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METHODICAL RECOMMENDATIONS FOR PRACTICAL TRAINING AND INDEPENDENT WORK OF RESIDENTS IN THE DISCIPLINE "DIABETOLOGY AND EMERGENCY ENDOCRINOLOGY"

31.05.01 «General Medicine»

Full-time education

Educational-methodological recommendations

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Educational and methodological recommendations for the discipline "Diabetology and emergency endocrinology", profile "Specialty" contain materials for the preparation and conduct of practical classes on diabetes and emergency endocrinology for students of the Faculty of Medicine, as well as topics and a set of tasks for independent work of students, teaching and information support of the discipline.

CONTENT

INTRODUCTION

«Diabetology and emergency endocrinology» refers to the discipline for choosing the optional part of block 1 of the specialty according to the Federal State Educational Standard 3+ of Higher Education (2016) and the Working Curriculum of the specialty 31.05.01 “General Medicine, approved by the rector of Ulyanovsk State University.

The objectives of mastering the discipline:
the formation and development in students of a holistic system of theoretical and practical knowledge and skills in diabetology and emergency endocrinology.

Tasks of mastering the discipline:
- know the etiology, pathogenesis, clinical symptoms of endocrinological diseases, their complications and emergency conditions;
- master the methods of examination, diagnosis and differential diagnosis of endocrinological diseases, their complications and emergency conditions;
- master the methods of assistance in emergency endocrinological conditions;
- to master the technique of organizing and conducting clinical examination of patients with endocrine diseases with the aim of timely prevention of their complications.

Forms of lectures and seminars, developed based on the "Regulation on the contact work of students with the teacher in the implementation of the educational process for educational programs of higher education." Types of independent work, forms and types of control of independent work are developed based on the "Regulation on the organization of independent work of students" of Ulyanovsk State University.

1. TRAINING AND METHODOLOGICAL RECOMMENDATIONS FOR PRACTICAL ACTIVITIES

Practical classes - a type of training aimed at developing students' independence and acquiring skills, the ability to actively participate in creative discussions, draw conclusions, reasonedly express their opinion and defend it. These training sessions deepen, expand, detail the knowledge gained at the lecture.

1.1. Themes of practical classes

Section 1. Diabetes mellitus

Theme 1. Differential diagnosis of hyperglycemia. Diagnosis and treatment of diabetes
Questions on the topics of the section (for discussion in the lesson):
1. Etiology, pathogenesis, clinical presentation of type 1 and type 2 diabetes.
2. Classification of diabetes mellitus: diagnostic criteria for diabetes mellitus, impaired fasting glucose and carbohydrate tolerance.
3. Clinical, hormonal and immunological differences between different types of diabetes.
4. Risk factors for diabetes, diet therapy, physical activity.
5. Treatment of type 2 diabetes. Classification and duration of insulin action, indications for insulin therapy.
6. Schemes of insulin therapy, calculation of doses of insulin.
7. The mechanism of action, indications and contraindications for groups of tablets of sugar-lowering drugs. Rational and irrational combinations.
8. Clinical examination, prognosis, medical and social examination of diabetes mellitus.

Theme 2. Diabetic microangiopathy. Diabetic retinopathy, nephropathy. Diabetic neuropathy
Questions on the topics of the section (for discussion in the lesson):
1. Diabetic nephropathy: etiology, pathogenesis, classification, clinic, treatment, prevention.
2. Microalbuminuria, the value of its definition. Stages of chronic kidney disease.
3. Diabetic retinopathy: etiology, pathogenesis, classification, clinic, treatment, prevention.

4. Changes in the vessels of the retina at various stages of diabetic retinopathy.
5. Diabetic polyneuropathy: etiology, pathogenesis, classification, treatment, prevention.
6. Vegetative forms of diabetic neuropathy: diagnosis, treatment.

Theme 3. Macroangiopathy. Diabetic foot. Diabetes mellitus and arterial hypertension

Questions on the topics of the section (for discussion in the lesson):

1. Risk factors for the development of macrovascular complications in diabetes mellitus. 2. Diabetic angiopathy of the lower extremities: etiology, pathogenesis, classification, clinic, treatment, prevention.
3. Diabetic foot syndrome: etiology, pathogenesis, classification, clinic, treatment approaches, prevention.
4. Features of the course and treatment of coronary heart disease in patients with diabetes mellitus.
5. ACS in diabetes mellitus, management tactics.
6. Features of the course and treatment of arterial hypertension in patients with diabetes mellitus.

Theme 4. Diabetes mellitus and pregnancy. Diabetes mellitus and surgical pathology

Questions on the topics of the section (for discussion in the lesson):

1. Contraindications to pregnancy in patients with diabetes
2. Criteria for gestational and manifest diabetes
3. Delivery tactics for gestational diabetes.
4. Management features for patients with diabetes during pregnancy and after the birth.
5. Features of delivery in the manifest diabetes.
6. Features of the treatment of patients with diabetes mellitus depending on the volume of surgical intervention.
7. Management of patients in the perioperative period, the target level of glycemia.

Theme 5. Emergency conditions for diabetes

Questions on the topics of the section (for discussion in the lesson):

1. Hypoglycemic coma: etiology, pathogenesis, clinical features, emergency therapy.

Theme 7. 2. Hyperosmolar coma: etiology, pathogenesis, clinic, emergency therapy.
3. Lactacidemic coma: etiology, pathogenesis, clinic, emergency therapy.
4. Diabetic ketoacitodic coma: etiology, pathogenesis, clinic, emergency therapy.
5. Differential diagnosis of com in diabetes.
6. Prevention of emergency conditions in diabetes.

Theme 6. Differential diagnosis and treatment of diabetes

Questions on the topics of the section (for discussion in the lesson):

1. Clinical manifestations of cerebral coma.
2. Exotoxic coma (carbon monoxide poisoning): etiology, clinic, treatment.
3. Endotoxic coma (uremic, hepatic): etiology, clinic, treatment.
4. Impairment of consciousness as a result of epilepsy.
5. Differential diagnosis between exo- and endotoxic comas.
6. Differential diagnosis between coma of different etiologies.

Section 2. Thyroid Disease

Emergency conditions for thyroid diseases

Questions on the topics of the section (for discussion in the lesson):

1. Etiology, pathogenesis, main clinical symptoms of thyrotoxic crisis.
2. The tactics of assisting with thyrotoxic crisis.
3. Etiology, pathogenesis, main clinical symptoms of hypothyroid coma.
4.Tactics for assisting with hypothyroid coma.
5. Differential diagnosis of thyrotoxic and hypothyroid com.
6. Prediction and prevention of thyrotoxic and hypothyroid com.
7. Heart damage in patients with thyroid pathology.

Section 3. Adrenal Diseases

Theme 8. Emergency conditions for adrenal gland diseases

Questions on the topics of the section (for discussion in the lesson):
1. Mechanisms for the development of hypoadrenal and catecholamine crises.
2. Clinic of hypoadrenal and catecholamine crises.
3. Emergency therapy, prognosis and prevention of hypoadrenal crisis.
4. Types and emergency treatment of catecholamine crisis.
5. Differential diagnosis of hypoadrenal and catecholamine crises.
6. ECG - signs of hypokalemia and hyperkalemia.
7. Arterial hypertension in patients with adrenal gland diseases.

Section 4. Disorders of mineral metabolism

Theme 9. Emergency conditions for disorders of mineral metabolism

Questions on the topics of the section (for discussion in the lesson):
1. Etiology and mechanisms of hypocalcemic crisis.
2. Symptoms of hypocalcemic crisis.
3. Emergency therapy of hypocalcemic crisis
4. ECG - signs of hypocalcemia and hypercalcemia
5. Etiology, pathogenesis and symptoms of hypercalcemic crisis.
6. Emergency therapy for hypercalcemic crisis.
7. Laboratory and instrumental diagnosis of hypo- and hyperparathyroidism

1.2. DIABETIC KETOACIDOSIS (DKA, DIABETIC KETOACIDOTIC COMA)

DKA - requiring acute hospitalization, acute decompensation of diabetes, with hyperglycemia (plasma glucose> 13 mmol / L * in adults and> 11 mmol / L in children), hyperketonemia (> 5 mmol / L), ketonuria (≥ ++), metabolic acidosis (pH <7.3, bicarbonate level <15 mmol / L) and varying degrees of impaired consciousness or without it.

The main reason: absolute or pronounced relative insulin deficiency.

Provoking factors:
- intercurrent diseases, operations and injuries;
- skipping or canceling insulin by patients, errors in the technique of injections, malfunctioning of means for administering insulin;
- insufficient self-control of glycemia, non-compliance by patients with the rules for self-increasing insulin doses;
- manifestation of diabetes, especially type 1;
- medical errors: untimely appointment or inadequate dose adjustment of insulin;
- chronic therapy with steroids, atypical antipsychotics, some targeted anticancer drugs, SGLT-2 inhibitors, etc.
- pregnancy.

Clinical picture: polyuria, thirst, signs of dehydration and hypovolemia (decreased blood pressure,oligo- and anuria are possible), weakness, lack of appetite, nausea, vomiting, smell exhaled acetone, headache, shortness of breath, in a terminal state Kussmaul's breathing, impaired consciousness - from drowsiness, lethargy to coma. Often - abdominal syndrome (false "acute abdomen", diabetic pseudoperitonitis) - abdominal pain, vomiting, tension and soreness of the abdominal walls, paresis of peristalsis or diarrhea.

Laboratory changes: diagnosis and differential diagnosis

General clinical blood analysis	Leukocytosis: <15000 - stressful, > 25000 - infection
Urinalysis	Glucosuria, ketonuria, proteinuria (intermittent)
Biochemical analysis blood	Hyperglycemia, hyperketonemia Increased creatinine (fickle; more likely to indicate transient "prerenal" renal hypovolemia

	deficiency) Transient increase in transaminases and creatine phosphokinase (proteolysis) Na + more often normal, less often reduced or increased, K + more often normal, less often, with CKD C3-5 and "Prerenal" (hypovolemic) renal failure can be increased
acid-base balance	Decompensated metabolic acidosis

Treatment

Main components:

1. The elimination of insulin deficiency;
2. The fight against dehydration and hypovolemia;
3. Recovery of electrolyte balance and acid-base balance;
4. Treatment of concomitant diseases and conditions that provoked DKA.

At the prehospital stage or in the ward

1. Express analysis of glycemia and analysis of any portion of urine on ketone bodies;
2. 0.9% solution of intravenous sodium chloride drip at a rate of 1 l / h.

In the intensive care unit or intensive care unit

Laboratory monitoring.

- Express analysis of glycemia - hourly until the level of plasma glucose (GP) decreases to 13 mmol / l, then 1 time in 3 hours.
- Urinalysis for ketone bodies - 2 times a day for the first 2 days, then 1 time per day.
- General analysis of blood and urine: initially, then 1 time in 2 days.
- Na +, K + serum: at least 2 times a day, if necessary, every 2 hours until resolution of DKA, then every 4-6 hours until complete recovery.
- Calculation of effective osmolarity.
- Biochemical blood test: urea, creatinine, chlorides, bicarbonate, preferably lactate - initially, then 1 time in 3 days, if necessary - more often.
- Gas analysis and pH (possible venous blood) 1-2 times a day until the normalization of the acid base.

Instrumental studies and events:

- catheterization of the central vein.
- hourly control of urine output; control of central venous pressure (CVP) (or another method for assessing volley), blood pressure, heart rate and body temperature every 2 hours; ECG at least 1 time per day or ECG monitoring; pulse oximetry.
- search for a possible infection site by common standards.

Therapeutic measures

Insulin therapy - a mode of small doses (the best management of glycemia and lower risk of hypoglycemia and hypokalemia than in high dose mode).

1.Intravenous insulin therapy:

1. The initial dose of Short acting insulin: 0.1 - 0.15 IU / kg of real body weight intravenous infusion bolus. The required dose is collected in an insulin syringe, 0.9%NaCl solution is taken up to 1 ml and injected very slowly (2-3 minutes). If a bolus dose of insulin is not administered, then the initial rate of continuous infusion should be 0.1 - 0.15 U / kg / h.
2. In the following hours: Short acting insulin at 0.1 U / kg / h in one of the options:

• Option 1 (via infusomat): continuous infusion of Short acting insulin 0.1 U / kg / h. Preparation of the infusion mixture: 50 U Short acting insulin + 2 ml of a 20% solution of albumin or 1 ml the patient's blood (to prevent insulin sorption in the system, which accounts for 10-50% of the dose); the volume was adjusted to 50 ml with 0.9% NaCl solution.

• Option 2 (in the absence of an infusomat):a solution with a concentration of Short acting insulin 1IU / ml or 1 IU / 10 ml of a 0.9% intravenous NaCl solution in drip (+ 4 ml of a 20% solution albumin / 100 ml of a solution to prevent insulin sorption).Disadvantages:dose

adjustment of Short acting insulin by the number of drops or ml of the mixture requires constant staff presence and careful counting; it is difficult to titrate small doses.

• Option 3 (more convenient in the absence of an infusomat): Short acting insulin intravenous bolus (slowly) 1 time / hour with a syringe into the injection port of the infusion system. The duration of the pharmacodynamic effect of short acting insulin in this case is up to 60 minutes.

Advantages: no insulin adsorption (add albumin or blood to the solution does not necessary), accurate accounting and correction of the administered dose, lesser staffing, than in option 2.

Intramuscular insulin therapy is performed if intravenous access is not possible: loading dose of short-acting insulin - 0.2 U / kg, then intramuscularly at 5-10 U / h. Disadvantages: with violation of microcirculation (collapse, coma) short-acting insulin is worse absorbed; small the length of the needle of the insulin syringe makes intramuscular injection difficult; 24 intramuscular injections per day uncomfortable for the patient. If 2 hours after the start of intramuscular therapy, glycemia does not decreases, switch to intravenous administration.

With a mild form of DKA in the absence of hemodynamic and consciousness disturbances and with the possibility of leaving the patient in the usual (non-resuscitation) ward in some cases, subcutaneous administration of insulin according to the basal bolus principle is permissible therapy, with the introduction of extended-acting insulin 1 or 2 times a day and short-acting insulin at least 1 time in 4 hours.

The rate of decrease in plasma glucose is optimally 3 mmol / l /h and not more than 4 mmol/l /h (danger reverse osmotic gradient between the intra- and extracellular space and cerebral edema); on the first day, plasma glucose levels should not be reduced to less than 13-15 mmol/l.

If in the first 2-3 hours the plasma glucose does not decrease by at least 3 mmol from the initial	-Double the next dose of short-acting insulin -Check for adequate hydration
If plasma glucose is reduced by 3-4 mmol / l /h	Continue at the same dose.
If the rate of decrease in plasma glucose is> 4, but ≤ 5 mmol / l / h.	The next dose of short-acting insulin should be halved.
With a decrease in plasma glucose to 13-14 mmol / L.	The next dose of short-acting insulin should be halved.
If the rate of decrease in plasma glucose> 5 mmol / l / h	The next dose of short-acting insulin must be skipped. Continue hourly determination of plasma glucose.

Transfer to subcutaneous insulin therapy: with improvement in condition, stable hemodynamics, plasma glucose levels ≤12 mmol / L and pH> 7.3 switch to subcutaneous administration of short-acting insulin every 4 to 6 hours in combination with extended-acting insulin .. If DKA developed on the background of taking ISGLT-2, their further use is contraindicated.

2.Rehydration

Solutions:

• 0.9% NaCl solution (at the level of corrected Na + plasma * <145 mmol / L);

• At a plasma glucose level ≤ 13 mmol / L: 5–10% glucose solution (+ 3–4 IU short-acting insulin) on every 20 g of glucose).

• Colloidal plasma substitutes (with hypovolemia - systolic blood pressure below 80 mm Hg or CVP (central venous pressure) below 4 millimetres of water column.)

• Advantages of other crystalloid solutions (Ringer, Ringer-Lock, Hartmann et al.) before a 0.9% NaCl solution, have not been proven in the treatment of DKA

* Corrected Na + = measured Na + + 1.6 (glucose mmol / l - 5.5)

Sodium Correction = measured Na + [(glucose level - 100) x 0.016]

Rehydration rate: Total water deficiency in the body with DKA: 5–10% of body weight, or 50-100 ml / kg of real body weight. This volume of fluid should be reimbursed for 24 - 48 hours. On the 1st day, at least half of the fluid deficiency should be replenished.The initial rate of rehydration using 0.9% NaCl solution: in the 1st hour - 1-1.5 l, or 15 to 20 ml / kg body weight.

Further rehydration rate is adjusted in depending on the clinical signs of dehydration, blood pressure, hourly diuresis and CVP: with CVP <4 cm H2O , 1 liter of liquid is introduced per hour, with a CVP of 5 -12 cm H2O - 0.5 l / h, above 12 cm H2O- 250-300 ml / h.
It is possible to use a slower rehydration mode: 2 l in the first 4 hours, still 2 liters in the next 8 hours, in the future - 1 liter for every 8 hours.
If rehydration with DKA begins with a 0.45% NaCl solution (with hypernatremia>145 mmol / l), then the infusion rate is less, about 4-14 ml / kg per hour.

3.Recovery of electrolyte disturbances (potassium)

Intravenous infusion of potassium begins simultaneously with the introduction of insulin from the calculation:

Plasma K + (mmol / L)	The rate of introduction of potassium chloride (g in h):
Unknown	Begin no later than 2 hours after the start of insulin therapy, under the control of an electrocardiogram and diuresis, at a speed of 1.5 g per hour.
< 3	Slow down or stop insulin administration and administer 2.5-3 g per hour.
3-3,9	2 g per hour
4-4,9	1,5 g per hour
5-5,5	1,0 g per hour
more than 5	Do not administer potassium preparations

Potassium infusion requiring a high rate of administration should be carried out in the central vein.

4.Metabolic Acidosis Correction

The etiological treatment of metabolic acidosis in DKA is insulin.
Indications for the introduction of sodium bicarbonate: blood pH ≤ 6.9 or standard bicarbonate <5 mmol / L. 4 g of sodium bicarbonate is introduced (200 ml of a 2% solution intravenously slowly for 1 h), the maximum dose is not more than 8 g of bicarbonate (400 ml of a 2% solution per 2 hours). **Without determination of pH / acid-base balance, the introduction of bicarbonate is contraindicated!**
DKA resolution criteria: plasma glucose <11 mmol / L and at least two out of three
acid-base balance indicators: bicarbonate ≥ 18 mmol / l, venous pH ≥ 7.3, anionic difference ≤ 12 mmol / l. Small ketonuria may persist for some time.
Food. After full recovery of consciousness, ability to swallow, in the absence of nausea and vomiting - fractional, sparing nutrition with enough carbohydrates and moderate the amount of protein (cereals, mashed potatoes, bread, broth, scrambled eggs, meatballs from lean meat, diluted juices without added sugar), with additional subcutaneous the introduction of short-acting insulin in 1-2 units per 1 XE. After 1-2 days from the start of a meal, in lack of acute gastrointestinal pathology, - the transition to normal nutrition.

