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«UZHHOROD NATIONAL UNIVERSITY»
MEDICAL FACULTY N 2
Department of the Physiology and Pathophysiology

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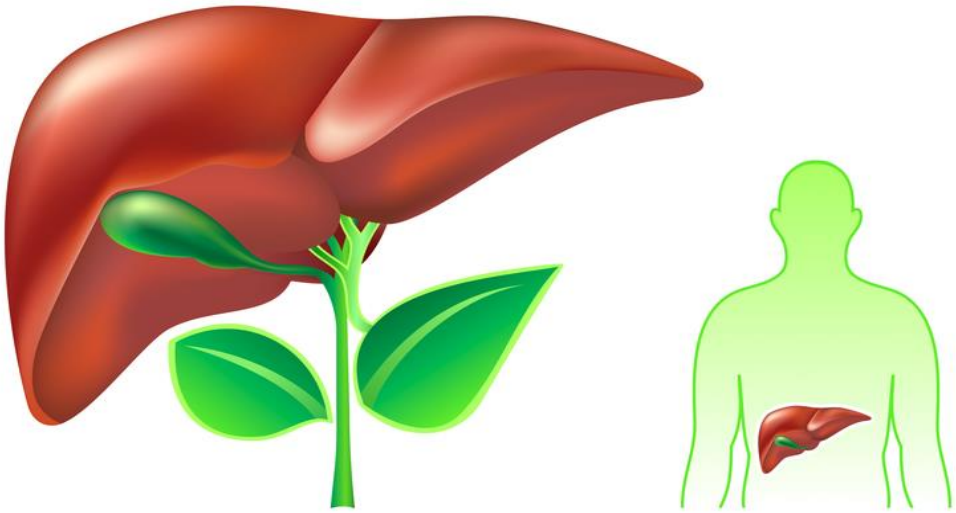
PATHOPHYSIOLOGY OF DIGESTION, LIVER, KIDNEYS, REGULATORY SYSTEMS AND EXTREME STATES

METHODICAL INSTRUCTIONS

for practical classes and self-study on Pathophysiology
for 3rd year students
of medical faculty №2, specialty 222 “Medicine”



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PATHOPHYSIOLOGY OF DIGESTION, LIVER, KIDNEYS, REGULATORY SYSTEMS AND EXTREME STATES. Methodical instructions for practical classes and self-study on Pathophysiology for 3rd year students of medical faculty №2, specialty 222 “Medicine” / Sheiko N.I., Slyvka Y.I. Uzhhorod: 2023. 80 p.

Methodological instructions for practical classes on Pathophysiology for students of the Medical faculty № 2 from the section “Pathophysiology of digestion, liver, kidneys. regulatory systems and extreme states" have been prepared in accordance with the requirements of the Syllabus on Pathophysiology for students of the medical faculty of higher medical educational institutions of the III-IV levels of accreditation.

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Methodological instruction to practical lesson № 28
Module 2. Pathophysiology of organs and systems

Theme: PATHOPHYSIOLOGY OF THE DIGESTIVE SYSTEM. INSUFFICIENCY OF DIGESTION

Student should know:

• Typical pathological states in the system of digestion: insufficiency of digestion (maldigestion) and disorder of absorbtion (malabsorbtion).

• Different principles for classification of the most widespread nosological forms of pathology of digestive tract.

Student should be able to:

• Estimate the role of experimental modelling of different forms of pathology of digestive channel for finding out of reasons and mechanisms of their origin and development.

• Apply knowledge about the role of the nervous and humorous regulation of different parts of digestive channel for the analysis of disorders of its motor, secretory and absorbtive functions.

LIST OF CONTROL QUESTIONS

1. General information of insufficiency of digestion, principles of classification. Reasons of insufficiency of digestion (maldigestion). Role of alimentary and infectious agents, disorders of the nervous and humoral regulation of functioning of the digestive system. Connection of disorders of digestion with disorders of metabolism and energetic balance in an organism.
2. Disorders of appetite. Anorexia. Types of starvation: physiological, pathological; complete, absolute, incomplete, partial. External and internal reasons of starvation. Characteristic of disorders of basic metabolism in certain periods of complete starvation with water. Pathophysiology features of incomplete starvation. Types, etiology, pathogenesis of partial (quality) starvation. Protein-calorie insufficiency, its forms: alimentary marasmus, kwashiorkor. Allimentary dystrophy.
3. Factors which influence on resistance of organism to starvation. A concept of medical starvation.
4. Reasons and mechanisms of disorder of digestion in the oral cavity. Etiology, pathogenesis, experimental models of caries and parodonthosis. Reasons, mechanisms and consequences of disorders of saline excretion.
5. Disorder of motor function of esophagus. Etiology, pathogenesis of heartburn.
6. Disorders of digestion in a stomach. General characteristic of disorders of motor and secretory functions of stomach. Pathological gastric secretion, types; reasons and mechanisms of development.
7. Etiology, pathogenesis of ulcerous illness of stomach and/or duodenum. Role of Helicobacter pilory. Etiology and pathogenesis of symptomatic ulcers of stomach and/or duodenum.
8. Disorder of digestion in bowels, etiology, pathogenesis. Disorders of digestion, related to insufficiency of secretion of pancreatic juice. Etiology, pathogenesis, complications of acute and chronic pancreatitis. Pathogenesis of pancreatic shock.

9. Intestinal dyskinesias. Reasons, mechanisms and signs of constipation and diarrhea. Intestinal ileus: types, etiology, pathogenesis.
10. Disorder of barrier function of bowels: intestinal autointoxication, coli-sepsis, dysbacteriosis. Syndrome of malabsobtion: determination of concept, signs (diarrhea, diminishing of weight of body, protein insufficiency, hypovitaminoses), reasons and mechanisms of development. Intestinal enzymopathies.

The insufficiency of digestion is the pathological state, when digestive system can't provide organism with nutrients. Classification of the insufficiency of digestion.
1) Depend on clinical course there are acute and chronic insufficiency of digestion.
2) Depend on anatomical location the insufficiency of digestion caused by disoders in the oral cavity, in stomach and in intestine.
3) Depend on deficiency of nutrients there are total and partial insufficiency of digestion.
Etiology of the insufficiency of digestion:

I. Hereditary and congenital origin.
II. Acquired origin:

1. infections;
2. physical affects (radiation etc.);
3. chemical affects;
4. disturbances of regulation
5. alimentary disturbances.

Disturbances of the basic functions of gastrointestinal tract: motor, secretory, absorbtive and excretory are observed at pathology of digestive system. The syndromes of the digestion insufficiency:
a) starvation;
b) dyspeptic syndrome;
c) dehydration;
d) disturbances of the acid-base balance;
e) intestinal autointoxication (copremia);
f) pain.
Digestion impairment in the oral cavity may be connected with pathology and dysfunction of:
• teeth in case of injury, absence or pathology due to dental caries or parodontosis;
• masticatory muscles (disorders of nervous regulation);
• temporomandibular joints;
• salivary glands.
Hypersalivation (in pathology the amount of saliva arises up to 6—7 1) is observed in stomatitis, gingivitis, pulpitis, parodontitis as well as during preparation of teeth with a dental drill.
Hyposalivation (reduction of saliva secretion) is connected with sympathetic nervous activation, injection of parasympathetic inhibitors (atropine), infectious and feverish processes.
Caries is a destruction of the hard tooth tissues with cavity formation, which may be complicated by pulpitis and periodontitis.

Parodontitis is an inflammatory-destructive process, which is characterized by damage of the parodentium, which surrounds the tooth root.

Pathology of the stomach may be primary (initially developing in the stomach) and secondary (as a result of pathology, which develops in other organs that may influence stomach functions).

All typical pathophysiological processes can develop in the stomach:

• inflammation (gastritis);
• allergy (autoimmune aggression);
• tumor (carcinoma);
• dystrophy up to necrosis (stomach ulceration);
• disorders of blood supply;
• hemorrhage;
• genetic disorders (which predispose to gastric pathology).

The pathogenesis of every named pathologic process is aggravated by the existence in the stomach of specific aggressive factors (pepsin and hydrochloric acid in large concentration).

Gastritis is an inflammation of the gastric mucosa. All the general laws governing inflammation as a typical pathological process can be applied to stomach inflammation (alteration, microcirculation disorders, BAS production, proliferation).

Three types of gastritis are differentiated.

1. Erosive and hemorrhagic gastritis develops due to the following causes:

• corrosive chemicals;
• radiation trauma;
• ischemia (vasculitis);
• alcohol abuse;
• side effects of nonsteroid and anti-inflammatory drugs, which have an inhibitory effect on cyclooxygenase, thus blocking prostaglandin synthesis. If used in the treatment for chronic inflammatory diseases (more frequently of allergic origin), they cause a systemic block of prostaglandins with their protective effect on the stomach mucosa. In addition, these drugs, introduced orally, damage the mucosa locally. An acute ulcer may develop in a couple of days or weeks. The inhibitory action of these drugs on platelet aggregation increases the danger of ulcer bleeding

2. Nonerosive chronic gastritis is usually restricted to the antrum and is associated with Helicobacter invasion, which not only diminishes mucosal protection, but can also stimulate gastrin liberation and thus gastric juice secretion in the fundus.

3. Atrophic gastritis is usually of autoimmune origin. It is most often limited to the fundus. In these cases the gastric juice and blood plasma contain autoantibodies (immunoglobulins G, infiltrates of plasmacytes and B lymphocytes) against parietal cells (their microsomal lipoproteins, gastrin receptors, carboanhydrase, etc.). Parietal cell atrophy ensues and secretion falls markedly (achlorhydria). If antibodies also block cobalamin binding, there develops pernicious anemia. As a variety of stimulating allergic reactions and receptor diseases autoantibodies to gastrin receptors of accessory stomach cells cause hypertrophy of gastrinproducing cells and thus more gastrin is liberated. As a consequence of high gastrin levels, hyperplasia of enterochromaffin-like cells may take place. These cells, carrying gastrin receptors, are responsible for histamine production in the gastric wall. Hyperplasia of the named

cells can be in progress causing mucosal metaplasia, which, as a precancerous condition, may lead to stomach carcinoma.

Ulcer is a recurrent disease characterized by areas of destruction in the mucous membrane under the influence of activated pepsin, hydrochloric acid and other aggressive factors.

Etiological factors of ulcer are divided into exogenous and endogenous, which in their turn are subdivided into physical, chemical and biological. The risk factors are drugs, alcohol abuse, smoking, eating pattern disorders, emotional stress.

Ulceration of the gastric mucosa is determined by the following pathogenetic mechanisms:

• activation of aggressive factors (corrosive effect of acid and pepsin secreted by the stomach);
• suppression of protective mechanisms;
• disorders of blood circulation in the gastric mucosa (ischemia, stasis);
• inhibition of regenerative ability of the gastric mucous cells.

Pancreatitis is an inflammation of the pancreas, which may be acute and chronic.

Etiological factors of pancreatitis are exogenous and endogenous. Exogenous factors include trauma and infection. Trauma may occur in surgical interventions. Infectious factors are bacterial infection, cocci, viruses (in parotitis and hepatitis), and tuberculosis agent.

Risk factors (the conditions aggravating the action of etiological factors) play a critical role in pancreatitis development. They are: overeating and abuse of fattening food (it causes increased secretion of pancreatic juice), intoxication including drug side effects (immunodepressants, thiazides, corticosteroids, etc.). Alcohol abuse associated with overeating is of great importance in the etiology of pancreatitis.

Among endogenous etiological factors the following ones are very important:

• disorders of blood circulation in the pancreas (thrombosis, ischemia);
• sclerosis of the pancreatic vessels; • occlusion of the pancreatic duct by edema, concrements (gallstones), polyps and tumors; • entry of bile into the pancreatic duct (bile reflux);
• autoimmune aggression (in chronic forms of pancreatitis).

As any other form of inflammation, pancreatitis proceeds in three stages — alteration, exudation and proliferation, has local (in the pancreas) and systemic (in the whole organism) manifestations. The acute form is dangerous for life for it is accompanied with pancreatic shock development.

Acute inflammation in this organ has the following peculiarities:

• Alteration (secondary) predominates over all other stages of inflammation.
• Systemic changes in the organism predominate over the local ones.
• Links of pathogenesis rapidly develop like chain branching reactions and vicious circles. An etiological factor starts inflammation (primary alteration). In response, which is characteristic of inflammation, microcirculation is impaired. Hyperemia and edema lead to pressure increase in the pancreatic duct. Pancreatic secret release becomes difficult. The bile and duodenal chyme (containing enterokinase) may enter the pancreatic duct by reflux. As in any other case of inflammation, BAS are formed. They activate intraorganic trypsinogen and chemotrypsinogen, which damage the pancreas. Secondary alteration is very severe. Pancreonecrosis develops, vascular

permeability rises. As a cascade, all systems of BAS formation are activated («proteolytic explosion»). Elastase and phospholipase A are prematurely activated in the ducts and cells of the pancreatic gland under the effect of bile, enterokinase and other BAS. Active trypsin, BAS and toxic products of tissue autolysis enter the blood. Activation of the blood kallikrein-kinin system aggravates the situation. All these substances are vasoactive and have a powerful vascular and hypotensive effect.

Pancreonecrosis involves the peritoneum (peritonitis) and causes severe pain. The latter together with systemic blood circulation disorder results in shock, which is called pancreatic shock. Severe disorders of hemodynamics, respiration and other vitally important functions ensue. This may lead to death of the patient if inhibitors of proteolytic enzymes are not injected. An important role in pancreatitis pathogenesis belongs to imbalance between proteolytic enzymes and their inhibitors (the latter are produced by the pancreas itself and other organs - the salivary glands, lungs). It is them that are used for acute pancreatitis treatment.

Syndrome of malabsorption may be primary (hereditary) or secondary (acquired). Hereditary syndrome of malabsorption is characterized by selective deficiency of enzymes. As a result, absorption of one or several nutrients is disturbed. This type of malabsorption includes:

• mono- (glucose, fructose, galactose) or disaccharides (lactose, saccharose, isomaltose) intolerance;
• deficit of peptidases (glutenic disease);
• malabsorption of amino acids (cystinuria, tryptophane malabsorption, methionine malabsorption);
• malabsorption of vitamins (cyanocobalamin, folic acid deficiency).

Acquired syndrome of malabsorption is observed:

• after gastrectomy;
• in intestinal diseases (enterocolitis, Crohn's disease);
• in diseases of the pancreas (pancreatitis);
• in diseases of the liver (acholic syndrome);
• after prolonged radiation or medicamentous therapy;
• in disorders of blood and lymph circulation in the intestine, which disturbs energy supply of active nutrient transport;
• under the influence of poisons blocking enzyme activity;
• in water-electrolyte imbalance;
• in ATP and sodium ion imbalance (which are of special importance in the active transport of glucose, amino acids and other compounds).

Disturbance of the motor function of the intestine manifests itself through peristalsis increase or decrease. Serotonin, P-substance, gastrin, and motilin activate peristalsis. Contraction of the intestinal muscles is activated by vagus nerve stimulation. Vasoactive intestinal peptide and glucagon inhibit peristalsis. Motility increases in:

• inflammation (enteritis, colitis);
• influence of mechanical or chemical stimuli due to consumption of undercooked food;
• effect of bacterial toxins;
• disturbance of nervous and humoral regulation. Increase of peristalsis usually leads to accelerated movement of nutrient masses in the intestine, disorders of their

digestion and absorption. Spasms of the intestinal muscles manifest themselves through spasmodic pain.

Constipation and diarrhea are clinical symptoms of decreased and increased intestinal motility and are connected with large bowel dysfunction. Irritable bowel syndrome is an example of disturbed nervous and humoral regulation of intestinal motility. Negative emotions change the motor and absorptive functions of the intestine and cause pain and diarrhea, frequently followed by constipation.

Krok 1 mcqs_A is correct answer:

1. A 57-year-old patient was admitted to the gastroenterological department with suspicion on Zollinger-Ellison syndrom because of rapid increase of gastrin level in the blood serum. What disorder of the secretory function of the stomach is the most likely?
A Hyperacid hypersecretion
B Hyperacid hyposecretion
C Achylia
D Hypoaci hyposecretion
E Hypoacid hypersecretion

2. A 40-year-old female patient diagnosed with acute pancreatitis has been delivered to the admission department of a regional hospital. What drug should be administered the patient in the first place?
A Contrycal
B Platyphyllin
C Atropine
D Metacin
E Pirenzepine

3. A patient has a critical impairment of protein, fat and hydrocarbon digestion. Most likely it has been caused by low secretion of the following digestive juice:
A Pancreatic juice
B Saliva
C Gastrijuice
D Bile
E Intestinal juice

4. A 49-year-old male patient with acute pancreatitis was likely to develop pancreatic necrosis, while active pancreatic proteases were absorbed into the blood stream and tissue proteins broke up. What protective factors of the body can inhibit these processes?
A α2-macroglobulin, α1-antitrypsin
B Immunoglobulin
C Cryoglobulin, interferon
D Ceruloplasmin, transferrin
E Hemoplexin, haptoglobin

5. To prevent attacks of acute pancreatitis a doctor prescribed the patient trasylol (contrycal, gordox), which is an inhibitor of:
A Trypsin
B Elastase
C Carboxypeptidase
D Chymotrypsin
E Gastricsin

6. A patient with hypersecretion of the gastric juices was recomended to exclude concentrated bouillons and vegetable decoctions from the diet because of their stimulation of gastric secretion. What is dominating mechanism of stimulation of secretion in this case?
A Stimulation of gastrin production by G-cells
B Irritation of taste receptors
C Irritation of mechanoreceptors of the oral cavity
D Irritation of mechanoreceptors of the stomach
E Stimulation of excretion of secretin in the duodenum

7. When the pH level of the stomach lumen decreases to less than 3, the antrum of the stomach releases peptide

that acts in paracrine fashion to inhibit gastrin release. This peptide is:
A GIF
B Acetylcholine
C Gastrin-releasing peptide (GRP)
D Somatostatin
E Vasoactive intestinal peptide (VIP)
8. A 57-year-old patient was admitted to the gastroenterological department with suspicion of Zollinger-Ellison syndrome because of rapid increase of gastrin level in the blood serum. What the most probable disorder of the secretory function of the stomach here?
A Hyperacidity hypersecretion
B Hyperacidity hyposecretion
C Achylia
D Hypoacidity hyposecretion
E Hypoacidity hypersecretion
9. Secretion of what gastrointestinal hormones will be primarily decreased as a result of ileoduodenum removal?
A Cholecystokinin and secretin
B Gastrin
C Histamine
D Gastrin an histamine
E Neurotensin
10. A 30-year-old woman was diagnosed with insufficiency of exocrinous function of pancreas. Hydrolysis of what nutrients will be disturbed?
A Proteins, fats, carbohydrates
B Proteins, fats
C Proteins, carbohydrates
D Fats, carbohydrates
E Proteins
11. After intake of rich food a patient feels nausea and sluggishness; with time there appeared signs of steatorrhea. Blood cholesterine concentration is 9,2micromole/l. This condition was caused by lack of:
A Bile acids
B Triglycerides
C Fatty acids
D Phospholipids
E Chylomicrons
12. After consumption of rich food a patient has nausea and heartburn, steatorrhea. This condition might be caused by:
A Bile acid deficiency
B Increased lipase secretion
C Disturbed tripsin synthesis
D Amylase deficiency
E Disturbed phospholipase synthesis
13. Examination of a 35 year old patient revealed high acidity of gastric juice. What receptors should be blocked in order to reduce it?
A Histamine
B α1-adrenoreceptors
C α2-adrenoreceptors
D β1-adrenoreceptors
E β2-adrenoreceptors
14. A patient was admitted to the infectious department. His symptoms: dry skin, decreased skin turgor, rice-water stool. The patient was diagnosed with cholera. What disorder of waterelectrolytic balance is most often observed in this disease?
A Isoosmotic hypohydration
B Hyperosmotic hyperhydration
C Hypoosmotihypohydration
D Hyperosmotic hypohydration
E Hypoosmotic hyperhydration
15. A 50-year-old man, who has been suffering from chronic hepatic failure for several years, has developed ascites. What is the main mechanism of this disorder development?
A. Increased pressure in portal vein system
B. Decrease of albumin and globulin synthesis in liver
C. Increased content of low-density and very low-density lipoproteins in blood
D. Neurotoxins appearing in blood
E. Increase of blood oncotic pressure
16. A patient presents with steatorrhea. This disorder can be linked to disturbed

supply of the intestine with the following substances:
A. Bile acids
B. Carbohydrates
C. Tripsin
D. Chymotrypsin
E. Amylase

Tests and Tasks for Self-Control

1. Caries was reproduced experimentally in rats. What compensatory reactions developed?
A. Formation of secondary dentine by fibroblasts.
B. Neogenesis of the enamel.
C. Hypotrophy of the salivary glands.
D. Inhibition of phagocytosis.
E. Hyperfunction of the parathyroid glands.

2. With the purpose of stomach ulcer modeling, sclerosis of animal gastric arteries was reproduced. What is the main mechanism of gastric mucosa damage in this experiment?
A. Disregulatory.
B. Neurodystrophic.
C. Mechanical.
D. Ischemic.
E. Neurohumoral.

3. A patient has Zollinger—Ellison syndrome (tumor of the pancreas). Elevation of gastric secretion and acidity, ulcers in the duodenum and jejunum are observed. What substance is produced by the tumor and provokes this syndrome?
A. Secretin.
B. Vasoactive intestinal peptide.
C. Pepsin.
D. Trypsin.
E. Gastrin.

4. A 20-year-old man, who participated in nuclear accident elimination, suffers from parodontosis. What is the main etiological factor of the development of this pathology?
A. Iron deficiency.
B. Emotional stress.
C. Malnutrition.
D. Increased mechanical load on the dentomandibular apparatus.
E. Streptococcus infection of the oral cavity.

5. A patient suffers from inflammation of the trigeminal nerve and progressive parodontosis. What is the pathogenesis of parodontosis in this case?
A. Decrease of immunoglobulin concentration in salvia.
B. Decrease of the phagocytic activity of leukocytes.
C. Dystrophic changes in the parodontium.
D. Hypertonus of the vagus nerve.
E. Hypersalivation.

6. A patient came to a doctor with complaints of purulent exudate from the gingival pocket and teeth loosening. What is the cause of purulent periodontitis in this case?
A. Hypersalivation.
B. Viral infection.
C. Bacterial infection.
D. Local anaphylaxis.
E. Generalized anaphylaxis.

7. A 57-year-old patient was delivered to the gastroenterological department with Zollinger—Ellison syndrome suspected. What kind of stomach secretory function disturbance is the most probable in this case?
A. Hyperacidic hypersecretion.
B. Low level of gastrin in the blood serum.
C. Achylia.
D. Hypoacidic hyposecretion.
E. Hypoacidic hypersecretion.

