

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

DISEASES OF ENDOCRINE SYSTEM
DIABETES MELLITUS, ETIOLOGY, PATHOGENESIS,
CLINICAL PICTURE, DIAGNOSTICS, CLASSIFICATION

Methodological recommendations
for students of 4 course

ЗАХВОРЮВАННЯ ЕНДОКРИННОЇ СИСТЕМИ.
ЦУКРОВИЙ ДІАБЕТ, ЕТІОЛОГІЯ, ПАТОГЕНЕЗ, КЛІНІКА,
ДІАГНОСТИКА, КЛАСИФІКАЦІЯ

Методичні вказівки
для студентів 4 курсу

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Topicality

3% of earth population have diabetes mellitus. Besides, there is permanent growth of incidence of this disease. Each 10-15 years the amount of such patients all over the world is doubled. In connection with large prevalence and the increase of amount of patients, diabetes mellitus is attributed to social diseases; it is included to the triad of diseases (together with oncology and vascular diseases) which are the principal reasons for disability and mortality. The great attention of researchers and doctors is aimed to resolve this problem.

Educational aims:

- to teach students to determine the etiologic and nosotropic factors of diabetes mellitus, type 1 and 2;
- to acquaint students with classification of diabetes mellitus after A.S. Yefimova (1983), classification of impaired glucose tolerance (WHO, 1985), and with etiologic classification of glycemic disorders (WHO, 1999);
- to teach students to determine the typical clinical presentation of diabetes mellitus;
- to acquaint students with the variants of development of diabetes mellitus type 1 and 2;
- to teach students to determine the basic diagnostic criteria of diabetes mellitus in accordance with WHO, 1999, and also to make the plan of examination of patients with diabetes mellitus;
- to acquaint students with the use of glucose tolerance test and the indications for its application;
- to teach students to substantiate and formulate the diagnosis of diabetes mellitus;
- to acquaint students with the main moral principles concerning diabetic patients.

What should a student know?

- definition of diabetes mellitus;
- epidemiology of diabetes mellitus in Ukraine and in the world, its prevalence in different age groups;
- risk factors for development of diabetes mellitus;
- mechanisms of development of carbohydrate, protein and fat metabolism disorders in patients with diabetes mellitus;
- etiology and pathogenesis of diabetes mellitus type 1 and 2;
- etiologic classification of glycemic disorders (WHO, 1999);
- clinical presentation of diabetes mellitus;

- the peculiarities of lesions of cardiovascular, hepatobiliary, urinary systems and osteoarthropathies in patients with diabetes mellitus;
- diagnostic criteria of diabetes mellitus according to WHO, 1999;
- indications and rules of glucose tolerance test;
- diagnostic value of determination of glycated hemoglobin, fructosamine, C-peptide, glucosuria, ketonuria
- What should a student be able to do?
- to define the risk factors for diabetes mellitus;
- to diagnose diabetes mellitus, including the early stages;
- to determine the type, character of progression, severity of the disease, degree of carbohydrate metabolism impairment;
- to estimate the type of tolerance to the carbohydrates;
- to use the methods of express diagnostics of glucosuria and ketonuria;
- to evaluate the glycemia and glycosuria types, the state of protein and fat metabolism, acid-base balance, electrolyte balance, C-peptide, glycated hemoglobin in patients with diabetes mellitus;

List of practical skills

- ✓ to define clinical symptoms, related to the hyperglycemia and concomitant diseases in patients with diabetes mellitus;
- ✓ to define the risk factors of diabetes mellitus, possible etiologic factors, initial signs of disease and methods of its diagnosis, character of the development of diabetes mellitus, methods of treatment, reasons for decompensation;
- ✓ to define the type of diabetes mellitus, degree of severity;
- ✓ to evaluate glycemia and glycosuria types, state of lipid, protein and mineral metabolism, C-peptide and glycated hemoglobin due to the results of laboratory tests;
- ✓ to define the degree of compensation of diabetes mellitus;
- ✓ to make and substantiate the diagnosis of diabetes mellitus;
- ✓ to perform the differential diagnosis for hyperglycemia and glucosuria

Topic content

- I. Diabetes mellitus: etiology, pathogenesis, clinical presentation, diagnosis. Classification.
- II. Definition: Diabetes mellitus is an endocrine and metabolic disease caused by deficit and/or ineffectiveness of insulin, leading to a state of chronic hyperglycemia and impairment of

all types of metabolism as well as multisystem lesions development.

- III. Insulin insufficiency can be acute and chronic, absolute and relative, and may induce the decompensation of carbohydrate and other types of metabolism.

Epidemiology

Diabetes mellitus is occupying the third place (after atherosclerosis and cancer) among diseases, which are the most frequent reasons for physical inability and death rate of patients. Diabetes is the reason for increase of death rate, because it produces many complications, it also causes premature death. Mortality of persons with diabetes is higher than the one of persons without diabetes.

Direct economic expenses on treatment of diabetes compose about 8% of the healthcare budget, among them 80% are spent for the treatment of diabetic complications. The morbidity caused by cardiovascular pathology is significantly higher in patients with diabetes. Coronary artery disease is observed in 10-20% of adults with diabetes, hypertension- in 60% of diabetics, they also tend to have strokes 3-4 times more often than general population. Diabetes is the most frequent reason for blindness in adults. Diabetic nephropathy is the most frequent reason for renal failure (34% of all cases). Diabetic polyneuropathy is the reason for 50% of nontraumatic amputations of lower extremities.

Morbidity of diabetes composes 1,5-4% of population in the industrially developed countries according to the data of WHO experts. In the Central-European region 5% of adults suffer from diabetes. The general number of patients includes about 60 million in the entire world, in Ukraine – more than 1 million. An opinion exists, that real morbidity of diabetes is two times higher than official data, that is caused by large number of the hidden (latent) forms of diabetes.

Annually the amount of patients is increasing on 10%, each 15 years the amount of patients is doubled.

The geographical and national factors influence the prevalence of disease. The disease is more widespread in Europe and USA, than in the countries of South-East Asia, North Africa, and among Eskimos.

The incidence of disease is increasing with age: the number of patients with diabetes in the age below 15 years composes 5% of their general number, the majority of patients (80%) are older than 40 years. Prevalence of diabetes is higher among elderlies, and also among obese persons (in 4-30 times).

Pathogenesis of diabetes mellitus type1

Various environmental factors play a role in the pathogenesis of type 1 diabetes. Most of these factors are unknown. However, viral infections (eg, enterovirus, rubella virus) and nutritional factors (eg, cow's milk in infancy) can boost an autoimmune process in susceptible individuals.

Risk factors include viruses or toxic substances that affect genetically determined antigens of HLA system and cause autoimmune destruction of beta cells in the islets of Langerhans.

Regardless of the primary mechanisms (virus induced, autoimmune or slowly progressive) degradation of b-cells in the next stages of the process leads to the decrease in their number up to almost complete disappearance of b-cells with the development of absolute insulin deficiency.

Pathogenesis of type 1 diabetes can be divided into six stages:

1. Genetic predisposition (due to the presence of genes haplotypes of HLA-I, II and III class. HLA DR3 and DR4 genotypes are associated with increased risk of diabetes type I, whereas HLA-DR2 genotype protects against the disease. Diabetes type 1 is either idiopathic or autoimmune; it is linked to the following antigens of HLA-system: U8, U15, DR, DRW 3-4, which are associated with genes of DQ locus, genes Fas and Fas-L. Susceptibility to type 1 diabetes is associated with genes of HLA DR3, DR4 or DR3/DR4 complex as well as with certain gene locus HLA DQ (DQA and DQB, DRB genes). The identified alleles of HLA-DR/DQ genes can mediate the susceptibility to diabetes or they may show a protective effect.)

