PATHOPHYSIOLOGY OF THE ORGANS AND SYSTEMS

PRACTICAL PART

Minsk BSMU 2024

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
КАФЕДРА ПАТОЛОГИЧЕСКОЙ ФИЗИОЛОГИИ

ПАТОФИЗИОЛОГИЯ ОРГАНОВ И СИСТЕМ

PATHOPHYSIOLOGY OF THE ORGANS AND SYSTEMS

Практикум

Минск БГМУ 2024

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А в т о р ы: Ф. И. Висмонт, С. А. Жадан, С. Н. Чепелев, Е. Н. Чепелева, Е. В. Переверзева, Т. В. Абакумова

Р е ц е н з е н т ы: д-р мед. наук, проф. каф. нормальной физиологии Белорусского государственного медицинского университета И. Н. Семененя; каф. патологической физиологии Витебского государственного ордена Дружбы народов медицинского университета

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Предназначен для студентов 3-го курса лечебного факультета, обучающихся на английском языке, для самостоятельной подготовки к занятиям, выполнения и оформления лабораторных работ.

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ABBREVIATIONS

ABB — acid-base balance
ADH — antidiuretic hormone
ADP — adenosine diphosphate
ALAT — alanine aminotransferase
APTT — activated partial thromboplastin time
ARF — acute renal failure
AsAT — asparagineaminotransferase
ATP — adenosine triphosphate
BAS — biologically active substances
BP — blood pressure
BT — bleeding time
CBC — complete blood count
CBV — circulating blood volume
CCF — chronic circulatory failure
CHH — compensatory hyperfunction of the heart
CRF — cronic renal failure
DIC — disseminated intravascular coagulation
DNA — deoxyribonucleic acid
ECG — electrocardiogram
EFP — effective filtration pressure
FDPs / Fg — degradation products of fibrin / fibrinogen
FRC — functional residual capacity
Gl-6-FDG — glucose-6-phosphate dehydrogenase
Gl-6-FDG — glucose-6-phosphate dehydrogenase
GTP — glutamine transpeptidase
HR — heart rate
HUS — hemolytic uremic syndrome
IHD — ischemic heart disease
INR — International Normalized Ratio
ITP — idiopathic thrombocytopenic purpura
LPO — lipid peroxidation process
MCV — mean cellular volume
MVV — maximal voluntary ventilation
NSI — nuclear shift index
PPP — pentose phosphate pathway
PT — prothrombin time
PTI — prothrombin index
RAAS — renin angiotensin aldosterone system
RR — respiration rate
RVT — right ventricular type
SAS — sympathoadrenal system
SFMC — soluble complexes of fibrin monomers
TLC — total lung capacity
TT — thrombin time
TTP — thrombotic thrombocytopenic purpura
VC — vital capacity of the lungs
VE — minute ventilation
WBCs — white blood cells
WHO — World Health Organization

LESSON 1. PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM. TYPICAL FORMS OF PATHOLOGY AND REACTIVE CHANGES IN THE ERYTHROCYTIC SYSTEM

Date: «____» _____ 20__

The purpose of the Lesson: to discuss the types of erythropoiesis and peculiarities of its impairment, to study basic morphofunctional peculiarities of erythrocytes and hemoglobin in pathology; to study etiology and pathogenesis of the most common anemias and erythrocytosis, blood pattern in this pathology.

Tasks:

– To get acquainted with general laws, types and basic impairments of blood formation (hemopoiesis).

– To study morphofunctional peculiarities of erythrocytes, hemoglobin and the character of peripheral blood in various pathology.

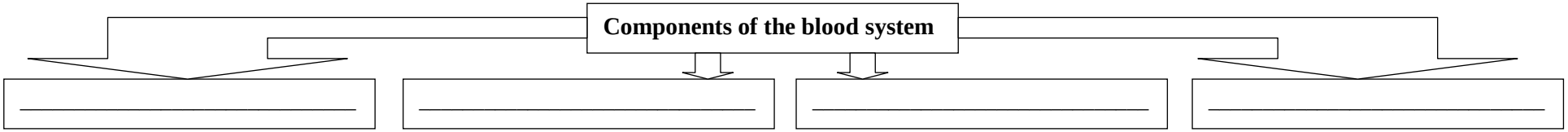
– To study under the microscope and draw the pattern of peripheral blood: a) after acute blood loss (on the fifth day); b) in iron-deficiency anemia; c) in B_{12}-deficiency anemia; d) in microspherocytosis (disease of Minkovsky–Shoffar).

– To analyze to total blood count (TBC) (№ 1–11, 20) and solve the situational tasks (№ 2–15) on the topic of the Lesson (see the "Situational tasks on Pathological Physiology").

– Control test on the topic of the Lesson.

PART 1. WORK WITH TRAINING MATERIALS

1. Fill in the Scheme.



2. Fill in the Table.

Periods of hematopoiesis

Yolk	Hepatic	Bone marrow
Period of time:		
Typical types of hematopoiesis:		
1 _____ _____	1 _____ 4 _____ 2 _____ 5 _____ 3 6	1 _____ 4 _____ 2 _____ 5 _____ 3

3. Fill in the Table by sketching the cells of the normo- and megaloblastic types of hematopoiesis.

Cells of normo- and megaloblastic types of hematopoiesis

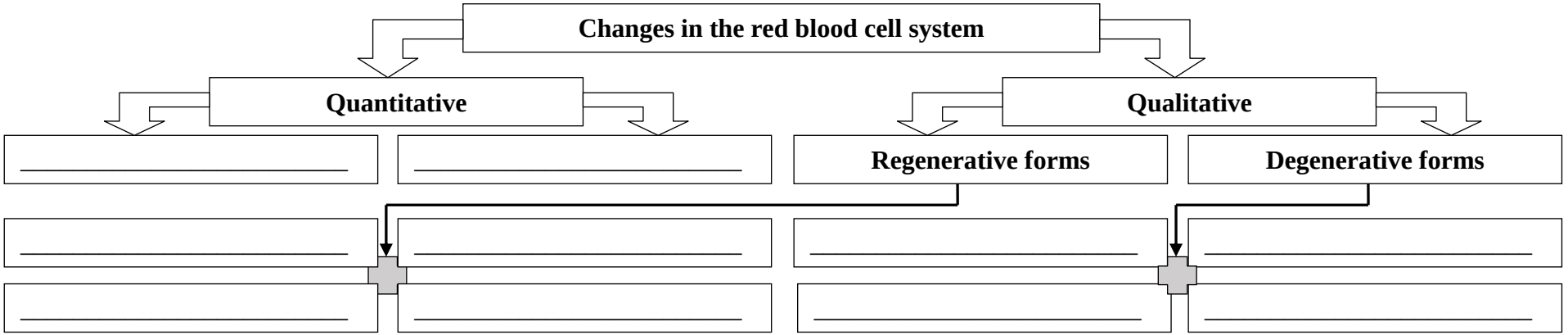
<table>
<tr><th>Normoblastic (erythroblastic) type</th><th>Megaloblastic type</th></tr>
<tr><td></td><td rowspan="3"></td></tr>
<tr><td>Erythroblast</td></tr>
<tr><td></td></tr>
<tr><td>Pronormoblast (-cyte)</td><td>Promegaloblast</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Basophilic normoblast (-cyte)</td><td>Basophilic megaloblast</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Polychromatophilic normoblast (-cyte)</td><td>Polychromatophilic megaloblast</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Oxyphilic normoblast (-cyte)</td><td>Oxyphilic megaloblast</td></tr>
<tr><td colspan="2"></td><td rowspan="3"></td></tr>
<tr><td>Reticulocyte</td><td>Polychromatophil</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td colspan="2">Erythrocyte (normocyte)</td><td>Megalocyte</td></tr>
</table>

4. Fill in the Table.

Comparative characteristics of normoblastic and megaloblastic types of hematopoiesis

Characteristic	Normoblastic type	Megaloblastic type
Number of stages		
The way the nucleus disappears from cells		
Mature cell:		
– the form		
– the presence of enlightenment in the center		
– type of Hb		
– life span of the cell		

5. Fill in the Sceme.



PART 2. PRACTICAL WORK

Work 1. STUDYING MORPHOFUNCTIONAL PECULIARITIES OF REGENERATIVE AND DEGENERATIVE FORMS OF ERYTHROCYTES

Study a blood smear under the microscope with 10 × 90 magnification that is supravitally stained with ***brilliant cresyl blue*** for revealing reticulocytes.

Erythrocytes	*Reticulocytes*

Work 2. STUDYING OF DEGENERATIVE FORMS OF ERYTHROCYTES

Having studied the tables and slides *"Erythropoiesis and its violations"*, fill in the Table:

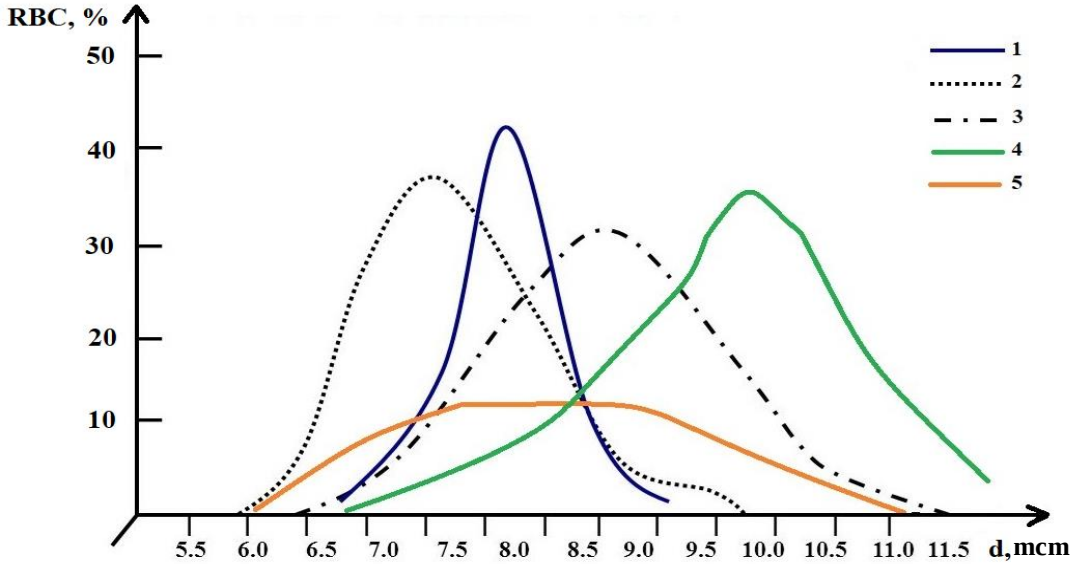
Degenerative forms of erythrocytes

<table>
<tr><td rowspan="2">1. Abnormalities of cell size (anisocytosis)
(sketch the cells and indicate their sizes comparing with normocytes)</td><td>Normocytes
_____ mkm, _____ fl</td><td>Microcytes
_____ mkm, _____ fl</td></tr>
<tr><td>Macrocytes
_____ mkm, _____ fl</td><td>Megalocytes
_____ mkm, _____ fl</td></tr>
<tr><td rowspan="4">2. Cell shape abnormalities (poikilocytosis)</td><td>Ovalocytes</td><td>Microspherocytes</td></tr>
<tr><td>Torocytes (codocytes, target-like cells)</td><td>Acanthocytes</td></tr>
<tr><td>Drepanocytes (sickle erythrocytes)</td><td>Echinocytes</td></tr>
<tr><td>Degmacytes (a nibbled erythrocytes)</td><td>Schistocytes</td></tr>
</table>

<table>
<tr><td rowspan="2">3. Cell staining abnormalities (anisochromia)
(sketch the cells noting the correlation between their color intensity and size comparison with normocytes,)</td><td>Normocytes (CI = _____)</td><td>Hyperchromous erythrocytes (CI > _____)</td></tr>
<tr><td colspan="2">Hypochromous erythrocytes (anulocytes) (CI < _____)</td></tr>
<tr><td rowspan="2">4. The presence of pathological inclusions</td><td>Howell-Jolly bodies</td><td>Cabot’s rings</td></tr>
<tr><td>Basophilic puncture</td><td>Heinz bodies</td></tr>
</table>

Work 3. STUDYING DIFFERENT VARIATIONS OF ANISOCYTOSIS ON THE ERYTHROCYTOMETRIC PRICE–JONES CURVE

Determine the forms of anisocytosis of erythrocytes using the variants of the Price–Jones curves presented in the figure.



Price–Jones curve in health and disease states

1. – Norm 2. – _____ 3. – _____ 4. – _____ 5. – _____

Work 4. In hemograms No. 1–11, 30 from the "Final lesson on the section "Pathophysiology of the blood system", identify regenerative and degenerative forms of erythrocytes; indicate the type of hematopoiesis if data are available

Control questions

1. The blood system, the definition of the notion, general characteristic.
2. Hemopoesis. General laws of blood formation. Periods and types of blood formation in ontogenesis.
3. The characteristic of the basic classes of blood cells according to the structure of blood formation (according to A. I. Vorobjev and I. P. Tchertkov).
4. Hemopoietic cells-progenitors: colony-forming units or colony-forming cells (CFC).
5. The development scheme of hemopoietic cells-progenitors and colony-stimulating factors regulating them.

6. Erythropoiesis. Cells-progenitors of erythropoiesis: BFU-E (burst-forming mature and immature units) and CFU-E (colony-forming erythrocyte unit).
7. Morphofunctional cellular characteristic of normoblastic and megaloblastic types of blood formation.
8. Morphofunctional peculiarities of erythrocytes in pathology. Regenerative and degenerative forms of erythrocytes.
9. Types and pathological forms of hemoglobin.
10. Neurohumoral regulation of erythropoiesis, its impairments.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 1).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 2. PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM. ANEMIA. ERYTHROCYTOSIS

Date: «____» _____ 20__

The purpose of the Lesson: to study etiology and pathogenesis of the most common anemias and erythrocytosis, blood pattern in this pathology.

Tasks:

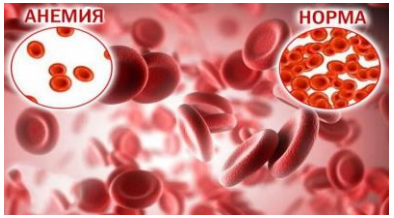
– To study under the microscope and draw the pattern of peripheral blood: a) after acute blood loss (on the fifth day); b) in iron-deficiency anemia; c) in B_{12}-deficiency anemia; d) in microspherocytosis (disease of Minkovsky–Shoffar).

– To analyze to total blood count (TBC) (№ 1–11, 30) and solve the situational tasks (№ 2–15) on the topic of the Lesson (see the "Situational tasks on Pathological Physiology").

– Control test on the topic of the Lesson.

PART 1. WORK WITH TRAINING MATERIALS

1. Give the definition of "anemia": _____
_____



2. List the compensatory reactions that occur in response to hypoxia in anemia: _____
_____

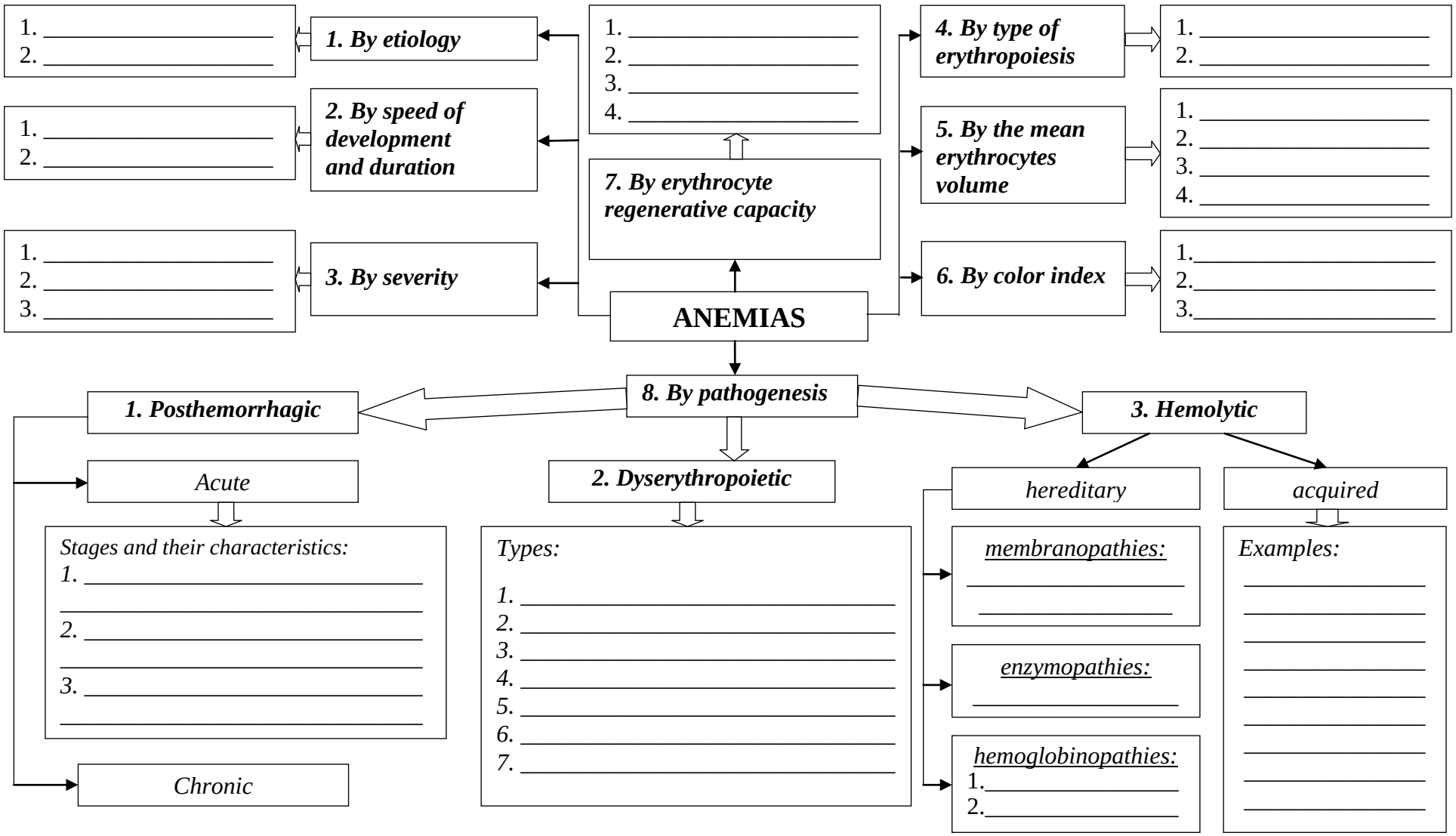
3. Fill in the Sceme.

ANEMIA

True	**False**
Characteristic: _____	*Characteristic:* _____

4. Fill in the Scheme.

Classification of anemias



5. Fill in the Scheme.

Pathogenesis of iron deficiency anemia

Iron deficiency

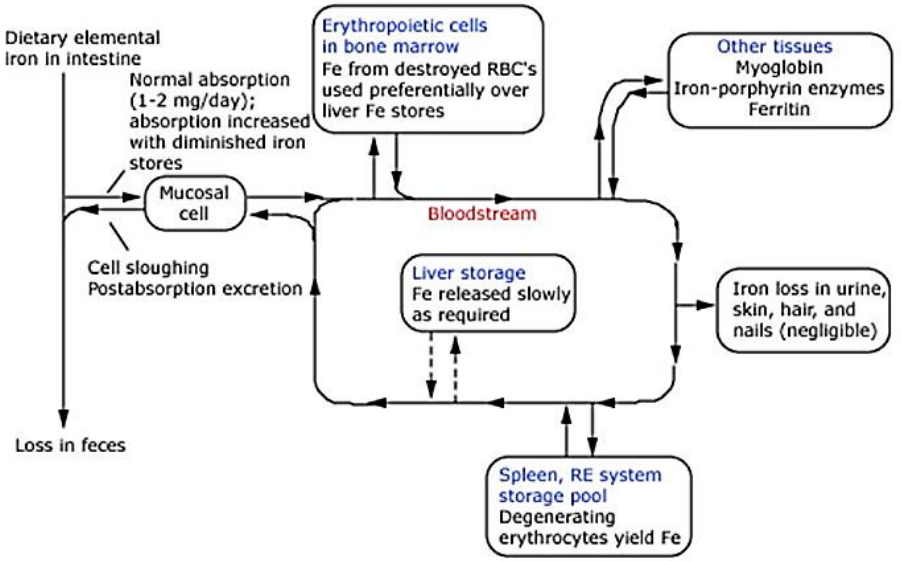
⇓

(indicate with arrows ↓ and ↑)
__ serum iron
__ iron binding capacity of blood serum
__ % of transferrin saturation
__ transport of iron in the bone marrow
__ content of iron and sideroblasts in the bone marrow

⇓

*Blood picture:*_____

Iron metabolism is norm



6. Fill in the Table.

The clinical picture of iron deficiency anemia

General anemic syndrome	Sideropenic syndrome
Characteristic manifestations	
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

7. Fill in the Table.

Iron-saturated anemia (porphyrin deficiency, sideroachrestic, sideroblastic, iron refractory)

Hereditary	**Acquired**
Etiology	
(fill in missing items) delta-aminolevulinic acid genetic defect _____ *inability to bind iron* iron deposition in various organs:	*Reasons:* 1. _____ 2. _____ 3. _____ 4. _____ 5. _____
Blood picture:	
Clinical manifestations:	

8. Fill in the Scheme.

Pathogenesis of B_{12}-deficiency anemia

In the norm: **External antianemic factor (vitamin B_{12})** **Internal antianemic factor (gastromucoprotein)**

Methylcobalamin | **Deoxyadenosylcobalamin**

Normally is responsible for: _____ | *Normally is responsible for:* _____

Interaction with specific ileal receptors

Absorption of vitamin B_{12}

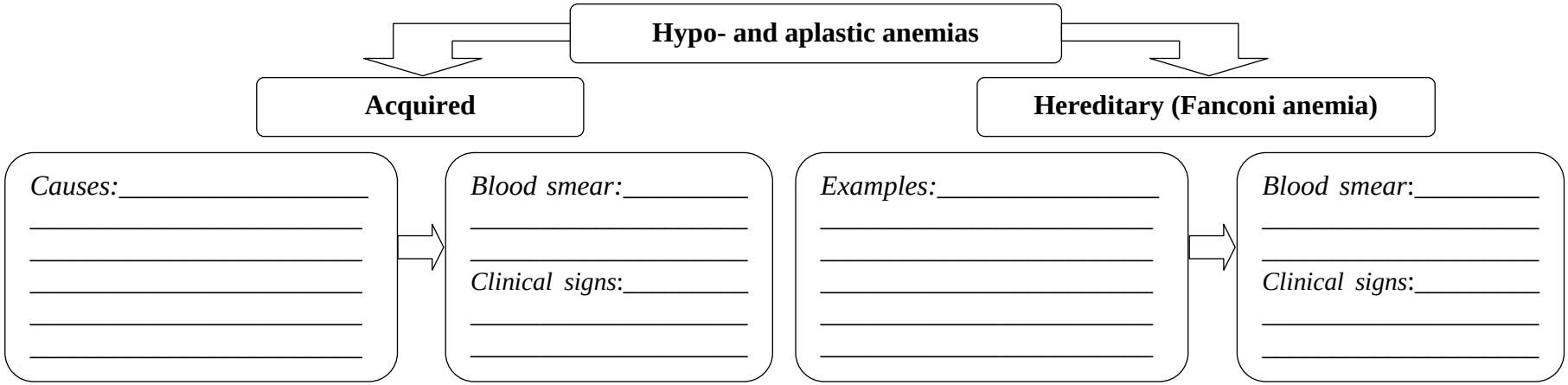
With vitamin B_{12} deficiency:

– DNA _____;
– cell division_____;
– normoblastic type →
– megaloblastic type

– accumulation_____;
– _____;
– _____;
– _____;

9. Fill in the Scheme.

Characteristics of hypo- and aplastic anemias



10. Fill in the Table.

Morphology of erythrocytes in anemias

Degenerative forms of erythrocytes	***Is most common in the pathology of:***
Microcytes	
Macro (megalo-)cytes	
Microspherocytes	
Sickle erythrocytes (drepanocytes)	
Torocytes (codocytes)	
Hypochromous erythrocytes (anulocytes)	
Hyperchromous erythrocytes	
Megaloblasts	
Erythrocytes with Howell–Jolly bodies, Cabot's rings	
Erythrocytes with Heinz bodies	
Anisocytosis, poikilocytosis	
Degmacyte («nibbled erythrocyte»)	
Echinocyte	
Schistocyte	

11. Fill in the Scheme.

HEREDITARY HEMOLYTIC ANEMIAS

Membranopathies are the group of hereditary hemolytic anemias associated with _____

_____

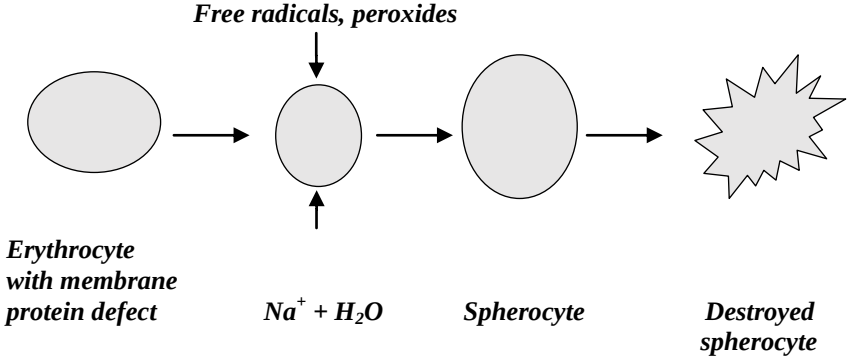
Inheritance type: _____

Enzymopathies are a group of hereditary hemolytic anemias associated with _____

_____

Inheritance type: _____

The pathogenesis of Minkowski-Shoffard anemia: an increase in the permeability of the erythrocyte membrane under the influence of free radicals, peroxides, → the entry of Na^+ and H_2O into the erythrocyte, → the formation of a spherocyte, → the destruction of a spherocyte.



Clinical manifestations: _____

_____

_____

_____

Blood picture: _____

_____

_____

Pathogenesis of anemia associated with a deficiency of glucose-6-phosphate dehydrogenase (Gl-6-FDG) in the erythrocyte membrane:

↓ GL-6-FDG → ↓ Oxidation reaction of Gl-6-FDG in PFC → ↓ Reduced glutathione →

→ ↓ SH- groups → ✸ ← Exogenous and endogenous oxidants

With a deficiency of Gl-6-FDG, the oxidation reaction of Gl-6-phosphate in PFC is blocked, the formation of reduced glutathione, which protects SH-groups from the action of various oxidants (free radicals, peroxides, sulfonamides) decreases which leads to erythrocyte destruction.

Clinical manifestations: _____

_____

_____

_____

_____

_____

Blood picture: _____

_____

_____

_____

_____

12. Fill in the Scheme.

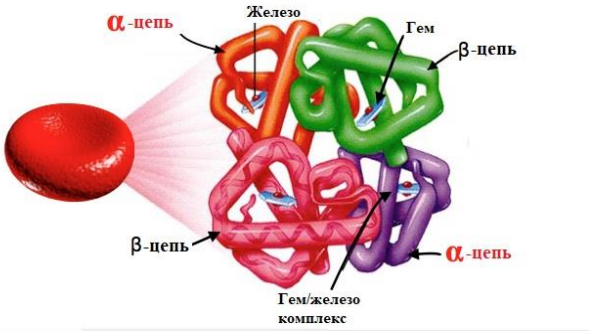
HEREDITARY HEMOLYTIC ANEMIAS

Hemoglobinopathies (quantitative)
Thalassemia

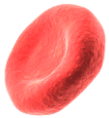
Inheritance type: _____

Pathogenesis of anemia:

The structure of hemoglobin is norm:



At thalassemia:


Erythrocyte is norm

→ **genetic defect of globin chains synthesis** →


Target-like erythrocyte (torocyte, codocyte)

A genetic defect of the α-chains synthesis — ***α-thalassemia***.
A genetic defect of the β-chains synthesis — ***β-thalassemia (Cooley's anemia)***.

Clinical manifestations: _____
_____
_____

Blood picture: _____
_____

Hemoglobinopathies (qualitative)
Sickle cell anemia

Inheritance type: _____

Pathogenesis of anemia:

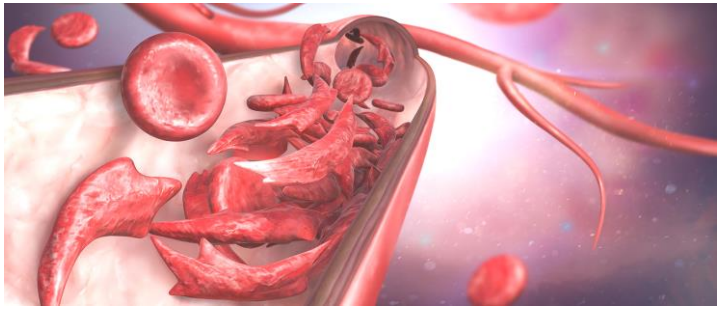

Erythrocyte in norm

→ **in β2-chain of globin glutamate is replaced by valine** →


Drepanocyte

Clinical manifestations: _____
_____
_____
_____
_____

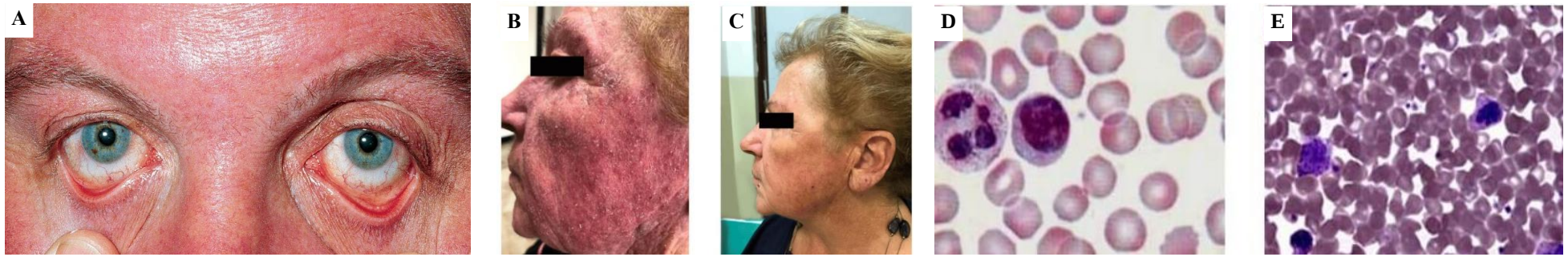
Blood picture: _____
_____
_____



13. Fill in the Table.

Erythrocytosis

Absolute		**Relative**
Develops due to:		
Primary	**Secondary**	*Examples:* _____
independent nosological forms	symptoms of a particular disease	_____
Examples: _____	*Examples:* _____	_____
_____	_____	_____
_____	_____	_____



Polycythemia vera: A — redness of the whites of the eyes (a symptom of the rabbit eyes); B — redness of the skin; C — the skin is normal; D — normal concentration of blood cells; E — increased production of blood cells

PART 2. PRACTICAL WORK

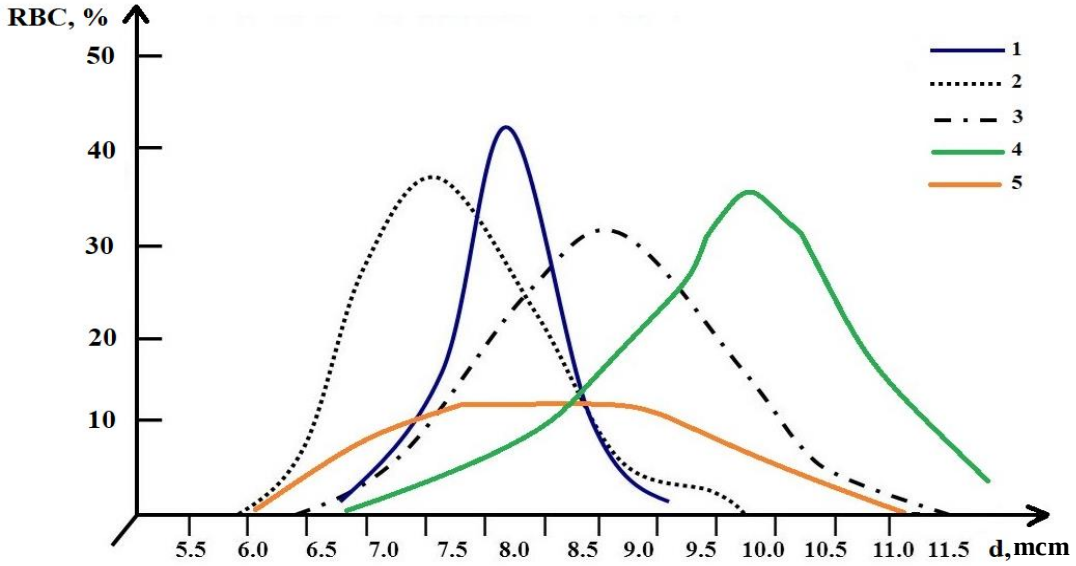
Work 1. STUDYING MORPHOFUNCTIONAL PECULIARITIES OF REGENERATIVE AND DEGENERATIVE FORMS OF ERYTHROCYTES

Study a blood smear under the microscope with 10 × 90 magnification that is supravitally stained with ***brilliant cresyl blue*** for revealing reticulocytes.

