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

31.05.01 «General Medicine»

Full-time education

Educational-methodological recommendations

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Educational and methodological recommendations for the discipline "Endocrinology", profile "Specialty" contain materials for the preparation and conduct of practical classes on 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

«Endocrinology» refers to the basic (compulsory) 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:
teach students methods of diagnosis, detection, treatment and prevention of endocrinological diseases.

Tasks of mastering the discipline:
- master the examination technique, knowledge of the clinical symptoms of endocrinological diseases, their complications;
- master the methods of diagnosis and differential diagnosis of endocrinological diseases, their complications;
- master the methods of treatment for endocrinological diseases, their complications;
- master the technique of organization, planning and medical examination of patients with endocrinological diseases.

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. The content of the discipline

Section 1. Diabetes

Theme 1. Diabetes mellitus

Questions on the topics of the section (for discussion in the lesson):
1. Definition and classification of diabetes;
2. Etiology and pathogenesis of type 1 diabetes mellitus, risk factors for its development;
3. Etiology and pathogenesis of type 2 diabetes mellitus, risk factors for development and prevention;
4. Criteria for diabetes, biological effects of insulin;
5. Differential diagnosis of diabetes mellitus type 1 and 2;
6. Atypical forms of diabetes (diabetes mellitus type Mody, LADA);
7. Prevention, clinical examination, issues of medical and social expertise in diabetes.
8. The mechanism of action of groups of sugar-lowering tablets;
9. Indications and contraindications for groups of sugar-lowering tablets.

Theme 2. Diabetes mellitus

Questions on the topics of the section (for discussion in the lesson):
1. Classification and duration of action of basal insulin;
2. Classification and duration of action of prandial insulin;

3. Hypoglycemic coma: etiology, pathogenesis, clinical features, treatment.
4. Ketoacidotic coma: etiology, pathogenesis, clinic, treatment.
5. Hyperosmolar coma: etiology, pathogenesis, clinic, treatment.
6. Lactacidemic coma +: etiology, pathogenesis, clinical features, treatment.
7. Differential diagnosis of com in diabetes.
8. Classification and clinic of microvascular complications of diabetes;
9. Classification and clinic of microvascular complications of diabetes.

Section 2. Thyroid Disease

Theme 3. Diffuse toxic goiter. Hypothyroidism Thyroiditis. Endemic and nodular goiter

Questions on the topics of the section (for discussion in the lesson):
1. Biological effects of thyroid hormones, hormonal regulation and degree of thyroid enlargement.
2. Diffuse toxic goiter. Etiology. Pathogenesis. Clinic. Diagnostics. Treatment;
2. Hypothyroidism. Etiology. Pathogenesis. Classification. Clinic. Diagnostics. Treatment;
3. Thyroiditis. Etiology. Pathogenesis. Classification. Clinic. Diagnostics. Treatment;
4. Diffuse goiter. Etiology. Pathogenesis. Clinic. Diagnostics. Treatment;
5. Nodular goiter. Etiology. Pathogenesis. Classification. Clinic. Diagnostics. Treatment;
6. Thyrotoxic coma. Etiology. Clinic. Treatment. Prevention
7. Hypothyroid coma. Etiology. Clinic. Treatment. Prevention
8. Diagnosis and differential diagnosis of thyroid diseases;
9. Prevention, clinical examination, issues of medical and social expertise in diseases of the thyroid gland.

Section 3. Neuroendocrinology

Theme 4. Disease and Itsenko-Cushing's syndrome.

Questions on the topics of the section (for discussion in the lesson):
1. Biological effects of pituitary hormones.
2. Hormonal regulation of hormones.
3. Etiology, pathogenesis of the disease and Itsenko-Cushing's syndrome;
4. Features of the clinic of the disease and Itsenko-Cushing's syndrome;
5. Laboratory diagnosis of the disease and Itsenko-Cushing's syndrome;
6. Diagnosis and differential diagnosis of the disease and Itsenko-Cushing's syndrome;
7. Large and small dexamethasone samples;
8. The principles of treatment of the disease and Itsenko-Cushing's syndrome;
9. Prevention, clinical examination, medical and social examination for the disease and Itsenko-Cushing's syndrome.

Section 4. Adrenal Diseases

Theme 5. Pheochromocytoma. Chronic adrenal insufficiency.

Questions on the topics of the section (for discussion in the lesson):
1. Biological effects of hormones of the adrenal cortex and catecholamines.
2. Pheochromocytoma. Etiology. Pathogenesis. Clinic. Diagnostics. Treatment;
3. Classification of pheochromocytoma and clinical manifestations of pheochromocytoma;
4. Chronic adrenal insufficiency. Etiology. Pathogenesis. Clinic. Diagnostics. Treatment;
5. Differential diagnosis of primary and secondary adrenal insufficiency;
6. Differential diagnosis of pheochromocytoma and chronic primary adrenal insufficiency;
7. Hypoadrenal crisis. Etiology. Clinic. Treatment. Prevention
8. Catecholamine crisis. Etiology. Clinic. Treatment. Prevention
9. Prevention, clinical examination, medical and social examination of pheochromocytoma and chronic adrenal insufficiency.

