Lviv National Medical University
named after Danylo Halytsky

METHODICAL GUIDE
OF PRACTICAL CLASSES IN
"Internal medicine, including endocrinology, medical genetics", individual profile course: «ENDOCRINE EMERGENCIES. Management of patients with endocrine system diseases»

for the sixth year students of medical faculty
Obstetrics and gynecology
Training
second (master's) level of higher education
field of knowledge 22 "Health"
specialty 222 "Medicine"

Lviv 2021

Methodical developments are made according to educational and qualification characteristics and educational and professional programs of preparation of experts, experimental curriculum developed on the basis of the credit transfer system, discussed and approved at the methodological meeting of the Department of Endocrinology (Protocol № 10 of February 4, 2021) and approved by the profile methodical commission on therapeutic disciplines of LNMU named after Danylo Halytsky (Protocol № 5 of 25.03.21).

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Topic 1. Features of management of pregnant women with diabetes

1. Relevance of the topic.

The prevalence of diabetes among pregnant women is growing at the same time as the global obesity epidemic. In women of reproductive age, the incidence of not only type 1 diabetes but also type 2 diabetes is increasing. Diabetes significantly increases the risks to the mother and fetus, largely due to the degree of hyperglycemia, chronic complications and comorbidities. In general, specific risks of diabetes during pregnancy include miscarriage, fetal malformations, preeclampsia, fetal death, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, and respiratory distress syndrome. In addition, diabetes during pregnancy may increase the risk of obesity and hypertension.

2. Educational objective.

Get acquainted with epidemiological studies of diabetes in Ukraine and in the world **(α = 1)**

The student must know (α = 2):

• Classification of diabetes mellitus;
• Diagnosis of diabetes mellitus during pregnancy;
• Differential diagnosis of gestational diabetes mellitus and gestational diabetes;
• Pre-pregnancy preparation and observation of a pregnant woman with type 1 diabetes.
• Pre-pregnancy preparation and follow-up of a pregnant woman with type 2 diabetes.

The student must be able to (α = 3):

• prescribe the necessary tests to detect diabetes in pregnant women;
• on the basis of the analysis of data of laboratory and instrumental inspections to substantiate and formulate the diagnosis of diabetes mellitus in pregnant women;
• to carry out differential diagnosis of gestational diabetes mellitus and type 1 and 2 diabetes mellitus;
• prescribe adequate treatment of diabetes mellitus during pregnancy: existing algorithms and standards according to world recommendations;
• dynamic monitoring of pregnant women with type 1 and type 2 diabetes:
• features of pregnancy and childbirth in women with diabetes;

3. Educational goal.

Pay attention and form a sense of responsibility in students who will be obstetricians and gynecologists, the timeliness of detection and proper treatment of diabetes on the background of pregnancy from pre-pregnancy preparation to childbirth.

4. Interdisciplinary integration:

Disciplines	*Know*	*Be able*
Disciplines studied earlier		
normal anatomy	topography, vascularization of the pancreas	
normal physiology	internal secretion of the pancreas and placenta	
histology	histological structure of pancreatic islets	
biochemistry	carbohydrate metabolism	
pathological anatomy	morphological changes in organs and tissues in diabetes mellitus	
pathological physiology.	pathogenesis of vascular complications and comatose states in diabetes mellitus on the background of pregnancy	
Disciplines to be studied later		conduct a clinical examination, prescribe appropriate diagnostic tests, consultations of related specialists to verify the diagnosis.
internal medicine	clinic, diagnosis, differential diagnosis, treatment, prevention of diabetes	
pediatrics	clinic, diagnosis, differential diagnosis, treatment, prevention of diabetes in children	
surgery	features of the course of diabetes mellitus in surgical pathology, timely diagnosis and management of such patients	
obstetrics and gynecology	features of the course of diabetes	

	mellitus during pregnancy, timely diagnosis and management of such patients.	
neurology	clinic, diagnosis, differential diagnosis, treatment, prevention of neurological complications of diabetes	
ophthalmology	clinic, diagnosis, differential diagnosis, treatment, prevention of diabetic retinopathy	
Intra-subject integration.	modern methods of examination of patients, in particular laboratory, instrumental adequate tactics of treatment.	Assign adequate treatment

5. Content of the lesson topic:

A. Classification of diabetes mellitus.

B. Etiology, pathogenesis of type 1 and 2 diabetes mellitus.

C. Type 1 diabetes and pregnancy: diagnosis, dynamic monitoring and treatment

D. Type 2 diabetes and pregnancy: diagnosis, dynamic monitoring and treatment

E. Type 1 and 2 diabetes mellitus: differential diagnosis with gestational diabetes mellitus.

F. Clinical manifestations of vascular disorders of the placenta in diabetes mellitus in pregnant women

6. Plan and organizational structure of the lesson

(see "Preface")

7. Materials of methodical providing of employment.

7.1 Materials of the preparatory stage of the lesson

Tests (α=2)

1. At what stage of pregnancy should a pregnant woman be diagnosed with

diabetes for the first time?

A. In early pregnancy
B. In the 1st trimester (up to the 12th week of gestation)
C. In the 2nd trimester (from the 13th to the 25th week of gestation)
D. In the 3rd trimester (from the 26th week of gestation)
E. Necessarily between 24-27 weeks of gestation.

2. At what stage of pregnancy should you first be screened for gestational diabetes?

A. In early pregnancy
B. In the 1st trimester (up to the 12th week of gestation)
C. In the 2nd trimester (from the 13th to the 25th week of gestation)
D. In the 3rd trimester (from the 26th week of gestation)
E. Necessarily between 24-27 weeks of gestation.

3. Macroangiopathy, as a complication of diabetes, most often affects such vessels:

A. The brain
B. Placenta
C. The retina
D. Kidney
E. Liver

4. Which of the following statements is correct about diabetes in pregnant women?

A. Same as gestational diabetes.
B. This is type 1 diabetes that first appeared during pregnancy.
C. It is type 2 diabetes that first appeared during pregnancy.
D. This is a pregnancy, against the background of type 1 and type 2 diabetes.
E. This is gestational diabetes.

5. Which of the following statements is correct about gestational diabetes?

A. Same as gestational diabetes.
B. This is type 1 diabetes that first appeared during pregnancy.
C. It is type 2 diabetes that first appeared during pregnancy.
D. This is a pregnancy, against the background of type 1 and type 2 diabetes.
E. This is gestational diabetes.

7.2. Materials of methodical maintenance of the main stage of employment:

Protocol of examination, diagnosis, treatment and prevention

Preconception counseling

ADA 2020 recommendations.

- 14.1. All women of childbearing potential with concomitant diabetes and reduced reproductive potential are encouraged to include pregnancy planning counseling in their standard diabetes management regimen. Recommendation A
- 14.2. It is recommended that family planning and contraception be discussed with women with diabetes until the woman's treatment regimen and glycosylated hemoglobin (HbA1c) levels are optimized for pregnancy. Recommendation A
- 14.3. Consultation before conception should address the issue of achieving a glucose level as close as possible to normal. To reduce the risk of congenital fetal abnormalities, preeclampsia, macrosomia and other associated complications, it is recommended to maintain HbA1c levels in the range of <6.5% (<48 mmol / mol). Recommendation B

All women of childbearing potential with concomitant diabetes should be informed of the importance of achieving and maintaining the safest level of euglycemia before conception and throughout pregnancy. Observational studies suggest that elevated HbA1c levels during the first 10 weeks of pregnancy are directly proportional to the increased risk of developing diabetic embryopathies (especially anencephaly, microcephaly, congenital heart disease, renal abnormalities, and caudal regression) (Guerin A. et al., 2007). The amount and sequence of data are convincing and confirm the recommendations for normalization of glycemia before conception, given that organogenesis occurs at 8 weeks of gestation, with HbA1c levels <6.5% (<48 mmol / mol) associated with the lowest risk congenital anomalies of the fetus.

- There is a need to inform all women of childbearing age with concomitant diabetes about the possible risks of unplanned pregnancy and the benefits of pregnancy planning for mother and fetus. Family planning, including possible contraception, should be discussed with women with pre-existing diabetes. In order to minimize the risks of embryopathies, it is necessary to inform all women of reproductive age about:

- possible risks of fetal malformations due to hyperglycaemia associated with unplanned pregnancy;
- possible methods of contraception, effective and permitted for women with concomitant diabetes.

Preconception training

Recommendations

- • 14.4. It is recommended that a multidisciplinary approach be used in the management of patients with concomitant diabetes, including an endocrinologist, perinatologist, nutritionist, and diabetes specialist. Recommendation B
- • 14.5. In addition to following recommendations 14.1 (Recommendation A) for maintaining glycemic levels, additional attention should be paid to the nutrition, examination and self-care training of patients with concomitant diabetes. Recommendation E
- 14.6. Women with type 1 or type 2 diabetes who are planning to become pregnant or are pregnant are advised to consult a specialist about the possible risks of developing and / or progressing diabetic retinopathy. It is recommended to have a vision test before pregnancy or in the first trimester, then it is recommended to perform a vision control every trimester for 1 year after delivery. Recommendation B
- • The importance of preconception training in all women with concomitant diabetes is noted in the opinion of the Committee of Obstetricians and Gynecologists of the American College of Obstetricians and Gynecologists (ACOG, committee opinion). Thus, a key point of the recommendations is the need to include the issue of pregnancy planning in routine primary and gynecological care. Preconception training should include standard examinations and training that are recommended for all women with diabetes. Prenatal vitamins should be prescribed to all women planning a pregnancy (at least 400 mg of folic acid and 150 mcg of potassium iodide) before conception. Examinations and surveys on the use of nicotine, alcohol and drugs are mandatory in preconception training.

Standard training for pregnant women should include screening for sexually transmitted diseases, thyroid disease, genetic screening, analysis of prescription drugs and supplements taken by women, and a review of travel history, focusing on

regions with Zika epidemics. Consultation with a nutritionist-nutritionist on the specific risks of obesity and lifestyle modifications is recommended in individual cases.

Counseling on the potential risks to the mother and fetus due to concomitant diabetes should include detailed information to the pregnant woman and possible ways to reduce the risk, including setting glycemic targets, lifestyle modifications, and diet therapy. The most important point of diabetes management is to set target blood glucose levels. Specific screening for diabetes should include determination of HbA1c, creatinine, and albumin-creatinine ratio. Particular attention should be paid to the review of pharmacological drugs used by pregnant women to exclude potentially harmful (angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (BRAII) and statins).

Women with diabetic retinopathy are recommended to closely monitor the condition of the visual organ during pregnancy, to assess the progression of retinopathy and prescribe treatment if necessary. To reduce the risk of preeclampsia, it is recommended to prescribe acetylsalicylic acid in a dose of 81-150 mg to all pregnant women with diabetes up to the 16th week of pregnancy.

Glycemic targets during pregnancy

- Recommendations
- • 14.7. Determination of fasting and postprandial glucose levels in gestational diabetes or a history of diabetes is necessary to achieve optimal glucose levels. Glycemic targets are glucose levels:
- - in fasting blood plasma <95 mg / dL (<5.3 mmol / l);
- - 1 h after a meal, the glucose level should be <140 mg / dl (<7.8 mmol / l) or;
- - 2 h after a meal <120 mg / dL (<6.7 mmol / l). Recommendation B
- • 14.8. Due to increased erythrocyte metabolism, HbA1c levels are slightly lower during pregnancy compared to non-pregnant women. Optimal HbA1c values during pregnancy should be <6% (<42 mmol / mol) if this can be achieved without significant hypoglycaemia, but the target level may be lower - up to <7% (<53 mmol / mol) if necessary for prevention of hypoglycemic state. Recommendation B

- • 14.9. Additional determination of blood glucose levels before and after meals can help achieve the target level of HbA1c in pregnant women with concomitant diabetes. Recommendation B
- • 14.10. Continuous glucose monitoring may reduce the risk of neonatal macrosomia and hypoglycaemia during pregnancy complicated by type 1 diabetes. Recommendation B

• 14.11. Continuous glucose monitoring should not be used as a substitute for blood glucose self-monitoring to achieve the optimal target fasting glucose level before and after meals in pregnant women with concomitant diabetes. Recommendation E

• 14.12. Commonly used estimates of HbA1c and glucose levels should not be used during pregnancy as a primary assessment of HbA1c levels. Recommendation C

Fasting blood glucose levels during pregnancy in women with normal glucose metabolism are lower than in non-pregnant women due to non-insulin-dependent glucose uptake by the fetus and placenta; also pregnant women with diabetes are characterized by mild postprandial hyperglycemia and carbohydrate intolerance due to diabetogenic placental hormones.

In patients with diabetes, glycemic goals are usually achieved through a combination of insulin and nutrition. Because glycemic targets during pregnancy are more stringent than in non-pregnant women, it is important that women with diabetes consume certain amounts of carbohydrates that are appropriate for insulin dosage and do not cause hyper- or hypoglycemia.

Physiology of insulin

Because early pregnancy is a period of hypersensitivity to insulin and low glucose levels, most women with type 1 diabetes may have lower insulin requirements and an increased risk of developing hypoglycemia. However, the situation changes rapidly around the 16th week of pregnancy, as insulin resistance increases significantly in the second and early third trimester. Insulin levels decrease by the end of the third trimester as the placenta ages. A rapid decrease in insulin requirements may indicate the development of placental insufficiency. In women with normal pancreatic function, insulin production is sufficient to address this physiological resistance and maintain normal glucose levels. However, in women with concomitant diabetes, hyperglycemia occurs if appropriate treatment is not used.

- ***Glucose monitoring***

- Reflecting the physiology of insulin, monitoring of blood glucose levels is recommended to achieve metabolic control in pregnant women with concomitant diabetes. Postprandial glucose testing is also recommended when using insulin pumps or basal bolus therapy to adjust insulin dose. Postprandial glucose monitoring is associated with better glycemic control and a lower risk of preeclampsia.
- Similar to the goals recommended by ACOG, the ADA sets its own glucose targets for type 1 and type 2 diabetes:

• fasting glucose <95 mg / dL (<5.3 mmol / l);
• glucose 1 h after a meal <140 mg / dL (<7.8 mmol / l) or
• glucose 2 h after a meal <120 mg / dL (<6.7 mmol / l).

These values are optimal for determining the level of glucose control, if they can be achieved safely. In practice, women with type 1 diabetes may find it difficult to achieve these goals without the risk of hypoglycemia, especially women who have a history of recurrent hypoglycemia. If women are unable to meet these targets, the ADA offers less stringent targets based on clinical experience and individualized care.

HbA1c during pregnancy

In a study of pregnant women without concomitant diabetes, an increase in normal HbA1c levels was associated with adverse effects during pregnancy (Ho Y.R. et al., 2017). Observational studies of pregnant women with a history of diabetes suggest that HbA1c levels in the range of <6–6.5% (<42–48 mmol / mol) are associated with the lowest adverse effects on the fetus at the beginning of gestation. Clinical trials have not evaluated the risks and benefits of achieving these target levels, and treatment goals should consider the risk of maternal hypoglycemia when setting an individualized HbA1c target of <6% (<42 mmol / mol) to <7% (<53 mmol / mol).

HbA1c levels fall during pregnancy because pregnant women have a greater need for red blood cells (see Insulin Physiology). In addition, because HbA1c is an integrated measure of glucose, it may not fully capture the increase in postprandial glucose, which carries the risk of macrosomia. Thus, although the determination of HbA1c levels may be useful, this diagnostic test should be used as a secondary method of glycemic control during pregnancy, after self-determination of blood glucose levels.

In the second and third trimesters of pregnancy, HbA1c levels <6% (<42 mmol / mol) have the lowest impact on the risks of preterm birth, preeclampsia and the development of adverse events for the fetus. Targeted HbA1c levels in pregnant women should be achieved without the risk of hypoglycaemia, which, in addition to the usual adverse effects, may increase the risk of giving birth to a child with malnutrition. Due to the physiology of erythrocytes and physiological changes in glycemic parameters during pregnancy, there may be a need for more frequent monitoring of HbA1c levels than usual (eg monthly).

Continuous monitoring of glucose levels during pregnancy

Continuous Glucose Monitoring in Pregnant Women with Type 1 Diabetes Trial (CONCEPTT) is a randomized controlled trial of continuous glucose monitoring in addition to standard therapy. before and after meals glucose levels, compared with standard management of type 1 diabetes. The results of the study showed that continuous glucose monitoring during pregnancy with concomitant type 1 diabetes indicates lower HbA1c levels, without increasing the risk of hypoglycemia, preterm birth and neonatal hypoglycemia (Feig D.S. et al., 2017).

Management of pregnant women with concomitant type 1 and type 2 diabetes

A. Insulin

Recommendations

• 14.16. Insulin is the drug of choice for the treatment of type 1 and type 2 diabetes during pregnancy. Recommendation E

• 14.17. Repeated injections or an insulin pump may be used during pregnancy complicated by type 1 diabetes. Recommendation C

The physiology of pregnancy requires frequent titration of insulin and emphasizes the importance of daily and frequent self-monitoring of blood glucose levels. Due to the complexity of insulin management during pregnancy, you can contact a specialized medical center that can provide a multidisciplinary approach to pregnancy management (perinatologist, endocrinologist, diabetologist-nutritionist and other professionals who have experience in managing pregnancy with concomitant diabetes).

To date, there is no evidence to support the ability of insulin to cross the placental barrier. A recent Cochrane systematic review failed to recommend any specific insulin regimen for the treatment of gestational diabetes (O'Neill S.M. et al., 2017). Although many physicians prefer insulin pumps during pregnancy, there are no data on their effectiveness compared to other insulin regimens.

DM type 1

Women with type 1 diabetes have an increased risk of developing hypoglycemia in the first trimester, and due to the physiological adjustment of the body during

pregnancy there is a risk of developing hypoglycemia. Therefore, educating patients and their families about the prevention, diagnosis, and treatment of hypoglycemia is important before, during, and after pregnancy to help prevent the risks of hypoglycemia and provide proper care. Insulin resistance passes quickly with the aging of the placenta.

Pregnancy is a ketogenic condition in a pregnant woman with concomitant diabetes. Therefore, it is recommended that all women with concomitant type 1 diabetes be prescribed ketone strips and provided information on the prevention and detection of diabetic ketoacidosis, which carries a high risk of stillbirth. Women with pre-existing diabetic ketoacidosis who do not have adequate nutrition often require the administration of 10% dextrose with a drop in insulin dosage to adequately meet the higher carbohydrate needs of the placenta and fetus in the third trimester of pregnancy.

Concomitant retinopathy is of particular concern during pregnancy. The rapid introduction of euglycemia in retinopathy is associated with a possible risk of disease progression.

DM type 2

Type 2 diabetes is often associated with an increased risk of obesity. The recommended weight gain during pregnancy for overweight women is 6.8-11.34 kg, and for obese women - 4.54-9.07 kg.

Glycemic control is often easier to achieve in women with type 2 diabetes than in patients with type 1 diabetes, but this may require significantly higher doses or concentrations of insulin. As with type 1 diabetes, insulin requirements fall sharply after delivery.

The risk of associated hypertension and other comorbidities may be as high or higher in type 2 diabetes as in type 1 diabetes, even if it is better controlled and shorter in duration, with abortions occurring more frequently in the third trimester. pregnancy in women with type 2 diabetes compared with the first trimester in women with type 1 diabetes.

Preeclampsia and acetylsalicylic acid

- Recommendations

• 14.18. It is recommended that women with type 1 or type 2 diabetes be given acetylsalicylic acid at a low dose of 60-150 mg / day (usual dose of 81 mg / day) by the end of the first trimester to reduce the risk of preeclampsia. Recommendation A

Concomitant diabetes during pregnancy is associated with an increased risk of

preeclampsia. Based on the results of clinical trials and meta-analyzes, the U.S. Preventive Services Task Force recommends prescribing low-dose acetylsalicylic acid as a prophylactic to pregnant women at high risk of preeclampsia up to 12 weeks. However, additional studies are needed to evaluate the long-term prenatal effects of acetylsalicylic acid on offspring.