Erythrocytes	*Reticulocytes*

Work 2. STUDYING DIFFERENT VARIATIONS OF ANISOCYTOSIS ON THE ERYTHROCYTOMETRIC PRICE–JONES CURVE

Determine the forms of anisocytosis of erythrocytes using the variants of the Price–Jones curves presented in the figure.



Price–Jones curve in health and disease states

1. – Norm 2. – _____ 3. – _____ 4. – _____ 5. – _____

Work 3. STUDYING THE BLOOD SMEAR IN ACUTE POSTHEMORRHAGIC ANEMIA **(5th day after acute blood loss)**

A. Smear staining according to **Romanowsky–Giemsa**.

Study a blood smear under the microscope with 10 × 90 magnification. Find in the smear immature (regenerative) forms of erythrocytes — polychromatophils (1–2 and more in the field of vision). Pay attention to moderately expressed poikilocytosis and anisocytosis of erythrocytes.

1 – erythrocytes	2 – polychromatophils	3 – poikilocytes

Fig. 1. Blood smear in the acute posthemorrhagic anemia (5th day after the blood loss)

B. Supravital staining of the smear with ***brilliant cresyl blue***.

Examine the smear under the microscope. Find 2–4 reticulocytes with characteristic cytoplasmatic inclusions of dark blue color as a small net in the field of vision. Draw the cells.

1 – erythrocytes;	2 – reticulocytes

Fig. 2. Blood smear at the acute posthemorrhagic anemia (5th day after blood loss)

Answer the questions:

1. What changes in the pattern of red blood are observed on the 5^{th} day after acute blood loss? _____

_____

_____

2. What processes in the erythron system do the revealed changes mean? _____

_____

3. Explain the origin of basophilic reticular substance in reticulocytes: _____

_____

Work 5. STUDYING THE BLOOD SMEAR IN IRON-DEFICIENCY ANEMIA

Study a peripheral blood smear of a patient with iron-deficiency anemia under the microscope with 10 × 90 magnification. Observe the presence of hypochromous erythrocytes; slight aniso- and poikilocytosis.

1 – hypochromic erythrocytes (anulocytes);	2 – poikilocytes;	3 – microcytes

Fig. 3. Blood smear in the iron-deficiency anemia

Answer the questions:

1. What changes in red blood cells (number of erythrocytes and hemoglobin content) and erythrocyte indices (MCV, MCH, RDW) are characteristic for iron-deficiency anemia? _____

_____

_____

2. What pathological forms of erythrocytes appear in peripheral blood in iron-deficiency anemia? _____

_____

_____

Work 6. STUDYING THE BLOOD SMEAR IN THE B_{12}-(FOLIC ACID) DEFICIENCY ANEMIA

Study a blood smear of the patient with the B_{12}-deficiency anemia under the microscope with 10 × 90 magnification. Pay attention to expressed anisocytosis, poikilocytosis (round, pear-shaped, oval erythrocytes); anisochromia and hyperchromia, the presence of megalocytes, erythrocytes with Howell-Jolly bodies, Cabot's rings, basophilic puncture; and also single megaloblasts and giant polysegmentonuclear leukocytes. Draw these cells.

1 – basophilic megaloblast;	2 – polychromatophilic megaloblast;	3 – oxyphilic megaloblast;
4 – megalocytes;	5 – poikilocytes;	6 – erythrocytes with Jolly bodies;
7 – erythrocytes with Cabot's rings;	8 – erythrocytes with basophilic puncture;	9 – giant polysegmented neutrophil

Fig. 4. Blood smear in the B_{12}-(folic acid) deficiency anemia

Answer the questions:

1. What type of hemopoiesis is characteristic for B_{12}-(folic acid)-deficiency anemia? _____

2. What quantitative changes in erythrocytes, hemoglobin content and erythrocyte indices (MCV, MCH, RDW) are characteristic for B_{12}-deficiency anemia? _____
_____

3. Explain the origin of pathological inclusions in erythrocytes in the given type of hemopoiesis:

– *Howell-Jolly bodies* are _____
_____

– *Cabot's rings* are _____
_____

– *Basophilic puncture is* _____
_____

Morphological characteristics of the main types of anemias taking into account the erythrocyte indices

Type of anemia	CI	Erythrocyte diameter, mcm	MCV, fl	MCH, pg	RDW, %	Characteristics
Acute posthemorrhagic (1–3 days)	0,80–1,05	7,2–7,5	80–90	27–33	norm	normochromic, normocytic
Fe-deficiency	< 0,80	< 6,5	< 79	< 27	> 14,5	hypochromic microcytic
B_{12}-deficiency	> 1,1	> 8	> 100	> 34	> 14,5	hyperchromic macrocytic
Hemolytic	0,80–1,05	< 6,5 or norm	< 79 or norm	> 34 or norm	> 14,5	normochromic, normocytic or hyperchromic, microspherocytic
Aplastic	0,80–1,05	7,2–7,5	80–90	27–33	norm	normochromic, normocytic

Characteristics of the severity of anemia *(according to E. D. Goldberg)*

Severity	Hemoglobin (g/l)	Erythrocytes × 10^{12}/l
Mild	> 100	> 3
Moderate	100–66	3-2
Severe	< 66	< 2

Blood parameters in norm

Parameters	System SI	Extra systemic units
Erythrocytes: female male	$(3.7–4.7) \times 10^{12}$/L $(3.9–5.1) \times 10^{12}$/ L	3.7–4.7 million per 1 μL 3.9–5.1 million в 1 μL
Hemoglobin (HGB): female male	120.0–140.0 g/ L 130.0–160.0 g/ L	12.0–14.0 g % 13.0–16.0 g %
Hematocrit (HCT): female male	0.36–0.42 0.40–0.48	36–42 % 40–48 %
Mean erythrocyte volume (mean corpuscular volume — MCV) MCV = HCT × 10 : RBC	80–100 phL (10^{-15} L)	80–100 μm^3
Mean hemoglobin content per erythrocyte (mean corpuscular hemoglobin — MCH) MCH = HGB : RBC	25.4–34.6 × 10^{-15} kg/cell	25,4–34,6 pg/cell*
Mean hemoglobin concentration per erythrocyte (mean corpuscular hemoglobin concentration — MCHC) MCHC = HGB × 10 : HCT	0.3–0.38 kg/l	30–38 /dl* 30–38 %
Erythrocytes distribution width over the volume (red cell distribution width — RDW) — anisocytosis factor	11.5–14.5 %	11.5–14.5 %
Color factor	0.8–1.05	0.8–1.05
Reticulocytes	0.2–1.5 %	20–150.0 ppm
ESR: female male	1–15 mm/h 1–10 mm/h	1–15 mm/h 1–10 mm/h

Control questions

1. The definition of the notions “anemia” and “erythrocytosis”.
2. Classification principles of anemia:
   a) by etiopathogenesis;
   b) by the color index;
   c) by the hemopoiesis type;
   d) by the ability of the bone marrow for regeneration;
   e) by erythrocyte size.
3. Etiology, pathogenesis, general characteristic, blood pattern in anemia due to blood loss:
   a) acute posthemorrhagic anemia;
   b) chronic posthemorrhagic anemia.

4. Etiology, pathogenesis, general characteristic, blood pattern in anemia due to impaired hemopoiesis (dyserythropoietic):
   a) iron-deficiency;
   b) sideroachrestic;
   c) B_{12}-(folic acid) deficiency;
   d) B_{12}-(folic acid)-achrestic;
   e) hypo- and aplastic, metaplastic.
5. Etiology, pathogenesis, general characteristic, blood pattern in anemia due to enhanced hemopoiesis:
   a) membranopathies (hereditary microspherocytosis);
   b) enzymopathies (deficiency of glucose-6-phosphatedehydrogenase of erythrocytes);
   c) hemoglobinopathies (sickle-cell anemia; thalassemia);
   d) anemia due to exposure of antibodies and other damaging factors.
6. Impairments and compensatory-adaptive processes in the organism in anemia.
7. Erythrocytosis. The definition of the notion. Types (primary and secondary, absolute and relative). Etiology and pathogenesis, blood pattern in erythremia (Vaquez disease, polycythemia Vera).

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 2).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
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Teacher's signature: _____

LESSON 3. PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM. TYPICAL FORMS OF PATHOLOGY AND REACTIVE CHANGES IN THE LEUKOCYTE SYSTEM. LEUKOCYTOSIS, LEUKOPENIA AND AGRANULOCYTOSIS

Date: «____» _____ 20__

The purpose of the Lesson: to study quantitative and qualitative changes in leukocyte system; typical forms of their impairments, types of blood leukocyte profile in pathology.

Tasks:

– To get acquainted with general laws and basic typical pathological forms and reactive changes in leukocyte system on the basis of materials presented on tables on the given topic and the blood pattern in peripheral blood smears of patients.

– To draw the cells of IV–VI classes of granulocyto-, lympho- and monocytopoiesis using materials of the textbook, hematologic atlas, album, slides and tables.

– To draw pathological forms of leukocytes showing some impairments in the leukocyte system using materials of the textbook, hematologic atlas and tables.

– To get acquainted with clinical characteristic of impairments in the leukocyte system.

– To study under the microscope and draw the blood pattern in neutrophilic and eosinophilic leukocytosis.

– To discuss some complete blood count (CBC) including typical pathological forms and reactive changes in leukocyte system (№ 12–20), to acquire skills of solving situational tasks (№ 16–18) on the topic of the Lesson (see the "Situational tasks on Pathological Physiology").

– Control test of the topic of the lesson.

PART 1. WORK WITH TRAINING MATERIALS

1. Fill in the Table.

Changes in leukocytes

Quantitative	Qualitative		
	Regenerative	Degenerative	Regenerative-degenerative
1. _____ _____ 2. _____ _____	_____ _____ _____ _____ _____ _____ _____	changes in the size, shape, structure of nucleus and cytoplasm of leukocytes: 1._____ 2._____ 3._____ 4._____ 5._____	_____ _____ _____ _____ _____ _____ _____

2. Fill in the Table.

Types of leukocytosis

According to the content of certain types of leukocytes in the leukocyte formula		*By biological value*	
Absolute	**Relative**	**Physiological**	**Pathological**
_____	_____	– _____	_____
_____	_____	– _____	_____
_____	_____	– _____	_____
_____	_____	– _____	_____
_____	_____	– _____	_____
_____	_____	– _____	_____

3. Fill in the Table, indicating the most common conditions for which these types of leukocytosis are characteristic; indicate the corresponding changes in the absolute and relative number of leukocytes.

Types of leukocytosis by morphological characteristics

Neutrophilia count of cells in the norm (% $\times 10^9$/L)	**Eosinophilia** in the norm (% $\times 10^9$/L)	**Basophilia** in the norm (% $\times 10^9$/L)	**Monocytosis** in the norm (% $\times 10^9$/L)	**Lymphocytosis** in the norm (% $\times 10^9$/L)
> _____ $\times 10^9$/L > _____ %	> _____ $\times 10^9$/L > _____ %	> _____ $\times 10^9$/L > _____ %	> _____ $\times 10^9$/L > _____ %	> _____ $\times 10^9$/L > _____ %
Blood picture: – *leukocytosis:* – *relative and absolute neutrophilia;* – *shift of the leukocyte formula to the left;* ***Observed at:*** _____ _____ _____	***Blood picture:*** – *leukocytosis:* – *relative and absolute eosinophilia;* ***Observed at:*** _____ _____ _____	***Blood picture:*** – *leukocytosis:* – *relative and absolute basophilia;* ***Observed at:*** _____ _____ _____	***Blood picture:*** – *leukocytosis:* – *relative and absolute monocytosis;* ***Observed at:*** _____ _____ _____	***Blood picture:*** – *leukocytosis:* – *relative and absolute lymphocytosis;* ***Observed at:*** _____ _____ _____

4. Fill in the Table.

Mechanisms of leukocytosis development

Mechanisms	**Characteristics, examples**
Enhancement of normal leukopoiesis	
Redistribution of leukocytes in the vascular bed	
Overproduction of leukocytes at tumor lesions of hematopoietic tissue	
Hemoconcentration	

5. Fill in the Table.

Types of leukopenia

According to the content of certain types of leukocytes in the leukocyte formula		*By biological value*	
Absolute	**Relative**	**Physiological**	**Pathological**

6. Fill in the Table, indicating the most common conditions for which these types of leukopenia are characteristic; indicate the corresponding changes in the absolute and relative number of leukocytes.

Types of leukopenia by morphological characteristics

Neutropenia	**Eosinopenia**	**Monocytopenia**	**Lymphopenia**
< _____ × 10^9/L, < _____ %	< _____ × 10^9/L < _____ %	< _____ × 10^9/L < _____ %	< _____ × 10^9/L < _____ %
Observed at: _____ _____ _____ _____ _____	***Observed at:*** _____ _____ _____ _____ _____	***Observed at:*** _____ _____ _____ _____ _____	***Observed at:*** _____ _____ _____ _____ _____

7. Fill in the Table.

The mechanisms of leukopenia development

Mechanisms	**Characteristics, examples**
Violation and (or) inhibition of leukopoiesis	_____ _____
Excessive destruction of leukocytes in the vascular bed or organs of hematopoiesis	_____ _____
Redistribution of leukocytes in the vascular bed	_____ _____
Increased loss of white blood cells by the body	_____ _____
Hemodilution	_____ _____

8. Complete the definition. ***Agranulocytosis*** is a clinical and hematological syndrome characterized by:

– _____
– _____
– _____

9. Fill in the Table.

Types of agranulocytosis

Myelotoxic	**Immune (haptenic)**
Etiology	
_____ _____ _____	_____ _____ _____
Pathogenesis	
_____ _____ _____	_____ _____ _____
Characteristic changes in the blood picture	
_____ _____ _____	_____ _____ _____

10. Give the definition of *"panmyelophthisis"*: _____
_____
_____

11. Typical manifestations of the blood picture in panmyelophthisis: _____
_____
_____
_____

12. Fill in the Table.

Characteristics of neutrophil nuclear shifts

Types of nuclear shift		**Total leukocyte count**	**Neutrophils**				**Pathological forms**	**Myelopoiesis activity level**	**Prognosis**
			myelocytes	**young**	**band**	**segmented**			
To the left	*Hyporegenerative (simple)*								
	Regenerative								
	Hyperregenerative: *– leukemoid* *– leukemic*								
	Degenerative								
	Regenerative-degenerative								
To the right	*Degenerative*								

Leukocyte formula changes in some pathological conditions

<table>
<tr><th colspan="2">Pathological condition</th><th colspan="2">Characteristic changes of the leukocyte formula</th></tr>
<tr><td rowspan="3">Acute bacterial (coccal) infection</td><td>Peak of the disease</td><td colspan="2"></td></tr>
<tr><td>Recovery period</td><td colspan="2"></td></tr>
<tr><td>Proceeding as a sepsis type</td><td colspan="2"></td></tr>
<tr><td colspan="2">Acute viral (flu, measles, German measles) infection, peak of the disease</td><td colspan="2"></td></tr>
<tr><td colspan="2">Chronic specific infection</td><td colspan="2"></td></tr>
<tr><td colspan="2">Allergic conditions, helminthic invasion</td><td colspan="2"></td></tr>
<tr><td colspan="2" rowspan="2">Agranulocytosis</td><td>myelotoxic</td><td>immune</td></tr>
<tr><td></td><td></td></tr>
</table>

13. Fill in the Scheme.

The formula for calculating the nuclear shift index:

NSI = ———————————————————

_____ *(specify the type of shift)* **NSI < 0.06**	**Normal value NSI:** _____	_____ *(specify the type of shift)* **NSI = 0.08–0.9**	_____ *(specify the type of shift)* **NSI = 1–2**

PART 2. PRACTICAL WORK

1. Draw pathological (degenerative) forms of leukocytes using presented tables, materials of the textbook, hematological atlas and album.

Degenerative forms of leukocytes

1 – neutrophilic leukocytes with toxic granularity;	2 – with vacuolization of the nucleus and cytoplasm;	3 – with hyper- and hyposegmentation of the nucleus;
4 – with bodies of Kniazkov–Dele;	5 – with chromatolysis;	6 – rod nuclear with thorns

Fig. 1. Degenerative forms of leukocytes

2. Examine a blood smear of the patient with neutrophilic leukocytosis under the microscope with 10 × 90 magnification. Pay attention to the great number of neutrophilic leukocytes of various degree of maturity in the field of vision. Draw them.

1 – a metamyelocyte;	2 – a rod neuclear neutrophil;
4 – a segmented neutrophil;	4 – a neutrophil with toxic granularity

Fig. 2. Blood smear in the neutrophilic leukocytosis

3. Study a blood smear of the patient with large eosinophilia under the microscope with 10 × 90 magnification. Pay attention to the great number of eosinophilic leukocytes of various degree of maturity in the field of vision. Draw them.

1 – a rod shaped eosinophil;	2 – a segmented eosinophil;	3 – a segmented neutrophil

Fig. 3. Blood smear in the eosinophilic leukocytosis (large eosinophilia)

Blood parameters (leukocytes) in norm

Parameters	Absolute and relative number of leukocytes in peripheral blood (SI)
Leukocytes (**WBC**)	4,0–9,0 × 10^9/L
Myeloblasts	0
Promyelocytes	0
Neutrophiles (**neu**): myelocytes (**myelo**) metamyelocytes (**meta**) band segmentated	 0 0 % (1 %) 1–6 % (0,040–0,300 × 10^9/L) 47–72 % (2,000–5,500 × 10^9/L)
Eosinophils (**eosin**)	1,0–5 % (0,020–0,300 × 10^9/L)
Basophils (**baso**)	0–1 % (0–0,0065 × 10^9/L)
Lymphoblasts Prolymphocytes	0 0
Lymphocytes (**lymph**)	19–37 % (1,200–3,000 × 10^9/L)
Monocytes (**mono**)	3–11 % (0,09–0,6 × 10^9/L)
Medium cells (**MID**) — mixture of monocytes, eosinophils, basophils and immature cells: **MID#** — absolute number of the medium cells from the general number of WBC in the blood test; **MID%** — percentage of the medium cells	 0,2–0,8 × 10^9/L 5–10 %

Control questions

1. Leukopoiesis, its impairments.
2. Pathological forms of leukocytes, their morphofunctional peculiarities.
3. Leukopenia, the definition of the notion, the cause and developmental mechanisms, its types.
4. Agranulocytosis, the definition of the notion. Types of agranulocytosis, the causes and their developmental mechanisms. Peripheral blood pattern in various types of agranulocytosis.
5. Panmyelophthisis. The causes and its developmental mechanisms, the pattern of peripheral blood and bone marrow in panmyelophthisis.
6. Leukocytosis, the definition of the notion, types, the causes and developmental mechanisms.
7. Leukocyte formula changes, absolute and relative changes of some types of leukocytes, pathogenetic and prognostic characteristic.
8. The characteristic, pathogenetic and prognostic characteristic of various types of the leukocyte formula shifts.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 3).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
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9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 4. PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM. HEMOBLASTOSES. LEUKEMOID REACTIONS

Date: «____» _____ 20__

Purpose of the Lesson: to study the causes, development mechanisms and hematological manifestations of leukemia (the main types of leukograms in leukemia).

Tasks:

– To get acquainted with the morphofunctional peculiarities of the cells observed in the patients with the certain types of leukemia.

– To study under the microscope the blood picture in some types of leukemia (acute and chronic myeloid and lymphoid) and draw it. To draw blood picture observed in acute myeloid leukemia using hematological atlas and tables.

– To interpret the hemograms (№ 21–29) on the topic of the Lesson.

– To solve the situational tasks (№ 15, 19–26) (see the "Situational tasks on Pathological Physiology").

– Control test.

PART 1. WORK WITH TRAINING MATERIALS

1. Give the definition of *"leukemia"*:_____
_____
_____
_____
_____

2. What is the difference between leukemic cells and blasts that are present in the process of normal hemopoiesis? _____
_____
_____

3. Describe the stages of leukemia pathogenesis:

I stage: _____
_____

II stage: _____
_____

III stage: _____
_____

4. Fill in the Table.

Classification of leukemias

Classification criteria	Types of leukemia
By histogenetic characteristic	– _____ –
By the degree of differentiation (maturity) of leukemic cells	– acute Classification of acute leukemias: *(indicate the basis for each classification)* FAB, 1976: _____ EGIL, 1995: _____ – chronic
By the number of WBC in the peripheral blood	1. _____ _____ 2. _____ _____ 3. _____ _____ 4. _____

5. Fill in the Table.

Comparative characteristics of blood picture in acute and chronic myeloid leukemias (at the developed stage)

Type of myeloid leukemia	Acute	Chronic
Presence/prevalence of blasts		
Presence of all maturing cells (+/–)		
Leukemic hiatus (+/–)		
Basophilic-eosinophilic association (+/–)		
Ph′-chromosome in the cells of myeloid row (+/–)		
Pancytopenia (+/–)		

6. Fill in the Table.

Comparative characteristic of blood picture in acute and chronic lymphoid leukemia (at the developed stage)

Type of lymphoid leukemia	Acute	Chronic
Presence/prevalence of blasts		
Presence of all maturing cells (+/–)		
Ph′-chromosome (+/–)		
Botkin-Gumprecht-Klein shadows (+/–)		
Pancytopenia (+/–)		

7. Fill in the Table.

The main syndromes in leukemia

Syndrome	Development mechanisms	The main manifestations
Anemic		
Hemorrhagic		
Infectious		
Intoxication		
Metastatic		
Osteoarthropathic		

8. Give the definition of *«leukemoid reactions»*: _____
_____
_____
_____

9. Fill in the Table.

The main types of leukemoid reactions

Types	Causes	Changes in the blood
Myeloid type		
Myelocytic, promyelocytic	_____ _____	_____ _____
Neutrophilic	_____ _____	_____ _____
Eosinophilic (“large eosinophilia”)	_____ _____	_____ _____
Lymphoid type		
Lymphocytic with the presence of lymphocytes with typical morphology	_____ _____	_____ _____
Lymphocytic with the prevalence of lymphocytes with atypical morphology	_____ _____	_____ _____
Plasmacytic	_____ _____	_____ _____
Immunoblastic	_____ _____	_____ _____

PART 2. PRACTICAL PART

1. Study the blood smears of the patient with leukemic type of acute myeloid leukemia under the microscope with magnification 10 × 90. While doing that pay attention to the number, morphology of blood cells, cellular polymorphism.

In particular, notice that in the blood smears of the patient with acute myeloid leukemia (sub- and leukemic types), not only an increase in leukocyte number is observed but also a lot of blasts, absence of intermediate forms of the cells and presence of single segmented neutrophils are found (*hiatus leukaemicus*) in the field of vision.

1 – blasts;	2 – segmented neutrophils

Fig. 1. Blood picture in subleukemic and leukemic types of acute myeloid leukemia

2. Study the blood smears of the patients with leukemic types of chronic leukemia under the microscope with magnification 10 × 90. Pay attention to the number, morphology of blood cells, cellular polymorphism.

In particular, notice that in the blood smears of the patients with chronic myeloid leukemia (sub- and leukemic types), not only an increase in leukocyte number is observed, but also:

– all morphologicaly detected cells of granulocytopoiesis: myeloblasts, promyelocytes, neutrophilic, eosinophilic and basophilic myelocytes, metamyelocytes band and segmented cells are found;

– an increase in the number of eosinophils and basophils (eosinophilic-basophilic association) is observed.

1 – myeloblast;	2 – promyelocyte;	3 – neutrophilic myelocyte;	4 – eosinophilic myelocyte;
5 – basophilic myelocyte;	6 – young neutrophil	7 –young eosinophil;	8 – young basophil;

9 – band neutrophil;	10 – band eosinophil;	11 – band basophil;	12 – segmented neutrophil;
13 – segmented eosinophil;		14 – segmented basophil	

Fig. 2. Blood picture in chronic myeloid leukemia

3. In the blood smears of the patients with chronic lymphoid leukemia (subleukemic and leukemic types) you may observe a large number of leukocytes, presence of all morphologically detected cells of the lymhocytopoiesis: lymphoblasts, prolymphocytes, lymphocytes (are prevalent in the field of vision). Lymphocyte shadows (Botkin–Gumprecht–Klein cells) are also detected.

1 – lymphoblast;	2 – prolymphocyte;
3 – lymphocytes;	4 – cells (shadows) of Botkin–Gumpreht

Fig. 3. Blood picture in chronic lymphoid leukemia

Cytochemical characteristics of different leukemia types

FAB	Type of acute leukemia	Reaction to the nutrients			Reactions to the enzymes			
		Glycogen (Schiff reaction)	**Glycosaminoglycans**	**Lipids (black sudan)**	**Peroxidase**	**Acid phosphatase**	**α-naphthyl-esterase**	**chloroacetate-esterase**
MO	Undifferentiated	–	–	–	–	–	–	–
M1 M2	Myeloblastic	+	-	+	+	+	weakly+	+
M3	Promyelocytic	strongly+	+	+	strongly+	weakly+	weakly+	strongly+
M4	Myelomonoblastic	+ (diffuse)	–	–	strongly+	+	+	weakly+
M5	Monoblastic	weakly+	–	weakly +	weakly +	strongly+	+	–
M6	Erythromyeloblastic	+	–	Reactions depend on what categories blasts refer to (myeloblasts, monoblasts, non-differentiated blasts)				
M7	Megakaryoblastic	Detection is based on the typical morphology of the cells						
	Lymphoblastic	+ (in the form of lumps)	–	–	–	sometimes+	–	–
	Plasmablastic	Detection is based on the typical morphology of the cells and the presence of paraprotein in the blood serum						

Control questions

1. Leukemia, definition. General characteristic and classification principles.
2. Etiology and pathogenesis of leukemia. Modern theories of leukemia development. Tumor nature of leukemia.
3. The peculiarities of leukemia cells, their morphological, cytochemical and cytogenetic characteristics.
4. The peculiarities of hemopoiesis and cell content of the blood at different types of leukemia.
5. The main body disorders at leukemia, their mechanisms.
6. Leukemoid reactions. The main types, causes, blood picture and the difference between leukemia and leukemoid reaction.
7. Diagnostic and treatment principles of leukemias.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 4).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.

5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.

6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.

7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.

8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.

9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 5. PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM. HEMOSTASIS DISORDERS

Date: «____» _____ 20__

Purpose of the Lesson: to study the main types of hemostasis disorders, their causes, development mechanisms, clinical and hematological manifestations.

Tasks:

– To study the disorders in the system of hemostasis and platelets.

– To acquire skills in solving the situational tasks (№ 27–34) on the topic of the Lesson (see the "Situational tasks on Pathological Physiology").

– To get acquainted with some diagnostic methods of hereditary coagulopathies, to analyze the given results after correction of hemostasis disorders, identify their type.

– Control test.