Section 5. Metabolic Syndrome and Obesity
Theme 6. Metabolic syndrome and obesity
Questions on the topics of the section (for discussion in the lesson):
1. Definition, etiology of obesity;
2. Risk factors for obesity and metabolic syndrome;
3. The pathogenesis of obesity;
4. Classification of obesity;
5. Clinical symptoms characteristic of exogenously constitutional obesity;
6. Criteria for metabolic syndrome;
7. The principles of treatment of obesity and metabolic syndrome;
8. Complications and prognosis of obesity;
9. Prevention, clinical examination, medical and social examination of obesity and metabolic syndrome.

1.2. Definition of diabetes mellitus, classification, diagnostic criteria

Diabetes mellitus (DM) is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action,or both. The chronic hyperglycemia of diabetes is associated with long–term damage,dysfunction and failure of different organs, especcially the eyes,kidneys,nerves,heart,and blood vessels.

Classification of diabetes mellitus (WHO, 1999, with additions):

I.Type 1 diabetes (destruction of β-cells of the pancreas, usually leading to absolute insulin deficiency)

A. Immune mediated

B. Idiopathic

II. Type 2 diabetes • with predominant insulin resistance and relative insulin deficiency or

• with predominantly impaired insulin secretion with or without insulin resistance.

III. Other specific types of diabetes.

• Genetic defects of β-cell function.

1).MODY 3 (Chromosome 12, HNF-1α),

2).MODY 1 (Chromosome 20, HNF-4α),

3).MODY 2 (Chromosome 7, glucokinase),

4).Other very rare forms of MODY (e.g., MODY 4: Chromosome 13, insulin promoter factor-1; MODY 6: Chromosome 2, *NeuroD1*; MODY 7: Chromosome 9, carboxyl ester lipase),

5).Transient neonatal diabetes (most commonly ZAC/HYAMI imprinting defect on 6q24)

6). Permanent neonatal diabetes (most commonly KCNJ11 gene encoding Kir6.2 subunit of β-cell K_{ATP} channel),

7).Mitochondrial DNA,

8).Others

• Genetic defects of insulin action (Type A insulin resistance, Leprechaunism, Rabson-Mendenhall syndrome, Lipoatrophic diabetes, Others)

• Diseases of the exocrine pancreas (Pancreatitis, Trauma/pancreatectomy, Neoplasia, Cystic fibrosis, Hemochromatosis, Fibrocalculous pancreatopathy, Others)

• Endocrinopathies (Acromegaly, Cushing's syndrome, Glucagonoma, Pheochromocytoma. Hyperthyroidism, Somatostatinoma, Aldosteronoma, Others)

• Diabetes mellitus induced by drugs or chemicals (Vacor, Pentamidine. Nicotinic acid, Glucocorticoids, Thyroid hormone, Diazoxide, β-Adrenergic agonists, Thiazides. Dilantin, γ-Interferon, Others)

• Infections (Congenital rubella, Cytomegalovirus, Others)

• Uncommon types of immune-mediated diabetes

("Stiff-man" syndrome, Anti-insulin receptor antibodies. Others)

• Other genetic syndromes, sometimes associated with diabetes

(Down syndrome, Klinefelter syndrome, Turner syndrome, Wolfram syndrome, Friedreich ataxia. Huntington chorea, Laurence-Moon-Biedl syndrome, Myotonic dystrophy, Porphyria, Prader-Willi syndrome, Others)

IV. Gestational diabetes mellitus (GDM). Occurs during pregnancy (except for manifest diabetes).

Diagnostic criteria for diabetes mellitus and other glycemic disorders (WHO, 1999-2013)

	Norm	Prediabetes	Diabetes mellitus
Criteria for diabetes mellitus (WHO)			
НвА1с	4-6%	6,1-6,4%	6.5% and above
Fasting capillary blood (mmol / L)	3.3-5.5	5,6-6,0	6,1 and above
Fasting plasma (venous blood) glucose(mmol / L)	3,3-6,0	6,1-6,9	7,0 and above
The oral glucose tolerance test (OGTT) is performed with 75 g of anhydrous glucose at 2 h after glucose intake	3,3-7,7	7,8-10	11,1 and above
Criteria for diabetes mellitus (ADA)			
НвА1с	*4-5,6%*	*5,7-6,4%*	*6,5% and above*
Venous blood (mg / dl)	*70-99*	*100-125*	*126 and above*
The oral glucose tolerance test (OGTT) is performed with 75 g of anhydrous glucose at 2 h after glucose intake(mg / dl)	*70-139*	*140-199*	*200 and above*
Criteria for diabetes mellitus in pregnant women (WHO)			
pregnant women fasting blood glucose	3,3-5,0	5,1-6,9	7,0 and above
The oral glucose tolerance test (OGTT) is performed with 75 g of anhydrous glucose at 1 h after glucose intake		10 and above	
The oral glucose tolerance test (OGTT) is performed with 75 g of anhydrous glucose at 2 h after glucose intake	3,3-8,4	8,5-11,0	11,1 and above
Criteria for diabetes mellitus in pregnant women (ADA)			
Fasting blood glucose (mg/dL)	*70-91*	*92-125*	*126 and above*
The oral glucose tolerance test (OGTT) is performed		*180 and above*	

with 75 g of anhydrous glucose at 1 h after glucose intake			
The oral glucose tolerance test (OGTT) is performed with 75 g of anhydrous glucose at 2 h after glucose intake	*70-152*	*153-199*	*200 and above*

Hemoglobin A1c was first separated from other forms of hemoglobin by Huisman and Meyering in 1958 using a chromatographic column. The use of hemoglobin A1c for monitoring the degree of control of glucose metabolism in diabetic patients was proposed in 1976 by Koenig and coworkers.

