LESSON № 8

Topic: DISORDERS OF CARBOHYDRATE METABOLISM

Aim of the lesson: to study disorders of carbohydrate metabolism, mechanisms of diabetes mellitus symptoms development and its complications.

QUESTIONS:

1. Typical forms of derangement of carbohydrate metabolism.
2. Causes and consequences of carbohydrate digestion disturbances. Symptoms. Lactase deficiency.
3. Hyperglycemia. Types. Causes and mechanisms. Consequences.
4. Hypoglycemia. Types. Consequences. Hypoglycemic coma.
5. Causes and consequences of carbohydrate intermediary metabolism disorders.
6. Glycogenoses: classification, manifestations, mechanisms of pathology.

Aglycogenoses.

7. Diabetes mellitus. Etiology. Types and particularities.
8. Pathogenesis of type I and type II forms diabetes mellitus. Main metabolic (carbohydrate, protein, lipid) disturbances in diabetes mellitus.
9. Clinical symptoms of diabetes mellitus and mechanisms of there development.
10. Complications of diabetes mellitus. Types of comas and their pathogenesis.
11. Diabetic vascular complications. Pathogenesis of atherosclerosis, diabetic nephropathy, diabetic retinopathy, peripheral neuropathy.
12. *Hexosemias. Galactosemia: manifestation and mechanisms of pathology.
13. *Pentosemias. Fructose intolerance: manifestations and mechanisms of pathology.

Tasks

1

A 50-year-old patient F. was admitted to hospital in an unconscious state. On examination: the skin appears dry, turgor of the skin and eye ball is reduced: shallow breathing; heart rate 96 beats/min; the tongue is dry; recurrent cramps of the extremities and face muscles. Blood tests show hyperglycemia (20mM glucose), hyperazotemia, hypernatremia, pH 7,32.

The relative who accompanied the patient to hospital told the physician that the patient had been suffering from diabetes mellitus and had ingested small doses of hypoglycemic medicines. During the last month he experienced exacerbation of chronic cholecystitis and colitis, suffered from vomiting and diarrhea which occurred quite often. The patient also felt constantly thirsty and frequently urinated.

- Define the pathological state of the patient on admission.
- What was the cause of this pathological state? Describe the main stages of its pathogenesis.
- Why do patients lose consciousness during the development of this pathological state and the similar ones?
- What methods are used to treat patients in this pathological state?

2

A 23-year-old male patient visited his physician with complaints of intermittent muscle weakness, dizziness, headache, episodes of poor vision, tremor of hands, irritability, and, occasionally, confusion. The paroxysms of this condition occurred more frequently during the last four months. The patient attributed his malaise to the psychological stress that accompanied his professional activity, and also associated it with an acute feeling of hunger. After evaluation of the patient the physician made a diagnosis of neurasthenia and recommended an appropriate treatment. However, the disease went on progressing, and 1,5 months later the patient was brought by ambulance to the emergency room with a diagnosis of coma of unclear etiology.

On admission: consciousness is lost; there is evidence of midriasis, muscle cramps; tachycardia, arterial hypotension; irregular breathing;

blood glucose level 30 mM.

• What form of pathology caused the clinical manifestations presented by the patient during his first visit to the physician?

• Define the pathological state of the patient in the emergency room.

• What are the main steps of pathogenesis of this pathological state?

• What other forms of pathology should be kept in mind when you are making a differential diagnosis of this pathological state?

3

A 43-year-old patient C. with an excessive body mass suffers from diabetes mellitus. To control his blood glucose he uses hypoglycemic drugs. Two weeks before he was admitted to hospital he had had an episode of excessive alcohol drinking, and soon after that he noticed an enhanced feeling of dry mouth. He drank a lot of water (up to 8-10 1 daily) and urinated frequently. He felt general weakness and pain in the legs. On the night before the admission the patient was delirious. When he woke up in the morning he was agitated, restless, and confused. The patient's relatives called in the ambulance. On admission: consciousness is absent; the skin is dry and pale. The results of the blood tests: glucose 45mM, lactic acid 2,9 mM, pH 7,29. Urine glucose level 2 mM.

• What other signs, in addition to the observed in this patient, may be found in a) diabetes mellitus and b) diabetic coma? Describe these signs and explain their pathogenesis.

• What are the main stages of pathogenesis of this coma?

4

A female patient, approximately 40 years of age, had been brought to the emergency room in an unconscious state. Witnesses of the incident told the physician that she had suddenly lost her consciousness in the bus on her way back from her summer house in the countryside. A card that was found among her papers indicated that she suffered from diabetes mellitus and took a slow-release form of insulin.

On examination: consciousness is absent, corneal and deep tendon reflexes are not observed, the pattern of breathing is unremarkable; blood pressure 80/60 mm Hg; tachycardia is present;

the skin appears moist: turgor of the eye balls is increased; general trembling is alternating with episodes of clonic and tonic seizures.

The patient was treated with insulin, but no improvement was observed: the patient's condition even worsened: breathing became irregular, blood pressure decreased to 70/50 mm Hg, tachycardia progressed, and the duration of seizures increased.

What pathological state developed in the patient before and after administration of insulin? Describe causes and mechanisms of this state. What therapeutic procedure would have been appropriate for pathient before and after the administration of insulin?

5

In two monozygous sibs (8 months of age) an examination revealed a significant increase in the liver size (hepatomegaly), decreased fasting level of blood glucose (hypoglycemia), and lack of fasting blood glucose changes after the adrenaline administration. The liver biopsy investigation showed an increased content of glycogen and a significantly diminished activity of glycogen phosphorylase in hepatocytes.