Frequent Concomitant Therapy

• Broad-spectrum antibiotics (high probability of infections as causes of DKA).
•The introduction of low molecular weight heparin in a prophylactic dose in the absence contraindications (high probability of thrombosis due to dehydration).

1.3.HYPEROMOSOLAR COMA (The hyperosmolar hyperglycemic state (HHS))

- acute decompensation of diabetes mellitus, with pronounced hyperglycemia (usually, plasma glucose levels> 35 mmol / l), high plasma osmolarity and pronounced dehydration, in the absence of ketosis and acidosis.
- acute decompensation of diabetes mellitus, with pronounced hyperglycemia (usually, plasma glucose levels> 35 mmol / l), high plasma osmolarity and pronounced dehydration, in the absence of ketosis and acidosis.

The main reason is pronounced relative insulin deficiency and severe dehydration.
Provoking factors: vomiting, diarrhea, fever, other acute diseases (myocardial infarction, pulmonary thromboembolism, stroke, massive bleeding, extensive burns, renal failure, dialysis, surgery, injuries, heat and sunstroke, the use of diuretics, concomitant diabetes insipidus; incorrect medical recommendations (prohibition of sufficient fluid intake during thirst); advanced age; administration of glucocorticoids, sex hormones, somatostatin analogues, etc., endocrinopathy (acromegaly, thyrotoxicosis, Cushing's disease).
The **Clinical picture:** severe polyuria (often later oligo- and anuria), severe thirst (in elderly may be absent), weakness, headaches; severe symptoms dehydration and hypovolemia: reduced skin turgor, softness of the eyeballs with palpation, tachycardia, later - arterial hypotension, then increase circulatory failure, up to collapse and hypovolemic shock; drowsiness, stupor and coma. There is no smell of acetone and Kussmaul breathing.
A feature of the GHS clinic is polymorphic neurological symptoms (convulsions, dysarthria, bilateral spontaneous nystagmus, hyper- or hypotonic muscles, paresis and paralysis; hemianopsia, vestibular disorders, etc.), which does not fits into any clear syndrome, is variable and disappears during normalization osmolarity.
A differential diagnosis with cerebral edema is crucial to avoid ERRORAL diuretic purpose INSTEAD OF REHYDRATION.
Laboratory changes: diagnostics and differential diagnostics.

General clinical blood analysis	Leukocytosis: <15000 - stressful, > 25000 - infection
General urine analysis	Massive glucosuria, proteinuria (intermittently); no ketonuria
Biochemical blood analysis	Extremely high hyperglycemia, no hyperketonemia High plasma osmolarity:> 320 mosmol / L1 Increased creatinine (inconstant; most often indicates transient renal failure caused by hypovolemia) the level of adjusted Na + is increased, the level of K + is normal, less often reduced, with CKD C3-5 and "Prerenal" (hypovolemic) renal failure it can be increased
acid-base balance	No acidosis: pH> 7.3, bicarbonate> 15 mmol/ L, anionic difference<12 mmol / l

Calculation of plasma osmolarity: 2(Na+K)+glucose (in mmol/L) (normal 285-295 mosmol/L).
Treatment
The main components:
1. The fight against dehydration and hypovolemia;
2. The elimination of insulin deficiency;
3. restoration of electrolyte balance,
4. identification and treatment of diseases that provoked HHS and its complications.
At the prehospital stage or in the emergency room:
1. Express analysis of plasma glucose and any portion of urine on ketone bodies;
2. 0.9% NaCl solution intravenously at a rate of 1 l / h.
In the intensive care unit or intensive care unit:
Laboratory monitoring As with DKA, with the following features:
1. Calculation of adjusted Na + (to select a solution for infusion).
2. Desirable - determination of the level of lactate (frequent combined presence lactic acidosis).
3. Coagulogram (minimum - prothrombin time).

Instrumental research as with DKA. If after a clear decrease in hyperosmolarity, neurological symptoms do not decrease, computed tomography of the brain is recommended.

Therapeutic measures

1.Rehydration

As with DKA, with the following features:

• in the first hour - 1 liter of 0.9% NaCl solution, then - depending on the level of Na + - with adjusted Na +> 165 mmol / L: saline solutions contraindicated, rehydration begins with a 5% glucose solution;

- with adjusted Na + 145–165mmol /L: rehydration is carried out 0.45%(hypotonic)NaC lsolution;

- when the adjusted Na + decreases to <145 mmol / L,they switch to 0.9%NaCl solution. In case of hypovolemic shock(blood pressure <80/50 mm Hg),it is first very quickly administered intravenously 1 l of a 0.9% NaCl solution or colloidal solutions.

Rehydration rate:1st hour - 1–1.5L of liquid,2nd and 3rd hours - 0.5–1 L,then 0.25–0.5 L(under the control of the CVP; the volume of fluid introduced per hour should not exceed hourly urine output by more than 0.5–1l).

2.Features of insulin therapy:

• Given the high sensitivity to insulin in HHS, at the beginning of the infusion insulin is not administered or is administered in very small doses - 0.5–2 units / h, maximum 4 units / h intravenously.

If after 4–5 hours from the start of the infusion, after partial rehydration and reduction level of Na +, pronounced hyperglycemia persists, switch to the regime insulin dosing recommended for the treatment of DKA.

If, simultaneously with the start of rehydration of a 0.45% (hypotonic) solution NaCl mistakenly administered higher doses of short-acting insulin (≥ 6 U / h), possibly a rapid decrease in plasma osmolarity with the development of pulmonary edema and cerebral edema.

Plasma glucose should not be reduced faster than 4 mmol / l / h, plasma osmolarity no more than 3-5 mosmol / l / h, and sodium level - no more than 10 mmol / lday.

3. Recovering Potassium Deficiency. It is carried out according to the same principles as with DKA. Potassium deficiency is usually greater expressed than with DKA.

4. **Frequent concomitant therapy**

Direct anticoagulants (unfractionated or low molecular weight heparin) due to the high probability of thrombosis and thromboembolism.

1.4.LACTIC ACIDOSIS (LACTATACIDOSIS)

Lactic acidosis - metabolic acidosis with a large anionic difference (≥10 mmol / L) and blood lactic acid> 4 mmol / L (some determinations> 2 mmol / l).

The main reason is increased formation and reduced utilization of lactate and hypoxia.

Provoking factors:

• Reception of biguanides, severe decompensation of diabetes, any acidosis, including DKA.

• Renal or liver failure.

• Alcohol abuse.

• intravenous the introduction of radiopaque agents.

• Tissue hypoxia (CHF, cardiogenic shock, hypovolemic shock, obliterating diseases of peripheral arteries, CO poisoning; syndrome compression, burns, injuries, extensive purulent-necrotic processes in the soft tissues, severe respiratory diseases, anemia, acute mesenteric ischemia, asphyxia).

• Acute stress, severe late complications of diabetes, senile age, severe general condition, advanced stages of malignant neoplasms and hemoblastosis.

• Overdose of nucleoside analogues, β-adrenergic agonists, cocaine, diethyl ether, propofol, isoniazid, strychnine, sulfasalazine, valproic acid, linezolid, paracetamol, salicylates; poisoning with alcohols, glycols; excessive parenteral administration of fructose, xylitol or sorbitol.

• Pregnancy.

Clinical picture: myalgia, non-stopping analgesics, heart pain,not stopping with antianginal drugs, abdominal pains, headaches, nausea, vomiting, weakness, adynamia, arterial hypotension, tachycardia, shortness of breath,subsequently Kussmaul's breathing, impaired consciousness from drowsiness to coma.

Laboratory changes: diagnosis and differential diagnosis

Biochemical blood analysis	The diagnosis of lactic acidosis is confirmed at a concentration of lactate> 5.0 mmol / L and pH <7.35 and very likely at lactate concentration 2.2–5 mmol / L in combination with arterial blood pH <7.25. Blood for determination of lactate, store in the cold for no more than 4 hours Glycemia: any, often hyperglycemia, Often - increased creatinine, hyperkalemia
acid-base balance	Decompensated metabolic acidosis: pH <7.3, plasma bicarbonate level ≤ 18 mmol / L, anionic the difference is 10-15 mmol / l (with correction for hypoalbuminemia)

Treatment

Main components.

1. Reduced lactate formation.
2. Excretion of lactate and metformin from the body.
3. The fight against shock, hypoxia, acidosis, electrolyte disorders.
4. Elimination of provoking factors.

At the prehospital stage: intravenous infusion of 0.9% NaCl solution.

In the intensive care unit or intensive care unit

Laboratory and instrumental monitoring:

carried out, as with DKA, with more frequent monitoring of lactate levels.

Therapeutic measures

1.Reduced lactate production:-short-acting insulin at 2–5 U / h iv, 5% solution glucose at 100 - 125 ml per hour.

2. Removal of excess lactate and biguanides (if used) (only effective measure for the elimination of metformin - hemodialysis with lactate-free buffer).

• In case of acute overdose of metformin - activated carbon or other sorbent inside.

3.Acid-base balance recovery

- Ventilation in hyperventilation mode to eliminate excess CO2 (target: pCO2 25-30 mm Hg. Art.).

• Introduction of sodium bicarbonate - only at pH <6.9, very carefully (danger a paradoxical increase in intracellular acidosis and lactate production), not more than 100 ml of a 4% solution once, iv slowly, followed by an increase ventilation to remove excess CO generated during iv bicarbonate.

4.The fight against shock and hypovolemia

According to the general principles of intensive care.

1.5.HYPOGLYCEMIA and HYPOGLYCEMIC COMA

Classification:

Level 1: plasma glucose values from 3.0 to <3.9 mmol / L (with symptoms or without) in patients with diabetes receiving glucose-lowering therapy, indicate a risk the development of hypoglycemia and require the start of measures to stop hypoglycemia

regardless of the presence or absence of symptoms.
Level 2: plasma glucose values <3.0 mmol / L, with or without symptoms -
clinically significant hypoglycemia requiring immediate relief.
Level 3: severe hypoglycemia - hypoglycemia within the above
range with such a violation of cognitive functions (including loss of consciousness, i.e. hypoglycemic coma), which requires the help of another person to stop.
Main reason: excess insulin in the body relative to intake carbohydrates from the outside (with food) or from endogenous sources (glucose production liver), as well as with accelerated utilization of carbohydrates (for example, muscle work).
Provoking factors:
• Directly associated with drug hypoglycemic therapy:
- an overdose of insulin, sulfonylurea or clay preparations: error patient, an error in the function of the insulin pen, glucometer, intentional overdose; doctor's error (target glycemia level is too low, too high doses);
- change in the pharmacokinetics of insulin or sugar-lowering tablets: change of drug, renal and liver failure, high titer of antibodies to insulin, abnormal injection technique, drug interactions of sulfonylureas;
- increased sensitivity to insulin: prolonged physical activity,early postpartum period, adrenal or pituitary insufficiency.
• Nutrition: skipping or insufficient XE, alcohol, restriction nutrition to reduce body weight (without corresponding dose reduction of sugar-lowering drugs); slowing down gastric emptying (with autonomous neuropathy), vomiting, malabsorption syndrome.
• Pregnancy (first trimester) and breastfeeding.
Clinical picture: • Vegetative symptoms: palpitations, trembling, pallor, sweating, mydriasis, nausea, severe hunger, anxiety, anxiety, aggressiveness.
• Neuroglycopenic symptoms: weakness, impaired concentration, headache pain, dizziness, drowsiness, paresthesia, visual impairment, confusion, disorientation, dysarthria, impaired coordination of movements, confusion consciousness, coma; cramps and other neurological symptoms are possible.
Laboratory changes: diagnosis and differential diagnosis
Blood analysis
Plasma glucose <3.0 mmol / L
(with coma - usually <2.2 mmol / L)
Treatment
Mild hypoglycemia (not requiring the assistance of another person)
Reception of 1-2 bread units of quickly acquired carbohydrates: sugar (2-4 pieces on 5 g, is better dissolve) or honey or jam (1–1.5 tablespoons), or 100–200 ml of fruit juice, or 100–200 ml sugar-lemonade, or 4-5 large glucose tablets (3-4 g each), or 1-2 tubes with carbohydrate syrup (each 5-10 g of carbohydrates). If hypoglycemia does not stop after 15 minutes, repeat treatment.
If hypoglycemia is caused by long-acting insulin, especially at night time, then additionally eat 1-2 bread units of slowly digestible carbohydrates (bread, porridge and etc.).
Severe hypoglycemia (requiring the help of another person, with loss of consciousness or without it).
Lay the patient on his side, free the oral cavity from food debris. Upon loss consciousness can not be poured into the oral cavity sweet solutions (danger of asphyxiation!).
• Intravenously inject 40 - 100 ml of a 40% glucose solution until complete recovery
consciousness.
• Alternative - 1 mg (small children 0.5 mg) glucagon subcutaneously or intramuscularly (administered relative of the patient).
• If consciousness does not recover after intravenous administration of 100 ml of a 40% solution glucose - start intravenous injection of a 5–10% glucose solution and to hospitalize.
• If the cause is an overdose of an sugar-lowering tablets with a long duration actions, i/v drip of

5-10% glucose solution continue until normalization of glycemia and complete elimination of the drug from the body.

1.6. HYPOTHYROID COMA

Hypothyroid coma is an extremely serious complication of hypothyroidism, manifested in a sharp exacerbation of all the symptoms of the disease, an increase in hypothermia, stupor, loss of consciousness against the background of hypoventilation and hypercapnia, in patients who do not receive adequate replacement therapy.

Epidemiology

Hypothyroid coma most often appears in patients with severe hypothyroidism in the elderly or senile, in most cases in women aged 60-80 years. The development of hypothyroid coma is most likely in the cold season. True hypothyroid coma is extremely rare, it is an extremely serious condition, mortality during its development is 50-80%.

Etiology

Untimely or inadequate treatment of hypothyroidism is most often a consequence of the late diagnosis of the disease as a result of the atypical clinical picture of the disease. Difficulties in the diagnosis of hypothyroidism more often arise with a monosymptomatic course of hypothyroidism in elderly patients, “masks” of hypothyroidism that can mimic a variety of pathologies:

1. Therapeutic (polyarthritis, polyserositis, myocarditis, IHD, neurocirculatory dystonia, hypertension, arterial hypotension, pyelonephritis, hepatitis, biliary tract hypokinesia, colon hypokinesia).
2. Hematologic (iron deficiency hypochromic and B12-folic deficiency anemia).
3. Endocrine (acromegaly, obesity, prolactinoma, delayed puberty)
4. Neurological (myopathy).
5. Psychiatric (depression, myxedema delirium, hypersomnia).
6. Gynecological (polycystic ovary, uterine fibroids, menometorrhagia, opsenomenorrhea, galactorrhea, hirsutism).
7. Dermatological (alopecia).
8. Surgical (gallstone disease).

Less often, the cause of an exacerbation of thyroid hormone deficiency also becomes observed as a result of the abolition of substitution, the termination of treatment with levothyroxine preparations or an increase in the need for this drug as a result of provoking factors:

- subcooling;
- concomitant diseases (trauma, blood loss, pneumonia, viral diseases, urogenital infection, acute and chronic infections, stroke, acute myocardial infarction, surgical interventions, radiation therapy and others);
- after taking medications that inhibit the functions of the central nervous system (tranquilizers, antipsychotics, drugs for anesthesia and barbiturates);
- hypoglycemia;
- with hypoxic conditions;
-after X-ray examination;
- as a result of taking a large dose of alcohol.

Pathogenesis

Severe deficiency of the level of thyroid hormones leads to a marked decrease in cardiac output, inhibition of tissue respiration, increased hypoxia, hypoventilation, renal hypoperfusion, decreased activity of metabolic processes in the brain, and syndrome of excessive production of vasopressin. All this leads to a significant metabolic disorder in organs and tissues, including the central nervous system, which leads to the development of a coma.

Clinical picture: Hypothyroid coma develops slowly, gradually progressing. First, a feeling of fatigue, lethargy, apathy appears, then you can observe a decrease in metabolic processes, heart failure, hypoxemia, hypercapnia develop. In patients with hypothyroid coma, the following

syndromes can be distinguished:
1) hypometabolism (increase in body weight, decrease in body temperature below 35 ° C);
2) cardiovascular disorders (bradycardia, low voltage of the teeth and diffuse metabolic changes on the ECG, hydropericardium, lowering blood pressure, primarily due to systolic);
3) hypoventilation-hypercapnic (bradypic, decreased respiratory rate, shallow breathing, decreased blood oxygen saturation, temporary respiratory arrest during sleep, increased hypoxemia, hypercapnia and respiratory acidosis);
4) oppression of the nervous system (decrease and disappearance of tendon reflexes, state of prostration, confusion, stupor of consciousness, cramps, progressive stupor gradually turning into a coma);
5) ectodermal disorders (dryness and thickening of the skin caused by accumulation of beta-carotene yellowness of the skin, diffuse alopecia, fragility and dull hair color, fragility and transverse striation of nails, hyperkeratosis in the elbow and knee joints);
6) edematous (pronounced swelling on the face or puffiness of the face, eyelids, dense subcutaneous edema of the hands, legs, pressure does not leave traces of pressure); hypervolemia, hyponatremia, problems with urination (up to anuria);
7) anemic (normochromic normocytic, hypochromic iron deficiency, as well as macrocytic anemia are possible);
8) insufficiency of contra-hormonal hormones (development of hypoglycemia);
9) gastrointestinal disorders (hepatomegaly, megacolon, weakening of peristaltic murmurs, up to their complete disappearance with the development of dynamic intestinal obstruction).
Often, concomitant pathology can cause an atypical course of a hypothyroid crisis. So, in 15-20% of cases with concomitant infectious and inflammatory diseases, hypothyroid coma develops at normal or even subfebrile body temperature. Progressive bradycardia may be absent if the patient has severe heart failure. With the initial arterial hypertension, which is often found in old age, the development of coma is possible against the background of normal or even high blood pressure. With an unfavorable outcome, the patient's death occurs with phenomena of increasing respiratory and cardiovascular failure.