The glycosylated hemoglobin test (A1C, HbA1c also called hemoglobin A1C or the glycosylated hemoglobin test) is an imortant blood test to diagnose diabetes or determine control of diabetes. It provides an average blood glucose measurement over the past 3 months and is used in conjunction with home glucose monitoring to make treatment adjustments.

People with diabetes should have this test 4 times a year (every 3 months).

3.Algorithm for individualized selection of treatment targets according to HbA1c

	Age					
	Young	Middle 45-60 years old	Elderly and/ or life expectancy <5 years			
			Functionally independent	Functionally dependent		
				Without senile asthenia and / or dementia	Senile asthenia and / or dementia	The final stage of life
No severe macrovascular complications and / or risk of severe hypoglycemia	<6,5%	< 7,0%	< 7,5%	< 8,0%	< 8,5%	Avoid hypoglycemia and hyperglycemia symptoms
Severe macrovascular complications and / or risk of severe hypoglycemia	< 7,0%	< 7,5%	< 8,0%	< 8,0%	< 8,5%	Avoid hypoglycemia and hyperglycemia symptoms
With a low life expectancy (<5 years), treatment goals may be less stringent.						

The following target values of pre- and postprandial plasma glucose levels will correspond to these target HbA1c levels.

HbA1c, %	Fasting plasma glucose,mmol/L	Plasma glucose level on OGTT, mmol/L
< 6,5	< 6,5	< 8,0
< 7,0	< 7,0	< 9,0
< 7,5	< 7,5	< 10,0
< 8,0	< 8,0	< 11,0

1.4. Groups of sugar-lowering drugs and their mechanism of action

Drug groups	Mechanism of action
Sulfonylurea drugs	• stimulate insulin secretion from the pancreas
Meglitinides (glinides)	• stimulate insulin secretion from the pancreas
Biguanides (Metformin)	•Decreased liver glucose production • Decreased insulin resistance in muscle and adipose tissue
Thiazolidinediones (glitazones, TZD)	• Decreased insulin resistance in muscle and adipose tissue • Decreased liver glucose production
Alpha-glucosidase inhibitors (AGIs)	• Slowing the absorption of carbohydrates in the intestines
Glucagon-like peptide-1 receptor agonists (GLP-1RAs)	• Glucose-dependent stimulation of insulin secretion • Glucose-dependent decrease in glucagon secretion and a decrease in liver glucose production • Slowing gastric emptying • Reduced food intake • Weight loss
Inhibitors of dipeptidyl peptidase 4 (DPP-4 inhibitors or gliptins)	• Glucose-dependent stimulation of insulin secretion • Glucose-dependent inhibition of glucagon secretion • Decreased liver glucose production • Do not cause delayed gastric emptying • Neutral effect on body weight
Sodium glucose cotransporter 2 (SGLT2) inhibitors (gliflozins)	•reduce renal reabsorption of g lucose • Weight loss •Insulin-independent mechanism of action
Insulin	•All mechanisms characteristic of insulin

1.5. Comparative effectiveness, advantages and disadvantages of sugar-lowering drugs

Group/ Decline HbA1C	Advantages	Disadvantages	Notes
Medications that affect insulin resistance.			
Biguanides - metformin - prolonged-action metformin 1-2%	- low risk of hypoglycemia - does not affect body weight - improves lipid profile - available in fixed combinations (with sulfonylurea, DPP-4 inhibitors, and SGLT2 inhibitors - reduces the risk of myocardial infarction in patients with type 2 diabetes and obesity - reduces the risk of development type 2 diabetes mellitus in patients with impaired glucose tolerance - potential cardioprotective effect (not proven in combination with sulfonylurea derivatives) - low price	gastrointestinal discomfort - risk of developing lactic acidosis (rare) - risk of developing vitamin B12 deficiency with prolonged use	Contraindicated with a glomerular filtration rate <30 ml / min / 1.73 m2 (with a glomerular filtration rate of 30-44 ml / min / 1.73 m 2, the maximum daily dose should not exceed 1000 mg), with liver failure; acute coronary syndrome; diseases accompanied by hypoxia; alcoholism; acidosis of any genesis; pregnancy and lactation. The drug should be canceled within 2 days before and after performing radiopaque procedures, large surgical interventions
Thiazolidinediones - Pioglitazone - Rosiglitazone 0,5-1,4%	Reducing the risk of macrovascular complications (pioglitazone) - low risk of hypoglycemia; improvement of blood lipid spectrum - potential protective effect in relation to β cells - reduce the risk of type 2 diabetes in people with impaired glucose tolerance.	- weight gain - peripheral edema - increased risk of fractures of the tubular bones in women - slow onset of action - high price	Contraindicated in liver disease; swelling of any genesis; heart failure of any functional class; acute coronary syndrome; Ischemic heart disease in combination with nitrate intake; ketoacidosis; in combination with insulin (with the exception of confirmed cases of severe insulin