PART 1. WORK WITH TRAINING MATERIALS

1. Fill in the Scheme.

Typical forms of the disorders and reactive changes in the platelet system

_____ | _____ | _____ | _____

2. Fill in the Scheme.

Thrombocytosis

Primary (_____)

Development basis — _____

_____

Disease examples: _____

_____

Secondary (_____)

Development basis — _____

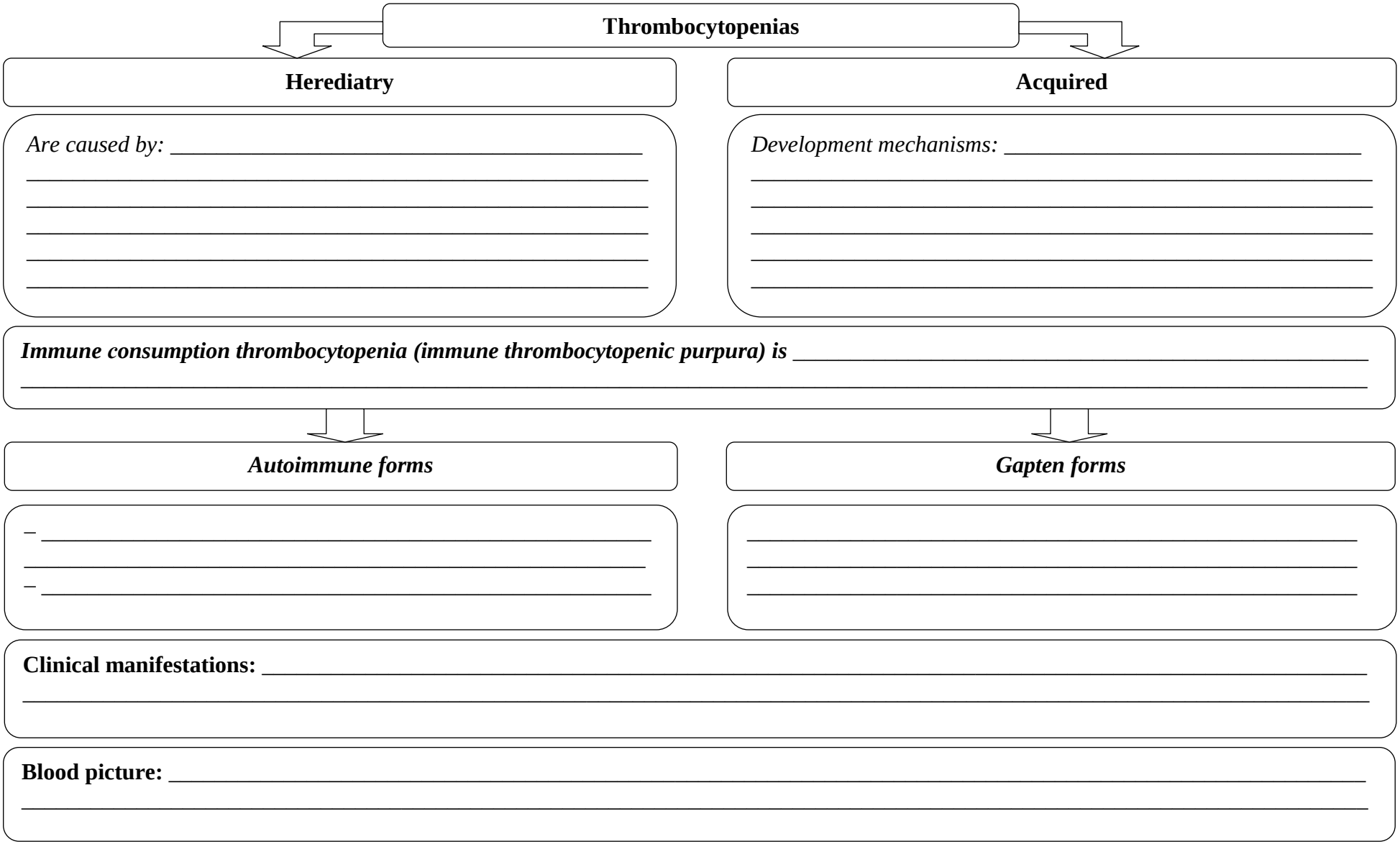
_____

Appear at: _____

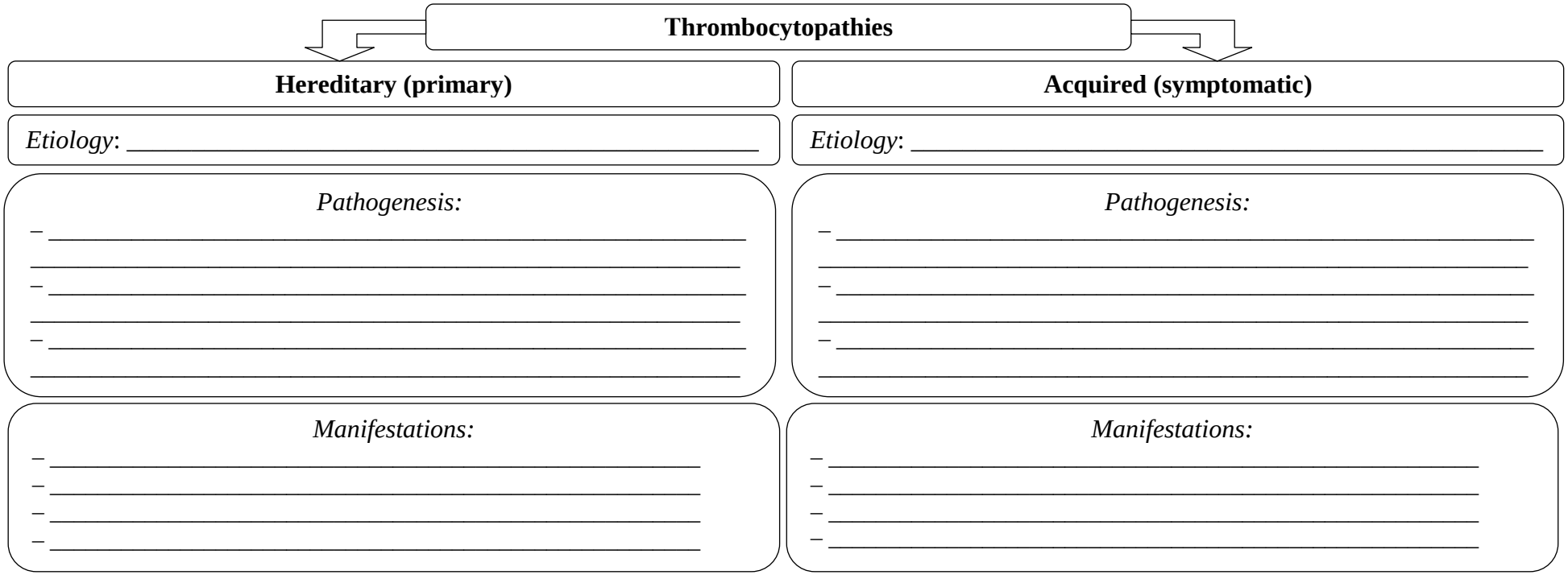
_____

Pathogenic significance: _____

3. Fill in the Scheme.



4. Fill in the Scheme.



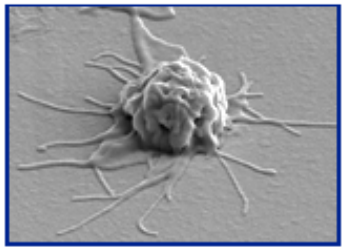
5. Fill in the Table.

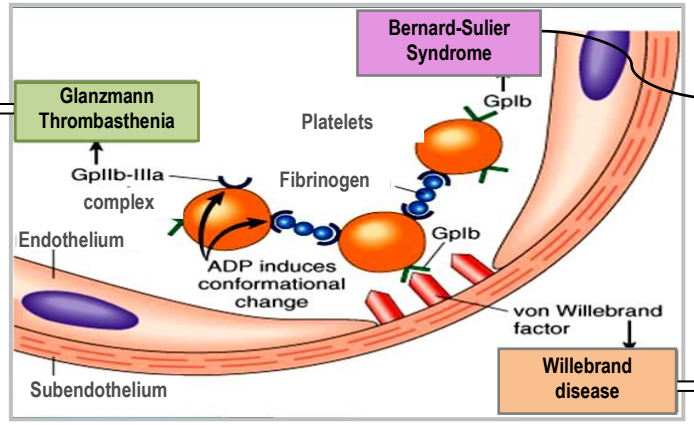
Characteristics of the primary thrombocytopathies

Characteristic	**Glanzmann thrombasthenia**	**Willebrand disease**	**Bernard–Soulier syndrome (disease) — giant platelet syndrome**
Inheritance type			
Pathogenesis	_____	_____	_____
Manifestations	_____ _____	_____ _____	_____ _____
Laboratory diagnosis	_____ _____	_____ _____	_____ _____

6. Fill in the Scheme, identifying the type of impaired platelet function at each certain syndrome.

What thrombocyte function is impaired?
_____
_____





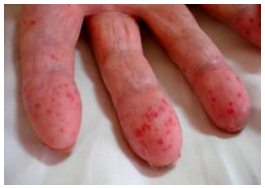
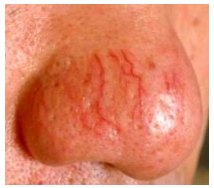
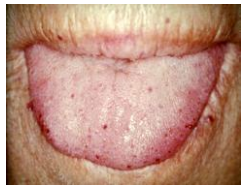
What thrombocyte function is impaired?
_____
_____

What thrombocyte function is impaired:
_____
_____

7. Fill in the Scheme.

Hemostasis disorders are caused by:

Pathology of the vascular wall (vasopathies)	***Thrombocyte pathology***	***Plasma system pathology***
– Rendu-Osler disease (_____) – Henoch-Schonlein purpura (_____)	– _____ _____ – _____ _____ – _____ _____	– _____ _____ – _____ _____ – _____ _____

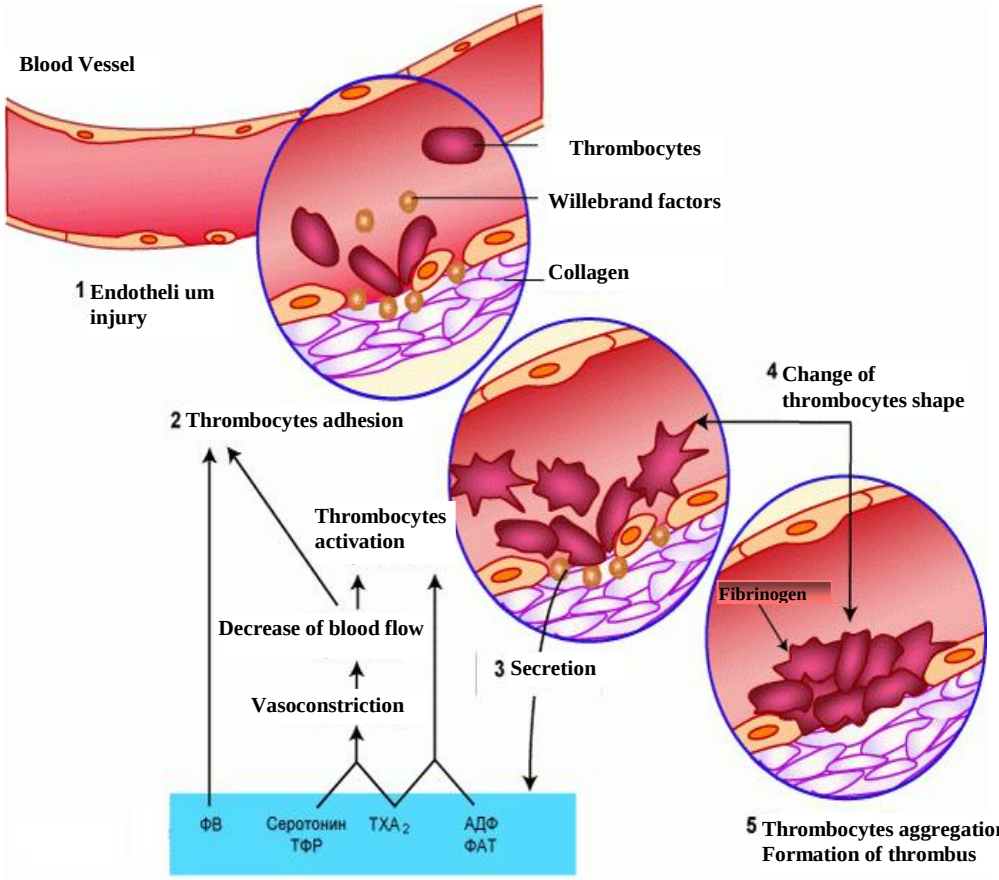




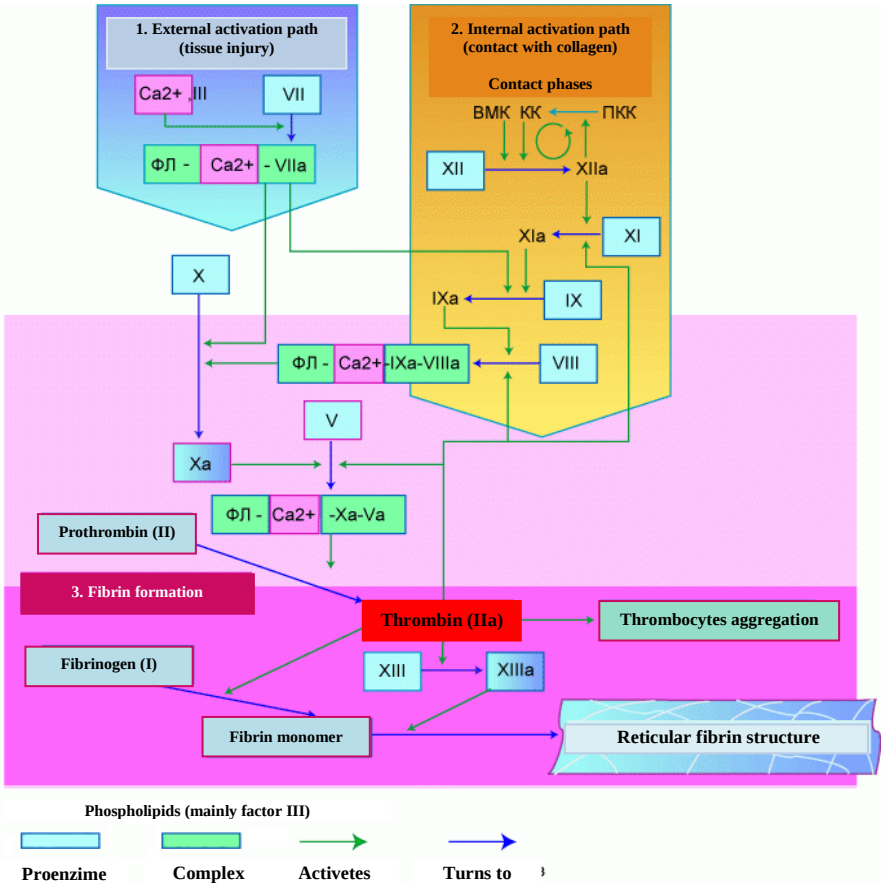
Typical manifestations of the disorders:

– _____
– _____
– _____

8. Define the types of hemostasis on the pictures. Answer the questions.

Hemostasis types





_____ _____

(hemostasis type) *(hemostasis type)*

Disorders

_____ _____

(What syndrome do they manifest by?) *(What syndrome do they manifest by?)*

9. Fill in the Scheme.

Thrombocytic syndrome (thrombophilia) is _____

Complex of the disorders leading to the development of the thrombosis, – _____:

1. _____
2. _____
3. _____

The main cause — pathology of anticoagulation system: _____

The main factors of the anticoagulation system: _____

Deficiency of the anticoagulation system factors

hereditary

Deficiency of the factors:

_____

acquired

Deficiency of the factors:

– _____

– antiphospholipid syndrome:

а) _____;

б) _____

Manifestations:

_____

Manifestations:

_____

10. Give the definition of *"hemorrhagic syndrome":* _____

11. Fill in the Table.

Types of bleeding

Type	Characteristics	Examples
Microcirculatory (capillary petechial-bruised)	_____	_____
Hematome	_____	_____
Microcirculatory-hematome (mixed)	_____	_____
Vasculitic-purplish	_____	_____
Angiomatous	_____	_____

12. Fill in the Table.

Hemostatic disorders with vascular genesis — vasopathies

Characteristics	Hereditary	Acquired
Name	_____	_____
Pathogenesis	_____ _____	_____ _____
Type of bleeding		
Clinical manifestations	_____ _____ _____ _____ _____	– _____ – _____ – _____ – _____ – _____ –
Blood picture	_____ _____	_____ _____

13. Fill in the Scheme.

Hemostasis disorders associated with the thrombocyte pathology

1. Hemorrhagic syndromes: _____

2. Coagulopathies

Hereditary

Disease	**Factor deficiency**	**Inheritance type**	**Clinical manifestations**
Hemophilia A			
Hemophilia B			
Hemophilia C			
Parahemophilia			
Willebrand disease			

Acquired

DIC-syndrome is _____
_____

Etiology: _____
_____

Pathogenesis:
– _____
– _____
– _____

Development stages

Name	**Characteristic**	**Manifestations**
1._____	_____	_____
2._____	_____	_____
3._____	_____	_____

PART 2. PRACTICAL PART

1. Look through the results of the laboratory test made for differential diagnosis of hereditary coagulopathies and make conclusions.

Test is based on the principle of correction of the plasma coagulation disorders with the help of specially prepared plasma samples with previously detected deficiency of certain coagulation factors.

If the added plasma (standard) corrects coagulation parameter disorder, it means that there is a deficiency of different coagulation factors in both plasma samples. If not, it means that they have the same defect.

Materials and methods:

0.2 ml of previously prepared plasma that is standard with the detected deficiency of the factors VIII, IX, XI, XII (factor concentration is less than 1 % of normal content) and 0.8 ml of plasma that is analyzed. Then activated partial thromboplastin time (APTT), thrombin time (TT) and prothrombin time (PT) are measured.

The results of hemostasis parameter correction in the analyzed plasma

Plasma samples with the hereditary coagulopathy		**Added plasma standards with previously detected deficiency of the plasma factors**				**Diagnostic conclusion about the deficiency of certain factors in the analyzed plasma**
		Deficiency of the factor				
		VIII	**IX**	**XI**	**XII**	
Analyzed plasma	1	APTT – 80 s TT – 14 s PT – 13 s	APTT – 54 s TT – 16 s PT – 12 s	APTT – 55 s TT – 15 s PT – 14 s	APTT – 54 s TT – 14 s PT – 16 s	_____ _____
	2	APTT – 55 s TT – 16 s PT – 12 s	APTT – 56 s TT – 16 s PT – 13 s	APTT – 54 s TT – 14 s PT – 15 s	APTT – 102 s TT – 15 s PT – 12 s	_____ _____
	3	APTT – 56 s TT – 15 s PT – 15 s	APTT – 55 s TT – 15 s PT – 12 s	APTT – 98 s TT – 16 s PT – 13 s	APTT – 55 s TT – 16 s PT – 15 s	_____ _____
	4	APTT – 57 s TT – 13 s PT – 14 s	APTT – 100 s TT – 14 s PT – 14 s	APTT – 55 s TT – 15 s PT – 16 s	APTT – 54 s TT – 15 s PT – 14 s	_____ _____
	5	APTT – 87 s TT – 14 s PT – 12 s	APTT – 93 s TT – 15 s PT – 12 s	APTT – 57 s TT – 16 s PT – 14 s	APTT – 55 s TT – 15 s PT – 16 s	_____ _____
	6	APTT – 56 s TT – 16 s PT – 16 s	APTT – 91 s TT – 16 s PT – 13 s	APTT – 96 s TT – 15 s PT – 15 s	APTT – 55 s TT – 14 s PT – 14 s	_____ _____

Answer the question: what phase and mechanism of blood coagulation activation are impaired in the given blood samples with the hereditary coagulopathy? _____
_____

2. Study the blood smear in the thrombocythemia.

Look at the blood smear under the microscope with magnification 10 × 90. Pay attention to the big amount of thrombocytes in the field of vision. Draw them.

1 – erythrocytes;	2 – neutrophilic leukocytes;	3 – thrombocytes

Fig. 1. Blood picture in thrombocythemia

3. Match the nosological forms of disease with their main manifestations.

Disease	The main manifestations
1. Antiphospholipid syndrome	a) hemorrhagic telangiectasia
2. Christmas disease	b) thrombocytopenia, arterial and venous thrombosis, repeated abortions
3. Bernard-Soulier syndrome	c) hematomes, hemartrosis
4. Randu-Osler disease	d) thrombocytopenia, presence of the giant thrombocytes in blood
5. Schoenlein-Henoch disease	e) multiple hemorrhagic immune thrombovasculitis

The correct answers: 1 – _____; 2 – _____; 3 – _____; 4 – _____; 5 – _____.

4. Match the type of bleeding with the pathology it is typical for:

Type of bleeding	Type of pathology
1. Petechial (microcirculatory, petechial-bruised)	a) infectious and immune vasculitis
2. Hematoma	b) deficiency of FVIII and FXIII, DIC-syndrome, severe form of the Villebrand disease, overdose of anticoagulants
3. Mixed capillary-hematoma	c) vasopathy, arterio-venous shunts, angioma, telangiectasia
4. Vasculitic-purplish	d) hemophilia A, hemophilia B, deficiency of FVIII, acquired coagulopathies, overdose of anticoagulants
5. Angiomatous	e) thrombocytopenia, trombocytopathy

The correct answers: 1 – _____; 2 – _____; 3 – _____; 4 – _____; 5 – _____.

5. Match the nosological forms of the disease with the causes of their development.

Diseases	Causes
1. DIC-syndrome	a) deficiency of IX plasma factor
2. Hemophilia A	b) vascular-thrombocytic and coagulation hemostasis disorders
3. Hemophilia B	c) hereditary defect of VIII plasma factor synthesis
4. Hemophilia C	d) deficiency of V plasma factor
5. Parahemophilia	e) deficiency of XI plasma factor

The correct answers: 1 – _____; 2 – _____; 3 – _____; 4 – _____; 5 – _____.

6. Match the main manifestations of the disease with their nosological forms.

The main manifestations	Diseases
1. Thrombocytopenic purpura, systemic vascular damage, brain damage symptoms. Anisopoikilocytosis, «helmet-shaped» erythrocytes	a) hemolytic-uremic syndrome (HUS)
2. Severe thrombocytosis, leukocytosis, anemia, microcirculatory disorders, thromboembolic syndrome, bleeding, acute pain in fingers and toes, their gangrene is possible	b) Werlhof's disease (ITP)
3. Thrombocytopenia, megakaryocytes, giant platelets, anti-platelet antibodies in the bone marrow, decreased platelet lifespan	c) hemophilia A
4. Thrombocytopenia, vascular damage of the microvasculature, mainly of the kidneys, acute renal failure	d) essential thrombocythemia
5. Hemorrhagic syndrome, hematomas, hemarthrosis, recurrent, spontaneous bleeding	e) Moszkowicz's disease (TTP)

The correct answers: 1 – _____; 2 – _____; 3 – _____; 4 – _____; 5 – _____.

7. Match the pathogenic factors with the diseases they cause.

Etiological factor	Disease
1. Absence or defect of glycoproteins GP IIb-IIIa of platelet membrane to fibrinogen	a) antiphospholipid syndrome
2. Deficiency or functional insufficiency of von Willebrand factor (f.W)	b) Christmas disease
3. The appearance of antiphospholipid antibodies in blood	c) Glanzmann's thrombasthenia
4. Factor IX deficiency	d) Bernard-Soulier syndrome
5. Absence of a specific glycoprotein that interacts with f.W-f.VIII in the platelet membrane	e) Willebrand disease

The correct answers: 1 – _____; 2 – _____; 3 – _____; 4 – _____; 5 – _____.

Platelet parameters of the hemogram in norm

Parameter	Value
Platelets (PLT)	150.0–450.0 × 10^9/l
Mean platelet volume (MPV)	7.4–10.4 fl.
Platelet distribution width (the degree of platelet anisocytosis) (PDW)	10.0–20.0 %
Plateletcrit (the percentage of the blood volume occupied by platelets in the total blood volume) (PCT)	0.15–0.40 %

METHODS FOR VASCULAR-THROMBOCYTIC HEMOSTASIS STUDYING

Rumpel–Leede test (the tourniquet test). On the inner surface of the upper third of the forearm a circle with a diameter of 5 cm is drawn, then the arm is compressed with a cuff from the device for measuring blood pressure for 5 minutes at a pressure of 90–100 mm Hg. Five minutes after removing the cuff, the number of petechiae in the outlined circle is counted (norm — up to 10 petechiae, weakly positive test — 11–20 petechiae, positive — 21–30 petechiae, strongly positive — more than 30). The tourniquet test is positive in case of hereditary and acquired thrombocytopenia and platelet dysfunction.

Bleeding time (BT). The method allows to determine the state of blood vessels after the interaction of platelets and the vascular wall. BT is determined by the modified IVY method. After applying the cuff to the upper part of the shoulder and creating a pressure of 40 mm Hg in it, an incision 1 × 9 mm is made on the skin of the flexor surface of the forearm measuring 1 × 9 mm with a disposable lancet. BT — the time required to stop bleeding is normally 3–8.5 minutes.

A progressive increase in bleeding time is observed with a decrease in the number of platelets, a primary damage of the vascular wall, qualitative changes of platelets, Willebrand disease.

Methods for determining the platelet functions

Study of the platelet adhesion ability. It is determined by passing blood through a glass bead filter, resulting in a decrease in platelet number. The difference between the number of platelets before and after filtration determines the degree of platelet adhesiveness, which is normally 20.

A sharp decrease in adhesiveness (< 10 %) is observed with qualitative changes of platelets, Willebrand disease.

Study of the platelet aggregation. The platelet aggregation test is performed in plasma rich in thrombocytes with the addition of inducers such as ADP, adrenalin, collagen, free fatty acids. The aggregatometer allows to constantly record fluctuations in the intensity of light transmission through the plasma. The formation of aggregates is accompanied by an increase in light transmission.

The addition of inducers at certain concentrations induces typical two-wave aggregation. The first wave determines the reduction of platelets, the second reflects the synthesis of thromboxane and platelet secretion (release reaction).

In thrombocytopathies, platelet aggregation under the influence of aggregating agents is absent.

METHODS FOR COAGULATION HEMOSTASIS STUDYING

A parameter characterizing the 1st phase of coagulation — prothrombinase formation

Activated partial thromboplastin time (APTT). It allows determining the presence of plasma coagulation factors that take part in the activation of blood coagulation by the internal mechanism. To carry out the test, an activating agent (crushed silicon oxide or kaolin) is used. It is a substitute for phospholipids of the platelet membrane, calcium and plasma of a patient or a healthy person. After adding an activating agent to the plasma, the active serine center of FXII "opens", leading to the subsequent activation of coagulation factors by the internal mechanism, as well as factors X, V, II, I. The activating agent binds activated factors IX, X, V, II. This process is accelerated in the presence of added calcium and is accompanied by the formation of a clot. The end of clotting is registered in seconds. The APTT value is normally 25–38 sec.

APTT increases with a deficiency of FXII, FXI, FX, FVIII, FV, FII, FI, precallikrein and high-molecular-weight kininogen.

Parameters characterizing the 2nd phase of coagulation — thrombin formation (PT, PTI, INR)

Prothrombin time (PT). This test makes it possible to assess the presence of FVII, which is involved in the external mechanism of activation of blood coagulation, as well as FX, FV, FI, FII. Tissue factor and calcium are added to the patient's plasma. Tissue factor activates FII, which in turn activates FX, FV, Ca and FII, leading to the formation of thrombin. Thrombin converts fibrinogen to fibrin. PT does not take into account the state of factors of the internal mechanism of blood coagulation. Normally, PT is 10–14 seconds.

PT increases in patients with hereditary deficiency of FVII, FX, FV, FII, FI or acquired combined factor deficiency, for example, with vitamin K deficiency, use of oral anticoagulants.

Determination of the prothrombin index (PTI). The index allows to assess the presence of hypocoagulation due to a deficiency of coagulation factors involved in the external mechanism. It is calculated using the determined prothrombin time.

$$\text{PTI} = \frac{\text{PT of the patient}}{\text{PT of the donor}} \times 100\ \% = 70\text{–}110\ \%\ (0.7\text{–}1.1).$$

Interpretation: PTI values < 70 % indicate hypocoagulation with hereditary or acquired deficiencies of FVII, FX, FV, FII, FI, as well as with use of indirect anticoagulants that block the synthesis of vitamin K-dependent factors in the liver.

PTI > 110 % cannot indicate hypercoagulability because this test is insensitive to it, this may indicate a defect in the determination.

Definition of International Normalized Ratio (INR). Unlike the previous test, where the standard is mixed plasma from 10 donors, this test uses a standardized thromboplastin, with a certain sensitivity, with an activity of about 12 seconds, which makes it possible to accurately assess the severity of hypocoagulation, to monitor patients taking indirect anticoagulants. The determination of the INR is made by hardware.

$$\text{INR} = \left(\frac{\text{PT of the donor}}{\text{PTof the patient}}\right)^{\text{ISI}} = 0.7\text{–}1.1,$$

where ISI is the international thromboplastin sensitivity index (index for a specific factory thromboplastin) = 1–1.9.

INR values > 1.1 indicate hypocoagulation in the 2nd phase of coagulation. The therapeutic range of INR values for anticoagulant therapy is 1.6–2.6. With an INR value of 4, there is a risk of severe bleeding. Like the previous index, it does not characterize hypercoagulability.

A parameter characterizing the 3rd phase of coagulation — fibrin formation

Thrombin time. Gives the information about the state of the final stage of blood coagulation. For this purpose, a thrombin solution is used, which, when mixed with an equal volume of plasma, causes it to clot in 15 seconds at a temperature of 37 °C.

An increase in thrombin time is observed at hypofibrinogenemia, excess heparin, accumulation of fibrinogen degradation products in the plasma, molecular abnormalities of fibrinogen, paraproteinemia.

METHODS FOR STUDYING COAGULATION HEMOSTASIS CHARACTERIZING HYPERCOAGULATION

Hypercoagulation can be determined by the following methods: APTT, TT, determination of the amount of D-Dimers, soluble complexes of fibrin monomers (SFMC), fibrin degradation products (FDPs).

SFMC (soluble complexes of fibrinogen / fibrin monomers) formed by the influence of thrombin on fibrinogen are found normally. They are fibrin monomers consisting of D – E – D domains with open polymerization centers. For the formation of fibrin-polymer from them, it is necessary to accumulate a sufficient amount of them in the blood because before they are soluble complexes of fibrin-monomer. They are determined semi-quantitatively by sediment tests: orthophenanthralin, β-naphthalan tests and are assessed in the number of plus points by the number and rate of floc loss. Plasma is not turbid - the result is negative. If the plasma becomes turbid, there are clots — "++++".

This test indicates the potential plasma thrombogenicity and possible hypercoagulation, the circulation of a large amount of thrombin in the blood, the test confirms the DIC syndrome.

The test is not strictly specific, other proteins not related to hemostasis (paraproteins, C-reactive protein) may be precipitated.

FDPs (degradation products of fibrinogen / fibrin) are formed as a result of plasmin influence on fibrinogen, fibrin monomer and non-crosslinked fibrin polymer. They are areas D – E – D or D – E with open centers of polymerization. They can attach to fibrinogen, fibrin monomer, block them and block coagulation. They have an inhibitory effect on fibrin self-assembly.

They are determined by paracoagulation tests. Ortrphenanthroline hydrochloric acid is added to the plasma, separating the bonds between FDPs, the polymerization centers of fibrinogen are unblocked and the released fibrinogen leads to blood coagulation (FDP test is positive). If there are no FDPs, then the addition of ortofenanthralin does not lead to blood clotting — the test is negative.

A positive test indicates the presence of hyperplasminemia, potential plasma thrombogenicity, and the possible presence of thrombosis.

Fibrin degradation products belong to late D-dimers and are currently determined by the test for the content of D-dimers.

D-Dimers. The level of D-dimers characterizes the activity of the fibrinolysis system. When cross-linked fibrin dissolves with the help of plasmin, regions consisting of D – D and D – D – E fragments of adjacent fibrin filaments are formed, as plasmin cuts longitudinal bonds between D – E – D fibrin domains, but not acts on cross-linking. Such fragments are called D-dimers.

D-dimers are determined using test strips by immunometric method using human monoclonal antibodies to the neo-antigen of D-dimers that do not cross-react with SFMC and FDPs. For determination, citrated platelet-free plasma is taken. The stability of D-dimers in citrate plasma at room temperature is 24 hours after collection of the material. The blood level is up to 500 ng/ml. The test is highly sensitive, but not very specific. At the level of D-dimers < 500 ng/ml. If the level of D-dimers is < 500 ng/ml (the test is negative) — the probability of thrombosis is 60 %, > 500 ng/ml — the probability of thrombosis is 98 %. At normal pregnancy, the level of D-dimers is 2 times higher.

An increase in the level of D-dimers can be observed in venous thrombosis, thrombophlebitis, pulmonary embolism, disseminated intravascular coagulation (all phases), myocardial infarction, after surgery.

