**STATE UNIVERSITY OF MEDICINE AND PHARMACY**

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**Department of pathology, discipline of pathophysiology**

**INDIVIDUAL WORKBOOK**

**Semester VI**

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

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

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

**Chișinău, 2025**

**Topic 1: Pathophysiology of the erythrocyte series. Erythrocytosis. Anaemia. Etiology. Pathogenesis. Haemogram changes.**

**Clinical case 1**

The 37-year-old patient presented to the gynaecologist with the following complaints: for several months she has been suffering from intermenstrual bleeding, menorrhagia (heavy bleeding), extreme fatigue and weakness. History: 5 years ago she was diagnosed with ankylosing spondylitis (chronic inflammation of the spinal column), for which she receives specific treatment.

Objective: pronounced pallor, brittle nails and hair, labial commissures and taste paresthesias.

**Patient's haemogram:**

|  |  |  |
| --- | --- | --- |
|  | **Patient values** | **Reference values** |
| **Hematocrit** | **32** | **Men 39-49%****Women 35-45%** |
| **Hemoglobin** | **9,0** | **Men 13,6-17,5 g/dL****Women 12,0-15,5 g/dL** |
| **Eritrocite** | **4,2** | **4,7-6,1 mln/mm3** |
| **Number of reticulocytes** | **0,5** | **0,5-1,5%** |
| **MCV** | **74** | **80 -100 fL** |
| **MCH** | **22** | **26 – 34 pg** |
| **MCHC** | **28** | **31 -36 g/dL** |
| **Leucocyte** | **5,7** | **4,800–9,000/mm3** |
| **Neutrophils** | **60** | **60 -62%** |
| **Basophiles** | **0** | **0- 1,0%****10 -120/ mm3** |
| **Eosinophil** | **3** | **1-4%****4- -500 mm3** |
| **Lymphocyte** | **32** | **25-35%****800 -3,500/ mm3** |
| **Monocyte** | **5** | **3-7%****200-800/ mm3** |
| **thrombocyte** | **258** | **150,000-450,000/ mm3** |
| **Morphological changes of blood cells** | **Anisocytosis, poikilocytosis, anulocytosis.** |  |

**1. What type of pathological process of the erythrocyte system is present in the patient? Explain the changes in the haemogram.**

**2. Describe the mechanism of iron absorption in the body.**

**3. What is the pathogenetic mechanism of this pathological process of the erythrocyte system, the etiological factor being metrorrhagia?**

**4. What is the pathogenetic mechanism of this pathological process in the erythrocyte system, the aetiological factor being chronic inflammation?**

**5. What is the pathogenetic mechanism of clinical signs such as brittle nails and hair, labial commissures and taste paresthesias?**

**6. In order to establish the diagnosis of this pathological process of the erythrocyte system, further biochemical tests (serum iron, serum ferritin, transferrin, transferrin saturation, serum iron binding capacity (TIBC)) are needed. What are they and how do they change?**

**7. What are the morphological changes and what are their mechanisms?**

**Clinical case N 2**

The patient, aged 47, was admitted with the following complaints: asthenia, irritability, unstable walking, headache, dizziness, paraesthesia, diarrhea. From the patient's history - one year ago he underwent gastric resection

Objective: teguments are pale, fissured, bright red tongue (Hunter's glossitis).

**Patient's haemogram:**

|  |  |  |
| --- | --- | --- |
| **CBC** | **Patient values** | **Reference values** |
| **Hematocrit** | 35 | **Men** 39-49%**Women** 35-45% |
| **Hemoglobin** | 11,7 | **Men** 13,6-17,5 g/dL**Women** 12,0-15,5 g/dL |
| **Eritrocite** | 3,6 | 4,7-6,1 milion/mm3 |
| **Number of reticulocytes** | 0,3 | 0,5-1,5% |
| **MCV** | 114 | 80 -100 fL |
| **MCH** | 38 | 26 – 34 pg |
| **MCHC** | 33 | 31 -36 g/dL |
| **Leucocyte** | 4,6 | 4,800–9,000/cumm |
| **Neutrophils** | 70 | 60 -62% |
| Segmented neutrophils | 65 | 40-60% |
| Nonsegmented neutrophils | 5 | 1-6% |
| Metamyelocytes | 0 | 0% |
| Myelocytes | 0 | 0% |
| **Basophiles** | 0 | 0- 1,0%10 -120/cu mm |
| **Eosinophil** | 2 | 1-4%4- -500 cu mm |
| **Lymphocyte** | 25 | 25-35%800 -3,500/cu mm |
| **Monocyte** | 3 | 3-7%200-800/cu mm |
| **thrombocyte** | 143 | 150,000-450,000/cu mm |
| **Morphological changes of blood cells** | Anisocytosis, poikilocytosis,Giant neutrophils withhypersegmented nuclei, erythrocytes with Cabot rings and Jolli bodies |  |

**1. What pathology of the erythrocyte system is present in this patient and what is the aetiological factor? Explain the haemogram changes.**

**2. What is the mechanism of vitamin malabsorption that caused this anaemia?**

**3. What is the pathogenetic mechanism of this erythrocyte system pathology in this patient?**

**4. The haemogram shows the values of the parameters MCV and MCH. What do these parameters indicate in this patient?**

**5. What is the pathogenetic mechanism of Hunter's glossitis (bright red coloured tongue) (reread by pathogenetic chain)?**

**6. What is the pathogenetic mechanism of diarrhoea in this? (Explain by pathogenetic chain)**

**7. What is the pathogenetic mechanism of neurological signs? (Explain by pathogenetic chain)**

**Clinical case 3**

The patient, 32 years old, presented with the following complaints: general weakness, drowsiness, dizziness. From the history the patient had breast cancer and was undergoing a course of cytostatic treatment.

Objective: marked pallor, petechiae, ecchymosis, gingival and nasal bleeding.

Very frequent develop respiratory infections.

**Patient's haemogram:**

|  |  |  |
| --- | --- | --- |
|  | **Patient values** | **Reference values** |
| **Hematocrit** | 29 | **Men**39-49%**Women**35-45% |
| **Hemoglobin** | 9,0 | **Men39**13,6-17,5 g/dL**Women35**12,0-15,5 g/dL |
| **Eritrocite** | 3,1 | 4,7-6,1 million/cu mm |
| **Number of reticulocytes** | 0 | 0,5-1,5% |
| **MCV** | 87 | 80 -100 fL |
| **MCH** | 29 | 26 – 34 pg |
| **MCHC** | 33 | 31 -36 g/dL |
| **Leucocyte** | 2,8 | 4,800–9,000/cumm |
| **Neutrophils** | 30 | 60-62% |
| **Basophiles** | 0 | 0- 1,0%10 -120/cu mm |
| **Eosinophil** | 0 | 1-4%4- -500 cu mm |
| **Lymphocyte** | 67 | 25-35%800 -3,500/cu mm |
| **Monocyte** | 3 | 3-7%200-800/cu mm |
| **thrombocyte** | 108,000 | 150,000-450,000/cu mm |
| **Morphological changes of blood cells** |  |  |

**1. What pathology of the erythrocyte system is present in this patient and what is the aetiological factor?**

**2. What is the pathogenetic mechanism of this pathology?**

**3. What are the signs of agranulocytosis in the patient's haemogram?**

**4. Identify whether pancytopenia is determined in the patient's laboratory analysis, argue.**

**5. What is the pathogenesis of the clinical signs: petechiae, ecchymoses, gingival and nasal bleeding? (Please summarise by pathogenetic chain)**

**6. What is the pathogenesis of common respiratory infections in this patient? (Please summarise by pathogenetic chain)**

**7. How does the number of lymphocytes in the blood count change, of what type and what is the pathogenetic mechanism of these changes?**

**Clinical case 4**

A 46-year-old man was admitted to the hospital with the following complaints: muscle weakness, dizziness, headache, poor appetite, yellowish skin colour, dark urine. According to the patient, 2 weeks ago he was treated with penicillin antibiotics. Physical examination revealed: jaundice and icteric conjunctivae, a soft abdomen on palpation without pain, rhythmic, sonorous heart sounds; auscultatory lungs - without pathological changes; peripheral lymph nodes - without changes. There was no evidence of hepato- and splenomegaly.

**Biochemical analysis**: total bilirubin - 3.2 mg/dL (N=0.1 - 1.2); conjugated bilirubin - 0.5 mg/dL (N=0.1 - 0.5); unconjugated bilirubin - 2.7 mg/dL (N=0.1 - 0.7); haptoglobin - 18 mg/dL (N=30 - 200);

**Urinalysis:** Hemosiderinuria, haemoglobinuria.

**Patient's haemogram**

|  |  |  |
| --- | --- | --- |
| **CBC** | **Patient values** | **Reference values** |
| **Hematocrit** | **29** | **Men39**39-49%**Women35**35-45% |
| **Hemoglobin** | **9,5** | **Men39**13,6-17,5 g/dL**Women35**12,0-15,5 g/dL |
| **Eritrocite** | **3,0** | **4,7-6,1 mln/mm3** |
| **Number of reticulocytes** | **3,5** | 0,5-1,5% |
| **MCV** | **87** | 80 -100 fL |
| **MCH** | **32** | 26 – 34 pg |
| **MCHC** | **33** | 31 -36 g/dL |
| **Leucocyte** | **5,7** | 4,800–9,000/cu mm |
| **Neutrophils** | **60** | 60 -62% |
| **Basophiles** | **0** | 0- 1,0%10 -120/cu mm |
| **Eosinophil** | **4** | 1-4%4- -500 cu mm |
| **Lymphocyte** | **31** | 25-35%800 -3,500/cu mm |
| **Monocyte** | **5** | 3-7%200-800/cu mm |
| **thrombocyte** | **278,000** | 150,000-450,000/cu mm |
| **Morphological changes of blood cells** |  |  |

**1. What type of pathological process of the erythrocyte system is present in the patient? Argue by changes in the haemogram.**

**2. What type of haemolytic anaemia is present in this patient? What are the distinguishing features between congenital and acquired haemolytic anaemia?**

**3. What is the pathogenetic mechanism of anaemia in the given patient? (Summarise by pathogenetic chain)**

**4. Which parameter indicates that the given anaemia is hyperregenerative and what is the mechanism?**

**5. What explains the elevated total and indirect bilirubin levels? (Summarise by pathogenetic chain)**

**6. What is the role of haptoglobin and how is its reduced level explained?**

**7. What is the mechanism of haemosiderinuria and haemoglobinuria in this patient?**

**Clinical case 5**

The 47-year-old patient was admitted to the haematology ward with the following complaints: general weakness, insomnia, headache, paraesthesia in the fingers, visual disturbances, loss of work capacity, pyrosis and eructation.