Differential diagnosis

Differential diagnosis is carried out with the following pathological conditions: renal failure, heart failure, cerebrovascular accident, general intoxication, mechanical intestinal obstruction, with insufficient function of the adrenal cortex.

Diagnostics

The main difficulties in the diagnosis of hypothyroid coma are associated with the extremely difficult general condition of patients, which impedes the carrying out of diagnostic measures, as well as the need to immediately begin treatment, without waiting for laboratory confirmation of hypothyroidism. When making this diagnosis, one has to rely on the anamnesis and the characteristic clinical symptoms described above and examination data:
- hormonal background: a decrease in blood levels of free T3, free T4, free cortisol; increase in TSH level;
- general blood test: anemia, leukopenia, increased hematocrit;
- biochemical analysis of blood: hypoglycemia, a decrease in the concentration of sodium in the blood; increased content increased production of creatine phosphokinase, aminotransferase;
- KShchS: development of respiratory acidosis;
- ECG: bradycardia, low voltage of the teeth and diffuse metabolic changes;
- Ultrasound: signs of ascites, pulmonary edema, hydropericardium, a decrease in the thyroid gland in volume, or its absence.

When analyzing anamnestic data in patients with hypothyroid coma, one should remember the possibility of an atypical course of hypothyroidism and take into account the possibility of increasing levels of transaminases and creatine phosphokinase, which together with nonspecific changes on the ECG can lead to an erroneous diagnosis of myocardial infarction.

Treatment

1. Emergency hospitalization in a specialized department with blood sampling to determine TSH, free T4 and free cortisol.
2. **Treatment with glucocorticoids** begins immediately, without waiting for the results of a study of hormone levels. The clinical symptomatology of hypothyroid coma does not allow to exclude concomitant hypocorticism, therefore, even before the administration of levothyroxine preparations, 100-200 mg of hydrocortisone hemisuccinate 3-4 times a day (daily dose up to 200 mg) or prednisolone 60-90 mg (daily dose up to 180- 240 mg) per 400 ml of 0.9% sodium chloride solution and / or 400 ml of 5% glucose solution intravenously. After 2-4 days, the dose of glucocorticoids is gradually reduced. After the patient's condition improves, glucocorticoid drugs are canceled.
3. **Substitution therapy with thyroid hormones**. With hypothyroid coma, atony of the gastrointestinal tract and a pronounced violation of intestinal absorption are observed, therefore, during the first day, 250 μg of levothyroxine is administered intravenously every 6 hours. The effect of levothyroxine becomes noticeable only after a few hours, therefore, triiodothyronine can be additionally prescribed in a dose of up to 50 μg per day. When conducting an intravenous infusion, it should be remembered that the amount of fluid transfused per day should not exceed 1 liter. On the second day, maintenance therapy with levothyroxine is carried out in a dose of up to 100 mg per day. In the following days, the dose of levothyroxine is reduced to 50-100 μg per day, then they switch to the usual replacement doses of the drug. In the absence of levothyroxine preparations for intravenous administration, triiodothyronine or levothyroxine can be administered through a gastric tube. The starting dose of triiodothyronine is 100 μg every 12 hours until the body temperature normalizes, then 20-50 μg every 12 hours until the condition improves (levothyroxine - 100 μg by mouth or through a stomach tube every 6-12 hours). The dose is adjusted depending on the dynamics of body temperature and clinical symptoms. Treatment with thyroid drugs is carried out under the supervision of an ECG, blood pressure, pulse and respiratory rate.
4. The fight against **hypoventilation, hypercapnia and hypoxia**. Severe hypoventilation and hypercapnia in patients with hypothyroid coma requires artificial lung ventilation and oxygen therapy. With a sharp decrease in the rhythm of breathing, 2-4 ml of cordiamine, which stimulates the respiratory center, should be administered intravenously. The introduction of cordiamine during the day can be repeated 3-4 times under the control of blood pressure.
5. Elimination of **hypoglycemia**. To eliminate hypoglycemia, intravenous administration of 20-30 ml of a 40% glucose solution and intravenous drip of 500-1000 ml of a 5% glucose solution are recommended, depending on the level of CVP, heart rate, and urine output.
6. Normalization of the **cardiovascular system**. Patients in a hypothyroid coma often have severe arterial hypotension, and often collapse and phenomena of left ventricular failure. Treatment of disorders of the cardiovascular system, in particular, lowering blood pressure, is carried out using reopoliglukin, 10% albumin. If, against the background of a decrease in blood pressure, heart failure develops, then the use of cardiac agents, for example, strophanthin, is used.
7. The fight against **anemia**. With severe anemia, a red blood cell transfusion of mass or single blood is indicated, in the most severe cases - repeatedly.
8. The fight against **hypothermia**. To warm the patient, it is necessary to wrap them with blankets, and also slowly increase the room temperature (by 1 ° C per hour, but not higher than 25 ° C). Active warming of the patient with heating pads, etc. is not recommended, because dilatation of blood vessels of the skin leads to increased vascular insufficiency and the development of collapse.
9. Elimination of provoking factors and treatment of **concomitant diseases**. In patients in a coma, atony of the bladder is constantly observed.
Prognosis.

In the absence of timely and adequate treatment, patients in a hypothyroid coma die mainly from respiratory and heart failure, in some cases from cardiac tamponade. Mortality in this

pathology remains high and exceeds 50%.

1.7. THYROTOXIC CRISIS

Thyrotoxic crisis is a syndrome of pronounced acute action of an excess of thyroid hormones and catecholamines, with a pronounced deficiency of glucocorticosteroids, with an avalanche-like increase in dangerous symptoms, mainly on the cardiovascular system and brain.

Epidemiology

The incidence of thyrotoxic crisis in patients with moderately severe and severe forms of hyperthyroidism is 0.5-19%. The ratio of cases of crisis in women and men is 9: 1.

The main provoking factors:

• thyroid surgery in the treatment of diffuse toxic goiter;
• tooth extraction;
• the use of ether anesthesia during surgical procedures;
• the use of radioactive iodine in the treatment of diffuse toxic goiter;
• treatment of the thyroid gland with x-rays;
• inadequate preparation for treatment with radioactive iodine or surgical treatment, consisting in the absence of the patient's euthyroid state.
• inadequate therapy, premature withdrawal or skipping of drugs, drug withdrawal after prolonged use used to correct hormonal status in hyperthyroidism;
• reception of funds containing iodine, the introduction of radiopaque agents;
• rough feeling of the thyroid gland with diffuse toxic goiter.
• infectious diseases (including respiratory tract);
• cerebrovascular accident;
• childbirth and complicated pregnancy in women;
• stressful situations;
• injuries;
• excessive physical activity;
• pulmonary embolism
• diseases of an infectious nature;
• some diseases (gastroenteritis, pneumonia);
• taking certain medications (insulin, glycosides, adrenergic agonists).

In some cases, the so-called spontaneous crisis is recorded, which manifests itself without visible provoking factors

Pathogenesis

The pathogenesis of thyrotoxic crisis is based on a sharp increase in the level of free thyroid hormones - triiodothyronine (T3) and thyroxine (T4). Critical conditions are characterized by the fact that a sudden increase in the level of thyroid hormones is accompanied by a lack of hormones in the adrenal cortex. In addition, the following processes are characteristic of this condition:

• increased adrenal insufficiency, which exacerbates the deficiency of their hormones;
• activation of the sympathetic-adrenal system, as well as the subcortical centers of the hypothalamus and the reticular formation of the brain;
• excessive synthesis of catecholamines - substances that stimulate the activity of endocrine glands.

These pathological changes lead to the fact that the reserve capacity of the body is depleted, and a life-threatening condition develops - a thyrotoxic crisis that requires emergency care.

Clinical picture:

The development of thyrotoxic crisis occurs suddenly, within a few hours. However, in some cases, a prodromal period is observed, during which a gradual subtle increase in symptoms occurs (within 2-3 days).

In the development of thyrotoxic crisis, 2 main stages can be distinguished: the period of excitation and the progression phase of cardiac pathologies. The first stage is associated with the

activation of the sympathoadrenal system, and the second stage is associated with the attenuation of compensatory mechanisms.

Signs of a crisis are intensely manifesting symptoms of a toxic goiter of a diffuse type with an avalanche-like increase.

The appearance of a person changes dramatically: a hyperemic face of a mask-like appearance with a pronounced state of horror, eyes wide open with rare blinking. The injured person takes a specific position: raising the arms and legs to the side, with the legs bent at the knees, muscle adynamia. The skin when feeling wet and hot, the temperature rises to 38-40 ° C. Rapid breathing is heard (this is a sign of suffocation).

Symptoms of cardiovascular system disorders are manifested in the form of severe tachycardia (above 190 beats per minute), atrial fibrillation, increased stroke volume and myocardial oxygen demand, increased blood pressure, shortness of breath, tachypnea, difficulty breathing. Often acute heart failure develops. An increase in blood pressure is determined by the severity of the attack. An increase in diastolic pressure indicates the development of heart failure.

Renal pathologies are clearly expressed as a significant decrease in the frequency of urination, up to anuria (complete blocking of urine output). The critical condition is exacerbated by acute hepatic atrophy.

Disorders in the central nervous system are observed in 90% of patients in a state of crisis. There is an indomitable fear of mortal danger, anxiety, headache, emotional lability, insomnia, excessive agitation; trembling in the limbs. Crisis progression leads to neurogenic and motor impairment. The following manifestations are possible: an acute form of psychosis, hallucinations and delirium, confusion with subsequent inhibition, loss of orientation in space, prostration and the onset of a coma.

The main gastrointestinal symptoms that occur during a crisis are a decrease in appetite, nausea, vomiting, abdominal pain cramps, diarrhea, and hyperdefecation. Nausea, uncontrollable vomiting, severe diarrhea, sweating - in severe cases, sweat is so plentiful that there is a risk of dehydration.

People older than 60 years often develop an apathetic version of the thyrotoxic crisis, which is characterized by apathy, a delayed reaction, a slight enlargement of the thyroid gland, the absence of the usual ophthalmic symptoms of hyperthyroidism (but blepharoptosis is possible - lowering of the upper eyelids), weight loss, muscle weakness and congestive heart failure are observed .

Diagnostics

Thyrotoxic crisis is diagnosed on the basis of the appearance of characteristic clinical symptoms (fever, tachycardia, CNS disorders and gastrointestinal disturbances) in the presence of toxic goiter. In addition, the previous action of the provoking factor is taken into account: surgical intervention, treatment with radioactive iodine, infectious disease, and so on. To confirm the diagnosis, studies are carried out: hormonal background: an increase in the level of free T4 and T3; decrease in cortisol and thyroid-stimulating hormone; general blood analysis; biochemical blood test: hyperglycemia; KShchS; ECG: tachycardia, heart rhythm disturbance; Ultrasound

Treatment

1. Emergency hospitalization in a specialized department.
2. Relieving **corticosteroid deficiency** caused by thyrotoxicosis. In order to eliminate adrenal insufficiency, 50-100 mg of hydrocortisone hemisuccinate is administered intravenously every 6 hours 4 times a day (daily dose 150-400-600 mg) or 60 mg prednisolone (daily dose 180-240-300 mg), in severe cases 5 -10 mg of DOXA intramuscularly. The daily dose is determined by the severity of the patient's condition. After the patient's condition improves, usually starting from the 2nd to 3rd day, a transition to the intramuscular route of glucocorticoid administration with a subsequent reduction in their dose is possible.
3. The appointment of high doses of **thyreostatics.** A decrease in the level of thyroid hormones

is achieved by using thyreostatics, iodine preparations or Lugol's solution. In thyrotoxic crisis, propylthiouracil (propicyl) is most effective, capable of not only inhibiting the synthesis of thyroid hormones, but also inhibiting the peripheral conversion of thyroxine to triiodothyronine. The initial dose of propylthiouracil is 600-800 mg, then this drug is administered every 6 hours in a single dose of 300-400 mg. In the absence of propylthiouracil, thiamazole 60 mg is used orally once, and then 20-30 mg every 6 hours (daily dose 100-120 mg). For patients unable to swallow, the drug is dissolved in 100-150 ml of 5% glucose and administered through a nasogastric tube. With vomiting, antithyroid drugs are used rectally.

As the crisis stops and the patient's condition improves (usually after 2-3 days), the doses of thyrostatics can be reduced by about 2-3 times. Further dosage adjustment is carried out according to the general principles of treatment of thyrotoxicosis.

4. Prescription of **iodine preparations**. To block the accumulation of iodine in the thyroid gland, the introduction of iodine preparations is started 1-2 hours after the appointment of thyreostatics. 5-10 ml of a 10% sterile solution of sodium iodide dissolved in 1.0 l of a 5% glucose solution every 8 hours is administered intravenously. After the cessation of vomiting and diarrhea, they switch to taking Lugol's solution in milk at a dose of 20-30 drops 3-4 times a day. After stabilization of the patient’s condition, the dose of Lugol’s solution is reduced to 10 drops 3 times a day, its administration is continued until the patient is withdrawn from the state of crisis (usually about 7-10 days). With vomiting, 50 drops of Lugol's solution are injected through the probe 3 times a day.

5. Correction of **water-electrolyte disturbances**. It is provided by intravenous drip of 500 ml of 5% glucose solution and isotonic sodium chloride solution. The total amount of parenteral fluid is determined by the severity of dehydration and hypovolemia and can reach 3 liters per day. To improve microcirculation, it is possible to prescribe reopoliglukin and albumin solution.

6. Eliminating the risk of **heart** failure. With the development of acute vascular insufficiency, an adequate amount of replacement therapy is supplemented by the introduction of higher doses of corticosteroids (hydrocortisone 400-600 mg per day, prednisone 200-300 mg / day, dopamine). With the development of acute left ventricular failure and pulmonary edema, intravenous administration of diuretics (60-80 mg of furosemide), cardiac glycosides (0.5 ml of 0.05% strophanthin solution; 0.5-1 ml of 0.06% corglycon) is shown, oxygen inhalation, saturated with vapors of alcohol. It is advisable to stop the arrhythmic syndrome with beta-blockers, cardiac glycosides. Violations of rhythm and conduction are stopped according to general principles. With paroxysm of atrial tachyarrhythmia, β-adrenergic blockers are prescribed orally (metoprolol, atenolol, propranolol) or 1-2 ml of 0.1% propranolol solution (1-2 mg) are dissolved intravenously, dissolved in 10 ml of isotonic sodium chloride solution every 3-6 hours . With insufficient effect and good tolerance, a single dose of propranolol can be gradually increased to 5-10 mg. After the termination of vomiting and restoration of consciousness, propranolol is prescribed orally at 40-60 mg 3-4 times a day. When prescribing β-adrenergic blockers during a thyrotoxic crisis, it should be borne in mind that, as a result of their negative inotropic effect, pulmonary edema may develop.

7. Relief of **psychomotor** agitation. To stop the nervous and psychomotor agitation, the introduction of phenobarbital at 0.3-0.4 grams per day, accelerating the inactivation of thyroxine, is recommended. Perhaps the intravenous administration of 2-4 ml of a 0.5% solution of seduxen or relanium, 2-4 ml of a 0.25% solution of droperidol.

8. The fight against **hyperthermia**. In order to lower body temperature, it is better to use physical methods (cooling the body with fans, wrapping the patient’s head, abdomen and heart region with ice bubbles, etc.). The introduction of antipyretic drugs, especially salicylates, is undesirable (they increase thyrotoxicosis due to its displacement from the connection with the protein).

An effective method of treating thyrotoxic crisis is plasmapheresis, which allows you to quickly remove large amounts of thyroid hormones and thyroid-stimulating antibodies.

Forecast

Thyrotoxic crisis has a favorable prognosis with adequate treatment. On average, 3 days after the start of therapy, the patient's condition improves. Then a constant correction of thyroid hormone levels is required.

Without emergency care, a thyrotoxic crisis is accompanied by a rapid aggravation of dehydration symptoms, the occurrence of refractory pulmonary edema, vascular collapse, geomegaly develops with subsequent necrosis of the liver, a person falls into a coma, and death may occur about 72 hours after the onset of signs of crisis.

1.8. ADRENAL CRISIS

The adrenal (addisonic, hypoadrenal) crisis is an acute severe complication of adrenal cortex insufficiency, which develops as a result of a pronounced mismatch between the low level in the body and the increased need for them and characterized by a sharp exacerbation of all symptoms of hypocorticism.

Etiology

The development of the adrenal crisis in patients with chronic insufficiency of the adrenal cortex is promoted by:

• acute infectious and inflammatory processes of any localization, especially extensive and significantly pronounced (for example, severe pneumonia, tuberculosis, meningitis, sepsis, etc.);

• surgical interventions without appropriate amendments to replacement therapy; severe blood loss, injuries, burn disease;

• severe psychoemotional stress; heavy, intense physical activity;

• pregnancy and childbirth;

• unreasonable dose reduction of glucocorticoids or discontinuation of replacement therapy;

• alcohol intoxication;

• treatment with insulin, morphine, sleeping pills, diuretics, warfarin;

when changing climate;

with acute hemorrhage in the adrenal gland or with the development of a heart attack in them, autoimmune or metastatic damage to the adrenal gland.

Pathogenesis

In a healthy person, glucocorticoids (cortisol), mineralocorticoids (aldosterone) and androgens are synthesized in the adrenal cortex. Glucocorticoids support metabolism, potentiate the effect of catecholamines, ACTH of the pituitary gland is regulated. Mineralocorticoids control sodium metabolism and fluid balance in the body, the reninangiotensin system and the level of K + serum.

The pathogenesis of the adrenal crisis is caused by a pronounced deficiency of gluco- and mineralocorticoids, which leads to a deep violation of all types of metabolism, a decrease in gluconeogenesis, hypoglycemia, a decrease in the volume of circulating blood, hypovolemia, collapse, hyponatremia, hyperkalemia, hypercalcemia, severe impaired renal function, arrhythmia, cardiovascular, respiratory, digestive and nervous systems.