2. The initiation of immune processes (autoimmune mechanism of the destruction of beta-cells caused by congenital loss of tolerance to autoantigens). Patients with type 1 diabetes produce various antibodies to antigens, which are the islet components: cytoplasmic antigens; superficial antigens of B-cells, cytotoxic complement-mediated antigens to insulin and proinsulin. Viruses can induce the autoimmune reaction or can directly affect the beta cells, which leads to rapid development of diabetes. B-cytotropic group of viruses includes Coxsackie virus, mumps, chicken pox, measles, cytomegalovirus. A seasonal increase in the frequency of diabetes is observed because these infections often affect children in the autumn and winter months.

3. The stage of active immunological processes (regardless of initiating factors and primary mechanisms of diabetes (virus induced, autoimmune, quickly progressing or slowly progressing) is characterized by destruction and progressive decrease of B-cells number in pancreatic

islets up to complete disappearance of B-cells and development of an absolute insulin deficiency. Recently, an important role in the destruction of B-cells has been given to nitric oxide (NO). NO is formed in the body from L-arginine under the influence of the NO-synthetase. Nitric oxide (NO) is a relatively stable free radical, its half-life is few seconds. The highly toxic substances (nitrates and nitrites) are produced as the result of NO oxidation. In addition to the mentioned above mechanisms of B-cells destruction an important role belongs to the autoimmune processes);

4. Progressive reduction of the first phase of insulin secretion stimulated by intravenous glucose injection (an autoimmune destruction of B-cells is slow and it may take months and years to develop the disorders of carbohydrate metabolism. This phase of disease belongs to pre-clinical period);

5. Clinically obvious or manifest diabetes (severe metabolic disorders and clinical presentation of the disease develop in case of an absolute lack of insulin, when 80-95% of B-cells are destroyed);

6. Complete destruction of B-cells (Any pathogenic variant causes the destruction of B-cells. Slowly progressive type 1 diabetes (Latent Autoimmune Diabetes in Adults, LADA), has a subtype - slowly progressive diabetes of adults of autoimmune genesis. This subtype of diabetes is called Latent Autoimmune Diabetes in Adults (LADA) - late onset of autoimmune diabetes in adults).

Pathogenesis of diabetes type 2

Pathogenesis of diabetes type 2 includes two leading factors: insulin resistance and defective insulin secretion, both of them are present in each patient, but in different proportions.

Risk factors for type 2 diabetes: obesity, wrong diet, lack of exercise, stress, old age.

The evidence of genetic stipulation of type 2 diabetes is a high incidence of disease in close relatives of patients (40%). The hereditary nature of the disease is also proved by its high prevalence in some ethnic populations: among Pima Indians (Arizona, USA) it is higher than 50%.

There are two types of genetic defects in diabetes type 2. Defects of the first type cause insulin resistance or obesity, which leads to insulin resistance. Defects of the second type are the causes for reduced secretory activity of B-cells or their insensitivity to hyperglycemia.

Insulin resistance is one of the factors causing poor metabolic control. It can be reduced by weight loss. Insulin resistance develops due to genetic factors, some environmental factors, and lifestyle

characteristics of the patient (wrong diet, lack of exercise, stress, old age).

Insulin resistance leads to compensatory increase of insulin secretion by beta cells as long as they retain the ability to hypersecrete insulin.

The key defect responsible for the progression of type 2 diabetes is not an insulin resistance but a decreased function of beta-cells. There is defective insulin secretion profile in diabetes type 2 - basal insulin secretion is not changed, but the secretion of insulin in response to meals (prandial insulin secretion) is smoothed and delayed.

A fundamental aspect of the pathophysiology of type 2 diabetes is a progressive decline of prandial insulin response, especially in the early phase. The absence of postprandial peak reduction of plasma glucose to physiological levels during the postprandial period causes permanent hyperglycemia. B-cells are unable to identify or to respond to changes in the concentration of plasma glucose and/or unable to compensate the insulin resistance by increased release of insulin.

The early phase of insulin response is especially impaired: it is slowed and reduced in comparison with a group of healthy individuals. Early phase of prandial insulin response plays a central role in the suppression of endogenous glucose production. In diabetes type 2 endogenous glucose production continues despite to the prandial load, and in combination with continued relative deficiency of insulin release leads to postprandial hyperglycemia.

Insulin secretion is always insufficient comparatively to existing hyperglycemia in type 2 diabetes. In case of severe disease, this deficit becomes absolute in comparison with healthy people. The biggest difference between insulin secretion and metabolic need for it is always found in prandial period (after meals).

The progressive nature of the disease is mainly the result of decreased function of B cells. The deterioration of the function of beta-cells is proved in patients with type 2 diabetes along with increase of the disease duration, while sensitivity to insulin remains virtually unchanged during the disease (except of cases of successful weight correction, the diet change and sufficient physical activity). The defect of prandial insulin secretion increases during the progression of type 2 diabetes; there is a progressive gradual steady decline of prandial insulin secretion.

High postprandial peaks of glucose concentration in plasma can show direct action, damaging the blood vessels and thus increasing the cardiovascular risk.

Classifications of diabetes mellitus

Classification of diabetes mellitus after A.S.Yefimova (1983). A clinical diagnosis, which is formulated according to this classification, reflects the nature of the clinical course of diabetes, and helps to determine the plan of examination and treatment.

1. Clinical forms:

- a) primary (essential)
- b) secondary (symptomatic)
- c) gestational diabetes,
- d) impaired glucose tolerance (latent)
- e) risk factors (pre-diabetes).

2. Types of diabetes:

- a) insulin dependent - Type 1 (IDDM)
- b) insulin independent - Type 2 (IIDD).

3. Degree of severity:

- a) mild,
- b) moderate,
- c) severe.

4. State of compensation:

- a) compensated,
- b) decompensated.

5. The presence of angiopathies and neuropathy:

- a) microangiopathies (retino-, nephro-, angiopathy of lower limbs)
- b) macroangiopathy,
- c) universal micro- and macroangiopathy,
- d) neuropathy (peripheral, visceral, encephalopathy).

6. Lesions of other organs and systems:

- a) hepatopathy, enteropathy,
- b) cataract, glaucoma,
- c) dermatopathy,
- d) osteoarthropathy and others.

7. Acute complications of diabetes (coma):

- a) Diabetic,
- b) Hyperosmolar,
- c) Lactic,
- d) hypoglycemic.

In 1985 the WHO Expert Committee recommended classification of diabetes, which was in use till 1999. Classification presents a list of carbohydrate metabolism disorders according to the scientific knowledge of that period.

Classification of diabetes mellitus and other categories of glucose regulation (WHO, 1985)

A. Clinical classes:

1. Diabetes mellitus:

- Insulin dependent is a type I,
- Insulin independent is a type II:
 - a) – in individuals with normal body weight,
 - b) - in individuals with obesity.

II. Other types, including diabetes, which accompanies certain states or syndromes:

- a) diseases of the pancreas;
- b) hormonal disease etiology;
- c) conditions caused by medications or chemicals;
- d) changes in insulin receptors;
- e) certain genetic syndromes;
- e) mixed states.