8. A patient with high mechanical intestinal obstruction complains of

abdominal pain, uncontrollable vomiting during the last 3 hours, dyspnea. Objectively: pulse is 110, arterial pressure — 90/50 mmHg, hematocrit value — 0.52, hyponatremia. What is the main mechanism of cardiovascular disorder?
A. Alkalosis.
B. Respiratory acidosis.
C. Dehydration, hypovolemia.
D. Intestinal endointoxication.
E. Hypoxia.
9. A patient has been taking glucocorticoids for a long time. Fibrogastroscopy revealed erosions and ulcers in the stomach and duodenum. What mechanism determines the development of ulcers?
A. Increasing production of PgE.
B. Decreased influence of histamine on the gastric mucus.
C. Increasing tone of the sympathetic nervous system.
D. Deficit of mucous protection factors.
E. Decrease of gastric secretion and acidity.
10. 5 years ago a patient underwent gastrectomy. Now a stomatologist found atrophic-inflammatory processes of the mucous membrane of the gums and tongue. What is the cause of these changes?
A. Vitamin C deficiency.
B. Vitamin B12 deficiency.
C. Vitamin B(deficiency.
D. Malnutrition.
E. Psychoemotional stress.

Recommended literature:

Basic

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4. Porth, Carol. Essentials of pathophysiology: concepts of altered health states /Carol Mattson Porth ; consultants, Kathryn J. Gaspard, Kim A. Noble. —3rd ed. 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins. – 2011. – 1282 p.
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Methodological instruction to practical lesson № 29
Module 2. Pathophysiology of organs and systems

Theme: PATHOPHYSIOLOGY OF LIVER. LIVER FAILURE

Student should know:

- Concept, criteria and classification of hepatic insufficiency, hepatic coma, icterus, portal hypertension.

Student should be able to:

- Analyze the different variants of hepatic insufficiency according to reasons and mechanisms of origin, course character, degree of severity.

LIST OF CONTROL QUESTIONS

1. Liver failure: determinations of concept, principles of classification. Etiology, pathogenesis, experimental models of hepatic insufficiency. Typical disorders of carbohydrate, protein, lipid, water-electrolyte metabolism, metabolism of microelements, vitamins and hormones, disorder of activity of the functional systems of organism at insufficiency of liver.
2. Insufficiency of antitoxic function of liver, mechanisms of basic signs. Types, reasons, pathogenesis of hepatic coma. Role of cerebrotoxic substances.
3. Insufficiency of excretory function of liver, basic signs. Determination of concept, criteria, types of jaundice, reasons and mechanisms. Comparative characteristic of disorders of pigment metabolism at hemolitic, hepatic and mechanical jaundices; syndromes of cholemias and hypo-, acholias. Gall-stone illness.
4. Syndrome of portal hypertension: etiology, pathogenesis, signs. Mechanisms of development of hydroperitoneum, hepato-lienal and hepato-renal syndromes.
5. Disorder of protein metabolism. Disorder of metabolism of purine and pirimidine bases. Positive and negative nitrous balance. Disorder of the basic stages of protein metabolism. Nitrigenemia, productive and retentional. Disorder of protein composition of blood: hyper-, hypo-, dysproteinemia. Disorder of a transport function of plasma proteins. Conformative changes of protein molecules, disorder of degradation of proteins in lysosomes and proteosomes, their role in pathology. Inherited disorders of metabolism of aminoacids.

Hepatic insufficiency is a group of syndromes characterized by impaired ability of the liver to fulfill its functions, which results in disorders of the organism's vital activity.

The liver performs a very large number of important physiological functions. It is involved in the synthesis of a number of plasma proteins (albumin, fibrinogen) in the intermediary metabolism of proteins, carbohydrates and fats, in the storage of various vitamins (B12), minerals, carbohydrates (glycogen). It is also responsible for detoxification and excretion into bile of endogenously produced waste products or

exogenous toxins and drugs. Specific function of the liver is the formation and secretion of bile. Accordingly, the liver is vulnerable to a wide variety of toxic, metabolic, infectious, and circulatory insults, and injury to it may have far-reaching consequences, given the critical dependence of other organs on the metabolic function of the liver.

Major causes of liver disease:

1) infections -viruses of hepatitis, bacteria of tuberculosis, syphilis, protozoa(amoeba, lamblia), helminth (echinococcus, ascarid) and others
2) chemical agents - alcohol, drugs, insecticides, vegetable poisons, products of tissue decay in burn, necrosis; gestational toxicosis
3) physical factors -ionizing radiation, trauma
4) disturbances of the blood circulation in the liver (local one – ischemia, thrombosis or general one – cardiovascular insufficiency)
5) lesions of the biliary tract
6) alimentary factors-protein, vitamin deprivation, fatty meal
7) endocrine and metabolic disorders-diabetes mellitus, thyrotoxicosis, obesity
8) genetic defects-hereditary enzymopathy The most severe clinical consequence of liver disease is liver failure.

Damage of the liver can be primary (by direct action of an etiological factor) and secondary (indirect affection of the liver in other pathology — allergy, systemic blood circulation disorders, heart insufficiency, hypoxia).

All typical pathological processes can occur in the liver.

Inflammation (hepatitis) is caused by infectious and noninfectious agents.

Allergy results from formation of cytotoxic autoantibodies against pathologically changed hepatocytes and development of autoallergic reactions of humoral and cellular types; then the liver is damaged by immune cytolysis with T-killers and BAS.

Tumors may be primary and metastatic.

Hypoxia of different origin creates a relative deficit of microsomal cytochrome P450 needed for the antitoxic function of the liver.

Metabolic disorders.

Dystrophy (hepatosis) is a result of primary or secondary metabolic changes in hepatocytes.

Sclerosis (cirrhosis), i.e. diffuse growth of the connective tissue (as a rule against the background of chronic inflammatory or metabolic affection of the liver); alcohol abuse plays a role.

Liver failure is a pathological condition in which some or all hepatic functions are reduced to provide the homeostasis. Liver failure may result from many factors which are able to cause massive hepatic destruction or lesions of the bile ducts.

Classification

<u>According to causes of hepatocyte damage, liver failure can be divided into</u>:

-hepatocellular

-hepatovascular
-cholestatic

Hepatocellular failure results from an immediate damage to liver cells by pathogenic agents including physical (ionizing radiation), chemical (aphlotoxin, muscarin) and biological (viruses of hepatitis) ones Hepatocellular failure occurs when total liver cell function falls below the minimum required to maintain a physiological state. It results from loss of a large number of liver cells.

Hepatovascular failure results from primary changes in the liver circulation, mainly due to portal hypertension. Portal hypertension is a syndrome characterized by increased portal pressure. It may be caused by a variety of conditions that increase resistance to blood flow through the liver, e. g., portal vein thrombosis, alcoholic cirrhosis, tumor and other. As a result of increased resistance to hepatic flow collateral channels open. It connects the portal circulation with the systemic one, so portal blood is shunted directly into the systemic one instead of passing through the liver. It leads to an increased blood level of toxic compounds absorbed from the gut.

Cholestatic failure develops as a result of primary changes in bile formation or bile secretion. It mostly occurs in obstructive jaundice. Pathogenesis includes: direct destruction of hepatocytes by bile and toxic influence of bilirubin on tissue respiration.

<u>According to number of functions reduced liver failure</u> can be either partial or total (all functions are fail)

<u>According to clinical course</u> acute and chronic liver failure are distinguished.

Clinical features of disturbed hepatic function

The manifestations of liver failure reflect various functions of the liversynthesis, storage, metabolic, detoxification, excretory, bile formation and bile secretion ones. Regardless of cause, the clinical signs of hepatic failure are much the same.

The more important effects include:

1) jaundice because of failure to remove bilirubin from the blood, to conjugate it and to excrete it in the bile

2) hypoalbuminemia which results from an impaired hepatic synthesis of albumin and that, in turn, predisposes peripheral edema

3) coagulopathy because of impaired hepatic synthesis of blood clotting factors. The resultant bleeding tendency may lead to massive gastrointestinal hemorrhage as well as bleeding elsewhere. 4) changes in nitrogen metabolism with a rise in blood level of toxic nitrogenous compounds produced by bacteria in the gut and normally metabolized by the liver. These compounds are harmful to the CNS causing encephalopathy

5) hyperammonemia which is due to defective hepatic urea metabolism and that mediates hepatic encephalopathy

6) hormonal disturbances attributable to interference with hepatic metabolism of various steroid and other hormones. Impaired estrogen metabolism and consequent hyperestrogenemia are putative causes of palmar erythema and spider angiomas of

the skin. In the male, hyperestrogenemia also leads to hypogonadism and gynecomastia.
7) circulatory disturbances with cyanosis and hypervolemic circulation
Hepatic encephalopathy (hepatic coma) is a feared complication of acute and chronic liver failure. Patients show a spectrum of disturbances in brain function, ranging from subtle behavioral abnormalities to marked confusion and stupor, to deep coma and death. Associated fluctuating neurologic signs include rigidity, hyper-reflexia, nonspecific electroencephalographic changes, and, rarely, seizures. Particularly characteristic is asterixis (also called flapping tremor), which is a pattern of nonrhythmic, rapid extension-flexion movements of the head and extremities.

Biochemical features of disturbed hepatic function
To access injury to liver cells measures of serum levels of transaminases are used. The key enzymes are ALT (alanine aminotransferase) and AST (aspartate aminotransferase). ALT is liver specific, whereas AST is derived from organs other than the liver. The liver‘s synthetic capacity is reflected in measures of serum protein levels and prohtrombin time. Hypoproteinemia is a characteristic of hepatic failure. Prothrombin time is prolonged. The liver‘s excretory function may be evaluated in measures of: - serum bilirubin - gamma-glutamyltransferase (GGT) - alkaline phosphatase Alkaline phosphatase is present in the membrane of cells that line the bile duct and is released by disorders affecting the bile duct.
GGT provides the transport of peptides and amino acids into liver cells. It is a sensitive indication of hepatobiliar diseases, especially in diagnosis alcoholic abuse.

Alterations in bile production and bile secretion function
The liver secrets bile, approximately 600 to 1200 ml daily. Bile function: - bile play an essential role in the digestion and absorption of fats and fat-soluble vitamins from the intestine - bile serves as a vehicle for excretion of bilirubin, excess cholesterol and metabolic and-products that cannot be eliminated in the urine Bile contains water, electrolytes, bile salts, bilirubin, cholesterol, and certain products of organic metabolism. Of these, only bile salts, which are formed from cholesterol, are important in digestion.
Bile salts:
- aid in emulsifying dietary fats
- they are necessary for the formation of the micelles that transport fatty acids and fat-soluble vitamins to the surface of the intestinal mucosa for absorption
Impairment of bile production and bile secretion results into:
- digestive disorders: malabsorption of fat and fat-soluble vitamins, fatty stools
- disorder of excretion of bilirubin, cholesterol, end-products of hormones and drugs degradation
- jaundice

EFFECTS OF HEPATIC INSUFFICIENCY

Main functions of liver	Disorders
Metabolic	1)**Disorders in carbohydrate metabolism – result abnormality of glucose level in blood :** • Decreased amount of glycogen in the liver (starvation, disorders of glycogenesis, glycogenolysis, synthesis of glucose from monosaccharides,…) • Disorders of splitting of glycogen into glucose – glycogenoses (different types); 2) **Disorders in lipid metabolism:** • Disorders in lipid digestion, bile acid formation; • Disorders in synthesis of TG, cholesterol, lipoproteins, phospholipids… • Disorders of absorption of some vitamins (D,E,K,A); • Increased formation of ketones; • Fatty infiltration of liver. 3) **Disorders of protein metabolism:** • Disorders of synthesis of proteins; • Disorders in amino acids metabolism; • Disorders in synthesis of urine; • Disorders in coagulative system, dysproteinemias 4) **Disorders of metabolism some vitamins (D,E,K,A; B_{12} deposition), microelements (Fe, Cu, Co, Zn, Mo)**
Defensive	1)**Disorders of antitoxic function of liver** • decrease amount of functionally active hepatocytes, • decreased activity of enzymes during detoxication, • depletion of ATP 2) **Disorders of phagocytosis, decreased bactericidal properties of bile, decreased regenerative properties of hepatocytes,…**
Excretory	**Disorders of 2 main processes:** • Excretion of products of metabolism like bilirubin, cholesterol… • Digestive function – mostly lipid metabolism. As a result – **jaundice, cholemia, acholia**
Hemodynamic	• Disorders in collecting blood from digestive tract ; • Abnormalities in blood deposition; • Disorders in vascular tone regulation (in synthesis of angiotensin precursor, ferritin – vasoconstriction and angiotensinase – vasodilation;

Fig 17. Effects of hepatic insufficiency

JAUNDICE

	PREHAPATIC (Hemolytic)	INTRAHEPATIC (Parenchimal)	POSTHEPATIC (Mechanical)
Etiology	The major cause of prehepatic jaundice is excessive red blood cell destruction that occurs in the following conditions: -hemolytic blood transfusion reaction, - hereditary disorders of the red blood cells: sickle cell anemia, thalassemia, spherocytosis, - acquired hemolytic disorders, - hemolytic disease of the new-born - autoimmune hemolytic anemia	Intrahepatic jaundice is caused by disorders that directly affect the ability of the liver to remove bilirubin from the blood or conjugate it so it can be eliminated in the bile. The most common causes include hepatitis, cirrhosis, cancer of the liver and drug-induced cholestasis.	Posthepatic or obstructive jaundice, also called cholestatic jaundice, occurs when bile flow is obstructed between the liver and the intestine. Causes of posthepatic jaundice include: -structural disorders of the bile duct -cholelitiasis -congenital atresia of the extrahepatic bile ducts -bile duct obstruction caused by tumors
Pathogenesis	Resulting from an excessive hemolisis, bilirubin is formed in so large amount that it fails to be excreted by the liver and is retained in the blood. In prehepatic jaundice, unconjugated bilirubin is elevated, the stools are of dark color because contain a large amount of sterkobilinogen, and there is no bilirubin in the urine. Urobilinogen can occur in the blood and urine because it is formed at a rate in excess of the liver's ability to utilize it.	Intrahepatic jaundice usually interferes with all phases of bilirubin transport – uptake, conjugation and excretion. Both unconjugated (disturbed uptake and conjugation) and conjugated (disturbed excretion) bilirubin are elevated and the urine often is dark because of the presence of bilirubin. There is cholemia (bile in the blood) as a result of damage to liver parenchyma.	Conjugated bilirubin levels usually are increased, the stools are clay colored because of the lack of bilirubin in the bile, the urine is dark, and the levels of serum alkaline phosphatase are markedly elevated. The effects of jaundice on the organism are related to two syndromes: cholemia and acholia.
Differential criteria of jaundice			
In the blood	• high level of unconjugated bilirubin • no cholemia • urobilinogen appears	• increase in unconjugated bilirubin • appearance of conjugated bilirubin • urobilinogen appears	• conjugated bilirubin appears • cholesterol increases (cholemia) • bile acids appear
In the faces	Stercobilin is increased	Stercobilin drops	Stercobilinogen is dropped or absent (acholia)
In the urine	Stercobilin is increased	• sterkobilin drops • urobilinogen appears • conjugated bilirubin appears	• stercobilinogen is dropped or absent • conjugated bilirubin appears • bile acids appear

Fig. 18 Jaundice

Krok 1 mcqs_A is correct answer:

1. A 48 y.o. patient was admitted to the hospital with complaints about weakness, irritability, sleep disturbance. Objectively: skin and scleras are yellow. In blood: conjugated bilirubin, cholalemia. Feces are acholic. Urine is of dark colour (bilirubin). What jaundice is it?
A Mechanic
B Hemolytic
C Parenchymatous
D Gilbert's syndrome
E Crigler-Najjar syndrome
2. Examination of a miner revealed pulmonary fibrosis accompanied by disturbance of alveolar ventilation. What is the main mechanism of this disturbance?
A Limitation of respiratory surface of lungs
B Constriction of superior respiratory tracts
C Disturbance of neural respiration control
D Limitation of breast mobility
E Bronchi spasm
3. A patient presents with icteritiousness of skin, scleras and mucous membranes. Blood plasma the total bilirubin is increased, stercobilin is increased in feces, urobilin is increased in urine. What type of jaundice is it?
A Haemolytic
B Gilbert's disease
C Parenchymatous
D Obturational
E Cholestatic
4. Hepatitis has led to the development of hepatic failure. Mechanism of edemata formation is activated by the impairment of the following liver function:
A Protein-synthetic
B Barrier
C Chologeneti
D Antitoxic
E Glycogen-synthetic
5. A patient being treated for viral hepatitis type B got symptoms of hepatic insufficiency. What blood changes indicative of protein metabolism disorder will be observed in this case?
A Absolute hypoalbuminemi
B Absolute hyperalbuminemia
C Absolute hyperfibrinogenemia
D Proteinic bloocomposition is unchange
E Absolute hyperglobulinemia
6. M-r S presents all signs of the hepatic coma: loss of consciousness, absence of reflexes, cramps, convulsion, disorder of heart activity, recurrent (periodical)respiration. What are cerebrotoxical substances which accumulate in blood under hepar insufficiency?
A Ammonia
B IL-1
C Autoantibody
D Necrosogenic substances
E Ketonic body
7. Analysis of blood serum of a patient revealed increase of alanineaminotransferase and aspartate aminotransferase level. What cytological changes can cause such a situation?
A Cellular breakdown
B Disturbed function of energy supply ofcells
C Disorder of enzyme systems of cells
D Disturbance of genetic apparatus of cells
E Disturbance of cellular interrelations
8. A patient complains of frequent diarrheas, especially after consumption

of fattening food, and of body weight loss. Laboratory examination revealed steatorrhea; hypocholic feces. What can be the cause of this condition?
A Obturation of biliary tracts
B Mucous membrane inflammation of small intestine
C Lack of pancreatic lipase
D Lack of pancreatic phospholipase
E Unbalanced diet
9. A patient suffers from hepatic cirrhosis. Examination of which of the following substances excreted by urine can characterize the state of antitoxic function of liver?
A Hippuric acid
B Ammonium salts
C Kreatinine
D Uric acid
E Aminoacids
10. A 48 y.o. patient was admitted to the hospital with complaints about weakness, irritability, sleep disturbance. Objectively: skin and scleras are yellow. In blood: conjugated bilirubin, cholalemia. Feces are acholic. Urine is of dark colour (bilirubin).What jaundice is it?
A Mechanic
B Hemolytic
C Parenchymatous
D Gilbert's syndrome
E Crigler-Najjar syndrome
11. A 4 y.o. boy has had recently serious viral hepatitis. Now there are such clinical presentations as vomiting, loss of consciousness, convulsions. Blood analysis revealed hyperammoniemia. Disturbance of which biochemical process caused such pathological condition of the patient?
A Disturbed neutralization of ammoni in liver
B Disturbed neutralization of biogenic amines
C Increased putrefaction of proteins in bowels
D Activation of aminoacide carboxylation
E Inhibition of transamination enzymes
12. A patient has a disturbed absorbtion of fat hydrolysates. It might have been caused by a deficit in the small intestine cavity:
A Of bile acids
B Of bile pigments
C Of lipolytienzymes
D Of sodium ions
E Of liposoluble vitamins
13. A patient has yellow skin colour, darkurine, dark-yellow feces. What substance will have strengthened concentration in the blood serum?
A Unconjugated bilirubin
B Conjugated bilirubin
C Mesobilirubin
D Verdoglobin
E Biliverdin
14. A patient being treated for viral hepatitis type B got symptoms of hepatic insufficiency. What blood changes indicative of protein metabolism disorder will be observed in this case?
A Absolute hypoalbuminemia
B Absolute hyperalbuminemia
C Absolute hyperfibrinogenemia
D Proteinic bloocomposition is unchanged
E Absolute hyperglobulinemia
15. A patient with jaundice has high total bilirubin that is mainly indirect (unconjugated), high concentration of stercobilin in the stool and urine. The level of direct (conjugated) bilirubin in the blood plasma is normal. What kind of jaundice can you think of?
A Hemolytic
B Parenchymal (hepatic)
C Mechanical

D Neonatal jaundice
E Gilbert's disease

16. A patient with biliary dyskinesia and constipations has been prescribed a cholagogue having also a laxative effect. What drug has been administered?
A Magnesium sulfate
B Allochol
C Cholosas
D Cholenzyme
E Nicodinum

17. An unconscious patient was taken by ambulance to the hospital. On objective examination the patient was found to have no reflexes, periodical convulsions, irregular breathing. After laboratory examination the patient was diagnosed with hepatic coma. Disorders of the central nervous system develop due to the accumulation of the following metabolite:
A Ammonia
B Urea
C Glutamine
D Bilirubin
E Histamine

18. Enzymatic jaundices are accompanied by abnormal activity of UDP glucuronyl transferase. What compound is accumulated in blood serum in case of these pathologies?
A Unconjugated bilirubin
B Conjugated bilrubin
C Dehydrobilirubin
D Hydrobilirubin
E Choleglobin

19. A drycleaner's worker has been found to have hepatic steatosis. This pathology can be caused by the disruption of synthesis of the following substance:
A Phosphatidylcholine
B Tristearin
C Urea
D Phosphatidic acid
E Cholic acid

20. A patient takes cholagogues. What other process besides biliary excretion will be stimulated?
A Intestinal motility
B Gastric juice secretion
C Pancreatijuice secretion
D Gastric motor activity
E Water absorption

21. A 53-year-old male patient complains of acute pain in the right hypochondrium. Objective examination revealed scleral icterus. Laboratory tests revealed increased ALT activity, and stercobilin was not detected in the stool. What disease is characterized by these symptoms?
A Cholelithiasis
B Hemolytic jaundice
C Hepatitis
D Chronic colitis
E Chronic gastritis

22. A patient has been admitted to the contagious isolation ward with signs of jaundice caused by hepatitis virus. Which of the symptoms given below is strictly specific for hepatocellular jaundice?
A Increase of ALT, AST level
B Hyperbilirubinemia
C Bilirubinuria
D Cholemia
E Urobilinuria

23. A tooth extraction in a patient with chronic persistent hepatitis was complicated with prolonged hemorrhage. What is the reason for the haemorrhagic syndrome?
A Decrease in thrombin production
B Increase in thromboplastin production
C Decrease in fibrin production
D Increase in fibrinogen synthesis

E Fibrinolysis intensification

24. A43-year-old patient suffers fromacute pancreatitis with disrupted common bile duct patency. What condition can develop in this case?