Objective: Teguments are red-purple in colour. The face is congested, the sclera injected, and on examination of the fundus of the eye, turgescent veins are seen. Blood pressure 160/85 mm Hg. Moderate hepatomegaly, increased blood viscosity.

**Patient's haemogram**

|  |  |  |
| --- | --- | --- |
| **CBC** | **Patient values** | **Reference values** |
| **Hematocrit** | 60 | **Males** 39-49%**Females** 35-45% |
| **Hemoglobin** | 29,9 | **Males** 13,6-17,5 g/dL**Females** 12,0-15,5 g/dL |
| **Eritrocite** | 9,4 | 4,7-6,1 million/cu mm |
| **Number of reticulocytes** | 3,7 | 0,5-1,5% |
| **MCV** | 75 | 80 -100 fL |
| **MCH** | 24 | 26 – 34 pg |
| **MCHC** | 30 | 31 -36 g/dL |
| **Leucocyte** | 11,500 | 4,800–9,000/cumm |
| **Neutrophils** | 69 | 60 -62% |
| **Basophiles** | 2 | 0- 1,0%10 -120/cu mm |
| **Eosinophil** | 6 | 1-4%4- -500 cu mm |
| **Lymphocyte** | 20 | 25-35%800 -3,500/cu mm |
| **Monocyte** | 3 | 3-7%200-800/cu mm |
| **thrombocyte** | 570 | 150,000-450,000/cu mm |
| **Morphological changes of blood cells** | **Anisocytosis, poikilocytosis, anulocytosis** |  |
| **EPO** | 2,5 | 4,3 – 29 UI/L |

**1. What type of pathological process of the erythrocyte system is present in the patient, absolute or relative? Explain the changes in the haemogram.**

**2. What type of erythrocyte pathological process is present in the patient, absolute primary or absolute secondary? Explain the changes in the haemogram.**

**3. What is the pathogenesis of this pathological process noted in the patient?**

**4. The haemogram shows the values of the parameters MCV, MCH and MCHC. What do these parameters indicate in this patient and what is the pathogenetic mechanism of these changes?**

**5. What is the pathogenetic mechanism of some neurological signs: insomnia, headache, visual disturbances?**

**6. How does blood pressure change and what is the pathogenetic mechanism (replay by pathogenetic chain)?**

**7. What is the pathogenetic mechanism of moderate hepatomegaly?**

**Topic 2: Pathophysiology of the leukocyte series. Leukocytosis. Leukopenia. Leukoses. Etiology. Pathogenesis**

**Clinical case 1**

A 65-year-old man, on public transport, loses consciousness after a coughing fit. He is transported by AMU to the Hospital, where he is admitted to the Therapy Department with the fallowing complaints: progressive dyspnea, dry cough, fever, petechiae in the thoracic region and ecchymoses on the abdomen and legs.

**Anamnesis:** chronic bronchitis, recurrent urogenital fungal infections, gingivorrhea after oral hygiene.

|  |  |  |  |
| --- | --- | --- | --- |
| **Terminology** | **Results of Patient**  | **Measurement units** | **Reference values** |
| **Hemoglobin (HGB)** | 88 | g/l | **Man 136-172 Woman 120-150** |
| **Erythrocytes (RBC)** | 2,5 | x 106/mm3 | **Man 4,3-5,9****Woman 3,5-5,0**  |
| **Hematocrit** | 30 | % | **Man 39-49 Woman 33-43** |
| **MCV** | 112 | fL | **82 - 96** |
| **MCH** | 39 | pg | **27 - 33** |
| **MCHC** | 34 | g/dl | **33-37** |
| **RDW** | 16 |  | **11.5 – 14.5** |
| **Reticulocytes** | 2 | % promiles | **5 - 10** |
| **Trombocytes** | 120 | x 103/μL | **150-450** |
| **Trombotocrit** | 0,8 | mL/L | **1.08-2.82** |
| **Leucocytes** | 200000 | leucocyte/mm3 | **6000-8000 leucocyte/mm3** |
| **Neutrophyls:**Myeloblasts | 64 | % | **0** |
| PromyelocytesMyelocytes | 00 | %% | **0****0** |
| Metamyelocytes | 0 | % | **0** |
| Nonsegmented | 3 | % | **1-6** |
| Segmented | 16 | % | **47-72** |
| **Eosinophyls** | 2 | % | **0.5-5** |
| **Basophyls** | 1 | % | **0-1** |
| **Lymphocytes** | 10 | % | **25-35** |
| **Monocytes** | 4 | % | **3-11** |

**Objective data:** auscultatory harsh breathing, the abdomen is difficult to palpation due to ascites. USG: splenomegaly and hepatomegaly/Radiography: bilateral pneumonia.

Blood smear: Blast cells ↑↑↑; containing azurophilic granules, MPOX test +; Lipid test +; Glycogen test -;

**Questions**

**1. What type of the leukocyte pathology system is attested in the patient and what is the etiological factor of it?**

**2. What are the differentiating criteria between acute and chronic myeloid leukemia?**

**3. Progressive dyspnea, attested in the patient, can be a criterion attributed to pulmonary leukostasis. Explain what does leukostasis represent, as a general clinical manifestation in leukemia.**

**4. List the general clinical manifestations of leukemia, tick which of them are present in the patient.**

**5. List 3 types of morphological changes that are related to the process of abnormal neutrophil differentiation in the patient as a manifestation of structural atypia in leukemia. Tick the change present in the patient.**

**6. Explain the pathogenetic mechanism of anemia in the patient.**

**7. Explain the pathogenetic mechanism of haemorrhagic syndrome in the patient.**

**Clinical case 2**

A 9-year-old boy, together with his father, addressees to the family doctor with complaints of: persistent headache, decreased visual acuity, permanent bone pain, enlargement of both testicles not accompanied by fever at the moment. Palpation: generalized symmetrical lymphadenopathy, hepato/splenomegaly

Blood smear: morphologically small blast cells, without granules, with little cytoplasm, PAS reaction + and acid phosphatase reaction +.

|  |  |  |  |
| --- | --- | --- | --- |
| **Terminology** | **Results of Patient**  | **Measurement units** | **Reference values** |
| **Hemoglobin (HGB)** |  80 | g/l | **Man 136-172 Woman 120-150** |
| **Erythrocytes (RBC)** | 2,1 | x 106/mm3 | **Man 4,3-5,9 Woman 3,5-5,0** |
| **Hematocrit** | 30 | % | **Man 39-49****Woman 33-43** |
| **MCV**  | 98 | fL | **82 - 96** |
| **MCH**  | 32 | pg | **27 - 33** |
| **MCHC**  | 38 | g/dl | **33-37** |
|  **RDW** | 15 |  | **11.5 – 14.5** |
| **Reticulocytes** | 2 | % promiles | **5 - 10** |
| **Thrombocytes** | 135 |  x 103/μL | **150-450** |
| **Thrombotocrit** | 0,9 | mL/L | **1.08-2.82** |
| **Leucocytes** | 150000 | leucocyte/mm3 | **6000-8000 leucocyte/mm3** |
| *Leukocyte formula* |  |  |  |
| **Neutrophils:**Myeloblasts | 0 | % | **0** |
| PromyelocytesMyelocytes | 00 | %% | **0****0** |
| Metamyelocytes | 0 | % | **0** |
| Nonsegmented | 2 | % | **1-6** |
| Segmented | 28 | % | **47-72** |
| **Eosinophils** | 2 | % | **0.5-5** |
| **Basophils** | 0 | % | **0-1** |
| **Lymphoblasts****Prolymphocytes****Lymphocytes** | 48017 | %%% | **0****0****25-35** |
| **Monocytes** | 3 | % | **3-11** |

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**Questions:**

**1. Identify what type of pathological process of the leukocyte system is present in the patient.**

**2. List the clinical and paraclinical criteria for identifying the pathological process.**

**3. There are 3 indispensable processes for any type of leukemia present in the given patient: anaplasia, hyperplasia, metaplasia. Give their definition.**

**4. Explain from a pathogenetic mechanism the bone pain in a child.**

**5. What is the pathogenetic mechanism of thrombocytopenia in the patient?**

**6. Describe the general pathogenesis of acute leukemia.**

**7. Specify the classification of leukemias depending on the number of leukocytes and blast cells detected in the peripheral blood. To what type is attributed the patient?**

**Clinical case 3**

A 68-year-old man, goes to his family doctor at the insistence of his wife who noticed that her husband had become jaundiced for about a month. The patient's complaints: permanent feeling of fatigue, lack of appetite and "catches colds" quickly and frequently (recurrent bronchitis and urethritis).

**Objective:** symmetrically enlarged submandibular, cervical, supra/subclavicular, inguinal lymph nodes, soft, painless on palpation. Splenomegaly. Hepatomegaly. **Immunophenotyping:** Absence of IgM in serum and absence of IgA in urethral secretions; IgG in serum=0.4g/l (<2g/l is already suggestive of immunodeficiency.