III. Diabetes, which is caused by malnutrition (tropical)

- a) pancreatic;
- b) pancreatogenic.

IV. Impaired glucose tolerance (IGT):

- a) in individuals with normal body weight;
- b) in individuals with obesity;
- c) IGT due to other conditions and syndromes.

5. Diabetes during pregnancy.

B. Reliable risk classes (persons with normal glucose tolerance, but with a significantly increased risk of developing diabetes):

- a) previous impaired glucose tolerance;
- b) potential impaired glucose intolerance.

Etiologic classification of violations of glycemia (CARTFUL, 1999)

The up to date information on genetic, immunological and metabolic features of diabetes allowed to establish specific causes and mechanisms of development of different types of diabetes. In 1999, the WHO Expert Committee approved the Etiological classification of disorders of glycemia.

1. Type 1 diabetes (β -cell destruction, usually leading to absolute insulin deficiency)

A. Autoimmune (immune-mediated)

B. Idiopathic

2. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)

3. Other specific types of diabetes

3.1. Genetic defects of b-cell function

- 3.2. Genetic defects of insulin action
- 3.3. Diseases of exocrine pancreas
- 3.4. Endocrinopathies
- 3.5. Drug- or chemical-induced diabetes
- 3.6. Infections
- 3.7. Uncommon forms of immune-mediated diabetes
- 3.8. Other genetic syndromes sometimes associated with diabetes
4. Gestational diabetes mellitus

In the new classification the names "insulin dependent" and "insulin dependent" were omitted and only the names "diabetes types 1 and 2" were preserved in order to indicate the type of diabetes using arabic numerals. Exclusion of the adjectives "insulin dependent" or "insulin independent" from the name of the disease is associated with the fact that until recently the basis for appropriate diagnosis was the therapy of diabetes, i.e. the need for insulin therapy instead of pathogenetic data.

1. Type 1 diabetes – disorder of carbohydrate metabolism caused by destruction of b-cells of the pancreas with absolute or relative insulin deficiency and bias to ketoacidosis. Diabetes is considered as autoimmune or immune-mediated disease in cases, when the destruction and reduction of b-cells number develops due to an immune or autoimmune process. Reduction of number or complete disappearance of b-cells leads to absolute insulin deficiency and total dependence of patient on administration of exogenous insulin (insulin dependence). Patient may develop ketoacidosis, coma and death if lacks insulin. More than 15% of those with type 1 diabetes die after 25 years of disease, life expectancy is reduced by 15 years.

Type 1 diabetes includes a heterogeneous group of diseases – the differences refer to the pace of absolute insulin deficiency development. With the rapid pace of progression the manifestation occurs in childhood (juvenile, quickly progressing diabetes). In case of slow progress of insular apparatus destruction, manifestation of carbohydrate metabolism disorders occurs in postpubertal period (slowly progressive type 1 diabetes of adults, LADA).

More than 90% of children with diabetes suffer from type 1 diabetes.

Among adults, who got sick with diabetes after the age of 35 years, the proportion of type 1 diabetes is about 20%.

Type 1 diabetes occurs equally among men and women.

A. Autoimmune (immune-mediated) type 1 diabetes is characterized by the presence of autoantibodies: antibodies to glutamatedecarboxylase (GAD-antibodies), antibodies to insulin, cytoplasmic autoantibodies and

antibodies to tyrosinphosphatase. The presence of these antibodies indicates autoimmune process.

B. Idiopathic type 1 diabetes is diagnosed in patients of African or Asian origin, when there is destruction and reduction of number of b-cells with a constant insulin deficiency and bias to ketoacidosis, but the etiology and pathogenesis are unknown. In these patients the phenomena of autoimmunity and association with certain HLA system genes are absent, but hereditary transmission of the disease is clearly traced.

2. Diabetes mellitus type 2 - carbohydrate metabolism disorders are caused by severe insulin resistance along with deficient insulin secretion or primary violation of insulin secretion and moderate insulinorezystentnostyu.

About 95% of all diabetics suffer from type 2 diabetes.

Type 2 diabetes is more common in older people, more often in women.

3. Other specific types of diabetes.

3.1. Genetic defects of b-cell function.

This group includes variants of diabetes of MODY-type. Diabetes MODY – Maturity Onset Diabetes of the Young, or "Masonic type of" diabetes, is also a heterogeneous disease. Among the diabetic children 10% have this variant of the disease. Molecular genetic studies show several syndromes:

1) diabetes MODY 1 (defect in chromosome 20, the gene HNF4a - hepatocyte nuclear transcription factor 4a);

2) diabetes MODY 2 (defect in chromosome 7, the gene glucokinase);

3) diabetes MODY 3 (defect in chromosome 7, the gene HNF1a hepatocyte nuclear transcription factor 1a, mutation of glucokinase gene); the genes of hepatocyte nuclear transcription factors 4a or 1a are expressed in the liver and b-cells of the pancreatic islets;

4) diabetes MODY4 (defect in chromosome 13, mutation of the IPF-1 gene of insulin promotor factor);

5) mitochondrial DNA mutation 3243;

6) other.

Other forms of diabetes include family cases of diabetes, which have a clinical presentation of diabetes type 2, and are caused by abnormal or mutant insulins: "Chicago insulin" - mutation of insulin molecule in which phenylalanine in position B-25 is replaced by leucine (pheno-leu); "Los Angeles insulin" - in which phenylalanine in position B-24 is replaced by serine (phen-ser); "Insulin Wakayama," in which the amino acid valine in position A-3 is replaced by leucine (val-leu).

3.2. Genetic defects of insulin action:

1) resistance to insulin type A, 2) leprechaunism 3) Rabson-Mendenhall's syndrome, 4) lipotrophic diabetes and 5) others.

3.3. Diseases of the exocrine pancreas:

1) Pancreatitis, 2) Trauma/pancreatectomy, 3) Neoplasia, 4) Cystic fibrosis, 5) Hemochromatosis, 6) Others

These diseases are characterized by the involvement of significant part of the pancreas in the pathological process. Such patients have marked disorders of exocrine function as well as deficiency of b-cell secretory function.

3.4. Endocrinopathies:

1) Cushing's syndrome, 2) acromegaly, 3) pheochromocytoma, 4) glucagonoma, 5) hyperthyroidism, 6) somatostatinoma and 7) other. These endocrine diseases result from excessive secretion of relevant hormones, which possess marked contrainsulinary action. Clinical manifestation of carbohydrate metabolism disorders thus depends on the compensatory reserve of B-cells

3.5. Diabetes induced by drugs or chemicals.

3.6. Infections.

Virus induced diabetes that occurs after acute viral infections (congenital rubella, Coxsackie virus B3 and B4, cytomegalovirus, mumps, adenovirus, etc.) may be associated with significant destruction of b-cells and might have a direct impact on the development of diabetes. Majority of such patients have HLA genes and immunological markers typical for type 1 diabetes.

3.7. Uncommon forms of immune-mediated diabetes.

3.8. Other genetic syndromes sometimes associated with diabetes.

The genetic syndromes associated with carbohydrate metabolism disorders are included in this group. These diseases are caused by lesions of certain chromosomes: Down's syndrome, Turner's syndrome, Klinefelter's syndrome, Wolfram syndrome, Friedreich's ataxia, Huntington's chorea, Lawrence-Moon-Beidel syndrome, Prader-Willi syndrome, porphyria, myotonic dystrophy and others.