A. Mechanical jaundice
B. Hemolytic jaundice
C. Hepatocellular jaundice
D. Hepatic coma
E. Portal hypertension

25. A 60-year-old man suffering from chronic hepatitis frequently observes nasal and gingival hemorrhages, spontaneous hemorrhagic rashes on the skin and mucosa. Such presentations result from:

A. Decreased synthesis of prothrombin and fibrinogen
B. Increased blood content of aminotransferases
C. Decreased synthesis of serum albumins
D. Increased blood content of macroglobulins and cryoglobulins
E. Decreased blood content of cholinesterase

26. Blood test of the patient revealed albumine content of 20 g/l and increased activity of lactate dehydrogenase isoenzyme 5 (LDH5). These results indicate disorder of the following organ:

A. Liver
B. Kidneys
C. Heart
D. Lungs
E. Spleen

27. A 46-year-old woman suffering from cholelithiasis developed jaundice. Her urine became dark yellow, while feces are lightcolored. What substance will be the most increased in concentration in the blood serum in this case?

A. Conjugated bilirubin
B. Unconjugated bilirubin
C. Biliverdine
D. Mesobilirubin
E. Urobilinogen

28. An unconscious patient was delivered by ambulance to the hospital. On objective examination the patient was found to have no reflexes, periodical convulsions, irregular breathing. After laboratory examination the patient was diagnosed with hepatic coma. Disorders of the central nervous system develop due to the accumulation of the following metabolite:

A. Ammonia
B. Urea
C. Glutamine
D. Bilirubin
E. Histamine

29**.** A patient has been admitted to the contagious isolation ward with signs of jaundice caused by hepatitis virus. Which of the symptoms given below is strictly specific for hepatocellular jaundice?

A. Increase of ALT, AST level
B. Hyperbilirubinemia
C. Bilirubinuria
D. Cholemia
E. Urobilinuria

30. A patient presents with acute attack of cholelithiasis. Laboratory examination of the patient’s feces will show the following in this case:

A. Negative reaction to stercobilin
B. Positive reaction to stercobilin
C. Connective tissue
D. Partially digested cellulose
E. Starch granules

31. Encephalopathy has developed in a child with hemolytic disease of the newborn. What substance had increased in the child’s blood, resulting in damage to the CNS?

A. Unconjugated bilirubin
B. Bilirubin-albumin complex
C. Bilirubin glucuronide
D. Verdohemoglobin
E. Bile acids

32. A patient has normally colored stool including a large amount of free fatty acids. The reason for this is a disturbance of the following process:
A. Fat absorption
B. Fat hydrolysis
C. Biliary excretion
D. Choleresis
E. Lipase secretion

33. Due to the blockage of the common bile duct (which was radiographically confirmed), the biliary flow to the duodenum was stopped. We should expect the impairment of:
A. Fatt emulsification
B. Protein absorption
C. Carbohydrate hydrolysis
D. Secretion of hydrochloric acid
E. Salivation inhibition

34. Feces of a patient contain high amount of undissociated fats and have grayish-white color.Specify the cause of this phenomenon:
A. Obturation of bile duct
B. Hypoactivation of pepsin by hydrochloric acid
C. Hypovitaminosis
D. Enteritis
E. Irritation of intestinal epithelium

Tests and Tasks For Self-Control

1.A patient complaining of yellowing of the scleras and skin, darkening of the urine and feces consulted a doctor. Analysis of blood: erythrocytes — 2.5 • 1012/1, hemoglobin - 80 g/1, color index - 0.9, a lot of reticulocytes. What form of jaundice has developed?
A. Mechanical.
B. Parenchymatous.
C. Nuclear.
D. Hemolytic.
E. Shunt.

2. In a hepatocirrhosis patient ascites, splenomegaly, dilatation of the subcutaneous veins of the anterior abdominal wall, and peripheral edemas are found. What pathological syndrome has developed?
A. Hepatocerebral.
B. Arterial hypertension.
C. Hepatocardiac.
D. Hepatorenal.
E. Portal hypertension.

3. A 35-year-old patient developed immune hemolytic anemia. The level of what substance increases in the blood serum most of all?
A. Stercobilirubin.
B. Stercobilinogen.
C. Direct bilirubin.
D. Indirect bilirubin.
E. Protoporphyrin.

4. A 55-year-old woman complains of tiredness, irritability, sleeplessness at night and sleepiness during daytime, skin itch. Pulse - 58, arterial pressure — 110/65 mmHg. The excrements are colorless and contain a lot of fat. The initial diagnosis is cholelithiasis with occlusion of the common bile duct with a stone. What is the cause of nervous symptoms?
A. Lipid absorption disorder.
B. Hyperbilirubinemia.
C. Hypercholesterinemia.
D. Disorder of fat-soluble vitamin

absorption.
E. Cholemia.

5. A woman with chronic hepatitis complains of sensitivity to barbiturates, which she used to tolerate without signs of intoxication. What function of the liver is damaged?
A. Excretory.
B. Antitoxic.
C. Hemodynamic.
D. Hemopoietic.
E. Digestive.

6. An ultrasound examination of a patient allowed establishing an initial diagnosis: cancer of the liver. What protein is found in the blood in this case?
A. y-Globulin.
B. Properdin.
C. Paraprotein.
D. C-reactive protein.
E. a-Fetoprotein.

7. A 58-year-old patient had hepatitis B. Later he developed signs of hepatocirrhosis with ascites and edema of the inferior extremities. What changes of blood composition led to edema development?
A. Hypoalbuminemia.
B. Hypogammaglobulinemia.
C. Hypocholesterinemia.
D. Hypokalemia.
E. Hypoglycemia.

8. In a patient, poisoning with mushrooms was followed by the development of yellow coloration of the skin and scleras, the urine became dark. What pigment colors the urine of the patient with hemolytic jaundice?
A. Free bilirubin.
B. Direct bilirubin.
C. Indirect bilirubin.
D. Stercobilin.
E. Hemoglobin.

Recommended literature:

Basic

1. Simeonova N.K. Pathophysiology/ N.Simeonova.// Kyiv, Ukraine. – 2010. – 430-454 pp.
2. Victor N. Jelski, Svetlana V. Kolesnikova. Handbook Of Pathophysiology Part 2: Pathophysiology of organs and systems. - Donetsk, Ukraine. – 2011. – 96-108 pp.
3. Krishtal N.V. Pathophysiology: textbook/ N.Krishtal et al.// Kyiv: AUS Medicine Publishing, 2017. – 490-507 pp.

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4. Porth, Carol. Essentials of pathophysiology: concepts of altered health states /Carol Mattson Porth ; consultants, Kathryn J. Gaspard, Kim A. Noble. —3rd ed. 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins. – 2011. – 1282 p.
5. Robbins Pathology basis of disease / Cotran R.S., Kumar V., Robbins S.L. - 2000

Methodological instruction to practical lesson № 30
Module 2. Pathophysiology of organs and systems

Theme: PATHOPHYSIOLOGY OF KIDNEYS. BASICS OF INTERPRETATION OF URINE ANALIZES. RENAL FAILURE

Student should know:

- Reasons and mechanisms of development of chronic kidney failure (CKF).
- Reactive changes of blood flow in kidneys at their impairment.

Student should be able to:

- Explain the metabolic disorders (metabolism of sodium and water, metabolism of potassium, acid-basic state, mineral metabolism, metabolism of xenobiotics/medications) and changes of endocrine function of kidneys at CKF.
- Estimate role of retentional nitrogenemia and other metabolic disorders in development of poliorganic insufficiency.
- Explain general principles of prophylaxis and treatment of acute and chronic renal failure.

LIST OF CONTROL QUESTIONS

1. A concept about renal failure, principles of classification. Prerenal, renal and postrenal mechanisms of disorders of kidney processes. Reasons and mechanisms of disorders of circulation of blood in kidneys.
2. Functional, physical and chemical bases of disorders of glomerular filtration. Reasons and mechanisms of disorders of canalicular reabsorbtion and secretion. Inherited tubulopathies. Basic indexes of kidney function. The use of functional tests for estimation of disorder type of kidney functions.
3. General signs of insufficiency of kidney functions. Reasons, signs and mechanisms of development of retentional nitrogenemia. Pathogenesis of kidneys edemas. Disorder of the acid-basic state: kidney nitrogenemic acidosis, proximal and distal canalicular acidosis. Pathogenesis and signs of kidney osteodystrophy.
4. Mechanisms of development of arterial hypertension, anaemia, disorders of hemostasis at kidney diseases.
5. Glomerulonephritis: determinatin of concept, principles of classification. Experimental models, etiology and pathogenesis of diffuse glomerulonephritis. Nephritic syndrome, primary and secondary. Reasons and mechanisms of formation of kidney stones, urolithiasis. Pielonephritis.
6. Quantitative and qualitative changes of composition of urine. Oliguria, anuria and poliuria. Water, osmotic and hypertensive diuresis. Hypo- and isosthenuria. Pathological components of urine: proteinuria, cylindruria, glucosuria, aminoaciduria, hematuria, leucocyteuria. A concept of selective and nonselective proteinuria and their mechanisms.

7. Syndromes of acute and chronic renal failure: criteria, reasons and mechanisms of development, clinical signs. Pathogenesis of uremic coma. Principles of therapy of kidney insufficiency. Concept about extracorporal and peritoneal hemodialisis, lymphodialisis, lymphosorbtion.

The kidney is a compound parenchymatous organ with numerous functions. It consists of nephrons (glomeruli, tubules) and interstitium. Each part has its own functions. There are diuretic and non-diuretic functions.

Excretory function is performed by nephrons. It is urine formation and elimination. The kidneys deal with the constancy of the volume of water and fluid (isovolemia), electrolytes (isoionia), osmotic concentration (isotonia), acid-base balance (isohydria). The kidneys excrete the end products of nitrogen metabolism (urea, uric acid, ammonia, creatinine) and amino acids. Under pathological conditions the kidneys excrete foreign and toxic substances.

Incretory function of the kidneys consists in production of the substances, which are increted directly into the blood, but not into the urine. They are renin, prostaglandins, and erythropoietin. The juxtaglomerular apparatus can be considered a small endocrine organ.

Hemodynamic function is participation of the kidneys in the regulation of arterial blood pressure and circulating blood volume.

Hemopoietic (erythropoietic) function of the kidneys consists in the formation of the stimulator (erythropoietin) and supposed inhibitor of erythropoiesis.

Hemostatic function is influence on blood coagulation, anticoagulation and fibrinolysis.

Three physiological processes are accomplished in the kidney parenchyma to form the urine: filtration, reabsorption and secretion.

Renal insufficiency is a group of syndromes of homeostasis disorder caused by renal function failure.

Etiological classification divides renal pathology into ***acquired and hereditary*** as well as infectious and noninfectious.

In clinical practice it is subdivided into ***traumatic, nephrotoxic, metabolic, immunological, and vascular (ischemic).***

Topographic classification divides it into ***prerenal, renal and postrenal***. This classification is built on the assumption that the initial reason for kidney pathology is localized. Division into ***glomerular, tubular and tubulointerstitial*** types is based on the morphological principle.

Pathogenetic classification divides renal pathology into ***primary*** (pathology begins in the kidney) ***and secondary*** (the kidney is involved in systemic disordes of the organism or as a complication of another disease) as well as ***total and partial*** (all or single renal functions are impaired).The latter in its turn is subdivided into ***filtrative, reabsorbtive, secretory and incretory***.

Clinical classification divides the pathology into ***acute and chronic***.

Etiological factors, which cause renal pathology, are divided into exogenous and endogenous, physical, chemical and biological as well as acquired and hereditary.

In addition to the mentioned classification of etiological factors, the following

division of initial causes into prerenal, renal and postrenal is useful for clinical practice.

Prerenal factors are those, which secondarily involve the kidneys into the following pathology:

• Systemic disorders of blood circulation resulting in a decrease of systemic blood pressure and circulating blood volume (blood loss, shock, collapse, acute cardiac insufficiency).

• Dehydratation of the organism and hemoconcentration (uncontrollable vomiting, profuse diarrhea).

• Increase of systemic blood pressure (arterial hypertension).

• Acute systemic intoxication (in massive crush of tissues including burns).

• Massive hemolysis (mismatched hemotransfusion).

Renal factors are those, which directly influence the kidneys — toxic (intoxication with nephritogenic poisons), bacterial, viral, immune, vascular (local disorders of blood supply).

Postrenal factors are connected with obstruction of the urinary tracts (calculi, tumors) and urine retention.

Conditions, which aggravate the action of etiological factors and predispose to renal pathology, are the following:

a) accessibility of the kidneys as organs of excretion to damaging factors;

b) infection entry into the kidneys not only by the hematogenic route but also by spreading upwards from the urinary tract.

The daily amount of urine is called diuresis, which is equal to the difference between the amount of fluid filtered in the glomeruli and its amount reabsorbed in the tubules. So, a change of diuresis may result from dysfunction of the glomeruli and tubules.

Polyuria is an increase in the total quantity of urine to more than 2 1.

Oliguria is diuresis decrease to less than 500 ml.

Anuria is the absence of urine excretion or diuresis decrease to less than 100 ml/day.

Specific gravity of the urine is characterized by the following terms. ***Hyposthenuria*** is a decrease of urine specific gravity to less than 1010 (to 1002). This specific gravity of the urine confirms the fact that the kidneys are capable of diluting the primary urine. Edema development is not typical of such patients. However, as to the ability to concentrate the urine, it is decreased. Consequently, uremia development is possible. ***Hypersthenuria*** is an increase in the specific gravity of the urine to more than 1010 (to 1040). This specific gravity of the urine confirms the fact that the kidneys are capable of concentrating the primary urine. Uremia development is not typical of such patients. However, the ability to dilute the primary urine is reduced. Consequently, the development of systemic edema is possible**.** ***Isosthenuria*** is a monotonic specific gravity with a constant index 1010. This specific gravity of the urine confirms the fact that the kidneys are not capable of neither concentrating nor diluting the primary urine. Consequently, the development of edema and uremia is possible.

Pathological admixtures of the urine is the presence of substances or cells, which are not typical of the standard urine composition.They are the following.

Proteinuria is the presence of protein in the urine. It is divided into true (proteins excreted into the urine by the kidneys) and false (proteins are not excreted by the kidneys but are admixed to the urine in inflammation of the urinary tracts), functional (transitory, which disappeares after elimination of the cause) and organic (in organic lesion of the kidneys — inflammation, nephrotic syndrome), extrarenal and renal. Renal (true) proteinuria is organic (acute and chronic glomerulonephritis, nephrotic syndrome, etc.) and is subdivided into glomerular and tubular, which have been described above. The gomerular one is a cardinal sign of an increased permeability of the glomerular filter for proteins due to physical and chemical changes in the basement membrane. Tubular proteinuria is connected with disorders of protein reabsorption from the primary urine as well as entry of protein molecules into the urine from destroyed tubular cells. Organic proteinuria is characterized by stableness, a large amount of protein in the urine — from 10—15 up to 120 g/1, the presence of fractions of high-molecular-weight plasma proteins. Functional proteinuria (false) is nonstable, inconsiderable, not more than 1 g/1 and disappears after causative factor elimination.

Glucosuria is the presence of glucose in the urine. It is the main symptom of DM.

Hematuria is the presence of erythrocytes in the final urine and is determined as cellular pathologic admixtures by microscopic examination of the urinary sediment. It is subdivided into renal and extrarenal. Renal hematuria, which is caused by increased permeability of the glomerular filter for blood cells, has been described above. Extrarenal hematuria is caused by traumas or inflammation of the urinary bladder or ureter (if there are stones). It is important to differentiate them in clinical practice. In the latter case there is a large amount of fresh erythrocytes in the urine. In renal hematuria shadows of erythrocytes are found in the urine (lixiviated erythrocytes).

Leukocyturia is the presence of leukocytes in the final urine. It may be of glomerular, tubular and exrtarenal origin. As a rule, it testifies to inflammation.

Urine acidity reflects disorders of the acid-base balance. Systemic acidosis is associated with an increased content of ammonium salts in the urine.

Salts (urates, phosphates, oxalates) are present in the final urine in systemic disorders of mineral balance in the organism.

Bacteria appear in the final urine in case of inflammation of the kidneys or urinary tract.

Glomerulonephritis is a bilateral diffusive infectious-allergic kidney disease of inflammatory origin with prevailing damage of the glomeruli. It may be primary and secondary (as a complication of other diseases, more often of diffuse lesions of the connective tissue), as well as acute and chronic.

Chronic glomerulonephritis is a prolonged progressive disease characterized by diffuse bilateral injury of the kidneys of inflammatory nature, heterogeneous by origin, pathogenesis and clinical manifestations.

Pyelonephritis is an infectious inflammatory disease of the mucous membrane of the urinary tract and renal parenchyma (simultaneous or subsequent) with predominant affection of the interstitial tissue.

Uremia is the end stage of chronic renal insuffitiency. It is characterized by dismetabolism and involvement of all physiological systems with grave disorders.
It is complete impairment of the excretory renal function and regulation of homeostasis with the following systemic changes:
• Intoxication is connected with retention in the blood of the substances, which must be excreted in the urine — urea and creatinine (azotemia), phenols, indoles, amino acids. Furthermore, many new toxic substances are formed — over 200 toxic substances are revealed. It is these substances that determine organism intoxication and associated clinical symptoms.
• Electrolyte disorders in the blood — decreased amount of Ca2+, increased amount of phosphorus, porassium.
• Acidosis. Uremia is not merely biochemical abnormalities mentioned above. There are a lot of external clinical manifestations. It is serious disorders of all functions.
Development of the following clinical syndromes is necessary for the diagnosis of uremia:
• Hemorhage syndrome (predisposition to bleeding, disorders of thrombocyte aggregation).
• Anemia (as a result of blood loss, uremic hemolysis, suppression of hemopoiesis due to bone marrow intoxication).
• Gastrointestinal syndrome (dyspeptic signs) — anorexia (loss of appetite), disorders of taste, vomiting, diarrhea, esophagitis, gastritis, colitis).
• Cardiovascular syndrome (uremic myocarditis and pericarditis, arterial hypertension).
• Neuromuscular syndrome (spasms, paresis, convulsions).
• Respiratory insufficiency (pulmonary congestion, dyspnea, uremic pleuritis, Kussmaul breathing).
• Peripheral neuropathy (tormenting itching).
• Encephalopathy (general weakness, apathy, headache, hearing disorders, coma).
• Endocrine disorders (connected with general intoxication).
• Body weight reduction.
• Arthritis. Uremic patients must be dialyzed.

Krok 1 mcqs_A is correct answer:

1. Shock and signs of acute renal failure (ARF) developed in the patient due to permanent injury. What is the leading cause of development of ARF in the case?
A Decreased arterial pressure
B Urine excretion violation
C Increased pressure in the nephron capsule
D Increasepressure in the renal arteries
E Decreased oncotic BP

2. Chronic glomerulonephritis was diagnosed in a 34-year-old patient 3 years ago. Edema has developed in the last 6 months. What caused it?
A Proteinuria
B Hyperproduction of vasopressin
C Disorder of albuminous kidneys function
D Hyperosmolarity of plasma
E Hyperaldosteronism

3. Two weeks after lacunar tonsillitis a

20-year-old man started complaining about general weakness, lower eyelid edemata. After examination the patient was diagnosed with acute glomerulonephritis. What are the most likely pathological changes in the urine formula?
A Proteinuri
B Cylindruria
C Presence of fresh erythrocytes
D Pyuria
E Natriuria
4. Violation of safety rules resulted in calomel intoxication. Two days later the daily diuresis was ml. A patient experienced headache, vomiting, convulsions, dyspnea, moist rales in lungs. What pathology is it?
A Acute renal insufficiency
B Chronic renal insufficiency
C Uraemicoma
D Glomerulonephritis
E Pyelonephritis
5. A 50-year-old patient complains of thirst, drinking of a lot of water, marked polyuria. Blood glucose is 4,8 mmol/L, urine glucose and acetone bodies are absent, urine is colorless, specific gravity is 1,002-1,004. What is the cause of polyuria?
A Vasopressin insufficiency
B Hypothyroidism
C Insulin insufficiency
D Aldosteronism
E Thyrotoxicosis
6. On the 6th day of treatment a patient with acute renal insufficiency developed polyuria. Diuresis intensification at the beginning of polyuria stage of acute renal insufficiency is caused by:
A Renewal of filtration in nephrons
B Volume expansion of circulating blood
C Growth of natriuretic factor
D Reduction of aldosteron content in plasma
E Reduction of vasopressin content in plasma
7. A 30 year old woman has face edemata. Examination revealed proteinuria (5,87 g/l), hypoproteinemia, dysproteinemia, hyperlipidemia. What condition is the set of these symptoms typical for?
A Nephrotic syndrome
B Nephritic syndrome
C Chronipyelonephritis
D Acute renal failure
E Chronic renal failure
8. The low specific gravity of thesecondary urine (1002) was found out inthe sick person. Wat is the most distantpart of nephron where concentration ofsecondary urine takes place?
A In the collecting duck
B In the nephron's glomerulus
C In proximal tubule of nephron
D In ascending part of loop of Henle
E In distal tubule of nephron
9. Periodic renal colics attacks are observed in a woman with primary hyperparathyroidizm. Ultrasonic examination revealed small stones in the kidneys. What is the most plausible reason of the stones's formation?
A Hypercalcemia
B Hyperphosphatemia
C Hypercholesterinemia
D Hyperuricemia
E Hyperkalemia
10. A man after 1,5 litr blood loss has suddenly reduced diuresis. The increased secretion of what hormone caused such diuresis alteration?
A Vasopressin
B Corticotropin
C Natriuretic
D Cortisol

E Parathormone

11. A 58-year-old patient with acute cardiac insufficiency has decreased volume of daily urine - oliguria. What is the mechanism of this phenomenon?

A Decreased glomerular filtration

B Decreased number of functioning glomerules

C Drop of oncotic blood pressure

D Rise of hydrostatic blood pressure in capillars

E Reduced permeability of renal filter

12.Violation of safety rules resulted in calomel intoxication. Two days later the daily diuresis was 620 ml. A patient experienced headache, vomiting, convulsions, dyspnea, moist rales in lungs. What pathology is it?

A Acute renal insufficiency

B Chronic renal insufficiency

C Uraemicoma

D Glomerulonephritis

E Pyelonephritis

13. On the 6th day of treatment a patient with acute renal insufficiency developed polyuria. Diuresis intensification at the beginning of polyuria stage of acute renal insufficiency is caused by:

A Renewal of filtration in nephrons

B Volume expansion of circulating blood

C Growth of natriuretic factor

D Reduction of aldosteron content in plasma

E Reduction of vasopressin content in plasma

14. A 30 year old woman has face edemata. Examination revealed proteinuria(5,87 g/l), hypoproteinemia, dysproteinemia, hyperlipidemia. What condition is the set of these symptoms typical for?