**Blood smear:** Gumprecht shadows

|  |  |  |  |
| --- | --- | --- | --- |
| **Terminology** | **Results of Patient 1** | **Measurement units** | **Reference values** |
| **Hemoglobin (HGB)** |  80 | g/l | **Man Woman** **136-172 120-150** |
| **Erythrocytes (RBC)** | 2,1 | x 106/mm3 | **Man Woman****4,3-5,9 3,5-5,0** |
| **Hematocrit** | 30 | % | **Man Woman****39-49 33-43** |
| **MCV**  | 98 | fL | **82 - 96** |
| **MCH**  | 32 | pg | **27 - 33** |
| **MCHC**  | 38 | g/dl | **33-37** |
|  **RDW** | 15 |  | **11.5 – 14.5** |
| **Reticulocytes** | 2 | % promiles | **5 - 10** |
| **Thrombocytes** | 135 |  x 103/μL | **150-450** |
| **Thrombotocrit** | 0,9 | mL/L | **1.08-2.82** |
| **Leucocytes** | 180000 | leucocyte/mm3 | **6000-8000 leucocyte/mm3** |
| *Leukocyte formula* |  |  |  |
| **Neutrophils:**Myeloblasts | 0 | % | **0** |
| PromyelocytesMyelocytes | 00 | %% | **0****0** |
| Metamyelocytes | 0 | % | **0** |
| Nonsegmented | 1 | % | **1-6** |
| Segmented | 8 | % | **47-72** |
| **Eosinophils** | 0 | % | **0.5-5** |
| **Basophils** | 0 | % | **0-1** |
| **Lymphoblasts****Prolymphocytes****Lymphocytes** | 3580 | %%% | **0****0****25-35** |
| **Monocytes** | 3 | % | **3-11** |

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**Questions:**

**1. Identify what type of pathological process of the leukocyte system is attested in the patient.**

**2. What is the etiology of this pathological process of the leukocyte series attested in the patient?**

**3. What are the pathogenetic factors that promote lymphoblast malignancy?**

**4. What is the pathogenetic mechanism of recurrent bacterial infections in the patient?**

**5. Explain what does Gumprecht fingerprints represent?**

**6. It is known that chronic lymphocytic leukemia can transform into the acute form. The basis of this process is "Tumor Progression". What is this process?**

**7. What is the pathogenetic mechanism of jaundice in the patient?**

**Clinical case 5**

A 45-year-old patient presents to the family doctor with the following complaints: cough with muco-purulent sputum, dyspnoea, fever 38.5○C, chest pain, muscle weakness. The symptoms started several days ago and gradually worsened. On auscultatory examination, the doctor found rales and crackles in the right lung and an increased respiratory rate (24 breaths per minute).

Chest X-ray: lobar pneumonia on the right side, middle lobe.

**Patient's haemogram**

|  |  |  |
| --- | --- | --- |
| **CBC** | **Valori** | **Valori de referință**  |
| **Hematocrit** | 45 | **Males** 39-49%**Females** 35-45% |
| **Hemoglobin** | 15,1 | **Males** 13,6-17,5 g/dL**Females** 12,0-15,5 g/dL |
| **Eritrocite**  | 5,6 |  4,7-6,1 million/cu mm |
| **Number of reticulocytes** | 1,3 | 0,5-1,5% |
| **MCV** | 97 | 80 -100 fL |
| **MCH** | 27 | 26 – 34 pg |
| **MCHC** | 34 | 31 -36 g/dL |
| **Leucocyte** | 15,7 | 4,800–9,000/cumm |
| **Neutrophils** | 72 | 60 -62% |
| Segmented neutrophils | 58 | 40-60% |
| Nonsegmented neutrophils | 10 | 1-6% |
| Metamyelocytes  | 4 | 0% |
| Myelocytes  | 0 | 0% |
| **Basophiles** | 0 | 0- 1,0%10 -120/cu mm |
| **Eosinophil**  | 1 | 1-4%4- -500 cu mm |
| **Lymphocyte** | 23 | 25-35%800 -3,500/cu mm |
| **Monocyte**  | 4 | 3-7%200-800/cu mm |
| **thrombocyte** | 357 | 150,000-450,000/cu mm |
| **Morphological changes of blood cells** |  |  |

**1. What type of pathological process of the leukocyte system is present in the patient? Argue the changes in the haemogram.**

**2. What is the pathogenetic mechanism of this pathological process of the leukocyte system?**

**3. What type of neutrophilia is seen in the patient, with left- or right-sided nuclear deviation? Please justify your answer. What are the types of left-shift neutrophilia?**

**4. What is the main function of migrating neutrophils in the inflammatory focus?**

**5. In severe pneumonia, a leukemoid reaction of the myeloid series may be present in the hemoleucogram. Is this change present in the patient? How is it characterised?**

**6. What is the pathogenetic mechanism of fever in this patient?**

**7. What type of inflammation predominates in the patient (acute or chronic)? Please justify your answer.**

**Topic 3: Pathophysiology of the cardiovascular system. Heart failure. Circulatory insufficiency. Etiology. Pathogenesis. Modification of intracardiac hemodynamics.**

**Clinical case 1**

Patient N., 66, 11 years old, hypertensive, complains of low tolerance to physical exertion, manifested by the appearance of dyspnea (the feeling of lack of air).

The estimated echocardiographic indices are:

♦Ejection fraction (EF) =59% (norm, EF>50%).

♦Systolic volume =51 ml (norm >70 ml).

♦Minute volume =3.1 L (norm =4-6 L).

♦Heart rate =60 b/min.

♦End-diastolic volume =100 ml (norm >120 ml).

♦End-systolic volume =41 ml (norm >55 ml).

♦End-diastolic diameter of the LV =40 mm (norm >43 ml).

**Questions:**

**1. What type of heart failure is present, and which functional indices have diagnostic value?**

**2. What type of myocardial remodeling is present, its genesis and pathogenetic contribution to the impairment of diastole?**

**3. What are the mechanisms of reduced oxygen supply of cardiomyocytes in a concentrically hypertrophied myocardium?**

**4. What are the mechanisms of impaired diastolic relaxation in the hypertensive heart?**

**5. Which remodeling patterns, apart from concentric hypertrophy, lead to impaired diastolic relaxation?**

**6. Explain the causes and nature of the alteration of the heterometric and homeometric response in diastolic heart failure?**

**7. What are the factors that activate fibroblasts and increase extracellular matrix growing in diastolic heart failure?**

**Clinical case 2**

Patient N., 67, 11 years old, complains of anginal pain and low tolerance to physical exertion. Edema of the legs periodically occurs.

Coronary angiography estimates stenosis of up to 80% of the left descending artery (LAD).

Estimated echocardiographic indices are:

♦Ejection fraction (EF) =39% (normal, EF>50%).

♦Heart rate =80 b/min

♦Systolic volume =48 ml (normal >70 ml).

♦Minute volume =3.6 L (normal =4-6 L).

♦End-systolic volume, end-diastolic volume and end-diastolic pressure of the left ventricle are elevated.

♦Circulating level of natriuretic peptide B (PNB) is elevated.

**Questions:**

**1. What type of heart failure is present, and which functional and biochemical indices have diagnostic value?**

**2. What are the causes of systolic heart failure in this patient?**

**3. What are the mechanisms of pulmonary arterial pressure elevation in systolic heart failure?**

**4. What are the causes of edema in systolic heart failure?**

**5. What are the consequences of calcium accumulation in cardiomyocytes caused by the energy deficiency attested in systolic heart failure?**

**6. What are the mechanisms of urgent activation of contractile function in systolic heart failure?**

**7. What are the early compensatory and decompensatory functional changes of systolic heart failure?**

**Topic 4: Dysregulation of vascular tone. Primary arterial hypertension. Secondary arterial hypertension. Etiology. Pathogenesis. Hemodynamic changes. Cardiac arrhythmias.**

**Clinical case 1**

Patient N., 57 years old, has been suffering from essential or primary arterial hypertension (PAH) for 9 years.

He complains of periodic headaches, low tolerance to physical exertion, sleep disorders.

Functional, instrumental and laboratory assessments:

♦Systolic blood pressure =170 mm Hg. Diastolic blood pressure =100 mm Hg. Heart rate =60 b/min.

♦Thickness of the intima-media complex of the common carotid artery =1.2 mm (norm<0.9 mm).

♦Reduced level of nitric oxide (NO). Hyperhomocysteinemia =21 μmol/L (norm<10 μmol/L).

♦Triglycerides =180 mg/dL (norm<150 mg/dL). Total cholesterol =6.8 mM/L (norm<5.4 mg/dL). Increased oxy-LDL levels.

♦Microalbuminuria =190 mg/24 hours (normal <30 mg/24 hours).

♦Vit.D (25.OH-D) level =30 nM/L (normal =50-70 nM/L).

♦C-reactive protein =4 mg/L (normal <1.0 mg/L). Elevated IL-1b, IL-6 and TNF-α.

**Questions:**

**1. What are the general etiological factors that lead to endothelial injury and dysfunction in patients with PAH?**

**2. What are the factors that lead to NO deficiency in patients with PAH that are dispensable from endothelial injury and the mechanism of their action?**

**3. The deficiency of which factors of endothelial origin have a pathogenetic role in vasoconstriction and the evolution of PAH?**

**4. What are the 3 components of the renin-angiotensin-aldosterone system with a pathogenetic role in the development of PAH and the imminent mechanisms?**

**5. Microalbuminuria is an early marker of renal dysfunction in patients with PAH (the kidney is a target organ). What are the mechanisms?**

**6. What are the mechanisms of pathogenetic contribution of hyperhomocysteinemia in the evolution of PAH?**

**7. What are the mechanisms of pathogenetic contribution of vitamin D deficiency in the evolution of PAH?**

**Clinical case 2**

Patient N., 41 years old, is diagnosed with Cushing's syndrome associated with secondary arterial hypertension (SAH).