Pregnancy and drugs

- Recommendations

• 14.19. In pregnant women with concomitant diabetes, hypertension or significant proteinuria, it is recommended to maintain blood pressure (BP) levels> 135/85 mm Hg. Art. to optimize the long-term health of the mother. The target blood pressure level should be at least 120/80 mm Hg. art., as lower rates may adversely affect fetal development. Recommendation A

• 14.20. It is recommended to cancel potentially dangerous drugs (ACE inhibitors, BRAII, statins) to all women of childbearing age who do not use reliable contraception. Recommendation B

In the normal course of pregnancy, blood pressure during pregnancy should be lower than in non-pregnant women. In case of pregnancy complicated by diabetes and chronic hypertension, the target blood pressure should be <135/85 mm Hg. Art. Lowering blood pressure below 120/80 mm Hg. Art. may be associated with impaired fetal growth and development, especially in placental insufficiency.

ACE inhibitors and BRAII are contraindicated during pregnancy because these groups of drugs can cause fetal renal dysplasia, oligohydramnios, pulmonary hypoplasia, and intrauterine growth retardation. Antihypertensive drugs that are allowed to be used during pregnancy include: methyldopa, nifedipine, labetalol, diltiazem, clonidine and prazosin. It is also possible to use drugs of the group of β-adrenoceptor blockers, with the exception of atenolol, which is prohibited for use in pregnant women. Continuous use of diuretics during pregnancy is not recommended because it is associated with limited maternal plasma volume, which may reduce intraplacental perfusion (Sibai B.M., 1996). Based on available data, the use of statins should be avoided during pregnancy (Kazmin A. et al., 2007).

- ***Postpartum care***
- ***Recommendations***

• 14.21. Immediately after delivery, insulin resistance decreases sharply, so it is recommended to evaluate and adjust the dose of insulin administered, as in most cases in the postpartum period, insulin requirements are halved. Recommendation C

• 14.22. The contraceptive plan should be discussed and used in all women of childbearing age with diabetes. Recommendation C

• 14.23. It is recommended that all women who have had gestational diabetes at 4–12 weeks postpartum be examined using a glucose tolerance test (75 g), and that clinically appropriate non-pregnancy diagnostic criteria be recommended. Recommendation B

• 14.24. Women diagnosed with prediabetes who have a history of gestational diabetes should lead an active lifestyle and / or use metformin to prevent progression to diabetes. Recommendation A

• 14.25. Women with a history of gestational diabetes should be screened for the development of type 2 diabetes or prediabetes at least every 3 years. Recommendation B

• 14.26. Women with a history of gestational diabetes should be pre-screened for diabetes to detect and treat hyperglycemia and prevent birth defects. Recommendation E

• 14.27. Postpartum care should include assessment of psychosocial status and support for self-care. Recommendation E

7.3. Materials of control of the final stage of employment:

Cases (α=3)

1. A 38-year-old woman went to the family doctor with complaints of itchy skin and genitals, slight thirst, dry mouth, nocturnal urination. The mother had type 2 diabetes. She is currently pregnant at the 20th week of gestation. Height 165 cm, weight 98 kg. Glycemia during the day: 8.4-10.3-12.6-6.9 mmol / liter. What preliminary diagnosis should be made?

A. Diabetes mellitus type 1.

B. Diabetes mellitus type 2.

C. Gestational diabetes mellitus

D Candidiasis.

E Dermatitis.

2. A pregnant woman at the 12th week of gestation, aged 28, complains of thirst, dry mouth, frequent urination. The fasting blood glucose content is 7.8 mmol / l, HbA1c - 9.8%. The examination revealed the smell of acetone in the mouth, dry skin. What diagnosis should be suspected?

A. Type 1 diabetes

B. Type 2 diabetes

C. Diabetes mellitus

D. Fasting glucose disorders
E. Gestational diabetes
3. A young couple plans to have a child. It is known that both partners have type 1 diabetes for more than 10 years. What recommendations will you give to the couple regarding pre-pregnancy training?
A. It is not desirable to get pregnant.
B. You can only get pregnant with IVF
C. Compensation for a woman's diabetes should be achieved first
D. It is necessary to first achieve compensation for diabetes in men
E. In both partners, diabetes should be compensated.

Protocol № 1 clinical examination of the patient

The patient's name _____
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Age _____

Complaints of the patient
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History of the disease _____
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Life history _____

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The results of the physical examination of the patient: _____

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Preliminary diagnosis: _____

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With what diseases it is necessary to make the differential diagnosis:

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Examination plan: _____

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Results of laboratory and instrumental examination:
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Rationale for clinical diagnosis: _____
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Clinical diagnosis: _____
The main disease: _____
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Complication: _____
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Concomitant diseases: _____
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Forecast: _____
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Efficiency: _____
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Treatment: _____

Topic 2. Features of management of pregnant women with gestational diabetes

1. Relevance of the topic.

Gestational diabetes is characterized by an increased risk of complications, macrosomia for the fetus and type 2 diabetes after pregnancy. That is, the risks of side effects increase in the presence of progressive hyperglycemia. Although there is some heterogeneity, many randomized controlled trials suggest that the risk of gestational diabetes may be reduced by diet, exercise, and lifestyle modification, especially when interventions begin in the first or early second trimester of pregnancy (Metzger BE et al., 2007; Koivusalo SB et al., 2016).

2. Learning objective.

Get acquainted with epidemiological studies of diabetes in Ukraine and in the world (α = 1)

The student must know (α = 2):

• Classification of diabetes mellitus;
• Diagnosis of diabetes mellitus during pregnancy;
• Differential diagnosis of gestational diabetes mellitus and gestational diabetes;
• Pre-pregnancy preparation and observation of a pregnant woman with type 1 diabetes.
• Pre-pregnancy preparation and follow-up of a pregnant woman with type 2 diabetes.

The student must be able to (α=3):

• prescribe the necessary tests to detect diabetes in pregnant women;
• on the basis of the analysis of data of laboratory and instrumental inspections to substantiate and formulate the diagnosis of diabetes mellitus in pregnant women;
• to carry out differential diagnosis of gestational diabetes mellitus and type 1 and 2 diabetes mellitus;
• prescribe adequate treatment of diabetes mellitus during pregnancy: existing algorithms and standards according to world recommendations;

• dynamic monitoring of pregnant women with type 1 and type 2 diabetes:
• features of pregnancy and childbirth in women with diabetes;

3. Educational goal.

Pay attention and form a sense of responsibility in students who will be obstetricians and gynecologists, the timeliness of detection and proper treatment of diabetes on the background of pregnancy from pre-pregnancy preparation to childbirth.

4. Interdisciplinary integration:

Disciplines	*Know*	*Be able*
Disciplines studied earlier		
normal anatomy	topography, vascularization of the pancreas	
normal physiology	internal secretion of the pancreas and placenta	
histology	histological structure of pancreatic islets	
biochemistry	carbohydrate metabolism	
pathological anatomy	morphological changes in organs and tissues in diabetes mellitus	
pathological physiology.	pathogenesis of vascular complications and comatose states in diabetes mellitus on the background of pregnancy	
Disciplines to be studied later		conduct a clinical examination, prescribe appropriate diagnostic tests, consultations of related specialists to verify the diagnosis.
internal medicine	clinic, diagnosis, differential diagnosis, treatment, prevention of diabetes	
pediatrics	clinic, diagnosis, differential diagnosis, treatment, prevention of diabetes in children	
surgery	features of the course of diabetes mellitus in surgical	

	pathology, timely diagnosis and management of such patients	
obstetrics and gynecology	features of the course of diabetes mellitus during pregnancy, timely diagnosis and management of such patients.	
neurology	clinic, diagnosis, differential diagnosis, treatment, prevention of neurological complications of diabetes	
ophthalmology	clinic, diagnosis, differential diagnosis, treatment, prevention of diabetic retinopathy	
Intra-subject integration.	modern methods of examination of patients, in particular laboratory, instrumental adequate tactics of treatment.	Assign adequate treatment

5. Content of the lesson topic:

1. Classification of diabetes.
2. Etiology, pathogenesis of gestational diabetes
3. Gestational diabetes: clinic, features of diagnosis.
4. Gestational diabetes and type 1 and 2 diabetes mellitus in pregnant women: differential diagnosis
5. Fetopathy in gestational diabetes.

1. 1. Plan and organizational structure of the lesson

(see "Preface")

7. Materials of methodical providing of employment.

7.1 Materials of the preparatory stage of the lesson

Tests (α = 2)

1. At what stage of pregnancy should you first be screened for gestational

diabetes?

A. In early pregnancy
B. In the 1st trimester (up to the 12th week of gestation)
C. In the 2nd trimester (from the 13th to the 25th week of gestation)
D. In the 3rd trimester (from the 26th week of gestation)
E. Necessarily between 24-28 weeks of gestation.

1. Criteria for the diagnosis of gestational diabetes.

A. on an empty stomach <5.3 mmol / l); 1 h after a meal <7.8 mmol / l) or 2 h after a meal <6.7 mmol / l).
B. fasting <6.1 mmol / L); 1 h after a meal <10.8 mmol / l) or 2 h after a meal <7.8 mmol / l).
C. on an empty stomach <5.5 mmol / l); 1 h after a meal <8.8 mmol / l) or 2 h after a meal <11.1 mmol / l).
D. on an empty stomach <4.5 mmol / L); 1 h after a meal <11.1 mmol / l) or 2 h after a meal <6.7 mmol / l).
E. on an empty stomach <5.5 mmol / l); 1 h after a meal <10.8 mmol / l) or 2 h after a meal <11.1 mmol / l).

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C. on an empty stomach <5.5 mmol / l); 1 h after a meal <8.8 mmol / l) or 2 h after a meal <11.1 mmol / l).
D. on an empty stomach <4.5 mmol / L); 1 h after a meal <11.1 mmol / l) or 2 h after a meal <6.7 mmol / l).
E. on an empty stomach <5.5 mmol / l); 1 h after a meal <10.8 mmol / l) or 2 h after a meal <11.1 mmol / l).

1. Which of the following statements is correct about gestational diabetes?

A. Same as gestational diabetes.
B. This is type 1 diabetes that first appeared during pregnancy.
C. It is type 2 diabetes that first appeared during pregnancy.
D. This is a pregnancy, against the background of type 1 and type 2 diabetes.
E. This is gestational diabetes.

7.2.Materials of methodical support of the main stage of employment:

Protocol of examination, diagnosis, treatment and prevention

Risk factors:

- • re-birth, pregnancy after the age of 35, birth of a child weighing> 4 kg in the past,
- • birth of a baby with a congenital malformation,
- • history of fading pregnancy, hypertension or BMI> 27 kg / m2 before pregnancy,
- • Type 2 diabetes in the family history,
- • transferred gestational diabetes (in ≈30% of women recur in the next pregnancy).

Diagnosis.

Determination of fasting blood glucose in each pregnant woman at the first examination. The pathological result requires urgent further diagnosis (diagnostic algorithm. If fasting blood glucose is within normal limits (<5.1 mmol / l [92 mg / dl]), perform diagnostic PGTT (with 75 g of glucose) at 24–28 weeks of pregnancy. - multiple measurement of concentration of glucose in plasma: on an empty stomach (before p / o reception of glucose solution), and also in 1 h and 2 h after loading by glucose.

In pregnant women with fasting blood glucose in the range of 5.1-6.9 mmol / l (92-125 mg / dl) or risk factors for hyperglycemia during pregnancy, perform a diagnostic PGTT as soon as possible, with the result within the norm to repeat the study at 24-28 weeks . pregnancy. Diabetes mellitus is diagnosed if at least one of the glycemic parameters during the test is pathological. Compliance with the general diagnostic criteria for diabetes at any stage of pregnancy requires referral of the patient to a specialized center. Determination of glycemia in the 1st hour of PGTT is only one of the criteria for diagnosis or exclusion of gestational diabetes - there are no (according to WHO) diagnostic criteria for diabetes based on blood glucose levels 1 hour after glucose intake and these values should not be used to diagnose diabetes in pregnant. After pregnancy and treatment, if blood glucose levels do not return to normal → determine the type of diabetes.

Diagnostic criteria for gestational diabetes based on PGTT using 75 g of glucose:

1) fasting blood glucose 5.3 mmol / l;
2) glycemia after 1 h PGTT <7.8 mmol / l;
3) glycemia after 2 h PGTT <6.7 mmol / l.

One of these criteria is sufficient to make a diagnosis.

Lifestyle modification

After diagnosis, it is recommended to start treatment with diet therapy, exercise and normalization of body weight, depending on its previous indicators. The recommended target glucose levels for type 2 diabetes are glucose:

• on an empty stomach <95 mg / dL (<5.3 mmol / l);
• 1 h after a meal <140 mg / dL (<7.8 mmol / l) or;
• 2 h after a meal <120 mg / dL (6.7 mmol / l).

Some studies suggest that 70-85% of women diagnosed with gestational diabetes can achieve disease control through lifestyle modification alone. It is believed that this proportion of women may be even higher if we use even lower targets of the International Association for Diabetes and Pregnancy Study Groups (Mayo K. et al., 2015)..

Diet therapy

Diet therapy is an individually designed nutrition plan between a woman and a nutritionist. The diet plan should ensure adequate calorie intake to promote fetal / neonatal and maternal health, achieve glycemic goals, and promote weight gain as recommended by the Institute of Medicine in 2009. There is no definitive study to determine the specific optimal intake calories for women with gestational diabetes. The diet plan should be based on an assessment of the diet from dietary guides. Thus, dietary guides for all pregnant women recommend a minimum of 175 g of carbohydrates, a minimum of 71 g of protein and 28 g of fiber. The diet should not be high in saturated fat.

Pharmacological therapy

Treatment for gestational diabetes with lifestyle modification and insulin demonstrated improved perinatal outcomes in two large randomized trials summarized in the U.S. Preventive Services Task Force review (Hartling L. et al., 2013). Insulin is a first-line drug recommended for the treatment of gestational diabetes in the United States. Although some randomized controlled trials support the limited efficacy of metformin and glibenclamide in lowering glucose in the treatment of gestational diabetes, these drugs are not recommended as first-line drugs because they cross the placental barrier and long-term safety data for offspring cause some concern. In addition, glibenclamide and metformin did not provide adequate glycemic control in separate studies.

Sulfonylurea preparations

Sulfonylurea derivatives are known to cross the placental barrier and are associated with a risk of neonatal hypoglycemia. The concentration of glibenclamide in umbilical cord blood is approximately 50-70% of maternal blood. In a 2015 meta-analysis and systematic review, glibenclamide was associated with higher neonatal hypoglycemia and macrosomia than insulin or metformin. There are also no long-term data on the safety of glibenclamide for offspring.

Metformin

In systematic reviews, metformin was associated with a lower risk of developing hypoglycemia in neonates and less weight gain in women than with insulin. However, metformin has the ability to cross the placental barrier, resulting in higher levels in umbilical cord blood than in maternal blood. In two randomized controlled trials, metformin during pregnancy with concomitant polycystic ovary syndrome showed a higher body mass index (BMI) and an increase in obesity in metformin-exposed offspring. Further research showed that the next generation had higher BMI, body weight to height ratio, waist circumference and postnatal fat gain (Hanem L.G. E. et al., 2018; Tarry-Adkins J.L. et al., 2019).

Studies comparing metformin with other regimens for ovulation induction in women with polycystic ovary syndrome have found no benefit in preventing miscarriage or gestational diabetes (Vanky E. et al., 2010), and there is no need to continue to recommend metformin in these patients.

Some women with gestational diabetes who need medication because of the high cost, language barriers, and misunderstandings are unable to use insulin safely and effectively during pregnancy. Oral medications may be an alternative for these women after discussing the potential risks and the need for longer safety data. However, due to possible adverse effects in placental insufficiency, metformin is not recommended for use in women with hypertension, preeclampsia or risk of fetal developmental delay.

Insulin

B. The purpose of insulin should be in accordance with the following recommendations. Both multiple daily insulin injections and continuous subcutaneous insulin infusion therapy are effective routes of administration, and none have shown benefits in pregnant women with concomitant diabetes.

Peculiarities of diabetes during pregnancy In the first half of pregnancy, episodes of hypoglycemia are often observed, which are associated with a decrease in insulin requirements under the influence of chorionic gonadotropin, the level of secretion of which reaches maximum values in the first trimester. Ketoacidosis (so-called starvation ketosis) often occurs during this period, which requires a reduction in insulin dose and an increase in the amount of carbohydrates in a woman's daily diet. From the second half of pregnancy (22-24 weeks) the need for insulin increases, which is due to the high hormonal activity of the fetoplacental complex and the pituitary-adrenal system of the pregnant woman. Cortisol, progesterone and estrogens act as peripheral insulin antagonists. Under the influence of these

hormones, insulin resistance develops, the body's sensitivity to both endogenous and exogenous insulin decreases, and as a result, the level of glycemia and glucosuria increases, and decompensation of diabetes often occurs. After the 35th week of pregnancy, the need for insulin decreases again. This is due to a significant increase in the function of the fetal insular apparatus and increased utilization of glucose from a woman's blood. At the end of pregnancy, the frequency of hypoglycemic episodes increases, which may be the cause of fetal stress

Postpartum observation

The glucose tolerance test is recommended at 4–12 weeks postpartum, as HbA1c levels may be constantly changing (decreasing) due to increased red blood cell counts associated with pregnancy, blood loss during delivery, or a previous glycemic profile at 3 months. The glucose tolerance test is sensitive to the detection of glucose intolerance, including both prediabetes and diabetes. Women of childbearing potential with pre-diabetes may develop type 2 diabetes before another pregnancy, so they need a preliminary assessment of glucose tolerance. Because gestational diabetes is associated with an increased risk of lifelong maternal diabetes (estimated at 50–70% 15–25 years after pregnancy), women are recommended to be screened every 1 to 3 years after pregnancy. Continuous evaluation may be performed using any of the recommended glycemic tests (eg, annual determination of HbA1c, fasting plasma glucose, or every 3 years for glucose tolerance testing using appropriate diagnostic criteria for non-pregnant women).

Gestational diabetes and type 2 diabetes

Women with a history of gestational diabetes have a significantly higher risk of developing type 2 diabetes. In a prospective study of nurses 'health studies II (Nurses' Health Study II), the subsequent risk of developing type 2 diabetes after gestational diabetes was significantly lower in women who followed a healthy diet (Tobias DK et al., 2012). Moderate but not complete BMI adjustments weakened this relationship. Body weight between pregnancies or postpartum weight gain is associated with an increased risk of adverse effects in subsequent pregnancies and earlier progression to type 2 diabetes.

Both metformin and lifestyle modifications prevent or delay the progression of diabetes in women with a history of prediabetes and gestational diabetes. Of all women with a history of gestational diabetes and prediabetes, only 5–6 require pharmacological treatment. In these women, lifestyle modifications and metformin reduction reduced diabetes progression by

35–40% over 10 years, respectively, compared with placebo.

Lactation

Given the nutritional and immunological benefits of breastfeeding, all women, including women with concomitant diabetes, should be supported in their desire to breastfeed. However, it should be borne in mind that lactation may increase the risk of hypoglycaemia overnight, and insulin dose adjustment may be requireda.