Clinical picture: The adrenal crisis develops from a few hours to several days. In the pre-crisis period, muscle weakness increases, skin pigmentation intensifies, appetite disappears, muscle pains appear, body weight decreases, blood pressure decreases. the patient’s consciousness is preserved, but he is very lethargic, dynamic, hardly speaks and turns in bed, his voice is quiet, slurred;

• patients are usually pale, cyanotic, dry, hyperpigmented skin, its turgor and elasticity are sharply reduced, the face is haggard, features are pointed, eyes are sunken; skin pigmentation is absent only with secondary adrenal insufficiency;

sharply reduced blood pressure, systolic pressure drops to 60 mm RT. Art. and below, diastolic pressure in the most severe cases may not be determined, which is manifested by profuse sweat, cooling hands and feet, sudden weakness, the pulse is threadlike, frequent, the heart is disturbed, arrhythmia, syncope develops;

• nausea and vomiting, severe abdominal pain, diarrhea;

• urine output decreases sharply (oligoanuria);
• symptoms of severe dysfunction of the central nervous system may occur: dimming of consciousness, stupor, convulsions, pseudomeningeal syndrome (due to hypoglycemia), delirious syndrome, hallucinations, fainting, coma occurs.
If such symptoms appear, urgent hospitalization is necessary.
Acute adrenal insufficiency can occur in three clinical forms:
1. Meningoencephalitic (neuropsychic form) in the clinical picture, adynamia or, on the contrary, agitation with impaired consciousness, delirium, seizures, epileptic seizures, and pseudomeningeal syndrome, inhibition, dimming of consciousness, stupor comes to the fore.
2. The gastrointestinal form is characterized by symptoms resembling an "acute abdomen" and is manifested by anorexia, nausea, vomiting, frequent loose stools, sometimes with an admixture of blood, epigastric pain spreading throughout the abdomen, pain in the lumbar region is possible, with palpation of the abdomen muscle tension of the abdominal wall is determined. All of these symptoms are accompanied by severe arterial hypotension.
3. Hypotonic form with a picture of collapse. There is severe arterial hypotension (refractory to vasopressors), hyponatremia, hypoglycemia, azotemia, dehydration, weakness, and circulatory collapse.

Differential diagnosis

- Shock, Sepsis, Dehydration, Overdose of drugs, Uremia, Hypothyroidism, Gastrointestinal diseases (appendicitis, peptic ulcer, gastroenteritis, pancreatitis, liver and gall bladder diseases), Myocardial infarction, heart failure, pulmonary embolism, Meningoencephalitis.

Table 1.Differential diagnosis of hypotonic forms of addison crisis and myocardial infarction.

	Addison crisis	**myocardial infarction**
Cause	Infection, physical or mental stress, surgery, decrease or stop taking gluco- and mineralocorticoids	Atherosclerosis of the coronary arteries, a history of coronary heart disease, various manifestations of cardiovascular failure, physical and mental stress.
Start	Gradual	usually acute
Age	More often young, average	Usually over 40
Leading complaints.	Asthenia, adynamia, dizziness, fainting, pain in the heart	Sharp growing pain behind the sternum, aggravated by physical exertion with radiation to the left shoulder blade, arm, neck; shortness of breath, fear, anxiety, general weakness
Consciousness	Retained consciousness but sick in prostration	Saved or may be lost
Skin and mucous membranes	Hyperpigmented pale, cold sweat	Pale with a transition to cyanosis, cold sweat
Pulse	Small, rare pulse	Filamentary, arrhythmic pulse.
Heart sounds	heart sounds are weakened	Heart sounds are weakened, often rhythm disturbance (extrasystole, atrial fibrillation), gallop rhythm, pericardial friction noise.

Electrocardiogram	The voltage is reduced, lengthening of the PQ interval, QRS complex, flattening of the T wave, lowering of the ST interval, lack of dynamics.	The characteristic changes inherent in one or another localization of myocardial infarction, the dynamics of the electrocardiogram during repeated examination
Blood glucose	Dramatically reduced	Norm or increase
Sodium in the blood	Reduced	norm
Potassium in the blood	Promoted	norm
Creatine phosphokinase activity	Norm	promoted.
Alanine aminotransferase (ALT) activity	Norm	Norm or increase
Aspartate transaminase activity	Norm	sharply increased
fibrinogen	Norm	increased
Fibrinolytic activity	not changed.	reduced
Blood levels of cortisol, 17-hydroxycorticosteroids,11-hydroxycorticosteroids.	Sharply reduced	norm or elevated.

Table 2. Differential diagnosis of the gastrointestinal form of addison crisis and acute gastroenteritis.

Signs	**Addison crisis**	**Acute gastroenteritis**
Anamnesis	Infection, trauma, surgery, insufficient hormone therapy, discontinuation of treatment.	The connection with the intake of food, drugs and other substances
Development	Often gradual	Fast
Adynamia	Severe	General weakness, moderate
Vomiting	not associated with food intake, initially rare, with increasing severity - more frequent, worsens the patient's condition	Vomiting pronounced at the beginning, single or repeated, subsequently decreases and disappears, facilitates the patient's condition
Abdominal pain	Spilled, less often in epigastrium	Cramping pain, usually in epigastrium
Abdominal Auscultation	Normal peristalsis	Peristalsis enhanced
Skin	Pigmented, rarely common color	Normal color
Pulse	pulse small, rare, less frequent	Pulse of Normal size, with dehydration - small, frequent
Blood pressure	sharply reduced	Normal or moderately reduced
Orthostatic Hypotension	Expressed	absent.
Eosinophilia	+	-
Lymphocytosis	+	-
Hyponatremia	+	-
Hyperkalemia	+	-
Hypoglycemia	+	-

Hypernatriuria	+	-
Hypokaliuria	+	-
General urine analysis	There may be albuminuria, cylindruria	Normal
17-hydroxycorticosteroids The ACTH test (also called the cosyntropin, tetracosactide, or Synacthen test)	Reduced	Norm +

Table 3. Differential diagnosis of meningoencephalic form of addison crisis and tuberculous meningoencephalitis

Signs	**Addison crisis**	**Meningoencephalitis**
Causes	Infection, trauma, physical, mental strain, surgery, decrease or stop taking glucocorticoids and mineralocorticoids.	Damage to the tubercle bacillus of the meninges.
Age	More often up to 40 years.	All age groups, most often children.
The onset of the disease.	More often a gradual onset.	Subacute onset
Body temperature	Normal or lowered (possible increase)	Low-grade fever(subfebrile temperature)
The main complaints.	Asthenia, adynamia, nausea, dizziness.	Sharp constant headache pain, pain in the eyes, photophobia, vomiting associated with a change in body position; in the absence of nausea - persistent constipation.
Skin and visible mucous membranes.	Hyperpigmented, especially in places of friction of clothes, in open areas of the skin, the presence of slate-blue spots on the mucous membranes of the lips, gums, cheeks.	Normal color with pronounced spontaneous red spots (Trousseau spots)
Muscle stiffness	moderately expressed (+)	Muscle rigidity is pronounced, there is an opisthotonus (++++)
Symptoms of root tension (Neri symptom, Lasegue's symptom, Wasserman symptom, Matskevych symptom)	-	+
Muscular-articular pain, "aches in the bones."	-	+
Tendon reflexes	Moderately elevated	Dramatically elevated, there are also pathological

Mental disorders	+	-
Motor disorders	Convulsions	Convulsions, paresis, paralysis, epileptiform seizures
Cranial nerve disorders	-	+
Pulse	Small, rare	rapid pulse
Blood pressure	Hypotension	blood pressure fluctuates
Ocular fundus	Normal	arterial spasm
General blood analysis	Eosinophilia, increased ESR	Neutrophilic leukocytosis, increased ESR
General urine analysis	Norm or albuminuria, cylindruria	Norm
Blood glucose	Decline	Norm or increase
Blood sodium	Decline	Norm or increase
Potassium blood	Increase	Norm
C-reactive protein (CRP)	-	+
ACTH test	-	+
Cerebrospinal fluid (CSF) examination	without features	Xanthochromic or transparent, opalescent, a fibrin membrane falls out; increase in protein, cytosis, lymphocytes; reduction in sugar and chloride; bacillus tuberculosis (+)

Diagnostics

For the diagnosis of acute adrenal insufficiency appoint:

- hormonal background: a sharp decrease in the number of corticosteroids (cortisol, aldosterone, etc.) is detected in urine and blood. The diagnosis of adrenal insufficiency is excluded with serum cortisol levels> 20 mmol / L;
- general blood test: erythrocytosis, an increase in the content of red blood cells and hemoglobin, leukocytosis with a shift to the left, an increase in ESR;
- biochemical analysis of blood: an increase in creatinine, urea (due to aldosterone deficiency), hyperkalemia, hypoglycemia, a decrease in the level of sodium, chlorides. With secondary adrenal insufficiency: hypernatremia, hypokalemia.
- general urinalysis: protein, single cylinders, red blood cells, sometimes acetone are determined;
- Electrocardiogram: signs of hyperkalemia: lengthening of the QT interval, pointed high T waves and heart block, slowing of atrioventricular conduction.

Computed tomography can be performed to rule out adrenal infarction.

Urgent care

Treatment

1. Substitution therapy with glucocorticoids and mineralocorticoids.
2. The fight against dehydration and hypoglycemia.
3. Restoring disturbed electrolyte balance.
4. Correction of protein metabolism disorders.
5. Fight against collapse.

When the initial symptoms of severe decompensation of Addison's disease appear

(increasing general weakness, the appearance and intensification of abdominal pain, nausea, vomiting, a significant decrease in blood pressure), immediate hospitalization in the intensive care unit or endocrinology department is necessary.

Before transportation, the patient should be administered intravenously (if not possible, administered intramuscularly) 50-70 mg of hydrocortisone hemisuccinate or phosphate or 30 mg (1 ml) of prednisone.

In the hospital, subclavian vein catheterization should be performed. An urgent blood test should be performed for the content of glucose, sodium, potassium, chlorides, urea, creatinine, total protein, as well as a general analysis of blood and urine, urine for acetone.

1. **Substitution therapy with glucocorticoids and mineralocorticoids**

- Glucocorticoid hydrocortisone is injected intravenously, drip (hydrocortisone hemisuccinate or cortisone) or intramuscularly (hydrocortisone acetate in suspension). Usually all three methods of administration are combined. Start with hydrocortisone hemisuccinate 100-150 mg intravenously. The same amount of the drug is dissolved in 500 ml of equal amounts of isotonic sodium chloride solution and 5% glucose solution and administered dropwise for 3-4 hours at a rate of 40-100 drops per minute. At the same time, an intramuscular injection of a drug suspension of 50–75 mg every 4–6 hours is performed. The dose depends on the severity of the condition, the dynamics of the increase in blood pressure and the normalization of electrolyte disturbances. During the first day, the total dose of hydrocortisone can range from 400-600 mg to 800-1500 mg or more.

Intravenous administration of hydrocortisone is continued until the patient is withdrawn from collapse and blood pressure rises above 100 mm Hg, then continue its intramuscular injection 4-6 times a day at a dose of 50-75 mg with a gradual decrease to 25-50 mg and an increase in the intervals of administration up to 2-4 times a day for 5-7 days. After this, the patient is transferred to oral treatment with prednisone (10-20 mg / day) in combination with cortisone (25-50 mg / day).

- The mineralocorticoid Deoxycorticosterone acetate is administered intramuscularly at the dose of 5 mg (1 ml 0.5%) after 6 hours (the highest daily dose is 25 mg) under the control of blood pressure and 1-2 times on the second day, then the dose is reduced to 5 mg daily or after 1 —2 days and as blood pressure normalizes, it is canceled.

With an increase in blood pressure to 115-120 / 60-70 mm Hg. replace intravenous drip of corticosteroids with intramuscular injection with prolonged intervals between administrations.

2. The fight against **dehydration and hypoglycemia**.

With dehydration, infusion therapy is carried out according to generally accepted methods under the control of central venous pressure and the control of hourly urine output. Hypoglycemia is eliminated by intravenous drip of a 5% glucose solution. About 3-4 liters of liquid are administered intravenously on the first day, and in the first 2 hours - 2 liters (1 liter of isotonic sodium chloride solution and 1 liter of 5% glucose solution).

3. Restoring disturbed **electrolyte balance**

The most characteristic electrolyte disturbances in the adrenal crisis are hyponatremia, hypochloremia, hyperkalemia. To eliminate hyponatremia and hypochloremia, an intravenous drip of isotonic sodium chloride solution is added with the addition of 20-30 ml of 10% sodium chloride solution, drinking salted water is prescribed (10 g of sodium chloride per 1 liter of boiled water).

To eliminate hyperkalemia, it is advisable to inject 30-40 ml of a 40% glucose solution intravenously (at the same time this eliminates hypoglycemia), you can enter 20 ml of a 10% solution of calcium gluconate. Intravenous administration of 30 ml of 10% sodium chloride solution also reduces hyperkalemia.

4. Correction of **protein metabolism** disorders.

In order to improve protein metabolism, an intravenous drip of 200 ml of a 20% solution of albumin, 400 ml of freshly frozen or native plasma is performed. These same drugs can increase the volume of circulating blood and stabilize blood pressure. An intravenous drip of amino acid

preparations (Alvesin «Neu», polyamine) in a daily dose of 400-600 ml is also recommended. Amino acids are used by the body to synthesize its own protein.

5. Fight against **collapse**. To eliminate the collapse, treatment with gluco- and mineralocorticoids, transfusion of polyglucin and reopoliglukin, saline solutions, 5% glucose solution under the control of central venous pressure are performed. The introduction of these solutions increases the volume of circulating blood and contributes to an increase in blood pressure. With the lack of effectiveness of these measures, dopamine is administered intravenously (80 mg of the drug is dissolved in 400 ml of 5% glucose solution and administered at a rate of 15-30 drops per minute). After the elimination of the adrenal crisis, patients with chronic insufficiency of the adrenal cortex gradually return to the doses of substitution therapy that they received before the development of the crisis and need lifelong replacement therapy.

Prognosis

To prevent the adrenal crisis, a constant lifelong conduct of adequate hormone replacement therapy is necessary. The prognosis is favorable with timely and adequate replacement therapy.

1.9. PHEOCHROMOCETOTIC CRISIS

Pheochromocytoma crisis is an acute developing syndrome of malignant arterial hypertension with severe neurovegetative disorders, due to the massive and rapid release of catecholamines (adrenaline and norepinephrine) into the blood by a hormone-active adrenal tumor.

Epidemiology.

The prevalence of the disease in the population is 0.5 per 100,000 of the population, the incidence is 1 per 1.5–2 million people per year. Adult men and women get sick with the same frequency, in children the disease develops more often in boys (in 60% of cases). For 100,000 autopsies, pheochromocytoma is detected in 20–150 observations. Among patients with arterial hypertension, the frequency of detection of pheochromocytes ranges from 0.1 to 0.7%, the highest frequency of pheochromocytoma is observed in patients with arterial hypertension aged 30-50 years (up to 1% of cases).

In 80% of cases, pheochromocytomas occur sporadically, in 10–20% of cases they are familial. In this case, pheochromocytomas can be a manifestation of several hereditary diseases transmitted by an autosomal dominant type:

- multiple endocrine neoplasia (MEN) 2A, or Sipple syndrome (in combination with medullary thyroid cancer (thyroid) and rarely with hyperplasia and / or parathyroid adenomas);
- MEN 2B type, or Gorlin syndrome (in combination with medullary thyroid cancer, marfan-like appearance, multiple ganglioneuromas of the gastrointestinal mucosa;
- von Recklinghausen's disease (in combination with cutaneous neurofibromatosis);
- von Hippel-Lindau syndrome (in combination with retinal hemangiomatosis, cerebrospinal hemangiomas and hemangioblastomas, less commonly with kidney cancer, multiple cysts of the kidneys, pancreas).

Pathogenesis.

In pheochromocytoma cells, catecholamines are synthesized and accumulated, as in normal cells of the adrenal medulla. The release of catecholamines can be triggered by changes in blood flow, necrosis in the tumor tissue and other causes. In addition, pheochromocytomas accumulate and secrete a large number of peptides, including endogenous opioids, adrenomedullin, endothelin, erythropoietin, neuropeptide Y (vasoconstrictor), and others. The main pathophysiological changes in the body with pheochromocytoma are associated with a high concentration of blood catecholamines adrenergic receptor apparatus in various organs. A change in the sensitivity of adrenoreceptors, a violation of the mechanisms of inactivation of catecholamines and energy depletion of vascular myocytes in the presence of an increased content of catecholamines in the vascular bed can lead to the development of catecholamine shock, which is characterized by a sharp increase in blood pressure in the central vessels (vasoconstrictor status) and a significant decrease in blood pressure on the periphery.

Paradoxical arterial hypotension with pheochromocytoma can be caused by precapillary shunting, profuse sweating, chronic constipation, as well as tumor hemorrhage, left ventricular failure, isolated influence of adrenaline on b2-adrenergic receptors, or the development of catecholamine shock (as a result of changes in the sensitivity of the mechanism of adrenol depletion of vascular myocytes).

Crisis can be triggered by slight physical exertion, abdominal palpation, sometimes taking b-blockers, anesthesia, and with the localization of pheochromocytoma in the bladder wall - urination, defecation, or other factors.

Clinical picture:

The most dangerous complication of pheochromocytoma is the catecholamine crisis. There are several important anamnestic and clinical guidelines that suggest the tumor nature of sympathoadrenal paroxysm:

The main symptom of the disease is high, mainly systolic **hypertension** (up to 250/130 mm Hg). The most characteristic crises are with a sudden increase in blood pressure (paroxysmal or persistent).

1. Repeated similar crises in the anamnesis
2. Connection of a hypertensive crisis with certain provoking factors
3. Tachycardia, tremor, hyperhidrosis, sharp blanching or redness of the skin, especially of the hands and feet, wide pupils.
4. The phenomena of hypermetabolism: fever, weight loss, hyperglycemia, glucosuria.
5. A paradoxical hypertensive reaction (increase in blood pressure in response to standard hypotensive therapy), to anesthetics and some antihypertensive drugs.
6. There is a headache, tinnitus, anxiety or fear, Often there are pains in the chest or abdomen, nausea, vomiting.

During a crisis, tachycardia (up to 180 / min), various cardiac arrhythmias, ventricular tachycardia, ventricular fibrillation, T wave inversion, blockade of the bundle of His bundle, and even a picture of acute myocardial infarction are noted on the electrocardiogram.

The occurrence of myocardial necrosis, arrhythmias, an increase in the level of cardiospecific enzymes are not associated with changes in coronary circulation, the cause of the changes is the so-called toxic catecholamine myocardial dystrophy. After the crisis, these violations disappear. Long-term hypercatecholaminemia due to increased afterload and the toxic effect of catecholamines on the myocardium causes the development of myocardial hypertrophy, the progression of cardiosclerosis, dilation of the heart chambers with the onset of symptoms of chronic left ventricular failure. Hypercatecholaminemia also causes an increased risk of sudden death.