4. Gestational diabetes.

The classification of carbohydrate metabolism disorders (1965 and 1985) included the term "impaired glucose tolerance" or chemical, hidden, latent diabetes. The present WHO classification (1999) has no "impaired glucose tolerance" and "credible risk classes" sections. These sections were omitted because episodic hyperglycemia itself is not a diabetes. "Impaired glucose tolerance" is considered as the stage of "impaired glucose regulation" and not as a separate class of

carbohydrate metabolism disorders. The term "impaired glucose regulation," according to WHO experts, more appropriately describes this condition.

CLINICAL MANIFESTATIONS OF DIABETES

Symptoms of diabetes depend on the state of compensation of carbohydrate metabolism and the presence of complications of the disease - symptoms of "late diabetic syndrome".

Clinical symptoms of decompensation of carbohydrate metabolism include the following:

1. Hyperglycemia – is clinically manifested by thirst (polidipsia), dryness of mouth mucosa, polyuria, and weight loss against the background of poliphagia. If patient adheres to diet and receives adequate treatment, the blood glucose level becomes normal, clinical signs of hyperglycemia disappear - the state of diabetes compensation is achieved.

Hyperglycemia in patients with diabetes is the result of an acute deficit of insulin and / or reduction of sensitivity of tissue receptors to insulin, leading to disorders of carbohydrate, fat, protein, and water-salt metabolism. Deficiency of insulin blocks the flow of glucose in insulin-dependent tissues, as the result they suffer from a marked energy deficit.

2. Dehydration, polidipsia.

Hyperglycemia causes relative and absolute tissue dehydration. Glucose has the high osmolality - the ability to "bind" the water. Hyperglycemia is accompanied by a redistribution of body fluids - water "leaves" tissues and relative intracellular dehydration develops. A significant amount of water is lost because of poliuria, thus causing absolute dehydration. The evidences of dehydration caused by hyperglycemia are the following: dry skin and mucosa, especially the mouth mucosa, decreased turgor of skin and subcutaneous fat. In severe decompensation dry mouth mucosa may cause the disorders of articulation - patient speaks with difficulty, there is a feeling that tongue "sticks" to the palate.

Dehydration causes compensatory disorders of thirst center; this results in polidipsia - increased intake of fluids by patients. Requirement in the fluid during the day is one of the clinical criteria for compensation of carbohydrate metabolism and the method of patient's self-control. Limitation of fluid intake is unacceptable - unresolved dehydration would lead to the development of disseminated intravascular clotting and severe consequences.

3. Glycosuria, polyuria.

Significant hyperglycemia (surpassing renal threshold for glucose) causes glycosuria - glucose excretion in the urine. Glycosuria due to the osmotic effect of glucose leads to polyuria. Polyuria often is expressed moderately - 2,5-6 liters per day. Daily maximum of polyuria depends on fluctuations in blood glucose level throughout the day. Amount of diuresis is one of the clinical criteria for compensation of carbohydrate metabolism. Patients are recommended to always determine the amount of daily urine in order to control the disease.

4. Weight loss.

Weight loss in patients who suffer from long-lasting decompensation of carbohydrate metabolism (more than 2-3 days) is the result of activation of endogenic gluconeogenesis. Formation of endogenous glucose is due to stimulation of glycogen decay in liver and muscles, increased decay of tissue proteins followed by deamination of amino acids in the liver.

The lack of insulin causes the changes in energy balance: free fatty acids, which are produced in adipose tissue as a result of increased lipolysis, become the main energy substrate for some tissues (muscles, myocardium, liver). Negative nitrogen balance, intense lipolysis causes weight loss. Biochemical markers of decompensation of carbohydrate metabolism and activation of gluconeogenesis are the accumulation of free fatty acids in blood, glycerol (hyperlipidemia) and amino acids.

Disorders of gastrointestinal tract in diabetes mellitus

Many gastrointestinal complications of diabetes seem to be related to dysfunction of the neurons supplying the enteric nervous system. An involvement of the intestinal nerves may lead to enteric neuropathy. This is a type of autonomic or "involuntary" neuropathy and may lead to abnormalities in intestinal motility, sensation, secretion, and absorption. Different nerve fibers can either stimulate or inhibit intestinal motility and function, and damage to these nerves can lead to a slowing or acceleration of intestinal function, giving rise to a variable symptom complex.

The Esophagus and Stomach in Diabetes

Gastroparesis

Diabetic gastroparesis is a condition in which emptying of food from the stomach is delayed, leading to retention of stomach contents. This may cause bloating, early satiety, distention, abdominal pain, nausea, or vomiting. Gastric stasis may lead to worsening of gastroesophageal reflux along with symptoms of heartburn and mechanical regurgitation of gastric contents. In addition, fatty foods and very fibrous foods normally exit the stomach slowly and may be poorly tolerated.

The diagnosis of gastroparesis is often suspected on the basis of symptoms alone. Upper GI endoscopy is helpful to rule out anatomic obstruction of the stomach or duodenum but does not provide an accurate physiological assessment of gastric emptying. Upper GI barium studies may confirm delayed gastric emptying with a dilated atonic/aperistaltic stomach with retained gastric contents. However, the upper GI series is more commonly nondiagnostic because liquids may empty normally from the stomach in spite of severe abnormalities in the ability to empty solid materials from the stomach into the duodenum.

The nuclear medicine gastric emptying test is the best confirmatory test for evaluation of gastroparesis. A test solid-food meal containing a technetium isotopic tracer is ingested, and scintigraphy is used to quantitatively measure the rate of gastric emptying. This test is highly sensitive and specific, although false positives and negatives may occur in response to medications that accelerate or slow the rate of gastric emptying. When performing initial diagnostic testing, it is best to measure gastric emptying rates when patients are off of medications that may affect the rate of gastric emptying.

The Small Intestine in Diabetes

In some cases of longstanding diabetes, the enteric nerves supplying the small intestine may be affected, leading to abnormal motility, secretion, or absorption. This leads to symptoms such as central abdominal pain, bloating, and diarrhea. Delayed emptying and stagnation of fluids in the small intestine may lead to bacterial overgrowth syndromes, resulting in diarrhea and abdominal pain.

Diagnosis can be quite difficult and may require small-bowel intubation for quantitative small-bowel bacterial cultures. Breath hydrogen testing and the [14C]-D-xylose test may be helpful in diagnosing bacterial overgrowth as well. All of these tests are somewhat cumbersome, and an empiric trial of antibiotics is often the most efficient means of diagnosing and treating this condition.

Individuals with diabetes also have an increased risk of celiac sprue. In this condition, an allergy to wheat gluten develops, leading to inflammation and thinning of the mucosa of the small intestine. Why this association occurs is not clear. However, sprue may lead to diarrhea, weight loss, and malabsorption of food.

The Colon in Diabetes

Enteric neuropathy may affect the nerves innervating the colon, leading to a decrease in colon motility and constipation. Anatomic abnormalities of the colon, such as structure, tumor, or diverticulitis, should be excluded with a barium enema or colonoscopy.

