Danylo Halytsky Lviv National Medical University

Methodological guidance for practical classes on
Internal medicine, including endocrinology, medical genetics.
The Individualized Major:
Endocrine emergencies.
Managing patients with endocrine diseases.
For sixth-year students
Surgery
Training specialists of the second (master's) level of higher education
Subject area 22 - **Healthcare**
Major 222 - **Medicine**

Lviv 2021

Methodological guidance compiled following educational and qualification

characteristics and professional specialist training programs, the experimental curriculum developed based on Credit Transfer System (CTS), discussed and approved at the Methodical Meeting of Endocrinology Department (Protocol No 10 dated February 04, 2021) and approved by the Subject-oriented Methodological Commission for Therapeutic Disciplines of Danylo Halytsky Lviv National Medical University (Protocol No. 5 dated 25.03.21).

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Theme 1. Managing a patient with chronic complications of diabetes mellitus. Peculiarities of the course of acute respiratory diseases COVID-19, caused by SARS-CoV-2 coronavirus in patients with diabetes mellitus.

1. Topicality.

Vascular events are one of the common syndromes in the manifestation of diabetes mellitus. In most cases, their intensity specifies the working capacity of patients, prognosis of the disease and the length of life. In this regard, the timely and accurate diagnostics, treatment of diabetic angiopathies acquires important significance

in diabetology. The problem of angiopathy is rather interdisciplinary than merely diabetic. It involves ophthalmology, surgery and nephrology. The knowledge of clinical features and treatment policy with different degrees of manifestation of angiopathy in different areas allow preserving the working capacity of patients for a longer period.

2. Learning goal.

To become acquainted with epidemiological surveys of diabetes mellitus in Ukraine and the world (α=1)

The student must know (α=2):

- Classification of diabetic angiopathies and neuropathies;
- Diabetic retinopathy: process stages, diagnosis, prevention and treatment;
- Diabetic nephropathy (diabetic chronic kidney disease (DCKD)): development stages, diagnosis, treatment and prevention
- Diabetic neuropathy, classification, diagnostics and treatment
- Diabetic foot: classification, diagnostics, treatment;

The student should be able to (α=3):

- order the necessary medical examinations to detect diabetic angiopathy (nephropathy, retinopathy, angiopathy of lower extremities), autonomic and peripheral neuropathy;
- based on analysis of laboratory findings and instrumental methods of examination justify and formulate a diagnosis of diabetes mellitus and its complications
- perform differential diagnosis of chronic complications of diabetes mellitus;
- order adequate treatment of chronic complications of diabetes mellitus.

- Managing a patient with chronic complications of diabetes mellitus: existing algorithms, standards for the diagnosis and treatment;
- Peculiarities of the course of acute respiratory diseases COVID-19, caused by SARS-CoV-2 coronavirus in patients with diabetes mellitus;

3. Educational goal.

Attract attention and form the sense of responsibility in students, who will be different types of doctors, to/for the timely detecting and the proper treatment of disease to achieve carbohydrate metabolic compensation as a principal factor

preventing complications of chronic diseases.

4. Interdisciplinary integration:

Subjects	*To know*	*To be able to*
Previously studied subjects		
Systemic Anatomy	the topography, the vascularization of the pancreas,	
Hominal Physiology	the internal secretion of the pancreas,	
Histology	the histologic structure of island of Langerhans,	
Biochemistry	the carbohydrate metabolism,	
Pathoanatomy	morphological changes in organs and tissues in patients with diabetes mellitus,	
Pathophysiology	pathogenesis of vascular events and comas in patients with diabetes mellitus	
Subjects that will be studied later		Perform a clinical review, order the corresponding
Therapy	Clinical picture, diagnostics, differential diagnostics, treatment, prevention of diabetes mellitus	diagnostic testing,

Pediatrics	Clinical picture, diagnostics, differential diagnostics, treatment, prevention of diabetes mellitus in children	Consultations by allied health professions to verify the diagnosis

Surgery	Peculiarities of the course of diabetes mellitus in the event of surgical pathology, timely diagnostics and surveillance of such patients	
Obstetrics & Gynaecology	Peculiarities of the course of diabetes mellitus during pregnancy, Timely diagnostics and surveillance of such patients	
Neurology	Clinical picture, diagnostics, differential diagnostics, treatment, prevention of neurological complication of diabetes mellitus	
Ophthalmology	Clinical picture, diagnostics, differential diagnostics, treatment, prevention of diabetic retinopathy	
Intersubject integration	Modern methods of patients' examination, in particular, laboratory, instrumental, adequate treatment strategy.	Order the adequate treatment

5. Training subjects:

- Etiology, the pathogenesis of diabetic macro- and microangiopathy, neuropathy, the biochemical effect of hyperglycemia.
- Classification of diabetic angiopathies.
- Classification of diabetic neuropathies.
- The definition of diabetic foot syndrome (classification, diagnostic and treatment approaches).
- Clinical manifestations of vascular events of diabetes mellitus
- Laboratory and instrumental diagnosis of diabetic angio- and neuropathies.
- Diabetic angio- and neuropathies treatment methods.

- Techniques preventing the development of chronic complications of diabetes mellitus

6. Plan and organizational structure of the class

(see «Introduction»)

7. Materials and methodological support of the class.

7.1 Materials of the preparatory stage of the class

Tests (α=2)

1. A teenage girl aged 18 is complaining about thirst, dry mouth, frequent urination. Fasting blood glucose level is 7,8 mmol/L, HbA1c – 9,8 %.
In the course of examination, there was detected acetone breath, dry skin. What diagnosis should be suspected?

A. Type 1 Diabetes Mellitus
B. Type 2 Diabetes Mellitus
C. Diabetes insipidus
D. Impaired fasting glycaemia
E. Gestational diabetes

2. A woman aged 50 visited a family physician. She was complaining about skin and genital itching, some thirst, dry mouth, nighttime urination.

Mother was suffering from type 2 diabetes mellitus. Height 165 cm, weight 90 kg. Daytime Glycemia: 8,4-10,3-12,6-6,9 mmol/L. What provisional diagnosis should be established?

A. Type 1 diabetes mellitus
B. Type 2 diabetes mellitus
C. Impaired glucose tolerance
D Candidiasis
E Dermatitis

3. Macroangiopathy, as the complication of diabetes mellitus, most often affects the vessels of:

A. Brain
B. Lungs
C. Retina
D. Kidneys
E. Liver

4. Which of the following assertions is not true as regards angiopathy of lower

extremities?

A. Occurence of paresthesia
B. Gradual trophic disturbance beginning with fingers
C. Leg Pain When Walking
D. Foot temperature decrease
E. Development of gangrene in the foot

5. Which of the following assertions is true as regards bone affection in patients with diabetes mellitus?

A. Dupuytren's contracture
B. Aseptic bone necrosis
C. Hyperostosis
D. Calcification of arthrodial cartilages
E. Seronegative polyarthritis

6. Define anti-hypertensive agents which are the most reasonable for the treatment of early nephropathy in teenagers:

A. ACE inhibitors

B. Loop diuretics.
C. Calcium antagonists
D. B-blockers
E. Statins

7.2. Methodological materials for the principal stage of the class:

Examination protocol, establishing a diagnosis, treatment and prevention

ACTIVITY SECTION	**GUIDELINES FOR ACTION**
Greeting	Greet and introduce yourself to a patient
Acquaintance	Collect personal information about a patient (full name, sex, age, place of residence, place of work and occupation)
Patient's complaints at the time of examination	Visual impairment, face oedema, limb swelling, a rise in arterial pressure, leg pain, foot ulcer formation

Managing patients with diabetic retinopathy

Diabetic retinopathy (DR) – a microvascular complication of diabetes damaging the back of the eye (retina). At the terminal stage, it can cause blindness.

Stages	***Diagnostic criteria***
I – non-proliferative retinopathy	• No complaints • Normal vision acuity • Retinal microaneurysm, swelling (predominantly in a macular zone), haemorrhage, hard and soft exudative focuses
II – preproliferative retinopathy	• Decrease in visual acuity • Alongside with changes, peculiar to I stage, there are vascular malformations (rosary-like, tortuosity, loops, duplication and significant fluctuations of the vessel calibre), a large amount of exudates, intraretinal microvascular abnormalities, numerous retinal haemorrhages, scotomas with varying intensity
III – proliferative retinopathy	• A sudden decrease in visual acuity to the complete blindness • Neovascularisation of the optic disc and other areas of the retina • Vitreous Hemorrhage • Fibrous tissue formation in the area of preretinal haemorrhages • Complications of diabetic retinopathy III: 1. Fractional retinal detachment 2. Rubeosis iridis 3. Secondary glaucoma

Diabetic retinopathy study methods:

1. Mandatory:
   - External examination of the eyeball, examination of visual acuity and visual fields once per 6 months
   - Defining the level of ophthalmotonous pressure once a year in patients suffering from diabetes mellitus for 10 or more years
   - biomicroscopy of the eye lens and vitreous body using a corneal microscope
   - direct or indirect ophthalmoscopy with dilated pupil once a year, in the event of discovered complications – every 3-6 months
2. Additional:
   - Photographing the vessels in the eye fundus using a fundus-camera

- Fluorescein angiography
- electrophysiological study methods to define the functional status of healthy ophthalmic nerve and retina

- ultrasound investigation in the event of significant opacities in the vitreous body and eye lens.

In the event of a sudden decrease in visual acuity or the occurrence of any other complaints about the sense of sight, you should be immediately examined by an ophthalmologist.

Diabetic retinopathy treatment:

Must be carried out jointly by endocrinologist and ophthalmologist.

- Perfect/optimal glycemic control (HbA1c <7,0-7,5%). There is clear dependence between glycemic control and the development of diabetic retinopathy.
- The use of vasoprotective drugs for treatment and prophylactic purposes has been recognized as poorly effective, especially against the background of inadequate glycemic control.
- Laser photocoagulation nowadays has become the most effective type of diabetic retinopathy treatment and prevention of blindness. There are used three basic methods of laser photocoagulation: focal laser photocoagulation, barrier laser photocoagulation, panretinal laser photocoagulation.