Sometimes, with extra-adrenal localization, catecholamine crises can occur under the guise of acute surgical or obstetric-gynecological pathology. Repeatedly reported diagnostic laparotomy undertaken during the catecholamine crisis, disguised as acute intestinal obstruction, destructive cholecystopancreatitis, perforated gastric ulcer. The tragic outcome of these errors is almost inevitable. It should also be remembered that the manifestation of a tumor in women often occurs during pregnancy and the catecholamine crisis is very similar to toxicosis of pregnant women.

The duration of the attack can be from several minutes to several hours. The catecholamine crisis is characterized by a high risk of life-threatening complications, it can end in a lethal picture of shock, reminiscent of acute adrenal insufficiency. Complications of pheochromocytoma include heart failure, pulmonary edema, arrhythmias, tachycardia, hypertension during shock or circulatory arrest during general anesthesia, catecholamine shock, cerebrovascular accident, renal failure in shock, hypertensive encephalopathy, ischemic colitis, dissecting aortic aneurysm, in pregnant women: fever, eclampsia, shock, death of the mother or fetus.

Diagnostics

Diagnosis of pheochromocytoma includes a hormonal background:

- determination of the concentration of catecholamines (adrenaline (epinephrine), norepinephrine) or their metabolites of vanillylmandelic acid (VMA) and homovanillic acid (HVA) in urine. The method is not specific enough: false-positive results are possible when taking rauwolfia, methyldopa, food with a high content of vanillin, after physical and emotional stress, as well as in patients with renal failure. The method is not very specific;
- determination of free catecholamines in plasma. Before blood sampling, the patient should lie quietly on his back for at least 30 minutes. The method is not very specific. An increase in the level of catecholamines is possible with anxiety, decreased circulating blood volume, acidosis, arterial hypotension, hypoxia, physical exertion, smoking, renal failure, increased intracranial pressure, obesity, while taking levodopa, methyldopa, administration of histamine or glucagon;
- determination of the total concentration of methanephrins (methanephrine and normetanephrine) in plasma and urine. Metanephrins are stable for 24 hours, therefore, their determination is not related in time to the moment of the release of hormones by the tumor. The method has high sensitivity and specificity (reach 98%);
- provocative tests (histamine, glucagon, metoclopramide, physical activity) and suppressive tests (clonidine, phentolamine). (For example, in a test with intravenous histamine, the administration of 0.05 mg of histamine to patients with pheochromocytoma after 2-3 minutes causes a marked increase in blood pressure; in a test with intravenous phentolamine, administration of 5 mg of phentolamine after 5 minutes leads to a decrease in systolic blood pressure by 35 mm Hg or more, diastolic blood pressure - by 25 mm Hg or more.) These samples are associated with a large number of complications, therefore they are used extremely rarely.
- topical diagnostics. For accurate topical diagnosis of pheochromocytoma, it is necessary to confirm its localization by two methods (for example, ultrasound and CT or ultrasound and MRI). The sensitivity of all methods is quite high, amounting to 90–96%.

To establish extra adrenal localization of the tumor or metastases of malignant pheochromocytoma, as well as for relapse of the disease after surgical treatment, iodine-131 meta-iodo-benzylguanidine (MIBG) scintiscanning or meta-123J-benzylguanidine is used.
- general blood test: neutrophilic leukocytosis;
- biochemical blood test: hyperglycemia;
- Electrocardiogram: tachycardia, various rhythm disturbances, ventricular fibrillation, T wave inversion, blockade of the bundle of His bundle, picture of acute heart attack.

Differential diagnosis

Diagnosis of pheochromocytoma is carried out with the following diseases and conditions:
- arterial hypertension of a different etiology (especially in severe renal failure);
- Anxiety, neurosis, psychosis; migraine, headaches with Horton's disease;
- paroxysmal tachycardia;
- endocrine diseases: thyrotoxicosis; diabetes mellitus (with hyperglycemia); hypoglycemia; menopause;
- addiction (taking amphetamines, cocaine, ergot alkaloids);
- caffeine abuse;
- medication: medications that increase blood pressure (for example, b-adrenergic agonists); atropine and atropine-like drugs; decongestants (e.g. phenylpropanolamine); clonidine withdrawal syndrome; MAO inhibitors in combination with certain foods and alcohol;
- diseases of the central nervous system: traumatic brain injury; stroke, transient ischemic attack; diencephalic syndrome; encephalitis; increased intracranial pressure; familial autonomic dysfunction;
- tumors (neuroblastoma, ganglioneuroma, ganglioneuroblastoma); carcinoid, mastocytosis; acrodinia; neurofibromatosis (von Recklinghausen disease); adrenal cancer, hormone-inactive adrenal tumors;
- diseases accompanied by sharp fluctuations in blood pressure: porphyria; lead poisoning; pain attacks with spinal cord; tetanus; Guillain-Barré syndrome.

Treatment

1. Immediately raise the head end of the bed to cause an orthostatic decrease in blood pressure.
2. Intravenously administered **α-blockers**, most often phentolamine (regitin) or tropaphen. Both drugs block both postsynaptic α1- and presynaptic α2-adrenergic receptors. Thus, they eliminate the effect of excess catecholamines and lower blood pressure

Phentolamine is injected intravenously every 5 minutes at a dose of 2-5 mg in 10 ml of isotonic sodium chloride solution until the crisis is stopped and blood pressure decreases.

Instead of phentolamine, 1-2 ml of a 2% solution of tropafen in 10 ml of an isotonic sodium chloride solution can be administered intravenously every 5 minutes until the crisis is stopped.

With a decrease and stabilization of blood pressure, α-blockers continue to be administered intramuscularly at the same dose every 2 or 4 hours during the day. Then they switch to taking phentolamine inside by 25-50 mg (1-2 tablets) every 3-6 hours and do not cancel it before surgery. For oral administration, instead of phentolamine, you can use the α-adrenergic blocking agent pyrroxan in tablets of 15 mg 1-2 tablets 3-4 times a day or prazosin (minipress, adversuten) in tablets of 1 or 5 mg in a daily dose of 6 to 15 mg per depending on the level of blood pressure. The advantage of prazosin is that it does not cause tachycardia. Long-acting α-blocker phenoxybenzamine is prescribed first at 10 mg 2 times a day, then the dose is gradually increased daily by 10-20 mg and adjusted to 40-200 mg per day. Prazosin (selective α1-blocker), usually prescribed in a dose of 1-2 mg 2-3 times a day, is no less effective.

3. In some cases, **β-adrenoblockers** are added to treatment with α-blockers. Indications for their appointment are severe tachycardia, arrhythmia. 1-2 ml of a 0.1% solution of anaprilin (obsidan) in 10 ml of isotonic sodium chloride solution is administered intravenously for 5-10 minutes. If necessary, the introduction can be repeated under the control of blood pressure. The total dose should not exceed 5-10 mg. In the future, they switch to taking the drug inside by 20-40 mg 3-4 times a day. The use of β-blockers, especially their intravenous administration, should be carried out under careful electrocardiographic monitoring.

4. If the above measures do not stop the pheochromocytoma crisis within 2-3 hours, it is necessary to carry out emergency surgical treatment - removal of the pheochromocytoma, because in this situation the crisis is exacerbated by “catecholamine shock”, a state of “uncontrolled hemodynamics”, which can cause the death of the patient. The development of “catecholamine shock” is due to a sudden change in the sensitivity of adrenergic receptors and a violation of the mechanism of inactivation and metabolism of catecholamines.

The state of “uncontrolled hemodynamics” is characterized by a quick and frequent change in hypertensive and hypotensive crises that are difficult to treat. Further, the development of severe arterial hypotension, which is not amenable to treatment with prednisone, vasopressor amines, polyglucin, antishock agents, is possible.

5. To reduce blood pressure, sodium nitroprusside is also used intravenously dropwise 100 mg in 500 ml of 5% glucose until the effect is achieved. To stabilize hemodynamics, captopril, verapamil or nifedipine can be prescribed.

If the operation is impossible due to the serious condition of the patient or in the presence of metastases of malignant pheochromocytoma, apply:

- metirosine inside 250 mg 4 times a day, if necessary, increase the dose to 4 g per day, before the operation (the dose is adjusted according to the level of daily urine catecholamines and hypotensive effect; before the operation, the drug must be taken for at least 1 week).

With metastatic pheochromocytoma, somatostatin is effective. For malignant pheochromocytoma, treatment with cyclophosphamide, vincristine and dacarbazine is used.

Surgical treatment and radiation therapy

The most effective and radical treatment for catecholamine-producing tumors is surgical. The necessary volume of surgery for unilateral lesions is unilateral adrenalectomy, and for bilateral, total adrenalectomy. After total (bilateral) adrenalectomy, the body loses sources of endogenous corticosteroids, and 5–10 hours after surgery, adrenal insufficiency develops. Such patients need lifelong replacement therapy with corticosteroids.

Radiation therapy of tumors from chromaffin cells has until recently been considered ineffective.
Preoperative preparation.

Preoperative preparation with selective and non-selective a-adrenergic receptor blockers is indicated for patients with severe pheochromocytoma, in the presence of frequent hypertensive crises, severe hypovolemic disorders, cardiovascular and cerebral complications or impaired renal function. The appointment of b-blockers is possible after achieving a-blocking effect.

In preparation for surgery or when **surgical treatment** is not possible (in this case, these drugs are taken continuously):

- doxazosin inside 1 mg 1-2 times a day, if necessary (preservation of crises, blood pressure> 160/90 mm Hg), the dose is increased by 1-2 mg every 1-2 weeks, to a maximum dose of 16 mg per day, before surgery or for life, or
- prazosin orally 1 mg 2-3 times a day, if necessary (preservation of crises, blood pressure> 160/90 mm Hg), the dose is increased by 1-2 mg once a week, up to 3-8 mg 2 times a day before surgery or for life, or
- proroxan orally 15-30 mg 2 times a day, if necessary (preservation of crises, blood pressure> 160/90 mm Hg), the dose is increased 1 time per week to a maximum of 180 mg per day, before surgery or for life, less effective contraindicated in cases of coronary and cerebral circulation, or
- phenoxybenzamine orally 10 mg 2 times a day, if necessary, increase the dose to 20–40 mg 2 times a day, dosed according to the hypotensive effect, before surgery or for life
- atenolol inside 12.5-100 mg 2 times a day, before surgery or for life, or
- bisoprolol inside 5-10 mg per day, before surgery or for life, or
- metoprolol orally 25-100 mg 2 times a day, before surgery or for life, or
- nebivolol orally 5-10 mg per day, before surgery or for life, or
- propranolol orally 20–40 mg 4 times a day, before surgery or for life.

Substitution therapy after bilateral adrenalectomy surgery:

- intravenous hydrocortisone 25-50 mg every 4 hours on the 1st – 2nd day after surgery, 25–50 mg every 5 hours on the 3rd day, 25–50 mg every 6 hours on the 4th day, 25–50 mg every 8 hours on the 5th day, 25-50 mg every 12 hours on the 6th day and 25-50 mg once a day in the morning on the 7th day, then the drug is canceled.
- hydrocortisone inside 10 mg 3 times a day from 3-4 days after surgery (after restoration of the functions of the gastrointestinal tract), for life

fludrocortisone 100 mg once daily in the morning, for life.

- correction of hypovolemia by intravenous drip of plasma exchange solutions in an amount of 1.5-2 liters. per day.

Errors and unreasonable appointments

It is unjustified to cancel prolonged a-blockers (phenoxybenzamine, doxazosin) or reduce their dose when developing orthostatic arterial hypotension at the beginning of use, due to a deficiency in the volume of circulating blood. The patient must comply with strict bed rest for 2-3 days, the dose of drugs must be gradually increased daily to achieve the above criteria for the effectiveness of treatment. The most severe category of patients are patients with persistent arterial hypotension or a tendency to hypotension in the interictal period. In these patients, prolonged-acting oral a-blockers are a means of choice that avoids the state of “uncontrolled hemodynamics”. Nevertheless, the presence of initial hypotension is often mistakenly considered a contraindication to the use of a-blockers.

With normal or moderately elevated blood pressure and the presence of tachycardia (persistent or paroxysmal), a typical mistake is the appointment of b-blockers without first taking a-blockers.

Evaluation of the effectiveness of treatment.

The criteria for the adequacy and duration of preoperative preparation are the reduction of hypertensive seizures (up to 1 time per day or less with a decrease in the amplitude of the rise in systolic blood pressure), a decrease in the difference in systolic blood pressure during an orthostatic test (a comparative measurement of blood pressure in horizontal and vertical position,

is considered positive when the difference systolic blood pressure over 20 mmHg), positive dynamics of myocardial status by yes nym electrocardiogram and Echocardiography (including reducing depression segment ST, slowing of arrhythmias, reduction in the size of the heart chambers, increasing left ventricular ejection fraction, etc.).

Prognosis.

In 30-60% of cases, the diagnosis of pheochromocytoma is posthumous. Patients with unrecognized tumors die, as a rule, from the consequences of severe vascular complications in the pool of cardiac or cerebral arteries on the background of malignant arterial hypertension. In surgical treatment, perioperative mortality in specialized institutions is 1–4%. More than 95% of patients usually survive within 5 years after surgery, the relapse rate does not reach 10%. The most common recurrence of pheochromocytoma develops in patients previously operated on for multiple ectopic tumors and in the familial form of the disease.

1.10. HYPOPARATHYROID CRISIS

An acute condition caused by insufficient formation of parathyroid hormone by the parathyroid glands is characterized by a decrease in calcium and an increase in the phosphorus content in the blood and the development of convulsive syndrome.

Etiology

There is congenital and acquired hypoparathyroidism. The cause of acquired hypoparathyroidism can be various infections and intoxications, as well as damage or removal of the parathyroid glands during operations on the thyroid gland. The main manifestations of hypoparathyroidism: tonic convulsions, attacks of which are preceded by numbness, cold extremities, a feeling of crawling ants, impaired bone sensitivity. Provoking moments can be various irritants - thermal, pain, physical stress.

Pathogenesis

Since the exchange of calcium and magnesium is closely interconnected, a patient with hypoparathyroidism develops not only hypocalcemia, but also hypomagnesemia. In addition, with a lack of parathyroid hormone, phosphaturia decreases, which leads to an increase in the level of blood phosphates. Impaired phosphate metabolism disorganizes the functioning of the blood buffer systems and leads to the development of alkalosis, which potentiates an increase in convulsive readiness. For hypocalcemia of another etiology, hyperphosphatemia is uncharacteristic. The developing electrolyte imbalance changes the permeability of the membranes of nerve cells, enhances the penetration of sodium into the cell and the output of potassium. As a result, the processes of polarization of neuronal membranes in the region of the synapses are disrupted, which significantly increases neuromuscular excitability and general autonomic reactivity. All this leads to the development of a convulsive syndrome, the extreme manifestation of which is hypoparathyroid tetany. The mechanism of development of hypocalcemia is caused by a deficiency of vitamin D and develops only with the combined influence of two factors: 1) insufficient intake of vitamin A in the body with food; 2) the absence of sunlight on the skin, where under the influence of ultraviolet radiation, its synthesis occurs.

Vitamin D deficiency leads to a disruption in the synthesis of calcium binding protein in the intestine and a slowdown in the absorption of calcium in the gastrointestinal tract. In addition, with vitamin D deficiency, calcium reabsorption in the distal renal tubules slows. This leads to impaired absorption and increased calcium excretion, the end result of which is hypocalcemia, with an exacerbation of which the development of a hypocalcemic crisis with attacks of tetany is possible. With tetany, convulsions are possible not only of skeletal muscles, but also of smooth muscles of internal organs, including coronary arteries. This can lead to the development of a typical clinical picture of ischemia and myocardial damage.

Clinical picture:

Symptom precursors usually precede the development of a crisis and the appearance of a convulsive syndrome: numbness, crawling sensation, burning, tingling, tension, stiffness in the muscles of the limbs. Occasionally, precursor symptoms may be absent. Paresthesia (numbness,

tingling, sensation of cold, heat) begins with the lips, gradually spreads to the hands and feet, accompanied by fibrillar muscle twitches and cramps in individual muscle groups. As hypocalcemia progresses, these symptoms turn into extremely painful transient tonic convulsions, which in typical cases first occur in the skeletal muscles of the upper and then lower limbs. As hypocalcemia progresses, seizures become generalized with the involvement of the trunk muscles, facial and respiratory muscles, as well as the muscles of the internal organs. From the side of the upper extremities during tetany, the tone of the flexors prevails, from the side of the lower extensors. During an attack, the hands are usually bent at the joints, the patient's hands take the form of an "obstetrician's arm". The patient's legs are extended, brought to each other, the patient's feet in a state of sharp plantar flexion ("horse foot", pedal spasm). There is a trism of masticatory muscles, a sardonic smile, a fish mouth, and eyelid cramps. In severe cases, opisthotonus develops - convulsive extension of the trunk posteriorly. Cramps in the intercostal muscles and diaphragm make breathing difficult. The most dangerous manifestation of tetany is laryngospasm, which is more common in children and is manifested by inspiratory dyspnea, noisy stenotic breathing, cyanosis, and the appearance of foam on the lips. The combination of laryngo- and bronchospasm with tonic seizures of the diaphragm and respiratory muscles can lead to asphyxiation, which ends lethally if intubation is not done. Sometimes a tracheostomy may be required. Death can also come from a heart-beating. The act of swallowing is disturbed due to a spasm of the smooth muscles of the esophagus. As a result of pylorospasm, nausea, vomiting, epigastric pain are possible. A spasm of the intestinal muscles causes intestinal colic, and the bladder leads to anuria. The duration of tetany attacks can be from minutes to several hours, their frequency varies widely. Attacks can occur both spontaneously and under the influence of mechanical, thermal, electrical or pain stimuli. Sometimes cramps can be triggered by muscle tension, nervous shock, hot bath, straightening of limbs. In addition to disorders of the somatic nervous system, concomitant dysvegetosis is observed, manifested by profuse sweating, bronchospasm, renal and (or) hepatic colic, vomiting, diarrhea. Hypocalcemic syndrome often proceeds under the guise of acute psychopathy (paranoid or hallucinatory syndromes, depressive-catatonic psychosis), as well as severe neurological pathology (dysarthria, dysphagia, paresis of the cranial nerves, extrapyramidal and stem disorders, spastic paresis of extremities, epileptic). When examining a patient with a hypocalcemic crisis, the following clinical syndromes can be distinguished.