She complains of periodic headaches, low tolerance to physical exertion.

Functional, instrumental and laboratory assessments:

♦Systolic blood pressure =170 mm Hg. Diastolic blood pressure =100 mm Hg.

♦Heart rate =64 beats/min.

♦The size of the left adrenal gland is enlarged on radiography.

♦Hypercortisolaemia. Reduced ACTH level. Hypernatremia. Hypokalemia. Hyperglycemia. Dyslipidemia.

**Questions:**

**1. What is the pathogenetic contribution of cortisol excess in connection with Ang II, regarding SAH?**

**2. What is the pathogenetic contribution of cortisol excess in connection with the sympathetic system, regarding SAH?**

**3. What is the pathogenetic contribution of cortisol excess in connection with mineralocorticoid activity, regarding SAH?**

**4. What is the pathogenetic contribution of cortisol excess in connection with nitric oxide (NO), regarding SAH?**

**5. What is the pathogenetic contribution of cortisol excess in connection with hyperglycemia, regarding SAH?**

**6. What is the pathogenetic contribution of cortisol excess in connection with insulin resistance and the associated metabolic syndrome, regarding SAH?**

**7. What is the pathogenetic contribution of cortisol excess in connection with autocosanoids (local hormones), regarding SAH?**

**Topic 5: Pathophysiology of breathing. Dysregulation of alveolar ventilation, pulmonary diffusion and perfusion. Obstructive and restrictive lung pathology. Respiratory failure**

**Clinical case 1**

Patient N., a 20-year-old, height - 164 cm, body weight - 65 kg, complains of periodic choking attacks with difficulty in exhalation, accompanied by thick, glassy sputum. The attacks started occurring in the last two years, after family had brought a dog, and are often triggered by inhaling of cold air or by strong emotions. The mother suffers from urticaria, and the brother has pollen allergy (pollinosis).

Blood count:

Erythrocytes – 4,5× 1012 /L

Hb – 136 g/L

Haematocrit– 48%

Leucocyte– 12×109 /L

basophiles– 1%,

eosinophile– 9%

segmented neutrophils - 55%

nonegmented neutrophils– 5%

lymphocyte– 25%

monocyte – 5%.

ESR– 20 mm/ hour.

ventilatory parameters:

FR (breathing rate) - 20/min,

TV (tidal volume) - 0,4L,

RV (respiratory volume) Maxim - 60L/min,

TLC (total lung capacity) - 3,7L,

FRC (forced residual capacity) - 3,8L,

FEV1 (forced expiratory volume per second) - 2L,

RV (residual volume) -1,8L,

inspiration/expiration ratio -1:1,5.

**Questions:**

**1. Explain the occurrence of choking and difficulty in expiration in the patient.**

**2. What is the role of corneal (bronchial mucosal) inflammation in the pathogenesis of bronchial asthma?**

**3. What is the mechanism of expiratory dyspnoea?**

**4. What does the Tiffneau index mean?**

**5. Calculate the Tiffneau index in the given patient. Characterise the Tiffneau index in obstructive and restrictive pathologies.**

**6. What are the features of pneumogram in obstructive respiratory diseases?**

**7. Are there pulmonary perfusion disturbances in lower obstructive diseases (as bronchial asthma)? Argue answer.**

**Clinical case 2**

Patient K., 43 years old, presented to the doctor with complaints of weakness, shortness of breath, high fever, and mucopurulent sputum with a rusty tint. Sputum microscopy revealed leukocytes and erythrocytes. On auscultation – wet rales in the lungs.

Blood count:

Erythrocytes – 4,8× 1012 /L

Hb – 132 g/L

Haematocrit – 48%

Leucocyte – 15×109 /L

basophiles – 1%,

eosinophile – 9%

segmented neutrophils – 52%

nonegmented neutrophils – 5%

metamielocite – 3 %

lymphocyte – 25%

monocyte – 5%. ESR – 26 mm/ hour.

Blood gases:

PaO2 – 50 mm Hg, PaCO2 – 42 mm Hg

ventilatory parameters:

FR (breathing rate) – 30 /min,

RV (respiratory volume) – 0,25 L,

inspiratory reserve volume– 1L,

vital lung capacity– 2,5 L,

forced vital capacity– 2,3 L,

FEV1 (forced expiratory volume per second) – 2 L,

RV (residual volume) – 3,7 L,

anatomical dead space capacity– 150 ml

**Questions:**

**1. What type of ventilatory disorder has this patient?**

**2. What type of Respiratory Failure has this patient according to pathogenesis?**

**3. How do you explain the pulmonary ventilation dysregulation in this patient?**

**4. How do you explain the dysregulation of gas diffusion in this patient?**

**5. How do pulmonary ventilation indices change in restrictive conditions?**

**6. Explain the mechanism of dyspnoea in this patient.**

**7. Explain the presence of leucocytes and red blood cells in the sputum.**

**Clinical case 3**

Patient K., aged 66 years, 5 weeks after a myocardial infarction, had frequent, increased shallow wheezing, during which a cough with a small amount of sputum and a mixture of blood occurred. The ECG showed characteristic signs of left ventricular posterior wall infarction.

Spirographic dates: RR = 26 pe min; forced vital capacity (FVC) = 3,23 l; total lung capacity (TLC) = 3,0 l; tidal volume (TV) = 0,7 l; FEV1 = 2 l/s; PaO2 in arterial blood before and after hyperventilation was 93 and respectively 92 mmHg.

Normal lung volume values:

Respiratory rate (RR) = 16-18/min

Forced vital capacity (FVC) = 3,5 L

Total lung capacity (TLC) = 3,5-6,0 L

Tidal volume (TV) = 0,3-0,9 l

Respiratory volume per minute (RVM) = 4,8 - 16,2 l

Forced expiratory volume per second (FEV1) = 3,2 l/s

Tiffneau index = 75-90%

**Questions.**

**1. Explain the emergent respiratory compensatory mechanisms present in this patient.**

**2. How do you explain the breathing disturbances in this patient?**

**3. How do you explain the productive cough with a small amount of sputum and a mixture of blood?**

**4. Calculate and evaluate: RVM, Tiffneau index.**

**5. What type of pulmonary alveolar ventilation disorder?**

**6. Does the patient have pulmonary diffusion disturbance?**

**7. Give a general conclusion about the condition of the patient's respiratory system.**

**Clinical case 4**

Patient, 57 years old. Smoker for 20 years, complaining of shortness of breath appeared during physical effort, fatigue. Objective: skin rose-pale, the rib cage is enlarged, the depth of respiration is decreased, respiratory rate 28 per minute. On chest palpation the intercostal spaces are enlarged. On comparative percussion of the rib cage is sound hypersonority of the entire lung surface. The lower pulmonary boundaries are lowered. Respiratory excursion reduced. On auscultation of the lungs - forced breathing. Comparative chest percussion shows hyperresonance over the entire lung surface. Absolute cardiac dullness is absent

**Questions.**

**1. How do you explain "feeling of air insufficiency"?**

**2. What is the general mechanism of dyspnea?**

**3. How do you explain that the rib cage is enlarged in this patient?**

**4. What do we call emphysema and what is the general characteristic of pulmonary emphysema?**

**5. What is the pathogenesis of emphysema?**

**6. What impact does cigarette smoke have on the pathogenesis of pulmonary emphysema?**

**7. How do pneumogram indices change in pulmonary emphysema?**

**Topic 6: Pathophysiology of the digestive system. Dysregulation of salivary secretion, gastric secretion, pancreatic insufficiency. Maldigestion and malabsorption in digestive pathology. Diarrhea.**

**Clinical case 1**

**Patient B., 45** years old, underwent subtotal resection of the stomach (antrectomy with vagotomy).

**Complaints:** general weakness, lack of appetite, diarrhea, impaired motility and sensitivity in the lower extremities. Over the past year, she has lost 5 kg.

**Objectively***:* pale skin, tachycardia, shortness of breath, atrophy of the oral mucosa.

**Blood test: erythrocytes** 1.7x1012/l; leukocytes – 3x109/l; platelets 100x109/l. MCV and MCH are increased. Blood smear – *megaloblasts, megalocytes, erythrocytes with basophilic granularity; Jolly bodies and Cabot rings; neutrophils with a hypersegmented nucleus.*

 **Questions**

**1. What changes in gastric secretion occurred in the patient after subtotal resection of the stomach and what is the pathogenesis?**

**2. How does the motor, evacuation, absorption, reservoir functions of the stomach change under conditions of hyposecretion and achlorhydria?**

**3. What metabolic disorders occur in gastric hyposecretion and achlorhydria?**

**4. What are the consequences of the rapid evacuation of an alimentary bolus with hyposecretion of the stomach?**

**5. Explain the pathogenesis of weight loss in this patient.**

**6. To remove the pathogenic chain of consequences of protein digestion and malabsorption in case of increased stomach acidity.**

**7. What is the pathogenesis of diarrhea and its consequences in gastric hyposecretion?**

**8. What is the pathogenesis of changes in the cytological picture of the patient's blood?**

**9. Explain the pathogenesis of motor and sensory disorders in the patient?**

**Clinical case 2**

**Patient A., 40 years old,** complains of pain in the epigastric region, heartburn, belching of acidic stomach contents, frequent constipation. The symptoms augmented in the last 2 years, when some problems appeared at work, but they became more pronounced in the last six months, when she lost 8 kg in weight.