Some parameters of the hemostasis system in the norm

Rumpel–Leede test (the tourniquet test).	Norm Weakly positive Positive Strongly positive	< 10 petechiae 11–20 21–30 > 30
Bleeding time **(BT)**	3–8,5 min	
Platelet number in blood	$150.0–450.0 \times 10^9$/L	

Coagulation hemostasis parameters

Activated partial thromboplastin time **(APTT)**	25–38 s
Prothrombin time **(PT)**	10–14 s
Prothrombin index **(PTI)**	70–110 %
International normalized ratio **(INR)**	0.7–1.1
Thrombin time **(TT)**	15–18 s

Parameters of activity of the fibrinolysis system

Degradation products of fibrin/fibrinogen **(FDPs/Fg)**	Negative test
D-dimer level	Up to 500 ng/ml

Control questions

1. Hemostasis system. Definition, function. Modern blood coagulation scheme, regulation mechanisms.
2. Hemostasiopathy. Definition. Classification of hemostasis system disorders.
3. Vascular-thrombocytic hemostasis disorders. Causes, mechanisms of development, clinical manifestations.
4. Causes, development mechanisms, clinical and hematological manifestations of thrombocytopathies (hereditary and acquired); thrombocytopenia; thrombocytosis (reactive and primary).
5. Coagulation hemostasis disorders caused by hereditary and (or) acquired deficiency of blood coagulation factor (hemophilia A, B, C, mixed hemophilia, parahemophilia, etc.), their pathogenesis, clinical manifestations, laboratory diagnostics, principles of treatment.
6. Anticoagulation system. Factors, mechanisms of regulation. Causes, mechanisms of development, consequences of the blood coagulation system disorders.

7. Hemostasis disorders of vascular (vasopathy) and mixed genesis, mechanisms of development, main clinical manifestations, laboratory diagnostics, principles of treatment.

8. Purpura and other hemorrhagic conditions (immune and non-immune thrombocytopenic purpura). Classification, main clinical manifestations, laboratory diagnostics, treatment principles.

9. Fibrinolysis and its disorders. Etiology, pathogenesis and clinical manifestations.

10. Thrombotic syndrome. Etiology and pathogenesis.

11. Hemorrhagic syndrome. Etiology and pathogenesis.

12. Thrombohemorrhagic syndrome (DIC syndrome) or intravascular microcoagulation syndrome. Etiological and pathogenetic factors, clinical manifestations, laboratory diagnostics, principles of treatment.

13. The main tests characterizing vascular-thrombocyte and coagulation hemostasis, their diagnostic value.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 5).

2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.

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4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.

5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.

6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.

7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.

8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.

9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 6. PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM. CHANGES IN THE TOTAL BLOOD VOLUME: HYPO- AND HYPERVOLEMIA. ACUTE BLOOD LOSS

Date: «____» _____ 20___

The purpose of the Lesson: to consider the typical impairment forms of the total blood volume, their causes and consequences, factors affecting their severity. To study etiology and pathogenesis of posthemorrhagic conditions, forms and mechanisms of compensatory reactions in blood loss. To get acquainted with treatment principles of acute blood loss.

Tasks: using ready-protocols of experiments to study: 1) the effect of acute blood loss on the severity of arising disorders depending on the rate of bleeding and the amount blood lost and; 2) manifestations of urgent compensatory reactions of the body in acute blood loss of varying severity; 3) influence of saline and blood transfusions on hemodynamic and respiratory parameters after acute massive blood loss.

PART 1. WORK WITH TRAINING MATERIALS

1. Fill in the Table.

Blood volume disorders

Type		Hematocrit (%)	Ratio of blood cells and plasma	Causes	Manifestations
Normovolemia	*Simple (normocythemic)*	For ♂ 40-46 For ♀ 36-42	_____	–	–
	Oligocythemic (hemodilution)	_____	normal blood volume; ↓ of blood cells (erythrocytes)	_____	_____
	Polycythemic (hemoconcentration)	_____	_____	_____	_____
Hypervolemia	*Simple (normocythemic)*	_____	_____	_____	_____
	Oligocythemic (hydremia)	_____	_____	_____	_____
	Polycythemic	_____	_____	_____	_____
Hypovolemia	*Simple (normocythemic)*	_____	_____	_____	_____
	Oligocythemic	_____	_____	_____	_____
	Polycythemic (anhydremia)	_____	_____	_____	_____

2. Give the definition of "*blood loss*": _____
_____
_____

3. Fill in the Scheme.

Causes of blood loss

_____ *(a cause)*	_____ *(a cause)*	_____ *(a cause)*
_____ *(latin name)*	_____ *(latin name)*	_____ *(latin name)*
_____ _____ *(examples)*	_____ _____ *(examples)*	_____ _____ *(examples)*

4. Fill in the Scheme.

Factors determining the nature and outcome of blood loss

_____ *(factor)*	_____ *(factor)*	_____ *(factor)*
Severity (% CBV): 1. _____ _____ 2. _____ _____ 3. _____ _____	*The lower the rate of blood loss, the* _____ _____ _____ _____ _____ _____	*Characteristic:* _____ _____ _____ _____ _____ _____

5. Fill in the Table.

Changes in the body in blood loss

Stages			**Characteristic**		
Initial					
Compensatory	***Phases***		***Time of appearance***	***Value***	***Peripheral blood indicators***
	Urgent mechanisms	*Hemodynamic (reflex) phase*	_____ _____	*SNS activation:* • _____ • _____ •	_____ _____ _____
		Hydraemic phase	_____ _____	• *volume reflex:* _____ _____ _____ • *osmo reflex:* _____ _____ _____ • *autohemodilution:* _____	_____ _____ _____ _____ _____ _____ _____ _____ _____
	Non-urgent mechanisms	*Protein phase*	_____ _____	_____ _____	_____ _____
		Bone marrow phase	_____ _____	_____ _____ _____	_____ _____ _____
Terminal			_____ _____		

PART 2. PRACTICAL WORK

Work 1. STUDYING THE EFFECTS OF BLOOD LOSS AND SUBSEQUENT INTRAVENOUS TRANSFUSIONS OF SALINE AND BLOOD ON THE DOG'S ORGANISM

Method: Both femoral arteries and a femoral vein of a narcotized dog are prepared. A cannula is inserted into the one of the arteries and is connected to the manometer, for registration of arterial pressure. Then cannulas are inserted into the other femoral artery and the vein for bloodletting and subsequent transfusion of blood or isotonic solution of sodium chloride.

For graphic registration of respiratory excursions a special cuff is fixed on the thorax of the animal, being connected by a rubber tube with the Marey's pressure gauge. The animal's circulating blood volume (CBV) is calculated on the basis of its body mass.

After the initial parameters have been recorded, 5 % of CBV is ***slowly*** let out from the artery into a glass vessel, meanwhile registering changes of heart rate (HR), arterial pressure (BP) and respiration rate (RR).

In 5 min ***stream*** bloodletting is repeated, the same volume of blood being taken out (total blood loss makes up 10 % of the animal's blood mass). Pay attention to distinctions of the registered parameters; analyze the causes and also the mechanisms of fast normalization of BP and HR. For revealing compensatory mechanisms of the organism carry out the third ***(stream)*** bloodletting in the volume of 10 % of blood; all parameters are being recorded.

In 5 min ***massive stream*** bloodletting is performed, about $^1/_3$ of the total blood mass being taken out. Observe the persistent significant decrease of BP, significant amplitude reduction of pulse waves of the 1st order, tachycardia, and insoleiratory breathlessness. Analyze the received results.

To decide, which of the factors (decrease of blood pressure or loss of erythrocytes) plays a leading ri in the development of hypoxia and death of the organism in acute massive blood loss, make sure that BP persists at a critically low level, the animal is IV injected 100–150 ml of warmed up saline and 5 min later — autogenic blood (60 % of the lost volume), BP and RR being registered.

Experimental results

Stages of experiment	Type of exposure	Blood pressure (mm Hg)	Pulse (beats/min)	Respiration (resp./min)
1	The initial data	130/100	86	12
2	Bloodletting(5 % of blood, slowly)	125/100	90	14
3	In 5 min	130/95	90	14
4	Bloodletting (5 % of blood, fast)	115/95	106	15
5	In 5 min	125/95	105	16
6	Bloodletting (10 % of blood, fast)	65/60	120	14
7	In 5 min	120/110	95	14
8	Bloodletting(30 % of blood, fast)	30/25	60	0
9	In 5 min	60/50	100	2
10	Intravenous injection of saline (150 ml)	85/65	80	4
11	In 5 min	80/65	90	8
12	Intravenous injection of 60 % of the lost blood	130/110	108	32
13	In 5 min	135/110	80	16

To resolve the question of which of the factors (lowering blood pressure or loss of red blood cells) plays a leading role in the development of hypoxia and death of the body in acute massive blood loss, making sure that blood pressure is stably kept at a critically low level, the animal is injected with 100–150 ml of heated saline solution, and after 5 minutes — autogenous blood (60 % of the lost volume), recording changes in blood pressure and respiratory rate.

Using the data given in the table of experimental results, create graphs reflecting changes in systolic (Fig. 1) and diastolic (Fig. 2) blood pressure, heart rate (Fig. 3) and respiration rate (Fig. 4) in the dynamics of the experiment. ***Mark with a vertical arrow the influence and nature of this or that influence.***

Fig. 1. Change in systolic pressure in a dog in the dynamics of acute blood loss and with various methods of its correction

Fig. 2. Change in diastolic pressure in a dog in the dynamics of acute blood loss and with various methods of its correction

Fig. 3. Change in heart rate in a dog in the dynamics of acute blood loss and with various methods of its correction

Fig. 4. Change in RR in a dog in the dynamics of acute blood loss and with various methods of its correction

Answer the questions:

1. What causes the absence of essential changes in BP, HR and respiration in slow blood loss comprising 5 % of the blood volume of the animal?

_____
_____

2. Why can you observe a visible (in blood loss of 5 % of the blood volume) and significant (in additional loss of 10 % of blood) decrease of BP?

_____
_____
_____

3. Due to what compensatory mechanisms is the BP normalization achieved 5 min later under the above mentioned variants of experiment?

_____
_____
_____

4. Taking into account the changes of analyzed parameters, estimate the condition of the organism 5 min later after the last stream massive bloodletting exceeding in total 50 % of blood volume? _____
_____
_____
_____

5. What caused some elevation of BP after transfusion of 150 ml of saline to the dog that has lost a half of its blood volume during 25–30 min?

_____
_____

Conclusions *(give the pathogenic background of performing stage-by-stage transfusion therapy to correct the state of vital functions in acute massive blood loss):* _____
_____
_____
_____
_____

Control questions

1. Typical forms of pathology and reactive changes of the total blood volume. Normo-, hypo- and hypervolemias and their types depending on the relationship of corpuscular elements and blood plasma. The causes of their incidence, clinical manifestations.
2. Blood loss: acute and chronic. Their causes, characteristic.
3. Factors determining the course and outcomes of posthemorrhagic conditions.
4. Basic components of pathogenesis of the posthemorrhagic conditions.
5. Types and mechanisms of compensatory reactions (urgent and long-term) in blood loss.
6. Centralization of blood circulation in acute blood loss; its essence, mechanisms, pathogenetic assessment.
7. The causes of death in acute blood loss.
8. Principles and methods of blood loss treatment.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 6).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
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Teacher's signature: _____

LESSON 7. FINAL LESSON ON THE SECTION "PATHOLOGICAL PHYSIOLOGY OF THE BLOOD SYSTEM". IMPROVEMENT OF PRACTICAL SKILLS (PATHOPHYSIOLOGICAL ANALYSIS OF HEMOGRAMS) COLLOQUIUM

Date: «____» _____ 20__

Purpose of the Lesson: to improve and evaluate the knowledge gained in practical classes on the section "Pathophysiology of the blood system" on issues related to the pathophysiological aspects of various variants of the blood system pathology; to develop practical skills in the analysis of hemograms with making a conclusion based on the available data.

Tasks:

– To analyze and give the conclusions on the presented hemograms.

– Examination "Analysis of hemograms".

Required level of knowledge and practical skills

The student should know:

– structural and functional features of blood cells of normoblastic, megaloblastic, myeloblastic, monoblastic, megakaryoblastic, lymphoblastic types of hematopoiesis, each of the stages of cell differentiation; pathological forms of erythrocytes and leukocytes;

– etiology and pathogenesis of typical blood system disorders: anemia, erythrocytosis, leukocytosis, leukopenia, agranulocytosis, panmyelophthisis, leukemoid reactions, leukemia; blood picture features, clinical manifestations and significance for the body.

The student should be able to:

– analyze and assess the state of the blood system according to its hematological and biochemical parameters.

Control questions

1. Typical forms of changes in total blood volume. Normo-, hypo- and hypervolemia and their types, depending on the ratio of formed elements and blood plasma; their causes and manifestations.
2. Blood loss and its types.
3. Factors determining the consequences of blood loss.
4. The main links of the pathogenesis of posthemorrhagic conditions.
5. Types and mechanisms of compensation for impaired functions at blood loss.
6. Centralization of blood flow in acute blood loss and its mechanisms, pathogenetic assessment.
7. Causes of death in acute blood loss.
8. Principles and methods of blood loss treatment.
9. Hematopoiesis and its disorders. General characteristics.

10. Anemia. Definition of the concept. Principles of classification. Anemia as a syndrome and as a nosological form. Qualitative and quantitative changes in erythron in anemia.

11. Etiology, pathogenesis, general characteristics of anemias resulting from blood loss. Blood picture.

12. Etiology, pathogenesis, general characteristics of anemias arising from disorders of hematopoiesis (dyserythropoietic). Blood picture.

13. Etiology, pathogenesis, general characteristics of anemias resulting from increased blood destruction. Blood picture.

14. Violations and compensatory-adaptive processes in the body in anemia.

15. Erythrocytosis, its types (primary and secondary, absolute and relative). Etiology and pathogenesis of erythremia (Vaquez disease), blood smear.

16. Leukocytosis and leukopenia, their types, causes and mechanisms of development, pathogenetic assessment.

17. Agranulocytosis. Definition, its types, etiology, pathogenesis. Blood picture in various types of agranulocytosis.

18. Panmielophthisis. Its causes, development mechanism and consequences. The picture of peripheral blood and bone marrow in panmyelophthisis.

19. Leukemia. Etiology and pathogenesis. Modern theories of leukemia development. Principles of classification. Blood picture.

20. Leukemoid reactions, their types. Etiology and pathogenesis, differences between leukocytosis and leukemia. Blood picture.

21. Hemostasis. Definition, types of hemostasis, general characteristics.

22. Hemostasiopathy. Definition. Classification of hemostasis system disorders.

23. Disorders of coagulation hemostasis caused by hereditary or acquired deficiency of blood coagulation factors, their pathogenesis, clinical manifestations. Hemophilia.

24. Quantitative and qualitative changes in platelets. Thrombocytosis, thrombocytopenia and thrombocytopathy, their types and distinctive features.

25. Disorders of hemostasis of vascular and mixed genesis (vasopathy), their mechanisms, main clinical manifestations.

26. Thrombotic syndrome. Etiology and pathogenesis.

27. Hemorrhagic syndrome. Etiology and pathogenesis.

28. Thrombohemorrhagic syndrome (disseminated intravascular coagulation syndrome) or intravascular microcoagulation syndrome. Etiology and pathogenesis.

Algorithm for making a conclusion based on the results of the hemogram analysis

1. To indicate the disorders identified during the analysis of the hemogram. To give the most complete description of them in accordance with the data available in the hemogram. For example to characterize the anemia according to the main criteria; leukocytosis or leukopenia — according to the relative and absolute content of a certain type of leukocytes; nuclear shift of neutrophils — by nature (to the left or to the right) and type of shift; leukemoid reactions — by the type (myeloid, lymphoid) and the form (myelocytic, lymphocytic, etc.); agranulocytosis — by the type (immune and myelotoxic), etc.

2. To indicate the possible cause and mechanism of the disorder development. For example, acute or chronic blood loss; anemia due to erythropoiesis disorders or increased destruction of red blood cells; state of hemolytic crisis at hemolytic anemia; bacterial processes: acute purulent coccal infections (pathogens: streptococci, staphylococci, meningococci, etc.); chronic specific processes: tuberculosis, syphilis, etc.; viral infections: infectious mononucleosis (Filatov's disease), influenza, etc.

3. To assess the functional activity of the hematopoietic system. For example, primary suppression of hematopoiesis in aplastic anemias, panmyelophthisis, myelotoxic agranulocytosis; secondary hyperreactive state of the bone marrow (with septic processes and endogenous intoxication) with its subsequent depletion (leukemoid reactions of the myeloid type); compensatory stimulation of hematopoiesis — at acute compensated blood loss; chronic hereditary hemolytic anemias, and the outcome of such stimulation in hemolytic anemias may be depletion of the hematopoietic function of the bone marrow (aplastic crises) and the development of myelofibrosis, etc.

4. To assume or establish the type of pathology in which the detected disorders would take place. For example, the identified abnormalities (leukocytosis or leukopenia) can be characteristic of acute or chronic inflammatory processes of a bacterial or viral nature. In case of a disease of the blood system, indicate its nosological form (for example, hereditary microspherocytic hemolytic anemia of Minkowski–Chauffard; sickle cell anemia, etc.).

5. To highlight the prognostic significance of hematological parameters, indicating the severity of the pathological process and the prognosis for complete recovery (mainly based on the prognostic value of changes in the leukocyte formula and the severity of bone marrow failure).

6. To indicate additional research methods required for a final conclusion. For example in diseases of the blood system, it is often necessary to examine the bone marrow as a defining diagnostic criterion; in sickle cell anemia and thalassemia — electrophoretic study of hemoglobin, etc.

EXAMPLES OF THE HEMOGRAM INTERPRETATION

Hemogram №1

Hemogram	Calculation and assessment of individual blood parameters	Identified violations
RBC – 1,4·10^{12}/л ↓ → Hb – 60 г/л ↓ → CI – 1,4 ↑ → Reticulocytes – 0,1% ↓ → HCT = 0,18 ↓ → RDW = 18,5% ↑ → MCV = 128 fl ↑ → MCH = 50,0 pg/cell MCHC = 39,0 г/dl **Leukocytes** –2,5·10^{9}/l ↓ → **Basophils** – 0% → **Eosinophils** – 2% → **Neutrophils** – 42% ↓ → myelocytes – 0% metamyelocytes – 0% band – 1% segmented – 41%↓ **Lymphocytes** – 50%↑ → **Monocytes** – 6% N → **Platelets** – 40,0·10^{9}/л **In a smear:** megalocytes, megaloblasts, poikilocytosis, macrocytosis, erythrocytes with Cabot rings, Howell–Jolly bodies, with basophilic granularity, giant hypersegmented neutrophils.	**severe anemia,** **hyperchromic,** **hyporegenerative** sign of severe anemia anisocytosis **macrocytic anemia** hyperchromic anemia leukopenia N N (0,05·10^{9}/л) abs. neutropenia (1,05·10^{9}/л ↓) SNI = 0,02 ↓ shift to the right rel. lymphocytosis (1,25·10^{9}/л - N). N → thrombocytopenia cells of megaloblastic type of hematopoiesis, degenerative forms of erythrocytes and leukocytes, characteristic of megaloblastic anemias; the presence of hypersegmented neutrophils indicates a shift in the leukocyte count to the right	**I. In the erythrocyte system.** Severe anemia, hyperchromic, aregenerative, macrocytic, megaloblastic. **II. In the leukocyte system.** Leukopenia, absolute and relative neutropenia with degenerative shift of lf to the right, relative lymphocytosis. **III. In the platelet system.** Thrombocytopenia.
Conclusion. Severe anemia, hyperchromic, aregenerative, megaloblastic, macrocytic; leukopenia, absolute and relative neutropenia with a shift of the leukocyte formula to the right, relative lymphocytosis; thrombocytopenia. Pancytopenia, aregenerative anemia, leukocyte counts to the right indicate a decrease in the level of bone marrow activity - suppression of hematopoiesis. The identified changes indicate B_{12}-deficiency anemia (possibly Addison-Birmer anemia). Bone marrow examination is required. ***The prognosis*** is difficult, but favorable for life and recovery with modern methods of treatment.		

Hemogram №2

Hemogram	Calculation and assessment of individual blood parameters	Identified violations
RBC – 3,2·10^{12}/л ↓ → Hb – 80 г/л ↓ → CI – 0,7 ↑ → Reticulocytes – 0,4% ↓ →	**moderate anemia, hypochromic,** **hyporegenerative.**	**I. In the erythrocyte system.** Severe anemia, hyperchromic, aregenerative, macrocytic, megaloblastic.
Leukocytes – 3,9·10^{9}/l ↓ → **Basophils** – 0% → **Eosinophils** – 0% → **Neutrophils** – 97% ↓ → myelocytes – 10% metamyelocytes – 25% band – 32% segmented – 20%↓ **Lymphocytes** – 2%↑ → **Monocytes** – 1% N → ESR – 69 mm ↑ **Platelets** – 120,0·10^{9}/л → **In a smear:** *toxic granularity of neutrophils.*	leukocytosis N aneosinophilia abs. and rel. neutrophilia (37,8·10^{9}/л), NSI = 2,2 hyperregenerative left shift abs. lymphocytopenia (0,78·10^{9}/л↓) rel. monocytopenia (0,39·10^{9}/л N) significantly increased thrombocytopenia degenerative forms of segmented neutrophils	**II. In the leukocyte system.** Leukocytosis; aneosinophilia; absolute and relative neutrophilia with a hyperregenerative shift to the left; relative and absolute lymphocytopenia; relative monocytopenia. **III. In the platelet system.** Thrombocytopenia.
Note. Bacteremia (staphylococci); severe endotoxemia and sepsis in anamnesis.		
Conclusion. Moderate anemia, hypochromic, normoblastic, hyporegenerative; leukocytosis, absolute and relative neutrophilia with a hyperregenerative shift to the left and the presence of neutrophils in the smear with toxic granularity; relative and absolute lymphocytopenia; relative monocytopenia; thrombocytopenia. Taking into account the bacteriological examination and anamnesis, the revealed disorders can be characteristic of a severe, acute, purulent process of coccal genesis, complicated by sepsis. ***The prognosis*** is extremely difficult, as indicated by a hyperregenerative shift of neutrophils to the left (a hyperreactive state of the bone marrow due to exposure to bacterial endotoxins), aneosinophilia, manifestations of sepsis: endotoxemia, bacteremia. But with modern methods of treatment, the prognosis for life is favorable.		

HEMOGRAMS

№ 1

RBC (erythrocytes)	**3.79×10^{12} /L**	
HGB (hemoglobin)	83 g/L	
CI (color index)	To calculate	
Ret (reticulocytes)	1 %	
HCT (hematocrit)	27.8 %	
MCV (mean corpuscular volume)	73.3 fL	
MCH (mean corpuscular hemoglobin)	21.9 pg/cell	
MCHC (mean Hb concentration)	29.9 g/dL	
RDW (red cell distribution width)	20.8 %	
WBC (leukocytes)	**6.4×10^{9} /L**	
Baso (basophils)	1 %	
Eosin (eosinophils)	3 %	
Neu (neutrophils):		
– myelo (myelocytes)	0 %	
– meta (metamyelocytes; young)	0 %	
– band	4 %	
– segmentated	62 %	
Lymph (lymphocytes)	20 %	
Mono (monocytes)	10 %	
PLT (platelets)	**415.0×10^{9} /L**	
ESR (erythrocyte sedimentation rate)	12 mm/h	

Serum iron – 6.85 mcmol/L.

Conclusion:

№ 2

RBC	**3.5×10^{12} /L**	
HGB	72 g/L	
CI	To calculate	
Ret	0.6 %	
HCT	25 %	
MCV	To calculate	
MCH	To calculate	
RDW	15.5 %	
WBC	**3.6×10^{9} /L**	
Baso	0 %	
Eosin	3 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	5 %	
– segmentated	64 %	
Lymph	23 %	
Mono	5 %	
PLT	**180.0×10^{9} /L**	
ESR	8 mm/h	

Serum iron – 58.3 mcmol/L.

Conclusion:

№ 3

RBC	**3.36×10^{12} /L**	
HGB	67 g/L	
Ret	0.5 %	
CI	To calculate	
WBC	**5.1×10^{9} /L**	
Baso	0 %	
Eosin	2 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	5 %	
– segmentated	51 %	
Lymph	38 %	
Mono	4 %	
PLT	**180.0×10^{9} /L**	
ESR	15 mm/h	

In the smear: poikilocytosis, microcytosis.

Conclusion:

№ 4

RBC	**1.58×10^{12} /L**	
HGB	68 g/L	
Ret	0 %	
CI	To calculate	
WBC	**2.8×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	1 %	
– segmentated	42 %	
Lymph	55 %	
Mono	2 %	
PLT	**85.0×10^{9} /L**	
ESR	28 mm/hour	

In the smear: megalocytes, megaloblasts, macrocytosis, anisocytosis, poikilocytosis, erythrocytes with Howell–Jolly bodies, Cabot rings, polysegmented neutrophils.

Conclusion:

№ 5

RBC	**2.0×10^{12} /L**	
HGB	70 g/L	
Ret	0.05 %	
HCT	20.5 %	
CI	To calculate	
MCV	102.5 fL	
MCH	35 pg/cell	
MCHC	To calculate	
RDW	15.2 %	
WBC	**2.5×10^{9} /L**	
Baso	1 %	
Eosin	2 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	2 %	
– segmentated	52 %	
Lymph	41 %	
Mono	2 %	
PLT	**80.0×10^{9} /L**	
ESR	30 mm/h	
In the smear: anisocytosis, toxic granularity of neutrophils.		
Conclusion:		

№ 6

RBC	**2.7×10^{12} /L**	
HGB	68 g/L	
Ret	5.0 %	
CI	To calculate	
MCV	88.9 fL	
WBC	**12.0×10^{9} /L**	
Baso	0 %	
Eosin	2 %	
Neu:		
– myelo	0 %	
– meta	7 %	
– band	17 %	
– segmentated	53 %	
Lymph	17 %	
Mono	4 %	
PLT	**150.0×10^{9} /L**	
ESR	18 mm/h	
In the smear: polychromatophils, single normoblasts.		
Conclusion:		

№ 7

RBC	**1.9×10^{12} /L**	
HGB	45 g/L	
Ret	12 %	
HCT	15 %	
CI	To calculate	
MCV	78.9 fL	
MCH	To calculate	
WBC	**7.8×10^{9} /L**	
Baso	0.5 %	
Eosin	1.5 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	4 %	
– segmentated	60 %	
Lymph	28 %	
Mono	6 %	
PLT	**350.0×10^{9} /L**	
ESR	1 mm/h	

In the smear: drepanocytes, meniscocytes, single normoblasts.

Conclusion:

№ 8

RBC	**3.32×10^{12} /L**	
HGB	72 g/L	
Ret	10 %	
HCT	18 %	
CI	To calculate	
MCV	54.2 fL	
MCH	To calculate	
MCHC	To calculate	
WBC	**4.4×10^{9} /L**	
Baso	0.5 %	
Eosin	2 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	3 %	
– segmentated	54.5 %	
Lymph	35 %	
Mono	5 %	
PLT	**180.0×10^{9} /L**	
ESR	20 mm/h	

In the smear: anisocytosis, poikilocytosis, punctuate basophilia in RBC, target cells, microcytosis. Serum iron is 64 μmol/L. Osmotic resistance of RBC is increased

Conclusion:

What additional research is needed to clarify the diagnosis?

_____

№ 9

RBC	**2.4×10^{12} /L**	
HGB	85 g/L	
Ret	35 %	
HCT	20 %	
CI	To calculate	
MCV	69 fL	
MCH	35.4	
MCHC	42.4	
WBC	**6.1×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	3 %	
– segmentated	60 %	
Lymph	32 %	
Mono	5 %	
PLT	**200.0×10^{9} /L**	
ESR	19 mm/h	

In the smear: microspherocytosis, normoblasts in all fields of vision. Osmotic resistance of RBC is decreased.

Conclusion:

№ 10

RBC	**6.6×10^{12} /L**	
HGB	174 g/L	
Ret	5 %	
HCT	60 %	
CI	To calculate	
MCV	90 fL	
MCH	To calculate	
MCHC	To calculate	
WBC	**8.7×10^{9} /l**	
Baso	0 %	
Eosin	1 %	
Neu:		
– myelo	0 %	
– meta	1 %	
– band	5 %	
– segmentated	65 %	
Lymph	24 %	
Mono	4 %	
PLT	**280.0×10^{9} /L**	
ESR	8 mm/h	

Conclusion:

№ 11

RBC	**7.32×10^{12} /L**	
HGB	180 g/L	
Ret	3 %	
HCT	57 %	
CI	To calculate	
MCV	77.8 fL	
MCH	To calculate	
MCHC	To calculate	
WBC	**16.4×10^{9} /L**	
Baso	0.5 %	
Eosin	7.5 %	
Neu:		
– myelo	0 %	
– meta	3 %	
– band	10 %	
– segmentated	59 %	
Lymph	17 %	
Mono	3 %	
PLT	**628.0×10^{9} /L**	
ESR	1 mm/h	

In the smear: polychromatophils, single normoblasts.

Conclusion:

№ 12

RBC	**4.2×10^{12} /L**	
HGB	125 g/L	
HCT	40 %	
CI	To calculate	
MCV	95 fL	
MCH	To calculate	
MCHC	To calculate	
WBC	**17.4×10^{9} /L**	
Baso	0 %	
Eosin	0.5 %	
Neu:		
– myelo	0 %	
– meta	5 %	
– band	12 %	
– segmentated	64 %	
Lymph	14 %	
Mono	4.5 %	
PLT	**290.0×10^{9} /L**	
ESR	25 mm/h	

Conclusion:

№ 13

RBC	**3.22×10^{12} /L**	
HGB	75 g/L	
HCT	32 %	
CI	To calculate	
MCV	99 fL	
MCH	To calculate	
MCHC	To calculate	
WBC	**30.0×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu:		
– myelo	6 %	
– meta	17 %	
– band	30 %	
– segmentated	42 %	
Lymph	4 %	
Mono	1 %	
PLT	**220.0×10^{9} /L**	
ESR	45 mm/h	

In the smear: toxic granularity of neutrophils.

Conclusion:

№ 14

RBC	**3.8×10^{12} /L**	
HGB	116 g/L	
HCT	36 %	
CI	To calculate	
MCV	94 fL	
MCH	To calculate	
MCHC	To calculate	
WBC	**14.8×10^{9} /L**	
Baso	0 %	
Eosin	2 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	5 %	
– segmentated	21 %	
Lymph	60 %	
Mono	12 %	
PLT	**185.0×10^{9} /L**	
ESR	17 mm/h	

Conclusion:

№ 15

RBC	**4.4 × 10^{12} /L**	
HGB	130 g/L	
HCT	40 %	
CI	To calculate	
MCV	To calculate	
MCH	To calculate	
MCHC	To calculate	
WBC	**8.8 × 10^{9} /L**	
Baso	1 %	
Eosin	11 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	5 %	
– segmentated	54 %	
Lymph	24 %	
Mono	5 %	
PLT	**200.0 × 10^{9} /L**	
ESR	10 mm/h	

Conclusion:

№ 16

RBC	**4.28 × 10^{12}/L**	
HGB	142 g/L	
HCT	38 %	
CI	To calculate	
MCV	To calculate	
MCH	To calculate	
WBC	**3.2 × 10^{9}/L**	
Baso	0 %	
Eosin	1 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	12 %	
– segmentated	23 %	
Lymph	57 %	
Mono	7 %	
PLT	**285.0 × 10^{9}/L**	
ESR	18 mm/h	

Conclusion:

№ 17

RBC	**3.84×10^{12} /L**	
HGB	120 g/L	
Ret	1 %	
HCT	35 %	
CI	To calculate	
MCV	90 fL	
MCH	To calculate	
WBC	**1.0×10^{9} /L**	
Baso	0 %	
Eosin	0.5 %	
Neu	0 %	
Lymph	82 %	
Mono	17.5 %	
PLT	**182.0×10^{9} /L**	
ESR	17 mm/h	

Conclusion:

№ 18

RBC	**2.96×10^{12} /L**	
HGB	97 g/L	
Ret	0.5 %	
HCT	25 %	
CI	To calculate	
MCV	97 fL	
MCH	To calculate	
WBC	**1.0×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	0 %	
– segmentated	15 %	
Lymph	68 %	
Mono	17 %	
PLT	**85.0×10^{9} /L**	
ESR	49 mm/h	

In the smear: toxic granularity of neutrophils.
Note: sore throat with necrotic coating.