Postpartum care

Recommendations

• 14.21. Immediately after delivery, insulin resistance decreases sharply, so it is recommended to evaluate and adjust the dose of insulin administered, as in most cases in the postpartum period, insulin requirements are halved. Recommendation C

• 14.22. The contraceptive plan should be discussed and used in all women of childbearing age with diabetes. Recommendation C

• 14.23. It is recommended that all women who have had gestational diabetes at 4–12 weeks postpartum be examined using a glucose tolerance test (75 g), and that clinically appropriate non-pregnancy diagnostic criteria be recommended. Recommendation B

• 14.24. Women diagnosed with prediabetes who have a history of gestational diabetes should lead an active lifestyle and / or use metformin to prevent progression to diabetes. Recommendation A

• 14.25. Women with a history of gestational diabetes should be screened for the development of type 2 diabetes or prediabetes at least every 3 years. Recommendation B

• 14.26. Women with a history of gestational diabetes should be pre-screened for diabetes to detect and treat hyperglycemia and prevent birth defects. Recommendation E

• 14.27. Postpartum care should include assessment of psychosocial status and support for self-care. Recommendation E

7.3. Materials of control of the final stage of employment:

Tasks (α=3)

1. A 38-year-old woman went to the family doctor with complaints of itchy skin and genitals, slight thirst, dry mouth, nocturnal urination. The mother had type 2 diabetes. She is currently pregnant at the 20th week of gestation. Height 165 cm, weight 98

kg. Glycemia during the day: 8.4-10.3-12.6-6.9 mmol / liter. What preliminary diagnosis should be made?

A. Diabetes mellitus type 1.
B. Type 2 diabetes.
C. Gestational diabetes mellitus
D. Candidiasis.
E. Dermatitis.

1. A pregnant woman at the 12th week of gestation, aged 28, complains of thirst, dry mouth, frequent urination. The fasting blood glucose content is 7.8 mmol / l, HbA1c - 9.8%. The examination revealed the smell of acetone in the mouth, dry skin. What diagnosis should be suspected?

A. Type 1 diabetes
B. Type 2 diabetes
C. Diabetes mellitus
D. Fasting glucose disorders
E. Gestational diabetes

1. A young couple plans to have a child. It is known that both partners have type 1 diabetes for more than 10 years. What recommendations will you give to the couple regarding pre-pregnancy training?

A. It is not desirable to get pregnant.
B. You can only get pregnant with IVF
C. Compensation for a woman's diabetes should be achieved first
D. It is necessary to first achieve compensation for diabetes in men
E. In both partners, diabetes should be compensated.

Protocol № 1 clinical examination of the patient

The patient's name _____

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Age _____

Complaints of the patient

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History of the disease _____

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Life history _____

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The results of the physical examination of the patient: _____

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Preliminary diagnosis: _____

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With what diseases it is necessary to make the differential diagnosis:

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Examination plan: _____

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Results of laboratory and instrumental examination:

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Rationale for clinical diagnosis: _____

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Clinical diagnosis: _____
The main disease: _____
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Complication: _____
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Concomitant diseases: _____
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Forecast: _____
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Efficiency: _____
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Treatment: _____
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Drug therapy: _____
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Glycemic control: _____

Notes on the acquisition of practical skills

№ з/п	Skills and manipulations	Signature student /

		supervisor
1.	Practical experience	
1.1.	Be able to conduct surveys, physical examinations of patients with diabetes.	
1.2.	Be able to analyze laboratory test data	
1.3.	Be able to prescribe antidiabetic therapy to a patient with diabetes	
2.	Be able to prescribe a treatment regimen for complications of diabetes:	
2.1.	Diabetic retinopathy	
2.2	Diabetic nephropathy	
2.3	Diabetic neuropathy	
2.4	Diabetic foot syndrome	

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Topic 3. Features of management of pregnant women with goiter syndrome

1. Relevance of the topic.

Goiter is a clinical concept that characterizes the presence of an increase in the size or volume of the thyroid gland, the presence of nodular goiter. It develops due to the realization of genetic predisposition under the influence of triggers.

Triggers are usually negative environmental factors: iodine and selenium deficiency, the action of digestible compounds, tobacco smoking and more. Goiter often accompanies a number of pathological conditions, such as diffuse toxic goiter, nodular goiter, chronic autoimmune thyroiditis, or may be the result of medical interventions and the use of a number of drugs.

Goiter can be diffuse when the total volume increases or nodular - in the presence of local additional inclusions in the thyroid gland (thyroid) tissue (adenoma, carcinoma, calcifications, in some cases - large cysts).

The scale of iodine deficiency and its consequences is truly impressive. The WHO estimates that about 2 billion people, or more than 30% of the world's population, live in iodine-deficient regions. The total number of patients with endemic goiter reaches 740 million, and patients with cretinism - 11 million. Cases of overt cretinism are rightly regarded as the "tip of the iceberg", given that less pronounced mental disorders (not always diagnosed) occur much more often . The course of endemic goiter, which is the most common and most well-known manifestation of iodine deficiency since ancient times, can be complicated by the development of local compression syndrome, iodine-induced thyrotoxicosis and / or malignancy. Thus, the problem of iodine deficiency in the world is recognized as relevant, because the combination of these disorders largely determines not only the health of the population, but also the intellectual level of society. It should be emphasized that under the condition of chronic "iodine starvation" the risk of radiation-induced thyroid pathology in the case of man-made disasters increases significantly.

Thyroiditis is a group of thyroid diseases that differ in etiology and pathogenesis, morphological picture and clinical course, a common component of which is a certain type of inflammation. The prevalence and clinical significance of certain forms of thyroiditis also vary significantly. Most doctors are faced with various variants of chronic autoimmune thyroiditis, which is considered the most common autoimmune disease in humans. It often leads to dysfunction of the thyroid gland (usually

hypothyroidism), which determines the main clinical aspect of this pathology. The second most common are subacute thyroiditis - granulomatous and lymphocytic - which, despite the rather bright symptoms, mostly do not leave persistent disorders. Other types of thyroiditis are much less common.

Thyrotoxicosis is a syndrome in which there are clinical and / or biochemical manifestations of excessive levels of thyroid hormones in the blood, regardless of the etiological factor. Diffuse toxic goiter and functional autonomy of the thyroid gland account for about 90% of cases of thyrotoxicosis. One of the most serious diseases is diffuse toxic goiter (Graves-Bazedov disease), which is a genetically determined systemic pathology of autoimmune genesis, which is manifested by diffuse thyroid disease and hyperthyroidism, often in combination with extrathyroid pathology. Timely diagnosis allows for adequate treatment, preventing the development of many serious complications of thyrotoxicosis - both chronic (cardiomyopathy, encephalopathy, myopathy, osteoporosis, cachexia) and acute (thyrotoxic crisis). The similarity of clinical symptoms dictates the need for differential diagnosis of thyrotoxicosis syndrome with numerous diseases of the cardiovascular, nervous and other systems, which may be a difficult task, but necessary in terms of medical tactics.

Cancer of thyroid gland it is considered a rare disease, which accounts for about 1-1.5% of all malignant neoplasms; at the same time, it occurs most often among endocrine tumors. Over the last 25 to 30 years, numerous reports have shown an increase in the incidence of thyroid cancer in many countries, especially among young people. In Europe, more than 20,000 new cases of thyroid cancer are diagnosed each year, and 1,500 to 2,000 patients die from the disease. In Ukraine, about 2,500 new patients are diagnosed during the year, ≈ 27,000 treated patients are registered, and the mortality rate is 10–12 per 1 million population.

Malignant thyroid tumors are quite unique and extremely diverse in their biological properties. This, on the one hand, often leads to diagnostic errors and long-term unsuccessful treatment by specialists in various fields (endocrinologists, surgeons, pediatricians, phthisiologists, otorhinolaryngologists). On the other hand, timely and adequate treatment of thyroid cancer provides quite good long-term results. This is facilitated by the low potential of malignancy, which is inherent in most of these tumors, and compliance with modern standards of their diagnosis and treatment. However, there are tumors with quite aggressive behavior, which are a real threat to life.

2. 2. Learning objective.

Get acquainted with the spread of diffuse and nodular non-toxic goiter, hypothyroidism, thyroiditis, thyroid cancer in Ukraine and in the world **(α = 1).**

The student must know (α=2):

• Biological action of thyroid hormones on the body and the mechanism of regulation of thyroid function in pregnant women;

• Definitions and risk factors for major thyroid diseases;

• Symptoms of major thyroid diseases in pregnant women;

• Diagnostic criteria for the main diseases of the thyroid gland in pregnant women;

• Classification of the degree of enlargement of the thyroid gland;

• Methods for assessing the functional status of the thyroid gland in pregnant women;

The student must be able to (α=3):

- • diagnose endemic and sporadic goiter, hypothyroidism, autoimmune, acute, subacute thyroiditis, thyroid cancer in pregnant women, determine treatment tactics and (if possible) preventive measures;
- • to carry out differential diagnosis of thyroid diseases;
- • examine the neck and palpation of the thyroid gland;
- • palpate the cervical lymph nodes;
- • effectively use the opportunities for mass and individual prevention of iodine deficiency diseases (IDD).

3. Educational goal.

To formulate deontological principles of work with patients with endocrine pathology. To draw students' attention to the role of the influence of environmental factors on the development of certain thyroid diseases. Develop a sense of responsibility for the timeliness of diagnosis, completeness of examination and choice of treatment tactics for patients with various thyroid pathologies, especially those that pose a potential threat to health or life.

4. Interdisciplinary integration:

Disciplines	*Know*	*Be able*
Disciplines studied earlier		
Normal anatomy	Anatomical structure of the thyroid gland	

Normal physiology	Synthesis, transport, effects, regulation of thyroid hormone secretion;	
Histology	Embryogenesis, histological structure of the thyroid gland;	
Pathological anatomy	Classification and nature of pathomorphological changes of the thyroid gland;	Evaluate the results of histopathological examination of the thyroid gland;
Pathological physiology	Etiology and pathogenesis of iodine deficiency diseases, hypothyroidism, thyroid tumors;	
Pharmacology	Preparations of iodine, thyroid hormones, anti-inflammatory drugs;	Write the appropriate recipes;
Radiation diagnostics	Ultrasonography, scintigraphy, X-ray diagnosis of thyroid diseases.	Evaluate the results of relevant research.
Disciplines to be studied later		
Internal diseases	Changes of internal organs at diseases of a thyroid gland, their differential diagnosis, the main methods of treatment;	Carry out a clinical examination of the patient, palpation of the thyroid gland, appoint the necessary diagnostic examinations and consultations of related specialists to verify the diagnosis, interpret their results (conclusions).
Pediatrics	Features of the course of thyroid pathology in childhood;	
Surgery	Surgical methods of treatment of thyroid pathology;	
Obstetrics and gynecology	Features of the course of thyroid disease during pregnancy, their impact on fetal development;	
Neurology, psychiatry	Psychoneurological manifestations of thyroid pathology.	
Intra-subject integration.	Modern methods of clinical, laboratory and instrumental examination of endocrine patients.	Carry out differential diagnosis of thyroid diseases with other pathology, prescribe

		adequate treatment.

5. Content of the lesson topic:

- • Definition and epidemiology of iodine deficiency diseases.
- • Pathogenesis, clinical manifestations and diagnosis of endemic goiter.
- • Modern approaches to the treatment of endemic goiter.
- • Clinical aspects of other iodine deficiency disorders.
- • Prevention of iodine deficiency diseases: forms, methods, control.
- • Sporadic goiter: etiology, pathogenesis, clinical manifestations, diagnosis, treatment.
- • Definition, epidemiology and classification of hypothyroidism.
- • Etiology and pathogenesis of various forms of hypothyroidism.
- • Clinical manifestations and diagnostic criteria of thyroid hypofunction; atypical variants of hypothyroidism.
- • Principles of treatment of hypothyroidism in different age groups.
- • Congenital hypothyroidism: pathogenesis, neonatal screening, features of replacement therapy.

• Clinical and morphological classification, etiology, pathogenesis, clinical manifestations, diagnosis, treatment of thyroiditis.
• Etiology, pathogenesis, clinic, diagnosis of diffuse toxic goiter;
• Epidemiology, etiological factors, morphological classification of thyroid tumors.
• Clinical picture of various forms of thyroid cancer.
• Possibilities and limitations of methods for diagnosing thyroid cancer.
• Modern approaches to the treatment of thyroid cancer.
• Dispensary supervision of patients with thyroid cancer. Forecast.

6. Plan and organizational structure of the lesson

(see "Preface")

7. Materials of methodical providing of employment.

7.1. Materials of the preparatory stage of the lesson

Tests (α = 2)

1. The infant was diagnosed with hypothyroidism as part of a neonatal screening program. At what age can a child be prescribed replacement therapy?

A. From the 1st month of life.
B. From the 3rd month of life.

C. From the 6th month of life.

D. Upon completion of breastfeeding.

E. Transfer the baby to artificial feeding, and then prescribe levothyroxine.

1. Determine the most informative laboratory indicator for the diagnosis of primary hypothyroidism in pregnant women:

A. TSH.

B. Total thyroxine.

C. Free thyroxine.

D. Triiodothyronine.

E. The level of antibodies to thyroperoxidase.

1. 1. The characteristic signs of hyperthyroidism in pregnant women include the following, except:

A. Weight gain

B. Hot skin

C. Emotional imbalance

D. Tachycardia

E. Exophthalmos.

2 Choose a drug that is used to treat accidents in pregnant women:

A. Thiamazole

B. Propylthiouracil

C. Iodine in high doses

D. Carbimazole

E. Dexamethasone.

7.2. Materials of methodical maintenance of the main stage of employment:

Degrees of enlargement of the thyroid gland (WHO, 1986) [used in clinical practice].

The degree of increase	**Characteristic:**
0	No goiter (volume of particles does not exceed size distal phalanx of the patient's thumb);

Ia	Goiter is determined only on palpation and is not visible when the head is
Iб	The goiter is palpable, but visible only when completely tilted back head (also includes a node at enlarged thyroid gland);
II	The thyroid gland is palpable, it is visible in a normal position the head of the subject
III	Large goiter, which can be recognized at a distance of 5 m and beyond

Degrees of enlargement of the thyroid gland (WHO, 1994) [used in epidemiological studies].

The degree of increase	**Characteristic:**
0	No goiter
I	Goiter is determined by palpation, but invisible to the eye
II	The goiter is palpable and visible to the eye

Laboratory methods of thyroid examination are divided into the following groups:
Functional status markers: TSH, zagT4, vT4, zagT3, vT3 •
Markers of autoimmune pathology: At-TG, At-TPO, At-TTG •
Markers of oncological pathology: thyroglobulin (TG), calcitonin

Diagnostic value of thyroid hormone levels

Thyroid function	**fT_3**	**fT_4**	**TSH**
Preserved (euthyroidism)	N	N	N
Subclinical dysfunction	N	N	increased (subclinical hypothyroidism); • reduced (subclinical thyrotoxicosis)
Manifest thyrotoxicosis	Increased	Increased	Reduced
Manifest hypothyroidism	Reduced/ normal	Reduced	increased (primary hypothyroidism); reduced / normal

			(secondary or tertiary hypothyroidism)

Iodine Consumption Standards (International Council for the Control of IDD, 2005)

Contingent	The need for iodine, mcg / day
Children aged 0 - 59 months	90
Children aged 6 to 12 years	120
Children over 12 years and adults	150
Women during pregnancy and lactation	250

Hypothyroidism is a clinical syndrome caused by a prolonged, persistent deficiency of thyroid hormones in the body or a decrease in their biological effect at the tissue level.

Classification.

By level of damage:

1. Primary (thyroid)
2. Secondary (pituitary), tertiary (hypothalamic)

a. Pangipopituitarism

b. Isolated TSH deficiency

c. Anomalies of the hypothalamic-pituitary area

3. Tissue (transport, peripheral) - resistance to thyroid hormones; hypothyroidism in nephrotic syndrome.

Originally:

1. Congenital:

a. abnormalities in the development of the thyroid gland: dysgenesis (agenesis, hypoplasia, dystopia, ectopia);

b. dyshormogenesis: congenital enzymopathies accompanied by impaired thyroid hormone biosynthesis; defect of TSH receptors;

c. congenital pangipopituitarism;

d. transient;

- Iatrogenic;
- Caused by maternal thyroid-blocking antibodies;
- Idiopathic.

2. Acquired:

- thyroiditis (autoimmune thyroiditis, hypothyroid phase, subacute viral),
- post-procedure (thyroid surgery),

-atrogenic (thyrostatic therapy with radioactive iodine, thyrostatics) - endemic goiter

By course:

1. Transient
2. Subclinical (minimal thyroid insufficiency)
3. Manifest

By state of compensation:

1. Compensated
2. Decompensated

Complications: thyrogenic dwarfism, encephalopathy, cretinism, polyneuropathy, myopathy, hypothyroid coma, sexual dysfunction (delayed or premature puberty), etc.

Diagnostic criteria:

1. Clinical:

- Decrease in intelligence of various degrees
- Growth retardation (thyrogenic dwarfism)
- Delay or advancement of sexual development
- Dryness, pale skin
- Brittle, dry hair
- Swelling of the face, limbs, tongue
- Bradycardia

2. Paraclinical studies:

- General blood test: anemia, sometimes accelerated ESR
- Increased levels of cholesterol, b-lipoproteins in the blood
- ECG: sinus bradycardia (in the first months of life the pulse may be normal), decreased voltage of the teeth, slow conduction, prolonged systole Visualization of the thyroid gland during its ultrasound.
- Hormonal diagnosis:
- In subclinical hypothyroidism: increase in thyroid-stimulating hormone (TSH) (above 2.5 mOD / l, but not above 10 mOD / l) at normal levels of BT4 and no clinical symptoms.
- At the manifest hypothyroidism - increase in TSH above 10 mOD / l and decrease in TT4; - With secondary hypothyroidism, the level of TSH is within normal limits or reduced, vT4 is reduced. - X-ray of the hands: delayed "bone" age, epiphyseal dysgenesis - For the diagnosis of AIT as a cause of hypothyroidism: the titer of antibodies to thyroperoxidase of thyrocytes (ATPO) - above the upper limit of normal by 2-3 times.

Prevention of iodine deficiency and treatment endemic goiter

See	Means
Prevention:	
Mass	iodization of table salt (40 g of potassium iodate per 1 t salts); as an alternative - iodization of bread, water, oil;
individual	prescribing iodine preparations to groups of the population or individuals with an increased need for iodine supply: children, adolescents, pregnant women and breastfeeding women; carried out by taking drugs of potassium iodide (Iodide-Farmak, Iodomarin), multivitamin drugs that cover the daily requirement of iodine.
Treatment:	
medicated	• preparations containing iodine: children - 100 mcg / day, adolescents and adults (<45 years) - 200-400 mcg / day for 6-12 months; • levothyroxine preparations (L-thyroxine, Euthyrox) in a suppressive mode, which provides the level of TSH in blood plasma 0.2–0.5 mIU / l; • preparations of thyroid hormones in combination with iodides (individually).
surgical	with goiter of large size; mechanical compression of the neck; nodular forms of goiter that do not respond to drug treatment, with a reasonable suspicion of malignancy.

Nodular / multinodular non-toxic goiter

M o r p h o l o g i c a l classification	• colloidal proliferating goiter; • follicular adenoma; • adenocarcinoma; • cyst; • focal thyroiditis.
Basic clinical manifestations	Часто відсутні. Можуть спостерігатися дискомфорт у стороннього тіла, видима припухлість.
Complication	• compression syndrome with dysfunction of neighborin • development of iodine-induced thyrotoxicosis (in iodi regions).
Diagnosis	• ultrasound, including Doppler; • TAB under ultrasound control - shown for nodes> 1 cm; • determination of TSH, if necessary fT4, fT3; • scintigraphy - if functional thyroid autonomy is suspected;

	• radiography, CT, MRI - in the presence of compression syndro
Therapeutic tactics	• dynamic monitoring - control every ≈ 6 months (ultrasound, if necessary, etc. methods); • suppressive therapy of L-T4 at the rate of 2.0-2.5 μg / kg / da regions should be combined with iodine preparations (as with endemic goiter); efficiency is generally low; • surgical treatment - according to the indications (see above).