**Objectively**: asthenic physique.

**Gastric secretion indicators:**

1. The volume of gastric juice collected on an empty stomach is 60 ml (N-up to 50);

2. Total acidity -50 UT (N-up to 40);

3. Free fraction HCl – 15 UT (N-up to 20)

4. Conjugate fraction HCl-30 (N- up to 25)

5. Gastric secretion under submaximal stimulation with histamine 110 (N-up to 100)

**Questions:**

**1. What changes in the secretion of gastric juice are indicated in this patient?**

**2. What paracrine mechanisms regulate gastric secretion and how?**

**3. What endocrine mechanisms regulate gastric secretion and how?**

**4. How does the motor, evacuation, absorption, reservoir function of the stomach change under conditions of gastric hypersecretion?**

**5. What is the mechanism of (pyrosis) heartburn and belching in the patient?**

**6. What is the pathogenesis of constipation and intestinal autointoxication in hyperchlorhydria?**

**7. How does the functionality of the gastrointestinal mucosa change under chronic stress?**

**Clinical case 3**

**Patient D., 60 years old,** complains of heartburn, constant epigastric pain, aggravated after meals, associated with nausea and periodic vomiting. Indicates weight loss (about 6 kg in the last 2 months). The patient regularly takes non-steroidal anti-inflammatory drugs for chronic back pain, smokes about 15 cigarettes a day, occasionally drinks alcohol

**Objectively:** epigastric tenderness is pronounced, but without signs of peritonitis.

**Endoscopy of the upper digestive tract** indicates the detection of an ulcerative lesion on the anterior wall of the stomach.

**Test for Helicobacter pylori +++**

**Questions:**

**1. Explain the pathogenesis of the ulcerogenesis due to administration of nonsteroidal anti-inflammatory drugs (NSAIDs).**

**2. How does *Helicobacter pylori* contribute to the pathogenesis of gastric ulcers?**

**3. What are the mechanisms by which *Helicobacter pylori* changes the functionality of the gastric mucosa?**

**4. List and explain the protective mechanisms of the gastric mucosa that resist the aggressive action of gastric juice.**

**5. What is the role of nicotine in ulcerogenesis?**

**6. What is the ulcerogenic mechanism of duodenal-gastric reflux?**

**Clinical case 4**

**Patient A., 55 years old,** complains of general weakness, nausea, vomiting, diarrhea, shingles pain that occurs after a large meal, frequent pain in the epigastric region. In 8 months, he lost 10 kg. He consumes a lot of fluids (6 l/24 hours), and also indicates polyuria.

**Anamnesis:** Alcohol abuse for 15 years. 8 years ago he suffered an attack of acute alcoholic pancreatitis.

**Laboratory tests***:* blood glucose level - 12 mmol/l; glucose -4% (diuresis 6 l/24 hours), low glucose tolerance; hypoalbuminemia, hypomagnesaemia and hypocalcemia.

**Pancreatic juice**: low trypsin activity; low concentration of bicarbonates.

**Urine** – creatinine increase

**Coprogram**: amylorrhea, steatorrhea.

**Questions**

**1. Clinical manifestations, data of laboratory and paraclinical studies indicate chronic exocrine and endocrine insufficiency of the pancreas. What is the pathogenesis of weight loss in pancreatic insufficiency?**

**2. What is the pathogenesis of general weakness in the patient?**

**3. What changes in carbohydrate metabolism indicate pancreatic insufficiency and what are the specific symptoms of the patient?**

**4. What is the pathogenesis of steatorrhea and amylorrhea in the patient?**

**5. What is the role of alcohol in the pathogenesis of exocrine pancreatic insufficiency?**

**6. What is the pathogenesis of hypocalcemia in exocrine pancreatic insufficiency?**

**7. What enzyme consequences accompany exocrine pancreatic insufficiency and which of these are seen in the patient?**

**8. One of the causes of B12-deficient anemia may be exocrine pancreatic insufficiency. Explain the pathogenesis.**

**9. What is the mechanism of vomiting and nausea in a patient with exocrine pancreatic insufficiency?**

**Topic 7: Pathophysiology of the liver. Liver failure. Etiology. Portal hypertension. Ascites. Hepatic encephalopathy.**

**Patient’s Chief Complaints**

Provided by wife: “My husband’s very confused and he has been acting strangely. This morning, he couldn’t answer my questions and seemed not to recognize me.”

**The patient S.** is a 46 years male with a history of chronic alcoholism. He was admitted to the hospital from the outpatient clinic with abdominal swelling and confusion. He has unintentionally gained 8 lbs during the past four weeks. Before becoming confusing the patient complains of abdominal pain, itching, nausea, vomiting, hematemesis, gum bleeding, loss of appetite, weakness, diarrhea.

**Medical history**

• Cirrhosis diagnosed 4 years ago with ultrasound and liver biopsy (micronodular cirrhosis)

• uncontrolled ascites

• two episodes of upper GI hemorrhages from esophageal varices (2 years ago)

• E. coli-induced bacterial peritonitis 3 years ago

• No history to suggest cardiac or gallbladder disease

• No previous diagnosis of viral or autoimmune hepatitis

**On physical examination**: The patient is restless, mildly jaundiced, and disoriented to time, place, and people.

• BP 110/65, Ps- 83, regular (supine)

• BP 95/60, Ps- 106, regular (standing); ECG – Sinus tachycardia. Low amplitude of T wave, U wave.

• Breathing rate - 27/min

**Skin.** Dry, warm with reduced turgor, hyperkeratosis, scratching. Jaundice. Palmar erythema. Ecchymoses on lower extremities. Gynecomastia.

**Abdomen** is moderately distended, firm, and slightly tender. Prominent veins observed around umbilicus.

**Diuresis** is reduced. Urine is dark.

**Feces** fade, presence of lipids.

**Laboratory Blood Test Results**

|  |  |  |
| --- | --- | --- |
| **CBC** | **VALUES** | **REFERENCE RANGES**  |
| **Hematocrit** | 36 | **Males** 39 - 49%**Females** 35 - 45% |
| **Hemoglobin**  | 11,8 | **Males** 13,6 - 17,5 g/dL**Females** 12,0 - 15,5 g/dL |
| **Red blood cells (RBC)** | 3,7 |  4,7-6,1 million/cu mm |
| **MCV** | 71 | 80 -100 fL |
| **MCH** | 19 | 26 – 34 pg |
| **MCHC** | 25 | 31 - 36 g/dL |
| **White blood cells** | 3.5 | 4,800–9,000/cu mm |
| **Basophil count** | 0,5 | 0 - 1,0 |
| **Eosinophil count** | 3 | 1. 4%
 |
| **Lymphocyte count** | 26 | 25 - 35% |
| **Monocyte count** | 5 | 3 - 7% |
| **Thrombocytes**  | 86,000 | 150,000 – 450,000/cu mm |

**BIOCHEMICAL BLOOD TESTS**

|  |  |  |
| --- | --- | --- |
| **Protein total** | 4,1 | 6,0 – 8,0 g/dL |
| **Albumin** | 2,2 | 3,4 – 4,7 g/dL |
| **Globulin** | 5,7 | 2.6 - 4.6g/dL |
| **Fibrinogen** | 98 | 160 – 450 mg/dL |
| **Prothrombin time**  | 20,2 | 11,0 -13,5 sec |
| **Glucose, *serum fasting*** | 46 | 60 – 110 mg/dL |
| **Glucose, *2 hours postprandial*** | 197 | < 150 mg/dL |
| **Triglyceride** | 145 | <165 mg/dL |
| **Cholesterol** | 109 | Desirable: < 200 mg/dLBorderline: 200–239 mg/dLHigh risk: >240 mg/dL |
| **Blood urea nitrogen (BUN)** | 5,8 | 8 – 20 mg/dL |
| **Creatinine** | 0,4 | 0,6-1,2 mg/dL |
| **Bilirubin total** | 3,8 | 0,1 – 1,2 mg/dL |
| **Direct or conjugated bilirubin** | 2,4 | 0,1 - 0,5 mg/dL |
| **Indirect or unconjugated bilirubin** | 1,4 | 0,1 – 0,7 mg/dL |
| **Alanine aminotransferase (ALT)** | 209 | 7-56 IU/L |
| **Aspartate aminotransferase (AST)** | 107 | 0 – 35 IU/Ll |
| **Ammonia (NH3)** | 250  | 18 – 60 µg/dL |
| **Lactic acid** | 2,8 | < 2,0 mmol/L |
| **Ketone bodies**  | 2,2 | < 1mg/dl |
| **Ca++** | 1,7 | 2,1 - 2,6 mmol/L |
| **Na+** | 156 | 135 - 145 mEq/L |
| **K+** | 3,3 | 3,5 – 5,5 mEq/L |
| **Folic acid** | 103 | 165 - 760 ng/mL |
| **B12 vitamin** | 98 | 140 - 820 pg/mL |
| **Vitamin A** | 21 | 30 – 65 mg/dL |
| **Vitamin E** | 0,3 | 0,5 – 0,7 mg/dL |
| **Vitamin D, 1,25OH** | 16 | 20 -76 pg/mL |

**Arterial Blood Gases**

|  |  |  |
| --- | --- | --- |
| Parameter | Value | Reference ranges |
| pH | 7,32 | 7,35 - 7,45 |
| PaO2 | 78 | 98 mmHg |
| PaCO2 | 32 | 35 - 40 mmHg |
| SaO2 | 85 | >95% |

|  |  |  |
| --- | --- | --- |
| **Bicarbonate** | 30 | 21 – 28 mEq/L |

**Questions:**

**1. What is etiology of this disease? Pathogenetic mechanism?**

**2. Explain the pathophysiology of liver fibrosis?**

**3. What are the pathogenetic mechanisms of ascites in the patient?**

**4. What is the pathogenetic mechanism of hepatic encephalopathy?**

**5. Which laboratory test strongly suggests that the patient has developed hepatic encephalopathy?**

**6. What is glycemic dyshomeostasis in the patient? Pathogenetic mechanism.**

**7. What are the changes in protein profile in the blood? Mechanisms?**

**8. What are the changes in lipid profile in the blood? Mechanisms? Consequences**

**9. Explain the hemodynamic changes in the patient?**

**10. Explain the respiratory changes in the patient?**

**11. Explain the cutaneous changes in the patient?**

**12. What biochemical tests shows impairment of liver function? What are liver-specific tests?**

**13. Explain the haematological changes in the patient. Pathogenetic mechanisms?**

**14. What is the pathogeny of anaemic syndrome in this patient?**

**15. What types of anemia can develop in patients with chronic liver failure? Pathogenetic mechanisms.**

**16. What are the hydro-electrolytic disturbances in the patient? Mechanisms?**

**17. What are the acid-base disorders in the patient? Mechanisms.**

**18. Explain the changes of diuresis?**

**Topic 8: Pre-hepatic, hepatic and post-hepatic jaundice. Dysregulation of bile pigment metabolism. Congenital hyperbilirubinemia.**

**Clinical case 1**

A 38-year-old male patient visited his therapist. The patient, 2 weeks ago, had a medical condition of pneumonia and received treatment with Benzylpenicillin 600mg × 4 times per day during 7 days.