Algorithm of remedial measures in the event of diabetic retinopathy:

Sight-threatening complications	***Remedial measures***
Non-proliferative diabetic retinopathy	Careful glycemic control
Retinal microbleeds	Laser photocoagulation of lesions
Significant macular oedema	Focal laser photocoagulation
Risk of proliferative diabetic retinopathy	Panretinal laser photocoagulation
Vitreous hemorrhage	Observation versus Vitrectomy
Tractional retinal detachment	Vitrectomy
Neovascular glaucoma	Panretinal laser photocoagulation, cryotherapy

The urgency of laser photocoagulation depends on the type and stage (is defined by ophthalmologist):

Macular oedema or macular retinopathy:

- In the event of acute type – urgently
- In the event of chronic type – within several days

Proliferative diabetic retinopathy:

- In the event of central type (newly formed vessels on optic disc) – urgently
- In the event of peripheral type (newly formed vessels in other areas of the retina) – without delay within 1-2 weeks

Preproliferative diabetic retinopathy:

- In the presence of additional risk factors – without delay within several weeks
- In the absence of risk factors – within 2-3 months

Criteria for treatment efficacy: Stabilisation of retinopathy progression

Regular medical check-up –lifetime:

<table>
<tr><th>Examination</th><th>Frequency</th><th>Remedial measures</th><th>Preventive measures</th></tr>
<tr><td colspan="4">Non-proliferative diabetic retinopathy</td></tr>
<tr><td>Examination by ophthalmologist: without macular retinopathy</td><td>Twice a year</td><td rowspan="3">Laser photocoagulation</td><td rowspan="3">Attaining of pefect /optimal glycemic control of diabetes mellitus.
Arterial blood pressure control and correction</td></tr>
<tr><td>with macular retinopathy</td><td>Three times a year</td></tr>
<tr><td>Measuring visual acuity.
Measuring ophthalmotonous pressure.
Direct ophthalmoscopy
Biomicroscopy of the eye lens and vitreous body
Fluorescein angiography of the retina
Photographing the vessels in the eye fundus</td><td>If necessary - more frequent</td></tr>
<tr><td colspan="4">Diabetic preproliferative retinopathy</td></tr>
</table>

Examination by ophthalmologist Measuring visual acuity. Measuring ophthalmotonous pressure. Direct ophthalmoscopy Biomicroscopy of the eye lens and vitreous body Fluorescein angiography of the retina Photographing the vessels in the eye fundus	3-4 times a year and if necessary	Laser photocoagulation	Maintenance of perfect /optimal glycemic control of diabetes mellitus. Arterial blood pressure control and correction
Diabetic proliferative retinopathy			
Examination by ophthalmologist Measuring visual acuity. Measuring ophthalmotonous pressure. Direct ophthalmoscopy Biomicroscopy of the eye lens and vitreous body Fluorescein angiography of the retina Photographing the vessels in the eye fundus	Urgently, then 3-4 times a year and if necessary	Laser photocoagulation Cryocoagulation core Vitrectomy	Maintenance of perfect /optimal glycemic control of diabetes mellitus. Arterial blood pressure control and correction

Managing patients with diabetic nephropathy

Diabetic nephropathy (diabetic chronic kidney disease) - specific renal vessels damage in patients with diabetes mellitus that is accompanied by the formation of nodular or diffuse glomerulosclerosis, the terminal stage of which is characterized by the development of CKD.

Classification of diabetic nephropathy (according to Mogensen) and its course

Duration of diabetes mellitus	Stage	Clinical picture	Prognosis
From the onset of disease	I – hyperfiltration, kidney hypertrophy	Increased glomerular filtrate rate up to 160 ml/min, enlarged kidneys	Possible full regression of changes
2–5 years	II – beginning of histological changes, change of the structure and functions of the basement membrane	Thickening of the basement membrane, mesangial expansion, absence of albuminuria	Possible partial regression of changes
5–10 (15) years	III – early clinical nephropathy	albuminuria, decrease of glomerular filtrate rate from 160 to 130 ml/min, arterial hypertension	Possible slowdown of changes progression, sometimes regression
10 (15)–25 years	IV – obvious nephropathy	constant proteinuria, decrease of glomerular filtrate rate up to 70 ml/min, then up to 10 ml/min, constant increase in arterial pressure, swelling, lipid storage disease	Possible slowdown of the course of changes progression, sometimes their delay
>15 years	V – kidney failure	increases in creatinine, arterial hypertension	Irreversible progression of changes to the terminal renal insufficiency
GFR - glomerular filtrate rate			

Diagnostics

Chronic kidney disease (CKD) must be actively detected during the screening study because for many years the disease may develop without any objective or subjective symptoms. It is necessary to carry out the clinical urine analysis, determine the creatinine concentration in serum and microalbuminuria in the urine from time to time in patients with an increased risk of chronic kidney disease, especially in patients with diabetes mellitus or arterial hypertension. In practice, the calculation of GFR but not the determination of creatinine concentration in blood serum, which depends on age and muscle mass, is the best indicator of kidney function.

Supplementary examinations:

1. Clinical urine analysis: albuminuria, proteinuria, micro- macrohematuria, casts, leukocyturia, low urine specific gravity.
2. Blood examination: anaemia (usually, normocytic and normochromic), an increase of creatinine, urea, uric acid, potassium, phosphates and parathormone, triglycerides, cholesterol concentration, hypocalcemia; metabolic acidosis.
3. Imaging: ultrasound investigation — kidneys, usually decreased in size (often <10 cm in long axis); exclusion (large kidney, despite chronic kidney disease) in the event of amyloidosis - nephropathy, diabetic nephropathy, multicystic kidney and nephropathy with HIV infection. Imaging using contrast (for example, CT) is carried out only in the case of an emergency, considering the high risk of contrast-induced nephropathy.
Diagnostic criteria:
The diagnosis of chronic kidney disease is established when during > 3 months, there are preserved morphological or functional kidney diseases (→Definition), or GFR

<60 ml/min/1,73 sq.m. The diagnosis of CKD is established in patients with chronic renal disease and GFR <60 ml/min/1,73 sq.m.

Treatment
Microalbuminuria stage:
carbohydrate metabolism compensation (HbA1c < 7%);
use of angiotensin-converting-enzyme inhibitors (ACE inhibitors) or ARA inhibitors in subpressor dose at normal arterial pressure and in median curative doses – at increased arterial pressure
over 130/80 mm Hg - constantly;
correction of dyslipidemia (if any);
a diet with mild restriction of animal protein (no more than 1 gr of protein per 1 kg of body weight);
Proteinuria stage:
Optimal carbohydrate metabolism compensation (HbA1c < 7%);
Maintenance of arterial pressure at a level of 130/80 mm Hg;
first choice drugs
- ACE or ARA inhibitors – constantly
correction of dyslipidemia (if any) – constantly;
restriction of animal protein up to 0,8 gr of protein per 1 kg of body weight – constantly;
prevent from using Nephrotoxic medications (contrasts, antibiotics, non-steroidal anti-inflammatory drugs);
erythropoietin if confirmed;
Chronic kidney disease stage:

carbohydrate metabolism compensation (HbA1c < 7%);
maintenance of arterial pressure at a level of 130/80 mm Hg; first choice drugs - ACE or ARA inhibitors (carefully – in the event the level of creatinine in blood is more than 330 mcmole/l). The combined antihypertensive therapy is recommended;
Restriction of animal protein p to 0,8 gr of protein per 1 kg of body weight – constantly;
correction of dyslipidemia (if any) – constantly;
treatment of renal anaemia (erythropoietin) – at the level of Hb< 110 gr/l (under the control of arterial pressure, Hb, Ht, platelets, iron and serum ferritin)
correction of hyperkalemia;
correction of calcium and phosphate metabolism;
hemodialysis;
peritoneal dialysis;

kidney transplantation (within the conditions of specialized centers);

Managing patients with diabetic neuropathy

Diabetic neuropathy (DN)– a complex of clinical and subclinical syndromes, characterized by diffuse or local lesion of peripheral and/or autonomic nerve fibers caused by diabetes mellitus.

Classification of diabetic neuropathy:

1. Peripheral:

1.1. Somatic
- diffusive symmetric distal sensory-motor neuropathy (called polyneuropathy)
- diabetic amyotrophy (proximal neuropathy causing significant acute disability)
- diffuse motor neuropathy (severe diabetic amyotrophy)
- acute painful neuropathy
- insulin neuritis
- mononeuropathy (damaging peripheral and cranial nerves)

1.2.Vegetative (autonomic) diabetic neuropathy
- cardiopathy
- neuropathy affecting the urinary bladder
- loop of thermal control
- stomach neuropathy
- colonic, enteric, pudendal neuropathy
- cutaneous neuropathy
- asymptomatic hypoglycemia (Hypoglycemia unawareness)
- vasomotor disorders (Charcot joint, neuropathic edema)

- bronchial dystonia
- venous distensibility in the feet
- pupillary reflex disorders
- sexual debility, retrograde ejaculation

2. Central (changes of the brain and spinal cord functions)
- cerebrasthenic syndrome
- encephalopathy
- dyscirculatory disorders of vascular genesis
- myelopathy

Diagnostics:

The examinations aimed at diagnosing diabetic neuropathy in patients with type 1 diabetes mellitus are carried out in a year after the occurrence of diabetes mellitus, and in patients with type 2 diabetes mellitus – from the moment the diabetes mellitus was diagnosed.

The list of mandatory examinations to diagnose diabetes mellitus:

- Lower limb examination to find symptoms of dry skin, hyperkeratosis, calluses, skin infection, abnormal toenail growths.
- Evaluation of tendon reflexes (patellar and Achilles reflexes).
- Evaluation of tactile sensitivity (using monofilament).
- Evaluation of pain sensitivity (using blunt end needle).
- Evaluation of temperature sense.
- Evaluation of proprioceptive sensibility (The Romberg test, used to investigate the cause of loss of motor coordination (sensitive ataxia)).
- Determination of the vibration perception (using graduated tuning fork).
- Electromyography (EMG) – stimulation of sensor sural nerve (n. suralis dextr.) and motor nerve (n. peroneus dextr.):
  - action potential amplitude
  - M amplitude of nerve conduction velocity
- Detecting orthostatic hypotension (arterial blood pressure reduction >30 mm Hg in the event of changing the position from supine to standing).
- The Valsalva maneuver (heart rate accelerates if you bear down, strain).