1. Tetanic (convulsive) syndrome. Unlike epilepsy, consciousness during tetany is preserved, however, with especially severe attacks, fainting may develop.
2. The syndrome of autonomic dysfunction. With a predominance of the tone of the sympathetic nervous system due to a spasm of the peripheral arteries, the attack proceeds with pallor, tachycardia, and an increase in blood pressure. If the tone of the parasympathetic division predominates, vomiting, diarrhea, polyuria, bradycardia, and arterial hypotension are typical.
3. The syndrome of damage to the central nervous system and brain disorders. During severe tetany attacks, it is possible to develop cerebral edema with stem and extrapyramidal symptoms, sometimes typical epileptiform attacks occur.
4. Visceropathy syndrome. During an X-ray examination, calcinates are often found in organs and tissues, intracranial calcification in the region of the basal ganglia, hypothalamus, cerebellum is possible, with a long history of hypoparathyroidism, cataracts are often detected.

Syndrome of damage to the skin and its derivatives. Dryness and peeling of the skin are characteristic, often the presence of eczema, exfoliative dermatitis, the appearance of pigmentation and depigmentation sites of the skin (vitiligo). Candidomycosis often develops. Bubbles with a clear liquid content (exfoliative dermatitis) may appear on the skin. Hair growth throughout the body is impaired, early gray hair and baldness appear. Fragility of nails is observed, the nail plates are pale, dull, often mycotically altered.

Diagnostics

Diagnosis of hypocalcemic crisis can be verified in the presence of: total calcemia less than 1.9-2.0 mmol / l and ionized calcium level less than 1 mmol / l; a typical Sulkovich reaction

(hypocalciuria up to 10-50 mg / day with a norm of 200-400 mg / day); urinary phosphorus excretion of less than 2.8 g / day; low levels of parathyroid hormone in the blood; ECG signs of hypocalcemia (lengthening of QT and ST intervals); typical radiological changes (signs of osteoporosis and osteosclerosis, periostosis of long tubular bones, ribbon-like compaction of metaphyses, calcification of costal cartilage, calcium deposits in the meninges and synaptic ganglia). When examining a patient who has a history of hypocalcemic tetany attacks, but at the time of examination is in the interictal period, it may be useful to know the samples to detect latent tetany. To identify signs of increased convulsive readiness, the presence and severity of the following symptoms are most often assessed.

1. Weiss symptom. In order to check this symptom, a neurological hammer is beaten along the outer edge of the orbit. With increased convulsive readiness as a result of striking, contraction of the circular muscle of the orbit and frontal muscle occurs.

2. Trousseau symptom. To identify the symptom, it is necessary to compress the shoulder by applying a tourniquet or inflating the cuff of the sphygmomanometer. 1-3 minutes after such compression, a characteristic spasm of the muscles of the hand occurs, giving it the shape of an "obstetrician's arm". Mechanical pressure on the brachial nerve located along the medial edge of the biceps of the shoulder leads to a similar spasm of the carpal muscles.

3. Chvostek's sign (symptom). In order to check this symptom, a neurological hammer is beaten at the exit site of the facial nerve in front of the external auditory meatus (in front of the tragus). With increased neuromuscular irritability, in response to this, a reduction in facial muscles is observed in the corresponding half of the face. Depending on the intensity of muscle contraction, three degrees of severity of this symptom are distinguished: III degree - only the muscles of the angle of the mouth contract (found in 25% of healthy people); II degree - contraction of the muscles of the angle of the mouth and wings of the nose; I degree - reduction of the entire facial muscles of the corresponding half of the face. Some authors (M.I. Balabolkin, 2002) regard the most intense expression of facial muscles as the III degree of symptom severity, and the minimum as I degree of response. However, a significant increase in neuromuscular excitability is indicated by a pronounced muscle spasm during a symptom check.

4. Schlesinger's symptom. To test this symptom, a straightened leg is passively quickly bent in the hip joint; during flexion in the hip joint, the leg remains straightened at the knee joint. With increased neuromuscular excitability, the patient has an involuntary convulsive contraction of the extensor muscles of the thigh and foot, leading to supination of the latter.

5. Symptom of Hoffmann. When checking this symptom, pressure is applied to areas located in the projection of the branching of peripheral nerves. In favor of increased neuromuscular excitability, the appearance of paresthesia in response to pressure in these areas indicates. If you get dubious results during the study of these symptoms, you can test with hyperventilation, after which re-study of the above symptoms.

First, convulsions of the arms and legs develop, then the trunk and face. In the region of the upper extremities, convulsions cover the flexor muscles, and the hands assume a characteristic position: they are pressed to the body and bent at the elbows, the hand is in the "obstetrician's hand" position. The lower limbs during cramps are pressed together, extended, fingers on the feet bent. In severe cases, convulsive contractions of the muscles of the face - chewing muscles (trismus) and muscles of the mouth develop. With cramps in the muscles of laughter, a so-called sardonic smile appears on the face. Muscle cramps are accompanied by severe pain. The muscles become very hard. In this case, spasm of the glottis, more often observed in children, is dangerous. Sometimes there is an isolated spasm of smooth muscles, in particular a spasm of the pylorus, accompanied by profuse vomiting; spasm of arteries of the heart, manifested by angina pectoris. Symptoms of acute hypoparathyroidism include the symptom of Chvostek I (contraction of the muscles of the upper eyelid along with contraction of the circular muscles of the mouth and muscles of the forehead when tapped with a hammer or finger anterior to the tragus in the region of the upper facial nerve). Symptoms for acute hypoparathyroidism are the Weiss symptom - contraction of the frontal and circular muscles of the eyelids when tapped with

a finger or percussion hammer at the outer edge of the orbit, where the upper branch of the trigeminal nerve passes, as well as diplopia, resulting from a violation of convergence or passing strabismus. In the chronic course of hypoparathyroidism, trophic disturbances of the skin, nails, and hair often occur, muscle weakness develops, which is more pronounced in the proximal limbs. The most characteristic ophthalmic manifestation of hypoparathyroidism is tetanic hypocalcemic cataract, which has some features in the initial stage of its development. Hypoparathyroid cataract, as a rule, is bilateral, although the clouding of the lenses in both eyes is not always parallel, it has the ability to quickly occur and ripen (against the background of tetany, clouding of the lens can develop within a few hours). Over time, cataract professes towards the central departments of the lens. In the late stage of development and with complete clouding of the lens, the hypoparathyroid cataract does not have any specific features. Complete hypoparathyroid cataract is subject to surgical removal performed during the replacement therapy of hypoparathyroidism with parathyroidin. The prognosis of tetanic cataract with congenital hypoparathyroidism is most serious.

Differential diagnosis

Stomach aunt can mimic the syndrome of "acute abdomen", and heart aunt is difficult to distinguish from an attack of angina pectoris or myocardial infarction. It is also difficult to exclude acute forms of coronary heart disease in these cases because not only prolongation of the QT interval, but also depression of the ST segment, sharpening or inversion of the T wave are often recorded as a result of coronary spasm during hypocalcemic crisis on the ECG. The study of calciumemia helps the correct diagnosis. During the differential diagnosis of hypocalcemic crisis, the presence of anamnestic data indicating damage to the parathyroid glands should also be taken into account. Most often these are surgical interventions on the thyroid and parathyroid glands, treatment with radioactive iodine, etc. Hypocalcemic tetany should be distinguished from normocalcemic, developing as a result of alkalosis. The cause of alkalosis in this case is most often the following reasons: hyperventilation (usually in patients with hysteria and neurosis); repeated vomiting (in patients with decompensated pyloric stenosis). The phenomena of tetany caused by hyperventilation have a clear relationship with respiratory failure and disappear a few minutes after its normalization. Patients with repeated vomiting usually have a characteristic history and clinical symptoms of a disease of the gastrointestinal tract. In addition, hypocalcemic tetany should be differentiated from convulsive syndrome of another etiology. Epilepsy. An epileptic seizure is accompanied by the development of a convulsive syndrome. But with a hypocalcemic crisis, in contrast to an epileptic seizure, the patient’s consciousness is usually preserved, there is no bite of the tongue characteristic of epilepsy and a period of amnesia. After an attack of epilepsy, the patient usually falls asleep, which is uncharacteristic for a hypocalcemic crisis. Achieving normocalcemia quickly stops not only the manifestations of the convulsive syndrome, but also the signs of increased convulsive readiness on the electroencephalogram. However, against the background of hypoparathyroidism, the development of typical epilepsy is possible.

Hypoglycemia. Severe hypoglycemia can be accompanied by the development of seizures, which should be differentiated not only from epilepsy, but also from hypocalcemic tetany. However, with severe hypoglycemia, the patient quickly falls into a coma, a history of diabetes mellitus is present. Laboratory examination reveals a low level of glycemia, after an intravenous administration of glucose, a pronounced positive effect is observed.

In patients with tetanus, the development of convulsive syndrome is preceded by a characteristic anamnesis: usually puncture wounds of the lower extremities contaminated with soil particles, as well as the absence of measures to prevent this disease (administration of toxoid, anti - tetanus serum, etc.). Sometimes the causative agent of tetanus enters the body due to damage to the skin as a result of burns or frostbite. The incubation period is from 3 to 30 days, but usually is within 1-2 weeks. With tetanus, prodromal symptoms can be observed: pain in the wound, muscle twitching around it. The development of convulsive syndrome begins with the involvement of facial muscles (trismus, a sardonic smile), then the process extends to the

muscles of the trunk and limbs. The muscles of the feet and hands are usually free of tension. Body temperature is increased, the degree of its increase is proportional to the severity of the convulsive syndrome.

Treatment

1. Emergency hospitalization in a specialized department.
2. Parenteral administration of **calcium** salts. Most preferred is an intravenous infusion of 10-20 ml of a 10% solution of calcium chloride, gluconate or lactate, dissolved in 500 ml of 5% glucose. It is also possible a very slow intravenous administration of these solutions in the same doses. However, with this method of administration, venous thromboses sometimes develop at the injection site. In addition, with extravasal ingestion of calcium solutions, massive necrosis of surrounding tissues develops. If the introduction of calcium does not stop the attack, and the presence of hypocalcemia is not in doubt, the presence of alkalosis or hypomagnesemia should be assumed. In such cases, trial treatment is indicated by intravenous administration of 10 ml of a 5% solution of ascorbic acid and 10 ml of a 25% solution of magnesia sulfate. After stopping hypocalcemia, the immediate appointment of replacement therapy with calcium preparations is shown (6-10 g of calcium gluconate or calcium lactate per day with a gradual decrease in the dose to the maintenance dose of 2-6 g / day), as well as with vitamin D.
3. Symptomatic treatment of **convulsive syndrome**. After stopping seizures by the intravenous administration of calcium, sedatives and antispasmodics are prescribed in usual doses (bromides, barbiturates, papaverine, tranquilizers, etc.).
4. The fight against **asphyxia.** With the development of laryngospasm and asphyxia, intubation and mechanical ventilation are indicated. Sometimes, to restore breathing, you have to resort to a tracheostomy.
5. Prescription of **vitamin D** preparations or its analogues. In case of hypocalcemic crisis, the most active vitamin D preparation is used - calcitriol (rockaltrol), which is prescribed orally at 0.25-1 mcg once a day. The dose is selected individually, depending on the severity of the clinical symptoms of convulsive readiness, as well as the results of monitoring levels of calcium, phosphorus and magnesium. Instead of calcitriol, it is possible to prescribe At-10 (tachistin), which is taken in 1-2 mg (40-80 drops) every 6 hours before the relief of the convulsive syndrome, followed by a dose reduction of 2 mg every 2 days.
6. The neutralization of the negative effects of **phosphates**. A calcium-rich milk-vegetable diet contains a lot of phosphorus, which enhances the excretion of calcium in the urine and its absorption by the skeleton. To bind phosphorus, the patient should take 20-40 ml of a 4% suspension of aluminum hydroxide with food.
7. Correction of **acid-base balance**. With a hypoparathyroid etiology of a hypocalcemic crisis, to eliminate the characteristic for these cases of alakalosis, it is indicated that 3–7 g per day of ammonium chloride is administered orally after meals.

In the treatment of hypoparathyroidism, normalization of calcium and phosphorus metabolism is of primary importance. To this end, in the interictal period, under the control of blood calcium concentration, substitution therapy with parathyroidin is carried out - a preparation of parathyroid hormone contained in the extract from the parathyroid glands of cattle, administered intramuscularly or subcutaneously 1-2 ml 1-2 times a day, daily or every other day, as well as ingestion of calcium preparations (5% calcium chloride solution, 1 tablespoon 3-6 times a day or calcium lactate, 0.5 g 3-4 times a day). A certain place in the treatment of hypoparathyroidism in the interictal period is occupied by calciferol and dihydrotachysterol, which improve the absorption of calcium in the intestine and maintain its normal concentration in the blood. Doses and duration of their use are strictly individual and are established on the basis of the general condition of the patient and the content of calcium and phosphorus in the blood. In an acute attack of tetany, the best cure for seizures is the intravenous administration of a 10% solution of calcium chloride (5-10 ml) or inside, 1 tablespoon of a 5% solution 5-6 times a day. In addition, parathyroidin (2–4 ml) is administered intramuscularly, the effect of which is manifested in 2–3 hours. Concerning the development of tetany (seizures) with hypoparathyroidism and its

differential diagnosis, one cannot help but remember that muscle cramps are not such a rare occurrence. They can also develop in healthy people after a fairly long physical exertion due to a decrease in the amount of substances necessary for muscle nutrition. Tetany is sometimes noted with rickets, varicose veins or thrombophlebitis, osteochondrosis of the spine, obliterating endarteritis, or obliterating atherosclerosis. Muscle seizures can be caused by hyperaldosteronism, respiratory or metabolic alkalosis, as well as prolonged neurotic hyperventilation of the lungs or prolonged vomiting (with narrowing of the pylorus). Seizures can be a symptom of adrenal or chronic renal failure. On the other hand, impaired renal function is one of the characteristic signs of primary hyperparathyroidism. During a parathyrotoxic crisis, this disorder can be critical. It is not difficult to understand how difficult the difficulties are in carrying out therapeutic measures aimed at stopping the hypercalcemic (parathyrotoxic) crisis if acute renal failure develops. Extracorporeal or peritoneal dialysis or intensive therapeutic plasmapheresis is sometimes the only way to preserve life in such cases. Acute renal failure, in turn, can cause the development of pulmonary edema, which creates additional difficulties in the treatment of such patients. The appointment in these cases of furosemide is especially important. Acute renal failure often develops after removal of an adenoma of the parathyroid glands or hyperplastic (all or three and a half) parathyroid glands, so it can be combined with acute hypocalcemic crisis. Moreover, intensive therapeutic plasmapheresis and hemodialysis and hemosorption are more indicated.

1.11. HYPERCALCEMIC CRISIS

Hypercalcemic crisis is an emergency caused by a sharp increase in serum calcium levels and is characterized by severe neuromuscular and neuropsychic disorders, increased blood coagulation up to the occurrence of thrombosis and DIC (Disseminated intravascular coagulation), as well as the development of acute cardiovascular insufficiency, which in the most severe cases accompanied by cardiac arrest in the systole phase. A life threat to the patient occurs when the calcium level is above 3.5-4.0 mmol / L. Mortality in a crisis can reach 50-60%.

Etiology

The development of a hypercalcemic crisis most often occurs against the background of adenoma or hyperplasia of the parathyroid glands, with vitamin D poisoning, as well as in patients with malignant tumors with massive bone metastases. Provoking factors: exacerbation of primary hyperparathyroidism in the absence of adequate treatment; rapid dehydration in patients with primary hyperparathyroidism and hypercalcemia; treatment with thiazide diuretics; hypervitaminosis of vitamin D, the consumption of a large amount of milk, calcium-rich food additives and soluble antacids (sodium bicarbonate, calcium carbonate, etc.) - milk-alkali syndrome or Burnett's syndrome.

Pathogenesis

An excess of parathyroid hormone leads to the mobilization of calcium from bone tissue due to the predominance of bone resorption processes over bone formation. This leads to demineralization of the bones and an increase in calcemia. In addition, the synthesis of calcitriol, a highly active form of vitamin D, is activated, which leads to excessive absorption of calcium in the intestine and an increase in its concentration in the blood.

Clinical picture:

Hypercalcemic crisis occurs against the background of primary hyperparathyroidism, and is manifested by the following syndromes.

1. Renal syndrome: polyuria, polydipsia, hypoisostenuria and nephrolithiasis.
2. Bone changes syndrome: diffuse osteopenia, subperiosteal resorption and osteolysis of the terminal phalanges of the hands and feet, fibrocystic osteitis with the development of skeletal deformities and pathological fractures.
3. Gastrointestinal syndrome: anorexia, nausea, flatulence, constipation, weight loss, the risk of developing peptic ulcers of the stomach and duodenum, pancreatitis, pancreaticcalculosis,

gallstone disease.

4. Syndrome of cardiovascular disorders: arterial hypertension, left ventricular myocardial hypertrophy, cardiac arrhythmias.

5. Visceropathy syndrome: associated with the deposition of calcium salts in various organs and tissues.

6. Syndrome of mental disorders: depression, drowsiness, memory impairment.

7. Syndrome of neurological disorders: radicular disorders, symptoms of tension, paresthesia, paresis of the muscles of the pelvic girdle and lower extremities. Under the influence of provoking factors, the patient's condition begins to rapidly deteriorate, appetite completely disappears, nausea, indomitable vomiting, abdominal pain, peritonism, constipation appear. Sometimes the pains are girdle-like, which leads to an erroneous diagnosis of acute pancreatitis. Body temperature rises, often up to 39-40 C. Sharp muscle weakness, decreased tone of skeletal muscles, weakening tendon reflexes, bone pain are observed. The skin is dry, due to severe itching, traces of scratching are often visible on it. Neuropsychiatric disorders occur and gradually increase in the form of depression or psychomotor agitation up to psychoses. As hypercalcemia progresses, consciousness becomes confused and a coma develops. Activation of blood coagulation factors against the background of severe hypercalcemia often leads to the development of intravascular thrombosis and even DIC. Intensive secretion of gastric juice on the background of hypercalcemic crisis often leads to ulcerative lesions of the walls of the stomach and duodenum with the development of severe gastrointestinal bleeding. In the first hours after the development of the crisis, an increase in blood pressure is possible, polyuria is replaced by oligo- and anuria, against which the symptoms of cardiovascular failure begin to progress and blood pressure decreases. With very high calcemia (up to 4.99 mmol / L), irreversible inhibition of the respiratory and vasomotor centers occurs, the clinical picture of shock develops and a lethal outcome occurs.

With hypercalcemic crisis, against the background of the clinical symptoms of hyperparathyroidism, the following clinical syndromes appear.