Conclusion:

№ 19

RBC	**0.56 × 10^{12} /L**	
HGB	17 g/L	
Ret	0 %	
HCT	6 %	
CI	To calculate	
MCV	107 fL	
MCH	30 pg/cell	
MCHC	28.3 g/dL	
WBC	**0.9 × 10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	0 %	
– segmentated	12 %	
Lymph	86 %	
Mono	2 %	
PLT	**25.0 × 10^{9} /L**	
ESR	40 mm/h	

In the smear: anisocytosis, poikilocytosis, toxic granularity of neutrophils.

Conclusion:

№ 20

RBC	**4.36 × 10^{12}/L**	
HGB	118 g/L	
HCT	38 %	
CI	To calculate	
MCV	86 fL	
MCH	To calculate	
WBC	**18.2 × 10^{9}/L**	
Baso	0 %	
Eosin	3 %	
Neu:		
– myelo	0 %	
– meta	1 %	
– band	5 %	
– segmentated	10 %	
Lymph (atypical lymphocytes)	67 %	
Mono	13 %	
PLT	**350 × 10^{9}/L**	

Plasma cells — 4 per 100 leukocytes.

Toxic granularity of neutrophils.

Conclusion:

№ 21

RBC	**2.4×10^{12} /L**	
HGB	75 g/L	
HCT	20 %	
CI	To calculate	
MCV	83 fL	
MCH	To calculate	
WBC	**3.2×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Myeloblast	30 %	
Pro	1 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	4 %	
– segmentated	30 %	
Lymph	30 %	
Mono	5 %	
PLT	**75.0×10^{9} /L**	
ESR	55 mm/h	
Conclusion:		

№ 22

RBC	**2.5×10^{12} /L**	
HGB	78 g/L	
Ret	0 %	
HCT	20 %	
CI	To calculate	
MCV	To calculate	
MCH	To calculate	
WBC	**200.0×10^{9} /L**	
Myeloblast	97 %	
Pro	0.5 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	0 %	
– segmentated	2.5 %	
Lymph	0 %	
Mono	0 %	
PLT	**48.0×10^{9} /L**	
ESR	60 mm/h	
Conclusion:		

№ 23

RBC	**1.1×10^{12} /L**	
HGB	37 g/L	
Ret	0 %	
HCT	10 %	
CI	To calculate	
MCV	90 fL	
WBC	**8.4×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu :		
– мyelo	0 %	
– мeta	0 %	
– band	2 %	
– segmentated	10 %	
Lymphoblast	62 %	
Lymph	20 %	
Mono	6 %	
PLT	**28.0×10^{9} /L**	
ESR	52 mm/h	

Conclusion:

№ 24

RBC	**2.0×10^{12} /L**	
HGB	64 g/L	
HCT	16 %	
CI	To calculate	
MCV	80 fL	
WBC	**8.4×10^{9} /L**	
Baso	0 %	
Eosin	0 %	
Neu:		
– segmentated	4.5 %	
Lymph	4 %	
Mono	1 %	
Blast	90.5 %	
PLT	**32×10^{9} /L**	

Note: reaction of blast cells to peroxidase is positive

Conclusion:

№ 25

RBC	**2.3×10^{12} /L**	
HGB	58 g/L	
HCT	20 %	
CI	To calculate	
MCV	To calculate	
MCH	To calculate	
WBC	**2.7×10^{9} /L**	
Baso	0.5 %	
Eosin	0 %	
Neu :		
– myelo	0 %	
– meta	0 %	
– band	1.5 %	
– segmentated	8.5 %	
Lymph	7.0 %	
Mono	4.5 %	
Blast	78 %	
()		
PLT	**93×10^{9}/L**	

Note: cytochemical reactions are negative in blast cells

Conclusion:

№ 26

RBC	**3.5×10^{12} /L**	
HGB	110 g/L	
HCT	35 %	
CI	To calculate	
MCV	100 fL	
WBC	**150.0×10^{9} /L**	
Baso	6 %	
Eosin	7.5 %	
Myeloblast	1 %	
Pro	2 %	
Neu:		
– myelo	25 %	
– meta	22.5 %	
– band	18 %	
– segmentated	14 %	
Lymph	3 %	
Mono	1 %	
PLT	**522.0×10^{9} /L**	
ESR	35 mm/h	

Conclusion:

№ 27

RBC	**3.2×10^{12} /L**	
HGB	87 g/L	
HCT	30 %	
CI	To calculate	
MCV	To calculate	
MCH	To calculate	
WBC	**38.0×10^{9} /L**	
Baso	8 %	
Eosin	3 %	
Myeloblast	1 %	
Pro	1 %	
Neu:		
– myelo	5 %	
– meta	4.5 %	
– band	5.5 %	
– segmentated	45 %	
Lymph	24 %	
Mono	3 %	
PLT	**380.0×10^{9} /L**	
ESR	35 mm/h	
Conclusion:		

№ 28

RBC	**2.8×10^{12} /L**	
HGB	68 g/L	
HCT	20 %	
CI	To calculate	
MCV	80 fL	
MCH	To calculate	
WBC	**300.0×10^{9} /L**	
Baso	0 %	
Eosin	1 %	
Neu:		
– myelo	0 %	
– meta	0 %	
– band	1 %	
– segmentated	2 %	
Lymphoblast	1 %	
Lymph	94 %	
Mono	1 %	
PLT	**87.0×10^{9} /L**	
ESR	40 mm/h	
In the smear: a large number of cells (shadows) of Botkin–Gumprecht		
Conclusion:		

№ 29

RBC	**2.1×10^{12} /L**	
HGB	61.1 g/L	
HCT	16 %	
CI	To calculate	
WBC	**176.5×10^{9} /L**	
Baso	10 %	
Eosin	3 %	
Myeloblast	10 %	
Pro	12 %	
Neu:		
– мyelo	16 %	
– мeta	17 %	
– band	9 %	
– segmentated	19 %	
Lymph	3 %	
Mono	1 %	
PLT	**93.6×10^{9} /L**	
ESR	50 mm/h	

Cytogenetic characteristics of blood cells: 95.5 % of cells contain Ph 't (9; 22) (q34; q11) chromosome

Conclusion:

№ 30

RBC	**2.1×10^{12} /L**	
HGB	70 g/L	
Ret	20 %	
HCT	15 %	
CI	To calculate	
MCV	71.4 fL	
WBC	**12×10^{9} /l**	
Baso	0 %	
Eosin	0 %	
Neu:		
– myelo	2 %	
– meta	4 %	
– band	8 %	
– segmentated	67 %	
Lymph	16 %	
Mono	3 %	
PLT	**199.0×10^{9} /L**	
ESR	18 mm/h	

In the smear: erythrocytes with Heinz bodies, anisocytosis, poylocytosis, degmacytes, schistocytes, punctate basophilia of erythrocytes, normoblasts.

Conclusion:

Control questions

1. Typical diorders of erythron, leukocytes, platelets and hemostasis systems: definition of the consepts, classification criteria, changes in peripheral blood.
2. Algorithm of pathophysiological analysis of hemogramms for the typical disorders of the blood system.
3. Criteria for assessing the severity of the patient's state and the prognosis of the disease according the hemogram data.
4. The principles of hemogramm conclusion makig as one of the most important link in the clinical diagnosis of patients.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 7).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 8. PATHOLOGICAL PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM. HEART FAILURE, ITS TYPES. OVERLOAD AND MYOCARDIAL FORMS OF HEART FAILURE

Date: «____» _____ 20__

Purpose of the Lesson: to discuss the basic types of blood circulation insufficiency, to study the causes, forms and development mechanisms of acute blood circulation insufficiency of cardiac genesis, to give the pathogenetic assessment of urgent and long-term compensation reactions for this form of circulatory failure.

Tasks:

– To study the causes, development mechanisms and manifestations of acute right ventricular failure.

– To get acquainted with modeling of experimental myocardial necrosis, to analyze some mechanisms of electrocardiographic abnormality formation in the given pathology.

– To study the causes, development mechanisms and manifestations of chronic right ventricular failure.

– To solve the situational tasks on the topic of the Lesson.

– Control test.

PART 1. WORKING WITH TRAINING MATERIALS

Answer the questions:

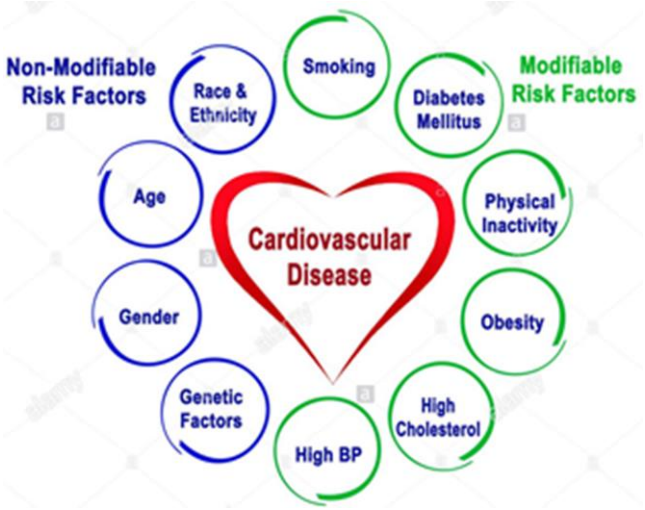
1. Give the definition of *"Risk factors for circulatory failure"*:

_____
_____
_____
_____
_____

According to the WHO there are more than _____ risk factors for the cardiovascular disease.

The presence of only one factor increases the probability of the disease development in _____ times.

The combination of risk factors for cardiovascular disease increases the probability of the disease development in _____ times.



2. Fill in the Table.

Classification of risk factors

Classification criteria	Types of risk factors	Examples
According to the primary effects on the heart and blood vessels	1. _____ _____ 2. _____ _____	1. _____ _____ 2. _____ _____
By possibility on the risk factors influence	1. _____ _____ 2. _____ _____	1. _____ _____ 2. _____ _____

3. Give the definition of "*circulatory failure*":_____
_____
_____

4. Fill in the Table.

Types of circulatory failure

By the course	– _____ _____ – _____ _____
By mechanisms	– _____ – _____ – _____
By compensation	– _____ _____ – _____ _____

5. Give the definition of "*Heart Failure*": _____
_____
_____
_____

6. Fill in the Table.

Types of Heart Failure

By origin	1. _____ 2. _____ – _____ _____ – _____ _____ 3. _____
According to the primary violations of myocardial contractile function or a decrease in venous return of blood	1. _____ _____ 2. _____ _____
By localization	1. _____ _____ 2. _____ _____ 3. _____ _____
By development speed	1. _____ 2. _____
Hemodynamic types	1. _____ _____ 2. _____ _____ 3. _____

7. List the possible causes of chronic circulatory failure: _____
_____

8. Fill in the Table.

Classification of chronic circulatory failure (by N. D. Strazhesko, V. Kh. Vasilenko)

Stage	Characteristic
1. Compensation	
2. Subcompensation	
2-A	
2-B	
3. Decompensation	

9. Fill in the Table.

Hemodynamic types of heart failure

Feature	Systolic Dysfunction	Diastolic Dysfunction
Definition	_____	_____
Etiology	1. _____ 2. _____ 3. _____ 4.	1. _____ 2. _____ 3. _____
Pathogenesis (continue the circuit)	↓ myocardial contractility ↓ ↓ of cardiac output ↓ organ hypoperfusion *(especially the brain, heart, kidneys, and muscles)* ↓ – SAS activation → _____ _____ – activation of RAAS → _____	↓ compliance and impaired filling of the ventricle with blood ↓ ↑ end-diastolic pressure ↓ ↓ of cardiac output ↓ _____ _____ ↓ _____
Clinical symptoms	_____	_____

10. Fill in the Table.

Types of Heart Failure

Type of insufficiency	**Left ventricular failure**	**Right ventricular failure**
Blood circulation		
Symptoms	_____ _____ _____	_____ _____ _____
	Common symptoms: _____ _____	

11. Give the definition of *"coronary insufficiency"*: _____
_____
_____

12. List the clinical forms of coronary heart disease:

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

13. List and describe the experimental methods of modeling of ischemic heart disease:

1. _____
_____
2. _____
_____
3. _____
_____

14. Fill in the Table.

The pathogenesis of coronary insufficiency

Ischemic syndrome	**Reperfusion syndrome**
The mechanisms: – _____ _____ _____ – _____ _____ _____ – _____ _____ _____ – _____ _____ _____	*Postischemic reperfusion syndrome is* _____ _____ _____ _____ <u>Pathogenesis</u>: blood flow to the previously ischemic myocardial zone with accumulation of unused excess oxygen ↓ activation of LPO processes ↓ _____ _____ _____

15. Fill in the Table.

The value of reperfusion for the organism

Positive	**Negative**
1. _____ _____ 2. _____ _____ 3. _____ _____ 4. _____	1. _____ _____ 2. _____ _____ 3. _____ _____

16. Give the definition to *"resorption-necrotic syndrome"* in myocardial infarction: _____
_____
_____

17. List and describe the symptoms typical for resorption-necrotic syndrome at myocardial infarction:

1._____
_____
2._____
_____
3._____
_____
4._____
_____

18. Sketch and briefly describe ECG changes typical for ischemia, ischemic damage, and myocardial necrosis.

Type of change	**Ischemia**	**Ischemic injury**	**Myocardial necrosis**
ECG			
Description of the changes	_____ _____	_____ _____	_____ _____

19. List and describe the main principles of coronary insufficiency therapy:

1._____
_____
2._____
_____
3._____
_____

20. Fill in the Table.

Compensation mechanisms for heart failure

<table>
<tr>
<th>Intracardiac</th>
<th>Extracardiac</th>
</tr>
<tr>
<td>

Urgent:

1. _____
2. _____
3. _____

Comparative characteristics of the heterometric and homeometric compensation mechanisms

<table>
<tr><th>Comparison criteria</th><th>Heterometric mechanism (Frank-Starling law)</th><th>Homeometric mechanism (Anrep phenomenon)</th></tr>
<tr><td>Occurs in response to overload</td><td></td><td></td></tr>
<tr><td>Change in the muscle fiber length (+/-)</td><td></td><td></td></tr>
<tr><td>When does it develop?</td><td></td><td></td></tr>
<tr><td>Energy benefit of the mechanism</td><td></td><td></td></tr>
</table>

Long-term:

***Myocardial remodeling* is** _____

_____

_____

Remodeling variants:

1. _____
2. _____
3. _____
4.

</td>
<td>

1. _____

_____

– _____

– _____

– _____

2. _____

_____

– _____

– _____

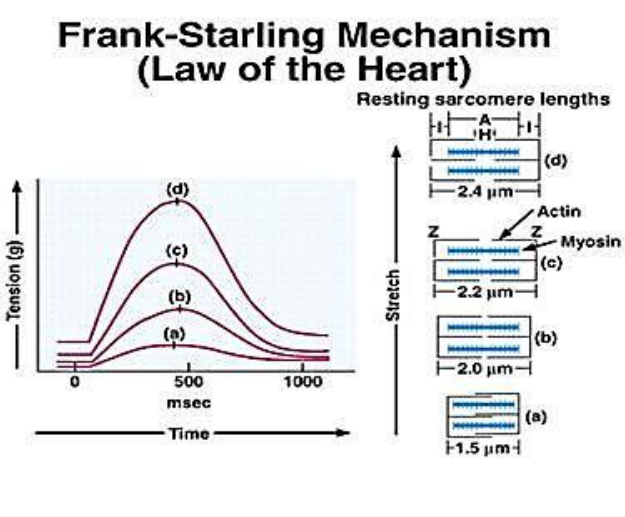
Manifestations:

_____

_____

Frank-Starling Law of the Heart

- Relationship between EDV, contraction strength and SV.
- Intrinsic mechanism:
  - Varying degree of stretching of myocardium by EDV.
  - As EDV increases, myocardium is increasingly stretched, and contracts more forcefully



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

21. What is meant by *"compensatory hyperfunction of the heart"* (according to F. Z. Meerson)?_____

_____

_____

22. List and describe the development stages of compensatory cardiac hyperfunction:

1. _____

_____

2. _____

_____

3. _____

_____

23. List the features of a hypertrophied myocardium:

1. _____

_____

2. _____

_____

3. _____

_____

4. _____

_____

5. _____

_____

6. _____

_____

24. List the principles of heart failure therapy (with examples):

1. _____

_____

2. _____

_____

3. _____

_____

PART 2. PRACTICAL PART

Work 1. INTRODUCTION TO THE MODELING OF EXPERIMENTAL MYOCARDIAL NECROSIS. ANALYSIS OF SOME MECHANISMS OF FORMATION OF ECG DISORDERS IN THE DEVELOPMENT OF MYOCARDIAL NECROSIS

The immobilized frog is fixed to a wooden board in the supine position. Needle electrodes from the electrocardiograph are inserted into both front and left hind limbs. The heart is exposed (with the opening of the pericardium). The initial electrocardiogram in I and III standard leads is recorded. A crystal of silver nitrate (lyapis), which causes myocardial necrosis, is placed on the anterior surface (left half) of the ventricle. The second electrocardiogram is registered: the rise of the ST segment (the so-called "coronal wave") is observed. Register the ECG changes, highlight the rise of the ST segment with a colored pencil:

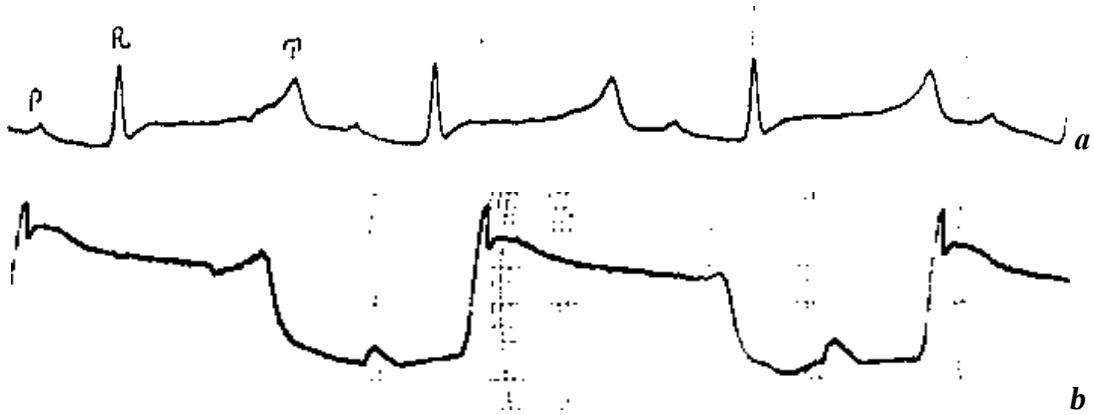


Fig. 1. Changes in the ECG of a frog in experimental myocardial necrosis caused by the action of a lapis crystal:
a — ECG of the frog in norm; *b* — ECG after applying lapis crystal to the myocardial surface

To explain the mechanism of ST interval elevation in myocardial necrosis, we compare ECG changes in the following experiments. We fix the second immobilized frog, expose the heart (with opening the pericardium), inject electrodes from the cardiograph into the corresponding limbs. We record an ECG in the same leads. Further, on the anterior surface of the heart, we apply:

1. A piece of necrotic cardiac muscle of the first frog. During the subsequent recording of the ECG, we note the rise in the ST interval, after which we wash the heart several times with Ringer's solution for cold-blooded and note the normalization of the ECG.

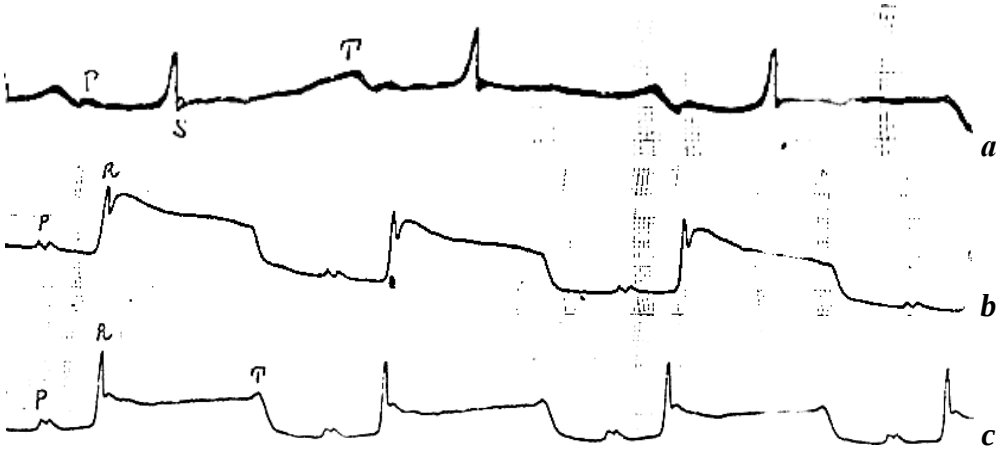


Fig. 2. Changes in the ECG of a frog under the influence of local application of a necrotic piece of the heart muscle followed by washing the heart with Ringer's solution: *a* — ECG in norm; *b* — ECG after application of a necrotic piece of the heart muscle; *c* — ECG after washing the heart with Ringer's solution

2. A cotton swab dipped in a 1 % solution of potassium chloride. We register an ECG, also note the rise of the ST segment, which disappears with repeated washing of the heart with Ringer's solution for cold-blooded.

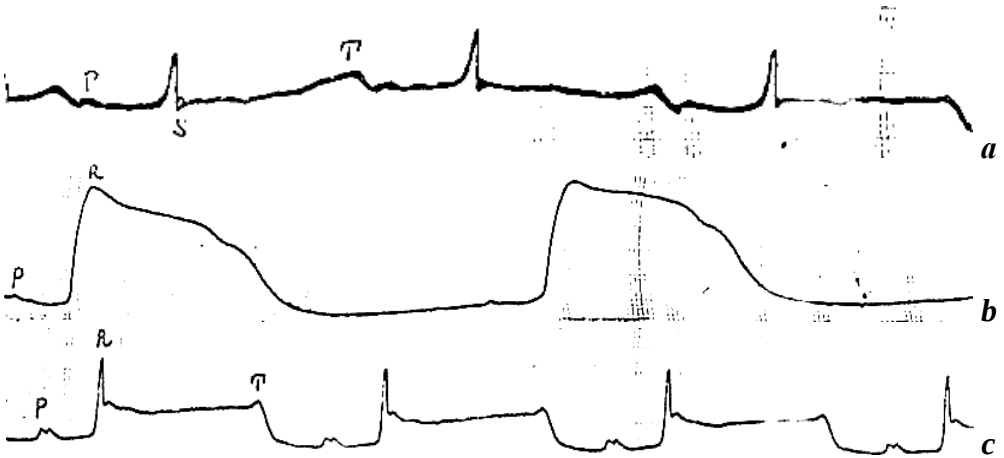


Fig. 3. Changes in the ECG of a frog under local application of cotton swab dipped in 1 % KCl solution, followed by washing Ringer's heart: *a* — ECG in norm; *b* — ECG after application of KCl; *c* — ECG after washing the heart with Ringer's solution

Make a conclusion about the possible mechanism of the formation of the ST segment elevation in myocardial necrosis: _____
_____
_____

PART 3. STUDYING MATERIALS OF EDUCATIONAL VIDEOS

Work 1. STUDY OF THE MATERIALS OF THE EDUCATIONAL VIDEO "ACUTE CIRCULATORY FAILURE OF THE RIGHT VENTRICULAR TYPE" (A. A. Krivchik et al., MSMI, 1978)

Analyze the watched material and answer the following **questions:**

1. What is the essence of the methodological technique used to model acute circulatory failure? _____
_____
_____

2. With the help of what technique was it possible to painlessly record the value of arterial, venous and portal pressure, the degree of blood oxygen saturation, etc. under the conditions of an experiment in non-anesthetized animal? _____
_____
_____

3. Underline in blue color the changes that reflect the development of pathological reactions in response to an acute disturbance of blood flow in the posterior vena cava:

1) a sharp drop in blood pressure, a collaptoid state with loss of consciousness;
2) increased pressure in the veins below the occlusion place;
3) pressure increase in the system of v. portae;
4) increased arterio-venous oxygen difference;
5) severe brain hypoxia;
6) hypoxia of the respiratory and vasomotor centers;
7) tachycardia;
8) dyspnea;
9) myocardial hypoxia;
10) decreased blood flow rate;
11) periodic breathing.

Which of them reflect changes of compensatory-adaptive nature (underline in red)?

4. Why should the changes you mentioned be regarded as compensatory-adaptive? What are they aimed at? In what cases does tachycardia not improve, but makes the situation worse and why? _____
_____
_____

5. What type of reactions (pathological or compensatory-adaptive) prevailed in the modeled form of acute circulatory failure?

_____

_____

6. Could the body independently, without medical assistance, get out of this state?_____

_____

_____

Work 2. STUDY OF THE MATERIALS OF THE EDUCATIONAL VIDEO "CHRONIC CIRCULATORY FAILURE OF THE RIGHT VENTRICULAR TYPE" (A. A. Krivchik et al., MSMI, 1979)

While watching the film, pay attention to the following information:

– features and advantages of the method used for modeling of chronic circulatory failure (CCF) of the right ventricular type (RVT);

– a methodological technique that provides the ability to control the severity of the phenomena of compensation at various stages of the CCF of RVT;

– the nature and dynamics of changes in arterial, venous and portal pressures, blood flow velocity, arterio-venous difference in O_2, myocardial contractility, ECG and EEG data as CCF develops;

– the influence of the increasing CCF of the RVT on the state of blood vessels, blood circulation, structure and functional state of the liver;

– symptoms from a number of organs and systems, reflecting mainly the phenomenon of "break", damage;

– reactions of compensatory-adaptive nature;

– manifestations of decompensation;

– the role of compensation mechanism training in achieving an adaptive effect in the development of CHF.

Answer the questions:

1. What are the features of the method used for modeling of chronic circulatory failure (CCF) of the right ventricular type (RVT)? What are its advantages in comparison with the imposition of a narrowing ligature on the vessel, usually used for these purposes?_____

_____

_____

_____

_____

2. Reflect the dynamics of changes in blood pressure in the posterior vena cava (PCV) (a), portal (b) veins and in the aorta (c) during the development of CCF of RVT on the corresponding graphs.

Fig. 1. Change in blood pressure in posterior vena cava during the development of CCF of RVT

Fig. 2. Change in blood pressure in the portal vein during the development of CCF of RVT

Fig. 3. Change in blood pressure in the aorta during the development of CCF of RVT

3. Underline in blue the signs that mainly reflect the phenomenon of "break", damage, i. e., the actual pathological reactions of the body that arise during the development of CCF of RVT?

1) significant increase in pressure in the posterior (inferior) vena cava;
2) the progressive increase in pressure in the system v. portae;
3) increasing slowdown in blood flow velocity;
4) moderate tachycardia;
5) decrease in blood oxygen saturation and increase in Δ A-V of O_2;
6) increasing signs of brain and heart hypoxia;
7) decreased pumping function of the heart;
8) deep and rapid breathing;
9) ↓ in the number of functioning vessels of the liver due to their obliteration;
10) development of collateral circulation (caput medusae);
11) liver congestion with parenchymal atrophy and fibrosis
12) development of hepatocellular failure;
13) extremity edema, ascites, hydrothorax.

Which of the changes shown in the film in case of CCF of RVT should be interpreted as the predominant manifestation of compensation reactions (underline in red), see above?

4. Underline <u>in red</u> the signs by which it is possible to make a conclusion about a gradual increase and about the achieved severity of compensation reactions?

1) sharp tissue swelling;
2) severe shortness of breath at rest;
3) relative stabilization of hemodynamics and liver function;
4) relative normalization of the general condition of the animal when the PCV is compressed;
5) ↑ of the period of life-safe clamping of the PCV (up to 2 hours);
6) repeated sharp increasing slowdown of blood flow velocity.

Which changes of registered parameters shown in the film should be regarded as a manifestation of decompensation (<u>underline in blue</u>) see above?

Work 3. SOLVING SITUATIONAL TASKS

№ 1

Patient K., 34 years, was delivered to clinic with a fracture of the right hip. On the next day severe pains in the thoracic cavity developed. The skin integuments became cyanotic. RR — 36 resp. per min. HR — 116 beats/min. BP — 85/60 mm Hg. The borders of the heart — in norm. Sharp swelling of cervical veins was observed. The liver is enlarged in size. On the X-ray film of the thoracic organs a cone-shaped shadowing is clearly marked in the lower lobe of the right lung. The oxyhemoglobin content in the arterial blood — 85 %, in the venous blood — 30 %. The erythrocyte count in the peripheral blood is 5.0×10^{12}/, leukocytes — 16×10^{9}/l.

Questions:

1. What caused the insufficiency development of blood circulation?
2. What type of cardiac insufficiency is there in the patient?
3. What is the pathogenesis of clinical symptoms?

№ 2

Patient M., 46 years, developed severe pains behind the breastbone during intensive physical work in the garden; they were controlled by nitroglycerin. Previously squeezing pains in the heart area had occurred on physical exertion, but they subsided quickly at rest. In the evening the pains relapsed and were not controlled by nitroglycerin. There appeared breathlessness and cough with profuse liquid sputum. The patient was hospitalized.

Objectively: the patient is of a medium height, hyperstenic, the skin integuments and visible mucous membranes are pale with a cyanotic shade. The respiration is frequent — 42 resp./min. HR — 110 beats/min. On auscultation various moist râles are heard over the whole surface of the right and left lungs. The minute volume of the lungs is 2.8 l, BP — 110/70 mm Hg. The oxyhemoglobin content in the arterial blood is 81 %, in venous — 45 %. The erythrocyte count in the peripheral blood is 5.0×10^{12}/, leukocytes — 11.9×10^{9}/l. The leukocyte formula: B — 0, E — 1, Y — 2, R — 7, S — 67, L — 19, M — 4.

Questions:

1. Is there any cardiac insufficiency in the patient?
2. Specify the main compensatory mechanism of hemodynamic impairments in the patient?
3. What syndrome is marked by an acute left-ventriular cardiac insufficiency in the patient?