Classification of diabetic peripheral neuropathy (DPN)according to the stages of severity (P.Dyck, P.Thomas, 1999)

DPN grading	***Characterization***

Grade 0. (neuropathy is absent)	There are no symptoms and signs of DPN, autonomic tests are negative, in the course of electromyography (EMG) of sensory and motor peripheral nerves (not less than 2 on one side) no pathologies have been detected.
Grade 1. Subclinical	1А. No symptoms and objective neurological signs of DPN. Existence of any 2 changes, detected in the course of electromyography (EMG) of sensory and motor nerves or positive autonomic tests (the Valsalva maneuver, deep breath test). 1Б. Without symptoms. In the course of clinical examination, there are detected 2 or more objective neurological signs of DPN on one side.

Grade 2. Clinical	2А. Complaints that are peculiar to DPN. Sensory Processing Disorder, movement disorder, autonomic disorders, without signs of weakness in the flexor digitorum brevis (a patient can remain standing on heels).
	2Б. The same + signs of weakness in the flexor digitorum brevis (a patient cannot remain standing on heels).
Grade 3. Severe	Neuropathy with performance impairment.

Treatment:

- Perfect/optimal glycaemic control (HbA1C <7,0-7,5%).
- Pharmacological therapy:
- α- lipoic (thioctic) acid

hypoglycemic activity (improvement of insulin sensitivity)
hypoglycemic activity
anti-oxidant action, detoxification activity (including as a donator of SH- groups)
neurotropic action – improves nerve impulse conduction (reduces lipid peroxygenation in peripheral nerves, improves endoneurial blood flow)
improves regeneration (encourages the growth of new nerve fibers)
immunotropic effect (increases the content of all T lymphocyte subpopulations)

- ***Vitamin B Complex*** in age-specific dosage variances during 2-3 months, a special liposoluble vitamin B1 – BENFOTIAMINUM (100mg 1-2 time(s) a day – during 1-3 months, 2 treatment courses a year).
- Reduction of pain and seizures: nonsteroidal anti-inflammatory drugs, (intramuscular administration every day or every other day №5-10)
- vasodilator (pentoxifyllinum, nicotinic acid products etc).
- metabolic therapy (actovegin, solcoseryl, cytochrome C, instenon, γ- linolenic acid, etc).

- in the event of vegetative disorders symptomatic medication is taken. Its effect is directed to compensation for the function that the organ has lost:
- Physiotherapy:
- diadinamometry
- inductothermy
- magnetotherapy
- laserpuncture
- nicotinic acid, euphylline, novocaine, proserine electrophoresis provided in the legs
- contrast baths for affected limbs
- lower limb massage
- hyperbaric oxygenation
- therapeutic exercise

Treatment efficiency criteria: absence of neuropathy clinical manifestations

Regular medical check-up:

Testing		***Regular medical check-up***
Examination, specialists	***Frequency***	
A neurologist with detection of all types of sensitivity (tactile, vibration, pain, temperature, proprioceptive), tendon reflexes	2 times a year	life long
Performance of orthostatic test (endocrinologist)	1 time a year	
The Valsalva maneuver (based on ECG)	1 time a year	
Analysis of heart rate variability	1 time a year if possible	
Electroneuromyography		
Cardiologist, gastroenterologist, urologist	if necessary	

Managing patients with diabetic foot disease

Diabetic foot disease (DFD) brings together pathological changes of the peripheral nervous system, arterial and microvascular bed, osseous-articular apparatus of the foot and directly threatens the development of ulcerous-necrotic processes and gangrene of the foot.

Classification (formulation of diagnosis)

- Neuropathic form:
  - preulcerative changes and foot ulcer
  - diabetic osteoarthropathy (Charcot's joint)
- neuro-ischaemic form
- ischaemic form

Mandatory study methods

- past medical history
- lower limb examination
- neurologic examination
- arterial bleeding assessment
- foot and ankle joints X-ray two projection imaging
- microbiological analysis of wound exudate

past medical history

NEUROPATHIC FORM	**ISCHAEMIC FORM**
long-term course of diabetes mellitus and/or occurrence of ischaemic foot ulcer, amputations in past medical history	long-term course of diabetes mellitus and/or occurrence of ischaemic foot ulcer, amputations in past medical history
alcohol abuse	tobacco abuse

<table>
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Lower limb examination

NEUROPATHIC FORM	ISCHAEMIC FORM
Dry skin, areas affected by hyperkeratosis in foot overload zones	Pale or cyanotic skin, Skin atrophy, often – skin cracking
Specific deformity of foot, toes, ankle joint	Nonspecific toe, foot deformities
Pulse on the pedal arteries has been preserved on both sides	Pulse on the pedal arteries has been reduced or is absent
Painless ulcerous defects in overloaded areas	Acral necrosis, severely painful
Absence of subjective symptoms	Intermittent claudication

Group risks of the diabetic foot disease development

- Patients with distal polyneuropathy at the stage of clinical manifestation depression of the peripheral nervous system function
- Patients with peripheral vascular diseases of any genesis
- Patients with foot deformity of any genesis
- Patients with diabetic retinopathy and nephropathy
- Single patients, aged patients
- People addicted to the alcohol
- Smokers

</td></tr>
<tr><td>Treatment</td><td>

Treatment of neuropathic form with preulcerative changes and foot ulcer

- carbohydrate metabolism compensation (HbA 1C < 7%)
- affected limb unloading (therapeutic and unloading footwear, individual unloading bandage, rocking chair)

</td></tr>
</table>

	• removal of hyperkeratosis areas and/or initial debridement of ulcerous defect • antibiotic therapy provided there are signs of infection and ulcerous defects at stage 2 and deeper • the use of modern atraumatic instruments. **Treatment of neuropathic form of diabetic foot disease with osteoarthropathy** • carbohydrate metabolism compensation (HbA 1C < 7%) • affected limb unloading (individual unloading bandage at the acute and subacute stages) • antibiotic therapy in the event of ulcerous defects with the signs of infection and wounds at stage 2 and deeper. • in the event of ulcerous defects – the use of modern atraumatic instruments for bandaging, which corresponds to the stage of the ulcerative process **Treatment of the ischemic form of diabetic foot disease** 1. Conservative treatment: • carbohydrate metabolism compensation (HbA 1C < 7%) • smoking cessation • the correction of arterial hypertension • treatment of dyslipidemia • elimination of limb ischemia phenomena: • disaggregant (coagulogram- guided and control of the state of the fundus of the eye), • vasodilators • anticoagulant (coagulogram-guided and control of the state of the fundus of the eye) 2. Reparative surgery on the arteries under the condition of separation of vascular surgery and/or percutaneous transluminal angioplasty (balloon angioplasty) 3. In the event of ulcerous defects – antimicrobial therapy **Prevention of diabetic foot disease** • Maintenance of the long-term steady-going carbohydrate metabolic compensation (HbA 1C < 7%) • Teaching patients to take care of feet/legs • the early detecting of patients that are among the risk group for diabetic foot disease • Wearing orthopedic footwear.

7.3. Control materials for the final stage of the class:

Assignments (α=3)

1. What forms of diabetic neuropathy are characterized by the presence of acute pain,

paresthesia, hyperesthesia and is fully reversible by its nature?
A. acute sensory diabetic neuropathy
B. chronic sensorimotor neuropathy
C. autonomic neuropathy
D. proximal motor neuropathy
E. chronic inflammatory demyelinating polyneuropathy

2. A patient aged 32, who was diagnosed with type 1 diabetes mellitus for the first time is complaining about acute pain in two legs, their hypersensitivity, especially about hip pain, a touch of clothes causes unbearable pain. The pain appeared along with diabetes symptoms. Its intensity increased after the normalisation of blood glucose level. It was accompanied by significant weight loss. Try to establish the provisional diagnosis?
A. type 1 diabetes mellitus, chronic sensorimotor neuropathy.
B. type 1 diabetes mellitus, acute sensory neuropathy.
C. type 1 diabetes mellitus, compressive mononeuropathy of lower limbs
D. type 1 diabetes mellitus, proximal motor neuropathy
E. type 1 diabetes mellitus, asthenoneurotic syndrome.

3. With what complications from among those listed below the diabetic patients are contraindicated in pregnancy?
A. non-proliferative diabetic retinopathy
B. stage 5 diabetic nephropathy
C. stage 1 diabetic neuropathy
D. metabolic liver disease
E. stage 1-2 diabetic neuropathy

Protocol № 1 clinical considerations for a patient

Patient’s full name _____
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Age _____ Occupation_____
patient's complaints_____
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past medical history_____
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patient's life history_____
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substantiation of clinical diagnosis: _____

Clinical diagnosis: _____
Prior disease: _____

Complications:

Intercurrent diseases: _____

Prognosis:

Treatment: _____

Medicamentous therapy: _____

Glycaemic control: _____

Marking of mastering pra

Order No.	Skills and procedures
1.	Practical skills
1.1.	Know how to interview, perfor examination of a patient with diabete
1.2.	Be able to analyze the laboratory exa
1.3.	Know how to assign a sugar-reducir patient with diabetes mellitus
2.	Know how to assign the diabetes treatment pattern
2.1.	Diabetic retinopathy
2.2.	Diabetic nephropathy
2.3.	Diabetic neuropathy
2.4.	Diabetic foot disease

Theme 2. Managing a patient with goitre. Peculiarities of the course of acute respiratory diseases COVID-19, caused by SARS-CoV-2 coronavirus in patients with thyroid problems.

3. Topicality

Goitre is a clinical concept characterizing the enlargement of the thyroid gland in size or volume, presence of nodular goitre. It develops because of genetic liability under the influence of triggers.

Triggers are usually represented by adverse environmental factors: iodine and selenium deficiency, the activity of goitrogenic substances, tobacco smoking etc. Goitre often accompanies the range of such pathological conditions as diffuse toxic goitre, nodular goitre, chronic autoimmune thyroiditis or it may result from medical interventions and some medication intake.

Goitre may be either diffuse (when the total volume increases) or nodular (in the event of the presence of local additional inclusions (adenomas, carcinomas, calcificates, in some cases – large cysts in thyroid tissue (TT)).