Diabetic Diarrhea

Patients with a longstanding history of diabetes may experience frequent diarrhea, and this has been reported to occur in up to 22% of patients. This may be related to problems in the small bowel or colon. Abnormally rapid transit of fluids may occur in the colon, leading to increased stool frequency and urgency. In addition, abnormalities in the absorption and secretion of colonic fluid may develop, leading to increased stool volume, frequency, and water content.

Diabetic diarrhea is a syndrome of unexplained persistent diarrhea in individuals with a longstanding history of diabetes. This may be due to autonomic neuropathy leading to abnormal motility and secretion of fluid in the colon. There are also a multitude of intestinal problems that are not unique to people with diabetes but that can cause diarrhea. The most common is the irritable bowel syndrome.

The Liver in Diabetes

Although liver function tests are commonly abnormal in patients with diabetes, it is unclear whether this is a reflection of the underlying obesity that is so common in patients with type 2 diabetes or whether it is an effect of poorly controlled diabetes. Fatty infiltration of the liver (nonalcoholic steatohepatitis) is common in obese individuals (up to 90%) as well as in type 2 diabetic individuals (up to 75%). People with type 1 diabetes in very poor control may also develop this syndrome, although it is much less common.

Fatty infiltration of the liver may lead to tender hepatomegally, elevated liver enzyme tests, and abdominal pain syndromes. Occasionally, this may progress to fibrosis and cirrhosis of the liver.

The diagnosis is usually suspected on the basis of the clinical presentation but can be confirmed with abdominal ultrasonography and, if needed, percutaneous liver biopsy. Metabolic abnormalities such as hemochromatosis and infectious etiologies such as viral hepatitis need to be excluded as part of the evaluation.

Diabetic patients seem to have an increased incidence of gallstones and gall bladder problems, but these, much like fatty infiltration of the liver, are primarily related to the obesity associated with type 2 diabetes and not to the diabetes itself. Obesity leads to secretion of bile by the liver that is supersaturated with cholesterol, leading to crystallization and stone formation. Typical symptoms of biliary colic include intermittent right upper abdominal pain, jaundice, or pancreatitis.

Disorders of the Cardiovascular system in diabetes mellitus

Atherosclerotic coronary artery disease (CAD)

Both type 1 diabetes and type 2 diabetes are independent risk factors for CAD. Moreover, myocardial ischemia due to coronary atherosclerosis commonly occurs without symptoms in patients with diabetes. As a result, multivessel atherosclerosis often is present before ischemic symptoms occur and before treatment is instituted. A delayed recognition of various forms of CAD undoubtedly worsens the prognosis for survival for many diabetic patients.

Diabetic Cardiomyopathy

One reason for the poor prognosis in patients with both diabetes and ischemic heart disease seems to be an enhanced myocardial dysfunction leading to accelerated heart failure (diabetic cardiomyopathy). Thus, patients with diabetes are unusually prone to congestive heart failure. Several factors probably underlie diabetic cardiomyopathy: severe coronary atherosclerosis, prolonged hypertension, chronic hyperglycemia, microvascular disease, glycosylation of myocardial proteins, and autonomic neuropathy. Improved glycemic control, better control of hypertension, and prevention of atherosclerosis with cholesterol-lowering therapy may prevent or mitigate diabetic cardiomyopathy.

Lesions of eyes in diabetes mellitus

Pathology of organ of sight can be associated with damage to the retina, iris, cornea, lens, optic nerve, extraocular muscles, orbital tissue and others. When the duration of diabetes is more than 15 years a dysfunction of organ of sight is found in 60-80% of cases. The most typical lesions of eyes in diabetes include proliferative retinopathy and blindness. The main risk factor concerning the development of diabetic retinopathy and papilledema is the duration of diabetes.

The lesions of sight organ in diabetes include:

- Diabetic retinopathy

- Inflammatory diseases of eyelids

- Diabetic (metabolic) cataract.

- Glaucoma.

- Disorders of oculomotor muscles (ophthalmoplegia).

- Transient disorders of visual acuity

- Changes of cornea.

- Changes of iris.

- Changes of vessels of conjunctiva.

- Lesions of orbital tissues.

Lesions of skin in diabetes mellitus

Almost all diabetic patients eventually develop skin complications from the long-term effects of diabetes mellitus on the microcirculation

and on skin collagen. Cutaneous infections are more common in type 2 diabetes, whereas autoimmune-related lesions are more common in type 1. Patients who have had diabetes for many years tend to develop the most devastating skin problems. However, problems can also develop in the short term, as insulins and oral hypoglycemic drugs can also have dermal side effects. Furthermore, diabetes-related cutaneous lesions may also serve as a port of entry for secondary infection.

Periungual telangiectasia

The lesions of periungual telangiectasia, appearing as red, dilated, capillary veins, are easily visible with the naked eye and are the result of a loss of capillary loops and dilation of the remaining capillaries. A prevalence up to 49% has been described in all diabetic patients. Connective tissue diseases may also involve periungual telangiectases, although these lesions are morphologically different. In diabetes, periungual telangiectasia is often associated with nail fold erythema, accompanied by fingertip tenderness and “ragged” cuticles.

Necrobiosis lipidica

Necrobiosis lipidica diabeticorum appears in 0.3% to 1.6% of diabetic patients. Its origin is unknown. The fully developed clinical appearance is diagnostic: nonscaling plaques with a yellow atrophic center, surface telangiectases, and an erythematous or violaceous border that may be raised. The pretibial region is the area typically affected. Ulceration occurs in up to 35% of cases. Women are affected more often than men. Patients with type 1 diabetes develop necrobiosis lipidica at an earlier mean age than those with type 2 and those without diabetes. The yellow aspect in the central area of the lesions is most likely due to thinning of the dermis, making subcutaneous fat more visible

Bullosis diabeticorum

Bullosis diabeticorum develops in approximately 0.5% of diabetic patients, but more often in those with type 1 diabetes, and more often in men and in patients with long-standing diabetes with peripheral neuropathy. It presents as asymptomatic bullae containing sterile fluid on a noninflamed base, usually arising spontaneously on the dorsa and sides of the lower legs and feet, sometimes on the hands or the forearms. The cause is unknown, and it is a diagnosis of exclusion. The differential diagnosis includes epidermolysis bullosa acquisita, porphyria cutanea tarda, bullous pemphigoid, bullous impetigo, coma blisters, and erythema multiforme.

Vitiligo

Vitiligo vulgaris, or skin depigmentation, occurs more often in type 1 diabetic patients. From 1% to 7% of all diabetic patients have vitiligo vs

0.2% to 1% of the general population. The mechanism behind the association has not been elucidated, although some have suggested polyglandular autoimmune syndrome (PAS), a rare immune endocrinopathy characterized by the coexistence of at least two endocrine gland insufficiencies that are based on autoimmune mechanisms. PAS type 2 is more common (estimated prevalence of 1:20,000), occurs mainly in the third or fourth decade, and is characterized by adrenal failure, autoimmune thyroid disease, or type 1 diabetes. Adrenal failure may precede other endocrinopathies. Vitiligo and gonadal failure occur more frequently in PAS type 1 than in PAS type 2, whereas immunogastritis, pernicious anemia, and alopecia areata are the main features of PAS type 2. In contrast to PAS type 1, family members of PAS type 2 patients are often affected as well. PAS type 2 is believed to be polygenic, with an autosomal dominant pattern of inheritance.

Diabetic dermopathy

Diabetic dermopathy (ie, shin spots and pigmented pretibial papules) affects 7% to 70% of all diabetic patients. It is not specific for diabetes: 20% of nondiabetic people show similar lesions. Men are affected more often than women, and the mean age is 50 years.