A Nephrotic syndrome

B Nephritic syndrome

C Chronic pyelonephritis

D Acute renal failure

E Chronic renal failure

15. A patient with nephrotic syndrome has massive edemata of his face and limbs. What is the leading pathogenetic mechanism of edemata development?

A Drop of oncotic blood pressure

B Increase of vascular permeability

C Rise of hydrodynamic blood pressure

D Lymphostasis

E Increase of lymph outflow

16. Due to the use of poor-quality measles vaccine for preventive vaccination, a 1-year-old child developed an autoimmune renal injury. The urine was found to contain macromolecular proteins. What process of urine formation was disturbed?

A Filtration

B Reabsorption

C Secretion

D Reabsorption ansecretion

E Secretion and filtration

17. Diabetic nephropathy with uremia has developed in a patient with pancreatic diabetes. The velocity of glomerular filtration is 9 ml/min. What mechanism of a decrease in glomerular filtration velocity and chronic renal failure development is most likely in the case of this patient?

A Reduction of active nephron mass

B Decrease in systemic arterial pressure

C Obstruction of nephron tubules with hyaline casts

D Tissue acidosis

E Arteriolar spasm

18. Due to the use of poor quality measles vaccine for preventive vaccination, a 1-year-old child has developed an autoimmune renal injury. The urine was found to contain macromolecular proteins. What process

of urine formation has been disturbed?
A Filtration
B Reabsorption
C Secretion
D Reabsorption ansecretion
E Secretion and filtration
19. Autopsy has revealed shrunken kidneys weighing 50 mg, with finegrained surface and uniformly thinned substance. Microscopic investigation has shown the thickening of arteriole walls due to accumulation of homogeneous anhistic pink-coloured masses in them. Glomerules were undersized, sclerotic, with atrophied tubules. What disease are these changes characteristic of?
A Essential hypertension
B Pyelonephritis with kidney shrinkage
C Renal amyloidosis
D Acute glomerulonephritis
E Membranous nephropathy
20. As a result of a road accident a driver has gotten a trauma. Now he is in shock condition and presents with a decrease in daily diuresis down to 300ml. What is the main pathogenetic factor of such alteration in the diuresis?
A Arterial pressure drop
B Oncotic blood pressure drop
C Increase in vascular permeability
D Secondary hyperaldosteronism
E Decrease in number of the functioning glomerules
21. A patient has a decreased vasopressin synthesis that causes polyuria and as a result of it evident organism dehydratation. What is the mechanism of polyuria development?
A Reduced tubular reabsorption of water
B Reduced tubular reabsorption of Na ions
C Reduced tubular reabsorption of protein
D Reduceglucose reabsorption
E Acceleration of glomerular filtration
22. A patient is 44 years old. Laboratory examination of his blood revealed that content of proteins in plasma was 40 g/l. What influence will be exerted on the transcapillary water metabolism?
A Filtration will be increased, reabsorption - decreased
B Both filtration and reabsorption will be increased
C Both filtration and reabsorption will be decreased
D Filtration will be decreased, reabsorption - increased
E Metabolism will stay unchanged
23. A patient with a history of chronic glomerulonephritis presents with azotemia, oliguria, hypo- and isosthenuria, proteinuria. What is the leading factor in the pathogenesis of these symptoms development under chronic renal failure?
A Mass decrease of active nephrons
B Intensification of glomerular filtration
C Tubular hyposecretion
D Disturbe permeability of glomerular membranes
E Intensification of sodium reabsorption
24. Poisoning caused by mercury (II) chloride (corrosive sublimate) occurred in the result of safety rules violation. In 2 days the patient's diurnal diuresis became 620 ml. The patient developed headache, vomiting, convulsions, dyspnea; moist crackles are observed in the lungs. Name this pathology:
A. Acute renal failure
B. Chronic renal failure
C. Uremic coma
D. Glomerulonephritis
E. Pyelonephritis

25. According to the results of glucose tolerance test a patient has no disorder of carbohydrate tolerance. Despite that glucose is detected in the patients's urine (5 mmol/l). The patient has been diagnosed with renal diabetes. What renal changes cause glucosuria in this case?
A. Decreased activity of glucose reabsorption enzymes
B. Increased activity of glucose reabsorption enzymes
C. Exceeded glucose reabsorption threshold
D. Increased glucose secretion
E. Increased glucose filtration
26. Urine analysis has shown high levels of protein and erythrocytes in urine. This can be caused by the following:
A. Renal filter permeability
B. Effective filter pressure
C. Hydrostatic blood pressure in glomerular capillaries
D. Hydrostatic primary urine pressure in capsule
E. Oncotic pressure of blood plasma
27. Poisoning caused by mercury (II) chloride (corrosive sublimate) occurred in the result of safety rules violation. In 2 days the patient's diurnal diuresis became 620 ml. The patient developed headache, vomiting, convulsions, dyspnea; moist crackles are observed in the lungs. Name this pathology:
A. Acute renal failure
B. Chronic renal failure
C. Uremic coma
D. Glomerulonephritis
E. Pyelonephritis
28. A 38-year-old man, who has been suffering from systemic lupus erythematosus for 3 years, developed diffuse renal lesions accompanied by massive edemas, marked proteinuria, hyperlipidemia, and dysproteinemia. What is the most likely mechanism of proteinuria develoment in this case?
A. Autoimmune damage to the nephrons
B. Inflammatory damage to the nephrons
C. Ischemic damage to the tubules
D. Increased blood proteins
E. Morbid affection of the urinary tracts
29. A 50-year-old inpatient during examination presents with glucosuria and blood glucose of 3,0 mmol/l, which are the most likely to be caused by:
A. Renal disorder
B. Diabetes insipidus
C. Myxedema
D. Essential hypertension
E. Pellagra
30. A 38-year-old man, who has been suffering from systemic lupus erythematosus for 3 years, developed diffuse renal lesions accompanied by massive edemas, marked proteinuria, hyperlipidemia, and dysproteinemia. What is the most likely mechanism of proteinuria develoment in this case?
A. Autoimmune damage to the nephrons
B. Inflammatory damage to the nephrons
C. Ischemic damage to the tubules
D. Increased blood proteins
E. Morbid affection of the urinary tracts
31. A 30-year-old woman developed facial edemas. Examination detected proteinuria (5.87 g/L), hypoproteinemia, dysproteinemia, and hyperlipidemia. Such combination of signs is characteristic of:
A. Nephrotic syndrome
B. Nephritic syndrome

C. Chronic pyelonephritis
D. Acute kidney failure
E. Chronic kidney failure

Tests fo Self-Control (give correct answers)

1. A 35-year-old patient complains of pain in the lumbar region, baggy lower eyelids, sickness. Erythrocytes and proteins were found in the urine of the patient. Arterial pressure - 160/110 mmHg. What pathology can be most probably suspected in this case?
A. Urethritis.
B. Pyelitis.
C. Cystitis.
D. Glomerulonephritis.
E. Pyelonephritis.
2. A nephrocytotoxic serum was injected to a rabbit. What pathology of the kidneys has been modeled in this experiment?
A. Acute diffuse glomerulonephritis.
B. Nephrotic syndrome.
C. Acute pyelonephritis.
D. Chronic renal failure.
E. Chronic pyelonephritis.
3. Mercury dichloride solution in the dose of 5 mg per 1 kg was injected subcutaneously to a white rat. In 24 h the concentration of creatinine in the blood plasma increased by several times. What is the mechanism of retentional azotemia in this case?
A. Increased glomerular filtration.
B. Increased formation of creatinine in the muscles.
C. Increased reabsorption of creatinine.
D. Decreased glomerular filtration.
E. Increased secretion of creatinine in the renal tubules.
4. Inspection of a patient showed that the clearance of endogenous creatinine makes 50 ml/min (normal — 110—150 ml/min). To a decrease of what function does it testify?
A. Ions excretion from the organism.
B. Tubular reabsorption.
C. Incretory function of the kidneys.
D. Glomerular filtration.
E. Tubular secretion.
5. During 17 years a man was ill with chronic glomerulonephritis. Pulse — 82, arterial pressure - 190/120 mmHg. What is the initial mechanism of arterial pressure rise?
A. Increased minute volume of the blood.
B. Decreased circulating blood volume.
C. Increased tone of the venous vessels.
D. Increased systolic blood output.
E. Increased peripheral resistance.
6. A 32-year-old man has been ill with chronic glomerulonephritis for 4 years. Inspection showed edemas on the face, legs and trunk, a high level of proteinuria. What is the mechanism of edemas?
A. Decreased oncotic pressure of the blood.
B. Increased hydrostatic pressure of the blood in the capillaries.
C. Increased oncotic pressure of the intracellular lymph.
D. Lymphatic drainage impairment.
E. Increased permeability of the capillaries.
7. A patient with a hemorrhage into the supraoptic region and periventricular nucleus of the hypothalamus suffers from polyuria. The level of vasopressin in the blood decreased. What is the main mechanism of polyuria development in this case?

A. Decreased reabsorbtion of sodium in the tubules.
B. Increased filtration of water in glomeruli.
C. Increased reabsorption of sodium in the tubules.
D. Decreased reabsorption of water in the tubules.
E. Increased excretion of potassium.

8. A patient has a diagnosis of initial nephrotic syndrome. The level of blood protein makes 40 g/1. What is the cause of hypoproteinemia in this case?
A. Decreased synthesis of protein in the liver.
B. Exudation of protein from vessels into tissues.
C. Proteinuria.
D. Increased proteolysis.
E. Decreased assimilation of protein from the intestine.

9. A patient has chronic glomerulonephritis. Glomerular
D. Increased glomerular filtration
filtration reduced to 20 %. What is the cause of decreased glomerular filtration in chronic renal failure?
A. Obstruction of the urinary tracts.
B. Tubulopathy.
C. Decreased amount of nephrons.
D. Ischemia of the kidneys.
E. Thrombosis of the renal arteries.

10. A 30-year-old patient was hospitalized with a diagnosis of acute glomerulonephritis. Proteinuria is observed. What is the mechanism of its origin?
A. Decreased oncotic pressure of the blood.
B. Delayed excretion of the products of nitrogen metabolism.
C. Increased permeability of the glomerular membrane.
D. Increased hydrostatic pressure in the capillaries.
E. Decreased amount of the functioning nephrons.

Recommended literature:

Basic

1. Simeonova N.K. Pathophysiology/ N.Simeonova.// Kyiv, Ukraine. – 2010. – 459-480 pp.
2. Victor N. Jelski, Svetlana V. Kolesnikova. Handbook Of Pathophysiology Part 2: Pathophysiology of organs and systems. - Donetsk, Ukraine. – 2011. – 109-123 pp.
3. Krishtal N.V. Pathophysiology: textbook/ N.Krishtal et al.// Kyiv: AUS Medicine Publishing, 2017. – 508-526 pp.

Additional

4. Porth, Carol. Essentials of pathophysiology: concepts of altered health states /Carol Mattson Porth ; consultants, Kathryn J. Gaspard, Kim A. Noble. —3rd ed. 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins. – 2011. – 1282 p.
5. Robbins Pathology basis of disease / Cotran R.S., Kumar V., Robbins S.L. - 2000.

Methodological instruction to practical lesson № 31
Module 2. Pathophysiology of organs and systems

Theme: PATHOPHYSIOLOGY OF THE ENDOCRINE SYSTEM. GENERAL CHARACTERISTIC OF DISORDERS OF ACTIVITY OF THE ENDOCRINE SYSTEM. PATHOLOGY OF THE HYPOTHALAMO-PITUITARY SYSTEM

Student should know:

- Reasons and general mechanisms of development of primary and secondary endocrinopathies.
- Neuroendocrinic pathology according to the reasons and mechanisms of its development.
- A concept "goiter", to analyze the types of goiter according to etiology, pathogenesis and functional state of thyroid gland.
- Reasons and typical disorders in an organism at hyper- and hypofunction of parathyroid glands.

Student should be able to:

- Analyze the consequences of disorders of secretion of hormones by adenohypophysis.
- Analyze the consequences of disorders of secretion of hormones by neurohypophysis.

LIST OF CONTROL QUESTIONS

1. General characteristic of disorders of activity of the endocrine system: hypofunction, hyperfunction, dysfunction of glands; primary, secondary endocrinopathies. Reasons of origin and mechanisms of development of endocrinopathies. Dysregulatory endocrinopathies: disorder of nervous, neuroendocrine, endocrine and metabolic regulation of glands functions. Disorders of direct and feed-back regulatory ties.
2. Glandular endocrinopathies: reasons and mechanisms of disorders of synthesis, depositing and secretion of hormones.
3. Peripheral disorders of endocrine function. Disorder of transport and metabolic inactivation of hormones. Disorders of reception of hormones, mechanisms of desensitization and hormonal resistance (prereceptor, receptor, postreceptor).
4. Pathology of the hypothalamo-pituitary system. Reasons of origin and mechanisms of development of syndromes caused by surplus or lack of pituitary hormones. General characteristic of disorders of activity of hypothalamo-pituitary-thyroid, hypothalamo-pituitary-adrenal, hypothalamo-pituitary-gonade systems.
5. Etiology, pathogenesis, clinical signs of panhypopituitarism. Reasons, mechanisms, clinical signs of partial insufficiency of hormones of adenohypophysis (STH, TTH, ACTH, gonadotropines). Etiology,

pathogenesis, clinical signs of the states of partial hyperfunction of adenohypophysis (STH, TTH, ACTH, gonadotropines, prolactine).

6. Pathophysiology of neurohypophysis. Diabetes insipidus: reasons and mechanisms of development, clinical signs.
7. Pathology of thyroid gland. Hypothyroidism: reasons and mechanisms of development, pathogenesis of basic disorders in an organism. Hyperthyroidism: reasons and mechanisms of development, pathogenesis of basic disorders in an organism. Goiter: types (endemic, sporadic, nodal and diffuse toxic), their etiology and pathogenesis; characteristic of disorders of the functional state of gland.
8. Disorder of function of parathyroid glands: types, reasons, mechanisms of development, clinical and pathophysiological signs.

The endocrine system presents an important communicative system that is responsible for regulation, integration, and coordination of a variety of physiological process, including growth, sex differentiation, metabolism, and adaptation to an ever-changing environment. The endocrine glands secrete their products, which are biologically active molecules called *hormones*, into the blood. The blood carries hormones to target cells that contain specific *receptor proteins* for the hormones and which can respond in a specific fashion to them.

Along with hormones other types or chemical messenger systems interact with one other to maintain homeostasis. They include:

1) Neurotransmitters, which are released by axon terminals of neurons into the synaptic junctions (e.g., acetylcholine, norepinephrine).

2) Cytokines, which are secreted by cells into the extracellular fluid (e.g., interleukins).

3) Eicosanoids, which are derived from arachidonic acid (prostaglandins and leukotriens).

4) ―Second messengers‖ (e.g., cAMP, cGMP, Ca2 + ions), which act inside the cell helping some hormones and neurotransmitters to exert their effects.

Disturbances of endocrine function

Disturbances of endocrine function can be divided into two categories: *hyperfunction and hypofunction.* Both hyper- and hypofunction of the endocrine gland can be *primary, secondary and tertiary.*

Primary defects in endocrine function originate in the target gland (e. g., primary deficiency of corticosteroid hormones caused by adrenalectomy).

In secondary disorders of endocrine function the target gland is essentially normal but its function is altered by a defective level of stimulating hormones from the anterior pituitary (e.g., a decrease in production of corticosteroids by the adrenal cortex caused by removal or destruction of the pituitary gland).

Tertiary disorders result from hypothalamic dysfunction when both the pituitary and target organ are under- or hyperstimulated.

Feedback control of hormone secretion. The activity of the most of endocrine glands is regulated by feedback mechanisms that involve the hypothalamic-pituitary-target cell system and ensure a proper level of hormone activity at the target tissue. The example is the hypothalamic-pituitary-thyroid axis. In this system, sensors defect a change in the hormone level and adjust hormone secretion so that body levels are maintained within an appropriate range. As an example, an increase in thyroid hormone is detected by sensors in the hypothalamus, and this causes a reduction in the hypothalamic secretion of thyrotropinreleasing hormone (TRH), with a subsequent decrease in the secretion of thyroid-stimulating hormone (TSH) by the anterior pituitary and resultant decrease in the output of thyroid hormone from the thyroid gland.

Disorders of negative feedback mechanism in the hypothalamic-pituitarytarget gland systems play an important role in the development of endocrine pathology. For example, a deficiency of iodine in a drinking water or food leads to a decreased synthesis of thyroid hormone. According to a principle of the negative feedback mechanism it results in an increase in TRH and TSH secretion. Hyperproduction of TSH in turn causes hyperplasia of the thyroid gland, the so-called struma. The other example is that, the administration of corticosteroid hormones causes suppression of the hypothalamic-pituitary-adrenal cortex axis resulting in a decreased production of own corticosteroids by the adreal cortex. In a case when a treatment with corticosteroid drug is stopped suddenly, the syndrome of abolition may occur. This is manifested by symptoms of acute adrenal failure.

Transport of hormones. Hormones that are released into the bloodstream circulate either free, unbound or attached to transport carriers. Peptide hormones and protein hormones usually circulate unbound in the blood. Steroid hormones and thyroid hormones are carried by specific carrier proteins synthesized in the liver. It is important, that *only free forms of hormones are biologically active.* Disturbances of a transport of hormones may manifest themselves by two types of disorders of endocrine function:

1) An increase in binding of a hormone with transport carriers leads to a decrease in an amount of the active unbound hormone and as a consequence to hypofunction of the given gland.

2) A decrease in binding of a hormone with transport carriers (e.g. in nephritic syndrome or cirrhosis that are associated with hypoproteinema) causes an increase in concentration of an active unbound form of hormone in the blood that, in its turn, leads to hyperfunction of the appropriate gland. Drugs that compete with a hormone for binding with transport carrier molecules increase hormone action by increasing the ability of the active unbound hormone. For example, aspirin competes with thyroid hormome for binding to transport proteins. When aspirin is administrated to persons with excessive levels of circulating thyroid hormone (such as thyroid crisis) serious effect may occur.

Metabolism and elimination In some cases, hormones are eliminated in the intact form. But the most of hormones must be inactivated to prevent their accumulation. Some hormones are enzimatically inactivated at receptor sites where they exert their action. Thus, catecholamines are degraded by monoamine oxydase (MAO) and

catechol-O-methyl transferase (COMT). Degradation of protein and peptide hormones occurs in the liver under action of enzymes peptidases. Adrenal and gonadal steroidal hormones like as thyroid hormone are inactivated in the liver by way of conjugation with glucuronic acids and then excreted in the bile or urine. In a human 65-95 % inactivated metabolites of all hormones excrete from the organism with urine.

Disturbances in metabolism of hormones may cause development of peripheral disorders of endocrine function. They are as follows:

1) Impairment of inactivation of hormones leads to an increase in amount of hormones in the blood that is accompanied by appropriate hyperfunction.

2) Increased transformation of hormones into their inactive forms accompanied with development of endocrine hypofunction (e.g., increased activity of insulinase, the enzyme that breaks down insulin, can cause diabetes mellitus 2 type).

Mechanisms of action Hormones produce their effects through interaction with high-affinity receptors located either or on the surface or inside the target cells. The function of these receptors is to recognize a specific hormone and translate the hormonal signal into a cellular response.

The response of a target cell to a hormone depends on

1) the number of receptors present and on

2) the affinity of these receptors for hormone binding.

There are approximately from 2000 to 100000 hormone receptors per cell. The number of hormone receptors on a cell may be altered for any of several reasons. They are as follows:

1) a destroy or block the receptor proteins by antibodies;

2) altered levels of hormone that influence the activity of the genes which are responcible for receptor synthesis. Decreased hormone levels produce an increase in receptor numbers; the process is called up-regulation. Excessive hormone levels produce a decrease in receptor numbers by down-regulation. The affinity of receptors for binding hormones is also affected by a number of conditions. For example, pH is a very important in the affinity of insulin receptors. In ketoacidosis insulin binding is decreased.

There are two types of hormone-receptor interactions:

1) surface receptor, and

2) intercellular receptor interactions.

Surface receptor interaction Peptide hormones and catecholamines interact with surface receptors. It is because they have low solubility in the lipid layer of cell membranes and cannot cross them. Interaction of these hormones with surface receptor leads to generation of an intercellular signal that is termed the second messenger, and the hormone is considered to be the first messenger. The second messenger activates enzymes or other proteins inside the cell and quick biochemical effects occur.

There are the following second messengers:

1) cyclic adenosine monophosphate (cAMP) that is the most widely distributed;

2) cyclic guanin monophosphate (cGMP)

Binding of hormones or neurotransmitters to surface receptors may also act directly

to open ion channels in the cell membrane, and often there are calcium channels. In this case influx of ions serves as an intracellular signal to convey the hormonal message to the cell interior. The increasing cytoplasmic concentration of calcium results in direct activation of calcium-dependent enzymes or calcium-calmodulin complexes with their attendant effects.

Intracellular receptor interaction Steroid and thyroid hormones act inside the cell. They are lipid soluble and pass freely throw the cell membrane. Then they are attached to intracellular receptors and form a hormone-receptor complex that travels to the cell nucleus. The hormone-messenger complex then activates or suppresses gene activity with a subsequent production or inhibition of protein synthesis.

The following proteins may be produced:

- enzymes;
- transport proteins;
- receptors;
- structural proteins.

Disturbances in interaction of hormones with peripheral target cells are mainly mediated by abnormalities of cell receptors. They are as follows:

1) a decrease in the amount of receptors or in the affinity of the receptors for hormone binding (i.e.,desensitization). In this case hypofunction of endocrine gland occurs despite the fact that the level of hormone in the blood is normal or even increased.

2) an increase in the number of receptors (i.e.,sensitization) is usually associated with development of endocrine hyperfunction.

Alterations in Pituitary function

Normal anatomy and function The pituitary gland is situated in the sella turcica, and it is divided into an anterior lobe (the adenohypophysis) and a posterior lobe (the neurohypophysis). Anterior pituitary and posterior pituitary are more or less separate endocrine organs. The adenohypophysis is embriologycally originated from glandular tissue, and it is connected with the hypothalamus by blood flow in the hypophyseal portal system. It represents approximately 90 % of the pituitary gland. Stimulated by hypothalamic hormones, the anterior pituitary produces tropic hormones that affect the endocrine target glands (thyroid, adrenal, and gonads), growth, and lactation. In addition, the anterior lobe of the pituitary secretes β-lipotropin (β-LPH) that affects lipid metabolism, and melanocytestimulating hormone (MSH) which controls skin coloration.