He had no deleterious habit of drinking alcohol or smoking.

General physical examination of the patient revealed generalized yellow discoloration of skin and sclera. Patient complains about fatigue and muscle weakness.

**On physical examination**, he is afebrile but deeply jaundiced.

**Blood pressure** = 105/60 mm Hg, FCC = 102 bpm;

**Shortness of breath and respiratory rate** = 21 bpm;

**Urine is dark: bilirubin** – abs, urobilinoids bodies ++, bile acids – abs

Dark faeces.

In the blood anti-erythrocytes antibodies.

**Laboratory Blood Test Results**

|  |  |  |
| --- | --- | --- |
| CBC | VALUES | REFERENCE RANGES |
| Hematocrit | 30 | Males 39 - 49%Females 35 - 45% |
| Hemoglobin  | 10,8 | Males 13,6 - 17,5 g/dLFemales 12,0 - 15,5 g/dL |
| Red blood cells (RBC) | 3,2 | 4,7 - 6,1 million/cu mm |
| Reticulocyte count | 2,2 | 0,5 - 1,5% |
| White blood cell (WBC) count | 5,800 | 4,800 – 9,000/cu mm |
| Neutrophil count | 60 | 60 - 62% |
| Basophil count | 0,5 | 0 - 1,0% |
| Eosinophil count | 3 | 1-4% |
| Lymphocyte count | 26 | 25 - 35% |
| Monocyte count | 5 | 3 - 7% |
| Thrombocytes  | 210,000 | 150,000 – 450,000/cu mm |
| MCV | 98 | 80 - 100 fL |
| MCH | 33 | 26 – 34 pg |
| MCHC | 34 | 31 - 36 g/dL |

**Biochemical blood tests**

|  |  |  |
| --- | --- | --- |
| Protein total | 7,1 | 6,0 – 8,0 g/dL |
| Albumin | 3,7 | 3,4 – 4,7 g/dL |
| Prothrombin time | 12,2 | 11,0 -13,5 sec |
| Glucose, *serum fasting* | 76 | 60 – 110 mg/dL |
| Glucose, *2 hours postprandial* | 143 | < 150 mg/dL |
| Bilirubin total | 3,1 | 0,1 – 1,2 mg/dL |
| Direct or conjugated bilirubin | 0,7 | 0,1 - 0,5 mg/dL |
| Indirect or unconjugated bilirubin | 2,4 | 0,1 – 0,7 mg/dL |
| Alanine aminotransferase (ALT) | 69 | 7 - 56 IU/L |
| Aspartate aminotransferase (AST) | 57 | 0 – 35 IU/Ll |
| Alkaline phosphatase  | 95 | 40 - 100 U/L |
| Gamma-glutamyl transpeptidase (GGT) | 40 | 9 – 48 U/L) |

**Questions:**

**1. What changes in bilirubin pigments is attested in this patient? Explain pathogenetic mechanisms**

**2. What changes in general blood analyses and biochemical blood test are in relation with this pathologic condition?**

**3. Give pathogenetic chain which reflects changes in steps of bilirubin metabolism in this patient**

**4. Explain changes of bilirubin fractions (total bilirubin, conjugated and unconjugated bilirubin) in the blood. Explain pathogenetic mechanisms.**

**5. Explain changes which are attested in the urine of this patient. Give pathogenetic mechanisms**

**6. Explain changes which are attested in the feces of this patient. Give pathogenetic mechanisms**

**7. What is the clinical significance of seric levels of alkaline phosphatase and Gamma-glutamyl transpeptidase in this patient?**

**Clinical case 2**

Patient T, is a 21 y.o. male presented to the emergent department after he noticed his “eyes looked yellow” for the past 1 month. He has no other symptoms but for the past 2 months he noticed easy fatigability, abdominal pain and mild pruritus. He also noted that his urine has become dark. There was no history of jaundice before and he did not report any history of fever, headache or confusion. He has not noted any abdominal swelling or weight loss.

**On physical examination**, he is afebrile but deeply jaundiced.

 **Blood pressure** = 90/60 mm Hg, pulse = 60 bpm and respiratory rate = 16 bpm.

Abdominal exam is notable for enlarged liver 15 cm but no shifting dullness, bulging flanks, or “fluid wave”. There was no splenomegaly.

Thyroid, skin, breast, cardiovascular, chest and neurological exams were unremarkable.

**Urine:** bilirubin++, urobilinoids bodies +, bile acids+

**Laboratory Blood Test Results**

|  |  |  |
| --- | --- | --- |
| CBC | VALUES | REFERENCE RANGES |
| Hematocrit | 41 | Males 39-49%Females 35-45% |
| Hemoglobin | 13,8 | Males 13,6-17,5 g/dLFemales 12,0-15,5 g/dL |
| Red blood cells (RBC) | 4,9 | 4,7-6,1 million/cu mm |
| White blood cell (WBC) count | 4,800 | 4,800–9,000/cu mm |
| Neutrophil count | 48 | 60 -62% |
| Basophil count | 0,5 | 0- 1,0% |
| Eosinophil count | 3 | 1-4% |
| Lymphocyte count | 26 | 25-35% |
| Monocyte count | 5 | 3-7% |
| Thrombocytes | 210,000 | 150,000 – 450,000/cu mm |

**Biochemical blood analysis**

|  |  |  |
| --- | --- | --- |
| Protein total | 5,5 | 6,0 – 8,0 g/dL |
| Albumin | 3,1 | 3,4 – 4,7 g/dL |
| Fibrinogen | 128 | 160 – 450 mgd/L |
| Prothrombin time | 20,2 | 11,0 -13,5 sec |
| Glucose, *serum fasting* | 46 | 60 – 110 mg/dL |
| Glucose, *2 hours postprandial* | 197 | < 150 mg/dL |
| Bilirubin total | 3,8 | 0,1 – 1,2 mg/dL |
| Direct or conjugated bilirubin | 2,4 | 0,1 - 0,5 mg/dL |
| Indirect or unconjugated bilirubin | 1,4 | 0,1 – 0,7 mg/dL |
| Alanine aminotransferase (ALT) | 209 | 7-56 IU/L |
| Aspartate aminotransferase (AST) | 107 | 0 – 35 IU/Ll |
| Alkaline phosphatase (AP) | 115 | 40-100 U/L |
| Gamma-glutamyl transpeptidase (GGT) | 50 | 9–48 U/L |
| Ca++ | 1.9 | 2,1 - 2,6 mmol/L |
| Vitamin A | 28 | 30 – 65 mg/dL |
| Vitamin E | 0,4 | 0,5 – 0,7 mg/dL |
| Vitamin D, 1,25OH | 19 | 20 -76 pg/mL |

**1. What changes in bilirubin pigments is attested in this patient? Explain pathogenetic mechanisms**

**2. What changes in biochemical blood test are in relation with this bilirubin pigment changes?**

**3. Give pathogenetic chain which reflects changes in steps of bilirubin metabolism in this patient**

**4. Explain changes of bilirubin fractions (total bilirubin, conjugated and unconjugated bilirubin) in the blood. Explain pathogenetic mechanisms.**

**5. Explain changes which are attested in the urine of this patient. Give pathogenetic mechanisms**

**6. Explain changes which are attested in the feces of this patient. Give pathogenetic mechanisms**

**7. What is the clinical significance of seric levels of alkaline phosphatase and Gamma-glutamyl transpeptidase in this patient?**

**8. What biochemical blood tests and clinical manifestations reflect hypocholia?**

**9. What biochemical blood tests and clinical manifestations reflect cholemia?**

**10. What biochemical blood tests reflect impairment of liver functions?**

**Clinical case 3**

An 64-year-old woman presented to the emergency department with a 5-day history of jaundice, fever and abdominal pain. The pain was sudden in onset and gradually intensifies in severity, located in the upper abdomen, which radiates directly through the abdomen to the back.

Also, patient has complained about nausea, vomiting and annoying itching. Feces are discoloured and fatty. Last month the patients lost appr. 5 kg and visual impairments was attested.

Physical examination showed sclera icterus and right upper quadrant tenderness, scratches on the skin of the abdomen and legs.

HR = 55 bpm, BP= 85/50mmHg

**Urine is dark:** bilirubin+++, bile acids +++

Abdominal USG – enlargement of the pancreatic head (tumor suspicion).

