 - 26 mEqL), PaCO2 - 32 mmol/L (norm 35 - 40 mmol/L), SaO2 - 85 %.

**Questions:**

1. **What acid-base dyshomeostasis developed in the patient and what is the pathogenetic mechanism?**
2. **Which biochemical pathogenetic links are involved in the development of ketoacidosis in insulin deficiency?**
3. **Explain the pH changes in the described clinical situation?**
4. **Explain the bicarbonate changes in the clinical situation described?**
5. **Reveal the pathogenetic mechanisms underlying the development of hyperpnea (frequent and accelerated breathing) in the acid-base dyshomeostasis present in the patient?**
6. **List the clinical and biochemical changes that reveal the presence of compensatory reactions in the given patient?**
7. **By which pathogenetic mechanisms can the hypernatremia in this patient be explained?**
8. **By which pathogenetic mechanisms can hyperkalemia be explained in this patient?**
9. **By which pathogenetic mechanisms can hyperkalemia be explained in this patient?**
10. **By which pathogenetic mechanisms can hypocapnia be explained in this patient? What is the biological significance of this compensatory reaction?**
11. **By which pathogenetic mechanisms can hypochloraemia be explained in this patient?**
12. **How can you explain the change in SaO2 in the given clinical situation?**

**Clinical case 2**

Patient B, 36 years old, was urgently hospitalized in deep coma after a benzodiazepine overdose.

**On objective examination**: shortness of breath (FR - 6/min), blood pressure 85/40 mmHg, tachycardia (FCC - 130/min).

**Blood biochemical analysis** reveals: Glucose - 106 mg/dL (norm 60 - 110 mg/dL) Sodium - 158 mEq/L (norm 135 - 145 mEq/L), Potassium - 6.1 mEq/L (norm 3.5 - 5.5 mEq/L), Calcium - 2.8 mmol/L (norm 2,1 - 2,6 mmol/L), Chloride - 90 mmol/L (norm 98 - 106 mmol/L), Ketone bodies 0,8 mg/dL (norm < 1,0 mg/dL), Lactic acid 0,9 mmol/L (norm < 2,0 mmol/L).

**Analysis of acid-base balance** reveals: pH - 7, 30 (norm 7, 35 - 7,45), Plasma bicarbonate - 32 mEq/L (norm 24 - 26 mEq/L), PaCO2 - 52 mmol/L (norm 35 - 40 mmol/L), SaO2 - 75 %.

**Questions:**

* 1. **What acid-base dyshomeostasis developed in the patient and what is the pathogenetic mechanism?**
1. **Explain the pH changes in the described clinical situation?**
2. **Explain the serum bicarbonate changes in the described clinical situation?**
3. **Explain the mechanisms by which the kidney is involved in compensating for the acid-base dyshomeostasis present in this patient.**
4. **By which pathogenetic mechanisms can the hypernatremia in this patient be explained?**
5. **By which pathogenetic mechanisms can hyperkalemia be explained in this patient?**
6. **By which pathogenetic mechanisms can hyperkalemia be explained in this patient?**
7. **By which pathogenetic mechanisms can the hypochloraemia in this patient be explained?**
8. **What clinical manifestations may be triggered by increased plasma CO2 (PaCO2) in the presence of this acid-base dyshomeostasis?**
9. **Explain the pathogenetic mechanisms underlying the decrease in blood pressure value in acid-base dyshomeostasis present in the patient.**
10. **This acid-base dyshomeostasis is associated with osmolarity disturbances. What osmolarity disturbances may be present and how do they manifest?**
11. **Which biochemical or blood gas parameter allows us to differentiate respiratory acidosis from metabolic acidosis?**

**Clinical case 3**

Patient A, 67 years old, was hospitalized with the following complaints: nausea and vomiting for 4 days, headache, dizziness, muscle cramps in the lower limbs.

**On objective examination**: low blood pressure, dry complexion, reduced skin turgor.

**Blood biochemical analysis** revealed: Glucose - 106 mg/dL (norm 60 - 110 mg/dL), Sodium - 128 mEq/L (norm 135 - 145 mEq/L), Potassium - 3.1 mEq/L (norm 3.5 - 5.5 mEq/L), Calcium - 1.9 mmol/L (norm 2.1 - 2.6 mmol/L), Chloride - 118 mmol/L (norm 98 - 106 mmol/L),

**Acid-base balance analysis** reveals: pH - 7,55 (norm 7,35- 7,45), Plasma bicarbonate - 32 mEqL (norm 24 - 26 mEqL), PaCO2 - 46 mmol/L (norm 35 - 40 mmol/L).

**Questions:**

1. **What acid-base dyshomeostasis developed in the patient and what is the pathogenetic mechanism?**
2. **Explain the pH changes in the described clinical situation?**
3. **By which pathogenetic mechanisms can the hyponatremia in this patient be explained?**
4. **By which pathogenetic mechanisms can hypokalemia be explained in this patient?**
5. **By which pathogenetic mechanisms can hypocalcemia be explained in this patient?**
6. **By which pathogenetic mechanisms can hypercapnia be explained in this patient? What is the biological significance of this change?**
7. **By which pathogenetic mechanisms can hyperchloremia be explained in this patient?**
8. **This acid-base dyshomeostasis is associated with osmolarity disturbances. What osmolarity dysregulations may be present and how do they manifest?**
9. **Which biochemical or blood gas parameter allows us to differentiate between metabolic and respiratory alkalosis?**