The scope of iodine deficiency and its consequences impresses. According to estimates of WHO, about 2 billion people or 30% of the world population live in areas severely affected by iodine deficiency. The total number of those suffering from endemic goitre reaches 740 million people, and those with infantile hypothyroidism – 11 million people. Herewith, the cases of discernible infantile hypothyroidism are quite fairly deemed to be «the tip of the iceberg», considering that less severe intellectual disabilities (not always diagnosed) occur much more frequently. The course of endemic goitre, which from olden times has been the most common and the best-known sign of iodine deficiency, may be complicated by the development of local compression syndrome, iodide-induced thyrotoxicosis and/or malignant change. Thus, the problem of iodine deficiency has been recognized as the immediate global problem, as long as all the specified disorders to a large extent determine not only the health status of the population but also the intelligence level of society. It is worth additionally emphasizing that under the condition of chronic iodine deficiency there significantly increases the risk of the thyroid gland radiation-induced pathology development in the event of industrial disasters.

Thyroiditis - a group of thyroid gland diseases that differ in etiology and pathogenesis, morphological pattern and clinical course. Thyroiditis is a general term that refers to "inflammation of the thyroid gland". The occurrence and clinical importance of types of thyroiditis also significantly differ. In most cases, physicians face different types

of chronic autoimmune thyroiditis, which is considered to be the most common autoimmune human disease. It often causes thyroid gland functional disorders (usually the development of hypothyroidism), which defines the main clinical aspect of this pathology. Subacute thyroiditis like granulomatous and lymphocytic are second by frequency. Notwithstanding their full-blown symptoms in most cases, they do not leave any persistent disorders behind. Other types of thyroiditis occur much less frequently.

Thyrotoxicosis – a syndrome with which there are observed clinical and/or biochemical manifestations of the excessive content of thyroid hormones in blood independent of the causative factor. About 90% of cases of thyrotoxicosis fall on diffuse toxic goitre and thyroid gland functional autonomy. *Diffuse toxic goitre* (Graves-Basedow disease) is one of the most severe diseases, which is a genetically determined system pathology of autoimmune genesis, which is manifested by diffuse thyroid disease and hyperthyreosis, often in combination with extrathyroidal pathology (infiltrative ophthalmopathy, dermopathy). Timely diagnosis enables adequate treatment, preventing the development of many severe complications of thyrotoxicosis both chronic (cardiomyopathy, encephalopathy, myopathy,

osteoporosis, cachexia) and acute (thyrotoxic crisis). The similarity of clinical symptomatology necessitates the differential diagnosis of thyrotoxicosis syndrome with numerous cardiovascular diseases, diseases of the nervous and other systems, which may be a difficult task, however, so necessary from the perspective of medical tactics.

It is believed that *thyroid cancer* is a rare disease, which is about 1–1,5 % of all malignant neoplasms, however, among endocrine tumors it occurs the most frequently. For the recent 25 – 30 years, numerous notifications show the increase of thyroid cancer cases in many countries, especially among youth. In Europe over 20000 new thyroid cancer cases are diagnosticated every year and 1500–2000 patients die from this disease. In Ukraine, during a year about 2500 new patients are detected. About 27000 patients are registered as such that have undergone treatment and 10–12 patients per 1 million of the population die.

Malignant thyroid neoplasms are quite specific and extremely diverse according to their biological attribute. On the one hand, it often leads to diagnostic errors and long–time ineffective treatment with different specialists (endocrinologists, surgeons, pediatricians, phthisiologists, otolaryngologists).

On the other hand, the timely delivered adequate treatment of thyroid cancer provides quite good long-term results. It is expediated by both the low malignant potential, peculiar to most of these tumors, and the compliance with up-to-date standards of their diagnostics and treatment. Nevertheless, there occur tumors with quite aggressive behaviour, which are life-threatening conditions.

4. Learning goal.

To become acquainted with spreading of diffuse and nodular nontoxic goitre, hypothyroidism, thyroiditis, thyroid cancer in Ukraine and the world (α=1).

The student must know (α=2):

- biological effect of thyroid hormones on human organism and mechanism of thyroid function regulation;
- determination and risk factors of the major thyroid disorders;
- symptoms and signs of the major thyroid disorders;
- diagnostic criteria of the major thyroid disorders;
- thyroid enlargement classification;
- methods of assessment of thyroid function;

The student should be able to (α=3):

- to diagnose endemic and sporadic goitre, hypothyroidism, autoimmune, acute, subacute thyroiditis, thyroid cancer, decide upon treatment policy and (if possible) the preventive measures;
- carry out the differential diagnosis of thyroid disorders;

- examine neck and thyroid;
- palpate cervical glands;
- effectively use the possibilities of public and personal preventive measures of iodine deficiency disorders (IDD).

3. Educational goal.

To formulate deontological principles of working with patients suffering from endocrine pathology. To attract students' attention to the influence of environmental factors on the development of certain thyroid disorders. To form the sense of responsibility for the timeliness of diagnostics, completeness of examination and selection of treatment policy for patients with different types of thyroid disorders especially the one, which may threaten life and health.

4. Interdisciplinary integration:

Subject	*To know*	*To be able to*
Previously studied subjects		
Systemic anatomy	Anatomy of the thyroid gland	
Hominal physiology	synthesis, transportation, effects, thyroid hormones' secretion regulation	
Histology	embryogenesis, histological structure of the thyroid gland	
Pathoanatomy	Classification and nature of pathomorphological changes of the thyroid gland ;	Evaluate results of pathohistological examination of the thyroid gland;
Pathophysiology	Etiology and pathogenesis of iodine deficiency disorders, hypothyroidism, thyroiditis, thyrophyma	
Pharmacology	Iodine-containing drugs, thyroid hormones, anti-inflammatory drugs;	Fill the corresponding prescriptions
Radiology	ultrasonography, scintigraphy, radiodiagnosis of thyroid disease	Evaluate results of corresponding examinations
Subjects that will be studied later		

Internal diseases	Changes of the internal organs in the event of thyroid diseases, their differential diagnostics, basic treatment methods;	Carry out clinical examination of a patient, palpate the thyroid gland; assign the necessary diagnostic examinations and

Pediatrics	Peculiarities of the course of the pathology of the thyroid gland at an early age;	and consulting of associated medical specialists to verify the diagnosis, interpret their results (conclusions).
Surgery	Surgical management of thyroid disease	
Obstetrics & Gynecology	Peculiarities of the course of thyroid diseases across pregnancy, their influence on fetal development;	
Neurology, psychiatry	psychoneurological symptoms of thyroid disease	
Intrasubject integration	Modern methods of clinical, laboratory and instrumental examination of patients with hormonal diseases.	Carry out differential diagnosis of thyroid diseases with other pathology, assign adequate treatment

5. Training subjects:

- Definition and epidemiology of iodine deficiency disorders.
- Pathogenesis, clinical manifestations and diagnosis of endemic goitre.
- Modern approaches to endemic goitre treatment.
- Clinical aspects of other iodine deficiency disorders.
- Iodine deficiency disorders prevention: forms, methods, control.
- Sporadic goitre: etiology, pathogenesis, clinical manifestations, diagnostics, treatment.
- Definition, epidemiology and classification of hypothyroidism.
- Etiology and pathogenesis of different types of hypothyroidism.

- Clinical manifestations and diagnostic criteria of thyroid hypofunction; atypical hypothyroidism.
- Principles of hypothyroidism treatment across different age groups.
- Congenital hypothyroidism: pathogenesis, the neonatal screening, peculiarities of substitution therapy.
- Clinical and morphological classification, etiology, pathogenesis, clinical

manifestations, diagnostics, treatment of thyroiditis.

- Etiology, pathogenesis, clinical picture, diagnosis of face different types;
- Epidemiology, causative factor, morphological classification of thyroid tumors.
- Clinical picture of different thyroid cancer types.
- Possibilities and restrictions of the thyroid cancer diagnosis methods.
- Modern methods to the thyroid cancer treatment.
- Regular medical check-up of patients with thyroid cancer. Prognosis.

6. Plan and organizational structure of the class

(see «Introduction»)

7. Materials and methodological support of the class.

7.1. Materials for the preparatory phase of the class

Tests (α=2)

- Within the framework of neonatal screening program, a newborn baby was diagnosed with hypothyroidism. Since what age the baby may be assigned the substitution therapy?
  - Since the 1st month of the new baby's life.
  - Since the 3d month of the new baby's life.
  - Since the 6th month of the new baby's life.
  - After termination of breastfeeding.
  - Transfer the baby into the artificial feeding, and then prescribe Levothyroxine.

- Define the most informative laboratory parameter for the diagnosis of primary hypothyroidism:
  - Thyrotropic hormone
  - General thyroxin.

C. Free thyroxin.
D. Triiodothyronine.
E. Antibodies level to thyroid peroxidase.

- To the characteristic symptoms of hypothyroidism refer all but…

A. Bodyweight gain
B. Warm skin
C. Emotional disequilibrium
D. Tachycardia

E. Exophthalmos

- Choose the drug that does not inhibit thyroid hormone synthesis:
- Thiamazolum
- Propylthiouracil
- High iodine doses
- Carbimazole
- Dexamethasone

7.2. Learning materials for the main stage of the lesson:

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

Grade of enlargement	**Characteristics:**
0	No goitre (the volume of elements does move beyond the size of distal phalanx of the patient's thumb);
Ia	Goitre is detected only on palpation and is invisible when the patient fully tilts the head backwards;
Ib	Palpable goitre, however, it is visible only when the patient fully tilts the head backwards; (including the nodule in the event of enlargement of the thyroid gland);
II	Palpable goitre. It is visible with the head in a normal position
III	A large goitre that is visible a distance of 5 m and more

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

Grade of enlargement	**Characteristics:**
0	No goitre
I	Palpable, however, invisible goitre
II	Palpable and visible goitre

Laboratory methods of study of the thyroid gland are divided into the following groups:
Markers of the functional status: thyrotropic hormone (TSH), general thyroxin, free thyroxin, general triiodothyronine, free triiodothyronine •
Markers for the autoimmune disease: anti-thyroglobulin autoantibodies, anti-thyroid peroxidase autoantibodies, TSH receptor antibodies •
Markers for oncologic pathology: thyroglobulin, calcitonin

Diagnostic value of thyroid hormone levels

thyroid function	fT_3	fT_4	TSH
Preserved (euthyroidism)	Normal	Normal	Normal
Subclinical dysfunction	Normal	Normal	• elevated (subclinical hypothyroidism); • lowered (subclinical thyrotoxicosis)
Manifest thyrotoxicosis	Elevated	Elevated	Lowered
Manifes hypothyroidism	Lowered/ normal	Lowered	• elevated (primary hypothyroidism); • lowered/normal (secondary or tertiary hypothyroidism)

Iodine consumption rate (the International Council for Control of Iodine Deficiency Disorders (ICCIDD), 2005)

Contingent	The need for iodine, mcg/day
Babies at the age of 0 – 59 months	90
Children at the age of 6 - 12	120
Children over 12 and adults	150
Women across pregnancy and lactating women	250

Hypothyroidism –a clinical syndrome caused by a long-term, persistent deficiency of thyroid hormones in the human body or the decrease of its biological effect in tissues.