Classification of thyroiditis (clinical and morphological)

Acute thyroiditis	• *purulent;* • non-purulent.
Subacute thyroiditis	granulomatous (de Kervena); lymphocytic: postpartum (post-partum thyroiditis); spontaneous.
Chronic thyroiditis	autoimmune (lymphocytic): hypertrophic form (Hashimoto's goiter); atrophic form (idiopathic hypothyroidism); focal (focal); fibrous (Riedel's goiter); specific (tuberculosis, sarcoidosis, etc.).

Differential diagnosis of thyroiditis

	Acute purulent	Sub-acute granulomates	Preparation lymphocytic striae	Autoimmune	
				Hypertrophic form	Atrophic form
Beginning	Acute	Acute	Acute	Gradual	Gradual
Pain in the neck	+++	+++	–	+/–	–
Hyperthermia	+++	++	–	–	–
Thyroid	Enlarged, contains dense sharply painful areas	Enlarged, painful, dense, often on one side	More often diffusely enlarged, dense, painless	Diffusely enlarged, compacted, pseudo-nodular	Not palpable
Dysfunction	–	+++	+++	++	+++
Antito-rheoid antibodies	–	+	++	+++	++
Cytological findings	Granulocytes	Giant multinucleated cells	Lymphocytes	Lymphocytes	–

Note: (+) - rarely, (++) - often, (+++) - very often.

Classification of thyrotoxicosis syndrome

Etiology	1. Thyrotoxicosis caused by hyperproduction of thyroid hormone • Graves-Bazedov disease (diffuse toxic goiter); • functional autonomy of the thyroid gland (nodular toxic goiter). 2. Thyrotoxicosis caused by hyperproduction of thyroid hormon gland: • hormonally active metastases of thyroid cancer. 3. Thyrotoxicosis not associated with hyperproduction of thyroid • drug-induced thyrotoxicosis; • thyrotoxic phase of destructive thyroiditis (subacute, postpartur
Sevirity	1. Subclinical (latent, latent) - basal TSH level is reduced, conc fT3 within normal limits; clinical manifestations are mostly abse

	2. Manifest - the concentration of fT4 and / or fT3 is increa manifestations varies from asymptomatic variants to a detailed cl 3. Complicated, including thyrotoxic crisis.
Grade	• compensation; • subcompensation; • decompensation.

Frequency of clinical signs in patients with diffuse toxic goiter

Symptom	**%**	**Symptom**	**%**
Goiter	85–100	Eye symptoms	50–70
Tachicardia	85–100	Muscle weakness	60–80
Irritability	80–95	Hyperkinesis	50–80
Tremor	70–90	Increased appetite	40–60
Hot wet brushes	60–80	Infiltrative ophthalmopathy	30–50
Hyperhidrosis	70–90	Frequent bowel movements	20–40
Hypersensitivity to heat	70–80	Atrial fibrillation	2–10
The growth of systolic blood pressure	60–80	Infiltrative dermopathy	2–3
Fatigue	80–90	Decreased appetite	≈ 23
Weight loss	60–80	Dysmenorrhea	3–5
Systolic murmur over the thyroid gland	60–70	Gynecomastia	≈ 5
Dyspnea	60–70	Weight gain	≈ 5

Ocular symptoms of thyrotoxicosis

Symptom	**Manifestations**

Dalrimple	Wide open eye slits
Grefe	Lag of the upper eyelid when looking down
Shtelvaga	Infrequent blinking
Moebius	Weakness of convergence
Kocher	Retraction of the upper eyelid, the strip of sclera between the edge of the eyelid and the iris
Krause	Increased eye brightness

Methods of treatment of diffuse toxic goiter.

Methods of treatment	***Indications***
Medicinal: pathogenetic drugs • antithyroid drugs (thyrostatics)	• • are always used: either as a stand-alone method or as a preparation for radical intervention.
symptomatic drugs	
β-blockers	are used, as a rule, in a complex with thyrostatics.
Iodine in large doses	• • preoperative preparation; treatment of thyrotoxic crisis.
Glucocorticoids	• • severe course, insufficient response to thyrostatics; preoperative preparation; endocrine ophthalmopathy.
Sedatives	• • are used almost always.
Surgical	• • large goiter; compression syndrome; retrosternal goiter; severe forms of thyrotoxicosis complicated by atrial fibrillation; lack of sustainable compensation from drug treatment; propensity to relapse; intolerance to thyrostatics; the presence of a thyroid gland node> 2 cm

Radioiodine therapy	• age after 40 years (in the USA and some European countries after 18); moderate and severe course with low efficiency of drug treatment; severe complications or concomitant pathology that significantly increase the risk of surgery; postoperative recurrence of toxic goiter; refusal of the patient from surgical treatment.

Thyrostatic therapy - practical recommendations

Terms	Means	Goal
Initial therapy moderate clinical activity; Monitoring every 2-4 weeks.	• thiamazole 10–30 mg / d; carbimazole 15–40 mg / d; propylthiouracil 100–300 mg / d.	Compensation (normalization of fT4 and fT3 concentrations).
high clinical activity; Monitoring every 2-4 weeks.	• thiamazole 20–40 mg / d; carbimazole 30–60 mg / d; propylthiouracil 300–500 mg / d.	Compensation (normalization of fT4 and fT3 concentrations).
Maintenance therapy (12-18 months); Monitoring every 6-12 weeks.	• thiamazole 2.5–10 mg / d; carbimazole 5–15 mg / d; propylthiouracil 50–100 mg / d.	Persistent euthyroidism (TSH ≈ 0.3–1.0 mIU / l).
Withdrawal therapy relapse relapse	Monitoring every 3-4 months. Radical treatment.	Persistent euthyroidism (TSH ≈ 0.3–2.0 mIU / l).

Features of the clinical course of morphological variants of thyroid cancer

Histological variant	Clinical features
Papillary	It happens most often (≈ 65–80%). Progressing

	slowly, often over many years. Multifocal in 25-30% of cases. It develops mainly in young patients, including children. It metastasizes mainly lymphogenically (40–50% of observations), primarily in the cervical lymph nodes.
Follicular	The second in frequency (10–25%), clinically somewhat more aggressive, although in general its course is long. It occurs mainly in the middle age group (peak 50 years), relatively often metastasizes hematogenously (11–20%, primarily to the bones) and rarely to regional lymph nodes (5–6%).
Low-differentiated	Frequency 4-7%. According to the morphological structure, clinical course and prognosis, it occupies an intermediate position between differentiated and anaplastic types of thyroid gland. It mostly appears over the age of 50, often infiltrates the surrounding tissues and metastasizes (30-50%).
Medullary	Frequency 5–10%. There are two forms of this tumor - sporadic (70-80%) and familial (20-30%). Produces a large amount of calcitonin, as well as other biologically active substances: serotonin, prostaglandins, ACTH-like peptides and others. The degree of malignancy of the tumor is close to low-grade thyroid.
Anaplastic	Rare (1-5%), mainly in the elderly. It is characterized by rapid growth, early germination in the surrounding organs with the development of compression syndrome, extensive metastasis. Only a few patients live more than 6 months.

Diagnosis and treatment of thyroid cancer

Diagnosis	Ultrasound of the thyroid gland and regional lymphatic collectors; TAB under ultrasound control; determination of calcitonin, TSH, if necessary fT4, fT3; radiography, CT, MRI - in the presence of compression syndrome.
Differential diagnosis	Other diseases that are manifested by focal changes (clinically occurring as nodular goiter).
Treatment	At highly differentiated: thyroidectomy + radioiodine

	therapy + suppressive therapy L-T4. In other forms: thyroidectomy (sometimes extended) + modified cervical lymphadenectomy, sometimes - remote radiation therapy and / or chemotherapy (partial effect).
Monitoring	Ultrasound of the neck; determination of thyroglobulin (differentiated cancer); determination of calcitonin and / or CEA (medullary cancer); TSH control, if necessary fT4, fT3; scintigraphy - to verify residual thyroid tissue and distant metastases (differentiated cancer); if necessary - other examinations.

7.3. Materials of control of the final stage of employment

Cases (α=3)

1. A 25-year-old pregnant woman, who is concerned about the feeling of compression in the left neck, went to the endocrinologist. Circumstances: the thyroid gland is enlarged due to the left lobe, where a vaguely demarcated dense formation with a diameter of up to 3 cm is palpated, with a bumpy surface, not painful. A fine-needle biopsy of the node was performed, polygonal and spindle-shaped tumor cells were present in the punctate, an immunocytochemically negative reaction to thyroglobulin and a positive reaction to calcitonin. Make a diagnosis.

A. Papillary cancer.
B. Follicular cancer.
C. Medullary cancer.
D. Anaplastic cancer.
E. Tumor of other histogenesis.

2. In pregnant C at the 5th week of gestation, living in a mountainous area, a diffuse enlargement of the thyroid gland of the first degree was detected. Laboratory: TSH 3.2 mIU / l (N: 0.3–4.0), vT4 1.36 ng / dL (N: 0.93–1.7), anti-TPO < 10 IU / ml (N : <100). Which treatment approach in this case is the most pathogenetically justified?

A. Levothyroxine.
B. Potassium iodide.
C. Levothyroxine + potassium iodide.
D. Surgical treatment.

E. Antioxidants.

3. In a 28-year-old pregnant woman, palpation in the right lobe of the thyroid gland revealed a formation of 3 cm, dense consistency, indistinctly demarcated, with a bumpy surface. On ultrasound, it is reduced echogenicity, with blurred contours, microcalcifications and increased blood flow. What is the probable diagnosis?

A. Nodular non-toxic goiter.
B. Thyroid cancer.
C. Nodular toxic goiter.
D. Subacute thyroiditis
E. Acute non-purulent thyroiditis.

4. In a pregnant woman, 30 years old, diffuse euthyroid goiter of II degree without compression symptoms was found. There are no concomitant diseases. Which of the following treatments is most appropriate?

A. Glucocorticoids.
B. Immunomodulators.
C. Surgical treatment.
D. Thyroid hormones.
E. Antioxidants.

5. Pregnant, 22 years old, complains of weight gain, weakness, constipation, memory impairment. Objectively: dry skin, moderate swelling of the face and extremities. Pulse 60 beats / min., Blood pressure 110/60 mm Hg. Art. Ultrasound: total thyroid volume 2.6 cm3, reduced echogenicity, heterogeneous structure. Laboratory: TSH 23.2 mIU / l (N: 0.3–4.0), antibodies to TG and TPO are moderately elevated. It is most likely that the patient

A. Endemic goiter, euthyroidism
B. Autoimmune thyroiditis (Hashimoto's), hypothyroidism
C. Autoimmune thyroiditis (atrophic form), hypothyroidism
D. Iodine deficiency hypothyroidism.
E. Fibrous thyroiditis.

6. A pregnant woman complains of irritability, sweating, hand tremors, palpitations, weight loss with preserved appetite. The thyroid gland is enlarged to the second degree, elastic, not painful. The specified symptomatology most corresponds:

A. Diffuse toxic goiter
B. Neurasthenia
C. Autoimmune thyroiditis
D. Hypothyroidism

E. Hypoparathyroidism.

Task 1. A 24-year-old woman, pregnant, complains of apathy, lethargy, memory impairment, chills, dry skin, constipation, facial edema. Considers himself ill for a year. Objectively: blood pressure - 110/80 mm Hg. Art. ECG: voltage reduction, reduction of the P wave and flattening of the T wave. Laboratory tests: free T4 - 7.5 pmol / l (N: 10–23), TSH - 16.4 mIU / l (N: 0.3–4.0), antibodies to TPO - 640 IU / ml (N : <100). Ultrasound: echogenicity is diffusely reduced, the structure is sharply inhomogeneous, without tissue formations.

• Formulate a diagnosis (nosology, the nature of structural and functional changes in the thyroid gland).

• Identify and justify optimal treatment tactics.

Topic 4. Features of management of pregnant women with pathology of the adrenal glands.

1. Relevance of the topic.

2. Learning objective.

Get acquainted with the spread of adrenal pathology in Ukraine and in the world (α = 1).

The student must know (α=2):

• anatomical and physiological data of the adrenal glands;

• prevalence, etiology, pathogenesis, clinic, diagnosis, prevention and treatment of chronic adrenal insufficiency (Addison's disease) and acute adrenal insufficiency;

• classification of adrenal tumors;

• clinic, diagnosis, differential diagnosis, treatment of Itsenko Cushing's syndrome (corticosterone, glucosteroma), androsteroma and corticosteroma, primary hyperaldosteronism (Kona syndrome), pheochromocytoma;

The student must be able to (α=3):

• recognize clinical symptoms;
• interpret laboratory data, results of determination of hormones, their precursors and metabolites;
• introduce differential diagnostics;
• make a plan of examination and treatment;
• diagnose, treat, introduce dispensary supervision in case of chronic adrenal insufficiency, hormonally active tumors of the adrenal glands;
• diagnose and treat acute adrenal insufficiency and Addison's disease under stress

Educational goal. To formulate deontological principles of work with patients with endocrine pathology. To draw students' attention to the role of environmental factors on the development of adrenal diseases, the course of pregnancy against the background of pathology of the adrenal glands. Develop a sense of responsibility for the timeliness of diagnosis, completeness of examination and choice of treatment tactics for pregnant

women with various adrenal pathologies, especially those that pose a potential threat to the health or life of mother and child.

3. Interdisciplinary integration:

Disciplines	*Know*	*Be able*
Disciplines studied earlier		
Normal anatomy	Anatomical structure of the adrenal glands	
Normal physiology	Synthesis, transport, effects, regulation of adrenal hormone secretion;	
Histology	Embryogenesis, histological structure of the adrenal glands;	
Pathological anatomy	Classification and nature of pathomorphological changes of the adrenal glands;	Evaluate the results of histopathological examination of the emergency;
Pathological physiology	Etiology and pathogenesis of adrenal diseases, hormonally active adrenal tumors;	
Pharmacology	Preparations of gluco- and mineralocorticosteroids and androgens;	Write the appropriate recipes;
Radiation diagnostics	Ultrasonography, scintigraphy, X-ray diagnosis of adrenal diseases.	Evaluate the results of relevant research.
Disciplines to be studied later		
Internal diseases	Changes of internal organs in diseases of the adrenal glands, their differential diagnosis, basic methods of treatment;	Carry out a clinical examination of a pregnant woman, appoint the necessary diagnostic tests and

Pediatrics Surgery Obstetrics and gynecology Neurology, psychiatry	Features of fetal development on the background of adrenal pathology in pregnant women Surgical methods of treatment of adrenal pathology; Features of pregnancy against the background of adrenal diseases, their impact on fetal development; Psychoneurological manifestations of adrenal gland pathology.	consultations of related specialists to verify the diagnosis, interpret their results (conclusions).
Intra-subject integration.	Modern methods of clinical, laboratory and instrumental examination of endocrine patients.	Carry out differential diagnosis of emergencies with other pathology, prescribe adequate treatment.

4. Content of the lesson topic:

• Definition and epidemiology of emergencies.
• Pathogenesis, clinical manifestations and diagnosis of Itsenko-Kushig syndrome.
• Modern approaches to the treatment of Itsenko-Cushing syndrome.
• Clinical aspects of other syndromes of pathological hypercortisolism.
• Addison's disease: etiology, pathogenesis, clinical manifestations, diagnosis, treatment.
• Etiology and pathogenesis of various forms of CRF.
• Clinical manifestations and diagnostic criteria for acute adrenal insufficiency;
• Principles of treatment of chronic and acute adrenal insufficiency during pregnancy.

• Conn's syndrome: pathogenesis, neonatal screening, features of antihypertensive therapy in pregnant women.
• Etiology, pathogenesis, clinic, diagnosis of pheochromocytoma;

5. Plan and organizational structure of the lesson

(see "Preface")

7Materials of methodical support of employment.

7.1. Materials of the preparatory stage of the lesson

Tests (α=2)

1 Which of the hormones are mainly produced in the glomerular zone of the adrenal cortex?
A-dehydroepiandrosterone;
B-cortisol;
C-deoxycorticosterone;
D-androstenediol;
Ealdosterone.
2 What hormones are produced in the bundle zone of the adrenal cortex?
A-aldosterone;
B-dehydroepiandrosterone;
C-androsterone;
D-cortisol;
E-estrone.
3 Which of these hormones are not produced in the adrenal retina?
A-dehydroepiandrosterone;
B-testosterone;
C-cortisol;
D-estradiol;
E-androsterone.
4 What is the interaction between glucocorticoids and glucagon in the regulation of gluconeogenesis?
A-glucocorticoids directly activate the action of glucagon;
B-do not affect the effects of glucagon;
C-glucocorticoids have a permissive effect on glucagon in the regulation of gluconeogenesis.
5 How do glucocorticoids interact with adrenaline in the regulation of gluconeogenesis?
A-do not affect the action of adrenaline;

B-suppress its effect on the processes of gluconeogenesis;
C-have a permissive effect on the effects of adrenaline.
7.2. Materials of methodical maintenance of the main stage of employment:

Anatomical and physiological data of the adrenal glands

Adrenal glands - paired endocrine glands, there are right and left adrenal glands. The adrenal glands are a complex consisting of two endocrine glands - the cortex and the brain, which have different embryonic origins, different histological structure and synthesize different types of hormones. The cortical substance (adrenal cortex) is formed from mesodermal cells located near the rudiments of the gonads and kidneys. The brain substance is a derivative of the ectodermal cells of the neural crest. In the fetus, the fetal adrenal glands are larger than the kidneys. In the postnatal period, a permanent adrenal cortex begins to form, and by the third year of life, 3 zones of the adrenal cortex are clearly defined: glomerular, bundle, and reticular, which borders the cerebral cortex. In adults, the adrenal glands have the shape of triangles measuring 4x2x0.3 cm and weighing about 5-7 g. The cortex accounts for about 80% of the adrenal glands. The cerebral layer of the adrenal glands (as well as the sympathetic nervous system) are derived from the neural crest, have a neuroectodermal origin, are the site of formation of catecholamines, which include dopamine, norepinephrine and adrenaline.

The adrenal glands secrete corticosteroids, which consist of 21 carbon atoms. Steroid hormones are divided into four groups: glucocorticoids, mineralocorticoids, androgens and estrogens. The precursor of steroid hormones is cholesterol, the share of which in the human adrenal glands is up to 10% of raw weight. A large proportion of cholesterol (80-90%) is associated with fatty acids, cholesterol esters are concentrated in the lipid droplets of the cytoplasm. Free cholesterol makes up only 10% of its total content in the adrenal glands, is localized mainly in endoplasmic reticulum and mitochondria. Cholesterol replenishment is controlled by ACTH. ACTH regulates the rate of steroidogenesis in the adrenal glands, changing the metabolism of cholesterol and its redistribution both inside the cell and in the mitochondria. Intracellular transport of cholesterol is carried out by the microvilli system. The biosynthesis of corticosteroids begins in mitochondria, where cholesterol is cleaved by the enzyme desmolase P450scc side chain from 6 carbon atoms to form pregnenolone, a polycyclic compound with 21 carbon atoms. Pregnenolone, formed from cholesterol in

mitochondrial crystals, is a precursor to most corticosteroids. Further transformation of glucocorticoids occurs in the smooth endoplasmic reticulum. ***From pregnenolone with the participation of the enzyme 17ahydroxylase-P450s17 occurs 17a-hydroxylation with the formation of 17-ahydroxypregnenolone (cortisol). The enzyme 21-hydroxylase-P450s21 provides further hydroxylation in the 21st position with the formation of corticosterone. The enzyme 11b-hydroxylase-P450s11 controls the subsequent hydroxylation in the 11th position with the formation of cortisone (11-dehydrocortisol).*** These metabolites, resulting from successive hydroxylation reactions, are present in the beam and partially in the reticular zones of the adrenal cortex.

The biosynthesis of mineralocorticoids is controlled by the enzyme P450-aldo (aldosterone synthase), which is present only in the glomerular zone. Therefore, mineralocorticoids (aldosterone) are formed only in the cells of the glomerular zone. Under the control of the enzyme P450-aldo are all three last stages of aldosterone synthesis - the formation of 11-deoxycorticosterone corticosterone, 18-hydroxycorticosterone and aldosterone (18-oxycorticosterone). The functions of aldosterone-forming cells are only partially controlled by ACTH.