			resistance); during pregnancy and lactation
Medicines that stimulate insulin secretion (secretagogues)			
Sulfonylurea preparations. - gliclazide - gliclazide MR(modified release) - glimepiride - gliquidone - glipizide - glipizide retard - glibenclamide 1-2%	- rapid achievement of sugar-lowering effect - indirectly reduce the risk of microvascular complications - nephro- and cardioprotection (gliclazide MR) - low price	- risk of hypoglycemia - rapid development of resistance - weight gain - there is no definite data on cardiovascular safety, especially in combination with metformin	Contraindicated in renal (except for gliclazide, glimepiride and gliquidone) and liver failure; ketoacidosis; pregnancy and lactation
Medicines with incretin activity (Incretin Mimetics)			
DPP-4 inhibitors or gliptins -sitagliptin, -saxagliptin, -vildagliptin, - linagliptin -gosogliptine -alogliptin. 0,5-1%	- low risk of hypoglycemia - do not affect body weight - available in fixed combinations with metformin Potential β-cell protective effect	- potential risk of pancreatitis (not confirmed) - high price	It is possible to use at all stages of chronic kidney disease, including terminal with a corresponding dose reduction (linagliptin without dose reduction). With caution in severe liver failure (except saxagliptin, linagliptin), heart failure; contraindicated in ketoacidosis; pregnancy and lactation
Glucagon-like peptide-1 receptor agonists (GLP-1RAs) – exenatide -Prolonged-release exenatide – liraglutide – lixisenatide – dulaglutide 0,8-1,8% Approved exenatide (Byetta, Bydureon), approved in 2005/2012 liraglutide (Victoza, Saxenda), approved 2010 lixisenatide (Lyxumia), approved in 2016	- low risk of hypoglycemia - weight loss - lowering blood pressure - potential protective effect on β-cells - available in fixed combinations with basal insulin - secondary prevention in patients with ASCVD (liraglutide, semaglutide #, dulaglutide)	gastrointestinal discomfort - the formation of antibodies (mainly on exenatide) - potential risk of pancreatitis (not confirmed) - injection form of administration - high price	Contraindicated in severe renal and hepatic failure; ketoacidosis; pregnancy and lactation

albiglutide (Tanzeum), approved in 2014 dulaglutide (Trulicity), approved in 2014— manufactured by Eli Lilly semaglutide (Ozempic), approved in 2017.	- possibly effective as primary prophylaxis in patients with cardiovascular risk factors - nephroprotection (liraglutide, semaglutide)		
Medications that block intestinal absorption of glucose.			
Alpha-glucosidase inhibitors (AGIs) Acarbose- Precose or Glucobay Miglitol – Glyset 0,5-0,8%	- do not affect body weight - low risk of hypoglycemia - reduce the risk of type 2 diabetes in people with impaired glucose tolerance	gastrointestinal discomfort - low efficiency - taking the drug 3 times a day	Contraindicated in diseases of the gastrointestinal tract; renal and liver failure; ketoacidosis; pregnancy and lactation
Medicines that inhibit glucose reabsorption in the kidneys.			
Sodium glucose cotransporter 2 (SGLT2) inhibitors (gliflozins) canagliflozin, dapagliflozin, empagliflozin ipragliflozin 0,8-0,9%	- low risk of hypoglycemia - weight loss - the effect does not depend on the presence of insulin in the blood - a moderate decrease in blood pressure - a significant reduction in the risk of hospitalization for heart failure -nephroprotection - available in fixed combinations with metformin - secondary prevention in patients with ASCVD - possibly effective as primary prophylaxis in individuals with cardiovascular risk factors	- risk of urogenital infections - risk of hypovolemia - risk of ketoacidosis - the risk of amputations of the lower extremities (canagliflozin), with other drugs with caution - risk of fractures (canagliflozin) - high price	Contraindicated in case of ketoacidosis, pregnancy, lactation, decreased glomerular filtration rate <45 ml / min / 1.73 m2. Caution is required in the appointment: - in old age (see instructions for use) - with chronic urogenital infections - when taking diuretics The drug should be discontinued within 2 days before and after radiopaque procedures, large surgical interventions
Insulins			
Human insulin analogues 1,5-3,5%	- pronounced hypoglycemic effect - reduce the risk of micro- and macrovascular	- high risk of hypoglycemia - weight gain - require frequent glycemic control	There are no contraindications and dose restrictions

	complications	- injection form - relatively high price	

1.6.Characteristic of insulin preparations

Type	Name	Action		
		Onset (how quickly they act)	Peak (how long it takes to achieve maximum impact)	Duration (how long they last before they wear off)
Prandial insulins (fast-acting insulin ,"bolus" insulins)				
Ultra-short-acting analogues (Insulin Rapid- Acting Insulin Analogues**)** (clear)	-Insulin Aspart(Novorapid), -Insulin Lispro(Humalog), -Insulin Glulisine(Apidra)	after 5-15 minutes	after 1-2 hours	4–5 hours
Short-acting **human insulins (clear)**	-Insulin soluble [human genetically engineered] (Actrapid HM, Humulin Regular, Biosulin R, Insuman Rapid GT, Rinsulin R et cetera)	after 20-30 minutes	after 2-4 hours	5-6 hours
Basal insulins				
Intermediate-acting insulin (cloudy)*	Insulin-isophan [human biosynthetic] (Protaphane HM, Humulin NPH (Neutral Protamine Hagedorn), Biosulin N , Insuman Basal GT, Rinsulin NPH (Neutral Protamine Hagedorn) et cetera)	after 2 hours	after 6-10 hours	12-16 hours
Long-acting basal insulin analogues (clear)	Insulin glargine 100 U/ml Lantus Solostar Insulin glargine 300 U/ml Toujeo Solostar Insulin Detemir (Levemir)	after 1-2 hours	- (peak is not pronounced)	up to 29 hours up to 36 hours up to 24 hours
Extra (Ultra)-long-acting insulin analogue	Insulin Degludec (Tresiba)	After 30-90 minutes	- (absent)	more than 42 hours
Mixed or combination insulins				
Mixtures of short-acting	Insulin biphasic [human biosynthetic]	Humulin M3, Insuman Comb 25		The same as for short-acting insulin