1. Abdominal syndrome (acute pain in the epigastrium, nausea, indomitable vomiting, possible gastric bleeding, perforation of gastric and duodenal ulcers, acute pancreatitis).

2. Syndrome of neuropsychiatric disorders (confusion, stupor or hallucinations, which are replaced by somialment and coma).

3. Dehydration syndrome (dry skin and visible mucous membranes, decreased skin turgor, sharpening facial features).

4. Thermoregulatory disorder syndrome (febrile body temperature).

5. Syndrome of acute cardiopulmonary failure (severe dyspnea, cyanosis, tachycardia, gallop rhythm, arrhythmias, hypotension, filamentous pulses, vascular collapse and cardiac arrest in the systole phase).

6. Renal syndrome (anuria, increasing azotemia).

7. Syndrome of neuromuscular disorders (hypo- and areflexia, severe muscle hypotension, because of the weakness of the respiratory muscles, there may be a need for artificial ventilation of the lungs).

8. Hypercoagulation syndrome (thromboembolic complications, possibly the development of DIC). The diagnosis of hypercalcemic crisis is confirmed by the presence of a high level of blood calcium, characteristic of hypercalcemia changes on the ECG (shortening of the QT interval, expansion of the QRS complex), the presence of a parathyroid tumor according to ultrasound and computed tomography. Differential diagnosis. In individuals with a characteristic history (hyperparathyroidism, tumors, vitamin D poisoning), problems with the diagnosis of hypercalcemic crisis do not arise. In the absence of a typical history, there may be a need for differential diagnosis with renal colic, peptic ulcer exacerbation, acute pancreatitis, myasthenic crises, and gastrointestinal bleeding. Differential diagnosis is based on a study of the level of calciumemia, which in hypercalcemic crisis exceeds 3.5 mmo l / l.

Treatment

The following measures are intended to stop this emergency

1. Emergency hospitalization in the endocrinological or intensive care unit.

2. **Forced diuresis**. Within 3 hours, 3.0 L of isotonic sodium chloride solution is administered intravenously dropwise in combination with 80-100 mg of furosemide per hour. Due to the threat of hypokalemia during the infusion, it is necessary to control the level of basic electrolytes. Subsequently, under the control of diuresis, arterial and central venous pressure, the volume of the transfused fluid can be brought up to 8-9 l / day, furosemide is administered every 2 hours at a dose of 100 mg. It should be remembered that ignoring these indicators can lead to an overload of the heart with volume and the development of pulmonary edema.

3. **Binding of calcium by complexones**. A 5% solution of sodium salt of ethylenediaminetetraacetic acid (EDTA- Na2) is dissolved in 300-400 ml of 5% glucose and injected intravenously based on the calculation of 50 mg / kg of weight. When determining the amount of EDTA- Na2, it should be remembered that 1 ml of its 5% solution contains 50 mg of the active substance (ampoules of 5 and 10 ml are released). The infusion should be very slow, at a rate of 8-12 drops per minute, for the infusion takes about 4-6 hours. With a more rapid introduction, there is a threat of glomerulosclerosis, hemorrhage in the parenchymal organs, collapse.

4. **Fixation of calcium in the bones**. For this purpose, calcitrin is administered intravenously every 8 hours at the rate of 1-4 U / kg body weight.

5. The appointment of **corticosteroids**. Hydrocortisone hemisuccinate is used, which is intravenously slowly administered 3 times a day at 50 mg.

6. **Extracorporeal** methods of treatment. To accelerate the excretion of calcium, hemodialysis or peritoneal dialysis with calcium-free dialysate is performed.

2. EDUCATIONAL AND METHODOLOGICAL RECOMMENDATIONS FOR INDEPENDENT WORK OF STUDENTS

Independent work is the planned work of students, carried out on assignment and with the methodological guidance of the teacher, but without his direct participation. According to the target sign, independent work of students can be carried out: for mastering knowledge, for consolidating and systematizing knowledge, for the formation of skills.

2.1 The main types of topics for the independent form of work full-time education

Name of sections and topics	Type of independent work (study of educational material, solving problems, abstract, report, test, preparation for passing the test, exam, etc.)	Control form (verification of problem solving, abstract, etc.)
Diabetes mellitus. Differential diagnosis of hyperglycemia. Diagnosis and treatment of diabetes mellitus	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Diabetic microangiopathy. Diabetic retinopathy, nephropathy. Diabetic neuropathy	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.

Macroangiopathy. Diabetic foot. Diabetes mellitus and arterial hypertension.	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Diabetes mellitus and pregnancy. Diabetes mellitus and surgical pathology	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Emergency conditions for diabetes	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Differential diagnosis and treatment of coma in diabetes	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Emergencies for thyroid disease	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Emergency conditions for adrenal gland diseases	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.
Emergency conditions for mineral metabolism disorders	Study of educational material, preparation for passing the credit	Interview in class, checking situational tasks.

2.2 Set of tasks for independent work

The number of task	Problem situation (the formulation of the assignment)
1	Patient I., 52 years old, has complained of dry mouth, thirst, weight gain, and hunger over the past 3 months. BMI is 36 kg / m2. Fasting blood sugar 11 mmol / L, glycated HB - 9.2%. Total cholesterol - 6.7 mmol / l, triglycerides - 302 mg% (normal less than 150 mg%), HDL cholesterol - 31 mg% (normal - less than 40 mg%), LDL cholesterol - 113 mg% (normal - less than 130 mg%). Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
2	Patient S., 47 years old, has been suffering from diabetes for 10 years, follows a diet, is engaged in physical exercises daily. Receives insulin therapy: humalogue of 8 units. before each meal and glargine 42 units. in the evening. He complained of sleep disturbances, nightmares, severe fatigue, sweating at night. On examination, the patient is of sufficient nutrition, the skin is of normal humidity. The vesicular breathing. Pulse 120 beats per minute. Blood pressure - 160/80 mm Hg Fasting blood sugar - 11.5 mmol / L, postprandial glycemia - 4.6 mmol / L. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
3	Patient M., 29 years old, has been suffering from diabetes for 16 years. Gets mixed insulin - Humulin M3 for 24 units. in the morning and 15 units. in the evening. The

	last 5 years have been controlling diabetes well. The last 3 years marks an increase in blood pressure to 160/100 mm Hg. A physical examination revealed no physical abnormalities. HELL 150/90 mm Hg In blood tests: fasting glucose - 5.6 mmol / L, HBA1c - 8.1%, sodium - 135 mmol / L, potassium - 4.6 mmol / L, urea - 7.3 mmol / L, creatinine - 110 mmol / l In repeated analyzes of daily urine for 6 months, microalbuminuria was determined with a level of 182 mg / day, 171 mg / day and 200 mg / day. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
4	Patient I., 44 years old, was operated on for diffuse toxic goiter of large sizes. In the postoperative period, convulsions of the upper and lower extremities were repeatedly observed, which were stopped by the introduction of 20 ml of a 10% solution of calcium gluconate. In blood tests: total calcium - 1.7 mmol /l. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
5	Patient E., 53 years old, has been observed by an endocrinologist for 20 years. For the first time at the age of 33 years, an increase in the thyroid gland and signs of hyperthyroidism were noted. Examination revealed high levels of thyroxine and triiodothyronine in peripheral blood. I took tyrosol for 18 months. I felt good. For the next 5 years she did not take any treatment. Once a year I monitored the thyroid gland by ultrasound and TSH level. Subsequently, there was weakness, weight gain, depression, headache, low blood pressure, coldness of the limbs. The patient herself considered her condition to be a consequence of unreasonably long treatment with tyrosol. For the last 10 years, he has been taking replacement therapy with L-thyroxine in an increasing dose. On the day of supervision takes 150 mg of levothyroxine. From the anamnesis it is known that the patient's mother and grandmother also had thyroid diseases. Mom was operated on. Objectively: the condition is satisfactory. The skin is pale, moderately dry. Adequate food. Shins are pasty. The vesicular breathing. respiratory rate - 20 per minute. Heart sounds are muffled, pulse 64 per minute, blood pressure 120/80 mm RT. The abdomen is soft, painless. On the ECG - nonspecific changes in the myocardium on the anterior and lateral wall, signs of left ventricular hypertrophy. OAC and biochemical parameters within normal limits. Hormones in the blood: TSH - 1.7 mU / l, T4 f. - 11 nmol / l. Ultrasound of the thyroid gland: dimensions increased, volume 23.5 cm3, diffuse-heterogeneous, reduced echogenicity. In the right lobe, 2 round knots with a diameter of 15 and 7 mm are defined. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
6	Patient K., 19 years old, unconscious was delivered to the emergency room. According to relatives, he is registered at the endocrinologist for hypocorticism since childhood. Takes prednisone - 4 tablets per day and Cortinef - 2 tablets per week. A few days ago, the patient experienced severe psycho-emotional stress. The condition has worsened. Weakness, dizziness, loss of appetite, weight loss increased. The night before, vomiting, diarrhea appeared, in the morning - cramps and loss of consciousness. Delivered by ambulance. Objectively: the patient is unconscious, exhausted, the skin is swarthy with pigmentation in the places of physiological folds, in the folds of the skin on the palmar surface. The skin is dry. The vesicular breathing is weakened. The pulse is threadlike, rare. Blood pressure 70/40 mm Hg.

	Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
7	Patient D., 32 years old, was admitted to the endocrinology department with complaints of palpitations, weight loss for 10 months at 10 kg, sweating, irritability, insomnia, hand tremor and severe weakness. Over the past month, notes "a feeling of sand in the eyes." Six months ago, suffered severe stress (conflict in the family). Since that time, she felt growing weakness, poor sleep, nightmares and weight loss while maintaining her appetite. Objectively: a satisfactory condition, low nutrition. The skin is pale, high humidity. Tremor of the hands and fingers, tremor of the eyelids. Height 170 cm., Weight 53 kg. Exophthalmos. Positive symptoms of Kocher, Gref, Moebius and Shtelvag. Pulse 120 beats per minute, blood pressure 140/80 mm Hg Heart sounds are rhythmic, 1 tone is amplified, systolic murmur is at the top of the heart. It is carried out at all points and on the vessels of the neck. The contours of the front surface of the neck are deformed. On palpation, the thyroid gland is enlarged, denser than usual, painless, mobile. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
8	Patient S., 25 years old, complained of convulsive conditions in the limbs, creeps in them (paresthesia). These complaints are worrying for six months. A history of frequent transferred sore throat, pain on the front of the neck, pain when swallowing. Sore throat was accompanied by a temperature of up to 39 ° C, weakness. and tachycardia. It was treated, as a rule, with antibiotics for about 7 days, but sometimes it cost only local gargling. When measuring blood pressure, convulsions appeared in the hand. During the examination: a general blood test and a general urinalysis are normal. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
9	Patient A., 56 years old, who was treated for a long time by nephrologists for urolithiasis with frequent exacerbations, with a minor injury received a pathological fracture of the right lower leg. The patient notes weakness, pain in the bones of a aching character, a change in the gait of the duck type, thirst, polyuria, and itchy skin. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
10	Patient K., 22 years old, suddenly ran ill after running a long distance: pallor of the skin, shortness of breath, severe weakness, palpitations, headache, dizziness, fear of death, trembling in the body, nausea, single vomiting, epigastric pain . When examined by a doctor on duty, a heartbeat of up to 125 per minute and an increase in blood pressure to 205/110 mm Hg are noteworthy. No words have been noted before. An ambulance was delivered to the hospital. Objectively: The skin is pale, the limbs are cold to the touch, moist. Body temperature is 36.6 degrees. The respiratory rate is 21 per minute. Heart rate 130 beats per minute, arrhythmia. Blood pressure 190/100 mm Hg Heart sounds are muffled. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
11	Patient K., 17 years old, height 172 cm, weight 55 kg. He was taken to an emergency room in an unconscious state. According to relatives, it was established

	that the patient has diabetes for 2 years. Hypoglycemic conditions have been repeatedly observed. Insufficient diabetes control. Poor diet. Irregularly puts insulin. Over the past 2 weeks after a viral infection, he noted increasing weakness, thirst for up to 3-4 liters of fluid per day, loss of appetite. 2 days ago, nausea appeared. A few hours before hospitalization, repeated vomiting, abdominal pain. Lost consciousness. Objectively: the patient is unconscious, undernourished, the skin and mucous membranes are dry, breathing is noisy, quickened. Pulse 110 per minute, blood pressure - 85/50 Hg The abdomen is soft, painful in the umbilical region. Symptoms of peritoneal irritation are negative. Blood tests: white blood cells 10.0x10 ml, urea 11.3 mmol / l, creatinine - 120 mmol / l, pH - 7.21. Urinalysis (taken by catheter): density - 1041, sugar - 8%, acetone ++++. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
12	Patient A., 39 years old, was taken to the emergency room of a clinical hospital in an extremely serious condition. Consciousness is confused, periodically raves, motor anxiety is noted. According to the attendant, in recent days she noted nausea, repeated vomiting, fever up to 38-39 ° C. Six months ago, the patient was diagnosed with diffuse toxic goiter, and treatment with tyrosol was prescribed. About a month ago, she independently stopped taking the drug after visiting the "healer". When viewed from a temperature of 39.2 ° C, respiratory rate of 28 per minute. The patient is exhausted. The skin is moist over the entire surface. Pronounced tremor of limbs. On the front surface of the neck, a thyroid gland enlarged to 2 degrees is visually determined, dense, painless, mobile. Positive eye symptoms: Gref, Moebius, Kocher and Delrimple. The pulse is 176 beats per minute. Heart sounds are arrhythmic, systolic murmur is heard, conducted to all points. blood pressure 90/40 mm Hg. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
13	Patient D., 28 years old, has been suffering from type 1 diabetes for 6 years. Insulin receives in the form of a basic bolus therapy (actrapid and protafan). In the morning and in the afternoon I put the usual dose of insulin. In the evening after work I drank a large amount of alcohol, I did not inject insulin. Suddenly lost consciousness and was taken to hospital. Objectively: the patient is unconscious. The skin is pale, moist. Muscle tone is increased, sometimes cramps. The breath is shallow. Pulse - 64 per minute, blood pressure 90/60 mm Hg. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
14	A girl of 19 years old was taken to the intensive care unit with symptoms: polyuria and polydipsia 3-4 days, disorientation and severe agitation 1 day, fever 3 days. Two weeks ago, she had severe flu. Objectively: stupor, temperature 400C, the skin is pale, dry, pronounced dehydration. Respiratory rate 60 per minute, deep breathing as Kussmaul. Pulse - 140 beats per minute. Blood pressure - 160/60 mm Hg Laboratory data: white blood cells 18x10 / 109, blood sugar 36.2 mmol / L, bicarbonates - 19.8 mmol / L, urea - 17.0 mmol / L, creatinine - 250 mmol / L, sodium - 132 mmol / L, potassium - 3.1 mmol / L; chlorides - 92 mmol / L. Urine Acetone is negative. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.

15	Patient V., 27 years old, was found unconscious, covered with drops of sweat with convulsive twitching on the street at 17 o'clock. Using a bracelet on his arm, it was established that the patient suffers from diabetes, receives 28 units of protafan and 32 units of actrapid per day. In the morning, according to relatives interviewed by telephone, I felt good. After the introduction of 100 ml of 40% glucose came to, but notes a decrease in vision in the right eye. Objectively: normal nutrition. The skin is ordinary. In the lungs, vesicular breathing. The respiratory rate is 14 per minute. Pulse 80 per minute, blood pressure - 120/80 mm Hg Heart sounds are rhythmic. The abdomen on palpation is soft, the liver along the edge of the costal arch. In the fundus: retinal hemorrhage. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
16	The patient is 23 years old (height - 156 cm, weight - 54 kg), pregnancy 7 weeks. Complaints of dizziness, fatigue, weight gain of 2 kg, tearfulness, constipation. In the anamnesis: without pathology. In the status: blood pressure - 110 / 60mm Hg, heart rate-48 per minute. Thyroid gland: not palpable, low located. Eye symptoms are negative. There is no tremor. Secondary sexual characteristics by age. There are no galactorrhea. There are no striae. Examination: Ultrasound of the thyroid gland: volume - 29.1 cm3. Structure with linear fibrosis. Glucose - 5.0. TSH - 4.5 μMU / ml. HbA1c - 5.1%. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
17	The patient is 18 years old (height 140 cm, weight 54 kg). Complaints about: after a physical education lesson, trembling in the hands, headaches, excessive sweating, headache appeared. History: type 1 diabetes mellitus, on insulin. Heredity: father is overweight. In the status: Blood pressure - 115/70; Heart rate 80. Thyroid gland: palpable to 0 degree soft. Eye symptoms are negative. Outstretched tremors. The skin is moist, moist, the forehead is covered with drops of sweat. Secondary sexual characteristics by age. There is no striae. Examination: Serum glucose - 2.7 mmol / L. Urine sugar - no. Acetone is urine negative. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
18	A 47-year-old patient was admitted to the clinic with multiple pathological, spontaneous fractures of the tubular claws, pronounced curvature of the spine and deformation of the skeleton. Upon admission, the patient complained of general weakness, extremely fatigue, muscle hypotension, severe polyuria. The patient has a history of urolithiasis and elevated urinary phosphate levels. A laboratory examination of the patient revealed: serum calcium - 3.5 mmol / L (norm 2.1-2.6 mmol / L), serum phosphorus - 0.64 mmol / L (norm 0.81-1.45 mmol / l). On radiography of the tubular bones - cysts up to 1cm. On radiography of the thoracic spine - a decrease in the height of the vertebral bodies, rarefaction of the bone structure. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
19	The patient is 25 years old (height 175 cm, weight 64 kg). Complaints: dry mouth, thirst, fatigue, trembling hands, headaches, weight loss of 2 kg over the past half year, decreased vision. In the anamnesis: without pathology. In status: previously

	without pathology. Blood pressure = 120/75 mm Hg; Heart rate-93. Thyroid: not palpable. There is no tremor. Eye symptoms are negative. Secondary sexual characteristics by age. There is no gynecomastia. There are no striae. Examination: Ultrasound of the thyroid gland: volume - 13.7 cm3. The structure is heterogeneous. TSH - 2.5 μMU / ml. HbA 1C - 7.7%. Glycemic profile: 8-00 - 7.9; at 18-00 - 11.0 mmol / l. Insulin 3.2 (NORM: 3-27 ng / dl). Urine Acetone. Potassium - 4.1.mmol / Cor- normal position of EOS. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
20	The patient is 55 years old (height - 160 cm, weight - 84 kg). Complaints: increased blood pressure to 170/90 mm Hg, dizziness, irritability, weight loss of 5 kg over the past 3 months, increased sweating, trembling in the body. In status: blood pressure = 135/85 mm Hg; Heart rate-107. Thyroid gland: palpable to 1 degree soft, diffuse. Eye symptoms: Gref +, Kocher +, Dalrympl +, Shtelvaga +. Tremor is small. Secondary sexual characteristics by age. There are no galactorrhea. There are no striae. Examination: Ultrasound of the thyroid gland: volume - 23.7 cm3. The structure is heterogeneous. Enhanced vascularization. TSH - 0.05 μMU / ml. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
21	A pregnant woman was delivered to the on-duty hospital. You were summoned to Cito's emergency room! Objectively: unconscious, the patient has a sharp smell of acetone, the skin is pale cold to the touch, dry with traces of scratching. Turgor reduced. The breath is noisy, like Kussmaul. In the lungs, harsh breathing. The pulse is weak, frequent, arrhythmic. Blood pressure 80/60 mm Hg The abdomen is enlarged due to the pregnant uterus. (20-22 weeks). The reaction of the pupils to the light is weak. Anuria During the examination: blood glucose 32 mmol / L, plasma osmolarity - 320 mmol / L. cholesterol - 7.0 mmol / l, creatinine - 115 mmol / l, urea - 9 mmol / l. Serum electrolytes: sodium -134 mmol /l, potassium-2.5 mmol /l. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
22	The patient is 70 years old (height - 167 cm, weight - 60 kg). Complaints on the eve of: dry mouth, thirst, shortness of breath with slight exertion, increased blood pressure to 180/100 mm Hg, dizziness, headaches, weight loss of 5 kg over the past three months. The last three days has become sleepy, constantly lying. History: coronary heart disease, a week ago suffered an acute myocardial infarction. Heredity: not burdened. In objective status: serious condition, severe acrocyanosis, shortness of breath at rest. The mucous lips and tongue are dry, cracks in the corners of the mouth. Blood pressure = 145/90; Heart rate-90. Thyroid gland: up to 1 degree densified. Eye symptoms are negative. There is no tremor. Secondary sexual characteristics by age. There are no galactorrhea. There are no striae. Swelling of the legs. There is no smell of acetone. Examination: ultrasound of the thyroid gland: volume - 15.2 cm3. The structure is heterogeneous. In the right lobe isoechogenic node 18 x 16.5mm. TSH-0.08 μMU / ml. NvA 1s - 8.5%. Glycemic profile: 8-00 - 17.7; at 18-00 - 21.3 mmol / l. Insulin-0.1 (NORM: 3-27ng / dl, after eating - 6-35). Acetone is urine-negative. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.

