

LESSON № 9

Topic: DISORDERS OF LIPID METABOLISM

Aim of the lesson: to study disorders of lipid metabolism, mechanisms of hyperlipidemia, obesity and atherosclerosis development and its complications.

QUESTIONS:

1. Biological role of lipids in the human body.
 2. Typical forms of disorders of lipid metabolism.
 3. Causes and consequences of lipid digestion disturbances. Symptoms. Steatorrhea.
 4. Causes and consequences of lipid intermediary metabolism.
 5. Pulmonary and hepatic role in lipid metabolism.
 6. Plasma lipoprotein's composition and functions.
- Apoproteins.
7. Characteristics and mechanisms of hypolipidemia.
 8. Hyperlipidemias. Types (classification) according to Fredrickson. Causes, mechanisms and consequences of hyperlipidemias.
 9. Atherosclerosis: description and pathological features.
 10. Pathogenesis of atherosclerosis. Atherogenic and antiatherogenic lipoproteins. Stages of atherogenesis: initiation; formation and evolution of atheroma; complications.
 11. Risk factors of atherosclerosis development.
 12. Obesity. Types and pathogenesis of obesity. Causes and consequences.
 13. Hepatic lipid infiltration and dystrophy. Causes and consequences.

Tasks

1

A 13-year-old boy visited a doctor with complaints of recurrent pain in the region of the heart. The pain was exacerbated at exertion. Examination of the patient showed the presence of small, firm, yellow nodules (xanthomas) over the course of the hand muscles tendons, the presence of corneal lipid arcus. Angiographic examination revealed the coronary artery stenosis. Blood test results demonstrate: total plasma cholesterol – 22 mM, triglycerides – 1,7 mM, HDL-cholesterol – 0,7 mM (normal values: >0,9 mM), LDL-cholesterol – 9 mM (normal values: 3.0-4.5 mM). The patient's parents also have increased plasma levels of cholesterol – more than 8mM. Immunocytochemical analysis of the patient's leukocytes revealed abnormality of the LDL-receptor.

- What type of hyperlipidemia is observed in the patient?
- Is heredity important in the development of this pathology? If it is, what is its type of inheritance? What is the prevalence of this pathology in general population?
- What mechanisms underlie hyperlipidemia in this patient?
- Assess the atherogenicity of the patient's plasma by calculating the index of atherogenicity.
- What are the pathological consequences of hyperlipidemia of this type? What therapeutic approaches may be used to treat this pathology?

2

During examination of a 5-year-old boy a physician found an enlargement of the liver and spleen (hepatosplenomegaly), swelling of the tonsils which had red-orange color, and an enlargement of inguinal, axillary, and other superficial lymph nodes. Also clouding of the cornea was observed.

Biochemical tests revealed: total cholesterol of the blood plasma 0,1 mM, triglycerides – 2,3 mM, HDL fraction almost absent. During electrophoretic separation of the patient's plasma apoproteins A-I and A-II bands were not observed.

- What type of disorders of lipid metabolism is observed in the patient?
- What mechanisms underlie the development of this disorder?

- Why is HDL fraction considered antiatherogenic? What factors determine HDL levels in the blood plasma?
- What role do apoproteins of the A class play in the cholesterol metabolism?

3

During experimental studies of atherosclerosis one group of rabbits was fed cholesterol added to a standard pelleted food in a dose of 5 g per day. Cholesterol was previously purified to remove contaminating oxides. The second group was treated similarly, but cholesterol was not purified, and the third group received the same diet with cholesterol that was previously subjected to peroxidation by hydrogen peroxide in the presence of ferrous chloride (FeCl_2).

Six months after the start of the experiment the rabbits were killed by a lethal dose of a narcotic drug; the abdominal portion of the aorta and coronary arteries were isolated and their internal surface were examined for the presence of lesions. Simultaneously blood samples were obtained from all rabbits of the experimental groups; plasma was separated from formal particles and used to isolate LDL fraction. In the following in vitro studies samples of the isolated LDL fractions from various groups were added to a media containing cultures of murine peritoneal macrophages, and the extent of intracellular accumulation of cholesterol esters was assessed following incubation for three days. LDL fraction of the intact rabbits was used as a control.

- Which group of the rabbits is supposed to incur the maximum damage to their arteries due to the excess of cholesterol in the food?
- Describe the pathways by which LDL can enter peripheral cells, including macrophages.
- What differences in accumulation of lipids in murine macrophages can be expected with LDL fraction isolated from various experimental animals? Compare LDLs of the control and experimental groups of rabbits.
- What role do monocytes/macrophages play in atherogenesis?

4

During his visit to the doctor a 55-year-old male patient complains

of anginal pain which recently has increased in frequency and intensity. The patient is the president of a big trading company. During the last months he has experienced great psychological stress, spent 12-14 hours at his office daily and slept little; he began smoking more than one pack of cigarettes per day. The patient is a hearty eater, preferring high-calorie fat food. His father died of myocardial infarction. On examination: his height is 173 cm, weight 89 kg, blood pressure 175/100 mm Hg. Blood tests show the following: total plasma cholesterol – 6,8 mM, triglycerides – 1,9 mM. HDL cholesterol 0.8 mM, LDL cholesterol – 5,3 mM; glucose tolerance is decreased.

- What form of pathology is the cause of angina pectoris in this patient?
- What risk factors of this pathology are observed in the patient?
- Does the patient have signs of lipid metabolism disorder? If he does, what forms of it?
- What therapeutic approaches can be used to treat lipid metabolism disorders in this case?

LITERATURE:

1. Lecture material.
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