The synthesis and release of anterior pituitary hormones are largely regulated by the action of hormones from the hypothalamus which is the coordinating center of the brain for endocrine, behavioral, and autonomic nervous system function. The hypothalamus integrates incoming neural signals initiated from the body and the environment, and it secretes various releasing or inhibiting factors that evoke specific hormonal responses from the pituitary gland.

The most important hypothalamic hormones that regulate the secretion of anterior pituitary hormones include:

1. Thyrotropin-releasing hormone (TRH), which stimulates pituitary release of thyrotropin;
2. Corticotropin-releasing hormone (CRH), which stimulates pituitary release of adrenocorticotropin;
3. Prolactine-inhibiting factor (PIF), or dopamine, which signals the pituitary to halt the release of prolactine;
4. Growth-hormone-releasing hormone (GHRH), which stimulates pituitary release of growth hormone.

The neurohypophysis is embriologycally originated from neural tissue, and it is connected with the hypothalamus by the nerve axons from hypothalamic the supraoptic and paraventricular nuclei. In contrast to the hormone-producing anterior lobe, the posterior pituitary stores and releases two hypothalamic hormones, oxytocin, which stimulates uterine contractions and initiates lactation, and vasopressin (antidiuretic hormone (ADH)) which regulates the maintenance of serum osmolality. Both oxytocin and ADH are produced by neurons in the nuclei of the hypothalamus that have axons which terminate on the capillary network in the posterior lobe, where they discharge hormones into the systemic circulation.
Alteration in pituitary function can be divided into
1)hypofunction, or hypopituitarism and
2)hyperfunction, or hyperpituitarism.

Hypopituitarism Hypopituitarism is characterized by a decreased secretion of a single (partial hypopituitarism), several (subtotal hypopituitarism), or all (total hypopituitarism) pituitary hormones. The anterior pituitary has a large reserve. Typically, 70 % to 90 % of the adenohypophysis must be destroyed before hypopituitarism becomes clinically evident. The cause may be congenital or result from a variety of acquired abnormalities.
Hypopituitarism may result from: 1. Primary pituitary lesions including
 pituitary tumor, either a primary adenoma that compresses the rest of a normal gland or metastasis to the pituitary;
 pituitary infarction, especially in the peripartum period;
 pituitary radiation therapy or surgery;
 genetic diseases – rare congenital defects of one or more pituitary hormones;
2. Secondary defects:
 hypothalamic disorders – tumors and mass lesions (e.g., hypothalamic radiation, tumor, trauma, infections).

Total hypopituitarism Although isolated pituitary hormone deficiencies can occur, total hypopituitarism (panhypopituitarism) from a destructive pituitary lesion is more common. Because of decreases or depletion of pituitary tropic hormones and the resultant nonstimulation of target endocrine organs, affected patients show symptoms of hypothyroidism (cold intolerance, lethargy), hypogonadism (infertility), and hypoadrenalism (susceptibility to infection, stress intolerance). In children, dwarfism also results because of a lack of GH.
Examples of panpituitarism include:

1. Pituitary cachexia (Simmond‘s disease) that is characterized by a severe cachexia and atrophy of the thyroid, adrenal, and sexual glands;
2. Pituitary necrosis (Sheehan‘s syndrome) that result from infarction of the pituitary gland after substantial blood loss during childbirth.

Partial hypopituitarism Isolated pituitary tropin deficiencies occur rare, and they are often due to hypothalamic (secondary hypopituitarism) rather than pituitary (primary hypopituitarism) disorders. For example, an appreciable numbers of patients with partial TSH deficiency show an increase in TSH secretion when TRH is injected.
The most common clinical syndromes associated with hypoproduction of a single pituitary hormone include:
1. Pituitary dwarfism (nanism), which results from a decreased secretion of GH.
2. Pituitary hypogonadism, which occurs due to an impaired secretion of gonadotropic hormones.
3. Pituitary hypocorticism, which is due to a decreased production of ACTH resulting in secondary adrenal failure.
Growth hormone deficiency can be primary (e.g., due to a pituitary tumor or agenesis of the pituitary) or secondary (due to a lack of hypothalamic GHRH). In children, GH deficiency interferes with linear bone growth, resulting in short stature or dwarfism. In adults, GH deficiency leads to an increased cardiovascular mortality (endothelial dysfunction, atherosclerosis). The GH deficiency syndrome is associated with a cluster of cardiovascular risk factors, including central adiposity, increased visceral fat, insulin resistance, and dyslipidemia, the so-called metabolic syndrome (syndrome X).

Posterior pituitary hypofunction Deficiency of vasopressin secretion leads to diabetes insipidus, clinically manifested by the excretion of large volumes of dilute urine (polyuria). Pituitary causes of vasopressin deficiency include compression or destruction of the neurohypophysis by local tumors, radiation, cranial vascular lesions, trauma, or surgery.

Hyperpituitarism Hyperpituitarism is characterized by increased secretion of pituitary hormones. Anterior pituitary hyperfunction Intrinsic hypersecretion of an anterior pituitary tropic hormone almost always is the result of a neoplasm (usually an adenoma). Although functioning adenomas occasionally cause multihormone production, the three most common clinical syndromes are associated with overproduction of a single hormone (partial hyperpituitarism).
They include:
1. Growth hormone overproduction.
2. Hyperprolactinemia
3. Hypercorticism.

Growth hormone overproduction The main cause of excessive GH secretion by the anterior pituitary is an acidophil cell (eosinophilic) pituitary adenoma. The effects vary with the patient‘s age. GH hypersecretion in a child leads to gigantism and in an

adult to acromegaly. Gigantism occurs in the prepubertal child when the epiphyses are not yet fused to the long bones, and high levels of GH stimulate excessive skeletal growth.

Acromegaly occurs in the adult when the epiphyses are closed, linear growth is no longer possible, and GH produces the pattern of bone and soft tissue deformities. There is enlargement of the hands and feet (acral parts; hence the term acromegaly) and a protrusion of the lower jaw called prognathism. Overgrowth of the malar, frontal, and basal bones combines with prognathism to produce the coarse facial features called acromegalic facies. About 50 % of patients have abnormal glucose tolerance test that is a result of GH-induced insulin resistance. GH exerts multiple effects on carbohydrate metabolism, including decreased glucose uptake by tissues such as skeletal muscle and adipose tissue, and increased glucose production by the liver. Each of these changes results in GH-induced insulin resistance which stimulates the β-cells of the pancreas to produce additional insulin. Long-term overstimulation of the β-cells can result in GH-induced diabetes mellitus.

Hyperprolactinemia The main cause of elevated serum prolactine level is a pituitary adenoma producing prolactine. In female, hyperprolactinemia is associated with a sustained milk secretion from the breast (galactorrhea) and secondary amenorrhea, the so-called amenorrhea-galactorrhea syndrome. Hyperprolactinemia in male is associated with loss of libido, and impotence, and rarely with gynecomastia.

Hypercorticism Pituitary hypercorticism is due to an overproduction of adrenocorticotropic
hormone resulting in adrenocortical hyperfunction. Adrenocortical hyperfunction that results from an excessive glucocorticoid production by the adrenal cortex (primary hypercorticism) is called Cushing's syndrome. By convention, when this symptom complex is due to ACTH hypersecretion by the pituitary glang, it is called Cushing's disease. Pituitary hypersecretion of ACTH may be caused by hypothalamic overproduction of CRH (tertiary hypercorticism) or by a tumor of the pituitary gland (secondary hypersecretion). Excessive ACTH levels may also due to ectopic ACTH production by a nonendocrine tumor (especially small-cell lung carcinoma).

Alteration in thyroid function

Normal anatomy and function The normal thyroid weighs approximately 25 g and is situated close the trachea. The follicle is the functional unit of the thyroid. It is composed of an epithelium-lined sac filed with colloid, which stores the thyroid hormones in the form of thyroglobulin. The thyroid follicle produces and secretes two thyroid hormones: thyroxin (T4) and triiodthyronine (T3). Thyroxin and triiodthyronine are iodinated derivates of the amino acid tyrosine. The thyroid is remarkably efficient in its use of iodide. The follicle cells have in their basement membrane an iodide-trapping mechanism which pumps dietary iodide into the cell against a concentration gradient. As a result, the cell concentrates iodide to 20-50 times its concentration in the plasma. Inside the cell, iodide is oxidized by the

enzyme thyroid peroxidase to the more reactive iodine, which immediately reacts with tyrosine residues on thyroglobulin to form monoiodotyrosine and then diiodotyrosine. Two diiodotyrosine residues are coupled to form T4, or a monoiodotyrosine and a diiodotyrosine are coupled to form T3. Triiodthyronine and thyroxin are released into the circulation, where they are bound to plasma proteins, including thyroid hormone – binding globulin(TBG). More than 99 % of T4 and T3 are carried in the bound form and therefore physiologically inactive, while only the free fraction is active. The secretion of thyroid hormone is regulated by the hypothalamicpituitary-thyroid feedback system. Normally, hypothalamic thyrotropinreleasing hormone (TRH) stimulates thyrotropin (TSH) release from the anterior pituitary. TSH then stimulates thyroid hormone release, which feeds back to the pituitary to limit TSH release.

Effects of thyroid hormone. There is evidence that T3 is the active form of the hormone and that T4 is converted to T3 before it can act physiologically.

Thyroid hormone has two major functions:

1. It increases metabolism and protein synthesis;
2. It plays key roles in the regulation of body development, including mental development and sexual maturity.

Thyroid hormone actions. These can be classified as nuclear (on nuclear receptor) and non-nuclear (on plasma membrane and mitochondria). At the membrane, the hormone stimulates the Na+-K+-ATP-ase pump, resulting in increased uptake of amino acids and glucose. Combining with specific receptors on mitochondria T3 causes an increase in mitichondrial oxygen consumption (calorigenic action), and production of adenosine triphosphate (ATP) which is required for the sodium pump, which uses up to 40 % of the total energy supply of the body. A greater rate of oxidative phosphorilation results in greater heat production. Old theory, that thyroid hormone produced heat by uncoupling oxidation of substrate from phosphorilation in the mitochondria has now been disproved. In the nuclei which are the main targets for the thyroid hormones, T3 binds to receptors resulting in an increased expression of specific genes. The resultant messenger RNAs trigger the production of various enzymes that alter cell function.

These enzymes include:

- Na+-K+-ATP-ase of plasmatic membrane;
- enzymes of mitochondrias;
- protein components of β-adrenergic receptors.

All biological effects of thyroid hormone can be divided into three groups: metabolic, anabolic, and permissive. Metabolic effects Most of the widespread effects of thyroid hormone in the body are secondary to stimulation of O2 consumption (calorigenic action). T3 increases the O2 consumption of almost all metabolically active tissues, except the brain, spleen, testes, and anterior pituitary. As a result of this higher metabolism, the rate of glucose, fat, and protein use increases.

Thyroid hormone is catabolic:

1) stimulating intestinal absorption of glucose;
2) stimulating hepatic glycogenolysis;
3) stimulating insulin breakdown;

4) potentiating the glycogenolytic action of epinephrine;
5) stimulating lipolysis;

6) permitting the lipolytic actions of other hormones, such as glucocorticoids, glucagon, growth hormone and epinephrine. These metabolic effects of thyroid hormone are high-dose; therefore they become evident at hyperthyroidism.

Anabolic effects Thyroid hormone is essential for growth and differentiation of body tissues. These effects are low-dose and occur in physiological conditions. An absence or a decrease of anabolic effects becomes evident at hypothyroidism and manifests itself by slowed bone growth and delayed epiphyseal closure, as well as by muscle atrophy and weakness, weight loss, and negative nitrogen balance.

Permissive effects represent the ability of thyroid hormone to increase the responsiveness of tissues to catecholamines and other hormones such as estrogens or steroids. Thyroid hormone increases the number and affinity of β-adrenoreceptors in the heart and possibly in some other tissues, and the effects of thyroid hormone on the heart resemble those of β-adrenergic stimulation (i.e., chronotropic and inotropic effects of catecholamines).

Disorders of thyroid function can represent a hypofunctional or hyperfunctional state. They may be caused by a congenital defect in thyroid development, or they may develop later in life. The pathogenesis of most common thyroid diseases involves autoimmune processes. Three major thyroid antigens have been documented: thyroglobulin (Tg), thyroid peroxidase (TPO) and TSH-receptor (TSH-R). Goiter is a nonspecific term denoting thyroid gland enlargement. Such increases in gland size and weight may have a variety of causes and occur in hypothyroid, euthyroid, and hyperthyroid states.

Hypothyroidism

Hypothyroidism represents a decrease in thyroid function resulting from destruction or dysfunction of the thyroid gland (primary hypothyroidism), or impaired hypothalamic or pituitary function (secondary hypothyroidism). Primary hypothyroidism is much more common than secondary one. It may result from:

- insufficient synthesis of thyroid hormones due to destruction of thyroid gland in autoimmune thyroiditis (Hashimoto‘s thyroiditis);
- surgical or radiation ―overkill‖ in removing thyroid tissue;
- dietary lack of iodine (endemic goiter);
- congenital lack of thyroid tissue (hypo- or aplasia of the thyroid gland, or enzymopathies);
-use of goitogens, which are drugs or foods that interfere with thyroid hormones synthesis (e.g., iodine-containing drugs, radiographic contrast media and other).

Congenital hypothyroidism Congenital hypothyroidism is a common cause of preventable mental retardation. Thyroid hormone is essential for normal brain development and growth. Children who are hypothyroid from birth are called cretins. They are dwarfed and mentally retarded, and have enlarged, protruding tongues and potbellies. Hypothyroidism in the infant can be caused by a congenital lack of the thyroid gland, abnormal biosynthesis of thyroid hormone, or impaired release of TSH. Before the use of ionized salt became widespread, the most common cause of

cretinism was maternal iodine deficiency.
T4 crosses the placenta, and unless the mother is hypothyroid, the infant with congenital lack of thyroid gland appears normal and functions normally. However, replacement thyroid hormone therapy must be started soon after birth if mental retardation (cretinism) is to be prevented.

Acquired hypothyroidism The syndrome of adult hypothyroidism is generally called myxedema, although the term is also used to refer specifically to the skin changes in this syndrome.
The skin normally contains a variety of protein combined with polysaccharides, hyaluronic acid, and chondroitin sulfuric acid. In hypothyroidism, these complexes accumulate in the connective tissues throughout the body, promoting water retention and the characteristic puffiness of the skin (myxedema). As a result of myxedematous fluid accumulation, the face takes on a characteristic puffy look, especially around the eyes, the tongue becomes enlarged, and the voice husky and slow. These characteristic changes of voice are the basis of the aphorism that ―myxedema is the one disease that can be diagnosed over the telephone‖.
The other clinical manifestations of hypothyroidism are related to the hypometabolic state resulting from thyroid hormone deficiency. The hypometabolic state is characterized by a decrease in the basal metabolic rate (BMR), a tendency to gain weight, and cold intolerance. As the condition progresses, the skin becomes dry and rough and acquires a pale yellowish colour resulting from carotene deposition. This is because that the thyroid hormone is necessary for hepatic conversion of carotene to vitamin A, and the accumulation of carotene in the blood-stream (carotenemia) in hypothyroidism is responsible for the yellowish tint of the skin. Thyroid hormone deficiency causes a decrease in number and affinity of β-adrenoreceptors in the heart that results in bradycardia, decreased cardiac output, and hypotension. Gastrointestinal motility is decreased, producing constipation, flatulence, and abnormal distension. Nervous system involvement is manifested in mental dullness, lethargy, and impaired memory. In some patients there are severe mental symptoms (―myxedema madness‖). The major cause of acquired hypothyroidism is an autoimmune disorder in which the thyroid gland may be totally destroyed by an immunologic process (Hashimoto's thyroiditis). Iodine deficiency also can reduce thyroid hormone concentrations, causing the pituitary gland to increase thyrotropin secretion and spur the thyroid gland to hyperplasia. The resultant iodine deficiency goiter may become very large. Before the practice of adding iodide to table salt became widespread, the condition was common in certain areas of the worldusually those distant from the sea (and hence from iodine), where endemic goiter occurred in up to 50 % of the population.

Hyperthyroidism Hyperthyroidism, or thyrotoxicosis, results from excessive delivery of thyroid hormone to the peripheral tissues. The most common cause of hyperthyroidism is Graves' disease, which is accompanied by ophthalmopathy (bulging of the eyeballs) and goiter. Other causes of hyperthyroidism include:
- functioning thyroid adenomas or carcinomas;

- pituitary tumors that secret thyrotropin (secondary hyperthyroidism);
and - ingestion of excessive thyroid hormone(rarely).
Clinical manifestations of hyperthyroidism are related largely to two factors:
1) hypermetabolic state associated with the increase in oxygen consumption (calorigenic action of thyroid hormone) and use of metabolic fuels, and
2) the increase in sympathetic nervous system activity (permissive action of thyroid hormone). With the hypermetabolic state, there are frequent complaints of nervousness, irritability, and fatigability, as well as weight loss despite a large appetite; and an increase in the BMR and heat intolerance. Thyroid hormone excess leads to an increase in number and affinity of βadrenoreceptors that enhances the effects of catecholamines causing the cardiovascular effects (tachycardia, increased pulse pressure), shortness of breath, excessive sweating, and a fine tremor of the outstretched fingers.

Graver's disease (diffuse toxic goiter) Graver's disease is a state of hyperthyroidism which is accompanied by a protrusion of the eyeballs (exophthalmus) and a symmetrical enlargement of the thyroid gland (goiter). The disease is associated with human leukocyte antigen (HLA), and a familial tendency is evident. Diffuse toxic goiter occurs five times more frequently in women than in man. Graver's disease is an autoimmune disease in which T-lymphocytes activated by antigens in the thyroid gland stimulate B-lymphocytes to produce circulating antibodies against components of the TSH receptors. These antibodies, which are called thyroid-stimulating immunoglobulins (TSI), react with normal TSH receptors and stimulate thyroid hormone production. There is marked stimulation of the secretion of thyroid hormones and the high circulatory T4 and T3 levels inhibit TSH secretion, so the circulating TSH level is decreased. The exophthalmus in Graver's disease is due to swelling of the tissue, particularly the extraocular muscles, within the rigid bony walls of the orbit. This pushes the eyeballs forward. The exophthalmus, which occurs in as many as one third of affected persons, is thought, due to deposition of thyroglobulin-antithyroglobulin and other thyroid immune complexes in the extraocular muscles, with the production of an immune-complex inflammatory reaction. Alternatively, it may be an autoimmune disease of the orbital muscles. Thyrotoxicosis places a considerable load on the cardiovascular system. Tachycardia, often with arrhythmia and palpitation can be most or even all of the symptoms in some patients with hyperthyroidism. High-output cardiac failure can develop in patient with thyrotoxicosis because of the drop in peripheral resistance caused by cutaneous vasodilatation and opening of a large arteriovenous fistula despite the cardiac output is elevated.

Alteration in endocrine regulation of calcium

Calcium is essential for many physiologic processes. It is a vital second messenger and is necessary for bone growth, blood coagulation, muscle contraction, and nerve function. Three hormones are primarily concerned with the regulation of calcium metabolism: 1. Parathyroid hormone (PTH), which is secreted by the parathyroid glands, maintains the calcium concentration of the extracellular fluids. It performs this function by - promoting the release of calcium from bone, and - stimulating

calcium conservation by the kidney while increasing phosphate excretion. 2. Calcitonin, which is secreted by the parafollicular cells of the thyroid, inhibits bone resorption, hence it is a calcium-lowering hormone. 3. 1,25-Dihydroxy-vitamin D3, which is formed from vitamin D in the liver and kidney, increases circulating Ca2+ ions as a means of enhancing intestinal absorption of calcium.

Parathyroid hormone disorders Parathyroid hormone, also called parathormone, is a major regulator of serum calcium and phosphate. The dominant regulator of PTH secretion is changes in serum calcium levels, and there is an inverse relationship between plasma Ca2+ and PTH.

Hypoparathyroidism reflects deficient PTH secretion resulting in hypocalcemia. The causes of hypothyroidism usually are iatrogenic consequences of thyroid surgery, radioiodine therapy, as well as a mechanical injury to the neck, as in a motor car accident, and, more rarely, a congenital absence of all of the parathyroid glands, such as occurs in Di George syndrome. Decrease in parathyroid function can result not only from a deficiency of PTH but also from a failure of target organs (bones and kidneys) to respond to PTH, a condition called pseudohypoparathyroidism. Manifestations of hypoparathyroidism are related to hypocalcemia and are chiefly neurologic: anxiety, depression, functional psychoses, and neuromuscular irritability. Severe hypocalcemia causes tetany with muscle cramps, carpopedal spasm, and convulsions. Patients have hypocalcemia and hyperphosphatemia.

Hyperparathyroidism is caused by hypersecretion of parathyroid hormone resulting in hypercalcemia. Hyperparathyroidism can manifests as a primary disorder caused by adenoma, carcinoma, or hyperplasia of the parathyroid glands, or as a secondary disorder associated with avitaminosis D, resulting in chronically decreased serum calcium, which in turn stimulates PTH release. Manifestations of primary hyperparothyroidism are related to hypercalcemia and include mental confusion, headache, polyuria, polydipsia, hypercalcuria, calcified cornea and renal and gallstone problems, including lithiasis (kidney and gallstone stones), and pancreatitis, which is associated with gallstones. Chronic bone resorption may produce diffuse demineralization, pathologic fractures, and cystic bone lesions. Secondary hyperparathyroidism involves hyperplasia of the parathyroid glands and occurs primarily in persons with renal failure who cannot synthesize active vitamin D, and therefore, develop hypocalcemia. The bone disease seen in persons with secondary hyperparathyroidism caused by renal failure is known as renal osteodystrophy.