Classification.

According to the level of lesion:

1. Primary (thyrogenic)
2. Secondary (hypophyseal), tertiary (hypothalamic)
   a. panhypopituitarism
   b. isolated TSH deficiency I
   c. disorders of the hypothalamus and pituitary gland
3. Tissue (transport, peripheral) – resistant to thyroid hormones; hypothyroidism in the event of nephrotic syndrome.

By origin:

1. Congenital:

a. Developmental abnormalities of the thyroid gland: dysgenesis (agenesia, hypoplasia, dystopia, ectopia);
b. dishormonosis: congenital enzymopathies, accompanied by thyroid hormone biosynthesis disorders; impaired sensitivity TSH;
c. congenital panhypopituitarism;
d. transient;
- iatrogenic;
- caused by mother's thyroid-blocking antibodies;
- idiopathic

5. Acquired:
- thyroiditis, (autoimmune thyroiditis, hypothyroid phase, subacute viral),
- postprocedure (thyroid surgery),
-iatrogenic (radioiodine therapy and thyrostatic drugs, thyrostatic drugs) - endemic goitre

According to the course:
1. transient
2. subclinical (minimal thyroid deficiency)
3. manifest

According to the compensation status:
1. Compensated
2.Decompensated

Complications: thyrogenic nanism, encephalopathy, cretinism, polyneuropathy, myopathy, hypothyreoid coma, sexual development disorders (delayed puberty or precocious sexual development) etc.

Diagnostic criteria:
1. Clinical:
- different stages of cognitive decline
- stunted growth (thyrogenic nanism)
- delayed puberty or precocious sexual development
- dry and pale skin
- fragile, dry hair
- swollen face, limbs, tongue
- brachycardia

2. Paraclinical tests:
- Complete blood count: anemia, sometimes accelerated erythrocyte sedimentation rate)
- Increase in cholesterol level of blood, b- lipoproteid
- Electrocardiography (ECG): sinus bradycardia (during the first months of life pulse

rate may be normal), voltage decrease, conduction delay, systolic lengthening
Thyroid visualization during its ultrasound investigation.
- Hormonal diagnostics:
- In the event of subclinical hypothyroidism: high TSH level
(higher than 2,5 mU/l, however, lower than 10 mU/l) with the normal level of free thyroxin and absence of clinical symptomatology.
- In the event of manifest hypothyroidism: high TSH level – higher than 10 mU/l and decrease of free thyroxin; - In the event of secondary hypothyroidism the level of TSH is within normal limits or decreased, a decrease of free thyroxin.

- X-Rays of the hands: delayed skeletal maturation, epiphyseal dysgenesis – To diagnosticate autoimmune thyroiditis as the reason for hypothyroidism: anti-thyroid peroxidase antibodies (TPOAb) – 2-3 times higher than the upper normal level.

Prevention of iodine-deficient conditions and treatment of endemic goitre

Types	Means
Prevention:	
Mass	Table salt iodizing (40 g of potassium iodate per 1 t of salt); as an alternative – bread, water, oil iodizing;
Individual	Prescription of drugs containing iodine to the population groups or private persons with increased demand for iodine: children, teenagers, pregnant and breastfeeding women; carried out by taking medicines containing potassium iodide (Iodid-Farmak, Jodomarin), multivitamin preparations that meet the daily demand for iodine.
Treatment	
drug	• drugs containing iodine: children – 100 mcg/day, teenagers and adults (< 45) – 200–400 mcg/day for 6-12 months; • drugs containing levothyroxine (L-thyroxin, Euthyrox) in suppressive regimen providing the level of TSH • blood plasma 0,2–0.5 mI U/L; • thyroid hormone preparations in combination with iodides (patient-specific).
surgical	In the event of large goitre; mechanical compression of neck; nodular types of goitre, that do not respond to drug treatment under substantiated suspicion in malignant change.

Nodular/multinodular nontoxic goitre

Morphological classification	• colloid proliferative goitre; • follicular adenoma; • adenocarcinoma; • cystic lesion; • focal thyroid lesion.
Main clinical manifestations	Often absent. There may be observed neck discomfort, the sensation of a foreign body,visible swelling.
Complications	• compression syndrome with other organs functional disorders; • malignant change; • development of Iodide-induced thyrotoxicosis (in regions that were affected by iodine deficiency).
Diagnostics	• ultrasound investigation, including Doppler sonography; • US-guided FNAB–indicated with nodules > 1 cm; • Definition of TSH, if needed fT_4, fT_3 ; • scintigraphy – at suspicion on functional autonomy of the thyroid gland; • X-ray radiography, computed tomography, magnetic resonance examination – in the presence of compression syndrome.
Treatment policy	• case follow-up – control every ≈ 6 (six) months (ultrasound investigation, where required –in. methods); • suppressive therapy L-T 4 with a view to 2,0-2,5 mcg/kg/day, which in the regions affected by iodine deficiency it is worth combining with drugs containing iodine (as in the event of an endemic goitre); low efficiency in general; • surgical treatment – as indicated (see above).

Thyroiditis. Classification (clinical and morphological)

Acute thyroiditis	• *purulent;* • *nonpurulent.*

Subacute thyroiditis	• granulomatous thyroiditis;
	• lymphocyte thyroiditis:
	  • post-partum thyreoiditis;
	  • spontaneous thyroiditis.

Chronic thyroiditis	• autoimmune (lymphocyte): • hypertrophic (Hashimoto thyroiditis); • Ord's thyroiditis (Idiopathic hypothyroidism); • focal; • fibrous (Riedel's thyroiditis (also known as Riedel struma)); • specific (tuberculosis, sarcoidosis etc).

Differential diagnosis for thyroiditis

	Acute purulent	Subacute granulomatous	Subacute lymphocytic	Autoimmune	
				hypertrophic	Ord's thyroiditis
Beginning	Acute	Acute	Acute	Gradual	Gradual
Neck pain	+++	+++	–	+/–	–
Hyperthermia	+++	++	–	–	–
Thyroid gland	Enlarged, contains, indurated acutely painful zones	Enlarged, painful, indurated, often one-sided	More often diffusely enlarged, indurated, painless	diffusely enlarged, indurated, pseudo-nodular	Does not palpate
Functional disorder	–	+++	+++	++	+++
Antithyroid antibodies	–	+	++	+++	++
Cytological Findings	Granulocyte	Multinucleate giant cells	Lymphocytes	Lymphocytes	–

Notes: (+) – seldom, (++) – often, (+++) – very often.

Classification of thyrotoxicosis

Etiology	1. Thyrotoxicosis, associated with the hyperproduction of thyroid hormones of the thyroid gland (hyperthyroidism): • Graves-Basedow disease (diffuse toxic goitre); • functional autonomy of the thyroid gland (toxic thyroid nodule). 2. Thyrotoxicosis, associated with the hyperproduction of thyroid hormones outside the thyroid gland: • hormone-responsive thyroid cancer metastasis. 3. Thyrotoxicosis, not associated with the hyperproduction of thyroid hormones: • Drug-induced thyrotoxicosis; • thyrotoxic phase of destructive thyroiditis (subacute, post-partum).
Severity	1. Subclinical (hidden, latent) – random level of TSH is lowered, the concentrations of fT_4 and fT_3 are within normal limits; clinical manifestations are generally absent. 2. Manifest – concentration of fT_4 and/or fT_3 is elevated; manifestation range varies from oligosymptomatic to the comprehensive clinical picture. 3. Complicated, including thyrotoxic crisis.

Stages	• compensation; • subcompensation; • decompensation.

Frequency of clinical signs in patients with diffuse toxic goitre

Symptom	%	Symptom	%
Goitre	85–100	Ocular symptoms	50–70
Tachycardia	85–100	Muscle weakness	60–80
Irritability	80–95	Hyperkinesis	50–80
Tremor	70–90	Increased appetite	40–60
Sweaty warm hands	60–80	Infiltrative ophthalmopathy	30–50
Hyperhidrosis	70–90	Frequent rectal discharge	20–40
Hypersensitivity to heat	70–80	Atrial fibrillation	2–10
Systolic blood pressure increase	60–80	Infiltrative dermopathy	2–3
Fatigue	80–90	Decreased appetite	≈ 23
Body weight loss	60–80	Dysmenorrhea	3–5
Thyroid bruit heard over the systolic	60–70	Gynecomastia	≈ 5
Dyspnea	60–70	Body weight gain	≈ 5

Thyroid Eye Disease

Symptoms	Signs
Dalrymple	wide open palpebral fissure
Graefe	the lagging of the upper eyelid on the downward rotation of the eye
Stellwag	sign of infrequent or incomplete blinking
Mebius	rare congenital neurological disorder
Kocher	upper eyelid retraction, a strip of sclera between eyelid margin and iris
Krause	The intensity of brightness of the eye

Treatment methods for diffuse toxic goitre

Treatment methods	Indications
Medicamentous: *Pathogenetic therapy* Antithyroid drugs (thyrostatic drugs)	• always taken: either as an independent method or as a preparation for radical intervention.
symptomatic medication	
β- adrenoceptor blocking agent	• usually taken along with thyrostatic drugs.
High doses of iodine	• preoperative preparation; • treatment of the thyrotoxic crisis.

Glucocorticoids	• severe course of the disease, insufficient response to thyrostatic drugs; • preoperative preparation; • endocrine ophthalmopathy.
Sedating	• taken almost always.
Surgical	• a large goitre; • compression syndrome; • substernal goitre; • severe forms of thyrotoxicosis, complicated by atrial fibrillation; • absence of steady compensation for medicamentous therapy; • liability to recurrence; • thyrostatic medication intolerance; • presence of thyroid nodule > 2 cm.
Radioactive iodine therapy	• age over 40 (in the USA and some countries of Europe over 18); • middle and severe course with low efficiency of medicamentous therapy; • severe complication or concomitant pathology, which substantially increases the risk of surgical intervention; • postsurgical recurrence of toxic goitre; • patient's refusal from surgical treatment;

Thyrostatic therapy – practical recommendations

Conditions	Means	Goal
Initial treatment • moderate clinical activity; Control every 2–4 weeks.	• thiamazol 10–30 mg/day; • carbimazole 15–40 mg/day; • propylthiouracil 100–300 mg/day.	Compensation (normalization of concentrations of fT_4 and fT_3).