**Laboratory Blood Test Results**

|  |  |  |
| --- | --- | --- |
| CBC | VALUES | REFERENCE RANGES |
| Hematocrit | 40 | Males 39 - 49%Females 35 - 45% |
| Hemoglobin | 13,8 | Males 13,6 - 17,5 g/dLFemales 12,0 - 15,5 g/dL |
| Red blood cells (RBC) | 4,9 | 4,7 - 6,1 million/cu mm |
| White blood cell (WBC) count | 12,800 | 4,800 – 9,000/cu mm |
| Neutrophil count | 70 | 60 - 62% |
| Basophil count | 0,5 | 0 - 1,0% |
| Eosinophil count | 3 | 1 - 4% |
| Lymphocyte count | 26 | 25 - 35% |
| Monocyte count | 5 | 3 - 7% |
| Thrombocytes | 210,000 | 150,000 – 450,000/cu mm |

**Biochemical blood tests**

|  |  |  |
| --- | --- | --- |
| Protein total | 6,8 | 6,0 – 8,0 g/dL |
| Albumin | 3,5 | 3,4 – 4,7 g/dL |
| Fibrinogen | 180 | 160 – 450 mg/dL |
| Prothrombin time | 15,5 | 11,0 - 13,5 sec |
| Bilirubin total | 6,8 | 0,1 – 1,2 mg/dL |
| Direct or conjugated bilirubin | 6,3 | 0,1 - 0,5 mg/dL |
| Indirect or unconjugated bilirubin | 0,5 | 0,1 – 0,7 mg/dL |
| Alanine aminotransferase (ALT) | 40 | 7 - 56 IU/L |
| Aspartate aminotransferase (AST) | 30 | 0 – 35 IU/Ll |
| Alkaline phosphatase  | 155 | 40 - 100 U/L |
| Gamma-glutamyl transpeptidase (GGT) | 105 | 9 – 48 U/L) |
| Serum amylase | 180 | <100 U/L3 |
| Lipase | 98 | < 60 U/L3     |
| Ca++ | 1,4 | 2,1 - 2,6 mmol/L |
| Vitamin A | 21 | 30 – 65 mg/dL |
| Vitamin E | 0,2 | 0,5 – 0,7 mg/dL |
| Vitamin D, 1,25OH | 16 | 20 -76 pg/mL |

**1. What changes in bilirubin pigments is attested in this patient? Explain pathogenetic mechanisms**

**2. What changes in biochemical blood test are in relation with this bilirubin pigment changes?**

**3. Give pathogenetic chain, which reflects changes in steps of bilirubin metabolism in this patient**

**4. Explain changes of bilirubin fractions (total bilirubin conjugated and unconjugated bilirubin) in the blood. Explain pathogenetic mechanisms.**

**5. Explain changes, which are attested in the urine of this patient. Give pathogenetic mechanisms**

**6. Explain changes, which are attested in the feces of this patient. Give pathogenetic mechanisms**

**7. What is the clinical significance of seric levels of alkaline phosphatase and Gamma-glutamyl transpeptidase in this patient?**

**8. What biochemical blood tests and clinical manifestations reflect acholia?**

**9. What biochemical blood tests and clinical manifestations reflect cholemia?**

**10. What biochemical blood test reflect impairment of liver functions?**

**Topic 9: Pathophysiology of the kidney. Acute renal failure. Chronic kidney disease. Etiology. Pathogenesis.**

**Normal Laboratory Values:**

* Creatinine clearance: **100-120 ml/min**
* Blood urea concentration: **2.5-8.3 mmol/L**
* Residual nitrogen: **14.3-28.5 mmol/L**
* Blood creatinine: **0.5-1.2 mg/%**

**Clinical Case 1**

**Patient A., 39 years old, admitted to the therapy department with the following complaints:**
Headache, decreased work capacity, chest pain, nausea, polydipsia, pruritus, localized facial and periorbital edema.

**Medical history:** Frequent episodes of angina.

**Objective examination:**

* Pale, dry skin with decreased turgor
* Blood pressure: **190/100 mmHg**
* **Blood tests:**
	+ Hemoglobin (Hb): **90 g/L**
	+ Erythrocytes: **3.2 × 10¹²/L**
	+ Leukocytes: **10.2 × 10⁹/L**
	+ pH: **7.3**
	+ Plasma osmolarity: **>290 mOsm/kg H₂O**
	+ Total protein: **50 g/L** (normal range: **65-85 g/L**)
	+ **Diuresis:** **500 mL/24h**, nocturia
	+ **Zimniţkii test:** Urine density in all samples: **1010-1012**
	+ **Creatinine clearance:** **40 ml/min** (**normal: 120 ml/min**)
	+ **Blood urea concentration:** **17 mmol/L**
	+ **Blood creatinine:** **5.0 mg/%** (**normal: 0.5-1.2 mg/%**)

**Urinalysis:**

* **Color:** Pink (resembling meat washings)
* **Proteins:** **1.92 g/L** (high molecular weight > 70,000)
* **Selectivity index:** IgG/transferrin ratio **> 0.1**
* **Leukocytes:** 2-3 per high power field
* **Modified erythrocytes:** Numerous per high power field
* **Casts:**
	+ Hyaline: **2-4 per high power field**
	+ Erythrocytic: **2-4 per high power field**
* **Antistreptolysin O titter:** Elevated

**Renal Biopsy Findings:**

* **Glomerular permeability:** Diffusely increased
* **Cellular infiltration:** Presence of leukocytes, neutrophils, monocytes
* **Endothelial and mesangial cell proliferation**
* **Interstitial edema**
* **Red blood cells in renal tubules**

**Immunofluorescence Findings:**

* **IgG and C3 deposits** in mesangial and basement membrane

**Diagnosis:** **Post-streptococcal glomerulonephritis**

**Questions**

**1. Based on clinical symptoms and laboratory findings, which syndrome does this case fall under? List its characteristic symptoms.**

**2. What is the pathogenesis of edema in nephritic syndrome?**

**3. What is the pathogenesis of haematuria in nephritic syndrome?**

**4. What is the pathogenesis of oliguria in nephritic syndrome?**

**5. What is the pathogenesis of hyperazotemia in nephritic syndrome?**

**6. What is the pathogenesis of glomerular lesions with loss of size selectivity in the filtration membrane?**

**7. What type of proteinuria is observed in nephritic syndrome, and what is its pathogenesis?**

**Clinical Case 2**

**Patient J., 46 years old**

**Diagnosis:** **Lipoid Nephrosis (Minimal Change Disease)**

**Symptoms:** Severe edema, weakness, loss of appetite.

**Objective findings:** Pale, swollen skin, ascites, **HR**: 90 bpm, dilated heart, muffled heart sounds.
**Blood tests:**

* **Albumin**: 15 g/L
* **Dysproteinaemia, hyperlipidemia, hypercholesterolemia**
* **Reduced antithrombin III, transferrin, gamma-globulins**

**Urinary findings:**

* **Proteinuria:** 20 g/L (molecular weight < 70,000, selectivity index < 0.1)
* **Casts:** Hyaline, waxy, epithelial, granular (up to 10 per field)

**Questions**

**1. What syndrome do these findings indicate?**

**2. What is the pathogenesis of albuminuria in nephrotic syndrome?**

**3. What is the mechanism of edema and hypercoagulability?**

**4. What is the mechanism of hypothyroidism and vitamin D deficiency in nephrotic syndrome?**

**5. What causes anemia and immune dysregulation?**

**6. What is the pathogenesis of hyperlipidemia?**

**7. Where do immune complexes deposit in glomerulopathies?**

**Clinical Case 3**

Patient E., 30 years old, has been working for many years in a chemical plant. He has not been previously diagnosed with renal pathology but complains of polydipsia, diuresis of 4 L/24 hours, clear urine, and a relative density of 1003. No proteins, glucose, or red blood cells are detected in the urine. The concentration of ADH in the blood is normal.

**1. Explain the pathogenesis of polyuria in this patient.**

**2. What is the pathogenesis of tubular polyuria in diabetes insipidus, and what test would differentiate these pathologies?**

**3. What is the mechanism of polyuria if glucosuria is detected in this patient?**

**4. What homeostatic imbalances can be detected in proximal tubulopathies? What are the consequences?**

**5. What changes in the urogram can be detected in distal tubulopathies? What are the consequences?**

**6. What is the pathogenesis of glomerular-origin polyuria?**

**7. Why does this patient have low urine density and osmolality? Explain the pathogenesis.**

**Clinical Case 4.**

Patient M., 38 years old, was admitted to the nephrology department with lower back pain and chills, with a history of chronic pyelonephritis.

**Objective findings:** Body temperature 38-39°C, pallor, BP – 130/90 mmHg. Daytime diuresis – 1200 mL, cloudy urine, density 1025.

**Urinalysis:** Albumin – traces, glucose – absent, leukocytes – 100 per HPF (pyuria), erythrocytes – 1-2 per HPF, leukocyte casts, granular casts, epithelial casts.

**Creatinine clearance:** 80 mL/min.

**Blood tests:** Residual nitrogen – 20 mmol/L, leukocytes – 14,000, metamyelocytes – 2%, band neutrophils – 15%, segmented neutrophils – 65%, lymphocytes – 15%, monocytes – 3%, ESR – 24 mm/hour.
**Urine culture:** 1 million Escherichia coli colonies/mL.

**1. Explain the pathogenesis of increased blood pressure in a patient with chronic pyelonephritis exacerbation.**

**2. Explain the pathogenesis of polyuria in this patient.**

**3. What is creatinine clearance, and how should its alteration be interpreted?**

**4. What is para-aminohippuric acid (PAH) clearance, and how should its alteration be interpreted?**

**5. Explain the pathogenesis of urinary casts (cylindruria) in this patient’s urinalysis.**

**6. Explain the pathogenesis of hyperazotemia in this patient.**

**Topic 10: Pathophysiology of the endocrine system. Dysregulation of endocrine function of the hypothalamus and pituitary gland. Hyper- and hyposecretion on the hypothalamus-adrenal cortex axis.**

**Clinical case 1**

Patient X, 38 years old, addresses the AMU with complaints of continuous abdominal pain, that appeared 4 hours ago. Gradually, the pain increases in intensity and fever appears. Other complaints: tremor, sweating, palpitations, severe asthenia. In the morning when she got out of bed, she lost the consciousness.