Krok 1 mcqs_A is correct answer:

1.There is only one hormone among the neuro hormones which refers to the derivatives of amino acids according to classification. Point it out:
A Melatonin
B Thyroliberin
C Vasopressin
D Oxytocin
E Somatotropin

2. A 46 year-old patient has complained of headache, fatigue, thirst, pains in the spine and joints for the last 2years. Clinically observed disproportional enlargement of hands,

feet, nose, superciliaryarches. He notes that he needed to buy bigger shoes three times. What is the main reason of such disproportional enlargement of different parts of the body?
A Cartilaginous tissue proliferation undergrowth hormone influence
B Increased sensitivity of the tissues to growth hormone
C Joints dystrophy development
D Increase sensitivity of the tissues to insulin
E Joints chronic inflammation development
3. Intake of oral contraceptives containing sex hormones inhibits secretion of the hypophysiae hormones. Secretion of which of the indicated hormones is inhibited while taking oral contraceptives with sex hormones?
A Follicle-stimulating
B Vasopressin
C Thyrotropic
D Somatotropic
E Oxytocin
4. Parents of a 10 y.o. boy consulted a doctor about extension of hair-covering, growth of beard and moustache, low voice. Intensified secretion of which hormone must be assumed? A Of testosterone
B Of somatotropin
C Of oestrogen
D Of progesterone
E Of cortisol
5. A girl is diagnosed with adreno-genital syndrome (pseudohermaphroditism).This pathology was caused by hypersecretion of the following adrenal hormone:
A Androgen
B Estrogen
C Aldosterone
D Cortisol
E Adrenalin
6. A 38-year-old female patient complains of general weakness, cardiac pain, increased appetite, no menstruation. Objectively: the height is 166 cm, weight 108 kg, the patient has moon-shaped face, subcutaneous fat is deposited mainly in the upper body, torso and hips. There are also blood-red streaks. Ps- 62/min, AP160/105 mm Hg. Which of the following diseases is the described pattern of obesity most typical for?
A Cushing pituitary basophilism
B Alimentary obesity
C Myxedema
D Insulinoma
E Babinski-Frohlich syndrome
7. A female patient with bronchial asthma had taken prednisolone tablets (1 tablet 3 times a day) for 2 months. Due to a significant improvement of her condition the patient suddenly stopped taking it. What complication is likely to develop in this case?
A Withdrawal syndrome
B Cushing's syndrome
C Gastrorrhagia
D Upper body obesity
E Hypotension
8. A 26-year-old woman at 40 weeks pregnant has been delivered to the maternity ward. Objectively: the uterine cervix is opened, but the contractions are absent. The doctor has administered her a hormonal drug to stimulate the labor. Name this drug:
A Oxytocin
B Hydrocortisone
C Estrone
D Testosterone
E ACTH
9. A 30-year-old female exhibits signs of virilism (growth of body hair, balding temples, menstrual disorders).

This condition can be caused by the overproduction of the following hormone:
A Testosterone
B Oestriol
C Relaxin
D Oxytocin
E Prolactin
10. In the course of an experiment adenohypophysis of an animal has been removed. The resulting atrophy of thyroid gland and adrenal cortex has been caused by deficiency of the following hormone:
A Tropic hormones
B Thyroid hormones
C Somatotropin
D Cortisol
E Thyroxin
11. Examination of a patient revealed overgrowth of facial bones and soft tissues, tongue enlargement, wide interdental spaces in the enlarged dental arch. What changes of the hormonal secretion are the most likely?
A Hypersecretion of the somatotropic hormone
B Hypersecretion of insulin
C Hyposecretion of insulin
D Hyposecretion of thyroxin
E Hyposecretion of the somatotropic hormone
12. A 2-year-old child experienced convulsions because of lowering calcium ions concentration in the blood plasma. Function of what structure is decreased?
A Parathyroid glands
B Hypophysis
C Adrenal cortex
D Pineal gland
E Thymus
13. Kidneys of a man under examination show increased resorbtion of calcium ions and decreased resorbtion of phosphate ions. What hormone causes this phenomenon?
A Parathormone
B Thyrocalcitonin
C Hormonal form D3
D Aldosterone
E Vasopressin
14. A patient with signs of osteoporosis and urolithiasis has been admitted to the endocrinology department. Blood test revealed hypercalcemia and hypophosphatemia. These changes are associated with abnormal synthesis of the following hormone:
A Parathyroid hormone
B Calcitonin
C Cortisol
D Aldosterone
E Calcitriol
15. A 4 year old child with hereditary renal lesion has signs of rickets, vitamin D concentration in blood is normal. What is the most probable cause of rickets development?
A Impaired synthesis of calcitriol
B Increased excretion of calcium
C Hyperfunction of parathyroid glands
D Hypofunction of parathyroiglands
E Lack of calcium in food
16. Periodic renal colics attackes are observed in the woman with primery hyperparathyroidizm. Ultrasonic examination revealed small stones in the kidneys. What is the cause of the formation of the stones?
A Hypercalcemia
B Hyperphosphatemia
C Hypercholesterinemia
D Hyperuricemia
E Hyperkalemia
17. A 46-year-old patient suffering from the diffuse toxic goiter underwent resection of the thyroid gland. After the surgery the patient presents with appetite loss, dyspepsia, increased

neuromuscular excitement. The body weight remained unchanged. Body temperature is normal. Which of the following has caused such a condition in this patient?
A Reduced production of parathormone
B Increased production of thyroxin
C Increased production of calcitonin
D Increaseproduction of thyroliberin
E Reduced production of thyroxin
18. A patient is followed up in an endocrinological dispensary on account of hyperthyreosis. Weight loss, tachycardia, finger tremor are accompanied by hypoxia symptoms - headache, fatigue, eye flicker. What mechanism of thyroid hormones action underlies the development of hypoxia?
A Disjunction, oxydation and phosphorilation
B Inhibition of respiratory ferment synthesis
C Competitive inhibition of respiratory ferments
D Intensification of respiratory ferment synthesis
E Specific binding of active centres of respiratory ferments
19. A 40-year-old female patient has undergone thyroidectomy. Histological study of thyroid gland found the follicles to be of different size and contain foamy colloid, follicle epithelium is high and forms papillae, there is focal lymphocytic infiltration in stroma. Diagnose the thyroid gland disease:
A Basedow's disease
B Hashimoto's thyroiditis
C Riedel's thyroiditis
D De Quervain's disease
E Nodular goiter
20. During regular check-up a child is detected with interrupted mineralization of the bones. What vitamin deficiency can be the cause?
A. Calciferol
B. Riboflavin
C. Tocopherol
D. Folic acid
E. Cobalamin
21. A patient with signs of osteoporosis and urolithiasis has been admitted to an endocrinology department. Blood test revealed hypercalcemia and hypophosphatemia. These changes are associated with abnormal synthesis of the following hormone:
A. Parathyroid hormone
B. Calcitonin
C. Cortisol
D. Aldosterone
E. Calcitriol
22. During removal of the hyperplastic thyroid gland of a 47-year-old woman, the parathyroid gland was damaged. One month after the surgery the patient developed signs of hypoparathyroidism: frequent convulsions, hyperreflexia, laryngospasm. What is the most likely cause of the patient's condition? A. Hypocalcemia
B. Hyponatremia
C. Hyperchlorhydria
D. Hypophosphatemia
E. Hyperkalemia
23. On examination the patient presents with hirsutism, moon-shaped face, stretch marks on the abdomen. BP is 190/100 mm Hg, blood glucose is 17,6 mmol/l. What pathology is such clinical presentation characteristic of?
A. Adrenocortical hyperfunction
B. Hyperthyroidism
C. Hypothyroidism
D. Gonadal hypofunction
E. Hyperfunction of the insular apparatus

24. On examination the patient is found to have low production of adrenocorticotropic hormone. How would this affect production of the other hormones?
A. Decrease adrenocorticotropic hormones synthesis
B. Decrease hormone synthesis in the adrenal medulla
C. Decrease insulin synthesis
D. Increase sex hormones synthesis
E. Increase thyroid hormones synthesis
25. A 40-year-old woman on examination presents with intensified basal metabolic rate. What hormone present in excess leads to such condition?
A. Triiodothyronine
B. Thyrocalcitonin
C. Glucagon
D. Aldosterone
E. Somatostatin
26. After a case of sepsis a 27-year-old woman developed ”bronzed” skin discoloration characteristic of Addison’s disease. Hyperpigmentation mechanism in this case is based on increased secretion of:
A. Melanocyte-stimulating hormone
B. Somatotropin
C. Gonadotropin
D. β-lipotropin
E. Thyroid-stimulating hormone
27. A laboratory rat with chronic kidney failure presents with osteoporosis, pathologic calcification of the internal organs, and arterial hypertension. These disturbances are associated with increased activity of the following hormone:
A. Parathyroid hormone
B. Thyroxin
C. Triiodothyronine
D. Calcitonin
E. Adrenaline

Tests for Self-Control (give correct answers)

1. In a patient with iodine-deficiency goiter who moves from an iodinedeficient area to an iodine-replete area, the occurrence of hyperthyroidism most likely represents
A. Graves’ disease
B. Jod-Basedow phenomenon
C. Choriocarcinoma
D. Struma ovarii
E. Toxic multinodular goiter
2. The most common cause of goiter in developing nations is
A. Iodine deficiency
B. Lithium
C. Hashimoto’s thyroiditis
D. Propylthiouracil
E. Toxic multinodular goiter
3. Elevated plasma calcitonin is seen with
A. Thyroid lymphoma
B. Medullary thyroid carcinoma
C. Papillary thyroid carcinoma
D. Anaplastic thyroid carcinoma
E. Follicular thyroid carcinoma
4. A 30-year-old woman presents with a 6-month history of amenorrhea. Your initial evaluation should include measurement of
A. Prolactin
B. Estradiol
C. Progesterone
D. Testosterone
E. DHEA-S
5. A 35-year-old man has a prolactinoma and a history of severe peptic ulcer disease. There is a family history of pituitary tumors. The findings of what other diagnostic test at this time may be abnormal and potentially useful in diagnosis?
A. Fasting blood sugar
B. Serum calcium
C. Serum calcitonin

D. Urinary metanephrine
E. Serum ferritin

Recommended literature:

Basic

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3. Krishtal N.V. Pathophysiology: textbook/ N.Krishtal et al.// Kyiv: AUS Medicine Publishing, 2017. – 527-541 pp.

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4. Porth, Carol. Essentials of pathophysiology: concepts of altered health states /Carol Mattson Porth ; consultants, Kathryn J. Gaspard, Kim A. Noble. —3rd ed. 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins. – 2011. – 1282 p.
5. Robbins Pathology basis of disease / Cotran R.S., Kumar V., Robbins S.L. - 2000.

Methodological instruction to practical lesson № 32
Module 2. Pathophysiology of organs and systems

Theme: PATHOPHYSIOLOGY OF THE ENDOCRINE SYSTEM. PATHOLOGY OF ADRENAL GLANDS. STRESS

Student should know:

- Reasons of primary and secondary hyper- and hypofunction of adrenal glands cortex.

Student should be able to:

- Analyze pathogenesis of disorders of metabolism and physiology functions at hyper- and hypofunction of adrenal glands.
- Explain the mechanisms of development of the hereditarily disorders of function of adrenal glands.

LIST OF CONTROL QUESTIONS

1. Disorder of function of sexual glands: primary and secondary hyper- and hypogonadism . Reasons and mechanisms of development, extragenital signs of disorders of function of sexual glands.
2. Pathology of epiphisis: hypo- and hyperfunction, basic signs.
3. Pathology of adrenal glands. Insufficiency of adrenal cortex: types (primary, secondary; acute, chronic), etiology, pathogenesis, clinical signs. Hyperfunction of adrenal cortex: types (primary, secondary), etiology, pathogenesis, clinical signs. Syndromes of Itsenko-Kushing, Cohn, innate hyperplasia of adrenal cortex(adrenogenital syndrome). Types, reasons, mechanisms of development, clinical signs of disorders of activity of cerebral substance of adrenal glands.
4. A concept of stress as heterospecific, stereotype adaptative reaction of organism on the action of extraordinary irritants. Stages of development of general adaptation syndrome. Mechanisms of a long-term adaptation. A concept of a stressor damage and "illnesses of adaptation". Principles of prevention of stressor damages.

Alteration in Adrenal function

Normal anatomy and function. The adrenal glands are small, bilateral structures that weigh approximately 5 g each and lie retroperitoneally at the apex of each kidney.
The adrenal gland actually divided on anatomical and functional grounds into two separate endocrine organs:
the adrenal cortex which secretes the steroid hormones;
and the adrenal medulla which is a modified ganglion and secretes the catecholamines. Adrenal medullary hormones are not essential for life because the sympathetic nervous system also secretes epinephrine and norepinephrine, but they

help to prepare the individual to deal with emergencies.
On the other hand, the adrenal cortex is essential for life. It secretes glucocorticoids which affect the metabolism of carbohydrate and protein, mineralocorticoids essential to the maintenance of sodium balance and extracellular fluid volume, and sex hormones that exert minor effects on reproductive function. Of these, the mineralocorticoids and glucocorticoids are necessary for survival.
Hormones of Adrenal cortex
The adrenal cortex has three zones, all of which produce steroid hormones:
 the outermost zona glomeruloza produces mineralocorticoids, principally aldosterone;
 the intermediate zona fasticulata produces glucocorticoids, principally cortisol;
 the innermost zona reticularis produces androgens.
The secretion of the glucocorticoids and the adrenal androgens is controlled by the ACTH secreted by the anterior pituitary gland. The secretion of the mineralocorticoids is controlled by circulatory factors, of which the most important is angiotensin II that is in turn dependent on renin secreted by the kidney.
Transport, metabolism, and mechanism of action. The glucocorticoids, like other steroid hormones, are poorly soluble in aqueous media, and they circulate bound to plasma proteins, largely to corticosteroid-binding globulin (CBG) and to a lesser extent to albumin. The mineralocorticoids bind mostly to albumin for transport in the circulatory system. Once bond, the steroid is physiologically inert. The free or unbound fraction (< 10 %) of the total plasma concentration is the biologically active form. Steroids that are free in the blood diffuse through the plasma membranes of target cells; once inside, they bind to cytoplasmic receptor proteins, resulting in formation of hormone-receptor complex, which translocates into the nucleus. These complexes then bind to target sites on the DNA that affects gene activity with subsequent production of messenger RNA and protein synthesis.
The main site for metabolism of the adrenal cortical hormones is the liver, where they are metabolized, conjugated and made water soluble. They are eliminated in either bile or urine.
Effects of the glucocorticoids can be divided into physiological and pathological. Physiological effects of the glucocorticoids are as follows:
Metabolic effect. Cortisol increases the synthesis of a number of enzymes which play key roles in hepatic gluconeogenesis (an anabolic action of cortisol). In adipose tissue and skeletal muscle, however, cortisol is catabolic, i.e., it causes a breakdown of body tissue in order to mobilize energy. As body proteins are broken down, amino acids are mobilized and transported to the liver, where they are used in the production of glucose (i.e., gluconeogenesis). Breakdown of triglycerides and mobilization of fatty acids converts cell metabolism from the use of glucose for ATP production to the use of fatty acids.As glucose production by the liver increases and peripheral glucose use decreases, moderate glucose intolerance develops. In persons who are predisposed to diabetes it results in hyperglycemia. Psychological effect. The glucocorticoid hormones appear to be involved directly or indirectly in emotional behavior, and they may contribute to emotional instability.
Permissive effecs. The glucocorticoids facilitate the response of the tissues to

humoral and neural influences, such as that of the catecholamines during trauma and extreme stress.

Pharmacological effects of the glucocorticoids include immunologic and anti-inflammatory ones. The glucocorticoids have little influence on the immune system under physiological conditions. However, when administered in large doses over a prolonged period they can suppress antibody formation and decrease the development of cell-mediated immunity. Immature T-cells in the thymus and immature B-cells and Tcells in lymph nodes can be killed by exposure to high concentration of the glucocorticoids, causing lymphopenia and atrophy of lymphoid tissue.

Anti-inflammatory action of the glucocorticoids is based mainly on their ability to inhibit the activity of phospholipase A2, reducing the amount of arachidonic acid available for conversion to prostaglandins and leucotrienes. A highly significant aspect of long-term therapy with pharmacologic preparations of the adrenal cortical hormones is adrenal insufficiency on withdrawal of the drugs. Prolonged treatment with the glucocorticoids drives down ACTH release; therefore endogenous cortisol production is extremely low. Chronic suppression causes atrophy of the adrenal gland, and the abrupt withdrawal of drugs can cause acute adrenal insufficiency. Thus, patients have to be weaned off the glucocorticoids slowly to allow the rise of plasma cortisol to normal levels. Recovery to a state of normal adrenal function may be prolonged, requiring 12 months or more.

Effects of the mineralocorticoids. The mineralocorticoids stimulate the active transport of sodium through the epithelial cell wall. In common with the other steroid hormones, aldosterone stimulates de novo synthesis of proteins, which enhance sodium transport in the epithelial cell of the distal convoluted tubule of the kidney.

There are three main mechanisms of aldosterone action:

1) it increases the number of sodium channels in the apical membrane;
2) it increases the number of Na+-K+-ATP-ase molecules;
3) it increases ATP molecule number within the cell.

Disorders of adrenal cortical function can be divided into:

1. Hypofunction of adrenal cortex (adrenocortical insufficiency);
2. Hyperfunction of the zona fasticulata (hypercortisolism);
3. Hyperfunction of the zona glomeruloza (hyperaldosteronism);
4. Dysfunction of the adrenal cortex (adrenogenital syndrome).

Adrenocortical insufficiency Adrenocortical insufficiency may be caused by destruction of the adrenal cortex (primary adrenal insufficiency), low pituitary ACTH secretion (secondary adrenal insufficiency), or deficient hypothalamic release of CRH (tertiary adrenal insufficiency).

Primary adrenal insufficiency or Addison's disease results from destruction of the adrenal cortex by microorganisms or autoimmune disease. Before effective control of tuberculosis, bilateral adrenal destruction by tuberculosis was the most common cause of the disease. Today, autoimmune destruction accounts for 70 % to 90 % of all cases, with the remainder the resulting from infection, cancer, or adrenal hemorrhage.

Antibodies involved in autoimmune adrenalitis development are mainly directed to the steroidogenic enzymes. Genetic susceptibility to autoimmune adrenal insufficiency is strongly linked with the HLA.
In primary adrenal insufficiency, all three zones of the adrenal cortex are usually involved. The result is inadequate secretion of glucocorticoids, mineralocorticoids and androgens. The adrenal cortex has a large reserve capacity, and the manifestations of adrenal insufficiency are not usually detected until 90 % of the gland has been destroyed.
The initial symptoms generally have a gradual onset, with only a partial glucocorticoid deficiency resulting in inadequate cortisol increase in response to stress. Progression to complete glucocorticoid deficiency results in hypoglycemia, lethargy, weakness, fever, and gastrointestinal symptoms, such as anorexia, nausea, vomiting, and weight loss.
Mineralocorticoids deficiency causes decreased renal potassium secretion, along with increased urinary losses of sodium and water. The result is hyponatriemia, loss of extracellular fluid, decreased cardiac output, and hyperkaliemia. The combined lack of glucocorticoid and mineralocorticoid can lead to collapse, shock, and death.
Adrenal androgen deficiency is observed in women only (men derive most of their androgen from the testis) as decreased pubic and axillary hair and decreased libido.
Addison‘s disease is characterized by a deficiency of adrenal cortical hormones and an elevated ACTH levels resulted from a lack of feedback inhibition. Elevated level of ACTH causes hyperpigmentation. The skin looks bronzed; the gums and oral mucous membranes may become bluishblack. A chemical structure of ACTH is strikingly similar to that of melanocyte-stimulating hormone, hyperpigmentation occurs in more than 90 % of persons with Addison‘s disease and is helpful in distinguishing the primary and secondary forms of adrenal insufficiency.
Addison‘s disease, like type 1 diabetes mellitus, is a chronic metabolic disorder that requires lifetime hormone replacement therapy.

Acute adrenal insufficiency (adrenal crisis) Acute adrenal insufficiency is a life-threatening situation. It is a rapidly progressive disorder (over hours or days) presenting clinically as shock. Such an illness may occur in septicemia, especially meningococcemia, adrenal trauma, anticoagulant therapy or adrenal vein thrombosis as a result of massive bilateral adrenal hemorrhage.

Hypercortisolism. Cushing’s syndrome Hyperfunction of the zona fasticulata of the adrenal cortex is characterized by increased secretion of the glucocorticoids by the adrenal gland (hypercortisolism). The term Cushing‘s syndrome refers to the manifestations of hypercortisolism from any cause.
They include:
1. Adrenal conditions result from adenoma or carcinoma of the adrenal cortex (primary hypercortisolism);
2. Pituitary conditions result from hypersecretion of ACTH, causing bilateral adrenocortical hyperplasia (often called Cushing‘s disease);
3. Ectopic ACTH syndrome results from secretion of ACTH by nonendocrine tumors,

usually small-cell carcinoma of the lung; 4. Iatrogenic conditions result from administration of excessive doses of corticosteroids or ACTH. The major manifestations of Cushing‘s syndrome represent an exaggeration of the many actions of cortisol.
Chronically increased plasma glucose (hyperglycemia) stimulates excess insulin secretion with consequent the β-cells exhaustion and diabetes mellitus, also called steroid diabetes, development. The kidneys have to eliminate excess glucose that results in polyuria and polydipsia. Altered fat metabolism causes truncal obesity and redistribution of truncal fat, with a characteristic ―buffalo hump‖, and a round, plethoric ―moon face‖. Both ACTH and glucocorticoids are lipolytic in normal fat stores, and the excess insulin may be lipogenic in the face, upper back and in the supraclavicular fat pads. The catabolic effect of glucocorticoids on protein causes negative nitrogen balance, with muscle wasting, weakness, and thinning of the extremities. Loss of the bone protein matrix results in osteoporosis, causing back pain, compression fractures of the vertebrae, and rib fractures. The glucocorticoids possess mineralocorticoids properties; this causes hypokaliemia as a result of excessive potassium excretion and hypertension resulting from sodium retention. The glucocorticoids suppress the immune system by atrophying lymphoid tissue and inhibiting lymphocyte function, resulting in increased susceptibility to infection. Excess levels of the glucocorticoids may give rise to extreme emotional lability, ranging from middle euphoria to grossly psychotic behavior.

Hyperaldosteronism Hyperfunction of the zona glomeruloza of the adrenal cortex is characterized by increased secretion of the mineralocorticoids (hyperaldosteronism). Hyperaldosteronism may be divided into primary and secondary ones. Primary hyperaldosteronism (Conn‘s syndrome) is due to a lesion of the adrenal gland and accounts for approximately one-third of all cases of adrenocortical hyperfunction. The most common lesion is an aldosteroneproducing adrenal adenoma. The aldosterone excess produces sodium retention, increased total plasma volume, increased renal artery pressure, and inhibition of renin secretion. Most patients with primary hyperaldosteronism are women aged 30 to 50 who present with hypertension and hypokalemic alkalosis that result from increased urinary losses of potassium. Secondary hyperaldosteronism is due to extraadrenal causes, and relates to renin hypersecretion. An important stimulus for the release of aldosterone is angiotensin II, which is formed in increased amounts via the renin-angiotensin system when the renal perfusion pressure is reduced. For example, if the pumping action of the heart is reduced (heart failure) or in peripheral vasodilatation (e.g., in sepsis or liver failure) the blood pressure can be maintained only by massive activation of the sympathetic nervous system, resulting in renal vasoconstriction, renin release, and hyperaldosteronism.