Shin spots present as multiple, bilateral, asymmetrical, annular or irregular red papules or plaques on the extensor surface of the lower legs and may precede abnormal glucose metabolism. The clinician usually sees only the end result: atrophic, scarred, hyperpigmented, finely scaled macules. Lesions may also be found on the forearms, thighs, and lateral malleoli. Several studies found severe microvascular complications in patients with diabetic dermopathy, indicating a close association with a high risk of accelerated diabetes complications.

Acanthosis nigricans

Acanthosis nigricans presents as hyperpigmented, velvety plaques in body folds. The dark color is due to thickening of keratin-containing superficial epithelium.³¹ It is traditionally classified as benign in insulin-resistant states. However, it can occur as a sign of paraneoplasm (particularly in stomach cancer), as an adverse effect of certain drugs (eg, nicotinic acid, corticosteroids), and in various endocrinopathies (eg, acromegaly, Cushing syndrome, leprechaunism). Even in the insulin-resistant diabetic patient, an underlying pathologic condition should be excluded.

Cutaneous infections

Skin infections occur in 20% to 50% of diabetic patients (more often in those with type 2 diabetes) and are often associated with poor

glycemic control). The most common infections are candidiasis, dermatophytes, pyodermic infections.

Lesions of respiratory system

The lesions of respiratory organs in diabetes mellitus are characterized by higher incidence of tuberculosis, greater predisposition to development of acute pneumonias, chronic bronchitis, pneumosclerosis, emphysema. The diseases of bronchopulmonary system in diabetes mellitus are characterized by progressive respiratory failure; they are quite often complicated with abscesses and pleurisies and are a causal factors for formation of chronic pulmonary heart.

Osteoarthropathies at patients by diabetes mellitus

Charcot neuropathic osteoarthropathy, commonly referred to as the Charcot foot, is a condition affecting the bones, joints, and soft tissues of the foot and ankle, characterized by inflammation in the earliest phase. The Charcot foot has been documented to occur as a consequence of various peripheral neuropathies; however, diabetic neuropathy has become the most common etiology. The interaction of several component factors (diabetes, sensory-motor neuropathy, autonomic neuropathy, trauma, and metabolic abnormalities of bone) results in an acute localized inflammatory condition that may lead to varying degrees and patterns of bone destruction, subluxation, dislocation, and deformity. The hallmark deformity associated with this condition is midfoot collapse, described as a “rocker-bottom” foot, although the condition appears in other joints and with other presentations. Pain or discomfort may be a feature of this disorder at the active (acute) stage, but the level of pain may be significantly diminished when compared with individuals with normal sensation and equivalent degrees of injury. Clinical findings in patients with an acute Charcot process also include warmth, erythema and swelling.

Radiographs are the primary initial imaging method for evaluation of the foot in diabetic patients. Easily available and inexpensive, they provide information on bone structure, alignment, and mineralization. X-rays may be normal or show subtle fractures and dislocations or later show more overt fractures and subluxations. In later stages, the calcaneal inclination angle is reduced and the talo-first metatarsal angle is broken. Medial calcification of the arteries is present in most Charcot feet and is a frequent secondary finding on radiographs. Magnetic resonance imaging allows detection of subtle changes in the early stages of active CN when X-rays could still be normal.

Laboratory diagnostics of diabetes mellitus

1. Determination of fasting plasma glucose is a basic diagnostic test. The most informative are two types of methods:

a) Method of Somogyi-Nelson. The normal indexes of glycemia are 3,33 - 5,55 mmol/l (60-100 mg %).

b) Methods of Hagedorn-Jenssen and others. The normal indexes of glycemia for a healthy individuals are 4,44 - 6,66 mmol/l (80 - 120 mg%).

c) A screening method is used for the examination of large number of people by the use of glucometer.

2. Oral glucose tolerance test (OGTT). This test is intended to measure the capability and timely response of the insulin-secreting cells to the integrated signals provided by gastrointestinal hormones and rising blood glucose levels. Preparation: patient needs to fast, usually overnight, for 8-12 hours before the test is taken. The only thing that can be ingested is water. In the morning, a blood sample is drawn and tested to give a baseline reading. While waiting for the results of the first test, the patient is given a drink of glucose solution (75 grams of anhydrous glucose dissolved in 200 ml of water). Another blood test is taken 30 minutes after the glucose solution has been ingested and is able to be absorbed into the bloodstream. Blood tests will continue to be drawn after 1 and 2 hours after drinking the glucose solution.

Interpretation: the 2 hour OGTT glucose level should be below 7.8 mmol/L (140 mg/dL). Levels between this and 11.1 mmol/L (200 mg/dL) indicate "impaired glucose tolerance". Glucose levels above 11.1 mmol/L (200 mg/dL) at 2 hours confirm a diagnosis of diabetes. In patients with carbohydrate malabsorption, an intravenous glucose tolerance test replaces the oral glucose tolerance test.

3. Glycosuria appears when the blood glucose level exceeds the renal threshold for reabsorption of glucose. This normally lies at about 8,9—10,0 mmol/L (160—180 mg/dL), but it may be lower in renal tubular disease or elevated in diabetics to above 300 mg/dL. Thus, glycosuria may be absent in these patients despite markedly elevated blood glucose levels.

4. Glycated hemoglobin (HbA1c). HbA1c measurements reflect glucose levels over the preceding 3 months. HbA1c measurements are now included in the diagnostic criteria for diabetes mellitus. $\text{HbA1c} \geq 6.5\% = \text{diabetes mellitus}$, $\text{HbA1c} 5.7 \text{ to } 6.4\% = \text{prediabetes or at risk of diabetes}$.

5. Determination of fructosamine in serum. It is proven that fructosamine, which represents a group of glycosylated proteins of blood and tissues is created during nonenzyme glycosylation of proteins.

The level of fructosamine in serum increases in case of transient elevations of blood glucose levels during 1-3 weeks. In healthy individuals, the level of fructosamine in serum is 2-2,8 mg / dL and it is significantly increased in patients with diabetes.

6. Determination of C-peptide. This research allows determining the functional state of β -cells. The assay is conducted by radioimmune tests. The level of C-peptide in the blood of healthy people is 0,1-1,79 mmol/l (from data of test-set by "Hoechst" or 0,17-0,99 nmol/l (from the data of "Byk-Mallincrodt", 1 nmol/l = 1 mg/ml of x 0,33). The level of C-peptide is lowered in case of diabetes mellitus type 1; it can be normal or increased in case of diabetes mellitus type 2; and increased in case of insulinoma. Endogenous secretion of insulin is evaluated according to the level of C-peptide.

9. Determination of glucagons. Study is conducted by radioimmunoassay. The level of glucagon in serum of healthy individuals is 50-125 ng/L ("Rodioassay systems laboratories"), 360-1260 ng / L ("Cambridge Nuclear Radiopharmaceuticals"). Increased glucagon levels are observed in decompensated forms of diabetes, starvation, physical activity, glucagonoma, chronic diseases of the liver and kidneys.