- Give the definition of the pathological process developed in the infants.
- What are the possible causes of this process?
- Explain the sequence of events leading to glycogen accumulation in the liver cells in this form of pathology.

Explain the association, if any, between the low activity of glycogen phosphorylase in the patients' liver and a) an increased content of glycogen in the hepatocytes; b) hepatomegaly; c) a decreased fasting blood glucose levels; d) lack of hyperglycemic effect of adrenaline.

6

Two series of experiments were performed with an aim to determine the effect of a new antibiotic drug on the skin epithelium. In the *in vivo* studies using rats, the solution of the tested drug was applied to the skin surface. The employed dose of the antibiotic was much higher than the therapeutic one. The results of this experiment were assessed by in vivo microscopy studies which were performed during the first 24 hours after the end of drug application with 8-hour intervals. In the in vitro experiments the tested drug was added to the suspension of epithelial cells isolated from the same stock of rats. Six hours later the cells were washed out by repetitive centrifugation and suspending in the same media containing no tested drug. The effects of

the antiobiotic were studied at the same time points using regular light microscopy and electron microscopy.

The results of the experiments.

- In vivo: 8 hours after the completion of the drug application the morphological analysis of the epithelial cells revealed the signs of dystrophy and focal necrosis; the extent of pathological alterations increased by the end of the 24-hour observation period.
- In vitro: no signs of the cellular or subsellular damage were seen in the isolated epithelial cells after the drug treatment. The only changes observed included a reversible cell aggregation found in the first test (8 hours after the drug withdrawal), but not in the tests that followed.
- How can you explain the difference in results of the in vivo and in vitro experiments?
- Was damage to the epithelial cells in the in vivo test direct or indirect? Explain your point of view.
- What are the possible mechanisms of the injurious action of the drug on the epithelium?
- Taking into account the results of the in vitro experiments, which of these mechanisms are most likely?
- What processes or cell functions should be studied in the further in vivo experiments to confirm your presumptions about the mechanisms of the pathogenic effect of the tested drug?

7

A 61-year-old female patient had been suffering from arterial hypertension many years. During the last 2 years she began to feel cold intolerance in his legs, numbness and pain in the gastrocnemius muscles on walking and then at rest. These symptoms were more intense at night and caused sleep disturbances. Six months ago she developed a skin lesion on the front surface of her right shin; later it transformed into ulcer. The ulcer was painless but resistant to therapy. During the visit to the doctor the patient complained of dryness in the mouth, constant feeling thirsty, frequent urination. On examination: the skin of the right shin was dry, pale, and cold; no pulsation of the sole artery was detected. Repeated blood tests showed increased levels of cholesterol, fibrinogen; high platelet counts; glucose

20-25 mM. The urine is positive for ketone bodies and glucose.

- What forms of pathology can be observed in the patient?
- Name the likely type of lesion affecting the patient's arteries? Name and characterize the main mechanisms of pathology underlying changes in the patient's arterial wall.
- What factors caused the development of erosion and ulcer on the patient 's shin?
- Can you assume the presence of the microcirculatory disorders in the vascular system of the patient's right leg? What are the likely causes of these disorders?

8

A 34-year-old female patient who had been suffering from diabetes mellitus for more than 13 years presented with visual losses manifested is blurring of vision, «sand in the eyes» when reading small prints. Dr. examination: a significant decrease in vision acuity, narrowing of several visual fields in both eyes; irregular thickening of the retinal – microvessels wall; capillary microaneurisms and mural thrombi in the retinal microvessels; focal serous exudates and hemorrhages in the retina, ir.d its neovascularization.

The doctor informed the patient that her vision impairment was the result the diabetic microangiopathy. The latter includes pathological alteration of the orbital microvessel wall. The patient received appropriate advice and treatment.

- What types of microcirculatory disorders can you distinguish in the patient's retina?
- Which form of microcirculation disorders may give rise to focal retinal edema? Can the microcirculatory changes described produce vision impairment in the patient?

9

A 19 year old male, body weight 80 kg, was suddenly complaining of fever during his work and ordered home to bed. The patient was living alone. Fortunately a colleague visited him the next morning. He had to break the door down and found the patient unconscious. The patient arrived at the hospital in deep coma. The urine contained glucose and ketone bodies.Explain the condition of the patient concerning thermo-balance, carbohydrate metabolism.

10

A 23-year old male was saved after 30 days in the ruins of a house following earth quake. There was no food but sufficient water. At the arrival to the hospital the patient was in syncope with frequent, deep respiration, and the expired air smelled of acetone. The skin was dirty with brown pigmentation. The cardiac rate was 85 bpm, and the arterial blood pressure was 11.3/7.3 kPa (85/55 mmHg).

The blood [glucose] was 2.2 mM, and the plasma [FFA] was increased. The serum concentrations of proteins and essential amino acids were reduced. The blood [haemoglobin] was 95 g l^{-1}. There was moderate antidiuresis with ketonuria with signs of water retention and a high nitrogen loss in the urine.

The patient was treated with parenteral administration of glucose, amino acids and electrolytes. Following the glucose intake, the blood [glucose] was increased to 10 mM, and glucosuria occurred. A glucose tolerance test was performed and resulted in a high blood [glucose] level that had not reached the normal level within 2 hours.

- Describe the energetic events leading to survival.
- Why did the patient smell of acetone?
- What happened to the carbohydrate metabolism of the patient?
- Explain the high nitrogen loss in the urine.

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