Adrenogenital syndrome Adrenogenital syndrome is a state of dysfunction of the adrenal cortex caused by inborn enzyme defects that inhibit cortisol synthesis. The result is a feedback overproduction of ACTH, causing adrenal hyperplasia and overproduction of the adrenal hormones that are not affected by the enzyme

deficiency, i.e. androgens.
In males the condition is seldom diagnosed, in females an increase in adrenal androgensadrenal androgens results in virilization with hirsutism (abnormally abundant and distributed body hair), balding and clitoral enlargement. These features are usually apparent at birth, but in some forms do not develop until later. Hormones of the adrenal medulla The adrenal medulla lies within the cortex and originates from the neural crest. The catecholamines, epinephrine and norepinephrine, are synthesized by the chromaffin cells of the adrenal medulla.

Effects of catecholamines. Epinephrine and norepinephrine produce widespread effects on the cardiovascular system, muscular system, and carbohydrate and lipid metabolism in the liver, muscle and adipose tissues. Most cells of the body have receptors for catecholamines and, thus, are their target cells. Stressors cause an immediate release of catecholamines, which prepare the body for extraordinary physical and mental exertion; hence epinephrine is called the hormone of ―flight or fight‖.

Disorders of adrenal medulla function Disorders of adrenal medulla function occur rarely. The most common clinical syndrome is associated with overproduction of catecholamines by chromaffin cell tumor (pheochromocytoma). The catecholamines released into the circulation by a pheochromocytoma cause paroxysmal or sustained hypertension, angina, cardiac arrhythmias, headache, and carbohydrate intolerance. If the tumor is untreated, a potentially fatal cerebrovascular accident, congestive heart failure with pulmonary edema, or ventricular fibrillation may result.

Krok 1 mcqs_A is correct answer:

1. A girl is diagnosed with adrenogenital syndrome (pseudohermaphroditism). This pathology was caused by hypersecretion of the following adrenal hormone:
A Androgen
B Estrogen
C Aldosterone
D Cortisol
E Adrenalin
2. A patient suffering from pheochromocytoma complains of thirst, dry mouth, hunger. Blood test for sugar revealed hyperglycemia. What type of hyperglycemia is it?
A Adrenal
B Hypercorticoid
C Alimentary
D Somatotropic
E Hypoinsulinemic
3. Examination of a 42 year old patient revealed a tumour of adenohypophysis. Objectively: the patient's weight is 117 kg, he has moon-like hyperemic face, red-blue striae of skin distension on his belly. Osteoporosis and muscle dystrophy are present. AP is 210/140 mm Hg. What is the most probable diagnosis?
A Cushing's disease
B Cushing's syndrome
C Conn's disease
D Diabetes mellitus

E Essential hypertension

4. The formation of a secondary mediator is obligatory in membrane-intracellular mechanism of hormone action. Point out the substance that is unable to be a secondary mediator:

A Glycerol
B Diacylglycerol
C Inositol-3,4,5-triphosphate
D CAMP E Ca2+

5. A patient had been taking glucocorticoids for a long time. When the preparation was withdrawn he developed the symptoms of disease aggravation, decreased blood pressure and weakness. What is the reason of this condition?

A Appearance of adrenal insufficiency
B Hyperproduction of ACTH
C Sensibilization
D Habituation
E Cumulation

6. A 19-year-old male was found to have an elevated level of potassium in the secondary urine. These changes might have been caused by the increase in the following hormone level:

A Aldosterone
B Oxytocin
C Adrenaline
D Glucagon
E Testosterone

7. A 41-year-old male patient has a history of recurrent attacks of heartbeats (paroxysms), profuse sweating, headaches. Examination revealed hypertension, hyperglycemia, increased basal metabolic rate, and tachycardia. These clinical presentations are typical for the following adrenal pathology:

A Hyperfunction of the medulla
B Hypofunction of the medulla
C Hyperfunction of the adrenal cortex
D Hypofunction of the adrenal cortex
E Primary aldosteronism

8. A 44 year old woman complains of general weakness, heart pain, significant increase of body weight. Objectively: moon face, hirsutism, AP is 165/100 mm Hg, height - 164 cm, weight - 103 kg; the fat is mostly accumulated on her neck, thoracic girdle, belly. What is the main pathogenetic mechanism of obesity?

A Hyperproduction of corticosteroids
B Reduced production of thyroid hormones
C Increased insulin production
D Reduceglucagon production
E Increased mineralocorticoid production

9. A concentrated solution of sodium chloride was intravenously injected to an animal. This caused decreased reabsorption of sodium ions in the renal tubules. It is the result of the following changes of hormonal secretion:

A Aldosterone reduction
B Aldosterone increase
C Vasopressin reduction
D Vasopressin increase
E Reduction of atrial natriuretic factor

10. People adapted to high external temperatures have such peculiarity: profuse sweating isn’t accompanied by loss of large volumes of sodium chloride. This is caused by the effect of the following hormone upon the perspiratory glands:

A Aldosterone
B Vasopressin
C Cortisol
D Thyroxin
E Natriuretic

11. A 44 year old woman complains of general weakness, heart pain, significant increase of body weight. Objectively: moon face, hirsutism, AP is 165/100 mm Hg, height - 164 cm,

weight - 103 kg; the fat is mostly accumulated on her neck, thoracic girdle, belly. What is the main pathogenetic mechanism of obesity?
A Increased production of glucocorticoids
B Reduced production of thyroid hormones
C Increased insulin production
D Reduce glucagon production
E Increased mineralocorticoid production
12. A 41-year-old man has a history of recurrent attacks of heartbeats (paroxysms), profuse sweating, headaches. Examination revealed hypertension, hyperglycemia, increased basal metabolic rate, and tachycardia. These clinical presentations are typical for the following adrenal pathology:
A. Hyperfunction of the medulla
B. Hypofunction of the medulla
C. Hyperfunction of the adrenal cortex
D. Hypofunction of the adrenal cortex
E. Primary aldosteronism
13. Examination of a 42-year-old patient revealed a tumour of adenohypophysis. Objectively: the patient's weight is 117 kg, he has moon-like hyperemic face, redblue striae of skin distension on his belly. Osteoporosis and muscle dystrophy are present. AP is 210/140 mm Hg. What is the most probable diagnosis?
A. Cushing's disease
B. Cushing's syndrome
C. Conn's disease
D. Diabetes mellitus
E. Essential hypertension
14. Autopsy of a40-year-old woman, who died of cerebral hemorrhage during hypertensic crisis, revealed: upperbody obesity, hypertrichosis, hirsutism, stretchmarks on the skin of thighsand abdomen. Pituitary basophil adenoma is detected in the anterior lobe .What diagnosis is the most likely?
A. Cushing's disease
B. Essential hypertension
C. Alimentary obesity
D. Simmonds' disease
E. Hypothalamic obesity
15. Histological specimen of an ovary demonstrates a spherical structure composed of large glandular cells containing lutein. What hormone is produced by cells of this structure?
A. Progesterone
B. Estrogens
C. Testosterone
D. Corticosterone
E. Aldosterone
16. A 30-year-old woman developed the signs of virilism (body hair growth, balding temples, disturbed menstrual cycle). What hormone can cause this condition when hyperproduced?
A. Testosterone
B. Estriol
C. Relaxin
D. Oxytocin
E. Prolactin
17. Corticosteroid hormones regulate the adaptation processes of the body as a whole to environmental changes and ensure the maintenance of internal homeostasis. What hormone activates the hypothalamopituitary-adrenal axis?
A. Corticoliberin
B. Somatoliberin
C. Somatostatin
D. Corticostatin
E. Thyroliberin
18. After a severe stress the patient presents with eosinopenia in the blood test. In this case the decreased number of eosinophils can explain changes in the level of the following hormones:
A. Glucocorticoids
B. Adrenaline

C. Insulin
D. Mineralocorticoids
E. Vasopressin

Tests for Self-Control (give correct answers)

1. Adenoma of the glomerular zone of the adrenal cortex was diagnosed in a patient. It caused the development of initial hyperaldosteronism (Conn's syndrome). The balance of what ion is changed in this case?
A. Calcium.
B. Chlorine.
C. Magnesium.
D. Sodium.
E. Iron.
2. A patient suffers from chronic failure of the adrenal cortex — Addison's disease. A lack of what hormone is observed in this case?
A. Vasopressin.
B. Insulin.
C. Epinephrine.
D. Thyroxin.
E. Aldosterone.
3. A 28-year-old patient complains of mental and physical weakness, dyspepsia. The tuberculin test is positive, hypoglycemia, arterial pressure — 90/60 mmHg, hyponatremia. The skin is overpigmented. In what pathology of the adrenal glands are such phenomena observed?
A. Addison's disease.
B. Itsenko—Cushing's syndrome.
C. Acute failure of the adrenal cortex.
D. Adrenogenital syndrome.
E. Conn's syndrome.
4. A 44-year-old woman complains of sickness, obesity of the upper part of the body, appearance of hair on the face, menstruation cessation, and hyperglycemia. Arterial pressure — 165/100 mmHg. Determination of what parameter will allow distinguishing Itsenko—Cushing's disease from Itsenko—Cushing's syndrome caused by adenoma of the adrenal glands?
A. Level of androgens in the blood plasma.
B. Level of hydrocortisone in the blood plasma.
C. Level of 17-oxysteroids in the urine.
D. Level of corticotropin in the blood.
E. Amount of eosinophils in the blood.
5. A woman had a complicated delivery. In some months after loss of hair and teeth, body weight decreased, she became very sick. Later arterial pressure, body temperature, concentration of glucose, somatotropin and corticotropin in the blood reduced. What pathology of the pituitary gland is observed?
A. Diabetes.
B. Pituitary nanism.
C. Acromegaly.
D. Itsenko—Cushing's disease.
E. Panhypopituitarism.
6. A 10-year-old child has a hyperergic form of rheumatism with extensive pain syndrome, which can't be treated with nonsteroid medicines. Therefore it was necessary to use an anti-inflammatory hormone. What hormone has an antiinflammatory action?
A. Epinephrine.
B. Hydrocortisone.
C. Somatotropin.
D. Testosterone.
E. Insulin.
7. A 53-year-old woman is 163 cm tall,

her body weight is 92 kg, there is edema of the face and upper extremities. When pressed, the skin does not form a pit, the skin is dry and yellowish. Arterial pressure — 90/60 mmHg. Pulse — 56. Failure of what endocrine gland can such symptoms be connected with?
A. Neurohypophysis.
B. Adrenal cortex.
C. Thyroid gland.
D. Ovaries.
E. Parathyroid glands.

8. A 50-year-old patient was ill with encephalitis. Later diuresis increased to 12 1. The level of blood glucose was 4.1 mmol/1. A lack of what hormone can the state be connected with?
A. Aldosterone.
B. Glucagon.
C. Insulin.
D. Hydrocortisone.
E. Vasopressin.

9. A patient has increased body temperature, tachycardia, emotional lability, tremor. The change of what hormone concentration is this state connected with?
A. Vasopressin.
B. Thyroxin.
C. Testosterone.
D. Aldosterone.
E. Insulin.

10. A 44-year-old woman complains of weakness, pain in the heart, weight gain. Objectively: «moon face», arterial pressure - 165/100 mmHg. Body height 164 cm, body weight 103 kg, obesity of the face, neck, shoulders, abdomen. What is the cause of the development of these signs?
A. Deficiency of thyroid hormones.
B. Excess of glucocorticoids.
C. Excess of insulin.
D. Deficiency of glucagon.
E. Excess of mineralocorticoids.

11. A 50-year-old patient complains of thirst, polyuria, drinking plenty of water. Blood glucose — 4.8 mmol/1. In the urine glucose and acetone are absent; the urine is colorless, relative density is 1002—1004. What has caused polyuria?
A. Thyrotoxicosis.
B. Hypothyroidism.
C. Lack of insulin.
D. Aldosteronism.
E. Lack of vasopressin.

12. A patient with hyperthyroidism complains of weight loss, tachycardia, finger tremor, fever. Basal metabolism increased by 40 %. What is the cause of basal metabolism increase?
A. Intensifying of glycogenesis.
B. Activation of glyconeogenesis.
C. Activation of oxidative processes.
D. Intensifying of lipogenesis.
E. Depression of proteolysis.

13. A woman complains of tachycardia, weight loss, tremor, intensified sweating. What endocrine pathology can cause it?
A. Hypergenitalism.
B. Hypothyroidism
C. Hyperthyroidism.
D. Hypogonadism.
E. Hypoaldosteronism.

14. A 16-year-old girl presents with no hair on the pubis and in the armpits, her mammary glands are underdeveloped, no menstruations. What hormone imbalance can it be indicative of?
A. Ovarian failure
B. Hyperthyroidism

C. Hypothyroidism
D. Pancreatic islet failure
E. Adrenal medulla hyperfunction

Recommended literature:

Basic

1. Simeonova N.K. Pathophysiology/ N.Simeonova.// Kyiv, Ukraine. – 2010. – 493-509 pp.
2. Victor N. Jelski, Svetlana V. Kolesnikova. Handbook Of Pathophysiology Part 2: Pathophysiology of organs and systems. - Donetsk, Ukraine. – 2011. – 139-161 pp.
3. Krishtal N.V. Pathophysiology: textbook/ N.Krishtal et al.// Kyiv: AUS Medicine Publishing, 2017. – 542-565 pp.

Additional

4. Porth, Carol. Essentials of pathophysiology: concepts of altered health states /Carol Mattson Porth ; consultants, Kathryn J. Gaspard, Kim A. Noble. —3rd ed. 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins. – 2011. – 1282 p.
5. Robbins Pathology basis of disease / Cotran R.S., Kumar V., Robbins S.L. - 2000.

Methodological instruction to practical lesson № 33
Module 2. Pathophysiology of organs and systems

Theme: PATHOPHYSIOLOGY OF THE NERVOUS SYSTEM. PATHOPHYSIOLOGY OF THE EXTREME STATES

Student should know:

- Typical disorders of the nervous system functions.
- Different principles for classification/characteristic of disorders of activity of the nervous system.

Student should be able to:

- To explain the mechanisms of development and basic signs of disorders of integrative functions of CNS on the basis of knowledge about general laws of its functioning.
- To determine a concept the "extreme states", shock/collapse, coma.
- To explain the principles of classification of the shock and comatose states.
- To analyze the reasons and mechanisms of development of the extreme states.
- To explain the principles of therapy of the extreme states.

LIST OF CONTROL QUESTIONS

1. General characteristic of pathology of the nervous system, principles of classification of disorders of its activity. Features of development of typical pathological processes in the nervous system.
2. Disorder of sensory functions of the nervous system. Disorders of mechano-, thermo-, proprio- and nociception. Disorder of conduction of sensory information. Syndrome of Brown-Sekar. Signs of damage of thalamic centers and sensory structures of cerebral cortex.
3. Pain. Pain peculiarities as a type of sensitivity. Principles of classification of pain. Somatic pain. Visceral pain. Etiology and pathogenesis of pain: theory of division of impulses ("theory of gate"), theory of specificity. Pathological pain: neuralgia, causalgia, phantomic, thalamic . Peripheral, peripheral-central and central mechanisms of development of pathological pain. Emotional, vegetative, motional reactions of organism on pain. Emotional-pain stress, pain shock. Natural antinociceptive mechanisms. Principles and methods of antipain therapy.
4. Disorder of motional function of the nervous system. Experimental modelling of motional disorders. Peripheral and central paralyses and pareses:reasons, mechanisms of development, basic signs. Spinal shock. Motional disorders of subcortical origin. Disorders, related to the impairment of cerebellum. Cramps, their types. Disorder of neuro-muscular transmission. Myastheny.
5. Disorders of vegetative functions of the nervous system, methods of experimental modelling. Syndrome of vegetovascular dystony.

6. Acute and chronic disorders of cerebral circulation of blood. Stroke. Edema and swelling of cerebrum, reasons and mechanisms of development. Intracraneal hypertension. A role of damages of neuroglia in development of pathological processes in CNS. Damage of hematoencephalic barrier and autoimmune impairment of cerebrum.
7. A concept of the extreme states.
8. Shock: types, clinical signs, reasons and mechanisms of development. Disorder of general hemodynamics and microcirculation in pathogenesis of the shock states. Stages of shock. A role of hormones and physiological active substances and products of damaged tissues in pathogenesis of the shock states. Concept about „shock organs". Participating of neuromechanisms in development of shock. Pathophysiological bases of prophylaxis and therapy of shock.
9. A concept of crush-syndrome. Reasons, mechanisms of development, signs.
10. Collapse. General and different signs of shock and collapse. Reasons and mechanisms of development of the collaptoid states.
11. Coma. Principles of classification. Reasons and mechanisms of development of the comatose states. A role of disorders of energetic supply of cerebrum, osmotic disorders, ionic and acid-basic homoeostasis in pathogenesis of coma. Principles of therapy of coma.

Alterations in the nervous system activity can be divided into:
-the sensory function disorders
-the effector function disorders
-the integrative function disorders.
Disorders can be either primary or secondary.
Primary disorders occur as direct reactions of different nervous structures on pathogenic stimuli. These stimuli include:
-physical (trauma, radiation, thermal effects),
-chemical (toxins – heavy metals, alcohol, drugs),
-biological (viruses, bacteria, prions),
-social factors (emotions)
Secondary disorders result from alterations in metabolism (hypoxia, hypoglycemia, acidosis, electrolyte abnormalities) or due to endocrine function disorders or immune reactions.

The sensory function disorders The somatosensory system relays information to the CNS about four major body sensations: touch, temperature, pain, and body position. The somatosensory sensitivity includes:
1) cutaneus sensitivity; Specialized receptors are located in the skin and mucous membranes and are stimulated by touch (pressure, vibration) or by temperature (heat and cold) receptors;
2) deep sensitivity; Stretch receptors (proprioreceptors) are located in muscles, tendons and joint capsules and transmit information about motor activity (body position);
3) visceral sensitivity; Interoreceptors are located in various internal organs and

provide information about stretching of hollow organs and concentration of certain substances (CO2, H+, glucose, osmolarity etc.).
Sensory impulses are transmitted to the spinal cord and there influence the activity of motoneurons via reflex. Via the dorsal column (discriminative) and the anterolateral column they are transmitted to the medulla oblongata, thalamus, and cortex (postcentral gyrus). Information about movements reaches the cerebellum via the spinocerebellar tracts.
Disorders in the somatosensory sensitivity include:
1*) hyperesthesia – increased sensitivity,*
2) hypoesthesia – diminished sensitivity,
3) anesthesia – lost sensitivity,
4) paresthesia or dysesthesia – sensory perception without adequate stimulus (abnormal sensation of pain, temperature (numbness prickling).
Lesions in the peripheral nerves or spinal nerves can cause hypoesthesia (or hyperesthesia) but not anesthesia in the affected dermatome (because of overlapping innervations areas).
Lesions in spinal cord
Hemisection of the spinal cord causes Brown-Sequard's syndrome: alterations in pain and temperature sensitivity occur on the side opposite to the site of injury whereas a loss of tactile sensitivity and motor function occur on the site of the injury.
Complete transaction of the spinal cord leads to spinal shock – all kinds of sensitivity are lost below the site of injury. Spinal shock – temporary areflexia and common paraplegia with anesthesia just after spinal trauma (lost months).
Injury of the anterolateral column is accompanied by superficial sensitivity loss on the opposite side. It especially impairs pressure, pain and temperature sensation.
An interruption in the dorsal column stops adequate vibratory sensation and diminishes the ability to precisely define mechanical stimuli in space and time. Proprioception is also affected. Thus, the control of muscular activity is impaired. One of the effects is ataxia.
Pain Pain is an unpleasant sensory and emotional experience associated with potential tissue damage. Pain is both a protective (serves as a warning signal) and pathological (unpleasant physical and emotionally disturbing) sensation.
Classification of pain:
According to a source from which it is originated pain can be somatic (superficial and deep) and visceral.
Superficial somatic pain originates in the skin and subcutaneous tissues; it is a sharp, burning, and easily localized.
Deep somatic pain originates in the periosteum, muscles, tendons, joints and vessels; it is poorly localized (more diffuse). It may be caused by strong pressure on bone, ischemia to a muscle, and it is frequently associated with sweating and changes in blood pressure.
Visceral pain originates in visceral structures; it is poorly localized, unpleasant and associated with some autonomic symptoms (vomiting, nausea etc.). It often radiates to other areas. There are relatively few pain receptors in the viscera – visceral pain is poorly localized. However, it may be very severe. Sources of visceral pain may be

peritoneum, mesentery, parietal pleura and pericardium, muscular organs (heart, hollow organs etc.).
Pain in the hollow viscera organs may be caused by rapid and sharp distension or intensive contractions (spasm) of these organs. For instance, in intestinal obstruction, intestinal colic is produced by dilation of the intestine above the obstruction.
Visceral pain, like deep somatic pain, initiates reflex contraction of nearly skeletal muscle. This reflex spasm is usually in the abdominal wall and marks the abdominal wall rigid (especially when visceral inflammatory process involves the peritoneum).
According to its duration pain can be acute or chronic. Acute pain results from tissue damage (trauma, surgery) and it is characterized by autonomic nervous system responses. It lasts less than 6 months. Chronic pain, a persistent pain, is accompanied by loss of appetite, sleep disturbances, depression and other debilitating responses (back pain). It lasts 6 months or longer.
There are two concepts that explain pain sensation- specificity theory and intensity theory.
Specificity theory: pain results from activation of specific nociceptive (nociception means ―pain sense‖) receptors. Pain stimuli are perceived by the nociceptors in the skin, motor apparatus, internal organs and vessels. Pain arises due to action of noxious (i.e., causing tissue damage) stimuli on nociceptive receptors. These stimuli include:
1) mechanical (press),
2) thermal (t0>450C),
3) chemical (ions H+, K+),
4) stretches
Intensity theory: specific nociceptive receptors are absent in the body. Pain arises when the mechanical or thermal receptors are activated by high-intensity, non-noxious stimuli. For instance, light applied to the skin would produce the sensation of touch through low-frequency firing of the touch receptor; intense pressure would produce pain through highfrequency firing of the same receptor. Both theories focus on the neurophysiologic basis of pain, and both probably apply. Specific nociceptive afferents have been identified, however, almost all afferent stimuli, if driven at a very high frequency, can be experienced as painful. Thus, stimuli that cause tissue lesions as well as high-intensity non-noxious stimuli (temperature, distension) activate nociceptors in the skin and the viscera.