insulin and NPH-insulin*		GT; Biosulin 30/70 et cetera	and NPH-insulin. That is, in a mixture, insulins act separately.
Mixtures of ultrashort-acting insulin analogues and protaminated insulin analogues	Insulin lispro biphasic Insulin aspart biphasic	Humalog mix 25 Humalog mix 50 NovoMix 30	The same as ultra-short-acting insulin analogues and NPH-insulins, that is in a mixture, insulins act separately
Combinations of extra-long-acting insulin analogs and ultra-short-acting insulin analogs	Insulin degludec + insulin aspart in a ratio of 70/30.	Ryzodeg	The same as those of extra-long-acting insulin analogues and ultra-short-acting insulin analogues, i.e., in a mixture, the insulins act separately
Insulins for children and pregnant women			
Insulins Humalog, NovoRapid, Lantus, Levemir are allowed for use in children from 2 years old and pregnant patients. Tresiba insulin is approved for use from 1 year. Insulin Ryzodeg approved for use from 2 years.			

*Before administration, the drug should be thoroughly mixed.

1.7. 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).

1.8.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.

1.9.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.

1.10.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)

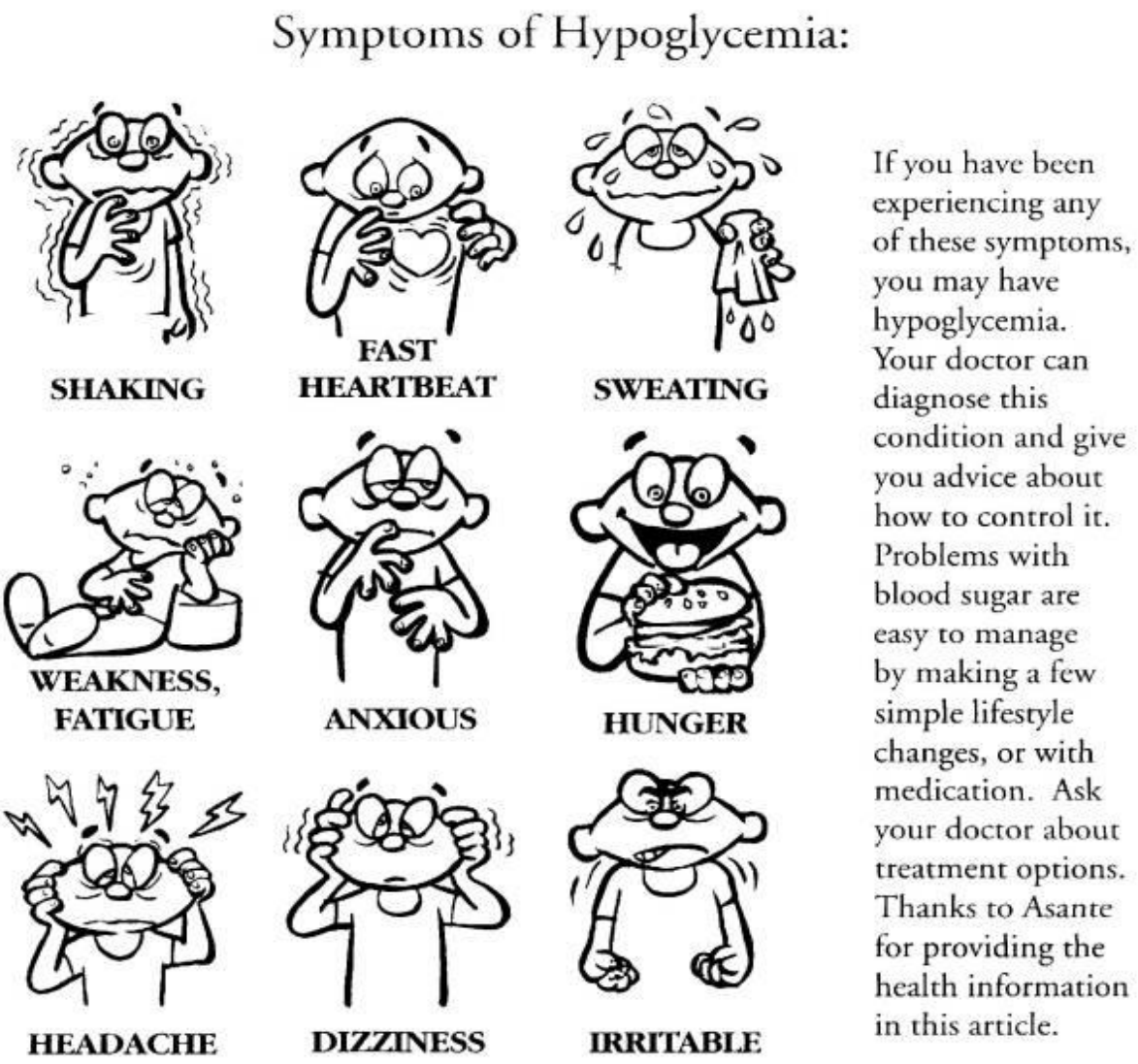
Treatment

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.