23	The patient is 45 years old (height - 176 cm, weight - 123 kg). Complaints about: a decrease in blood pressure to 80/50 mm Hg. with dizziness, headaches, weakness, darkening of skin color, periodic nausea. History: previous tuberculosis. Heredity: not burdened. Status: swarthy skin, increased pigmentation in places of friction of clothing. Blood pressure = 85 / 55mm Hg; Heart rate-82; Thyroid: not palpable. Eye symptoms are negative. There is no tremor. Secondary sexual characteristics by age. There are no striae. Examination: ultrasound of the thyroid gland: volume - 12.4 cm3. The structure is homogeneous. TSH-2.1 μmU / ml. Urine cortisol - 109 (normal: 138-635). Glycemic profile: 8-00 - 3.5; in 18-00 -4.6 mmol l. Urine sugar - no. Acetone urine-no. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
24	Patient X. 56 years old has repeatedly turned to a cardiologist for a paroxysmal increase in blood pressure to high figures - 200 / 100mm Hg, accompanied by palpitations, arrhythmias, trembling in the body, headaches, dizziness, a sense of fear of death. Such conditions often appear after physical exertion or plentiful food and pass spontaneously. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
25	The patient is 31 years old (height - 162 cm., Weight - 73 kg). Complaints: cramps in the limbs, numbness and crawling creeps. In the anamnesis: underwent a stumectomy a year ago. It takes levothyroxine at a dose of 75 mcg per day. Heredity is not burdened. In status: blood pressure = 120/70 mm Hg; Heart rate-71. Thyroid: not palpable. Eye symptoms are negative. There is no tremor, the skin is of normal moisture. Secondary sexual characteristics by age. There are no striae. Examination: ultrasound of the thyroid gland: volume - 17.5 cm3. The structure is saved. TSH - 2.7 μMU / ml. HBA1c-5.8%. ATPO-0. Serum glucose 4.9 mmol /l. Calcium ionized 0.9 mmol /l. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
26	An 18-year-old patient (height - 167 cm, weight - 63 kg) was called an ambulance. Complaints: weakness, dizziness, thirst, dry mouth, nausea, vomiting once, stable weight, lump in throat. History: Diabetes. A week without insulin. Heredity in the father Diabetes mellitus. Status: Sluggish, lying in bed. Blood pressure = 110/65 mm Hg; Heart rate-64. Thyroid gland: up to 0 degree, mobile, densified. Eye symptoms are negative. There is no tremor, the skin is dry, flabby. Secondary sexual characteristics by age. There is no gynecomastia. There are no striae. Examination: Glycemic profile: 8-00 -18.7; at 18-00 -20.5 mmol / l. НвА1с - 11.3%. Acetone is urine positive. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
27	A 54-year-old patient, an assistant secretary, went to the doctor with complaints of hot flashes several times a day against a background of a constant heartbeat, insomnia, tearfulness, and intolerance to stuffiness. From the anamnesis it is known that over the last year after stress, she lost 10 kg. Since childhood, vitiligo. The menstrual cycle from 15 years to date, regular, 2 pregnancies and 2 births. On examination: the condition is satisfactory, the patient is emotionally labile, fussy, finely spread tremor of the eyelids, fingers. BMI-24. The skin is elastic, diffusely

	moist, warm. No peripheral edema. Hyperemia of the neck, decollete, depigmented hands. The respiratory rate is 16 per minute. The vesicular breathing. Pulse -118 per minute. Heart tones are loud, the rhythm is correct. Blood pressure - 130/60 mm RT. Art. Liver at the edge of the costal arch. The thyroid gland is visible to the eye, enlarged by palpation, elastic, mobile when swallowing, painless. Symptoms of Moebius, Gref, Kocher, Krause are positive; edematous exophthalmos on both sides. Hormonal profile: TSH = 0.05 μIU / ml (0.3-3.2); f T4 =76.2 pmol /l (N:12.3-25.6); AT to TSH receptors = 47 (0). Heart rate -116 per minute, sinus rhythm. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
28	.A 40-year-old patient (height 159 cm, weight 45 kg) complaints of: periodic sudden increase in blood pressure to 180/100 mm Hg. with dizziness, headaches, a sense of fear of death, trembling in the body, weight loss of 4 kg over the past half year, shortness of breath, palpitations. In the anamnesis: without pathology. Heredity: not burdened. BMI-25 Blood pressure = 160/90 mm Hg; Heart rate-89. Thyroid gland: up to 0 degree, mobile, densified. Eye symptoms are negative. There is no tremor, the skin is damp. Secondary sexual characteristics by age. There are no galactorrhea. Striae are white on the stomach. Examination: Ultrasound of the thyroid gland: volume - 15.2 cm3. The structure is homogeneous. TSH-2.9 μMU / ml. HBA1s-5.5%. The glycemic profile in a crisis: 8-00 - 6.2; at 18-00 -6.3 mmol / l. C-peptide -2.6 ng / ml (normal: 1.1-4.4 ng / ml). Urine sugar - no. Acetone urine-no. Cortisol-17 (norm: 4-23). Urine methanephrine: 2145 mcg / day (normal: up to 320); Urine normetanephrine: 240cmkg / day (normal: up to 390). Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
29	ммоль/л. НвА1с - 9,4%. Сахар мочи +++. Ацетон мочи- отриA 65-year-old patient (height 166 cm, weight 104 kg) was called an ambulance. In the anamnesis: a week ago, in order to reduce weight, I began to take diuretics and laxatives. Three days after the start of their intake, thirst, nausea, loss of appetite, frequent loose stools, and rare vomiting appeared. In an unconscious state, she was taken to the intensive care unit. Heredity is not burdened. In objective status: the skin and mucous membranes are dry, there is no smell of acetone, left-side hemiparesis, blood pressure = 180/95 mm Hg; Heart rate-96 per minute. Thyroid gland: palpable to 0 degree, soft. Secondary sexual characteristics by age. There are no striae. Examination: Serum glucose: 8-00 - 43 mmol / L. HbA1C - 9.4%. Urine Sugar +++. Acetone is urine negative. Questions: Assume and justify the diagnosis. Assign additional examination and treatment.
30	53-year-old patient for 7 years suffers from chronic adrenal insufficiency, constantly takes hormone replacement therapy. Received in the regional clinical hospital, department of endocrinology. From the anamnesis: ten days ago I had an acute respiratory viral infection with a runny nose, the temperature increased to 37.4 ° C over 3 days. The last week, appetite decreased, pigmentation of the skin increased, headaches and epigastric pains appeared. Objectively: a serious condition, acrocyanosis, severe hypotension, nausea, periodic vomiting, dry skin and mucous membranes, turgor is reduced. Questions: Assume and justify the diagnosis.

	Assign additional examination and treatment.

3. LIST OF QUESTIONS TO CREDIT

№ tasks	The formulation of the question
1	Classification of insulin by duration of action, indications for insulin therapy
2	Groups of tablet sugar-lowering drugs: mechanism of action, indications, contraindications
3	Target glycated hemoglobin levels in patients with diabetes mellitus
4	Etiopathogenesis and clinical manifestations of microvascular complications of diabetes
5	Diabetic retinopathy: etiology, pathogenesis, clinic, treatment
6	Diabetic nephropathy: etiology, pathogenesis, clinic, treatment
7	Tactics for the treatment of microvascular complications of diabetes
8	Diabetic polyneuropathy: etiology, pathogenesis, clinic, treatment
9	Etiopathogenesis and clinical manifestations of macrovascular complications of diabetes
10	Tactics for the treatment of macrovascular complications of diabetes
11	Laboratory differential diagnosis of hyperglycemic com
12	Diabetic coma: etiology, clinic, diagnosis
13	Hyperosmolar coma: etiology, clinic, diagnosis
14	Lactacidemic coma: etiology, clinic, diagnosis
15	Clinical symptoms and differential diagnosis of hypoglycemic conditions
16	Features of laboratory and instrumental diagnostics in exo- and endotoxic coma
17	Diagnostic criteria for manifest diabetes during pregnancy
18	Criteria and features of the treatment of gestational diabetes
19	Management of patients with gestational diabetes during pregnancy
20	Management of patients with diabetes mellitus in the perioperative period
21	Features of management of patients with diabetes during pregnancy, childbirth and lactation
22	Differential diagnosis of gestational and manifest diabetes in a pregnant woman
23	Features of the treatment of arterial hypertension in patients with diabetes mellitus
24	Differential diagnosis of thyrotoxic crisis and hypothyroid coma
25	Features of laboratory and instrumental diagnostics of addison crisis
26	Pheochromocytoma crisis. Clinical options, diagnosis
27	Clinical manifestations of hyper- and hypoparathyroidism
28	Features of laboratory and instrumental diagnosis of hypo- and hyperparathyroid crisis
29	Symptoms and laboratory diagnosis of hypoparathyroid coma
30	Emergency therapy for hypoglycemic coma
31	Emergency therapy for ketoacidotic coma
32	Emergency therapy for hyperosmolar coma
33	Emergency therapy for lactacidemic coma
34	Emergency therapy for thyrotoxic crisis
35	Emergency treatment for hypothyroid coma
36	Emergency therapy for hypoadrenal crisis
37	Emergency therapy for pheochromocytoma crisis
38	Emergency therapy for hypoparathyroid crisis
39	Emergency therapy for hyperparathyroid crisis

4. EDUCATIONAL-METHODOLOGICAL AND INFORMATION SUPPORT OF DISCIPLINE

a) List of recommended literature

Primary:

1. Dedov I.I., Endocrinology [Electronic resource]: a textbook / II I. Dedov, G. A. Melnichenko, V. V. Fadeev - M.: Litterra, 2020. - 416 p. - ISBN 978-5-4235-0159-4 - Access mode: http://www.studentlibrary.ru/book/ISBN9785423501594.html

2. Dedov II, Pediatric endocrinology [Electronic resource]: textbook / II. Grandfathers, V.A. Peterkova, O.A. Malievsky, T.Yu. Shiryaeva - M.: GEOTAR-Media, 2020 .-- 256 p. - ISBN 978-5-9704-3899-2 - Access mode: : http://www.studentlibrary.ru/book/ISBN9785970438992.html

3. Mkrtumyan AM, Emergency endocrinology [Electronic resource] / Mkrtumyan AM, Nelaeva A.A. - M.: GEOTAR-Media, 2010.-128 p. (Series "Library of a specialist") - ISBN 978-5-9704-1836-9 - Access mode: http://www.studentlibrary.ru/book/ISBN9785970418369.html

4. Harrison`s Endocrinology by Jameson, J. Larry, 2010.(https://www.pdfdrive.com/harrison-endocrinology-e34584578.html

Additional literature:

1. Grandfather II, Pediatric endocrinology. Atlas [Electronic resource] / ed. I.I.Dedova, V.A. Peterkova. - M.: GEOTAR-Media, 2020 .-240 p. - ISBN 978-5-9704-3614-1 - Access mode: http://www.studentlibrary.ru/book/ISBN9785970436141.html

2. Kukes V.G., Medical diagnostic methods [Electronic resource]: study guide / Kukes V.G., Marinina V.F. et al. - M.: GEOTAR-Media, 2006. - 720 p. - ISBN 5-9704-0262-1 - Access mode: http://www.studentlibrary.ru/book/ISBN5970402621.html

3. Order of the Ministry of Health of Russia dated 09.11.2012 N 872н "On approval of the standard of primary health care for thyrotoxicosis" (Registered in the Ministry of Justice of Russia on 06.03.2013 N 27537) - http://www.consultant.ru/document/cons_doc_LAW_144463/

Educational-methodical literature:

1.Hormones and hormonal drugs: textbook. Method. manual for universities / S. M. Napalkova [et al.]; UlSU, IMEiFK. - Ulyanovsk: UlSU, 2014 .-120 p. – URL.- ftp://10.2.96.134/Text/Napalkova2014.pdf

2.Slobodnyuk N. A. Methodological recommendations for practical training and independent work of residents in the discipline "Diabetology and emergency endocrinology": a methodological manual / N. A. Slobodnyuk, M. V. Frolova; Ulyanovsk State University, Institute of Medicine, Ecology and Physical Culture. - Ulyanovsk : UlSU, 2019. - Загл. с экрана; На англ. яз.; Неопубликованный ресурс. - Электрон. текстовые дан. (1 файл : 784 Кб). - Текст : электронный. http://lib.ulsu.ru/MegaPro/Download/MObject/4902

b) Software

OC Windows

c) Professional databases, information and reference systems

1. Electronic library systems:

1.1. IPRbooks [Electronic resource]: electronic library system / group of companies IPR Media. - Electron. Dan. - Saratov, [2020]. - Access mode: http://www.iprbookshop.ru.

1.2. YURAYT [Electronic resource]: electronic library system / LLC Electronic publishing house YURAYT. - Electron. Dan. - Moscow, [2020]. - Access mode: https://www.biblio-online.ru.

1.3. Student consultant [Electronic resource]: electronic library system / Polytekhresurs LLC. - Electron. Dan. - Moscow, [2020]. - Access mode: http://www.studentlibrary.ru/pages/catalogue.html.

1.4. Lan [Electronic resource]: electronic library system / LLC EBS Lan. - Electron. Dan. - St.

Petersburg, [2020]. - Access mode: https://e.lanbook.com.
1.5. Znanium.com [Electronic resource]: electronic library system / Znanium LLC. - Electron. Dan. - Moscow, [2020]. - Access mode: http://znanium.com.
1.6. Clinical Collection: collection for medical universities, clinics, medical libraries // EBSCOhost: [portal]. - URL: http://web.a.ebscohost.com/ehost/search/advanced?vid=1&sid=e3ddfb99-a1a7-46dd-a6eb-2185f3e0876a%40sessionmgr4008. - Access mode: for authorization. users. - Text: electronic.
2. ConsultantPlus [Electronic resource]: reference legal system. / Company "Consultant Plus" - Electron. Dan. - Moscow: ConsultantPlus, [2020].
3. Database of periodicals:
3.1 Database of periodicals [Electronic resource]: electronic journals / LLC IVIS. - Electron. Dan. - Moscow, [2020]. - Access mode: https://dlib.eastview.com/browse/udb/12.
3.2. eLIBRARY.RU: scientific electronic library: site / Scientific Electronic Library LLC. - Moscow, [2020]. - URL: http://elibrary.ru. - Access mode: for authorization. users. - Text: electronic
3.3. "Grebennikon": electronic library / ID Grebennikov. - Moscow, [2020]. - URL: https://id2.action-media.ru/Personal/Products. - Access mode: for authorization. users. - Text: electronic.
4. National Electronic Library [Electronic resource]: electronic library. - Electron. Dan. - Moscow, [2020]. - Access mode: https: //neb.rf.
5. Electronic library of dissertations of the RSL [Electronic resource]: electronic library / FGBU RSL. - Electron. Dan. - Moscow, [2020]. - Access mode: https://dvs.rsl.ru.
5. SMART Imagebase // EBSCOhost: [portal]. - URL: https://ebsco.smartimagebase.com/?TOKEN=EBSCO-1a2ff8c55aa76d8229047223a7d6dc9c&custid=s6895741. - Access mode: for authorization. users. - Image: electronic.
6. Federal information and educational portals:
6.1. Single window of access to educational resources: federal portal / founder of FGAOU DPO TsRGOP and IT. - URL: http://window.edu.ru/. - Text: electronic.
6.2. Russian education: federal portal / founder of FGAOU DPO TsRGOP and IT. - URL: http://www.edu.ru. - Text: electronic.
7. Educational resources of UlSU:
7.1. Electronic library of UlSU: module ABIS Mega-PRO / LLC "Data Express". - URL: http://lib.ulsu.ru/MegaPro/Web. - Access mode: for users of the scientific library. - Text: electronic.
7.2. UlSU educational portal. - URL: http://edu.ulsu.ru. - Access mode: for register. users. - Text: electronic.

"Approving"

Head of Department

faculty therapy  / Ruzov V.I.