The formation of androgens in the adrenal cortex is carried out in its reticular layer and partially in the beam zone by conversion of 17-a-hydroxypregnenolone to C-19 steroids, which include dehydroepiandrosterone and dehydroepiandrosterone sulfate. Androstenedione is formed from 17-α-hydroxyprogesterone by the enzyme 17,20-desmolase. Androstenedione can be converted to testosterone. In men, testosterone of adrenal origin is only a small fraction of total testosterone circulating in the blood and excreted in the urine. Under the influence of ACTH in adrenal tissues there is an increase in DNA and RNA synthesis, cell size, nucleus volume increases, nucleoli and lamellar complex are hypertrophied, the number of lipid inclusions and mitochondria increases, the volume of smooth endoplasmic reticulum increases, enzymes are formed and activated. rate of steroidogenesis (cholesterol esterase, desmolase P 450-scc, etc.).

Biologically active glucocorticoids in descending order of activity are cortisol, cortisone, corticosterone, 11-deoxycortisol and 11-dehydrocorticosterone. The adrenal glands secrete 18-20 mg of cortisol per day. Cortisol entering the bloodstream is bound by α-2-globulin (corticosteroid-binding globulin, or transcortin). More than 95% of blood cortisol is associated with transcortin and is in constant equilibrium with the

free fraction of the hormone, which has a biological effect. However, cortisol also binds to albumin, which has a low affinity for it compared to transcortin. In the glomeruli of the kidneys, only free cortisol is filtered, about 90% of which is reabsorbed in the renal tubules, and the rest - about 330 nmol (120 milligrams) - is excreted in the urine during the day. The main site of cortisol metabolism is the liver, but the kidneys, intestines and lungs are also involved in the metabolism of corticosteroids. The half-life of cortisol is 80-110 minutes. Cortisol secretion, like ACTH, has a characteristic circadian rhythm. The maximum secretion occurs in the morning (6-8 g). Glucocorticoids are important, vital hormones involved in the regulation of metabolism in the body: - increase blood glucose due to a sharp increase in gluconeogenesis in the liver and reduce glucose utilization in the periphery (contrainsular action, peripheral antagonism of insulin); - have a catabolic effect on the metabolism of proteins and fats - activate their breakdown and inhibit synthesis; - activation of lipolysis in adipose tissue leads to the release into the blood serum of glycerol, free fatty acids and other lipids (hyperlipidemia and hypercholesterolemia). - suppress all components of the inflammatory reaction and are natural anti-inflammatory factors; - together with aldosterone, catecholamines and other vasoactive peptides are involved in maintaining normal blood pressure, potentiate mainly the effect of catecholamines on the vascular wall. In addition, this increases the formation of angiotensinogen, which is converted into angiotensin, has its own pressor effect and at the same time stimulates the secretion of aldosterone; - increase diuresis, stimulating the glomerular filtration rate and reducing water reabsorption (probably due to inhibition of antidiuretic hormone production). Cortisol has low mineralocorticoid activity - enhances sodium reabsorption in exchange for potassium ions in the distal tubules of the kidneys, which leads to sodium retention in the body, increased extracellular fluid volume and hypokalemia. Cortisol is the main corticosteroid that controls the secretion of corticoliberin and ACTH. Biologically active mineralocorticoids in descending order of activity are aldosterone, deoxycorticosterone, 18-oxycorticosterone and 18-oxydeoxycorticosterone. Aldosterone contributes to the retention of sodium and water in the body, stimulates potassium excretion, and has a weak glucocorticoid effect. Adrenal secreted aldosterone binds to specific cytoplasmic receptors of epithelial cells of the distal tubules of the kidneys. The aldosterone receptor complex then moves to the nucleus and binds to nuclear receptors, causing mRNA stimulation and protein-enzyme synthesis, which carries out increased potassium secretion and sodium retention,

ensuring the exchange of sodium ions for potassium in the distal tubules. In the reticular layer of the adrenal cortex is the secretion of sex hormones (androgens and estrogens).

Catecholamines are formed in the chromaffin cells of the adrenal medulla, CNS, adrenergic sympathetic fibers of postganglionic neurons. Catecholamines are both hormones and neurotransmitters that play a leading role in regulating the functioning of the cardiovascular system. The starting product for the formation of catecholamines is tyrosine. Initially, the mitochondria of chromaffin cells undergo hydroxylation of tyrosine with the participation of the enzyme tyrosine hydroxylase with the formation of dihydroxyphenylalanine (DOPA). The activity of tyrosine hydroxylase and hydroxylation of tyrosine is a major link in the biosynthesis of catecholamines, limiting its rate. DOPA is a precursor of catecholamines, has no biological activity, but easily crosses the blood-brain barrier. With the help of DOPA decarboxylase DOPA is converted into dehydroxyphenylethylamine (dopamine). Decarboxylation of DOPA and the formation of dopamine is carried out in the cytoplasm, where in dissolved form there are DOPA decarboxylase and other enzymes required for this stage of catecholamine biosynthesis. Dopamine enters the granules of chromaffin cells or axon terminals and in the presence of the enzyme dopamine-b-oxidase is converted to norepinephrine. Next, norepinephrine is re-released into the cytoplasm and by the enzyme norepinephrine-N-methyltransferase is transformed into adrenaline, which is re-absorbed by the granules. The granules perform the following specific functions: absorb dopamine from the cytosol of the cell and convert it to norepinephrine; granules are the place of "storage" of adrenaline and noradrenaline; protect them from the action of monoamine oxidase and destruction; in response to nerve stimulation, catecholamines are released into the blood. The granules function as tissue buffer systems for catecholamines; this function can be compared with the function of serum transport proteins for thyroid hormones and corticosteroids.

CHRONIC INFLAMMATION OF THE ADRENAL CORE (ADDISON'S DISEASE)

Chronic adrenal insufficiency is a disease caused by a sharp decrease in the production of hormones of the adrenal cortex. Chronic insufficiency of the adrenal cortex caused by tuberculous lesions was first described in 1855 by the English clinician Thomas Addison. Chronic adrenal insufficiency is more common in men aged 20-40 years; the ratio of men and women suffering from this disease - 2:

1.**Ethiology**

The primary form may be associated with damage to the cortical substance of the adrenal glands by destructive processes of various origins or with progressive atrophy of the adrenal glands of autoimmune origin. The development of the secondary form of the disease is more often associated with hypoplasia or atrophy of the adrenal cortex caused by primary damage to the hypothalamic-pituitary system, which leads to insufficient secretion of corticotropin by the pituitary gland. Previously, the main cause of chronic adrenal insufficiency was tuberculosis infection, which accounted for up to 80% of all cases. At this time, in approximately 50-65% of cases, primary chronic adrenal insufficiency occurs as a result of autoimmune adrenalitis. Often in the same patients, along with the presence of autoantibodies to the cell of the adrenal cortex, antibodies to the islets of the pancreas are detected.

Autoimmune lesions of the adrenal cortex are often found as a component of autoimmune polyglandular syndrome type I and II. Autoimmune polyglandular syndrome type I develops in childhood (about 10-12 years) and includes hypoparathyroidism, adrenal insufficiency and candidiasis. Often this insufficiency of these glands is combined with hypogonadism, pernicious anemia, alopecia, vitiligo and chronic active hepatitis.

Autoimmune polyglandular syndrome type II is observed in adults, usually after the age of 20 and is characterized by a triad: diabetes, autoimmune diseases of the thyroid gland and adrenal insufficiency. In autoimmune polyglandular syndrome type II there is an association with the genes of the HLA-DR3 and DR4 systems, whereas in autoimmune polyglandular syndrome type I there is no such association.

Schmidt's syndrome is characterized by autoimmune damage to the adrenal glands, thyroid and gonads. At tuberculous defeat adrenal glands can be enlarged, however they are more often shrunken, fibrosed, only at a microscopy it is possible to reveal small sites of a hyperplasia of cells of adrenal cortex. The cerebral layer of the adrenal glands is involved in the pathological process, which can be completely destroyed. Other pathological processes (blastomycosis, amyloidosis, histoplasmosis, coccidioidomycosis, hemochromatosis, etc.) in bilateral lesions of the adrenal cortex are the cause of chronic adrenal insufficiency in 10% of cases.

Primary chronic insufficiency of the adrenal cortex is rarely associated with amyloid degeneration of the adrenal cortex, adrenal vascular thrombosis, hemorrhage, lesions in purulent processes, brucellosis,

helminthic infestations, coccidioidomycosis, histoplasmosis, syphilis or raccoonitis glands, after bilateral adrenalectomy for adrenal tumors and Itsenko-Cushing's disease.

The secondary form of chronic insufficiency of the adrenal cortex is most often caused by inflammatory diseases of the brain and its membranes (encephalitis, arachnoiditis). Addison's disease can also occur as a result of long-term corticosteroid therapy for rheumatism, collagenosis, blood diseases, bronchial asthma, resulting in dysfunction of the hypothalamic-pituitary-adrenal cortex, leading to hypoplasia and atrophy of the adrenal cortex.

Pathogenesis

Damage to the adrenal cortex leads to a decrease in the formation of glucocorticoids, to a lesser extent mineralocorticoids and androgens. Hormone deficiency causes complex metabolic disorders in the body, as well as the functional state of many organs and systems. Glucocorticoid deficiency causes severe carbohydrate metabolism. Decreased activity of gluconeogenesis, in the intervals between meals there are episodes of hypoglycemia. There is no anabolic effect of glucocorticoids on the liver - reduced glycogen stores in the liver, mainly a "depot" of carbohydrates in the body. Even against the background of carbohydrate load, the level of glucose in the blood remains low - a flat glycemic curve. Low levels of glucose in the tissues cause dystrophic changes and various functional disorders - including muscle weakness and lethargy. Glucocorticoid deficiency causes inhibition of protein synthesis in the liver, decreased activity of intracellular enzymes, slows erythropoiesis and leukopoiesis, reduced adaptation to stressful situations and infections. Slowing of anabolic processes causes a decrease in muscle volume, various dystrophic and dysregenerative changes in the internal organs. Lack of mineralocorticoids causes increased sodium loss, dehydration, decreased circulating blood volume (loss of 1 mmol of sodium in the urine leads to the release of 6.5-8.5 ml of water, additional water loss per day can be 300-850 ml). Reducing the sodium content in the walls of arterioles reduces the pressor effect of other vasoactive substances (norepinephrine, etc.). Decreased plasma sodium causes a decrease in osmotic pressure, a decrease in circulating blood volume, which also leads to a decrease in blood pressure. Androgen deficiency causes dysfunction of the gonads, worsens anabolic processes. The combination of these disorders with dehydration, decreased glycogen content in the muscles, anorexia, hypoplasia and muscle atrophy leads to progressive weight loss. Decreased synthesis of mineral and glucocorticoids,

as well as androgens leads to dysfunction of the cardiovascular, digestive, hepatobiliary systems and kidneys.

Clinical manifestations

Patients, as a rule, can not determine the time of onset of the disease and indicate a constantly progressing general and muscular weakness, which worsens by the end of the day.

1. Arterial hypotension is found in 88-90% of patients and is one of the early manifestations of chronic adrenal insufficiency. Both diastolic and systolic pressure decreases to 80/60 mm Hg. and below. In some cases, diastolic pressure may be normal. In the presence of concomitant hypertension or in patients after bilateral adrenalectomy for Itsenko-Cushing's disease, normal or elevated blood pressure is observed. Arterial hypotension is clinically manifested by progressive weakness, dizziness, episodes of fainting. Regardless of the value of blood pressure, patients have orthostatic hypotension (Shellong's symptom). Violation of all types of metabolism leads to profound dystrophic changes in the myocardium, while reducing the contractile capacity of the myocardium, reduces cardiac output. Tachycardia is often observed. The pulse is soft, small. The ECG shows a decrease in the voltage of the teeth, a decrease in the interval S-T, lengthening the interval P-Q, Q-T, expansion of the QRS complex, a decrease in the tooth T.

2. Mental asthenia - severe general weakness, malaise, fatigue, apathy, loss of interest in life, depressive reactions. At the same time episodes of the increased irritability up to development of psychosis are possible. Decreased intellectual performance, memory, ability to concentrate. A good night's sleep does not improve your health. Patients can not lead a normal life, even the usual load for them is unbearable. At the expressed decompensation patients cannot get out of bed in the morning. Attacks of hypoglycemia develop as a result of decreased cortisol secretion, decreased gluconeogenesis, depletion of glycogen stores in the liver. Hypoglycemia manifests itself in the form of attacks characterized by severe weakness, irritability, psychotic reactions, hunger, sweating. Such seizures usually develop in the morning on an empty stomach or after a long break between meals. Psycho-emotional disorders are caused by frequent hypoglycemia and high levels of ACTH. Replacement therapy normalizes CNS function and these symptoms decrease in direct proportion to the normalization of cortisol levels in the blood

3. Physical asthenia - muscle weakness. Muscle strength and muscle volume decrease, dystrophic changes in myofibrils develop.

Dyselectrolyte disturbances, dehydration, arterial hypotension, decreased protein and glycogen production in muscles, decreased tissue macroerg formation, and decreased tissue oxygen utilization are causes of adynamia and asthenia. Along with the general weakness there is a decrease in body weight. Weight loss occurs both due to dehydration and due to decreased appetite and the addition of nausea and vomiting. Weight loss is due to a sharp suppression of anabolic processes with a decrease in the amount of muscle tissue and fluid loss. The rate of weight loss can be different.

4. Hyperpigmentation of the skin and mucous membranes Melanoderma is a specific symptom of primary adrenal involvement, the symptom is never observed in secondary adrenal insufficiency. Very rarely, hyperpigmentation is absent in primary adrenal insufficiency - "white" addisonism. The pathogenesis of melanoderma is associated with increased ACTH synthesis in primary adrenal insufficiency - melanostimulating hormone is formed in cells located near the corticotropin-forming zones. The accumulation of melanin pigment occurs primarily on exposed parts of the body, in places of friction of clothing, on the palmar lines, postoperative scars, on the mucous membranes of the mouth, in the anal area and areola of the nipples, on the external genitalia. Subsequently, diffuse hyperpigmentation develops. The severity of melanoderma correlates with the severity of adrenal insufficiency - increased severity of melanoderma is an unfavorable prognostic sign, a harbinger of the development of Addison's crisis. Achieving compensation for insufficiency is accompanied by lightening of the skin and mucous membranes.

5. Abdominal syndrome - loss of appetite up to anorexia - dystrophic changes in the gastric mucosa cause a decrease in the secretion of pepsin and hydrochloric acid, there are often manifestations of hypoacid gastritis. During the period of decompensation of the disease there are abdominal pain without a clear localization, nausea, vomiting, anorexia, constipation, alternating with diarrhea due to increased secretion of sodium chloride into the intestinal lumen. Vomiting and diarrhea increase sodium loss and lead to the development of acute adrenal insufficiency. Sometimes accompanied by ulcerative lesions of the stomach and duodenum, spastic colitis. Weight loss correlates with the degree of loss of appetite and digestive function.

6. Sexual dysfunction. Decreased function of the gonads. In men, decreased libido, impotence develops. Androgen deficiency occurs in women: pubic hair loss, in the armpits, because in a woman's body androgens are formed only in the adrenal glands, while in men androgens

are synthesized mainly by the testes. Women are also characterized by menstrual irregularities.

7. Nocturia is one of the most common symptoms of chronic adrenal insufficiency.

Classification

According to the clinical course:

1 - typical form - severe weakness, fatigue, lethargy, anorexia, weight loss, dyspepsia, hyperpigmentation of the skin and mucous membranes.

2 - atypical forms: a) mineral (by type of hypoaldosteronism); b) pigment-free; c) diencephalic-pituitary, etc.По ступеню тяжкості:

Mild form (satisfactory condition, preserved efficiency, systematic hormone replacement therapy is not required, enough dietary correction - the addition of salt, restriction of foods high in potassium, as well as taking ascorbic acid);

Moderate form (to achieve clinical effect, restoration of metabolic processes, reduction of pigmentation and adynamia, normalization of blood pressure and body weight, recovery requires hormonal replacement therapy - glucocorticoids cortisone, hydrocortisone, prednisolone, etc.);

Severe form - a history of addisonic crises; the clinical effect is achieved only with continuous glucocorticoid replacement therapy in combination with mineralocorticoids.

Additional studies Clinical analysis of blood - anemia, often of complex genesis - iron deficiency, B12- and folate-deficient, hyporegenerative. Possible eosinophyllocytophilia, relative lymphocytosis, sometimes leukopenia. Biochemical studies - lowering fasting blood glucose. When performing a glucose tolerance test - a flat glycemic curve with a pronounced hypoglycemic phase. Decreased insulin tolerance - a pronounced drop in blood glucose. Electrolyte imbalance. Deficiency of glucocorticoids and mineralocorticoids is the cause of excessive excretion of sodium in the urine, and its level in the blood decreases to 110 mmol / l, chloride - below 98.4 mmol / l, and potassium concentration rises above 5 mmol / l. Increased sodium / potassium ratio. Sometimes the serum calcium content is increased to 4.2 mmol / l. Hypercalcemia in such cases is combined with hypercalciuria, thirst, polyuria and hypostenuria. The absorption of calcium in the intestine and its release from the bones increase. Normalization of calcium metabolism occurs with adequate replacement therapy. There are impaired renal function: decreased glomerular filtration rate and renal blood flow, increased serum creatinine.

Typical hypoalbuminemia, sometimes also hypoproteinemia. Hormonal background disorders. The level of ACTH increases in primary adrenal insufficiency and decreases the content of ACTH in secondary insufficiency. The circadian rhythm of ACTH secretion is disturbed - high level both in the morning and in the evening.

A direct confirmation of hormonal insufficiency of the adrenal cortex is the determination of fluorogenic corticosteroids in plasma. If the level of corticosteroids in the blood taken at 8-10 am is less than 170 nmol / l (6 μg / 100 ml), the diagnosis of adrenal insufficiency is not in doubt. The content of cortisol, corticosterone, aldosterone in the blood decreases. Decreased urinary excretion of 17-ACS and 17-CS. More accurately reflects the functional state of the adrenal glands conducting stimulation tests.

1. Short-term ACTH test After determining the level of fluorogenic corticosteroids or cortisol in plasma, 0.25 mg (25 U) of synthetic ACTH (synactin) is administered intramuscularly or intravenously. After 30 minutes, the concentration of corticosteroids is examined again. If the function of the adrenal cortex is not impaired, there is at least a twofold increase in corticosteroids in the blood of the subject. A negative test (no increase in the content of hormones in the blood) indicates a decrease in adrenal function. The synacthen test should be combined with prednisolone treatment as it does not interfere with the determination of fluorogenic cortisol.

2. Long-term stimulating test with ACTH characterizes the potential reserves of the adrenal cortex, is used for the differential diagnosis of primary and secondary adrenal insufficiency. The drug of prolonged action depo-synactin (1 mg) is administered parenterally (intramuscularly). Plasma corticosteroid levels are determined 1, 4, 8 and 24 h after the administration of depo-synactin. At primary insufficiency of adrenal glands in all tests the level of cortisol will be low. At secondary insufficiency in 4 h. cortisol levels rise to 700 nmol / l (25 μg / 100 ml) and above. To avoid acute adrenal insufficiency, this test should be performed without interrupting prednisolone replacement therapy. If acute adrenal insufficiency is suspected, the patient should be given an infusion of prednisolone solution (30-60 mg) at the same time as synactin and the fluorogenic cortisol concentration in the blood should be examined periodically once an hour. If after 4-6 hours. it remains low, we can talk about adrenal insufficiency.