10. Methods for detection of potentially impaired glucose tolerance (IGT). Individuals with potential IGT include: children, whose both parents have diabetes; healthy twin from the pair of monoovular twins if the other one has diabetes, mostly type 2; mothers who gave birth to a child over 4 kg of body weight, patients with the presence of a genetic marker of type 1 diabetes. Potentially impaired glucose tolerance also includes manifestations of spontaneous hypoglycemia and prolonged increase of patient's body weight. Indexes of IGT in this cohort of people are characterized by hyperinsulinemic type of glucose curve.

Criteria for severity of diabetes mellitus

Moderate degree of severity of type 1 diabetes is characterized by the absence of complications or by the presence of retinopathy stage 1,2; nephropathy stage 1, peripheral polyneuropathy without marked pain syndrome and venous stasis ulcers. The average daily dose of insulin (daily insulin requirement) is not a criterion of degree of diabetes severity.

Severe degree of type 1 diabetes is characterized by pronounced complications – retinopathy stage 2, 3; nephropathy stage 2,3; peripheral polyneuropathy with severe pain syndrome or trophic ulcers, neurodegenerative blindness, encephalopathy, severe autonomic neuropathy, bias to ketoacidosis, recurrent coma, labile course of

diabetes. The need for insulin as well as glycemic indices are not the criteria of disease severity.

Mild form of type 2 diabetes is characterized by the possibility to compensate diabetes only by proper diet. Mild complications are possible – retinopathy stage 1, nephropathy stage 1, transient neuropathy.

The moderate degree of type 2 diabetes is characterized by compensation of carbohydrate metabolism by oral glucose lowering drugs. Complications: retinopathy stages 1 or 2, transient neuropathy.

Severe degree of type 2 diabetes is characterized by severe complications: retinopathy stage 3, nephropathy stage 2 or 3, severe symptoms of peripheral or autonomic neuropathy, encephalopathy. Any method can be chosen for achievement of compensation– diet, oral glucose lowering drugs, insulin therapy.

Criteria of compensation of diabetes:

1. Normoglycemia during the day, not exceeding 9-10 mmol / L, Fasting optimally 4,4-6,0 mmol /L; allowed up to 7.7 mmol / L; Plasma glucose after eating optimally 4,4-8,0 mmol / L; allowed up to 10.0 mmol / L.
2. The level of glycosylated hemoglobin (Hb1, HbA1c) below 9%.
3. Aglycosuria.
4. Normal content of lipids in the blood serum.
5. No episodes of hypoglycemia.
6. No clinical signs of hyperglycemia.

Control of initial level of knowledge

1. The pancreatic islets secrete all of hormones, except of:

- A. Insulin
- B. Glucagon
- C. Somatostatin
- D. Pancreatic polypeptide
- E. Adrenalin

2. All of the mentioned below substances stimulate the secretion of insulin, except of:

- A. Somatostatin
- B. Glucagon
- C. Glucocorticoids
- D. Corticotropin
- E. Gastrointestinal hormones

3. What biological effect is nontypical for insulin:

- A. Increases lipid synthesis
- B. Slows albumin degradation

C. Provides transport of glucose into the cell

D. Increases lipolysis

E. Stimulates the synthesis of RNA

4. *The typical complaints of patients with diabetes mellitus are all of the following, except of:*

A. Polyuria

B. Polydipsia

C. Anorexia

D. Skin itch

E. Weight loss

5. *The skin lesions typical for diabetes are all of the following, except of:*

A. Xanthomatosis

B. Hirsutism

C. Rubeosis

D. Necrobiosis lipoidica

E. Annular granuloma

6. *To determine the severity of diabetes all of listed features are taken into consideration, except:*

A. Duration of disease

B. Significance of clinical symptoms

C. Presence of angiopathies

D. Glycemia

E. Glucosuria

7. *The normal glycemic parameters by the method of Nelson-Somogyi do not include:*

A. 3,8 mmol/l

B. 5,8 mmol/l

C. 4,8 mmol/l

D. 5,2 mmol/l

E. 4,2 mmol/l

8. *The normal glycemic parameters by the method of Hagedorn-Jensen do not include:*

A. 3,8 mmol/l

B. 5,8 mmol/l

C. 4,8 mmol/l

D. 5,2 mmol/l

E. 6,2 mmol/l

9. *The level of glycated hemoglobin in healthy individuals should not exceed:*

A. 6%

- B. 7%
- C. 8%
- D. 9%
- E. 10%

10. For the standard glucose tolerance test the one-time load is used:

- A. 85 g of glucose
- B. 45 g of glucose
- C. 65 g of glucose
- D. 75 g of glucose
- E. 100 g of glucose

Endocrinology (initial level of knowledge's)

1. E
2. A
3. D
4. B
5. B
6. A
7. B
8. A
9. A
10. D

Control of final level of knowledge

1. For type 1 diabetes all statements are true, except of:

- A. Develops mainly at young age
- B. Rapid development microangiopathies
- C. The level of immunoreactive insulin does not change
- D. Episodes of ketoacidosis

E. Correction of carbohydrate metabolism achieved by insulin therapy

2. *For diabetes mellitus 2 type all of statements are typical, except of:*

A. It is inherited by dominant type

B. Signs of disease usually occur in childhood and adolescence

C. Often occurs in patients with obesity

D. Level of C-peptide is normal

E. Correction of carbohydrate metabolism is achieved by oral glucose lowering drugs

3. *Pathogenetic stages of type 1 diabetes include all mentioned below, except of:*

A. Genetic predisposition

B. Initiation of immune processes

C. Clinically explicit diabetes

D. Insulin resistance

E. Complete destruction of B-cells

4. *The most important role in the pathogenesis of type 1 diabetes belongs to:*

A. The genetic defect of antivirus immunity

B. The genetic defect of T lymphocytes

C. Contrainsulinary hormones

D. Primary destructive process of the pancreas

5. *Which hormones inhibit insulin secretion most potently:*

A. Epinephrine

B. Somatostatin

C. Glucagon

D. Norepinephrine

E. Prolactin

6. *Which tissues are the most insulin dependent:*

A. Muscle

B. Nervous

C. Fat

7. *In case of insulin deficiency the most activated processes are:*

A. Neoglucogenesis

B. ketogenesis

C. glycogenolysis

D. lipolysis

E. glycogenesis

8. *The influence of insulin on carbohydrate metabolism is characterized by all the features listed below, except of:*

- A. Increased permeability of cell membranes to glucose
- B. Activation of glucose utilization by cells
- C. Inhibition of glycogenolysis in liver
- D. Intensification of the neoglucogenesis
- E. Increased synthesis of glycogen

9. *The most characteristic effect of physiological doses of glucagon is:*

- A. Stimulation of neoglucogenesis
- B. Stimulation of insulin secretion
- C. Increased plasma glucose

10. *The most characteristic feature of type 1 diabetes is:*

- A. Association of HbA - antigens
- B. The presence of antibodies to pancreatic islets
- C. Reduced number of insulin receptors

Endocrinology (final level of knowledge)

1. C
2. B
3. D
4. D
5. B
6. A
7. C
8. D
9. C
10. B

Test tasks

1. A man of 36 years old, is being sick for 1-1,5 years. Complaints: pronounced weakness, bad appetite, nausea. He lost 10 kg of body

weight during last year. Fasting plasma glucose – 8,1 mmol/l.
Preliminary diagnosis?

- A. *Chronic gastritis.*
- B. *Cushing's disease.*
- C. *Diabetes mellitus.*
- D. *Chronic hepatitis.*
- E. *Insufficiency of adrenal glands.*

2. A woman of 53 years old suffers from the skin itch that appeared after severe stress. Her body height is 167 cm, body weight is 89 kg. Fasting plasma glucose – 8,4 mmol/l. Possible diagnosis?