• High clinical activity; Control every 2–4 weeks.	• thiamazol 20–40 mg/day; • carbimazole 30–60 mg/day; • propylthiouracil 300–500 mg/day.	Compensation (normalization of concentrations of fT_4 and fT_3).
Maintenance therapy (12–18 months); Control every 6–12 weeks.	• thiamazol 2,5–10 mg/day; • carbimazole 5–15 mg/day; • propylthiouracil 50–100 mg/day.	Persistent euthyroidism (TSH ≈ 0,3–1,0 mIU/L).
Cessation of therapy • remission • recurrence	Control every 3–4 months. Curative treatment.	Persistent euthyroidism (TSH ≈ 0,3–2,0 mIU/L).

Peculiarities of the clinical course of the morphological variant of thyroid cancer

Histological variant	Clinical features
Papillary	is the most common (≈ 65–80%). It progresses slowly. It often takes many years. It is multifocal in 25-30% of cases. It develops predominantly among young patients, in particular, children. Metastasizing occurs in a mainly lymphogenic way (40–50% of observations),first and foremost in cervical nodes.
Follicular	It is second in terms of occurrence (10–25%). It is clinically rather more aggressive, however, its course is usually long-term. It usually occurs among middle-aged people (maximum 50 years old). Predominantly hematogenous spread (11–20%, primarily in bones) and seldom in regional lymph nodes (5–6%).
Poorly differentiated	Frequency 4–7%. According to the morphological structure, clinical course and prognosis it falls in between differentiated and anaplastic types of thyroid cancer. It mainly occurs at the age of over 50, often infiltrates into adjacent tissues and is metastasizing (30–50%).
Medullary	Frequency 5–10%. There are two types of this tumor – sporadic (70–80%) and familial (20–30%). It secretes large quantities of calcitonin as well as other bioactive substances: serotonin, prostaglandin, corticotropin-like peptides etc. According to the degree of malignancy, the tumor approximates poorly differentiated thyroid cancer.

Anaplastic	It seldom occurs (1–5%). In most cases at an elderly age. It is fast-growing, early infiltrates into the adjacent organs, which is accompanied by the development of compression syndrome, wide-spreading. Only single patients live more than 6 months.

Diagnosis and treatment of thyroid cancer

Diagnosis	• ultrasound investigation of the thyroid gland and regional lymph node basins; • US-guided FNAB; • Definition of calcitonin, TSH, fT_4 , fT_3 where required ; • X-ray radiography, computed tomography (CT), magnetic resonance examination (MRT) – in the event of compression syndrome.

Differential diagnostics	Other diseases that manifest as focal abnormalities (their clinical course is the same as the course of a nodular goitre).
Treatment	In the event of highly-differentiated: thyroidectomy + radioiodine therapy + suppressive therapy L-T_4. In the event of other types: thyroidectomy (sometimes widened) + modified cervical lymphadenectomy, sometimes – External beam radiation and/or chemotherapy (partial effect).
MonitoringМоніторинг	• Neck ultrasound; • Determination of thyroglobulin (differentiated cancer); • Determination of calcitonin and/or carcinoembryonic antigen (CEA) (medullary thyroid cancer); • Control of TSH, if necessary fT_4 , fT_3 ; • scintigraphy – to verify the residual thyroid tissue and distant metastases (differentiated cancer); • if necessary – other examinations.

7.3. Control materials for the final stage of the class

Assignments (α=3)

1.A man, aged 45 years old visited an endocrinologist. He was complaining about a feeling of cervical compression at the left. Clinician-observed: enlarged thyroid caused by enlargement at the left in the place there was palpated a nondistinctively separated solid painless nodular lump 3 cm in diameter. There was carried out a fine needle biopsy of the node. A punctate contained polygonal and spindle tumor cells. Immunocytochemically– negative response to thyroglobulin and positive response to calcitonin. Establish the diagnosis.

A. Papillary carcinoma.
B. Follicular carcinoma.
C. Medullary carcinoma
D. Anaplastic thyroid cancer

E. Tumors of other histogeneses.

6. A patient S., aged 20 years old is living in a mountainous area. She was detected the first stage diffuse enlargement of the thyroid. Laboratorially: TSH 2,2 mIU/L (N: 0,3–4,0), free thyroxin 1,36 ng / dl (N: 0,93–1,7), anti-TPO < 10 IU/mL (N:< 100). What treatment approach in this particular case is the most pathogenetically substantiated?

- Levothyroxine

B. Potassium iodide
C. Levothyroxine + potassium iodide
D. Surgical treatment
E. Antioxidant

7. A man, aged 58 years old, in the course of palpation in the right lobe of the thyroid gland was detected an indefinite nodular mass Ø 3 in diameter, with dense consistency. In the course of ultrasound examination, it was detected that it has a decreased echogenicity, indistinct boundaries, microcalcifications and intensified blood flow. What is the most provisional diagnosis?

A. nodular nontoxic goitre.
B. thyroid cancer
C. nodular toxic goitre
D. subacute thyroiditis
E. acute non-purulent thyroiditis

8. A patient S., aged 40 years old was detected the second stage diffuse euthyroid goitre without compression symptoms. There are no intercurrent diseases. Which of the following treatment methods is the most reasonable?

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

9. A patient S., aged 52 years old is complaining about body weight gain, weakness,

faecal retention, memory impairment. Objective findings: dry skin, mild facial and limb swelling. Heart rate 60 beats per minute, arterial blood pressure 110/60 millimetres of

mercury. Ultrasound investigation: the thyroid gland volume2,6 c.m., decreaed echogenicity, inhomogeneous structure. Laboratorially: TSH 23,2 mIU/L (N: 0,3–4,0), thyroglobulin (TG) and thyroperoxidase (TPO) antibodies are moderately increased. It is the most probable that the patient has been suffering from

A. endemic goitre, euthyroidism
B. autoimmune thyroiditis (Riedel thyroiditis), hypothyroidism
C. autoimmune thyroiditis (atrophic), hypothyroidism
D. hypothyroidism caused by iodine deficiency
E. Riedel thyroiditis

10. A patient is complaining about annoyance, hyperhidrosis, hand tremor, heartbeats, bodyweight loss with preserved appetite. Enlarged thyroid gland up to the second stage, elastic, painless. The following symptomatology is best matched to:

A. diffuse Toxic Goitre
B. neurasthenia
C. autoimmune thyroiditis
D. hypothyroidism
E. hypoparathyroidism

Assignment 1. A woman, aged 44 years old is complaining about apathy, slowness, memory impairment, chills, dry skin, fecal retention, facial swelling. She has been considering herself ill for a year. Objective findings: temperature 36,0°C, heart rate – 56 beats per minute, arterial blood pressure – 110/80 mm Hg ECG: voltage reduction, a decrease of P wave and flattening of T wave. Enlarged thyroid gland because of enlargement of all the regions is visible with the normal position of the neck. It is moderately indurated and non-homogenous, painless. Laboratory examination: free thyroxin – 7,5 pmol/l (N: 10–23), TSH – 16,4 mIU/L (N: 0,3–4,0), TPO antibodies – 640 mIU/L (N: <100). Ultrasound investigation: diffusely decreased echogenicity, markedly inhomogeneous structure, with no tissue masses.

- Formulate the diagnosis (nosology, the nature of structural and diffuse changes of the thyroid gland).
- Define and explain the optimal treatment policy.

Assignment 2. A patient, aged 35 years old in the course of medical examination has been detected a nodule in the right thyroid lobe. No complaints. Negative family history. From the past medical history, it is known that as a teenager he was undergoing numerous X-ray examinations because of a cervical spine injury.

Objective findings: the lower part of the right lobe takes the nodular mass ≈ 2,5 cm in diameter. It has a dense consistency, is nodular, movable and painless. The left lobe is

not enlarged. It is soft and homogeneous. Cervical glands do not palpate.

- What is the most provisional diagnosis?
- What test he must be referred for and which one is the most informative?

Protocol № 2 clinical considerations for a patient

Patient's full name _____

Age _____ Occupation_____

patient's complaints_____

past medical history_____

patient's life history_____

Results of physical examination of patients: ___

Provisional diagnosis: _____

What diseases may require the performance of c

Examination plan: _____

Results of laboratory and instrumental examinat

substantiation of clinical diagnosis: _____

Clinical diagnosis: _____
Prior disease: _____

Complications:

Intercurrent diseases: _____

Prognosis:

Treatment: _____

Medicamentous therapy: _____

Marks of mastering prac

Order No.	Skills and procedures
1.	Practical skills
1.1.	Know how to interview, perform a pl examination of a patient with thyroid
1.2.	Be able to analyze the laboratory and examination data in patients with thy
1.3.	Be able to assign therapy to a patient thyrotoxicosis syndrome, hypothyroi event of thyroid and iodine deficienc
2.	Medical emergencies
2.1.	Be able to render aid in the event crisis

3.Management of a patient with hyperglycemic (ketoacidotic), hypoglycemic comas, thyrotoxic crisis, acute adrenal insufficiency.

1. Topicality**:** the knowledge of the peculiarities of the course and treatment of medical emergencies in the event of diabetes mellitus is mandatory for the physicians independent of the discipline they are specialized in. The reasons for the occurrence and development of acute complications of diabetes include acute disorders of the vital functions of the body like respiratory homeostasis, blood circulation etc. These disorders threaten life and require emergency assistance. Thus the study of comatose states in patients with diabetes mellitus is of the most immediate interest in future doctor training.

Treatment of diabetes mellitus with insulin and oral blood sugar-lowering drugs is often accompanied by the occurrence of hypoglycemic states.

The physicians must be acutely aware of the signs and symptoms of hypoglycemia and promptly assist in the occurrence of hypoglycemic states independent of their origin.
The problem of timely diagnosis and provision of emergency assistance in the event of hypoglycemic states is topical as long as the latter if untreated lead to high mortality rates, post hypoglycemic encephalopathy and disability.