№ 3

Patient A., 56 years, is in the department of intensive care with the diagnosis "Acute expanded myocardial infarction". On the 2nd day after a short-term improvement of the condition, despite the continuing therapeutic measures, breathlessness increased, profuse fine-vesicular râles in the lungs appeared.

Questions:

1. What pathologic processes in the respiratory and/or cardio-vascular system could cause the clinical picture of the patient's condition on the 2nd day?

2. What factors of the intracardiac and systemic hemodynamics can prove the presence and progressing of cardiac insufficiency in the patient? Specify these factors and point out the trend of their changes.

3. In case the version of cardiac insufficiency in this patient is confirmed, specify its type (by the affected part of the heart and the speed of its development). Is it possible to suggest that this insufficiency is of a) an overstrain type; b) a myocardial type; c) a mixed type? Prove your answer.

№ 4

Patient A., 50 years, was admitted to the intensive care department with complaints of squeezing pains behind the breastbone, weakness, breathlessness lasting for 20 h.

On examination: the state of a moderate severity, hyperemia of the face. On auscultation the respiration in the lungs is vesicular, no râles. RR — 16 resp./min, heart sounds are dull, rhythmic. HR — 80 beats/min. BP — 130/85 mm Hg. ECG: the rhythm is sinus, Q-segment is deepened and elevation of ST-segment in the first outlet with a mirror reflection in the III outlet. The activity of AST and LDH in the blood is sharply increased. Leukocytes — 12.3×10^9/l. Thrombocytes — 450×10^9/l. Prothrombin index — 120 % (the norm up to 105 %).

Questions:

1. The development of what disease does the described changes evidence?
2. In what department of the heart is the pathologic process localized?
3. Explain, what is the cause of the AST activity increase in this type of pathology?
4. What basic syndromes characteristic of this disease developed in the patient?
5. What is a possible development cause of this disease?

№ 5

Patient T., 45 years, suffers from a combined heart defect developed on the background of rheumatism she had suffered in youth. For many years she felt satisfactory. However after quinsy she has suffered this year her condition considerably aggravated. The patient is troubled with breathlessness, palpitation, pain in the heart area, hemoptisis, edemas.

Objectively: the skin integuments and visible mucous membranes are cyanotic. Percussion established dilation of the heart boarders to all sides. A cardiac beat is generalized, weak. Systolic and diastolic murmurs are heard at the apex. The second sound over the pulmonary artery is increased and split. The pulse — 96 beats/min, arrhythmic. BP — 130/80 mm Hg. Moist râles are heard in the lungs. The liver is enlarged, tender on palpation. Marked edemas on the legs. Erythrocyte count in the blood is elevated. The circulating blood volume is increased. The stroke volume is decreased.

Questions:

1. What signs of circulatory insufficiency are there in the patient?
2. Explain the pathogenesis of clinical manifestations of circulatory insufficiency.
3. Why do the changes of factors of the central hemodynamics and circulatory system in the patient occur?

№ 6

Patient A., 62 years, is in hospital for expressed left-ventricular insufficiency due to myocardial infarction that he had suffered a month before. He is in a forced position. A considerable part of the day and night he is sitting on the bed with his feet on the floor. On an attempt to lie down his breathlessness sharply increases.

Questions:

1. What is the pathogenesis of breathlessness in left-ventricular insufficiency?
2. Why the severity of breathlessness in the patient in a sitting position is less than in a lying position?

.

Control questions

1. Insufficiency of blood circulation. Definition, types.
2. Heart failure. Definition. The main causes of heart failure. Classification of heart failure by pathogenesis, localization, course. The concept of primary and secondary heart failure.
3. Hemodynamic classification of heart failure. Concept of systolic and diastolic dysfunction. Etiology, pathogenesis, hemodynamic disturbances and clinical manifestations of systolic and diastolic dysfunction.
4. The main indicators of changes in intracardiac and systemic hemodynamics in all forms of heart failure.
5. Etiology, pathogenesis and manifestations of acute left and right ventricular heart failure.
6. Coronary insufficiency. Definition, clinical forms of ischemic heart disease. Relative and absolute coronary insufficiency.
7. Etiological risk factors for ischemic heart disease. Experimental methods of modeling. The main causes of non-coronary necrosis of the myocardium.
8. Pathogenesis of ischemic and reperfusion syndromes in coronary insufficiency, their manifestations.
9. Myocardial infarction. Pathogenesis and manifestations of the main clinical and laboratory syndromes: pain, acute left ventricular failure (cardiac asthma, cardiogenic shock), resorption-necrotic syndrome. Impairment of metabolism, bioelectric and contractile properties of the myocardium.
10. Classification of chronic circulatory insufficiency of cardiac genesis by severity (Vasilenko-Strazhenko).
11. Mechanisms for compensation of heart failure. Their types, manifestations and pathogenetic assessment.
12. Comparative assessment of heterometric and homeometric mechanisms of intracardiac compensation in cardiac overload.
13. The concept of myocardial remodeling. Outcomes of myocardial remodeling depending on the type of hemodynamic overload and myocardial injury.
14. Etiology, pathogenesis, mechanisms of urgent and long-term intracardiac compensation in chronic myocardial overload with volume and pressure, outcomes, the nature of hemodynamic disturbances, clinical manifestations.
15. Pathogenesis and clinical manifestations of low ejection and stagnation syndromes on the pathways of inflow to the weakened heart. Signs of stagnation in the pulmonary and systemic circulation.

16. Extracardiac mechanisms of compensation of heart failure, their pathogenetic assessment. The role of the autonomic nervous system in the compensation of chronic heart failure. The concept of hormone-neurotransmitter dissociation. Its pathogenetic assessment.

17. The main effects of hyperactivation of the sympatho-adrenal and renin-angiotensin-aldosterone systems in chronic heart failure. Mechanisms of the cardiotoxic effect of catecholamines. Pathogenetic assessment of tachycardia in cardiac overload.

18. Reactions of the respiratory system and the hematopoietic system during the development of heart failure, the mechanisms of switching on these systems.

19. Etiology, pathogenesis and manifestations of chronic left and right ventricular heart failure.

20. Characteristics of compensatory hyperfunction of the heart in acute experimental overload of the left ventricle with resistance (according to F. Z. Meerson). Stages of development of compensatory cardiac hyperfunction.

21. Myocardial hypertrophy, causes and mechanisms of its development. Functional and metabolic features of the hypertrophied myocardium. Mechanisms of the development of decompensation in pathological myocardial hypertrophy.

22. Pathogenetic principles of heart failure therapy.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 8).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 9. PATHOLOGICAL PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM. HEART RATE DISORDERS (ARRHYTHMIAS), TYPES, CAUSES, MECHANISMS

Date: «____» _____ 20__

Purpose of the Lesson: to study heart rhythm disorders: disturbances of excitability, automatism and conductivity of the heart, their types, causes, and mechanisms of development, electrocardiographic and hemodynamic manifestations.

Tasks:

– To study the electrocardiographic manifestations of changes in the heart rate during irritation of the frog's stomach.

– To study the electrocardiographic manifestations of rabbit heart rhythm disturbances after intravenous injection of barium chloride solution and inhalation of NH_4OH.

– To study the sequence of electrocardiographic disturbances in the conduction of excitation along the conducting system of the rat heart during the development of hypothermia.

– To get acquainted with typical disorders of automatism, excitability and conductivity of the heart muscle of experimental animals and humans on the basis of a set of electrocardiograms.

– Solving of situational tasks. Control test.

PART 1. WORKING WITH TRAINING MATERIALS

1. Give the definition of *"arrhythmia":*_____

_____

_____

_____

2. List the main causes of arrhythmias:

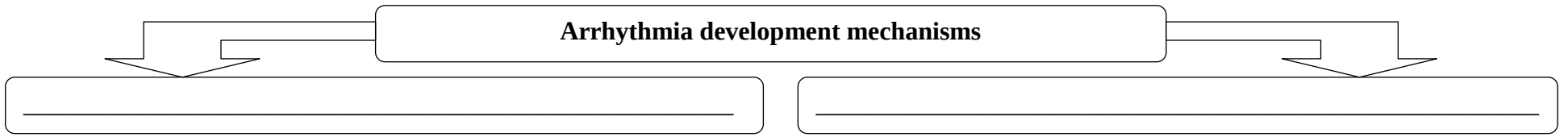
– _____

– _____

– _____

– _____

3. Fill in the Scheme.

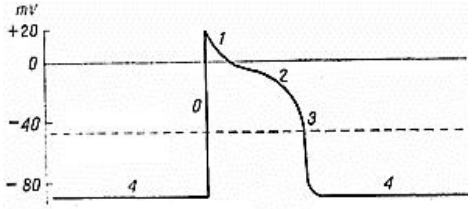


4. Fill in the Scheme.

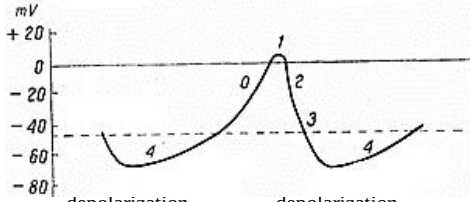
Impulse formation disorders

Normal automatism changes

The process of automatism is based on _____



Transmembrane electric potential of the contractile myocardium cell



depolarization depolarization

Transmembrane electric potential of a conduction system cell with automatic properties (pacemaker cell)

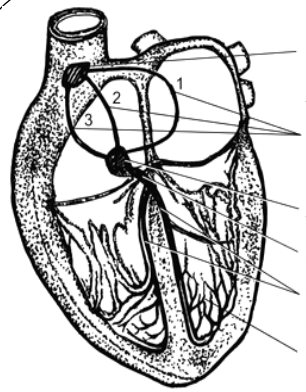
The frequency of generation of impulses by the cells of the SA-node depends on:

1. _____
_____
2. _____
_____
3. _____
_____

Abnormal automatism

A heterotopic focus of excitation is _____
_____

Name	Impulse generation frequency



Sinoatrial node (heart pacemaker)

Internodal atrial ventricular tracts:
1) front (Bachmann);
2) medium (Wenckebach);
3) back (Torelya)

Atrioventricular node

Bundle of His

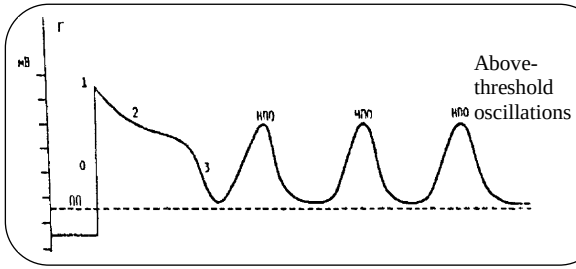
Right and left feet bundle of His

Purkinje fibers

Trigger activity

Early post-depolarization is _____
_____
_____

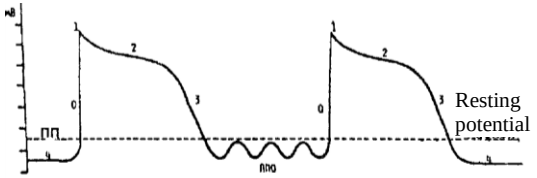
Occurs when: _____



Above-threshold oscillations

Late post-depolarization is _____
_____
_____

*Occurs when:*_____



Resting potential

Subthreshold oscillations

5. Fill in the Scheme.

Impulse conduction disorders

Slowdown (blockade) of impulse conduction

Types of impulse conduction blockade:

_____ – _____

_____ – _____

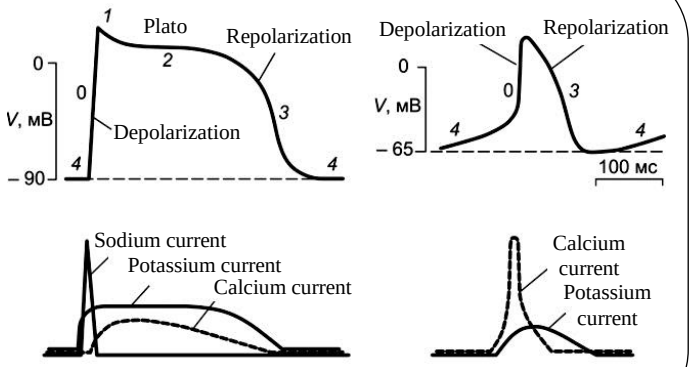
The main reason for the slowing down of the excitation impulse conduction or its blockade is

_____

_____

_____

_____



Re-entry mechanism

Essence: _____

_____

_____

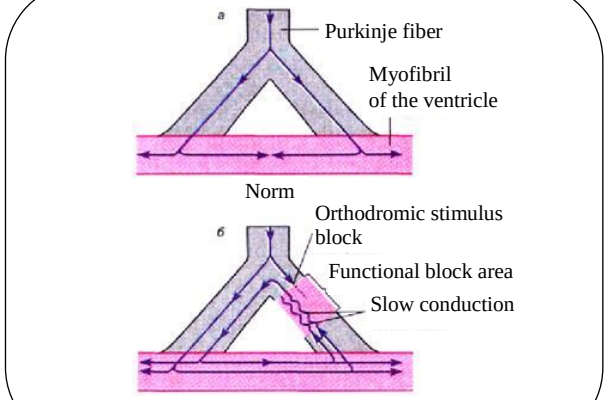
_____

Conditions for the development of the re-entry mechanism: _____

_____

– _____

– _____



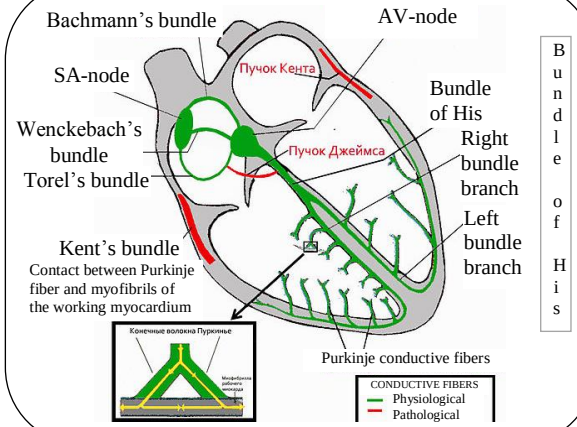
Supernormal conduction

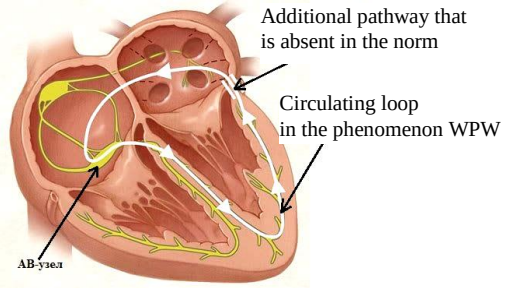
Essence: _____

_____

_____

_____

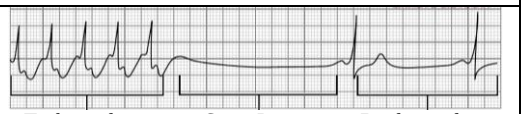




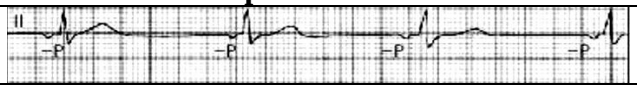
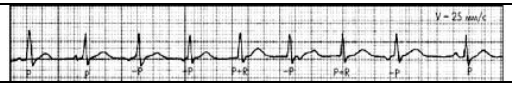
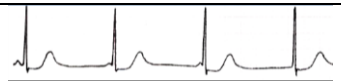
6. Fill in the Scheme.

Arrhythmias resulting from automatism disorders

Nomotopic arrhythmias

Sinus tachycardia	**Sinus bradycardia**	**Sinus arrhythmia**	**Sick sinus syndrome**
Electrophysiological mechanism:			
Development causes:			
– _____ – _____ –	– _____ – _____ –	– _____ – _____ –	– _____ – _____ –
Schematic representation of an ECG:			
			 Tachycardia Sinus Pause Bradyycardia
ECG signs:			
Changes in hemodynamic parameters:			

Heterotopic arrhythmias

Type	**Schematic representation of an ECG**	**ECG signs**
Atrial slow rhythm		
Atrioventricular (junctional) rhythm		
Pacemaker migration		
Idioventricular rhythm		
Dissociation with interference		

7. Fill in the Scheme.

Arrhythmias resulting from conduction disorders

Slowdown or blockade of conduction of excitation impulses

Causes:

– _____

– _____

Type by localization:

– _____ – _____

– _____ – _____

Atrioventricular block

Type		Schematic representation of an ECG	ECG signs
I degree			
II degree	*Mobitz type I*		
	Mobitz type 2		
III degree (complete block)			

Morgagni–Adams–Stokes syndrome

Occurs when: _____

_____

Pathogenetic basis: _____

_____

Clinical manifestations: _____

_____

Acceleration of conduction of excitation impulses

Cause:

_____

_____

Wolff–Parkinson–White syndrome (WPW syndrome)

Two ways of excitation passing along the ventricles:

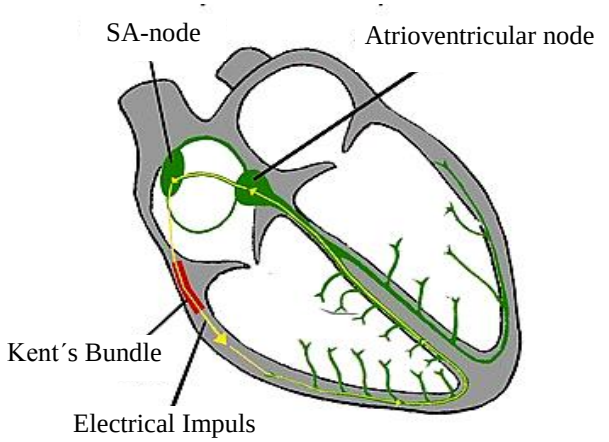
1) _____

2) _____

⇩

_____

_____



8. Fill in the Scheme.

Arrhythmias resulting from combined disorders of excitability and myocardial conduction

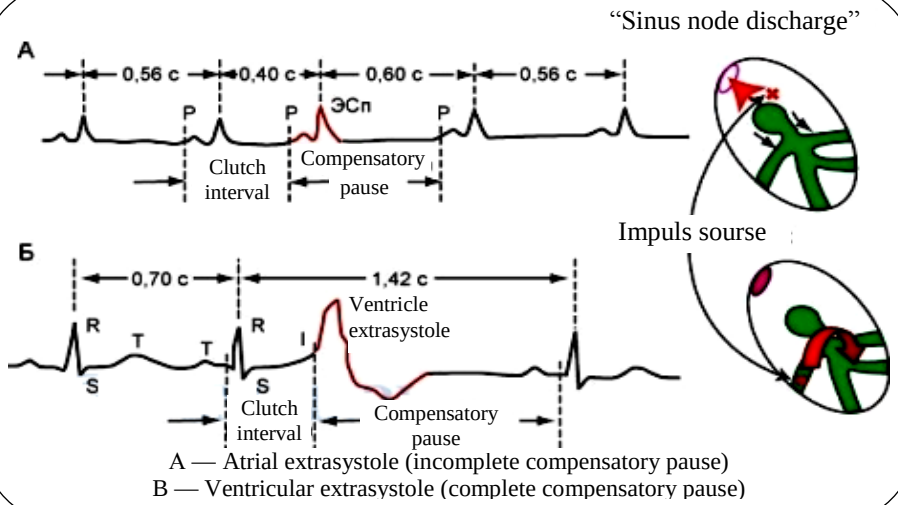
Extrasystole

Extrasystole is _____
_____
_____

A compensatory pause is _____
_____
_____

Extrasystole classification

Criteria	Types
The number of sinus impulses preceding the extrasystole	– _____ – _____ – _____
Depending on the localization of the focus of impulse activity	– _____ _____ – _____ _____
Depending on the number of ectopic foci of impulse activity	– _____ – _____



A — Atrial extrasystole (incomplete compensatory pause)
B — Ventricular extrasystole (complete compensatory pause)

Extrasystole type	Schematic representation of an ECG	ECG signs
Atrial extrasystole		
Atrioventricular extrasystole		
Ventricular extrasystole		

Arrhythmias resulting from combined disorders of excitability and conduction of the myocardium (continued)

Type	Schematic representation of an ECG	ECG signs
Supraventricular paroxysmal tachycardia		
Ventricular paroxysmal tachycardia		
Atrial flutter		
Ventricularl flutter		
Atrial fibrillation		
Ventricular fibrillation		

PART 2. PRACTICAL PART

Work 1. ELECTROCARDIOGRAPHIC MANIFESTATIONS OF HEART RATE CHANGES WHILE IRRITATING THE FROG STOMACH (GASTROCARDIAL REFLEX)

The immobilized frog is fixed with pins to a wooden board with the stomach up. The heart is exposed by excision of the sternum and soft tissues. Electrodes from the electrocardiograph are injected into both front and left hind limbs. The initial electrocardiogram in the II standard lead is recorder. The abdominal cavity is opened and stomach is removed. The stomach is irritated with an induction current and the ECG is recordered again.

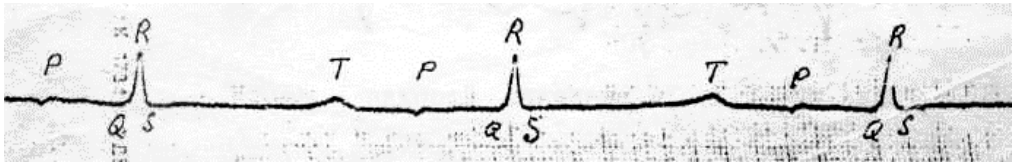


Fig. 1. ECG of the frog in norm. RR = 1,2’’. HR = 60 s/RR = _____

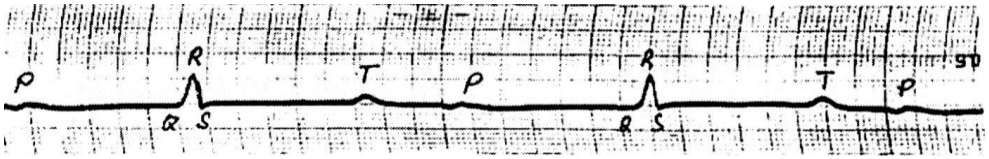


Fig. 2. ECG of a frog after gastric irritation by induction current

R–R'' = 1,5''. HR = _____

Answer the questions:

1. What ECG changes were observed in the experiment? _____
2. What type of rhythm disorders do they refer to? _____
3. What is the mechanism of these disorders? _____

Work 2. ELECTROCARDIOGRAPHIC MANIFESTATIONS OF HEART RATE DISORDERS IN THE INTRAVENOUS INJECTION OF BARIUM CHLORIDE AND IN THE INHALATION OF NH_4OH

We take an adult rabbit for experiment and fix it in a special machine. Then the animal is injected with needle electrodes from the electrocardiograph into both front and back left extremities. We record the initial electrocardiogram in the first standard lead, after which we inject 1 ml of 1 % barium chloride solution into the marginal vein of the rabbit's ear, and after 20–30 s we re-record the electrocardiogram. We register and analyze ECG changes. After normalization of the electrocardiogram, we bring a cotton swab moistened with NH_4OH to the rabbit's nose. We again record the ECG, note the rhythm disorder.

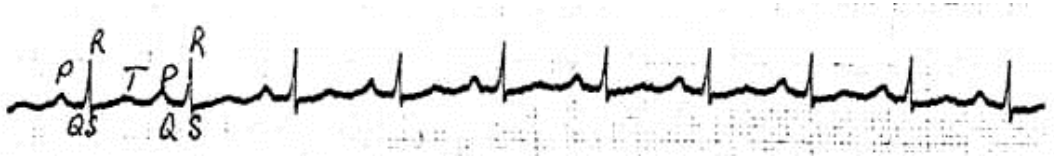


Fig. 3. ECG of the rabit in norm

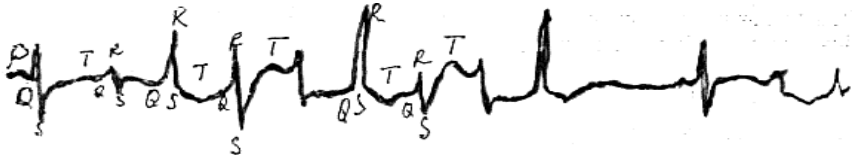


Fig. 4. ECG of the rabbit immediately after injection of barium chloride

Name the type of heart rhythm disorder:_____

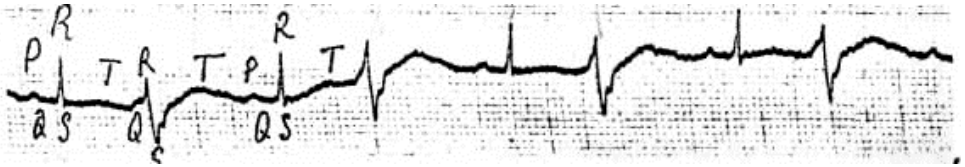


Fig. 5. ECG of the rabbit 1 minute after the injection of barium chloride

Name the type of heart rhythm disorder:_____

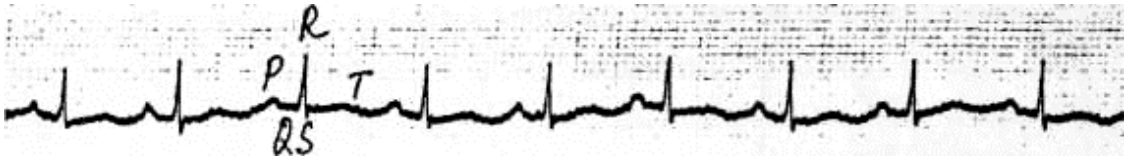


Fig. 6. ECG of the rabbit 15 minutes after the injection of barium chloride

Name the type of heart rhythm disorder:_____

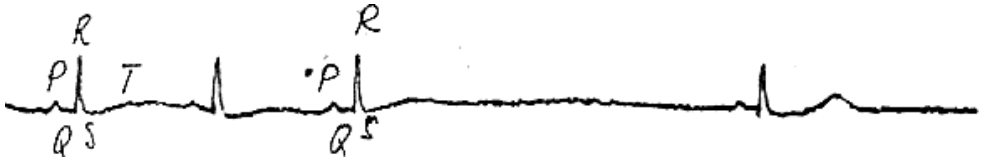


Fig. 7. ECG of the rabbit immediately after inhalation of NH_4OH

Name the type of heart rhythm disorder:_____

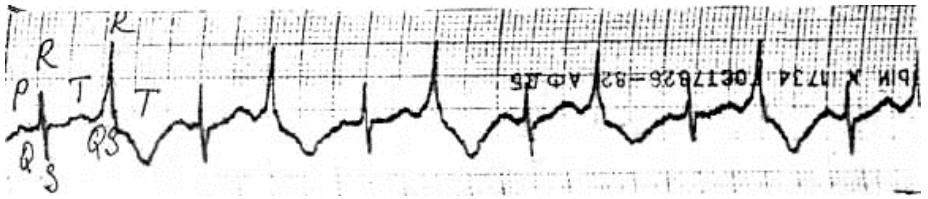


Fig. 8. ECG of the rabbit 1 minute after NH_4OH inhalation

Name the type of heart rhythm disorder:_____

Work 3. FILL IN THE TABLE

ECG in norm:	
CARDIAC ARRHYTHMIA	
I. Violation of automatism: 1. _____ 2. _____ 3. _____ **II.** Violation of exitability: – *extrasystoles*: 1. _____ 2. _____ 3. _____ 4. _____ – *atrial flutter, atrial fibrillation*; – *ventricular flutter, ventricular fibrillation*; – *paroxysmal tachycardia (supraventricular; ventricular).* **III.** Violation of conductivity: blocks — 1. _____ 2. _____3. _____ 4. _____	
ARRHYTHMIAS RESULTING FROM AUTOMATISM DISORDERS	
Sinus bradycardia *is*	
	ECG signs: _____ _____ _____
Sinus tachycardia *is*	
	ECG signs: _____ _____ _____
Sinus arrhythmia *is*	
	ECG signs: _____ _____ _____

ARRHYTHMIAS RESULTING FROM MYOCARDIUM EXCITABILITY AND CONDUCTIVITY DISORDERS	
1. Extrasystole	
Extrasystole is _____	
Atrial extrasystole	
from the upper part of atria:	
	ECG signs: _____ _____ _____
from the middle part of atria:	
	ECG signs: _____ _____ _____
from the lower part of atria:	
	ECG signs: _____ _____ _____
Atrioventricular extrasystole	
from the upper part of the AV-node:	
	ECG signs: _____ _____ _____

<table>
<tr><td colspan="2">from the middle part of the AV-node:</td></tr>
<tr><td></td><td>ECG signs:
_____
_____
_____</td></tr>
<tr><td colspan="2">from the lower part of the AV-node:</td></tr>
<tr><td></td><td>ECG signs:
_____
_____
_____</td></tr>
<tr><td colspan="2">Ventricular extrasystole (signs):
1. _____ 3. _____
2. _____ 4. _____
5. _____</td></tr>
<tr><td colspan="2">left ventricular extrasystole:</td></tr>
<tr><td>I lead
_____
III lead</td><td>ECG signs:
_____
_____
_____
_____
_____</td></tr>
<tr><td colspan="2">right ventricular extrasystole:</td></tr>
<tr><td>I lead.
_____
III lead</td><td>ECG signs:
_____
_____
_____
_____
_____</td></tr>
</table>

ATRIAL FLUTTER is	
Regular rhythm: Irregular rhythm:	**ECG signs:** _____ _____ _____ **ECG signs:** _____ _____
ATRIAL FIBRILLATION is	
	ECG signs: _____ _____ _____
VENTRICULAR FLUTTER is	
	ECG signs: _____ _____ _____
VENTRICULAR FIBRILLATION is	
	ECG signs: _____ _____ _____
PAROXYSMAL (JUNCTIONAL) TACHYCARDIA —	
Supraventricular paroxysmal tachycardia is	
	ECG signs: _____ _____ _____

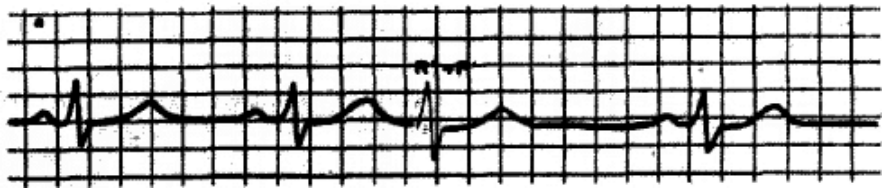
Ventricular paroxysmal tachycardia is	
	ECG signs: _____ _____ _____
ARRHYTHMIAS RESULTING FROM CONDUCTIVITY DISORDERS	
SA nodal blocks is	
	ECG signs: _____ _____ _____
Atrial block is	
	ECG signs: _____ _____ _____
AV nodal blocks is _____	
First degree AV block is	
	ECG signs: _____ _____ _____
Second degree AV block Type 1 (Wenckebach/Mobitz I) is	
	ECG signs: _____ _____ _____

Second degree AV block Type 2 (Mobitz II) is	
	ECG signs: _____ _____ _____
Third degree AV block III degree is	
	ECG signs: _____ _____ _____
Complete AV block is	
	ECG signs: _____ _____ _____
Ventricular block is	
Left bundle branch block (LBBB) is	**ECG signs:** _____ _____ _____
Right bundle branch block (RBBB) is	**ECG signs:** _____ _____ _____

Work 4. SOLVING SITUATIONAL PROBLEMS

Tasks: make a conclusion about the type of arrhythmia presented in the ECG fragment; list the mechanisms of pathogenesis for each variant; justify the effect on systemic hemodynamics (if any); indicate possible diseases in which this type of arrhythmia occurs.