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.)	Volume in hours	Control form (verification of problem solving, abstract, etc.)
Diabetes mellitus	Study material set-up preparation	8	Interview in the lesson, checking situational tasks.
Diabetes mellitus	Study material set-up preparation	4	Interview in the lesson, checking situational tasks.
Diffuse toxic goiter. Hypothyroidism.Thyroiditis. Endemic and nodular goiter.	Study material set-up preparation	4	Interview in the lesson, checking situational tasks.
Itsenko-Cushing's disease and syndrome.	Study material set-up preparation	4	Interview in the lesson, checking situational tasks.
Pheochromocytoma. Chronic adrenal insufficiency.	Study material set-up preparation	4	Interview in the lesson, checking situational tasks
Metabolic syndrome and obesity.	Study material set-up preparation	4	Interview in the lesson, checking situational tasks

2.2 Set of tasks for independent work

The number of task	Problem situation (the formulation of the assignment)
1	An ambulance was called for a 45-year-old patient. On examination: unconscious, pallor and dry skin, noisy breathing, narrow pupils, reduced reflexes, “soft” eyeballs, the smell of acetone. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination. **Answer standard:** Presumptive diagnosis: Diabetic ketoacidotic coma. Treatment: the introduction of short-acting insulin at 0.1 units / kg of weight per hour. Rehydration with 0.9% sodium chloride solution, control and administration of

	potassium chloride. Additional examination: glycemic control every hour, control of the general analysis of urine and urine for acetone, HBA1c.
2	A 26-year-old patient was admitted with complaints of irritability, fatigue, unmotivated mood swings. On examination, a diffuse increase in both lobes of the thyroid gland was found. Positive eye symptoms: widening of the palpebral fissures, occasional blinking. Pulse - 115 beats / min. For 2 years, it was periodically treated with thyreostatic drugs without a big effect. The diagnosis was made: diffuse goiter of the 2nd degree with moderate thyrotoxicosis. Questions: Prescribe a treatment. Assign an additional examination. **Answer standard:** Presumptive diagnosis: diffuse toxic goiter of the 2nd degree. Treatment: tiamazole 10 mg x 3 times a day after meals until the hormone levels normalize, then a dose reduction of 5 mg per week to a maintenance dose of 5 or 10 mg. The maintenance dose of tiamazole is taken up to 18 months. Additional examination: ultrasound of the thyroid gland, determination of antibodies to the TSH receptor. T4sv, TSH - to assess thyroid function. Complete blood count, transaminases, bilirubin - to exclude side effects of the drug.
3	A 66-year-old patient is 177 cm tall and weighs 98 kg with newly diagnosed type 2 diabetes. Questions: Prescribe a treatment. Assign an additional examination.
4	A 18-year-old patient is 154 cm tall and weighs 60 kg acne complaints. On examination, fasting venous blood sugar 7.7 mmol / L. Glycated hemoglobin - 6.6%. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
5	A 31-year-old patient complains of dry mouth, thirst, weight loss, and weakness. Fasting venous blood sugar 6.3 mmol / L. Glycated hemoglobin - 6.1%. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
6	A 67-year-old patient was operated on for nodular goiter. Immediately after the operation, hoarseness of the voice, swelling on the face, and dry skin appeared. Questions: What complication arose in this patient after surgical treatment? Prescribe a treatment. Assign an additional examination.
7	A patient 62 years after loading coal appeared pallor of the skin, trembling hands, sweating, motor excitement, increased tone of the eyeballs. A history of diabetes. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
8	A 56-year-old patient X. repeatedly turned to a cardiologist for a paroxysmal increase in blood pressure to high figures - 200/100 mmHg, accompanied by palpitations, arrhythmias, trembling in the body, headaches, dizziness, and a sense of fear of death.

	Such conditions often appear after physical exertion or plentiful food and pass spontaneously. Assume a diagnosis, schedule an examination and treatment. Questions: Prescribe a treatment. Assign an additional examination.
9	A 37-year-old patient, BMI-21, complains of weakness, fatigue, weight loss, nausea, and periodic vomiting. On examination: adinomic, low nutrition, skin swarthy, Blood Ppressure 90 / 55mm.rt.st. Heart rate-88 per minute. Assume a diagnosis, schedule an examination and treatment. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
10	A 30-year-old patient showed a dense consistency of a nodular formation in the right lobe of the thyroid gland measuring 20x16 mm. Peripheral lymph nodes are not enlarged. Radioisotope scan data confirm the diagnosis of nodular euthyroid goiter. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
11	A 18-year-old patient was admitted with complaints of pain when swallowing and neck formation. From the anamnesis it is known that recently the patient suffered a follicular tonsillitis. On examination: temperature 38 ° C, thyroid gland enlarged, tightened, painful. PS-100 per minute In a blood test: leukocytosis with a shift in the formula to the left, ESR - 30 mm / hour. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
12	A 57-year-old patient came in with complaints of an increase in blood pressure to 200/100 mmHg, gained 6 kg in weight over the past 3 months, and wide pink striae appeared on her hips and abdomen. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
13	The patient has 63 years of complaints of dry mouth, dizziness, and poor sleep. Fasting capillary blood sugar 9.4 mmol / L. On examination, BMI-31, BP-150/90 mm Hg Glycated hemoglobin - 8.5%. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
14	On the second day after surgery for diffuse toxic goiter, the patient suddenly appeared motor and mental agitation, tachycardia 130 per minute, body temperature 39.8 ° C. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
15	A preventive ultrasound study of a 40-year-old man revealed: a change in the thyroid gland in the form of areas of increased and decreased echogenicity, a thyroid volume of 32 cm3, and regional lymph nodes are not visualized.

	Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
16	A 36-year-old patient complained of constipation, poor memory, fatigue, and depression. A history of anemia. On examination, BP-100 / 65mm.Hg; 54 heart rate per minute; swelling of the eyelids, hoarseness of the voice. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
17	An 18-year-old patient (height - 167 cm, weight - 63 kg) was called an ambulance. Complaints about: weakness, dizziness, thirst, dry mouth, nausea, vomiting once, lost weight. In the anamnesis: DM. A week without insulin. Heredity in the father of diabetes. In the status: lethargic, lies in bed. AD = 110/65; Heart rate-64. The TG: it is not palpable. Eye symptoms are negative. There is no tremor, the skin is dry, flabby. Secondary sexual characteristics by age. There are no striae. On examination: HBA1C - 11.3%. Glycemic profile: 8-00 -18.7; at 18-00 -20.5 mmol / l. C-peptide - 13 pmol / L (normal: 298-1324 pmol / L). Acetone is urine positive. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
18	The patient is 23 years old (height 180 cm, weight 54 kg). Complaints: dry mouth, thirst, fatigue, trembling hands, headaches, weight loss of 2 kg over the past half year, decreased vision. In status: Blood pressure = 120/75 mm Hg; Heart rate-93. The Thyroid gland is not palpable. There is no tremor. Eye symptoms are negative. Secondary sexual characteristics by age. There is no gynecomastia. There are no striae. During the examination: HbA1c - 7.7%. Glycemic profile: 8-00 - 6.9; at 18-00 - 9.0 mmol / l. Urine Acetone. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
19	A 27-year-old patient complains of irritability, heat intolerance, weight loss, palpitations, and excessive sweating. Heart rate-102 per minute. There are no eye symptoms. With ultrasound of the thyroid gland, the volume is 35 cm3. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
20	A 32-year-old patient complains of furunculosis, thirst, polyuria, weight loss, periodontal disease. Fasting capillary blood sugar 13.2 mmol / L. Glycated hemoglobin - 10%. .Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
21	The patient is 52 years old, weight - 72 kg. From the anamnesis it is known that he has been ill for about 2 years. Because of diffuse toxic goiter, he took propicil for 18 months. 3 months after discontinuation of the drug, I felt fatigue, constant palpitations, the last month there was a low-grade fever. On ultrasound thyroid gland V = 44 cm3,

	TSH - 0.02. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
22	Patient L., aged 29, complains of headaches, muscle pain, pain in the spine, dry mouth. From the anamnesis: increased blood pressure about 2 years. Stumbled a week ago, fell, broke his shoulder. There were two suicidal attempts. On examination: depressed, over-nourished, round face, blush of cheeks, broad striae of crimson-red color on hips, abdomen, in the lumbar region. BMI-32, BP = 220 / 130mm.Hg. Heart rate-73. Blood sugar -12.3 mmol / L. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
23	Patient I., 38 years old, complains of constantly high blood pressure, up to a maximum of 230 / 120mm Hg, which are accompanied by nausea, occasionally vomiting, abdominal pain, sweating, trembling in the body. Antihypertensive therapy prescribed by a doctor (lisinopril and indapamide) - blood pressure is not reduced. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
24	What groups of drugs do you recommend to a patient of 60 years old, BMI 22, with decompensated type 2 diabetes, leading a healthy lifestyle. Over the past 6 months, he lost 8 kg. It takes metformin in a dose of 1000 mg at dinner + glimepiride 4 mg before breakfast. On examination: HBA1C - 9.5%. The department has Humulin NPH and Actrapid, Metformin, Empagliflozin, Vildagliptin, Glibenclamide. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
25	What groups of hypoglycemic drugs are recommended for a 58-year-old patient with HBA1C 9.1% who had first diagnosed diabetes mellitus a week ago who had acute myocardial infarction. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
26	Patient S. 72 years old, BMI-21, complains of fatigue, weight loss, poor appetite, the need for salty foods, nausea, and periodic vomiting. On examination: low nutrition, pigmentation of the palmar folds, skin swarthy, blood pressure 100 / 60mm Hg. Heart rate-85 per minute. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
27	A 53-year-old patient with alimentary obesity (BMI 32 kg / m2) and dyslipidemia, combined with type 2 diabetes. He takes vildagliptin 50 mg in the morning. HbA1C - 8.8%. Questions: Assume and justify the diagnosis.