3. Test with lysine-vasopressin. Perform an intravenous infusion of 4 UNITS of lysine vasopressin for 2 hours. Normally, the level of blood corticosteroids should increase 3-3.5 times compared to the initial.

Lysine-vasopressin often causes nausea, increased intestinal motility and frequent urge to defecate. The test is contraindicated in coronary heart disease.

4. Insulin tolerance test. It is performed by intravenous administration of simple insulin at a dose of 0.1 IU per 1 kg of body weight. The test method and its interpretation are similar to the ACTH test. The insulin test is contraindicated in persons with coronary heart disease, epilepsy, patients with initially low levels of fluorogenic corticosteroids in the blood (below 170 nmol / l). To diagnose hypoaldosteronism, the concentration of aldosterone in blood plasma or its excretion in the urine is determined. Pharmacodynamic tests allow to estimate its balance in an organism more reliably, than one-moment definition of level of aldosterone.

5. Test with angiotensin. Angiotensin is a specific stimulant of aldosterone secretion. 0.5 mg of angiotensin in 50-100 ml of isotonic solution of sodium chloride or glucose is administered intravenously over 50-60 minutes under constant control of blood pressure. No increase in aldosterone concentration at the end of the infusion indicates hypoaldosteronism.

6. A test with a low-salt diet is used to detect latent insufficiency of aldosterone secretion. Determination of aldosterone in primary chronic adrenal insufficiency shows that blood aldosterone levels may be normal or decreased, while renin levels are elevated due to decreased plasma volume. Visualization of the adrenal glands. Computed tomography, angiography, ultrasound, radioisotope scanning can determine the topographic changes of the adrenal glands and the nature of the pathological process that caused their functional impairment. Radiography of the kidneys allows in some cases to detect calcification in the adrenal glands. Percutaneous aspiration adrenal biopsy is sometimes used. The change in the ECG is due to metabolic and electrolyte disturbances. Usually there is a high-amplitude pointed tooth T, which in some leads may even exceed the height of the largest tooth of the QRS complex. Slowing of atrioventricular or intraventricular conduction is possible. Immunological studies A specific marker of "autoimmune adrenalitis" - antibodies to the adrenal enzyme 21-hydroxylase (P450s21). Characterized by high titers of antibodies to adrenal antigens, violation of cellular immunity in the autoimmune nature of the process. Differential diagnosis should be made between primary and secondary adrenal insufficiency, as well as diseases characterized by hyperpigmentation, hypotension and gastrointestinal disorders. With secondary adrenal insufficiency of pituitary origin, in contrast to the

primary, there is pallor of the skin, signs of endocrine insufficiency - hypothyroidism, hypogonadism, insufficient growth and low levels of corticotropin in blood plasma. In contrast to pituitary insufficiency, in polyglandular insufficiency of autoimmune origin in the blood of patients are determined organ-specific autoantibodies. Hyperpigmentation can be hereditary, national or caused by individual sensitivity to sunlight. It is also observed in pellagra, dermatomyositis, scleroderma, melanoma metastases, liver cirrhosis, hemochromatosis, long-term use of drugs containing arsenic, silver, gold, bismuth. Hemochromatosis is characterized by the absence of hyperpigmentation on the mucous membranes and the characteristic deposition of hemosiderin in the sweat glands, the presence of pigmentary cirrhosis of the liver and diabetes, gray-brown pigmentation of the skin. Porphyria is also accompanied by generalized brown pigmentation, but is characterized by the presence of large amounts of uroporphyrin in plasma, urine and feces. Poisoning by salts of heavy metals (arsenic, zinc, lead, mercury, etc.) may be accompanied by pigmentation of the skin and gums, but there is no pigmentation of the mucous membranes. Local pigmentation occurs in ulcerative colitis, liver cirrhosis, melanosarcoma, papillary dystrophy (acanthosis nigricans), neurofibromatosis. With pellagra on pigmented areas of skin, which on the extremities have the appearance of socks and gloves, there are signs of dermatitis. In addition, this disease is constantly diarrhea and dementia. The racial affiliation of the patient, as well as the possibility of sunburn should be taken into account. Relatively often latent chronic adrenal insufficiency under the influence of excessive solar radiation turns into clinically severe adrenal insufficiency. With hypotonic disease, the differential diagnosis is simple and is performed using laboratory tests. Anorexia and gastrointestinal disorders occur in diseases of the digestive system, pregnancy, nephritis, neurasthenia. Weight loss is always observed in chronic adrenal insufficiency, so in the differential diagnosis should also be borne in mind diseases accompanied by weight loss: chronic infections (tuberculosis), malabsorption syndrome, malignant neoplasms, leukemia. The level of glucocorticoids in the blood in these cases is normal or slightly reduced, but in response to ACTH stimulation, the response is not changed.

Treatment

In hypocorticism, the diet should be high-calorie, contain a sufficient amount of proteins, an increased amount of salt (8-10 g per day) and vitamins, especially ascorbic acid.

I. Elimination of causal factors that caused adinaly lesions. In tuberculosis etiology, tuberculosis treatment is carried out, with autoimmune lesions, treatment involves differentiated use of immunomodulators, taking into account the deficiency of T-supresors (thymosin, levomizole, etc.).

II. Hormone replacement therapy. Patients with primary chronic adestina insufficiency need constant intake of corticosteroids. In most patients, for complete compensation, it is enough to administer only glucocorticoids; in some cases, additional use and mineralcorticoids are required. Hydrocortisone (cortisol) is a drug of choice and is prescribed 30 mg per day (20 mg in the morning and 10 mg in the evening). Cortisone is usually used at a rate of 40-50 mg (25 mg in the morning and 12- 15 mg in the evening). Other synthetic glucocorticoids (prednisolone, dexamethasone, triamcinolone, etc.) are less desirable because they do not exhibit a mineralcorticoid effect.

With a mild degree of chronic adrenal insufficiency, cortisone is used at a rate of 12.5-25 mg per day in combination with ascorbic acid of 1.0-1.5 g per day during meals. In case of medium-severe and severe forms of chronic adrenal insufficiency, mineralocorticoids are prescribed in addition to glucocorticoids, the average daily need for deoxycorticosterone aceticate is 1 mg. DOXA (deoxycorticosterone acetate) in tablets of 5 mg is used sublingually, intramuscularly prescribed 0.5% oil solution of 1 ml; trimethyl-acetate deoxycorticosterone, a prolonged drug, is prescribed 1 ml of 2.5% solution intramuscularly 1 time in 2-3 weeks; fluorhydrocortisone (cortinef, florineph) is used 0.05-0.1 mg once a day during the subcompensation period and 2-3 times a day during the period of decompensation of the disease. Objective criteria for the effective action of glucocorticoids are: weight gain, disappearance or reduction of dyspepsic syndrome, reduction of pigmentation of the skin and mucous membranes, improvement or restoration of glucose tolerance. Laboratory indicators of the effective action of mineralcorticoids is an increase in sodium content and a decrease in potassium in blood plasma.

After removing one adrenal gland about Itsenko-Cushing's disease, hormonal drugs are not prescribed, after the removal of the second adrenal gland (stage 2) on the first day, 75-100 mg of water-solute hydrocortisone is used intravenously and simultaneously intramuscularly according to the scheme: 1-2 days - 50-75 mg every 3 hours, From the day - 50 mg every 4-5 hours, 4-5 days - 50 mg every 5 hours, 6-7th day - 50 mg after 8 hours, 9-10th day - 50 mg 2 times a day. From the 8th-9th day they switch to oral administration of corticosteroids, prednisolone is prescribed at 5-10 mg per

day, or 5 mg in the morning in combination with 1 DOXA tablet, or 1 cortineph tablet and 25 mg of cortisone in the afternoon.

|Change in the function of the adrenal glands during pregnancy.

During pregnancy, there is an increase in the functional activity of the adrenal cortical layer, which is associated with the secretion of the placenta ACTH and cortisone-like substances, a change in the metabolism of cortisol in the liver, an increase in the level of transcortine in the blood and hyperestrogenia. The placenta is permeable to corticosteroids of both maternal and fetal origin.

Conditions of positive prognosis of pregnancy: After adrenalectomy, pregnancy is recommended a year later in case of compensation for adrenal insufficiency and with constant intake of small doses of adrenal cortex drugs. Prolongation of pregnancy is allowed in the absence of exacerbation and the presence of the effectiveness of appropriate therapy. Pregnant women who have previously suffered an adrenalinectomy are subject to medical observation of the endocrinologist and obstetrician During pregnancy, accompanied by hypocorticism, a number of complications are found. Thus, the possible development of an acute crisis is accompanied by adrenal insufficiency. At the same time, there are three periods that are dangerous in relation to the development of the crisis: early gestation; childbirth; postpartum period. The development of gestosis from the early stages of pregnancy is characteristic, which leads toa violation of the electrolyte balance, fluid loss, hypoglycemic and hypochloric condition. From 28-30 weeks of pregnancy comes a clinical improvement in the condition of the pregnant woman due to fetal, placental and suprarenal secretion of cortisone and aldosterone. However, these shifts do not give the right to stop hormonal treatment. The THIRD trimester of pregnancy, especially the last 4-5 weeks, is more difficult to tolerate. Possible development and strengthening ofgestosis associatedwiththe use of steroid hormones. Sometimes there is a favorable course of pregnancy due to compensatory "help" of fetal hormones and placenta, and pregnant women do not need treatment. The danger of developing a crisis exists in the 1st day of the postpartum period, which is associated with a sharp drop in corticosteroid products due to the birth of the fetus, the absence of placenta and the inevitable blood loss in childbirth. In the process of keeping pregnant women with Hypocorticism and anumber of conditions should be observed. It is necessary to monitor the body weight, blood electrolyte content, blood pressure, cardiovascular system, blood glucose levels.

pregnant to the hospital in the first trimester, at 28 weeks and 3 weeks before giving birth. With increasing phenomena of adrenal insufficiency, which is not therapyable, early birth is shown. In case of abortion the day before for 2 days, prednisolone or 125 mg of hydrocortisone is prescribed with a repeat of it immediately after an abortion. During pregnancy, systematic treatment with glucocorticosteroids continues. In the first half of pregnancy, prednisolone is prescribed at 10-15 mg / day or dexamethasone 1-2 mg / day and Dox 5 mg intramuscularly after 2 days. In the second half of pregnancy, the dose of prednisolone is reduced to 5 mg / day or dexamethasone up to 0.5 mg / day and connected to DOXA to improve electrolyte metabolism (delays sodium ions in the body and increases potassium secretion). The dose of hormonal drugs is selected under the control of level 17-COP. Additionally, they recommend good nutrition, table salt up to 10 g, ascorbic acid 1 g per day, limit the intake of potassium salts. In childbirth and in the 1st day of the postpartum period, acute adrebral failure may occur with Hypocorticism. In patients whoreceived prednisolone,in the postpartumperiod,dehydration may develop due toincreased diurisis and the absence of thefetus and placentain the maternal body as ahormonally activecomplex. Often in childbirth there is a weakness of the declining activity of the uterus. In patients whoreceived prednisolone,in the postpartumperiod,dehydration may develop due toincreased diurisis and the absence of thefetus and placentain the maternal body as ahormonally activecomplex. Often in childbirth there is a weakness of the declining activity of the uterus. In childbirth, be sure to carry out adequate phased anesthesiation. By timely elimination of the weakness of childbirth, protracted childbirth is warned. In the first period of childbirth, 500 ml of glucose solution, 0.9% sodium chloride solution, 1 ml of 0.06% corglucon, 10 ml of 5% ascorbic acid solution are administered intravenously. Hydrocortisone is also injected 50 mg intramuscularly, then 5 mg of DOXA. This treatment is repeated every 3-4 hours. When blood pressure drops, repeat the introduction of DOXA. Mandatory is the prevention of bleeding in the third period of childbirth and the early postpartum period. Blood loss should be minimal and fully reimbursed. In the postpartum period, the interval of administration of hydrocortisone and DOXA increases simultaneously with the subsequent transition to its ingestion. On the 3rd-4th day after childbirth, hydrocortisone is prescribed 50 mg after 8 hours and DOXA 5 mg once a day. On the 5th day, hydrocortisone is prescribed 50 mg 2 times a day and prednisolone 10-15 mg. On the 7-8th day - hydrocortisone 50 mg in the morning and prednisolone - 10-15 mg. In the future, patients

are transferred to fixed doses that were used earlier. When overdose of steroid hormones, hypertension, edema, dyspeptic phenomena occur. Treatment with steroid hormones is carried out under the control of blood pressure and depending on the level of 17-COP, 17-OX. If it is necessary to perform the planned abdominal degeneration a day before the operation, hydrocortisone is prescribed 50 mg intramuscularly 3 times during the day. On the day of the operation - 75 mg of hydrocortisone intramuscularly, during the operation intravenously drip 75 - 100 mg of hydrocortisone in a saline solution of sodium chloride. It is mandatory to adequately fill the blood loss. With this pathology, healthy newborns are born with a frequency of 1:500. Fetal hypotrophy often, congenital anomalies up to 2% are possible. Stillbirth is on average noted in 3 cases per 100 genera.

Guypercorticism and pregnancy

Hyperfunction of the adrenal cortex is associated with the increased formation ofcorticoliberanu, an increase in acth secretion followed by stimulation of the function of theadrenal glands. The pathology of the adrenal cortex with the manifestation of primary hypercorticism includes a tumor of the adrenal cortex - corticosterome (Itsenko-Cushing syndrome) or tumors of other organs that produce ACTH-like substances.

Secondarypercorticism of functional genesisdevelops as a result of disorders in thehypothalamo-pituitary-adrenal system or as a result of corticotropic effects of pituitary adenome (Itsenko-Cushing's disease).

Primary hypercorticism. In primary hypercorticism, the manifestations of the disease are due to a tumor of the adrenal cortex - corticosterome, which occurs in 25-30% of observations. With this tumor there is an excess release of glucocorticosteroids, partly androgens or estrogens and mineralcorticosteroids.

With Itsenko-Cushing syndrome, the adinaly slightly increase. Atrophic changes in the organs of the reproductive system are noted. There are disorders of menstrual and reproductive function (amenorrhea, infertility). In this regard, pregnancy occurs only in the initial stages of the disease or after hormonal therapy of the underlying disease. The general symptoms of Itsenko-Cushing syndrome are characterized byhip of the adrenal gland-yizic disorders with a pronounced manifestation of hirsutism and endocrine-metabolic disorders. With corticosterome there is a violation of all types of metabolism. These patients have general weakness; depression; dry skin with a tendency to hyperkeratosis; pigment spots; hypertricosis; striae atrophicae on the abdomen, buttocks, less often - on the shoulders and thighs; hyperpigmentation; "moon-shaped"; deposits of fat on

the abdomen and torsoand; osteoporosis; curvature of the spine; spontaneous bone fractures; fluid retention; neurological disorders; cardiovascular disorders; arterial hypertension (due to hyperkalemia); meager menstruation or amenorrhea (due to changes in the hypothalama-pituitary mechanisms of regulation of menstrual function under the influence of an excessive amount of androgen corticosterome produced and cortisol); lactore up to 22% (due to a significant number of prolactin receptors in the adrenal filament); infertility; hypertrophy of the clitoris; hypoplasia of the uterus and ovaries; atrophy of the mammary glands; insulin-reticulated steroid diabetes mellitus or hyperglycemia; polyglobulinemia; hypercholesterolemia; increase in blood plasma ACTH; 2 - a 3x increase in blood plasma level of general and free cortisol (unlike Itsenko-Cushing's disease); absence of daily fluctuations in cortisol levels in blood plasma when sampling with hydrocortisone; in urine increased the amount of 11-oxyketosteroids. For diagnosis and differential diagnosis, determination of hormone secretion levels is used; hormonal samples (dexamethasone); ultrasound; CT adrenal glands (radiation load with this research method is at the upper limit of the dose available during pregnancy); determination of the content of glucocorticoid drugs in blood lymphocytes; crystallographic study of blood serum using MRI. Pregnancy in patients with corticosterome occurs relatively rarely (in 4-8% of cases). Corticosteromes in pregnant women in 18-30% of observations are malignant. Difficultyin pregnancy with primary hypercorticism is most often associated with a deterioration in the course of the underlying disease, a violation of the fetal condition, accompanied by a significant increase in the level of 17-COP, 17-OKS, somewhiteness of pregnandiol, ola pregnantry, a decrease in the number of estrogens (especially estriol). Pregnancy is often complicated by involuntary abortion, stillbirth. Often there is an early development of severe forms of gestosis. Due to the decrease in estriol and the development of gestosis, intrauterine asphyxia occurs and fetal development delay. Regardless of the gestation period with corticosterome, the removal of the tumor and abortion are shown. It is recommended to terminate the pregnancy within a period of up to 12 weeks with the use of enhanced steroid therapy. In case of preservation of pregnancy in the II trimester, metapyrone treatment is carried out up to childbirth (500 mg every 6 hours). In the III trimester, urgent rebirth is recommended after preparatory symptomatic therapy. The question of pregnancy tactics in women who have suffered previously total adrenalectomy is the appointment of corticosteroid therapy, since after adrenaline therapy until the end of pregnancy and especially in childbirth

there is a real threat of acute adrenal insufficiency. During pregnancy, thorough monitoring of the state of the fetoplacentar system is carried out. Timely prevention, diagnosis of gelrose and FPN should be carried out. Early birth is carried out according to indications.

Childbirth should be waited. In childbirth, intensive glucocorticosteroid therapy is indicated. Adequate anesthesia and prevention of bleeding should be carried out. Indications for a caesarean section are strictly obstetric. Childbirth after bilateral adrenalectomy against the background of adequate substitution therapy proceeds in the same way as in healthy women. However, it should be remembered that in these women in childbirth there is a threat of the development of acute adrenal insufficiency. In this regard, in childbirth should increase the dose of corticosteroids and use parenteral administration.

In the postpartum period, corticosteroid therapy is prescribed from 1 days under the control of the level of excretion 17 - COP. The lactation period can worsen the course of the underlying disease. Children of mothers sufferingfrom hypotrophy are born with signs of hypotrophy, with diabetics traits associated with carbohydrate metabolism in themother. However, on the other hand, as the results of clinical observations show, the vast majority of babies born to mothers who suffer from corticosterome but have been in persistent clinical remission and adrenal insufficiency compensation are practically healthy, without pronounced changes in the endocrine system. Secondaryhypercorticism (Itsenko-Cushing's disease). Due to the defeat of subcortical and stem formations (limbic zone, hypothalamus) with the subsequent involvement of the pituitary gland with the development of adenoma, the formation of secondary hyperplasia of the adrenal cortical substance and hypercorticism. The pituitary adenome is characterized by increased excretion of its anterior fate ACTH, impaired function of the hypothalamo-pituitary-adrenal system with excessive secretion of all steroids by the adrenal glands, especially 11-OX. The amount of 17-OX increased by 2-3 times, and 17-COP slightly (as opposed to adrogenic syndrome, corticosterome, etc.) Clinical manifestations of Itsenko-Cushing's disease are identical to Itsenko-Cushing syndrome of various origins with severe metabolic disorders, changes in the hypothalamic-pituitary-ovary system, etc. All these clinical signs are a significant risk factor for fetal and newborn developmental disorders. According to X-rayraniography, only a few years after the onset of the disease, the Turkish saddle becomes sparse and slightly enlarged, since corticotropic adenomes are small in size. Often there is a spilled or focal threshold of bones adjacent to the Turkish saddle.