№ 1



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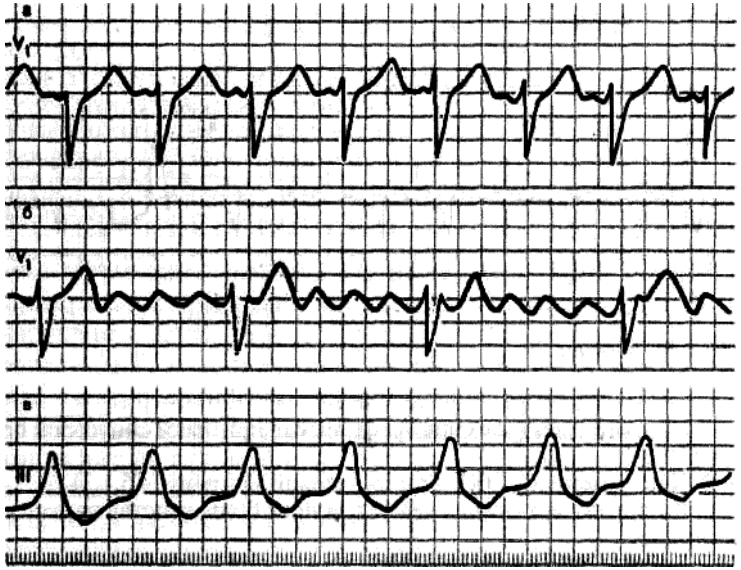

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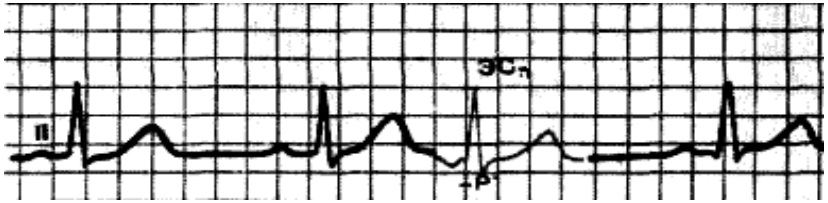

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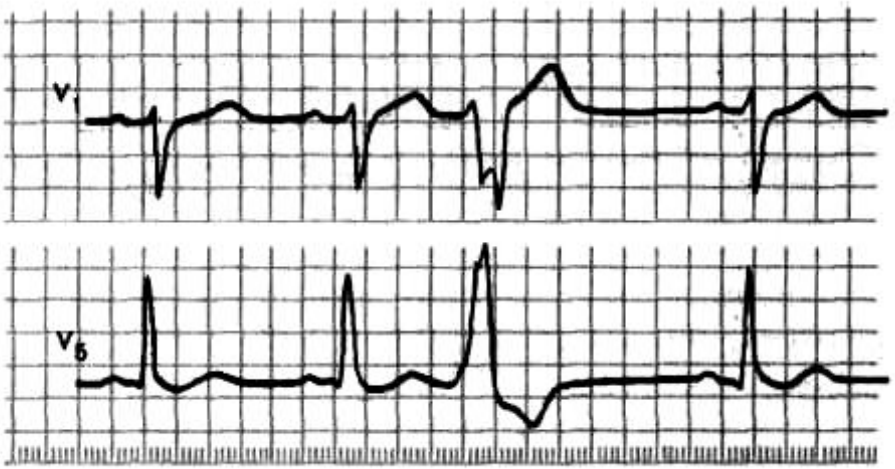

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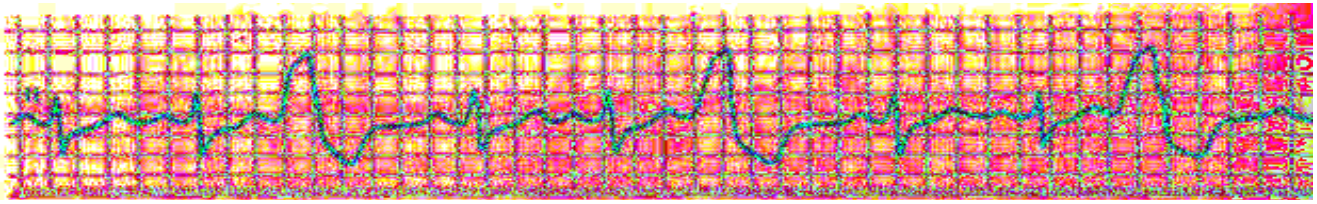

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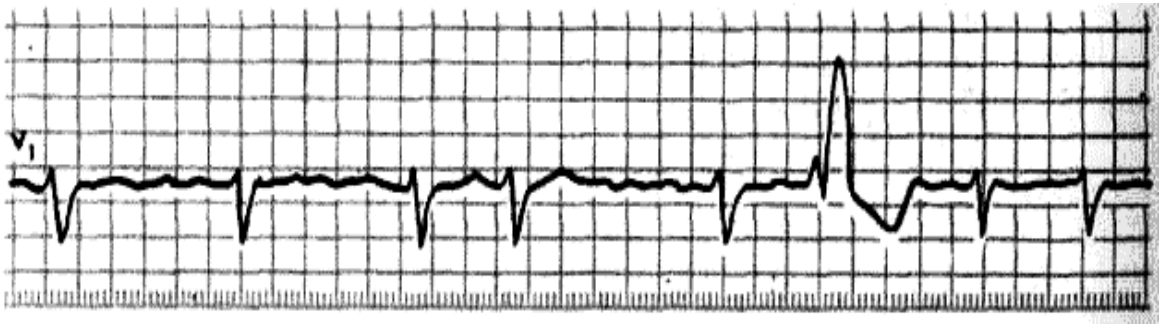

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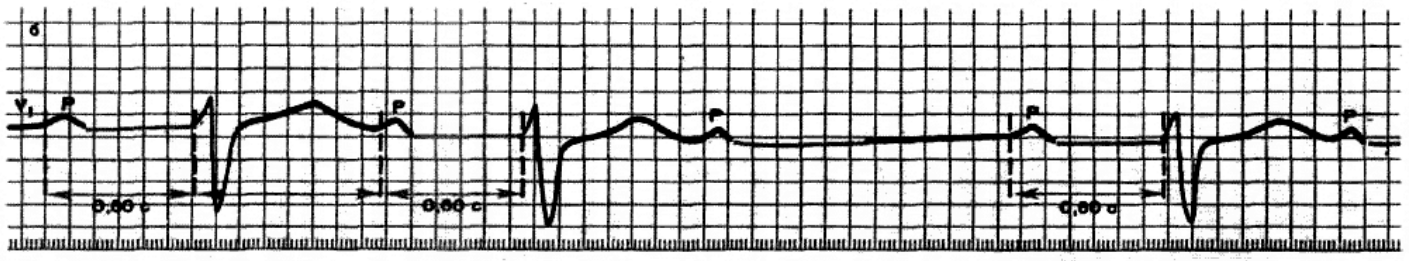

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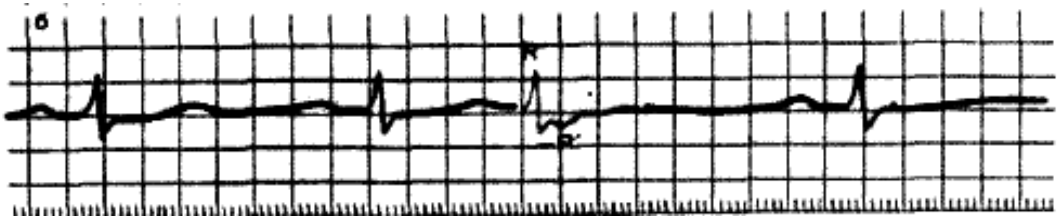

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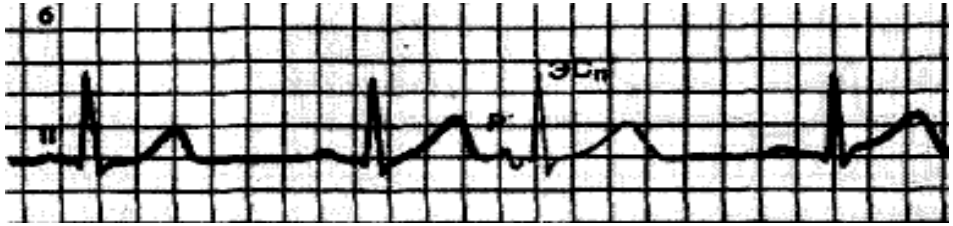

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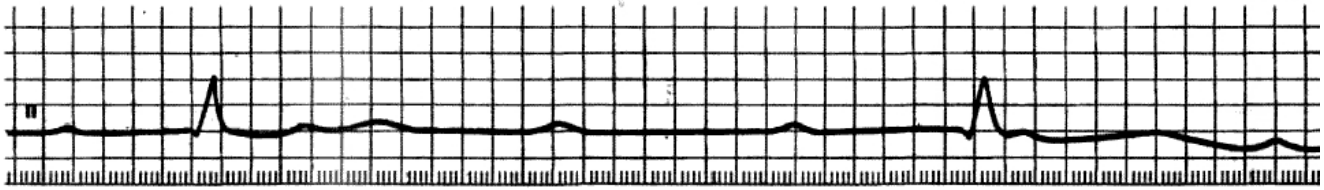

Control questions

1. Definition of “cardiac arrhythmias”. Arrhythmia classification.
2. Disorders of excitability of the heart: extrasystoles (definition, causes, types, characteristics, ECG manifestations, hemodynamic disorders).
3. Disorders of the automatism of the heart (types, causes, characteristics, mechanisms of development, ECG manifestations, hemodynamic disorders).
4. Disorders of conductivity of the heart: heart block (definition, causes, types, characteristics, ECG manifestations, hemodynamic disorders).
5. Disorders of excitability and conductivity of the heart:

a) atrial flutter and atrial fibrillation (causes, characteristics, ECG manifestations, hemodynamic disorders);

b) ventricular fibrillation (causes, characteristics, ECG manifestations, hemodynamic disturbances).

6. Cardiac defibrillation.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 9).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
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5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher’s signature: _____

LESSON 10. PATHOLOGICAL PHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM. VIOLATIONS OF THE REGULATION OF VASCULAR TONE. ARTERIAL HYPERTENSION AND HYPOTENSION. TYPES, ETIOLOGY AND PATHOGENESIS. COLLOQUIUM ON THE SECTION "PATHOPHYSIOLOGY OF THE CARDIOVASCULAR SYSTEM"

Date: «____» _____ 20__

The purpose of the Lesson: to improve and evaluate the knowledge obtained at lectures and practical classes on issues of systemic circulation disorders (etiology, pathogenesis, main clinical manifestations and hemodynamic disorders).

Tasks:

1. To study:

– regulation disorders of the vascular tone (arterial hyper- and hypotension), etiology, pathogenesis, mechanisms of hemodynamic impairments and manifestations;

– types, development mechanisms and manifestations of cerebrovascular insufficiency: paroxysms, crises, strokes;

– etiology and pathogenesis of atherosclerosis.

2. Solving the situational tasks.

3. Computer control test on the topics: "Pathological physiology of the blood circulatory system", "Arrhythmias. Typical impairments of excitability, automatism and conductivity of the heart" and "Violations of vascular tone regulation. Arterial hypertension and hypotension".

PART 1. WORK WITH TRAINING MATERIALS

1. Fill in the Table.

Classification of Dystonia

By change of vascular tone	1. _____ 2. _____
By etiology	1. _____ _____ 2. _____ _____
By prevalence	1. _____ _____ 2. _____ _____

2. Give the definition of “arterial hypertension” _____
_____

3. Fill in the Table.

Classification of Arterial Hypertension

By etiology	1. _____ _____ 2. _____ _____		
By clinical course	1. _____ 2. _____		
By type of predominantly high blood pressure	1. _____ 2. _____ 3. _____		
By initial pathogenesis link	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		
Hemodynamic options	1. _____ 2. _____ 3. _____		
By the degree of increase in blood pressure	**Category**	**Systolic blood pressure (mmHg)**	**Diastolic blood pressure (mmHg)**
	Degree I (mild)	_____	_____
	Degree II (moderate)	_____	_____
	Degree III (severe)	_____	_____
	Isolated systolic	_____	_____

4. What factors determine the level of systemic blood pressure?

1._____
2._____
3._____
4._____

5. Fill in the Table.

Theories of the development of essential hypertension

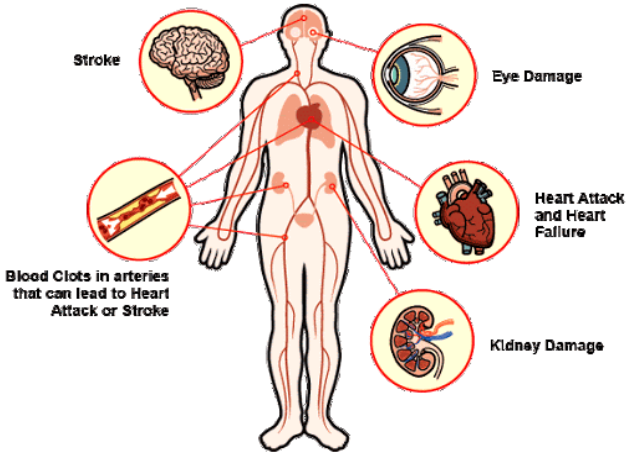
Theory Name	Authors	Essence
Neurogenic theory	_____ _____ _____	_____ _____ _____ _____ _____
Concept of an increase in the tone of sympathetic nervous system	_____ _____ _____	_____ _____ _____ *Causes leading to increased activity of the sympathetic nervous system:* 1. _____ _____ 2. _____ _____ _____ 3. _____ _____ _____ 4. _____ _____ _____ 5. _____ _____

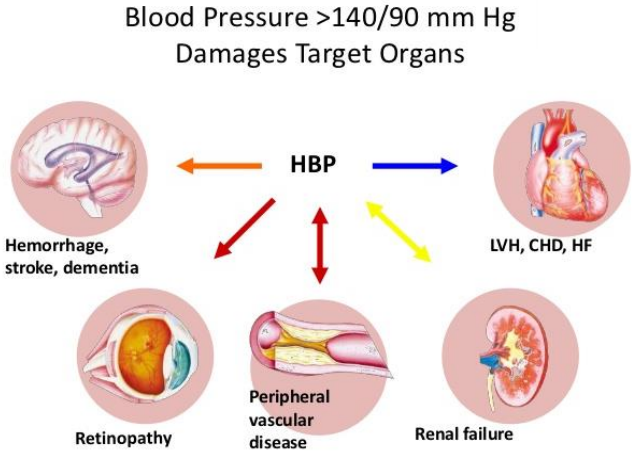
Theory Name	Authors	Essence
Theory of "cell membrane pathology"	_____ _____ _____	_____ _____ _____ _____ _____ _____
Increased blood pressure as a compensatory reaction	_____ _____ _____	_____ _____ _____ _____ _____
Cerebro-ischemic theory	_____ _____ _____	_____ _____ _____ _____ _____
Theory of "salt-sensitive hypertension" (Gyton, 1987)	_____ _____ _____	_____ _____ _____ _____ _____ _____
Endothelium dysfunction	_____ _____ _____	*Endothelium dysfunction* is _____ _____ _____ _____ _____ _____

6. Fill in the Scheme.

Major vicious circles in hypertension

Renal and related to it endocrine mechanisms	spasm of blood vessels ↓ _____ ↓ activation of RAAS, _____
Baroreceptor mechanism	↑ BP ↓ _____ ↓ weakening of depressive mechanisms ↓ further ↑ of BP
Chemoreceptor mechanism	↑BP (long period of time) ↓_____ _____ ↓ ↑ BP _____

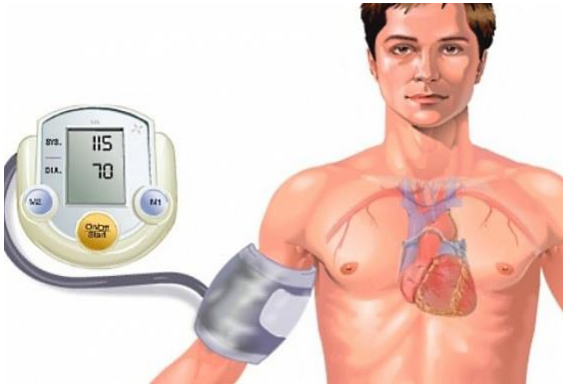




7. Give the definition of *"arterial hypotension"*:_____
_____
_____

8. Fill in the Table.

Classification of arterial hypotension

Physiological	**Pathological**	
– _____ _____ – _____ _____ – _____ _____ 	*By speed of development*	1. _____ _____ 2. _____ – _____ _____ – _____ _____
	Hemodynamic forms	– _____ _____ – _____ _____ – _____ _____
	According to the initial link of pathogenesis	– _____ – _____ – _____

PART 2. PRACTICAL WORK

Work 1. SOLVING SITUATIONAL PROBLEMS

№ 1

Patient G., 47 years, complains of a headache, mainly, in the occipital area, memory impairment, decrease of workability, dizziness, a periodically arising pain in the heart area, nausea, flashes before the eyes. Has been ill for 2 years, self-treatment was of no effect, the condition

becomes gradually worse. The anamnesis revealed that the patient spent practically the whole day at work (works as an investigator at the Procurator's), smokes per 1–1.5 packs of cigarettes a day. Has an aggravated heredity on cardiovascular diseases: his father suffered two strokes at the age of 52 and 58 years.

On examination: the patient of increased nutrition, his body weight index — 30, the pulse — 96 per minute, of increased tension, the heart borders are shifted to the left by 1 cm, arterial pressure — 155/95 mm Hg.

Results of additional investigation: the total urine test — without pathological changes; on the electrocardiogram — hypertrophy signs of the left ventricle, on examination of the eye ground there was revealed dilation of veins and narrowing of arteries of the retina; biochemical blood test: the glucose level — 6.8 mmol/l, the content of total cholesterol —— 7.1 mmol/l.

Questions:

1. What is your suggested diagnosis? Specify the stage.
2. List the regulated and non-regulated risk factors in the given patient.
3. Specify possible approaches to correct the regulated risk factors.
4. List the organs-targets affected in the given pathology.

№ 2

Patient C., 38 years, was admitted to the therapeutic department for a severe headache manifested as periodical recurrent attacks accompanied by the feeling of fear, palpitation, shivering, sensation of heat in the whole body, profuse perspiration, impairment of sight and increase of arterial pressure up to 250/130 mm Hg. The attacks last 10–25 minutes, subside by themselves, they appeared 3 years ago for the first time. APF inhibitors are inefficient.

On examination: the condition is satisfactory, the pulse — 90 per minute, is moderately tense, BP — 160/90 mm Hg. The heart sounds are high, the accent of sound II over the aorta. The abdomen is tenderless. The ophthalmologist revealed hypertonic angiopathy on the eye ground. The total tests of blood and urine — within the normal limits.

The sugar curve before loading — 5.4 mmol/l, after loading with 100 g glucose: 9.7 mmol/l – 12.3 mmol/l – 18.3 mmol/l – 7.2 mmol/l. Reaction to vanillin — almond acid (+++). The content of adrenaline and noradrenaline in the blood is elevated.

Questions:

1. What is your suggested diagnosis?
2. What is the arterial hypertension in the given patient caused by?

№ 3

A student of a medical college K., 16 years, being present at a surgical operation for the first time, suddenly felt "faintness", which was accompanied by noise in the ears, dizziness, nausea and loss of consciousness. Objectively: the skin integuments were very pale, extremities — cold to touch. The pupils — narrowed. The heart sounds — dull. The pulse — 40 per minute, of weak filling. BP — 70/30 mm Hg. Respiration — rare. Spraying the face with cold water and inhalation of liquid ammonia vapors helped the patient to recover her consciousness quickly.

Questions:

1. To what pathology do the specified symptoms testify?
2. What are the development mechanisms of this condition?
3. What are the principal causes of the given pathology?

№ 4

Patient Zh., 52 years, was admitted to the pulmonological department with a bilateral pneumonia. Fell ill 5 days ago. Objectively: the condition of a moderate severity. The body temperature — 40,2 ºC. The heart borders — dilated, heart sounds — dull. Systolic murmur is heard at the apex. BP — 105/70 mm Hg. The pulse — 105 beats/min, of weak filling. The percussion sound over the lower lobes of the right and left lung — dull, fine vesicular râles and crepitations were heard. Antibacterial therapy was administered. The patient developed profuse perspiration at night. The body temperature returned to the norm by the morning. The condition became considerably worse, dizziness and nausea appeared. The pulse became threadlike, BP decreased. The patient lost consciousness. Emergency medical therapy allowed to control this condition.

Questions:

1. To what pathology do the specified symptoms testify?
2. What is its pathogenesis?
3. List the types and major factors of the given pathology pathogenesis?

Control questions

1. Arterial hypertension, classification. Experimental forms. Symptomatic arterial hypertension.
2. Etiology and basic theories of the hypertension pathogenesis.
3. The role of hyperactivation of the renin-angiotensin-aldosterone system (RAAS) in the development of target organ dysfunction and stabilization of arterial hypertension. Clinical manifestations of target organ damage in arterial hypertension.
4. Arterial hypotension. Classification. Vascular circulatory failure: syncope, collapse. Etiology, pathogenesis, manifestations.
5. Dysregulation of cerebral circulation. Etiology, pathogenesis, manifestations. Pathological reactions of cerebral arteries, their types, characteristics.
6. Subclavian steal syndrome, Robin Hood syndrome, excessive cerebral perfusion; their characteristics, pathogenetic assessment.
7. Cerebrovascular insufficiency, its types. Paroxysms, crises, strokes. Pathogenetic principles of treatment of cerebral circulation insufficiency.
8. Atherosclerosis, its etiology and pathogenesis. The role of LDL-receptor interaction disorders in atherogenesis. The concept of pathological and modified lipoproteins, their elimination from the body using scavenger receptors.
9. Participation of vascular wall cells in interaction with modified lipoproteins and the mechanism of atherosclerotic plaque formation. Basic experimental models of atherosclerosis.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 10).

2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.

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7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.

8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.

9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 11. PATHOLOGICAL PHYSIOLOGY OF THE EXTERNAL RESPIRATION

Date: «____» _____ 20__

The purpose of the Lesson: to study etiology, pathogenesis, basic impairment forms of the external respiration system caused by the disorders of alveolar ventilation and perfusion; ventilation-perfusion relationships, diffusion in the lungs; development mechanisms of respiratory insufficiency, its stages.

Tasks:

- To study the effect of increased intraalveolar pressure on parameters of respiration and blood circulation in the dog;
- To study the acidosis effect on parameters of pulmonary ventilation in experiment;
- To draw schematically and give a brief characteristic of pneumogram changes in typical impairments of pulmonary ventilation;
- Solving the situational tasks;
- Control test.

PART 1. WORK WITH TRAINING MATERIALS

1. Give the definition of "*external respiration*": _____
_____
_____
_____

2. The main task of the functional system of external respiration is _____
_____

3. Fill in the Table.

Parameters of homeostasis in a blood at normal ventilation

Parameter	Normal range
pH art blood	
P_aO_2	
P_aCO_2	
buffer bases (BB)	
standard bicarbonate (SB)	
excess (deficiency) of buffer bases (BE)	

4. Fill in the Scheme.

Typical respiratory disorders

I. Disorders of lung ventilation

Alveolar hypoventilation

__ pO_2, __ PaO_2, __ $PaCO_2$
(indicate with arrows — ↑, ↓)

The development is based on

_____
_____

biomechanical disturbances

1. _____
Pathogenetic basis:
_____
_____
_____

2. _____
Pathogenetic basis:
_____
_____
_____

Alveolar hyperventilation

__ pO_2, __ PaO_2, __ $PaCO_2$
(indicate with arrows — ↑, ↓)

Types:
– _____
– _____
– _____
– _____

Manifestations:
_____
_____
_____
_____

II. Impaired lung perfusion

Perfusion of the lungs is ensured by pressure equal to ____ mmHg.

The driving force of pulmonary blood flow —
_____
_____

Factors leading to lung perfusion reduction:
1. _____
2. _____
3. _____
4. _____
5. _____

III. Violation of the ventilation-perfusion relationship

$\dot{V}/\dot{Q}$ ratio in norm is _____

$\dot{V}/\dot{Q}$	Causes	Alveolar air	Gas composition arter. blood
< 0,8			
> 1			

IV. Disorder of gases diffusion through the ACM

A decrease in the diffusion capacity of the lungs occurs when: _____
_____

V. Impairment of respiration regulation

Types:
– _____
– _____
– _____
– _____

5. Fill in the Table.

Manifestations of obstructive and restrictive disorders of alveolar hypoventilation

(indicate changes with arrows — ↑ or ↓)

Indicators	Obstructive type	Restrictive type
Breathing type		
VE		
MVV		
Tidal volume		
Vital capacity		
TLC		
FRC		
Tiffno Index		

6. Fill in the Table.

Pathological types of breathing

Types of respiration	Mechanism, characteristic	Occurs in pathological conditions	Pneumogram
Normal (eupnea)	–	–	
Deep accelerated (hyperpnea)			
Hurried superficial (polipnea)			
Stenosed			

Types of respiration		Mechanism, characteristic	Occurs in pathological conditions	Pneumogram
Breathlessness	**Inspirat.**			
	Expirat.			
Periodic	**Chain–Stocks**			
	Wavy			
	Biot			
Terminal	**Hasping**			
	Apneusis			
	Kussmaul			

7. Fill in the Table.

Clinical forms and manifestations of respiratory failure

Respiratory failure form	Basic development causes	Arterial blood gas composition	Clinical manifestations

8. Fill in the Table.

Types of Respiratory Failure

<table>
<tr><td colspan="2">Acute
(development time – _____)</td><td>Subacute
(development time – _____)</td><td colspan="3">Chronic
(development time – _____)</td></tr>
<tr><td colspan="2">3 degrees of severity:</td><td rowspan="4">Examples:</td><td colspan="3">3 stages of chronic respiratory failure (complete the table):</td></tr>
<tr><td>Types</td><td>Characteristics</td><td colspan="2">Types</td><td>Characteristics</td></tr>
<tr><td rowspan="2"></td><td rowspan="2"></td><td></td><td>P_aO_2
P_aCO_2
HbO_2
Compensation mechanisms</td><td rowspan="2"></td></tr>
<tr><td></td><td>P_aO_2
P_aCO_2
HbO_2
Compensation mechanisms</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>P_aO_2
P_aCO_2
HbO_2
Compensation mechanisms</td></tr>
</table>

9. Fill in the Table.

Functional impairments of organs and systems in acute mechanical asphyxia

Functions of organs and systems		**1 stage**	**2 stage**	**3 stage**	**Functions of organs and systems**
CNS (central nervous system)					
Autonomic nervous system					
System of blood circulation	*HR*				
	RR				
Respiratory system (type of breathing disorder)					

PART 2. PRACTICAL WORK

Work 1. THE EFFECT OF INTRAARTERIAL PRESSURE ELEVATION ON PARAMETERS OF RESPIRATION AND BLOOD CIRCULATION IN THE DOG

A femoral artery is allocated in a narcotized dog and a cannula is injected into it, then using the tubes filled with the solution of magnesia sulphate it is connected to the mercury manometer for arterial pressure registration.

The trachea is allocated and a tracheal cannula is injected into it; the last one (the lateral aperture being open) is connected with the artificial respiration apparatus.

The pneumograph cuff is fixed on the thorax and by means of a tube it is connected with Marey's capsule for registration of a pneumogram.

Having fixed the initial level of blood pressure and respiration rate, the intraalveolar pressure is elevated by closing the aperture in the tracheal cannula and blowing the air by means of the artificial respiration apparatus (5–6 inflations). Mark respiration changes and arterial pressure caused by these manipulations.

In subsequent opening of the lateral aperture of the tracheal cannula and letting out the excess of air from the lungs the pneumogram and the curve of blood pressure quickly return to their initial states (Fig. 1).

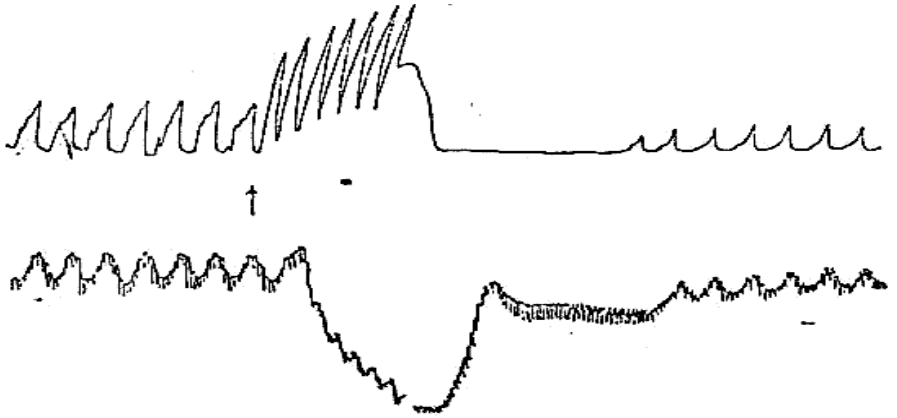


Fig. 1. Changes of respiration (the top curve) and arterial pressure (the bottom curve) in elevating the intraalveolar pressure of the dog. The arrows correspond to the moment of inflating air into the lungs

Answer the questions:

1. What changes of respiration and arterial pressure are noted in the dog after inflation of air into the lungs?

_____
_____

2. What is a possible mechanism of these changes?

_____
_____

3. In what diseases, pathological processes can similar phenomena arise?

_____
_____

Work 2. RESPIRATION CHANGES IN THE DOG IN ACIDOSIS

The initial parameters of respiration (pneumogram) and arterial pressure of the dog are recorded, then 5 ml of 10 % solution of acetic acid are injected into its vein. Changes of registered parameters and their subsequent normalization are noted. After the establishment of the initial pneumogram and arterial pressure value, 10 ml of 25 % solutions of sodium dihydrogen phosphate (NaH_2PO_4) are injected into the vein (Fig. 2).

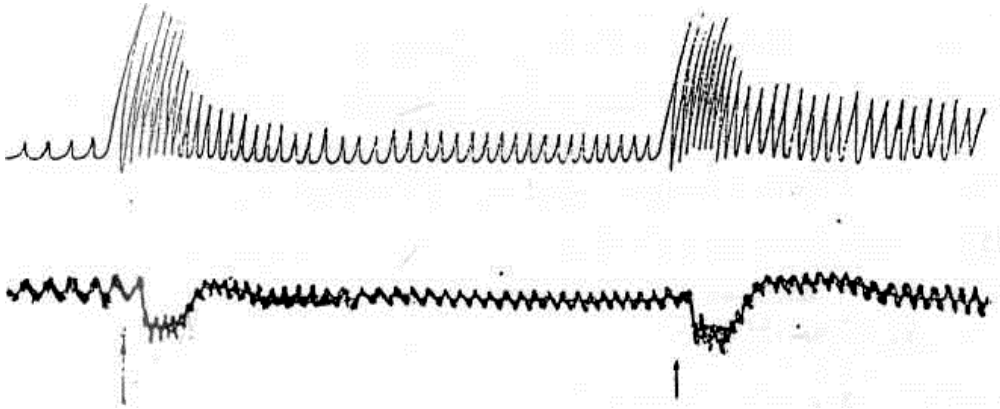


Fig. 2. Changes of respiration (the top curve) and arterial pressure (the bottom curve) in the development of acidosis in the dog. The first arrow corresponds to the injection of the acetic acid solution into the blood, the second arrow — to injection of the sodium dihydrogen phosphate solution

Answer the questions:

1. What changes of respiration and arterial pressure are observed in the dog while injection of the acetic acid and sodium dihydrogen phosphate solutions into the vein?