	Prescribe a treatment. Assign an additional examination.
28	Patient M., 51, complains of headaches, dizziness, swirling when swallowing, dry mouth and thirst, muscle pain. A history of arterial hypertension last 5-7 years to high numbers, takes antihypertensive therapy. Acute cerebrovascular accident suffered a month ago. On examination: increased nutrition, weight loss of the extremities is noted, on the skin of the abdomen, hips, and mammary glands - striae of crimson-red color, growth of a beard and mustache, male pattern bald patches. BMI-25, blood pressure-230/120 mmHg, Heart rate 65. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.ледование.
29	Select the drug for a 72-year-old patient, height - 165cm, weight-89 kg in with the first detected diabetes mellitus, suffering from Chronic obstructive pulmonary disease. HBA1C 7.7%. The department has Humulin NPH and Actrapid, Metformin, Empagliflozin, Vildagliptin, Glibenclamide. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.
30	Patient Sh. 44, the last six months, began to notice a periodic increase in blood pressure, accompanied by sweating, trembling in the body, headaches, fear and anxiety. Questions: Assume and justify the diagnosis. Prescribe a treatment. Assign an additional examination.

3. LIST OF QUESTIONS TO CREDIT

№ tasks	The formulation of the question
1	The mechanism of action of groups of tablets of sugar-lowering drugs
2	Classification, effects of action and indications for insulin therapy
3	Emergency therapy and diagnosis of hypoglycemic conditions
4	Features of diagnosis and emergency treatment of diabetic coma
5	Features of the treatment of the disease and Itsenko-Cushing's syndrome
6	Thyroid hormones and thyreostatic drugs: indications, contraindications, features of use.
7	Risk factors, prevention, medical and social expertise of diabetes mellitus
8	Risk factors, prevention, clinical examination, medical and social expertise of diffuse toxic goiter
9	Risk factors, prevention, clinical examination, medical and social expertise of hypothyroidism
10	Risk factors, prophylaxis, clinical examination, medical and social expertise of Itsenko-Cushing's disease
11	Risk factors, prophylaxis, clinical examination, medical and social expertise of chronic adrenal insufficiency
12	Risk factors, prevention, clinical examination, medical and social expertise of obesity and metabolic syndrome
13	Diagnosis of chronic complications of diabetes mellitus

14	Diagnosis of various types of diabetes
15	Differential diagnosis of hyperglycemic com
16	Differential diagnosis of the disease and Itsenko-Cushing's syndrome
17	Hormonal, laboratory, instrumental diagnosis of thyroiditis
18	Differential diagnosis of diffuse toxic goiter and hypothyroidism
19	Diagnosis and clinical manifestations of pheochromocytoma
20	Differential diagnosis of primary and secondary adrenal insufficiency
21	Metabolic Syndrome Criteria
22	Etiology, clinical manifestations of hypoglycemic coma
23	Clinical manifestations of primary adrenal insufficiency
24	Clinical symptoms characteristic of exogenous- constitutional obesity
25	Clinical symptoms and differential diagnosis of hypoglycemic conditions
26	Features of laboratory, instrumental diagnosis and treatment of chronic complications of diabetes
27	Classification, clinical manifestations of obesity
28	Features of laboratory and instrumental diagnostics, clinics for hypo- and hyperparathyroid crisis
29	Laboratory differential diagnosis of hyperglycemic com
30	Clinical manifestations and diagnosis and treatment of autoimmune thyroiditis
31	Management of patients with diffuse and nodular goiter
32	Management of patients with diabetes with lactacidemic coma
33	Features of management of patients with obesity and metabolic syndrome
34	Management of patients with diabetes with hyperosmolar coma
35	Diagnosis and management of patients with atypical forms of diabetes (diabetes mellitus type Mody, LADA)
36	Emergency care tactics for pheochromocytoma crisis

4. EDUCATIONAL-METHODOLOGICAL AND INFORMATION SUPPORT OF DISCIPLINE

a) List of recommended literature

Primary:

1. Ametov AS, Endocrinology [Electronic resource] / AS. Ametov, S.B. Shustov, Yu.Sh. Halimov, - M.: GEOTAR-Media, 2016 .-- 352 p. - ISBN 978-5-9704-3613-4 - Access mode: http://www.studentlibrary.ru/book/ISBN9785970436134.html

2. Dedov II, Endocrinology [Electronic resource]: textbook / II Dedov, GA Melnichenko, VV Fadeev - M.: Litterra, 2020. - 416 p. - ISBN 978-5-4235-0159-4 - Access mode: http://www.studentlibrary.ru/book/ISBN9785423501594.html

3. Mkrtumyan AM, Emergency endocrinology [Electronic resource] / Mkrtumyan AM, Nelaeva A.A. - M.: GEOTAR-Media, 2010 .-- 128 p. (Series "Doctor's Library") - 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. Dedov II, Pediatric endocrinology. Atlas [Electronic resource] / ed. I. I. Dedov, V. A. Peterkova. - M.: GEOTAR-Media, 2016 .-- 240 p. - ISBN 978-5-9704-3614-1 - Access mode: http://www.studentlibrary.ru/book/ISBN9785970436141.html

2. Kukes VG, Medical diagnostic methods [Electronic resource]: tutorial / Kukes VG, Marinina V.F. and others - 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:

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

2. Slobodnyuk N. A. Methodological recommendations for practical training and independent work of residents in the discipline "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 : 730 Кб). - Текст : электронный. http://lib.ulsu.ru/MegaPro/Download/MObject/4903

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.