In this situation, an MRI can be shown. Based on the dynamics of changes in the condition of the Turkish saddle, when diagnosing this disease, it is necessary to pay attention to the history, general status and data of laboratory research of hormones. To establish the diagnosis and differential diagnosis, hormonal samples with dexamethasone, metapyrone are used. With dexamethasone probing, there is a decrease in daily excretion of 17-OX by 15% or more due to inhibition of dexamethasone production by the pituitary gynae AKG with a further decrease in 17-OX excretion. When conducting a sample with metappirone (500 mg every 4-6 hours during the day), the excretion of 17-OX increases. Metapiron inhibits the production of 11-Hydroxylyase - an enzyme that ultimately synthesizes cortisol, which causes a decrease in its secretion and leads to increased secretion of AKG (according to the feedback system), whileincreasing the level of 17-OX. Corticotropic adenum pituitary gland from adrenal corticosterome and adrenal hyperplasia can be differentiated and X-rayed. In corticotropic adenome of the pituitary gland, the adrenal glands are hyperplasia and their shadow on X-rays is more intense than with adrenal tumors (corticosterome). In the event of pregnancy at the active stage of secondary hypercorticism, it must be interrupted in the early stages. A favorable prognosis of pregnancy and the result of childbirth in Itsenko-Cushing's disease is possible only with complete remission of the disease, with normalization of blood pressure, carbohydrate metabolism and adequate substitution therapy. The question of the possibility of prolongation of pregnancy is solved with a joint consultation of an endocrinologist, radiation diagnostics specialist and obstetrician-gynecologist. Pregnancy in these patients is a high risk factor for the life of the mother and child. Regardless of the nature of treatment (medical, radiation, surgical) the normal course of pregnancy in Itsenko-Cushing's disease is observed only in 30% of cases. Typical complications of pregnancy with this pathology are the threat of abortion in the early stages; premature birth; early onset of gestosis; arterial hypertension.

In the process of keeping pregnant women, careful monitoring of the general condition of the patient is required; blood pressure levels; body weight; dioresis; the presence of edema; hormone level indicators; blood glucose content. In each trimester of pregnancy, a joint consultation with an endocrinologist is necessary to resolve the issue of the possibility of prolongation of pregnancy and hormonal correction. It is recommended a diet with a restriction of salt, carbohydrates, with the appointment of vitamins, diphenine (a drug that reduces the function of the adrenal cortex,

at a dose of 1 tablet 3 times a day for 3 weeks). Typical complications in childbirth and in the postpartum period with secondaryhypercorticism are weakness of genera; prematurely gone amnio-like waters; aggravation of gestosis with high arterial hypertension; fetal intrauterinal asphyxia; acute adestine insufficiency in the early postpartum period due to the shutdown of placental corticosteroids; complications from the cardiovascular system or hemorrhage in the brain; bleeding in the consistent and early postpartum period; relapse of the underlying disease after childbirth. In the process of childbirth with an increase in blood pressure, controlled hypotensive therapy (arphonade or hygrony) is carried out; carry out adequate phased anesthesiation; assess the condition of the fetus in dynamics; carry out the prevention of anomalies of genera and bleeding. In the presence of an active phase of the disease in the patient, children are born cushioningoid type due to intrauterine insufficiency of synthesis of steroid hormones. Possible development of diabetes mellitus. In addition, hypotrophy in newborns may occur. In the presence of a newborn of low body weight, low blood pressure and increased excretion with urine of 17-COP and 17-OX, glucocorticosteroids are required. In the future, these children should be on dispensary accounting with an endocrinologist and a neurologist.

Adrenal cortex dysfunction (adrogenic syndrome) and pregnancy

Adrhenogenic syndrome (AGS) is a hereditary congenital disease characterized by inferiority of enzyme systems involved in the synthesis of steroid hormones of the adrenal cortical substance, which leads to a decrease in cortisol production. This causes (according to the feedback mechanism) an increase in the secretion of the pituitary gland acth, the development of adrenal cortex hyperplasia and activation of the synthesis of androgens with subsequent impaired sexual development and reproductive function. The frequency of AGD varies from 1 to 5000-10 000 newborns. Excessive production of androgens is the main reason for the development of verilyzation of the female body, the manifestation of which depends on the severity of the secretion of androgens and the time of the beginning of the implementation of this disease.

Adrhenogenic syndrome by clinical signs is divided into three forms:

congenital, prepubertate and postpuberta.

In the latter form, the violation of steroid synthesis can be asymptomatic for a long time and be compensated by adrenal hyperplasia.

Clinical signs of the disease are not detected until any stressor factor provokes the implementation of a latent form of violation of the function of the adrenal cortical substance. The first symptoms of hyperproduction of androgens in post-puberty form occur after the completion of the processes of oxenation and the formation of primary and secondary sexual characteristics. The following clinical signs are characteristic of the post-puberty form of AGS: well-defined female phenotype; hirsutism (excess growth of facial hair, around the nipples, on the limbs); normal on the structure of the genital organs and mammary glands; menstrual function disorders (anovulation, hypolygomenorrhea, amenorrhea); infertility; general weakness; headaches and muscle pain; reduced efficiency; arterial hypotension. Diagnosis of typical cases of AGS is not particularly difficult. An important diagnostic value is to determine the level of excretion of androgen metabolite, 17-COP and intermediate products for the synthesis of glucocorticosteroids - progesterone and 17-oxyprogesterone. With AHS, the excretion of 17-OX is at a low level (due to a deficiency of glucocorticosteroids), and neutral 17-COP increases by 5-10 times compared to the age norm. Similarly, the level of pregnandiol in urine changes. In the blood significantly increases the concentration of testosterone, 17-hydroxy-progesterone and DHEA. Differential diagnosis should be carried out with virilisurizing tumors of the adlands, Itsenko-Cushing's disease, sclera-cystic ovaries. The differential-diagnostic value acquires a dexamethasone trial. The drug has a inhibiting effect on the secretion of ACTH, which leads to a decrease in the excretion of not only the total 17-COP, but also androsterone, DHEA and pregnandiol.

A samba with AKG is characterized by an increase of 17-COP by 3 times with a slight increase of 17 COP. The onset of pregnancy in erased forms of AGA in women is not such a rare fact, and evidence of this is the large share of adrenal hyperandrogenia in the structure of the causes of the usual pregnancy innocence. Often in the postpubertal form of AGS, despite the fact that ovulation occurs and fertilization of the egg occurs, the pregnancy is interrupted in the early stages until the formation of the placenta for the inferiority of the yellow body. Excessive amounts of androgens cause circulatory disorders in the uterus, blood stasis, sclerotic change of blood vessels of myometry and chorion, which leads to an increase in the fragility of blood vessels, their ruptures. As a result, hemorrhagics occur in the decidual membrane with the formation of a retroplacentar hematoma and partial detachment of the chorion. The frequency of pregnancy innocence at AGS reaches 26%. An important

problem is the effect of high levels of androgens in the mother on the development of the embryo and fetus during pregnancy. It is known that androgens freely penetrate the placental barrier and affect the formation of external genital organs in the fetus of the female sex. The effect of increased levels of mother's androgens on the fetus manifests itself differently depending on the stage of intrauterinous fetal development. With the action of an increased concentration of androgens in the period between the 8th and 12th weeks, the external genitalia of the fetus of the female are formed according to the male type (female pseudogermaphroditism), with the action between the 13th and 20th weeks sinus urogenitales develop, and with the action after the 20th week there is an increase in the clitoris degree of different. In addition, androgens can affect the formation and proper functioning of neuroendocrine mechanisms of regulation and the so-called sexual differentiation of the fetal brain. During pregnancy, it is necessary to continue the use of corticosteroid therapy started before pregnancy, since when these drugs are canceled, abortions and the negative effects of hyperandrogenia on the fetus are possible. Treatment is carried out under the control of level 17-COP. Dexamethasone is usually used from glucocorticosteroids. At an elevated level, 17-COP prescribe a hormone at a dose of 0.5 mg or 0.375 mg to normalize 17-COP excretion with a gradual decrease in dose to 0.125 mg. This treatment must be combined with the prescription of potassium preparations. In terms of 16, 20 and 28 minutes, careful control over the level of 17-COP is required, since during these periods the production of hormones of the adrenal fetus increases. Due to the widespread use of corticosteroids during pregnancy, the frequency of gestosis increases, accompanied by fetoplacentar insufficiency and often delayed fetal development. Prevention of abortion is carried out by generally accepted methods. In a timely manner, prevention, diagnosis and therapy of gestosis and FPN are carried out, control the state of the fetoplacentar system. Children born to mothers with AGD require careful observation and examination of the function of the cortical substance of the adrenal glands.

Primary aldosteronism and pregnancy

D. Conn in 1955 described primary aldosteronism as a result of the development of benign adestine adenome. This tumor is more common in women and manifests itself clinically during pregnancy. With this tumor, the release of aldosterone increases by 40-400 times (normally 5.5 - 28 nmol / day). There are significant disorders of the metabolism of electrolyte: hypernatremia, hypokalemia with an increase in potassium secretion with

urine. Primary aldosteronism can occur both as an independent endocrine disease, and as a manifestation or consequences of heart failure, liver cirrhosis, nephrosis, potassium insufficiency.

This disease against the background of enhanced production of aldosterone is accompanied by hypertension, is characterized by a severe course and requires timely treatment. Clinical signs of primary alde sideism are muscle weakness due to hypokalemia; paralysis, paresthesia, convulsions, tetany. There are violations of the urinary system in the form of polyuria, polydisia, nikturia, moderate proteinuria, alkaline urine reaction. There are symptoms associated with aterial hypertension: headaches, changes in the full-time, persistent diastolic hypertension. For the diagnosis of this pathology use ultrasound; CT; MRI. As part of laboratory tests, the content of potassium and sodium is evaluated to detect hypokalemia and hypernatremia; study the content of aldosterone, determine the presence of protein in the urine. In primary aldosteronism, pregnancy is contraindicated and in case of its onset should be interrupted with the subsequent removal of the tumor and the treatment of diseases that led to its development.

Feochromocytoma and pregnancy

Theochromocytomaa is a catecholamine-promoting tumor originating from the brain matter of the adrenal glands or chromafin tissue from the paraganglia of the cervical, the bottomof thecavalry, portal,lower pi etc. and other plexus of the sympathy of the thymph nervous system. equally common in women and men. Its size is from 1 to 15 cm, weight from 1 to 75-100 g, usually one-sided, placed in a capsule and hasa rounded shape, more often the right adestum is affected. Described family diseases, established autosoman-dominant transmission pathway. The symptoms of the tumor are due to the influence of an excessive number of cathol-ninas. There are paroxysmal taicardia and sudden attacks of hypertension up to 300/190 mmHg. c., related to the periodic release of noradrenaline and adrenaline. Hypertension crises are accompanied by attacks of heart asthma, hyperglycemia and glucose, leukocytosis, fever, the appearance of pain in the extremities, paresthesia. During the crisis, sharp pallor of the face, limbs, cooling of brushes and feet, convulsions, shortness of breath, anxiety, vomiting, headaches are noted. The crisis can last up to 2-3 hours. When noradrenaline is ejected, crises last for hours and even around the clock. Hypertensive crises can be repeated 1 to 2 times a day or once a month and are accompanied by a series of vegetative symptoms in the form of headaches; nausea; vomiting; taicardia; sweating; weaknesses; pain in the

heart, abdomen, muscles of the limbs; body tremors; court; hyperthermia up to 40 ° C (due to the delay in heat transfer due to vascular spasm). In some cases, the disease can occur without crises, but with high blood pressure. Renal failure occurs with malignanthypertension syndrome. Angiopathy is noted on the side of the fundus. According to the ECG, signs of non-short-pathogenic necrose are detected. In severe crises, hemorrhage in the brain, mental disorders, the development of uncontrollable hemodynamics are possible, in which hypertension is replaced by hypotension. All these phenomena are explained by intoxication by cathécholys. With pheochromocytoma, the development of multiple tumors in the adrenal glands, thyroid gland, parathyroid glands is possible. In these cases, multicentric tumors (bilateral feochromocytoma and parathyroid tumor) develop. Most often, such a process occurs in family diseases. Metastasis of the feochromocytoma occurs in the regional lymph nodes, liver, lungs, bones. For the diagnosis of the pheochromocytoma, examination radiography of the abdominal cavity, ultrasound, CT, MRI is used. Determine the excretion of cathécholyamines and their metabolite - vanillinidal acid - in the daily urine after the crisis. Conduct a test with trophafen, which is aimed at blockade of vasopressor action of cathécholyamines. To do this, intravenously inject 1 ml of 2% trophafen solution. After 1 min, systolic blood pressure decreases by 40-30 mmHg. c., and diastolic - 20-25 mmD. Century. They also perform a fentolyamine test. Fentolytholin (5 mg) is administered intravenously or intramuscularly. The test is considered positive if after 2 minutes systolic blood pressure decreases by 30-35 mmHg. p., and diastolic - 20 - 25 mmD. Century. Theochromocytoma can be combined with diabetes due to the intense breakdown of glycogen in the liver and the depressing action of adrenaline on langerganza island; thyroid hyperfuncture; hyperfuncture of the adrenal cortex. Pregnancy with feochromocytoma is rare and is contraindicational. Perinatal mortality in this pathology is 40-50%, and mortality of newborns - more than 75%. Maternal mortality reaches 11%. Such adverse results are due to the fact that during pregnancy with feochromocytoma there is a persistent hypertension with paroxysmic crises. Hypertension crises often change shock-like condition, often fatal. Hemorrhagics occur in the brain, in the tissue of the adrenal glands or in the tumor itself. Cardiovascular system ("categorychoamine myocarditis")with dystrophy and myophybril nephrosis may be injured. In addition, there is often premature detachment of the placenta. In pregnant women, cathocolamine crises can develop after a change in body position, during contractions in childbirth, during obstetric

examinations, with fetal movements. Sudden death or shock in pregnant women is possible with the appearance of the first contractions. High perinatal mortality is explained by a decrease in the intensity of IPC due to injuries. the content of cathécholyamines and premature detachment of the placenta. Differential diagnosis during pregnancy is carried out with gestosis, diabetes mellitus, hypertension, thyrotoxicosis. Due to the threat to the life and health of the patient with this disease, it is advisable to convince the pregnant woman and her family of the need to interrupt the pregnancy. In any period of pregnancy, immediate removal of the tumor is shown. Abortion is carried out after the preliminary removal of the tumor.

In the case of prolongation of pregnancy in the II and III trimestics, three options for surgical treatment tactics are possible:

1) cesarean section with simultaneous removal of the tumor;

2) cesarean section with subsequent removal of the tumor;

3) childbirth through the natural birth canal, followed by the removal of the tumor.

Preference is given to the first option. Degeneration through the natural birth canal is dangerous due to the fact that with the contraction of the uterus there is a mechanical squeezing of the tumor with an increase in the release of cathécholyamines with all the negative consequences. In childbirth through natural birth canals, it is recommended to prescrib drugs that stop crises:

- phenoxybenzamin (daily dose from 20 to 200 mg)
- the effect occurs 2 hours after administration and lasts several days;
- phentolamin (pentamile) -α-Short-action adrenoblokator;
- sodium nitroprusid - 0.3-0.4 mg per 1 kg of body weight;
- cardioselective blockers;
- heart products;
- corticosteroids.

Tasks 1 How to prepare a patient with manifestations of adestine insufficiency for cesarean section?

A week before the planned operation to increase the dose of glucocorticoids;

B-enhance therapy by adding mineralcorticoids;

C-before starting the operation, introduce a large dose of glucocorticoids.

D - no need to ice hormones.

E-additionally prescribe saline solutions

Task 2 In which trimester of pregnancy do patients with adrenal insufficiency need to increase the doses of glucocorticoids?

A-in the first;
B-th second;
C-th third.
D – do not adjust at all
E – adjust only during childbirth

Task 3: How does therapy change in pregnant women with adestron insufficiency in the presence of early pregnancy toxicosis?

A-remains unchanged;
B-reduced doses of glucocorticoids;
C-therapy is carried out exclusively with mineralcorticoids;
D-increases the dose of glucocorticoids.
E-only to salt food

Task 4 A pregnant woman is 26 years old, on the 18th term of gestion. Complaints: severe weakness, poor appetite, nausea.

A. Chronic gastritis.
V. Itsenko-Cushing's disease.
C. Diabetes mellitus.
D. Toxicosis pregnant
E. Adrenal insufficiency. =

Sick M., pregnant at the 39th week of pregnancy,complains of weakness in themuscles, periodic seizures, seizures of sharp general weakness, polyuria, nicturium increase AT. Sick 8 months. Tones of the heart muffled, accent II tone over the aorta, AT - 170/100 mmHg. p., there is no edema in the blood: potassium - 3.0 mmol/l, glucose - 5.3 mmol/l.

A. Primary hyperaldosteronism
A. Hypertension
S. Late Gestosis
D.Itzenka-Cushing's disease
E. Feochromocytoma

Topic 5. Curation of a patient with hyperglycemic (ketoacidemic), hypoglycemic coma, thyrotoxic crisis, acute adhesive insufficiency.

1. **Relevance:** Knowledge of the peculiarities of the course and treatment of emergency conditions in conditions of diabetes mellitus is mandatory for doctors of all specialties. At the heart of the occurrence and development of acute complications of diabetes mellitus are acute disorders of vital functions of the body: homeostasis of breathing, circulation, etc. Therefore, the study of coma conditions in diabetes mellitus is extremely relevant in the preparation of the future doctor. Treatment of diabetes mellitus with insulin and oral sugar-reducing drugs is often accompanied by the occurrence of hypoglycemia in. Doctors should clearly know the signs of hypoglycemia and promptly provide assistance in case of hypoglycemic conditions of various origins. The problem of timely diagnosis and emergency care in hypoglycemic conditions is relevant due to the fact that the latter in the absence of treatment lead to high mortality; the occurrence of posthypoglycemic encephalopathy and disability.

Thyrotoxic crisis is a severe, life-threatening condition that is a complication of thyrotoxicosis, which most often develops in diffuse toxic goiter (Graves' disease). Most often, thyrotoxic crises occur after surgery to remove diffuse goiter, as well as when using an overdose of radioactive iodine during treatment of thyrotoxicosis.

Waterhouse Friedrichsen syndrome is an urgent clinical syndrome caused by acute dysfunction of the adrenal cortex due to hemorrhage (hemorrhagic infarction) in the adrenal cortex.

2. Educational goal.

Get acquainted with epidemiological studies in Ukraine and in the world (α=1)

The student should know (α=2):

• The main clinical signs of ketoacidosis and ketoacidotic coma.
• Pathogenesis of the main symptoms of ketoacidosis and ketoacidotic coma.
• Modern methods of diagnosis and differential diagnosis of ketoacidosis

and ketoacidotic coma.
• Classification of emergencies
• Causes and pathogenesis of hypoglycemic state and coma
• Clinical manifestations of hypoglycemia and hypoglycemic coma
• Tactics and methods of treatment of hypoglycemia and hypoglycemic coma in diabetes
• Definition, etiology and pathogenesis of thyrotoxic crisis.
• The main causes of thyrotoxic crisis. The role of surgical interventions on the thyroid gland, sudden cessation of thyrostatic therapy, stress factors, radioactive iodine therapy, some drugs in the development of thyrotoxic crisis.
• Staged thyrotoxic crisis (in typical cases).
• Tactics of management (examination, treatment) of patients with thyrotoxic crisis.
• Criteria for compensation of thyrotoxic crisis.
• Recommendations for choosing a modern method of treatment of thyrotoxic crisis
• Tactics of management of the patient at various clinical options of a course of pathologies of adrenal glands.
• Emergency care for acute adrenal insufficiency (Waterhausen-Friedrichsen syndrome).

The student must be able to (α=3):

• Have a method of diagnosis and analysis of data obtained during the survey and direct examination of patients with hypoglycemic conditions
• Assign the necessary examinations to detect hypoglycemic conditions and hypoglycemic coma;
• Carry out diagnostics and differential diagnosis of hypoglycemic conditions and hypoglycemic coma;
• To determine the tactics of treatment and prevention of hypoglycemia, hypoglycemic coma in conditions of diabetes mellitus;

3. Educational goal.

Pay attention and form a sense of responsibility in students who will be doctors of different specialties, the timeliness of detection and proper treatment of emergencies.