2. Learning goal.

Familiarize with epidemiological studies of diabetes mellitus in Ukraine and the world (α=1)

The student must know (α=2):

- The main clinical signs of ketoacidosis and ketoacidotic coma.
- Pathogenesis of the main symptoms of ketoacidosis and ketoacidotic coma.
- Modern diagnostic methods and differential diagnosis of ketoacidosis and ketoacidotic coma
- Classification of medical emergencies
- Reasons and pathogenesis of hypoglycemic state and coma
- Clinical manifestation of hypoglycemia and hypoglycemic coma
- Hypoglycemia and hypoglycemic coma treatment strategy and methods in patients with diabetes mellitus

The student must (α=3):

- Know the methods of establishing the diagnosis and data analysis, received during the interview and direct examination of patients with hypoglycemic states.
- Assign the necessary tests to identify hypoglycemic states and hypoglycemic coma;
- Perform diagnosis and differential diagnosis of hypoglycemic states and hypoglycemic coma;
- Decide upon the treatment strategy and prevention of hypoglycemia, hypoglycemic coma in patients with diabetes mellitus;

3. Educational goal.

Form the sense of responsibility and attract the attention of students, who will become physicians, to the timeliness of detecting and correctness of treatment of the disease.

4. Content of the training subject:

- Etiology, the pathogenesis of the diabetic macro – and microangiopathy, neuropathy, the biological effect of hyperglycemia.
- Classification of diabetic angiopathies.
- Classification of diabetic neuropathies.

- The concept of diabetic foot disease (classification, diagnostic and treatment approaches).
- Clinical manifestations of vascular events caused by diabetes mellitus
- Laboratory and instrumental diagnosis of diabetic angio- and neuropathies.

- Diabetic angio- and neuropathies treatment methods.
- Methods preventing the development of chronic complications caused by diabetes mellitus.

Training goal: teach the students how to diagnose the hyperglycemic (ketoacidotic) coma and precoma using the example of a clinical discussion of patients with ketoacidosis, perform differential diagnosis with hyperosmolar and lactic acidosis comas, use modern diagnostic standards for the diabetic ketoacidotic coma treatment.

Differential diagnosis of comas

Clinical of laboratory signs	Hyperglycemic (ketoacidosis)	Hypoglycemic coma
Age	**Different**	**Different**
Past medical history	First detected diabetes mellitus, diet violation, disturbance of insulin therapy regimen, infection, stress	insulin overdose, oral sugar-lowering drugs, strenuous physical activity, hunger
Precursor	weakness, nausea, thirst, vomiting, dry mouth, polyuria	hunger, sweatiness, tremor
Coma development	Gradual (2-3 days), against the background of concomitant pathology – 1 day rapid (minutes) Peculiarities of precoma – a gradual loss of consciousness	rapid (minutes) the agitation which develops into a coma
Temperature	normal, subfebrile	normal
Skin	dry, hyperemia, decreased turgor	wetness, normal turgor
Muscle, reflexes	reduced tone	hypersthenia
Tongue	dry	wet
Eyebulb	soft, reduced tone	normal tonus
Pupils	narrowed	dilated
Respiration	Kussmaul, acetone-odour	normal
Arterial blood pressure	reduced	norm
Heart rate	frequent	frequent

Signs of dehydration	prominent	absent
Urine output	polyuria , then oliguria	norm
Glycemia	high	low
Glycosuria	high	absent
Ketonuria	present	absent
Natriemia	norm, increased	norm
Kalemia	reduced	norm
Blood lactate	moderately increased	norm
Blood pH	reduced	norm

Basic measures in the treatment of ketoacidotic coma

Rehydration	• 1st hour – 1L isotonic sodium chloride solution; • 2nd, 3d hour – 0,L isotonic sodium chloride solution; • Then until the elimination of dehydration, 0,25-0,5L/h of isotonic sodium chloride solution
Renewal of potassium deficiency	Depends on kidney functional status and initial level of kalemia: if the potassium level is less than 3 mol/L there are transfused 3 g/h 4% of KCl solution, in the event of kalemia 3-4 mol/L – 2 g/h, in the event of kalemia 4-5 mol/L – 1,5 g/h
Insulin therapy	The initial short-acting insulin dose of 10-16 units was given intravenously as a bolus dose, further, there is administered 0.1 unit/kg/h of short-acting insulin as an intravenous bolus injection, subcutaneously insulin is introduced with the speed of 3-4 units/h only under the condition the glycemia decrease <14 mol/L and normal findings of acid-alkali balance.
Renewal of acid-alkali balance	If in an hour after performing rehydration with sol and insulin therapy shock preserves and pH remains < 7,0, bicarbonate is administered with a view to 1-2 mol/kg of body weight. Half of the dose is administered for 30 min, and the other half of the dose – within 1–2 hours. Additional administration of potassium solution is mandatory. If pH reaches > 7,0 the administration of bicarbonate ends.
Prevention of disseminated intravascular coagulation (DIC)	Heparin 2500-5000 is administered twice during the first day (prothrombin time is under control).
Treatment and prevention of contagious diseases	Broad-spectrum antibiotics are prescribed at a dose that depends on the patient's age.

Levels of hypoglycemia	**Measures**
Mild	• take 10–20 g of simple carbohydrates (1–2 slices of bread, glucose tabs, fruit juice concentrate, sugary drinks etc); • if you failed to get rid of hypoglycemia in 10-20 min, then it is necessary to test for glycemia (make sure that it is low), take 10-20 g of complex carbohydrates to avoid rebound hypoglycemia
Moderate	• 10–20 g of simple carbohydrates and 10-20 g of complex carbohydrates

Severe	• 40% glucose solution as an intravenous bolus injection from 20 to 100ml; • 1 ml of glucagon (1 mg) subcutaneously or intramuscularly; • 0,1% 1 ml of epinephrine subcutaneously; • In the event of inefficiency - as an intravenous bolus injection of 5% glucose solution until the normalization of glycemia level; • 75-100 mg of hydrocortisone or 30-60 mg of prednisolone - intravenously; • 100 mg of co-carboxylase, 5 ml of 5% ascorbic acid solution intravenously, if medically required - symptomatic agents for the performance of oxygen therapy; • In the event of a lasting coma to prevent cerebral oedema 5-10 ml of 25% magnesium sulfate solution intravenously or 15-20% Mannitol solution (0,5-1,0 h/kg) intravenously.

Basic measures in the treatment of hypoglycemic coma

Thyrotoxic crisis is a life-threatening condition that may develop in a patient with non-compensated thyrotoxicosis. It is characterized by the marked aggravation of its clinical signs and worsening of homeostasis disorders. In the absence of adequate treatment, a patient usually dies. Infections, traumas, severe diseases or surgical treatment of diffuse toxic goitre without corresponding antithyroid drugs are usually the provocative factors.

In the event of rapid deterioration in a patient's condition with hyperthyroidism it is always necessary to keep in mind a possible occurrence of the thyrotoxic crisis. Symptoms of the disease that caused the thyrotoxic crisis may come into the picture. In typical situations, the clinical course of thyrotoxic crisis is characterized by occurrence in stages.

1. Prodromal signs, which include agitation, insomnia (sleep hallucinations and other psychic dysfunctions), massive weight loss, intensification of muscle tremors and hyperhidrosis, fever, nausea and vomiting; most of them are caused by hyperactivity of the sympathoadrenal system.

2. Thyrotoxic crisis, the defining attributes of which includes a conspicuous aggravation of thyrotoxicosis symptoms, primarily on the part of nervous, cardiovascular and digestive systems, signs of dehydration, worsening multiple organ failure and development of the comatose state.

The classic clinical picture of thyrotoxic crisis is so vivid and notable that it is enough to see once to remember for the rest of your life. It includes fever (up to 38–41 °C), hyperhidrosis, severe tachycardia, cardiac insufficiency, tremor, nausea and vomiting, diarrhea, dehydration, extreme excitation, delirium or coma. In 90 % of cases of the central nervous system, disorders occur. At the first stage symptoms of motor and

psychic excitement predominate: patients are worrying, emotionally unstable (they are crying, attack, laugh), hyperactive and not goal-oriented in their behaviour, possible development of mental affection. With the progression of crisis such state changes by retardation, apathy, emotional enfeeblement, pronounced muscular weakness. It is important to remember that psychoneurological manifestations of thyrotoxic crisis have also prognostic significance, as long as their rapid progression, usually, is a premonitory symptom of comatose state. Thyrotoxic myopathy manifests as reduction of tone and rapid fatigability of the muscles of the neck, shoulder –blades, arms and legs, more seldom — face and trunk. There may be observed pains, involuntary jerks, convulsions and hypokalemic paroxysmal paralysis episodes. Excessive sweating, promptly intensifying dehydration. Symptoms on the part of the gastrointestinal tract include nausea, vomiting, decreased appetite, crampy abdominal pain, uncontrollable diarrhea and as a result - body weight loss.
Hepatomegaly and abnormal liver function tests often result from cardiac insufficiency, however, there was sometimes observed jaundice with necrosis involving hepatocytes. Heart rate (up to 140– 200 per 1 min) and

pulse pressure increases, short breath occurs. Permanent atrial fibrillation may lead to congestive heart failure among people, who did not suffer from heart diseases in the past medical history. Vascular collapse often becomes a harbinger of a patient's death.

Screening protocol, establishing the diagnosis, treatment and prevention

SECTION OF ACTIVITY	GUIDELINES FOR ACTION
Greeting	Greet and introduce yourself to a patient
Acquaintance	Collect the passport details of the patient (full name, sex, age, place of residence, place of work and occupation)
Patient's complaints at the time of examination	Define and present the details of the patient's complaints. When defining the complaints of the patient pay attention to the occurrence of: - nausea, vomiting, diarrhea); - xerosis, poor skin turgor; - hyperemia caused by heating of the human skin, febricity (a rise in the temperature of the body; frequently a symptom of infection); - severe tachycardia, low-tension pulse; - severe psychomotor agitation up to and including acute psychosis, changed for sleepiness, disorientation, semicoma; - bulbar palsy, Parkinsonism, convulsion.