**From the anamnesis:** The patient suffers from pulmonary TB, and 2 years ago, following a diagnostic laparoscopy (performed to determine the cause of infertility in the couple), the ovarian tuberculosis was established. She is considered ill for 2 years since she complaints of muscular weakness, border-line states between irritability and depression, periodic diarrhea (not accompanied by fever) and frequent states of lipothymia, polyuria and nocturia. She complaints of weight loss (18 kg in 2 years). 6 months ago, atrophic gastritis was determined at the FGDS. The condition worsens when the patient is submitted to a stressful situation.

**Objective data:** The patient is 172 cm, 60 kg. BP on admission 90/45, Pulse=105, RR=22. She has a tanned skin appearance.

**Paraclinical exams:**

***General blood analysis:*** Hb=85 g/l; Erythrocytes=2.1x10⁹/l, Leukocytes=14x10⁹/l; Ht=52%;

***Biochemical blood analysis:*** Na⁺-122mEq/l (135-145 mEq/l); K⁺-6 (3.5-5.5 mEq/l); pH- 7.32 (7.35-7.45); Blood osmolarity-275 (285-295 mOsmol/l); Creatinine-2.4 (<1 mg/dl).

***Endocrine markers:*** Cortisol (7:00-10:00) = 50 (172-497 nmol/l); ACTH (7:00-10:00) = 120 (7.2-63.3 pg/ml; Aldosterone = 0.5 (1.76-23.2 ng/dl).

Taking into account the acute abdomen, pain unresponsive to spasmolytics, leukocytosis with increasing dynamics, after 24 hours, a diagnostic laparoscopy is done, which proceeds to laparotomy. Intraoperatively: necrosis of the small intestine, intestinal resection and end-to-end anastomosis of the small intestine are performed.

**Diagnosis:** Primary adrenocortical insufficiency (Addison's disease). Mesenteric artery thrombosis.

**Questions:**

**1. What is the pathogenetic mechanism of arterial hypotension in Addison's disease?**

**2. Explain the pathogenetic mechanisms of tachycardia in the patient.**

**3. Describe the pathogenetic chain leading to hypoglycemia in the patient.**

**4. What are the compensatory reactions in case of hypocortisolism-induced hypoglycemia?**

**5. What is the pathogenetic mechanism of diarrhea and that of mesenteric artery thrombosis in the patient?**

**6. Explain from the pathogenetic point of view why the creatinine level is increased in this patient.**

**7. It is known that cortisol deficiency inhibits lipolysis; instead, lipolysis is activated in the patient. What are the reasons?**

**Clinical case N.2**

Patient x, a 42-year-old man, addresses to family doctor with skin and soft tissue lesions and fever. His medical history shows that he is a forest worker and 2 days ago, following an accident at work, he lost control of his chainsaw and cut his leg. He took ibuprofen, dexalgin and treated the wound with hydrogen peroxide solution. The wound became infected and, in the evening, appears fever. However, the family doctor was surprised by the patient's physical appearance, whom he had not seen at the clinic for 2 years: the patient had gained 18 kg in weight, with adipose tissue distributed mainly in the trunk and face, cherry-coloured striae appeared on the abdomen, and white, depigmented, itchy spots on the chest and back, with pronounced acne on the face. The patient complained of muscle weakness in his hands and legs and twice within a year, he had injured his leg when lifting weights, which is why he finds it increasingly difficult to go to work to the forest.

The patient was admitted to the traumatological hospital, where he underwent surgical intervention, requiring repeated cleaning and drainage of the postoperative wound, which had healed very slowly. Upon discharge from hospital, the family doctor contacted him to come to the medical center for **additional investigations, which are attached:**

1. Cortisol (7:00-10:00) = 900 (172-497 nmol/l)

ACTH (7:00-10:00) = 120 (7.2-63.3 pg/ml)

K⁺= 2.9 (3.5-5.5 mEq/l)

Fasting blood sugar = 145 mg/dl (70-126 mg/dl)

BP=165/100 mmHg, Ps=98 /min

2. USG-bilateral enlargement of the adrenal glands.

3. Brain MRI determined a pituitary adenoma of 1.5 cm in diameter.

With the attached results, he was referred to an endocrinologist to confirm the diagnosis and establish treatment tactics.

**Diagnosis:** Cushing's disease, secondary hypercortisolism.

**Questions:**

**1. Explain the pathogenetic mechanism of the increased susceptibility to infections in the given patient.**

**2. Explain from a pathogenetic point of view why there is a slow healing of the postoperative wound in the given patient.**

**3. List the criteria for differentiating Cushing's Disease from Cushing's Syndrome.**

**4. What is the pathogenetic mechanism of hyperglycemia in the patient?**

**5. What are the pathogenetic mechanisms of chronic arterial hypertension in the given patient?**

**6. Specify the pathogenetic mechanisms of bone fractures in the given patient.**

**7. How do we pathogenetically explain the appearance of depigmented and pruritic spots in the patient?**

**Topic 11: Pathophysiology of the endocrine system. Dysregulation of thyroid hormone secretion. Absolute and relative insulin deficiency.**

**Clinical case 1**

Patient X, 60 years old age, addresses to the family doctor with the following ***complaints:***

-Using the maximum dose of metformin and sulfonylurea derivatives, the patient cannot maintain adequate glycemic control

-The patient, being on antihypertensive treatment, has had frequent hypertensive crises for the last 3 months

-Weight gain +4 kg within 2 months

-Burning sensation starting with the fingers and toes and spreading throughout the limbs.

**From the anamnesis:** he is a mayor in the village, a stressful job. He frequently copes with stress, according to the patient, with "wine", does not follow the diet, prefers meals with fatty grilled meat. He has been diagnosed with diabetes mellitus for 8 years, and 2 years ago he suffered a myocardial infarction, and 1 year ago he underwent laser ophthalmological intervention. Frequent urinary infections on the background of erectile dysfunction. The patient's mother also died from complications of diabetes mellitus.

**Objective data:** BP: 170/100 mmHg, Ps: 68 -/min, Weight: 115 kg, Waist 182 cm,

**Paraclinical exams:** fasting blood sugar 182 mg/dl, total cholesterol= 52 (<200 mg/dl), HDL=25 (>40 mg/dl), LDL= 210 (<100mg/dl), TG 290 (<150mg/dl), glycosylated Hb=11% (N=4.8-5.6 %), Serum sodium-160 mEq/l, potassium =3.1 mEq/l.

Diagnosis: Type 2 diabetes complicated with diabetic macroangiopathy (coronary artery atherosclerosis) and microangiopathy (proliferative diabetic retinopathy/peripheral diabetic neuropathy). HTN gr. II additional very high risk. Obesity gr. II. Dyslipidemia.

**Questions:**

**1. Explain the pathogenesis of insulin resistance in the case of genetic defects occurring at the insulin receptor level and intracellular signaling pathways.**

**2. List 3 pathogenetic mechanisms by which obesity induces insulin resistance.**

**3. Describe the pathogenetic mechanisms of insulin resistance in the case of increased non-esterified fatty acids in the specific patient with type 2 diabetes.**

**4. Explain the role of adipokines in the occurrence of insulin resistance.**

**5. What are the pathogenetic mechanisms of hyperlipidemia in the patient? (High LDL and TG).**

**6. The given patient has a history of myocardial infarction caused by coronary artery atherosclerosis. What is the mechanism of atherosclerosis in the patient with type 2 diabetes?**

**7. One of the mechanisms of diabetic neuropathy is the activation of the polyol pathway. Explain, using a pathogenetic chain, how neuronal damage occurs upon activation of this pathway.**

**8. Microvascular complications in the patient can also be explained by activation of the protein kinase C pathway. List the resulting effects on the vascular endothelium.**

**Clinical case N.4**

Patient A., 34 years old, addresses the gynaecologist with complaints of primary infertility in a couple for 8 years, amenorrhea and watery discharge from the nipples of both mammary glands. Other complaints: feeling of chronic fatigue, weight gain (12 kg over 5 years), decreased work capacity, intolerance to cold, feeling of suffocation if the coat, scarf touches the neck area, chronic constipation.

**Objective data:** Weight 98 kg, Waist=1.65 m, BP=100/60, Ps=54 b/min, pastiness of the face, abdominal striae. Palpation - thyroid gland enlarged in volume.

**Paraclinical exams:** Hb=100g/l, RBC=2.7x10⁹/l; TSH=6.2 μIU/ml (0.27-4.2 μIU/ml), T₃=0.5 nmol/l (1.3-3.1 nmol/l), T₄= 40 nmol/l (66-181 nmol/l); PRL=920 (127-637μIU/ml), Na⁺= 125 mEq/l (135-145 mEq/l), blood sugar=3.9 mmol/l, cortisol= 600 nmol/l(172-497 nmol/l), total cholesterol=380 mg/dl (< 240 mg/dl), LDL=200 mg/dl (100-129 mg/dl), TG= 450 mg/dl (<150 mg/dl).

**Diagnosis:** Primary hypothyroidism. Endemic goitre. Myxedema. Hyperprolactinemia. Primary infertility. Dyslipidemia.

**Questions:**

**1. Describe the pathogenetic chain of hypercholesterolemia in the patient.**

**2. What is the pathogenetic mechanism of goitre in the patient with hypothyroidism?**

**3. Explain the pathogenetic mechanism of hypoglycemia in the patient.**

**4. Specify the pathogenetic factors of the pathological weight gain in the patient.**

**5. Explain why despite the low glomerular filtration in the patient with hypothyroidism, BP has low values.**

**6. Describe the pathogenetic link of infertility in the patient with primary hypothyroidism.**

**7. Explain, by pathogenetic mechanism, why the patient has anemia.**