The somatic motor activity disorders The somatic motor activity disorders include: hypokinesis, hyperkinesis, and ataxia.
Hypokinesis Hypokinesis is a disorder characterized by diminished movement. Hypokinesis includes:
- paresis – incomplete loss of motor functions, i.e. weakening of voluntary movement;
-paralysis –complete loss of motor functions, i.e. total inability to perform voluntary movement.
According to a level of the motor nervous system affection, paresis and paralysis can be peripheral, central and extrapyramidal.

Peripheral paralysis (paresis) arises due to destruction of a peripheral motor neuron (lower motoneuron located in the anterior horns of the spinal cord) or peripheral motor nerves. This leads to a complete disruption in nerve conduction.
Peripheral paresis may be caused by trauma, infections (poliomyelitis), allergic or degenerative (avitaminoses) process, and some intoxication. Experimentally a peripheral paralysis can be produced by transsection of any peripheral nerve which contains motor fibers. For example, in a dog, transsection of the sciatic nerve causes paralysis of shin flexors and muscles of the paws; when the animal moves it drags the lower part of the affected limb.
Peripheral paralysis is characterized by the following features:
1) muscular atonia (hypotonia) that develops due to complete absence of efferent impulses. Both voluntary and reflex movements are lost. As a result the muscles lose their tone and offer no resistance in passive movements. Hence, sluggish paralysis;
2) muscular atrophy that develops gradually as a result of muscular inactivity;
3) areflexia (hyporeflexia) In peripheral paralysis tendon reflexes disappear because impulses from the muscles cannot evoke reflex contractions of these muscles.
Central paralysis (paresis) results from an affection of a central motor neuron (upper motoneuron located in the motor area of the cortex) or their axons in the pyramidal tracts. The peripheral motor neuron remains intact. It may be caused by hemorrhages into the internal capsule, thrombosis and embolism of cerebral vessels, cerebral tumors.
The following types of central paralysis (paresis) are distinguished:
-hemiplegia – affection of half of the body opposite to the site of affection in the CNS;
-monoplegia – affection of one limp;
-paraplegia – simultaneous affection of either the upper or lower limbs;
-tetraplegia – paralysis of the muscles of both sides of the body.
Central paralysis is characterized by the following features:
1) muscular hypertonia – excessive, or spasticity, muscle tone. It manifests itself on attempts to perform passive movements for example, to flex an arm or leg. In this case the investigator feels a characteristic springy resistance. Hence, spastic paralysis;
2) hyperreflexia In central paralysis, there are hyperactive tendon reflexes and an increase in resistance to rapid muscle stretch. Voluntary movements are lost, but tendon reflexes are intensified because the inhibitory influences on the reflexes (coupling in the spinal cord) are weakened as a result of affection of the central apparatus. Atrophy is negligible or does not develop at all.
3) pathological reflexes.
Disinhibition manifests itself also in appearance of pathological reflexes such as:
-Babinski‘s one – extension of the great toe with fanning of the other toes on exciting the sole,
-Bekhterev –Mendel‘s one – flexion of the second to fifth toes when the dorsum of the food is tapped.
Extrapyramidal paralysis (paresis) is characterized not so much by loss of motor functions as by phenomena of loss of synkinetic movements. Extrapyramidal paralysis occurs due to affection in basal ganglia and it is characterized by:
1) loss of synkinetic movements - the movements are generally insufficiently

coordinated: - voluntary movements become difficult and slow (diminished automatism), - a patient appears fixed in his posture and moves like a robot
2) increased plastic muscle tone (rigidity) develops owing to affection of the strio-pallidal region.

Hyperkinesis Hyperkinesis is a disorder characterized by involuntary excessive movements. They are divided into: spinal, pyramidal, extrapyramidal.
Hyperkinesis of spinal origin is characterized by fibrillary contractions, i.e. isolated contractions of various muscle fibers. This is a result of stimulation of a peripheral motor neuron.
Hyperkinesis of pyramidal origin is most commonly manifested in convulsive state. The convulsions may be:
tonic – periodic protracted involuntary muscular contraction;
clonic – intermittent rhythmic involuntary muscular contractions alternating with relaxations. The cause of the convulsions is an excessive excitation of subcortex structures of the brain.
Hyperkinesis of extrapyramidal origin develops as a result of affection in basal ganglia. They include:
-chorea (from the Greek word ―choreia‖ – dance) is characterized by irregular, spasmodic involuntary movements of the limbs or facial muscles (―dancing‖ movement), often accompanied by hypotonia. This syndrome is a complete opposite to Parkinsonism. It is based on morphological disturbances in striatum (putamen and caudate nucleus).
-athetosis (from the Greek word ―athetos‖ – without position) is due to lesions in the lenticular nucleus (putamen and pallidum) is characterized by convulsive, slow movements primarily in distal parts of the extremities (writhing movements).
-ballism is a type of involuntary movement affecting the proximal limb musculature, manifested as jerking, flinging movements of the extremity. This appears due to a lesion of or near the contralateral subthalamic nucleus. Usually only one side of the body is involved, hence hemiballism.
Parkinson's disease (paralysis agitans), a neurologic syndrome, usually results from a lack of neurotransmitter dopamine as a consequent of degenerative, vascular or inflammatory changes in the basal ganglia (in the nigrostriatal system).
Parkinson's disease can be caused by:
- influenza (during World War I),
- idiopathic form in elderly individuals,
- treatment with drugs that block D2 dopamine receptors (some tranquilizer).
Parkinsonism is characterized by:
- akinesia (or poverty of movement)
- hypokinetic feature,
- rigidity (resistance to passive movements) and tremor -hyperkinetic features.
Ataxia Ataxia (from the Greek word ―ataxia‖ – disorder) is manifested in lack of coordination in standing still (static ataxia) or in movement (dynamic ataxia). Ataxia caused by affection of the cerebellum.

Shock is a pathological condition caused by the influence of extremely nocuous challengers on the organism and it is characterized by a critical decrease in tissue perfusion and eventually by dysfunctions of the vital organs.
According to etiology the following types of shock are distinguished:
• hemorrhagic
• traumatic
• burn
• cardiogenic
• septic
• anaphylactic
• hypovolemic
• neurogenic
According to pathogenesis shock is classifies as:
• hypovolemic
• obstructive
• distributive
• cardiogenic

According to modern views shock develops as a result of primary disturbances in neuroendocrine regulation of the organism's functions caused by the action of extremely nocuous challengers on the organism (the neurogenic theory). Hemodynamic disturbances are very important characteristic of shock, but they develop at second time, as a result of disturbances in the CNS activity. This feature distinguishes shock from collapse- the latter starts from disturbances in the systemic circulation.

Collapse or acute vascular insufficiency results from a loss of blood vessel tone and it is characterized by an acute decrease in arterial blood pressure (BP).
Coma (from the Greek word koma meaning a deep sleep) is a condition characterized by deep depression of the CNS, loss of consciousness, loss of reaction to external stimuli (absence of reflexes) and disturbances in vital functions of the organism.
According to etiology coma is divided into:
• neurologic (primary defect in the CNS: trauma, tumor, insult, infection)
• endocrine (diabetic, hypoglycemic, thyrotoxic)
• toxic(exogenous- alcohol, barbiturates; endogenous-uremic, hepatic)
General pathogenetic mechanisms of coma are the following:
• hypoxia and energy deficiency of neurons
• intoxication (alcohol, narcotic substances, urea, ammonia)

Krok 1 mcqs_A is correct answer:

1. A 68-year-old woman can't move the upper and lower right extremities due to insult. Muscle tone of these extremities and reflexes are increased. There are pathological reflexes. What form of the paralysis is it?
A Hemiplegia
B Paraplegia
C Tetraplegia
D Monoplegia

E Dissociation

2. A patient caught a cold after which there appeared facial expression disorder. He cannot close his eyes, raise his eyebrows, bare his teeth. What nerve is damaged?

A Facial
B Vagus
C Trigeminus
D Glossopharyngeal
E Infraorbital

3. An experimental rat with extremity paralysis has no tendon and cutaneous reflexes, muscle tone is decreased, but muscles of the affected extremity maintain their ability to react with excitation to the direct action of continuous current. What type of paralysis is it?

A Flaccid peripheral
B Flaccid central
C Spastiperipheral
D Spastic central
E Extrapyramidal

4. A 28 year old man had a gunshot wound of shin that resulted in an ulcer from the side of the injury. What is the main factor of neurodystrophy pathogenesis in this case?

A Traumatization of peripheral nerve
B Psychical stress
C Microcirculation disturbance
D Infection
E Tissue damage

5. A patient with obliterating atherosclerosis underwent sympathectomy of femoral artery in the region of femoral trigone. What type of arterial hyperemia was induced by the operation?

A Neuroparalytic
B Reactive
C Metaboli
D Neurotonic
E Functional

6.When a patient with traumatic impairment of the brain was examined, it was discovered that he had stopped to distinguish displacement of an object on the skin. What part of the brain was damaged?

A Posterior central gurus
B Occipital zone of the cortex
C Parietal zone of the cortex
D Frontal central gurus
E Frontal zone

7. A patient after hypertension stroke does not have voluntary movements in his right arm and leg with the increased muscle tone in these extremites. What type of dysfunction of nervous system is it? A Central paralysis
B Peripheral paralysis
C Peripheral paresis
D Reflex paresis
E Central paresis

8. A 50 year-old patient was injured on the occipital region of the head. The closed skull's trauma was diagnosed. She was taken to the hospital. The medical examination: deregulation of walking and balance, trembling of arms. What part of brain was injured?

A The cerebellum
B The medulla oblongata
C The mind-brain
D The inter-brain
E The spinal cord

9. A student is thoroughly summarizing a lecture. When his groupmates begin talking the quality of the summarizing worsens greatly. What type of inhibition in the cerebral cortex is the cause of it?

A External
B Protective
C Dying
D Differential
E Delayed

10. A 60-year-old patient was

diagnosed with hypothalamic lateral nuclei stroke. What changes in patient's behavior maybe expected?
A The rejection of food
B Aggressive behaviour
C Depression
D Thirst
E Unsatisfied hunger
11. A 68-year-old woman can not move her upper and lower right extremities after stroke. Muscle tone of these extremities and reflexes are increased. There are pathological reflexes. What form of the paralysis is it?
A Hemiplegia
B Paraplegia
C Tetraplegia
D Monoplegia
E Dissociation
12. As a result of craniocerebral trauma a patient reveals the following symptoms: intention tremor, dysmetry, adiadochokinesis, dysarthria. What structure of the brain is injured?
A Cerebellum
B Striatum
C Motor cortex
D Pale sphere
E Black substance
13. A 60-year-old man felt asleep after cerebral hemorrhage for a long time. Damage of what structure caused this state?
A Reticular formation
B Hippocampus
C Nuclears of the cerebral nerves
D Cortex of the large hemispheres
E Black substance
14. A patient has a transverse disruption of spinal cord below the IV thoracic segment. What changes of respiration will it cause?
A Respiration will stay unchanged
B Respiration will stop
C Respiration will become less frequent
D Respiration will become deeper
E Respiration will become more frequent
15. As a result of spinal-cord trauma a 33 y.o. man has a disturbed pain and temperature sensitivity that is caused by damage of the following tract:
A Spinothalamic
B Medial spinocortical
C Posterior spinocerebellar
D Lateral spinocortical
E Anterior spinocerebellar
16. Glutamate decarboxylation results in formation of inhibitory transmitter in CNS. Name it:
A GABA
B Glutathione
C Histamine
D Serotonin
E Asparagine
17. As a result of damage to certain structures of brainstem an animal lost orientation reflexes. What structures were damaged?
A Quadritubercular bodies
B Medial nuclei of reticular formation
C Red nuclei
D Vestibular nuclei
E Black substance
18. A patient has a haemorrhage into the posterior central gyrus. What type of sensitivity on the opposite side will be disturbed?
A Skin and proprioceptive
B Visual
C Auditory
D Olfactory
E Auditory and visual
19. An experimental rat with extremity paralysis has no tendon and cutaneous reflexes, muscle tone is decreased, but muscles of the affected extremity maintainheir ability to react with

excitation to the direct action of continuous current. What type of paralysis is it?
A Flaccid peripheral
B Flaccid central
C Spastiperipheral
D Spastic central
E Extrapyramidal
20. A patient with disturbed cerebral circulation has problems with deglutition. What part of brain was damaged?
A Brainstem
B Cervical part of spinal cord
C Forebrain
D Interbrain
E Midbrain
21. A 28 year old man had a gunshot wound of shin that resulted in an ulcer from the side of the injury. What is the main factor of neurodystrophy pathogenesis in this case?
A Traumatization of peripheral nerve
B Psychical stress
C Microcirculation disturbance
D Infection
E Tissue damage
22. A 35 year old man got an injury that caused complete disruption of spinal cord at the level of the first cervical segment. What respiration changes will be observed?
A It will come to standstill
B No changes will be observed
C Diaphragmal respiration will be maintained, thoracirespiration will disappear
D Thoracic respiration will be maintained, diaphragmal respiration will disappear
E It will become infrequent and deep
23. In course of an experiment a peripheralsection of vagus of an expiremental animal is being stimulated. What changes will be observed?
A Heart rate fall
B Heart hurry
C Pupil dilation
D Increase of respiration rate
E Bronchi dilation
24. By the decarboxylation of glutamate in the CNS an inhibitory mediator is formed. Name it:
A GABA
B Glutathione
C Histamine
D Serotonin
E Asparagine
25. It has been experimentally proven that the excitation of the motor neurons of flexor muscles is accompanied by the inhibition of the motor neurons of extensor muscles. What type of inhibition underlies this phenomenon?
A Reciprocal
B Inhibition after excitation
C Pessimal
D Feedback
E Lateral
26. A patient got a gunshot wound of hip which damaged the sciatic nerve. Any impact on the affected limb causes severe, excruciating pain. What mechanism of pain is most likely in this case?
A Causalgic
B Reflex
C Phantom
D Endorphin hypofunction
E Enkephalin hypofunction
27. A man sitting with his eyes closed, undergoes electroencephalography. What rhythm will be recorded on the EEG if there is an audible signal?
A Betrhythm
B Theta rhythm
C Delta rhythm
D Alpha rhythm

E Gamma rhythm

28. A male with a lesion of one of the CNS parts has asthenia, muscular dystonia, balance disorder. Which CNS part has been affected?

A Cerebellum
B Black substance
C Reticular formation
D Renuclei
E Vestibular nuclei

29. As a result of a craniocerebral injury a patient has a decreased skin sensitivity. What area of the cerebral cortex may be damaged?

A Posterior central gyrus
B Occipital region
C Cingulate gyrus
D Frontal cortex
E Anterior central gyrus

30. Workers of a conveyor workshop received recommendations for the effective organization of working time and higher working efficiency. What peculiarity of work in this workshop causes the greatest stress for the workers?

A Monotony of work
B State of "operating rest"
C Increased intellectual component
D Increase responsibility
E Social inefficiency of labor

31. A 66-year-old patient with Parkinson disease (Please chose the best treatment)

A Levodopa
B Naloxone
C Celecoxib
D Droperidol
E Chlorpromazine

32. A patient has recurrent attacks of epileptic seizures and stays unconscious between them. In order to stop convulsions the drugs of the following group should be used in the first place:

A Tranquilizers
B Neuroleptics
C Muscle relaxants
D Sedatives
E Analeptics

33. A patient complains that at the bare mention of the tragic events that once occurred in his life he experiences tachycardia, dyspnea and an abrupt rise in blood pressure. What structures of the CNS are responsible for these cardiorespiratory reactions in this patient?

A Cerebral cortex
B Cerebellum
C Lateral hypothalaminuclei
D Specific thalamic nuclei
E Quadrigemina of mesencephalon

34. After a craniocerebral injury a patient is unable to recognize objects by touch. What part of brain has been damaged?

A Postcentral gyrus
B Occipital lobe
C Temporal lobe
D Precentral gyrus
E Cerebellum

35. As a result of a continuous chronic encephalopathy, a patient has developed spontaneous motions and a disorder of torso muscle tone. These are the symptoms of the disorder of the following conduction tract:

A Tractus rubrospinalis
B Tractus corticospinalis
C Tractus corticonuclearis
D Tractus spinothalamicus
E Tractus tectospinalis

36. As a result of a craniocerebral injury, a patient has a decreased skin sensitivity. What area of the cerebral cortex is likely to be damaged?

A Posterior central gyrus
B Occipital region

C Cingulate gyrus
D Frontal cortex
E Anterior central gyrus

37. A patient complaining of pain in the left shoulder-blade region has been diagnosed with miocardial infarction. What kind of pain does the patient have?
A Radiating
B Visceral
C Phantom
D Protopathic
E Epicritic

38. When measuring total muscle action potential it was revealed that it was subject to the power-law relationship. The reason for this is that individual muscle fibers differ in:
A Depolarization threshold
B Diameter
C Conduction velocity
D Resting potential
E Critical level of depolarization

39. In a cat with decerebrate rigidity the muscle tone is to be decreased. This can be achieved
by:
A Destruction of the vestibular nuclei of Deiters
B Stimulation of the otolithic vestibular receptors
C Stimulation of the vestibular nuclei of Deiters
D Stimulation of the vestibulocochlear nerve
E Stimulation of the ampullar vestibular receptors

40. Degenerative changes in posterior and lateral columns of spinal cord (funicular myelosis) caused by methylmalonic acid accumulation occurinpatientswithB12-deficiency anemia. This results in synthesis disruption of the following substance:
A Myelin
B Acetylcholine
C Norepinephrine
D Dopamine
E Serotonin

41. As a result of an injury, the integrity of the anterior spinal cord root was broken. Specify the neurons and their processes that had been damaged:
A Axons of motor neurons
B Motor neuron dendrites
C Axons of sensory neurons
D Dendrites of sensory neurons
E Dendrites of association neurons

42. As a result of a road accident a 37year-old female victim developed urinary incontinence. What segments of the spinal cord had been damaged?
A S2 − S4
B Th1 − Th5
C L1 − L2
D Th2 − Th5
E Th1 − L1

43. Decarboxylation of glutamate induces production of gamma-aminobutyric acid and CO2
A Succinate
B Citric acid
C Malate
D Fumarate
E Oxaloacetate

44. A 49-year old female patient has limitation of left limbs arbitrary movements. Muscular tonus of left hand and leg is overstrained and spasmodic, local tendon reflexes are strong, pathological reflexes are presented. What is the most likely development mechanism of hypertension and hyperreflexia?
A Reduction of descending inhibitory influence
B Motoneuron activation induced by stroke
C Activation of excitatory influence from the focus of stroke

D Activation of synaptic transmission
E Ihibition of cerebral cortex Motoneurons

45. There are several groups of molecular mechanisms playing important part in pathogenesis of insult to cells (stroke?)which contributes to the pathology development. What processes are stimulated by proteinic damage mechanisms?
A Enzyme inhibition
B Lipid peroxidation
C Phospholipase activation
D Osmotic membrane distension
E Acidosis

46. As a result of a trauma a patient has developed traumatic shock that led to the following disorders: AP is 140/90 mm Hg, Ps is 120 bpm. The patient is fussy, talkative, pale. Such state relates to the following shock phase:
A Erectile
B Latent period
C Terminal
D Torpi
E -

47. Rats being under stress have muscular hypertonia and high arterial pressure, high glucose concentration in blood and intensified secretion of corticotropin and corticosteroids. In what stress phase are these animals?
A Antishock phase
B Exhaustion
C Shock phase
D Erectile
E Terminal

48. A 26 year old man is in the torpid shock phase as a result of a car accident. In blood: 3,2*109/l. What is the leading mechanism of leukopenia development?
A Redistribution of leukocytes in bloodstream
B Leikopoiesis inhibition
C Disturbed going out of mature leukocytes from the marrow into the blood
D Lysis of leukocytes in the blood-forming organs
E Intensified elimination of leukocytes from the organism

49. Purulent endometritis developed in a woman after delivery. Treating with antibiotics inhibitors of murein synthesis was ineffective. Wide spectrum bactericidal antibiotic was administered to her. In 6 hours temperature rapidly increased up to 400C with shiver. Muscle pains have appeared. BP dropped down to 70/40mmHg. Oligura has developed. What is the main reason for the development of this condition?
A Endotoxic shock
B Toxic effect of preparation
C Internal bleeding
D Anaphylactic shock
E Bacteremia

50. A 16 year-old patient got numerous traumas in automobile accident. Now the patient is having a shock. AP - 80/60 mmHg. daily urine volume 60-80 ml. What pathogenic mechanism leads to kidneys function violation?
A Decreased hydrostatic pressure inglomerular capillaries
B Increased osmotic pressure inglomerular capillaries
C Increased pressure in Bowman's capsule
D Increase vasopressin blood concentration
E Trauma of the urinary bladder

51. A highly injured person has gradually died. Please choose the indicator of biological
death:
A Autolysis and decay in the cells
B Disarray of chemical processes

C Loss of consciousness
D Absence of palpitation anbreathing
E Absence of movements
52. A patient who suffers from acute myocarditis has clinical signs of cardiogenic shock. What of the under-mentioned pathogenetic mechanisms plays the main part in shock development?
A Disturbance of pumping ability of heart
B Depositing of blood in organs
C Reduction of diastolic flow to the heart
D Decrease of vascular tone
E Increase of peripheral vascular resistance
53. A driver who got a trauma in a road accident and is shocked has reduction of daily urinary output down to 300 ml. What is the main pathogenetic factor of such diuresis change?
A Drop of arterial pressure
B Drop of oncotic blood pressure
C Increased vascular permeability
D Decrease number of functioning glomerules
E Secondary hyperaldosteronism
54. Rats being under stress have muscular hypertonia and high arterial pressure, high glucose concentration in blood and intensified secretion of corticotropin and corticosteroids. In what stress phase are these animals?
A Antishock phase
B Exhaustion
C Shock phase
D Erectile
E Terminal
55. As a result of a home injury, a patient suffered a significant blood loss, which led to a fall in blood pressure. Rapid blood pressure recovery after the blood loss is provided by the following hormones: A Adrenaline, vasopressin
B Cortisol
C Sex hormones
D Oxytocin
E Aldosterone
56. A 62-year-old patient has been hospitalized due to massive cerebral hemorrhage. Blood pressureis70/30mmHg, heart rateis120/min., respiratory rateis4/min., unconscious, no response to external stimuli. Such condition can be determined as:
A. Coma
B. Shock
C. Collapse
D. Stress
E. Agony
57. A patient with signs of emotional lability that result in troubled sleep has been prescribed nitrazepam. Specify the sleepinducing mechanism of this drug:
A. GABA-ergic system activation
B. Blockade of opiate receptors
C. Inhibition of stimulating amino acids
D. H1-histamine receptors stimulation
E. Supression of serotonergic neurotransmission

Recommended literature:

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