Examine organs and systems.Physical examination	Define the course of the disease, examine organs and systems. 1. Availability of risk factors. In the course of the interview pay attention to the information about: - sudden stop of thyrostatic therapy; - any stresses against the background of thyrotoxicosis, which exhaust adaptive capacities of the organism: -- extreme emotional stress; -- bodily injuries, including rough palpation of the thyroid gland; -- acute infectious or noninfectious disease; -- exposure to the sun; -- hypoglycemia; -- childbirth. - radioiodine therapies (at a high dose), decompensation of thyrotoxicosis. - drug administration: -- iodine-containing, in particular, radioopaque; -- hypoglycemic; -- salicylate; -- adrenergic agonists; -- cardiac glycosides. 2. Existence of syndromes/symptoms of damage - central nervous system damage (severe psychomotor agitation up to and including acute psychosis, which is replaced with sleepiness, disorientation, semicoma); - neurological disturbance (bulbar palsy, Parkinsonism, convulsion).

Survey design	Levels of thyroid hormones, especially free ones; preprandial glycemia; values of white blood cell differential; calcium and alkaline phosphatase; total bilirubin and aminotransferases; cortisol, gases and blood pH. Blood and urine culture. Chest X-ray examination; ECG monitoring.

Laboratory and instrumental examinations	Evaluate the levels of: - thyroid hormones, especially free ones; - preprandial glycemia; - values of white blood cell differential; - calcium and alkaline phosphatase; • bilirubin and aminotransferases; - cortisol.
	Evaluate the values of: - chest X-ray examination; - ECG monitoring; - blood and urine culture; - gases and blood pH
Formulation of diagnosis	Level I thyrotoxic crisis with the dyspeptic syndrome with no evidence of central nervous system damage. Level II thyrotoxic crisis with impairment of consciousness, spatial disorientation and disorientation in time, psychotic symptoms of somnolence, stupor. Level III thyrotoxic crisis (comatose state). Nephropathy (specify the stage) Cardiac insufficiency (specify the stage according to New York Heart Association (NYHA). Cerebrovascular disease (specify). Intercurrent diseases
Treatment plan	Draw up a treatment plan, which must include pathogenetic, symptomatic, efferent therapy and preventive treatment
Managing patients with thyrotoxic crisis	

Diagnosis	Basic principles of thyrotoxic crisis development: - sudden increase of thyroid hormones concentration in the blood; - decrease of thyroid hormones - transport proteins in human serum binding, and correspondingly, the increase of the rate of free fractions (fT_4 , fT_3); - progression of suprarenal cortex insufficiency against the background of accelerated metabolism of cortisol and increased demand of the organism for corticosteroids; - dramatic increase of catecholamines effect caused by the increase of the quantity and sensitivity of adrenoreceptors; - serious abnormality of biochemical processes on the cellular level, primarily oxidational phosphorylation, which makes the consuming of energy by cells impossible, because of delivering it to the unproductive direction of excessive heat production. Provocative factors: - sudden stop of thyrostatic therapy; - any stresses against the background of thyrotoxicosis, which exhaust the adaptive capacities of the organism: extreme emotional stress; -- bodily injuries, including rough palpation of the thyroid gland; -- acute infectious or noninfectious disease; -- exposure to the sun; -- hypoglycemia; -- childbirth. - radioiodine therapies (at a high dose), decompensation of thyrotoxicosis. - drug administration: -- iodine-containing, in particular, radioopaque; -- hypoglycemic; -- salicylate; -- adrenergic agonists; -- cardiac glycosides. 1. Clinical picture. Main syndromes:

	- dyspeptic (nausea, vomiting, diarrhea); - dehydration (xerosis, poor skin turgor); - overproduction of heat (hyperemia caused by heating of the human skin, febricity); - cardiovascular collapse (against the background of severe tachycardia, the pulse of poor volume there occurs a collapse, possible pulmonary edema); - visceropathy (hepatodystrophy with jaundice development, myocardiodystrophy with occurrence of arrhythmia); - injury of the central nervous system (sudden psychomotor agitation up to and including acute psychosis, changed for sleepiness, disorientation, semicoma); - neurological disturbances (bulbar palsy, Parkinsonism, convulsion). 2. Complete blood count: - left-shifted leukocytosis in WBC differential. 3. Biochemical blood assay: - increase of thyroid hormones concentration, especially free ones, in serum, however, they do not differ fundamentally from those that are observed in the event of uncomplicated thyrotoxicosis. Moreover, in the event of intercurrent severe diseases these figures may be either normal or even decreased (Low-T3-Syndrom); - calcium and alkaline phosphatase level increase; - increase in figures of bilirubin and aminotransferases; - cortisol level increase, which is typical for severe stress. - moderate hyperglycemia.

Adrenal crisis (Friderichsen-Waterhouse syndrome)

Etiology: adrenal crisis may be caused by acute thrombosis or adrenal vascular embolism, adrenal hemorrhage.

It is usually a complication of severe infection (meningococcaemia, streptococcus (pneumococcus) or staphylococcus bacteria, diphtheria, poliomyelitis), some systemic diseases (periarteritis nodosa, systemic lupus erythematosus). Systemic suprarenal cortex hemorrhage may occur during the complicated delivery, in the event of acute disseminated intravascular coagulation syndrome. Its course may have a form of Addisonian crisis – acute decompensation of chronic primary and secondary suprarenal gland inefficiency, congenital dysfunction of the suprarenal cortex (congenital adrenal hyperplasia).

Clinical variants of the course of acute adrenal insufficiency:

1. Cardiovascular – predominates collapse, hypotonia, manifestations of cardiovascular inefficiency: cyanose, hypothermia, cardiac dullness, the pulse of poor volume.

2. Intestinal – food refusal, nausea, vomiting (often continuous), diarrhea, abdominal extended spastic pain, symptoms of acute abdomen.

3. Neuropsychic – adynamia, asthenia, depression, delirium with visual hallucinations. Possible meningeal symptoms, convulsions similar to epileptic seizures. There gradually occurs an impairment of consciousness: retardation, brown-out, stupor. It is caused by cerebral edema development. Waterhouse–Friderichsen syndrome rapidly develops, in some hours, in a flash.

Diagnostic Criteria:

1. Electrolyte disturbance: hyperkalemia more than 5 mmol/L, hyponatremia less than 140 mmol/L, hypochloremia less than 90 mmol/L. The sodium-potassium correlation exceeds 20.
2. Hormonal imbalances : cortisol and aldosterone level decrease with aldosterone level increase. Because of the immediate development of the acute state there is usually no time to define the hormone level.
3.Changes in general clinical analysis: leucocytosis, eosinophilia, increased hematoglobulin level, hypoglycemia. Ketonuria, proteinuria, cylindruria (hyaline, granular casts), leucocytosis, microhematuria
4. Signs of hyperkalemia according to estimates of ECG.

Waterhouse–Friderichsen syndrome treatment:

1. Massive corticosteroid therapy.
2. Intravenous infusion therapy

3. Etiotropic treatment – antibacterial, antitoxic.
4. Symptomatic treatment – cardioprotectors, hepatoprotective agents, vitamin, sedating and other medication if medically required.

Control materials for the final stage of the class:

Assignments (α=3)

1. A patient was taken by an ambulance vehicle to the resuscitation department unconscious. There was detected a diabetes mellitus patient history. Stertorous Kussmaul's respiration, acetone breath, dry skin, decreased turgor, pinched face, periosteal reflexes are absent, sunken eyes. Blood contains lactic acids 1,2 mmol/L (norm 0,62-1,3 mmol/L), glycemia 29 mmol/L. The development of what emergency may be suspected?

A. Lactic acidosis a.
B. Hyperosmolar coma
C. Hypoglycemic coma
D. Ketoacidotic coma.
E. Uremic coma.

2. In the life of a patient aged 40 years old, suffering from a severe form of type 1 diabetes mellitus occurred decompensation, which was accompanied by the development of ketoacidosis. Metabolic diseases were treated with intravenous administration of small amounts of rapid-acting insulin and isotonic sodium chloride solution. In an hour the patient started suffering from headache, sweatiness, heart disorders. Blood sugar – 2,8 mmol/L, content of sodium - 140 mmol/L. What caused such a state?

A. Hyperhydration
B. Hypokalemia
C. Ketoacidotic intoxication.
D. Hyponatremia
E. Hypoglycemia

3. A man, aged 36 years old lost consciousness in the street. He was detected diabetes mellitus patient history. Alcohol breathe. Skin cover is excessively wet, warm. Arterial blood pressure – 140/90 mm Hg, convulsive reflexes. Shallow breathing, preserved eyeglobe tone, enlarged pupils, hyperreflexia. What medical assistance must be provided?

A. Subcutaneous administration of short-acting insulin 10 units.
B. Intravenous stream introduction of 40-80 ml of 40% glucose solution.
C. Intravenous administration of short-acting insulin 10 units.
D. Intravenous stream introduction of 100-120 ml of 40% glucose solution.
E. Intravenous drip-feed introduction of 500 ml of 5 % glucose solution.

4.A patient was performed an operation because of diffuse toxic goitre. Before the operation the heart rate - 96 beats per minute, arterial blood pressure - 125/70 mm Hg. On the second day there occurred a breakdown in health: the patient was excited, her consciousness was clouded, palpitation, excessive sweating, vomiting. The heart rate 166 beats per minute, atrial fibrillation. Arterial blood pressure 80/40 mm Hg. Temperature 39^0C.
What is the most provisional diagnosis?

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

5. A patient, K., aged 25 years old, is complaining about diarrhea, poor appetite and increase of the demand for salt, sleeping disorder, lack of conversation with friends who are absent at this time. Objective findings: brown skin with hyperpigmentation on elbows and knees; arterial blood pressure 75/40 mm Hg, heart rate 106 beats per minute. A boy suffers from physical and sexual development delay. Natrium level – 126 mmol/L, chlorides 74 mmol/L, cortisol 80 nmol/L (N 130 – 360).
What is the most provisional diagnosis?

A. Chronic adrenal insufficiency.
B. Acute adrenal insufficiency.
C. Dietary deficiency.
D. Acute pancreatitis.
E. Acute cholecystitis

6. A patient with meningococcal encephalomeningitis suddenly started suffering from a decrease of arterial blood pressure, resistance to sympathomimetics, brachycardia, nausea, vomiting. What is the most provisional diagnosis?

A. Acute adrenal insufficiency (Friderichsen-Waterhouse syndrome)
B. Internal bleeding
C. Food toxicoinfection
D. Addisonian crisis (disease)
E. Complete atrioventricular block

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