- A. *Impaired glucose tolerance.*
- B. *Steroid diabetes mellitus.*
- C. *Insulin dependent diabetes mellitus.*
- D. *Neurodermatitis.*
- E. *Insulin independent diabetes mellitus.*

3. The patient had large-focal myocardial infarction. Body weight exceeds the normal on 36%. BP - 150/90 mmHg, Fasting plasma glucose - 5.9 mmol / L, total cholesterol - 4.9 mmol / L, uric acid - 0.211 mmol / L. Which existing risk factors should be eliminated first of all during the process of secondary prevention?

- A. *Hyperglycemia.*
- B. *Arterial hypertonia.*
- C. *Obesity.*
- D. *Hypercholesterolemia.*
- E. *Hyperuricemia.*

4. How to evaluate the results of glucose tolerance test in 16-year-old boy: Fasting - 5.78 mmol / L, 1 hour after intake of 75 g glucose - 7.21 mmol / L, in 2 hours - 5,68 mmol / L.

- A. *Diabetes mellitus, latent form.*
- B. *Diabetes mellitus of moderate severity.*
- C. *Glucose tolerance is not impaired*
- D. *Diabetes mellitus, mild form*
- E. *Symptomatic hyperglycemia.*

5. A young man of 18 years old was first detected with glucose in urine- 5 g / L. Fasting plasma glucose - 5.1 mmol / L. No complaints. What study would reliably exclude diabetes?

- A. *Oral glucose tolerance test.*
- B. *Daily fluctuations of glycemia.*
- C. *Level of insulin in plasma.*
- D. *Daily glucosuria.*
- E. *Postprandial glycemia.*

6. Male of 26 years old, complains on thirst, increased urination, fatigue, weight loss. OBJECTIVE data: dry skin, red cheeks, vesicular breathing. Normal cardiac sounds. Tongue is dry. No symptoms of irritation of the peritoneum. What are the most informative studies for making of diagnosis?

- A. *Fasting plasma glucose*
- B. *General blood count*
- C. *General urinalysis*
- D. *Zimnitskiy's test*
- E. *Liver tests*

7. Patient of 27 years old with satisfactorily compensated diabetes mellitus type 1 has frequent hypoglycemia, nausea, intestinal disorders, skin hyperpigmentation, BP decreased to 80/50 mm Hg., Hb -105 g/l. What may be the reason for decrease of blood pressure?

- A. *Diabetic enteropathy*
- B. *Diabetic gastropathy*
- C. *Chronic insufficiency of adrenal glands*
- D. *The overdose of antidiabetic preparations*
- E. *Development of diabetes insipidus*

8. The woman of 64 years old complains on skin itch after respiratory infection. Height - 161 cm. Weight - 80 kg. Fasting plasma glucose - 9.2 mmol / L. What is the most likely diagnosis?

- A. *Diabetes mellitus, type 1*
- B. *Diabetes mellitus, type 2.*
- C. *Impaired glucose tolerance*
- D. *Steroid diabetes mellitus*
- E. *Neurodermatitis*

9. The woman of 30 years old, who was recently sick with influenza, has fasting plasma glucose level -11.3 mmol/L, glucosuria - 25 g / L. Height - 168 cm Weight - 67 kg. What is the most informative study to clarify the diagnosis?

- A. *Daily variation of glucosuria*
- B. *Daily variations of glycemias*
- C. *Determination of C-peptide*
- D. *Glycemia 1 hour after meals*
- E. *Oral glucose tolerance test*

10. Patient K., 37 years old, complains on thirst, polyuria (up to 5 liters per day), weakness. General tests: fasting plasma glucose - 9.2 mmol/L. What is the preliminary diagnosis?

- A. *Chronic glomerulonephritis*
- B. *Psychogenic polydipsia*

- C. Diabetes mellitus*
D. Primary hyperaldosteronism
E. Diabetes insipidus

CORRECT ANSWERS

1. C	5. A	9. C
2. E	6. A	10. C
3. C	7. C	
4. C	8. E	

Control questions

1. Epidemiology of DM.
2. Etiology of DM.
3. Pathogenesis of DM.
4. Mechanism of development of carbohydrate, protein and fat metabolism disorders in DM.
5. Classification of glycemia disorders (WHO, 1999).
6. Reliable risk classes of DM, diagnostic criteria.
7. Indications and rules of oral glucose tolerance test (OGTT).
8. Differential diagnostics of diabetes I and II types.
9. 1 type of DM, description, peculiarities of clinical course in the individuals of young age.
10. 2 type of DM, description, peculiarities of clinical course in elderly individuals.
11. Criteria of evaluation of DM severity.
12. Clinical signs of DM.
13. Lesions of GIT in diabetes.
14. Lesions of CVS in diabetes.
15. Lesions of the urinary system at diabetes.
16. Osteoarthropathies.
17. Criteria for diagnostics of DM and other categories of hyperglycemia (WHO, 1999).
18. Diagnostic value of C-peptide determination.
29. Diagnostic value of HbA1c determination.

Practical tasks

- to define clinical symptoms, related to the hyperglycemia and concomitant diseases in patients with diabetes mellitus;
- to define the risk factors of diabetes mellitus, possible etiologic factors, initial signs of disease and methods of diagnostics, clinical course of diabetes mellitus, methods of treatment, reasons for decompensation;
- to determine the type of diabetes mellitus, degree of severity;

- to evaluate the level of glycemia and glucosuria, state of lipid, protein and mineral metabolism, C-peptide and HbA1c levels due to results of laboratory assays;
- to determine the degree of compensation of diabetes mellitus;
- to make and substantiate the diagnosis of diabetes mellitus;
- to perform the differential diagnosis of hyperglycemia and glucosuria

Materials, necessary for self preparation

1. Endocrinology: textbook stud. of higher med. Institution / edited by prof. Petro N. Bodnar.- Second edition, update. - Vinnytsia: Нова Книга, 2012.- 328 p.
2. Essential Endocrinology and Diabetes. Richard Holt and Neil Hanley. Blackwell Publishing. Fifth edition. 2007. – 272 p.
3. Oxford handbook of endocrinology and diabetes. Edited by Helen E. Turner, John A.N.Wass.-Oxford University press. 2006.-1005p.
4. Williams Textbook of Endocrinology. Ed. By Henry M. Kronenberg, Shlomo Melmed, Kenneth S. Polonsky, P. Reed Larsen. Saunders 11 edition, 2008.- 1936p.
- 5.Harrison's Endocrinology/ Editor J.Larry Jameson. – McGraw-Hill Medical Publishing Division.-2006. – New York.- 563p.
6. Joslin's Diabetes Mellitus/ Edited by C.Ronald Kahn m.d., Cordon C.Weir m.d., George L.King m.d.- Lippincott Williams & Wilkins a Wolters Kluwer Business.-2006.-USA.- 328p.

Навчальне видання

ЗАХВОРЮВАННЯ ЕНДОКРИННОЇ СИСТЕМИ
ЦУКРОВИЙ ДІАБЕТ, ЕТІОЛОГІЯ, ПАТОГЕНЕЗ, КЛІНІКА,
ДІАГНОСТИКА, КЛАСИФІКАЦІЯ.

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