4. **Interdisciplinary integration:**

Disciplines	*Know*	*Be able*
Disciplines studied earlier		
Normal anatomy	Anatomical structure of the thyroid gland, adrenal glands	
Normal physiology	Synthesis, transport, effects, regulation of thyroid hormone secretion	
Histology	Know the histological structure of the hypothalamic-pituitary system, cortex and cerebral layer of the adrenal glands	
Pathological anatomy	Classification and nature of pathomorphological changes;	
Pathological physiology	Etiology and pathogenesis of iodine deficiency diseases, hypothyroidism, thyroid tumors;	
Pharmacology	Preparations of iodine, thyroid hormones, anti-inflammatory drugs;	Write the appropriate recipes;
Radiation diagnostics	Ultrasonography, scintigraphy, X-ray diagnosis of thyroid diseases.	Evaluate the results of relevant research.
Disciplines to be studied later		
Internal diseases	Changes of internal organs at diseases of a thyroid gland, their	Carry out a clinical examination of

Pediatrics Surgery Obstetrics and gynecology Neurology, psychiatry	differential diagnosis, the main methods of treatment; Features of the course of thyroid pathology in childhood; Surgical methods of treatment of thyroid pathology; Features of the course of thyroid disease during pregnancy, their impact on fetal development; Psychoneurological manifestations of thyroid pathology.	the patient, palpation of the thyroid gland, appoint the necessary diagnostic examinations and consultations of related specialists to verify the diagnosis, interpret their results (conclusions).
Intra-subject integration.	Modern methods of clinical, laboratory and instrumental examination of endocrine patients.	Carry out differential diagnosis of thyroid diseases with other pathology, prescribe adequate treatment.

5. Content of the lesson topic:

Etiopathogenesis of hyperketonemic coma.

Clinic, diagnosis, treatment of hyperketonemic coma.

Etiopathogenesis of hypoglycemic coma.

Clinic, diagnosis, treatment of hypoglycemic coma.

Differential diagnosis of various emergencies in diabetes.

Etiological factors, pathogenesis, clinic, diagnosis and intensive care of thyrotoxic crisis.

Acute adrenal insufficiency: pathogenesis, clinic, diagnosis and treatment.

6. Lesson plan and organizational structure

(see "Prerunciation")

7. Materials of methodological support.

7.1. Materials of the preparatory stage

1. Patient K. has been suffering from diabetes for 8 years. He is currently in a coma. The skin is dry, Kussmaul's breath, the smell of acetone from a mouth is noted. Name someone.
A. Ketoacidosis coma
B. Hypoglycemic coma
C. Lactic acid coma
D. Hyperosmolar coma
E. Cerebral coma
2. The characteristic signs of hyperthyroidism include the following, except:
A. Weight gain
B. Hot skin
C. Emotional imbalance
D. Tachycardia
E. Exophthalmos
3. The main clinical signs of acute adrenal insufficiency are:
A. Odor of acetone from the mouth, aggression, increased blood pressure
B. Loud breathing, bradycardia, general weakness
C. Vomiting, diarrhea, general weakness
D. Polydipsia, polyuria, decreased urine specific gravity
E. Kussmaul respiration, acetonuria, decreased blood pressure

7.2. Materials of methodical providing of the basic stage of employment:

Differential diagnostics of comas

Clinical and laboratory signs	Hyperglycemic (ketoacidotic)	Hypoglycemic coma
Age	different	different

Anamnesis	first detected diabetes, eating disorders, insulin therapy, infection, stress	excessive intake of insulin, oral hypoglycemic drugs, excessive physical work, hunger
Predecessors	weakness, nausea, thirst, vomiting, dry mouth, polyuria	hunger, sweating, trembling
Development of coma	gradual (2-3 days), on the background of concomitant pathology - 1 day fast (minutes). Features of precomatose state gradual loss of consciousness	fast (minutes) excitement that turns into a coma
Temperature	normal, subfebrile	normal
Skin	dry, redness, low turgor	moisture, turgor is normal
Muscles, reflexes	the tone is reduced	the tone is increased
Tongue	dry	wet
Eyeballs	soft, the tone is reduced	the tone is normal
Pupils	narrowed	extended
Breath	Kussmaul, smell of acetone	normal
BP	reduced	norm
Pulse	frequent	frequent
Signs of dehydration	expressed	missing
Diuresis	polyuria, then oliguria	norm
Glycemia	high	low
Glucosuria	high	is absent
Ketonuria	takes place	is absent
Sodium	increased rate	norm
Potassium	reduced	norm
Blood lactate	moderately elevated	norm
blood pH	reduced	norm

The main measures in the treatment of ketoacidotic coma

Rehydration	• 1st hour - 1 liter of isotonic sodium chloride solution; • 2nd, 3rd hour - 0.5 l of isotonic sodium chloride solution; • further to eliminate dehydration, 0.25-0.5 l / h isotonic sodium chloride solution
Restoration of potassium deficiency	Depends on the functional state of the kidneys and the initial level of potassium: when the potassium level is less than 3 mmol / l pour 3 g / h 4% solution of KCl, with potassium 3-4 mmol / l - 2 g / h, with potassium 4-5 mmol / h - 1.5 g / year
Insulin therapy	The initial dose of short-acting insulin is 10-16 units intravenously, then 0.1 units / kg / h of short-acting insulin is administered intravenously, for subcutaneous administration of insulin at a rate of 3-4 units / h only if the glycemia is reduced □14 mmol / l and at normal acid-base balance.
Restoration of acid-base balance	If one hour after rehydration with colloidal solutions and insulin therapy, the shock persists and the pH remains <7.0, bicarbonate is administered at a rate of 1-2 mmol / kg body weight. Half of the dose is administered within 30 minutes, the other half of the dose - within 1-2 hours. Additional introduction of potassium solution is obligatory. When the pH> 7.0, the introduction of bicarbonate is stopped.
Prevention of DIC syndrome	Twice during the first day, heparin is administered at 2500-5000 IU (under the control of blood clotting time).
Treatment and prevention of infectious diseases	Broad-spectrum antibiotics are prescribed in an age-appropriate dose.

The main measures in the treatment of hypoglycemic coma

The severity of hypoglycemia	**Activities**
Easy	consume 10-20 g of "fast" carbohydrates (1-2 slices of bread, glucose in tablets, concentrated fruit juices, sweet drinks, etc.); if the hypoglycemia is not eliminated after 10-20 minutes, you should check the glycemia (make sure

	it is low), consume 10-20 g of "long" carbohydrates - to avoid a rebound of hypoglycemia.
Moderate	10-20 g of "fast" carbohydrates and 10-20 g of "long" carbohydrates
Heavy	• 40% glucose solution pre-jet from 20 to 100 ml; • 1 ml of glucagon (1 mg) subcutaneously or intramuscularly; • 0.1% 1 ml of adrenaline subcutaneously; • in case of ineffectiveness, drip 5% glucose solution to normalize blood glucose levels; • 75-100 mg of hydrocortisone or 30-60 mg of prednisolone before; • 100 mg of cocarboxylase, 5 ml of 5% solution of ascorbic acid before, according to the indications of symptomatic drugs, oxygen therapy; • with a prolonged coma to prevent cerebral edema 5-10 ml of 25% solution of magnesium sulfate before or 15-20% solution of mannitol (0.5-1.0 g / kg) before.

Thyrotoxic crisis — this is a life-threatening condition that can develop in a patient with uncompensated thyrotoxicosis, characterized by a sharp exacerbation of its clinical manifestations and progressive disorders of homeostasis; in the absence of adequate treatment, it usually ends in death. The provoking factors are mostly infections, injuries, serious illnesses or surgical treatment of an accident without proper antithyroid therapy. In the event of a sudden deterioration in the condition of a patient with hyperthyroidism, the possibility of a thyrotoxic crisis should always be borne in mind. Symptoms of the disease that caused the thyrotoxic crisis may come to the fore. In typical cases, the clinical course of thyrotoxic crisis is characterized by a certain stage.

2. **Prodromal symptoms,** which include agitation, insomnia (night hallucinations and other mental disorders), significant weight loss, increased muscle tremor and hyperhidrosis, fever, nausea and vomiting; most of them are caused by hyperactivity of the sympathoadrenal system.

3. **Detailed crisis**, defining features of which are the rapid exacerbation of symptoms of thyrotoxicosis, especially from the nervous, cardiovascular and digestive systems, signs of dehydration, progressive multiorgan failure and the development of coma

The classic clinical picture of a thyrotoxic crisis is so vivid and characteristic that once seen, it is easy to remember for a lifetime. It includes fever (up to 38–41 ° C), hyperhidrosis, severe tachycardia, heart failure, tremor, nausea and vomiting, diarrhea, dehydration, extreme agitation, delirium or coma. In 90% of cases, there are CNS disorders. At the first stage, the symptoms of motor and mental arousal predominate: patients are anxious, emotionally unstable (crying, showing aggression, laughing), hyperactive and not purposeful in behavior, the possible development of psychosis. As the crisis progresses, this condition is replaced by inhibition, apathy, emotional numbness, and severe muscle weakness. It is important to remember that psychoneurological manifestations of thyrotoxic crisis also have prognostic value, as their rapid progression is usually a precursor to coma. Thyrotoxic myopathy is manifested by decreased tone and rapid fatigue of the muscles of the neck, shoulders, arms and legs, less often - the face and torso. Pain, involuntary twitching, convulsions, and attacks of hypokalemic paroxysmal paralysis may occur. Sweat is released in large quantities, rapidly increasing dehydration. Symptoms from the gastrointestinal tract include nausea, vomiting, loss of appetite, spastic abdominal pain, uncontrollable diarrhea and, as a consequence, weight loss. Hepatomegaly and abnormal liver function tests are more commonly caused by heart failure, but jaundice with hepatocyte necrosis has occasionally been observed. The heart rate increases (up to 140-200 per 1 min), pulse pressure increases, shortness of breath occurs. Persistent atrial fibrillation can lead to congestive heart failure even in those who have no history of heart disease. Vascular collapse often becomes a harbinger of the patient's death.

Protocol of examination, diagnosis, treatment and prevention

SECTION OF ACTIVITIES	GUIDELINES FOR ACTION
Greeting	Say hello and introduce yourself to the patient

Acquaintance	Collect passport data of the patient (name, sex, age, place of residence, place of work and specialty)
Complaints of the patient at the time of examination	Identify and detail patient complaints. When determining the patient's complaints, pay attention to the presence of: - nausea, vomiting, diarrhea); - dryness of the mucous membranes, reduced skin turgor; - hot hyperemic skin, fever; - severe tachycardia, weak pulse filling; - sharp psychomotor arousal, including acute psychosis, which is replaced by drowsiness, disorientation, constipation; - bulbar disorders, parkinsonism, seizures.
Examination plan	Levels of thyroid hormones, especially free; preprandial glycemia; indicators of leukocyte formula; calcium and alkaline phosphatase; bilirubin and aminotransferases; cortisol, gases and blood pH. Blood and urine culture. Chest radiography; ECG monitoring.
Laboratory and instrumental research	Rate the levels: - thyroid hormones, especially free; - preprandial glycemia; - indicators of leukocyte formula; - calcium and alkaline phosphatase; - bilirubin and aminotransferases; - cortisol.
	Evaluate the indicators: - radiography of the chest; - ECG monitoring; - blood and urine cultures; - gases and blood pH.
Formulation of the diagnosis	Stage I thyrotoxic crisis with dyspeptic syndrome without signs of CNS damage. Stage II thyrotoxic crisis with disturbance of consciousness, disorientation in space and time, psychotic manifestations of somnolence, stupor. Stage III thyrotoxic crisis (coma). Nephropathy (specify stage) Heart failure (specify NYHA grade). Cerebrovascular diseases (specify which). Concomitant diseases.

Treatment plan	Make a treatment plan that should include pathogenetic, symptomatic, efferent therapy and prophylactic treatment
Management of patients with thyrotoxic crisis	
Diagnosis	The main reasons for the development of thyrotoxic crisis: - sudden increase in blood concentrations of thyroid hormones; - decrease in binding of thyroid hormones with transport proteins of serum and, accordingly, increase in a share of free fractions (fT4, fT3); - progression of cortical insufficiency - sudden cessation of thyrostatic therapy; - any stressful effects on the background of thyrotoxicosis, which deplete the adaptive capacity of the organism: 1. Clinical picture. Main syndromes: - dyspeptic (nausea, vomiting, diarrhea); - dehydration (dryness of mucous membranes, reduced skin turgor); - heat overproduction (hot hyperemic skin, fever); - cardiovascular insufficiency (against the background of severe tachycardia, weak pulse filling there is a collapse, possible pulmonary edema); - - CNS damage (sharp psychomotor arousal, including acute psychosis, which is replaced by drowsiness, disorientation, constipation); - neurological disorders (bulbar disorders, parkinsonism, convulsions). 2. General blood test: - leukocytosis with a shift of the leukocyte formula to the left. 3. Biochemical analysis of blood: - increase in thyroid hormones -increased levels of calcium and alkaline phosphatase; - increase in bilirubin and aminotransferases; - increase in cortisol levels - moderate hyperglycemia.

Acute adrenal insufficiency (Waterhouse-Friedrichsen syndrome)

Etiology: Acute adrenal insufficiency is caused by acute thrombosis or embolism of the vessels of the adrenal glands, hemorrhage in them. It is

usually a complication of a severe infectious process (meningococcemia, pneumococcal or staphylococcal bacteremia, diphtheria, polio), some systemic diseases (nodular periarteritis, systemic lupus erythematosus). Systemic hemorrhage in the adrenal cortex may occur during difficult or complicated childbirth, with acute disseminated intravascular coagulation syndrome. It can also occur as Addison's crisis - acute decompensation of chronic primary and secondary adrenal insufficiency, congenital dysfunction of the adrenal cortex (adreno-genital syndrome).

Clinical variants of acute adrenal insufficiency:

1. Cardiovascular – collapse, hypotension, manifestations of cardiovascular insufficiency dominate: cyanosis, hypothermia, deafness of heart tones, pulse of weak filling.

2. Gastrointestinal – refusal to eat, nausea, vomiting (often incessant), diarrhea, abdominal pain spilled spastic nature, symptoms of "acute abdomen".

3. Neuropsychological – lethargy, asthenia, depression, delusions with visual hallucinations. Possible meningeal symptoms, seizures of the epileptic type. Consciousness is gradually disturbed: inhibition, darkening, stupor. Due to the development of cerebral edema.

Waterhausen-Friedrichsen syndrome develops rapidly, in a few hours proceeds in a flash.

Diagnostic criteria:

1. Electrolyte imbalance: hyperkalemia more than 5 mmol / l, hyponatremia less than 140 mmol / l, hypochloremia less than 90 mmol / l. The sodium / potassium ratio exceeds 20.

2. Disorders of hormone levels: a decrease in cortisol and aldosterone with increasing levels of ACTH. Due to the instantaneous development of an acute condition, it is usually not time to determine the level of hormones.

3. Changes in general clinical tests: leukocytosis, eosinophilia, increased hemoglobin, hypoglycemia. Ketonuria, proteinuria, cylindruria (hyaline, granular cylinders), leukocytosis, microhematuria.

4. Signs of hyperkalemia according to ECG data.

Treatment of Waterhouse-Friedrichsen syndrome:

1. Massive corticosteroid therapy.

2. Intravenous infusion therapy

3. Etiotropic treatment - antibacterial, antitoxic.

4. Symptomatic treatment - cardioprotectors, hepatoprotectors, vitamins, sedatives and other drugs according to the indications

7.3. Materials of control of the final stage of employment

Cases (α=3)

1. The patient was transported by ambulance to the intensive care unit without consciousness. A card of a patient with diabetes was found. Kussmaul's breath, the smell of acetone from the mouth, the skin is dry, turgor is reduced, facial contours are sharpened, periosteal reflexes are absent, the tone of the eyeballs is reduced. The content of lactic acid in the blood is 1.2 mmol / l (norm 0.62-1.3 mmol / l), glycemia is 29 mmol / l. What emergency condition can be suspected?

A. Lactic acid coma.

B. Hyperosmolar coma.

C. Hypoglycemic coma.

D. Ketoacidotic coma.

1. A 20-year-old patient with severe type 1 diabetes mellitus developed decompensation of the disease, which was accompanied by the development of ketoacidosis. Treatment of metabolic disorders was performed by d / v administration of small doses of short-acting insulin and isotonic sodium chloride solution. An hour later, the patient developed a headache, sweating, and heart failure. Blood sugar - 2.8 mmol / l, sodium content - 140 mmol / l. What caused this condition?

A. Hyperhydration.

B. Hypokalemia.

C. Ketoacytic intoxication.

D. Hyponatremia.

E. Hypoglycemia.

2. A 36-year-old woman lost consciousness on the street. He was found with a card of a patient with diabetes. The smell of alcohol from the mouth. The skin is excessively moist, warm. Blood pressure - 140/90 mm Hg, convulsive muscle twitching. Breathing is shallow, the tone of the eyeballs is

preserved, the pupils are dilated, hyperreflexia. What medical care should be provided?

A. Administration of short-acting insulin 10 UNITS subcutaneously.
B. Introduction of 40-80 ml of 40% glucose solution intravenously.
C. Administration of short-acting insulin 10 IU IV.
D. Introduction of 100-120 ml of 40% glucose solution intravenously.

2. The patient underwent surgery for diffuse toxic goiter. Before surgery, the pulse is 96 beats / min., Blood pressure 125/70 mm Hg. Art. On the second day, the condition deteriorated sharply: the patient was agitated, consciousness was darkened, palpitations, severe sweating, vomiting. Pulse 166 beats / min., Atrial fibrillation. BP 80/40 mm Hg. Art. Temperature 390 C. What is the most likely diagnosis?

A. Postoperative sepsis
B. Acute respiratory failure
C. Thyrotoxic crisis
D. Hypoparathyroidism

3. Patient, K., 25 years old, complaints of diarrhea, loss of appetite and increased need for salt, sleep disorders, the boy's conversation with friends who are currently absent. Objectively: skin, brown, hyperpigmented on the elbows and knees; AT 75/40 mm Hg, Ps106 beats / min. The boy lags behind in physical and sexual development. The level of Na is 126 mmol / l, chlorides are 74 mmol / l, cortisol is 80 nmol / l (N 130 - 360). What is the most likely diagnosis?

A. Chronic adrenal insufficiency.
B. Acute adrenal insufficiency.
C. Food poisoning.
D. Acute pancreatitis.
E. Acute adrenal insufficiency (Waterhouse-Friedrichsen syndrome)

Protocol № 3 clinical examination of the patient

The patient's name _____
_____
_____
Age _____
Complaints of the patient _____

History of the disease _____

Life history _____

The results of the physical examination of the patient: _____

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Preliminary diagnosis: _____
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_____
With what diseases it is necessary to make the differential diagnosis:
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Examination plan: _____
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Results of laboratory and instrumental examination:
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Rationale for clinical diagnosis: _____
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_____
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Clinical diagnosis: _____
The main disease: _____

_____
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Complication: _____
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Concomitant diseases: _____
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Forecast: _____
_____
_____
Efficiency: _____
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Treatment: _____
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Drug therapy: _____
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Notes on the acquisition of practical skills

№ з/п	**Skills and manipulations**	**Signature student / supervisor**
1.	Practical experience	
1.1.	Be able to conduct surveys, physical examinations of the patient	
1.2.	Be able to analyze the data of laboratory and instrumental examination in patients with acute	

	conditions	
1.3.	Urgent conditions	
2.	Be able to provide assistance in an emergency	

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Educational and methodical literature:

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7. Ендокринологія: навч. посіб. для студ. вищ. мед. закладів / за ред. проф. П.М. Боднара. Вінниця: Нова Книга, 2012. – 360с.
8. Basic & ClinicalEndocrinology. Seventhedition. EditedbyFrancis S. Greenspan, David G. Gardner. McGrew HillCompanies, USA, 2004. – 976p.