_____

_____

2. What are the mechanisms of these changes?

_____

_____

3. In what diseases, pathological processes can similar phenomena arise?

_____

_____

Work 3. SOLVING SITUATIONAL PROBLEMS

№ 1

Patient C., 24 years, was admitted to clinic with complaints of breathlessness and palpitation on physical exertion, dull pains in the heart area. During especially marked breathlessness a small amount of mucous sputum with blood is discharged. On the basis of the above complaints of the patient and subsequent examination the impairment of pulmonary circulation due to mitral stenosis was suggested.

Test results of the external respiration system:

Respiration rate — 20 per minute;

PC (pulmonary capacity), % of the proper value — 81;

RPC (residual pulmonary capacity), % of the proper value — 76;

MV (minute volume), % of the proper value — 133;

FPC/PC, % — 80.

Questions:

1. What impairment types of pulmonary perfusion are possible in the given patient? Prove the answer.
2. Explain the possible mechanisms of reducing PC and RPC in the patient.
3. Is there any impairment of alveolar ventilation of an obstructive type in the given patient? Prove the answer.

№ 2

Patient A., 43 years, a press operator of fire-resistant bricks with 20-year experience of work, complained that he had difficulty while coping with work because of breathlessness on physical exertion.

On objective examination the pallor of integuments was noted. The thorax was of a regular shape, both halves of it actively participate in the respiration act. The mobility of pulmonary edges was limited. Respiration — rough; dry scattered râles are heard.

On X-ray — the pulmonary pattern is changed on a cellular pneumosclerosis type.

Moderate reduction of external respiration efficiency is revealed — saturation of arterial blood with oxygen is 74 %.

Questions:

1. The functional impairment of what component of the external respiration system is the Min cause of its insufficiency in this case?
2. What is your explanation of the fact that breathlessness in the patient develops only on physical exertion?
3. What elementary functional test allows estimating the condition of diffuse pulmonary capacity in the patient?

№ 3

Patient G., 38 years, is in hospital for a closed fracture of X and XI ribs on the right, not complicated by the damage of pulmonary tissue.

The general condition is satisfactory. The respiration rate — 13 resp. per minute, respiration is superficial. The right half of the thorax lags behind during respiration. General spirography revealed: the tidal volume is 83 %, minute volume — 82 %, pulmonary capacity — 90 % of the norm.

Question: What type of the pulmonary ventilation impairment takes place in this case?

№ 4

Patient T., 19 years, on the 3-rd day of the disease applied to the doctor and was referred to hospital with the diagnosis of "acute pneumonia".

On admission the respiration was — 32 per minute, superficial. Intercostal muscles participate in respiratory movements. On auscultation fine bubbling moist and dry râles are heard.

On X-ray of the lungs — changes, characteristic of bilateral croupous pneumonia.

On examination of the external respiration efficiency a decrease of blood oxygenation is revealed — saturation of arterial blood was 86 %.

Questions:

1. What pathological type is present in the patient and what is the mechanism of its development?
2. What impairment of external respiration processes is the main cause of the blood oxygenation decrease in this case?

№ 5

The blood test for gases of patient M., 49 years, with respiratory insufficiency revealed, that at rest: PaO_2 — 83 mm Hg, $PaCO_2$ — 40 mm Hg. After the test with arbitrary hyperventilation within 2 minutes: PaO_2 — 65 mm Hg, $PaCO_2$ — 38 mm Hg.

Questions:

1. What is a possible cause of developing respiratory insufficiency by the patient?
2. Why does hyperventilation aggravate hypoxemia?

№ 6

Patient B., 56 years, was admitted to the neurological department for a cerebral stroke. On admission the condition was severe. Periodic respiration of a tidal type is observed. On the 2^{nd} day of the patient's staying in hospital the tidal respiration in the patient changed for Biot's (meningitic) respiration.

Questions:

1. Is it possible to regard the appearance of Biot's (meningitic) respiration as a prognostically favorable symptom?
2. What factor is of major importance in the pathogenesis of periodic respiration?

№ 7

Patient P., 52 years, is delivered to hospital with uremia. The patient is adynamic, sleepy. The face is puffy; the skin is dry and flabby with traces of multiple scratches. Breathlessness is observed, the phase of an inhalation and an exhalation being intensified and the rhythm being accelerated.

On 4-th day of staying in hospital, despite the undertaken measures, deterioration occurred: the patient developed a coma, the reaction of pupils to light — inert, she is in unconscious state. Some kind of noisy accelerated respiration appeared, deep inhalations are regularly alternated with deep exhalations.

Questions:

1. What form of respiration impairment appeared in the patient?
2. Will the breathlessness persist in the patient in a coma? Prove the answer.

Control questions

1. Insufficiency of the external respiration system. The definition of the notion, classification. Causes and development mechanisms. Stages of chronic respiratory insufficiency, its clinical manifestations.
2. Impairments of pulmonary ventilation: obstructive, restrictive and mixed, principal causes and manifestations. Changes of alveolar air gas content and arterial blood in the impairment of ventilation.
3. Impairments of gas diffusion through the lung membrane, principal causes and manifestations. Changes of gas content of alveolar air and arterial blood in the impairment of gas diffusion. Etiology and pathogenesis of respiratory distress-syndrome of adults.
4. Principal causes of the impairment of pulmonary perfusion. Forms and causes of pulmonary hypertension. Chronic pulmonary-cardiac insufficiency: pulmonary heart, etiology, pathogenesis, clinical manifestations.
5. Regulation impairments of respiration. Breathlessness, periodic and terminal respiration. Their forms, pathogenic characteristic, development mechanisms.
6. Asphyxia. Etiology, pathogenesis, development stages.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 11).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins and Cotran Pathologic Basis of Disease. V. II / V. Kumar, A. K. Abbas, J. C. Aster. South Asia ed. India : Elsevier, 2015. 1391 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 2nd ed. NY : Appleton & Lange, 2000.

Teacher's signature: _____

LESSON 12. PATHOLOGICAL PHYSIOLOGY OF DIGESTION AND LIVER

Date: «____» _____ 20__

The purpose of the Lesson: to study the causes, development mechanisms and manifestations of impairments in secretory, motor and absorption functions of the gastrointestinal tract. To characterize the typical forms of liver functional impairments.

Tasks:

– To determine the types of gastric secretion of patients by the presented graphs and tables, to get acquainted with clinical assessment of the secretory activity impairment of the stomach.

– To make a conclusion about violations of acid-producing and acid-neutralizing functions of the stomach in patients on the basis of gastric pH-metry data.

– To study the causes and mechanisms of the main syndromes in liver pathology.

– To study the mechanisms and manifestations of the general toxic effect of bile, its effect on the nervous system and heart muscle.

– Solving the situational tasks. Control test.

PART 1. WORKING WITH TRAINING MATERIALS

1. Give the definition of "*insufficiency of digestion*": _____

_____

2. Fill in the Table.

General etiology of digestion disorders

Exogenous factors		**Endogenous factors**
Physical	_____ _____	1. _____ 2. _____
Chemical	_____ _____	3. _____ 4. _____
Biological	_____ _____	5. _____ 6. _____
Psychogenic	_____ _____	7. _____ 8. _____

3. List the conditions that affect the occurrence and manifestation of digestive pathology: _____
_____

4. Fill in the Table.

Typical forms of digestive system pathology

Digestive disorders in the oral cavity	**Disorders of swallowing and movement of food through the esophagus**	**Digestive disorders in the stomach**	**Disorders of digestion in the gut**
1. _____ _____ 2. _____ _____ 3. _____ _____ 4. _____ _____	1. Swallowing disorders: – _____ – _____ 2. Esophageal pathology accompanied by dysphagia — _____ _____ _____ _____	*Functional disorders (list):* 1. _____ 2. _____ 3. _____ 4. _____ 5. _____	*Functional disorders (list):* 1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ 7. _____ 8. _____

5. Fill in the Table.

Eating disorders

Type of violation	**Hyporexia (anorexia)**	**Hyperrexia**	**Pararexia**
Definition	_____	_____	_____
Causes	1. _____ _____ 2. _____ _____ 3. _____ _____ 4. _____ _____ 5. _____ _____	1. _____ _____ 2. _____ _____ 3. _____ _____ 4. _____ _____	1. _____ _____ 2. _____ _____ 

6. Fill in the Table.

Salivation Disorders

Type of violation	**Hypersalivation**	**Hyposalivation**
Definition of the concept	_____	_____
Main causes	1. of central genesis: _____ _____ _____ 2. of peripheral genesis: _____ _____	_____ _____ _____ _____ _____
Negative consequences	_____ _____ _____	_____ _____ _____

7. Fill in the Table.

Characteristics of the swallowing disorders

Type of violation	**Dysphagia**	**Aphagia**
Definition of the concept	_____ _____ *Types of Dysphagia:* – _____ – _____ – _____ – _____	_____ _____ _____ _____ _____ _____ _____
Main causes	_____ _____	_____ _____
Negative consequences	_____	

8. Give the definition of *"achalasia"*: _____
_____

9. Fill in the Table.

Disorders of motor function of the stomach

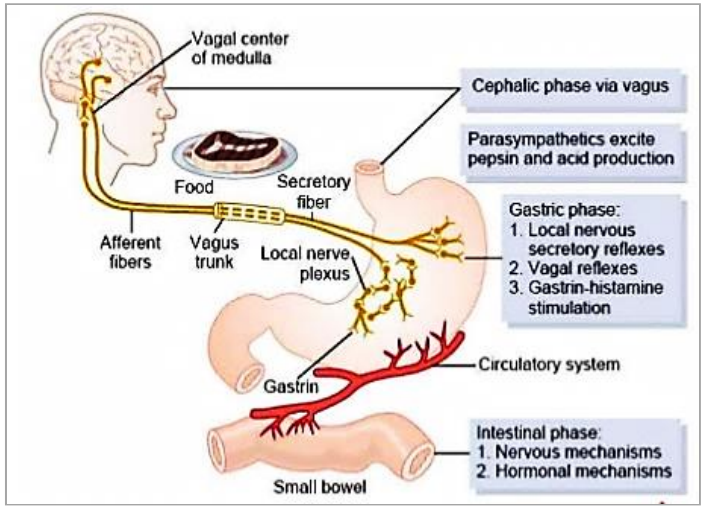
<table>
<tr><td rowspan="2">Typical forms of disorders</td><td>1. Change in muscle tone of the stomach:
– _____
– _____</td><td>3. Peristalsis change:
– _____
– _____</td></tr>
<tr><td>2. Change in muscle tone of sphincters:
– _____
– _____</td><td>4. Intestinal evacuation disorder:
– _____
– _____</td></tr>
<tr><td>The main causes of disorders</td><td colspan="2">– _____
_____
– _____
_____</td></tr>
<tr><td>The consequences</td><td colspan="2">1. Early satiety syndrome — _____
_____
2. Heartburn —_____
_____
3. Nausea — _____
_____
4. Vomiting — _____
Development mechanism: _____
_____
Value:
а) _____
_____
б) _____
_____
5. Dumping syndrome — _____
_____</td></tr>
</table>

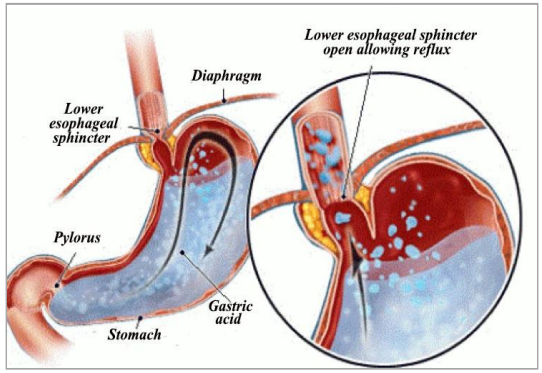
10. Fill in the Table.

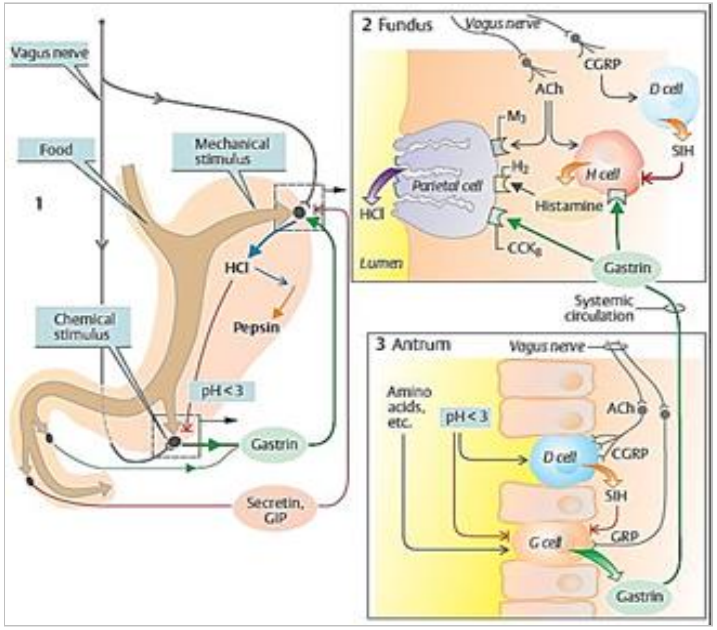
Quantitative changes in gastric secretion

Type of violation	Hypersecretion	Hyposecretion
Definition of the concept	_____ _____	_____ _____
Main causes	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____	1. _____ 2. _____ 3. _____ 4. _____ 5. _____
Possible consequences	_____ _____ _____	_____ _____ _____

11. Give the definition of *"achilia"*: _____
_____







12. Fill in the Table.

Qualitative changes in gastric secretion

Clinical manifestation	Hyperchlorhydria with pepsin hypersecretion	Hypo- and achlorhydria with hypocretion of pepsin
Acidity and volume of gastric contents		
The speed of evacuation of chyme and its neutralization in the duodenum		
Pyloric sphincter (mainly spasmodic/gaping)		
Pain syndrome (+/–)		
Muscle tone of the stomach (↑↓)		
Antiperistalsis (+/–)		
Heartburn (+/–)		
Belching (+/–), its character		
Vomiting (+/–), its nature		
Intestinal motility disorder (+/–), type (diarrhea / constipation)		

13. What is the essence of modern ulcer theory? _____

_____

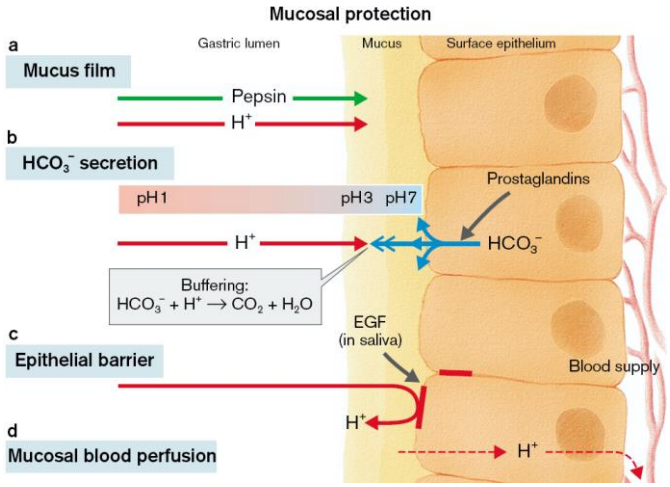
_____

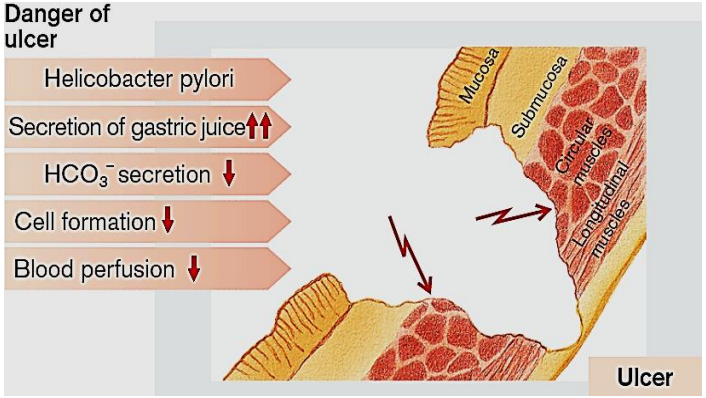
14. Complete the Scheme.

SHEY'S BALANCE

(ratio of protection and aggression factors of the gastric mucosa)

Protection factors **Aggression factors**





Factors of gastric mucus protection:

1. _____
2. _____
3. _____
4. _____
5. _____

Factors of aggression towards gastric mucus:

1. _____
2. _____
3. _____
4. _____

15. List the main forms of pyloric reflex violation and their consequences:

– _____

– _____

– _____

16. Fill in the Table.

The main theory of ulcer development

Name of the theory	**Authors**	**The essence**
Mechanical	_____ _____	_____ _____
Inflammatory	_____ _____	_____ _____
Peptic	_____ _____	_____ _____
Vascular	_____ _____	_____ _____
Vegetative	_____ _____	_____ _____
Endocrine	_____ _____	_____ _____
Cortical-visceral (neurogenic)	_____ _____	_____ _____

17. Fill in the Table.

Maldigestion — a syndrome of insufficient digestion

Type of violation	**Violation of cavity digestion**	**Violation of membrane digestion**
Causes	_____	_____
Consequences	_____ _____	_____ _____

18. Give the definition of *"malabsorption syndrome"* _____

_____

_____

19. Study the scheme and indicate the hereditary [1] and acquired [2] causes of malabsorbtion syndrome.

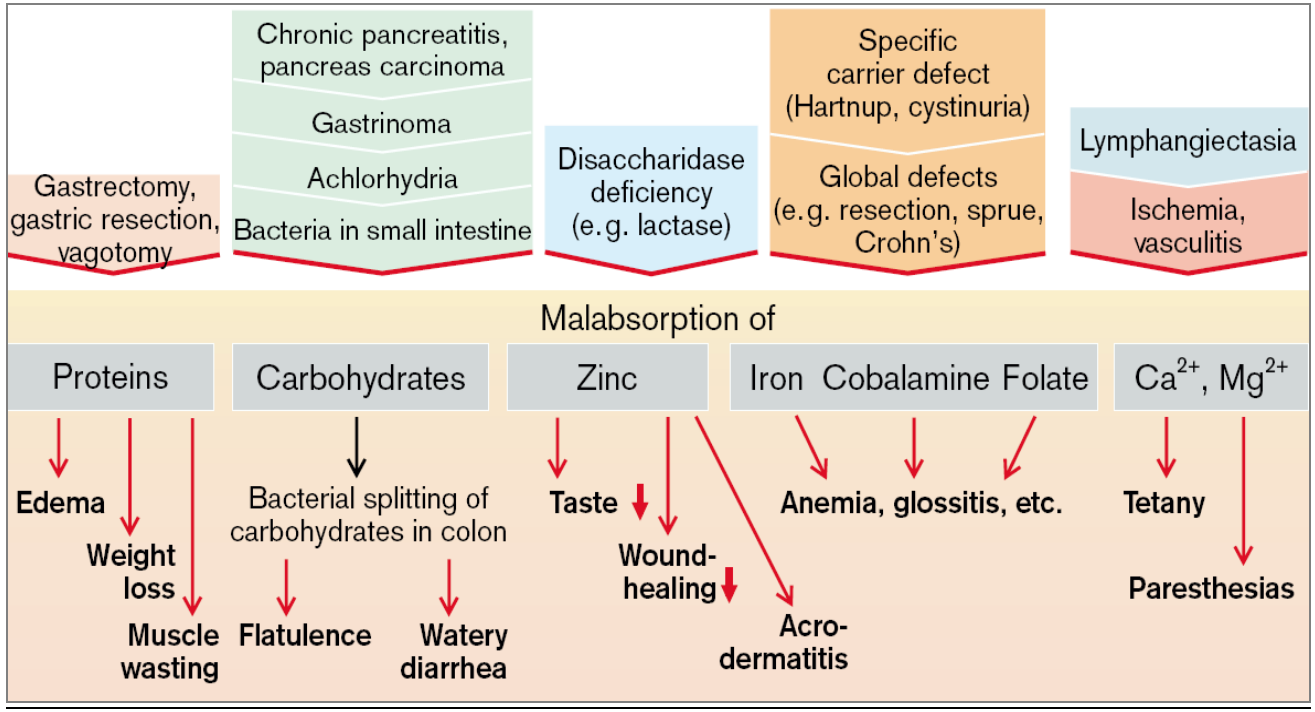


Fig. 1. Causes and consequences of malabsorption

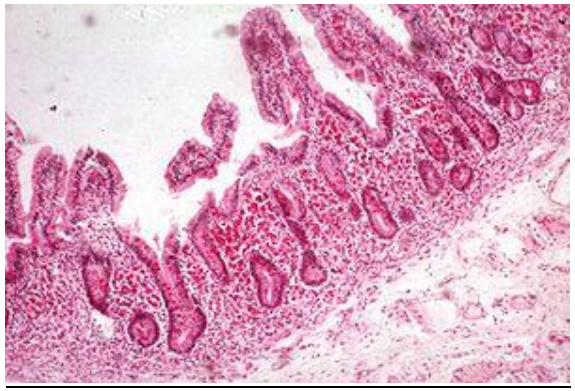


Fig. 2. Malabsorption: enlarged villi with many macrophages

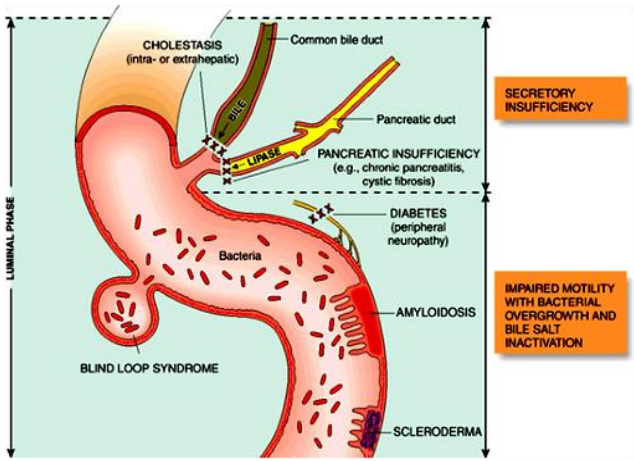


Fig. 3. Etiology of malabsorption

20. Fill in the Table.

Malabsorption syndrome

Malabsorption syndrome is _____		
Type	**Primary**	**Secondary**
Etiology	_____ _____	_____ _____

21. Give the definition of *"malassimilation syndrome"*: _____
_____

22. List the main manifestations of malassimilation syndrome: _____
_____

23. Fill in the Table.

Typical forms of impaired intestinal motor function

Diarrhea			**Constipation (constipation)**	
Type of diarrhea by pathogenesis	**Causes**	**Characteristics**	**Type by pathogenesis**	**Causes**
Osmotic	1. _____ _____ 2. _____ _____	_____ _____ _____ _____	*Spastic*	_____ _____
			Atonic	_____ _____
Secretory	1. _____ _____ 2. _____ _____	_____ _____ _____ _____	*Proctogenic*	_____ _____ _____

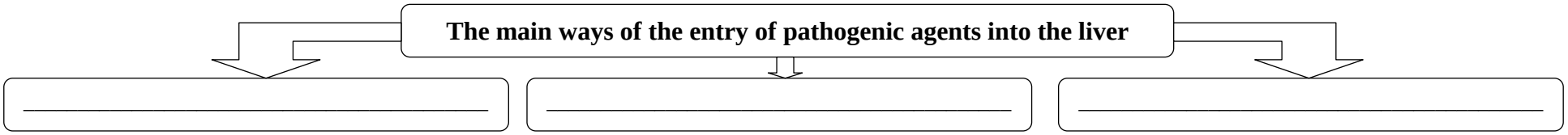
24. What does the symptom of intestinal intoxication include?_____
_____
_____

25. Fill in the Table.

The Liver Functions

Function	The essence
Digestion	
Protein synthesis	
Carbohydrate metabolism	
Lipid metabolism	
Participation in the exchange of vitamins	
Participation in mineral metabolism	
Participation in pigment exchange	
Influence on the processes of hemocoagulation	
Part of the body's immune system	
Providing Barrier Function	
Ensuring normal blood circulation	
Involved in hormone metabolism	
Participation in the regulation of ABB	
Hematopoiesis in the fetus	
Participation in thermoregulation	

26. Fill in the Scheme.



27. Give the definition of "*liver failure":* _____
_____

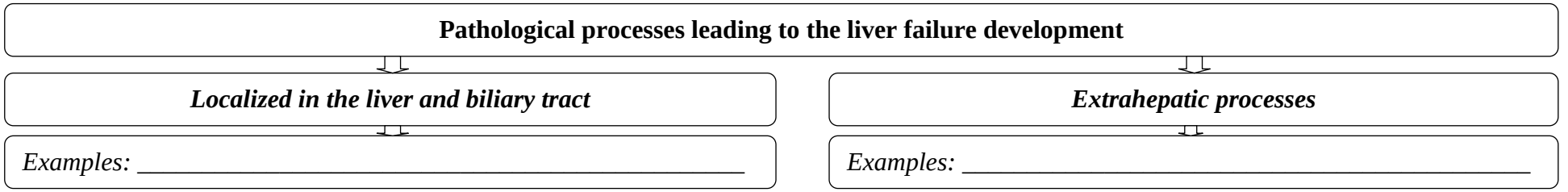
28. List the functions that are primarily impaired at the liver failure: _____
_____

29. Fill in the Table.

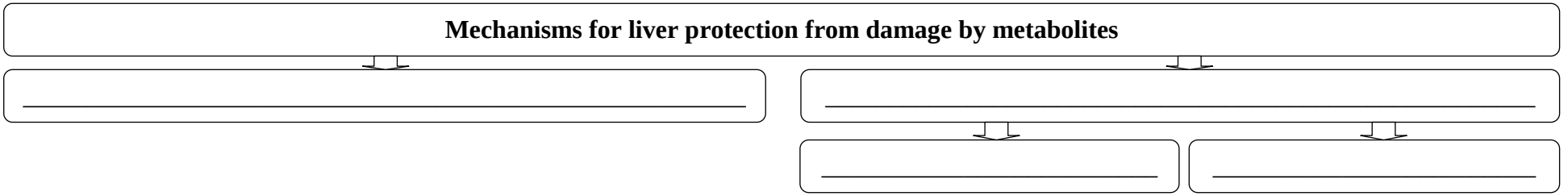
Classification of the liver failure

Classification criteria	Types, characteristics
By etiology	1. _____ 2.
By pathogenesis	1. _____ 2. _____ 3.
By primary damage of the liver or increased load on the liver	1. _____ 2.
Depending on the number of disturbed functions	1. _____ 2.
By the duration of the disease and the rate of development	1. _____ 2.

30. Fill in the Scheme.



31. Fill in the Scheme.

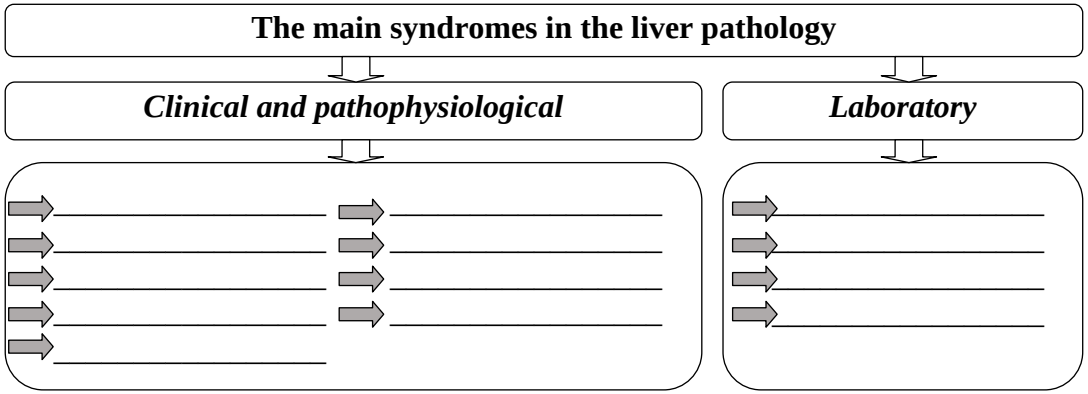


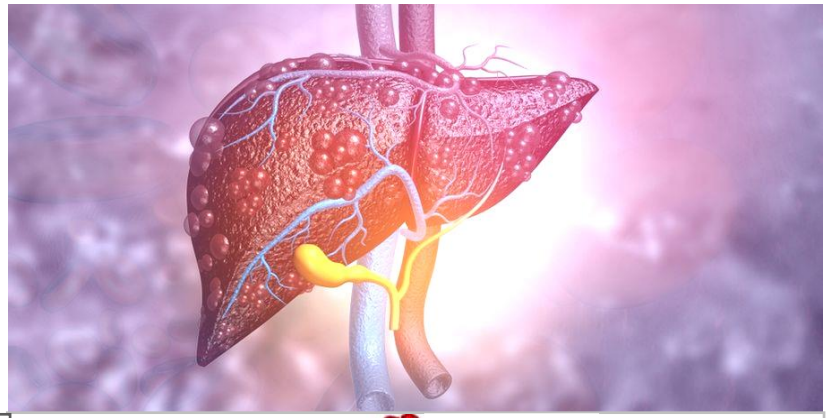
32. The main liver diseases include:_____

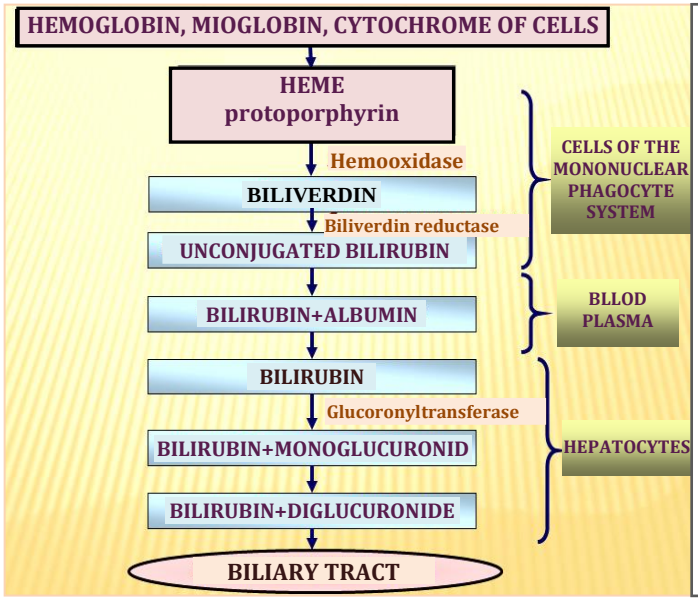
_____

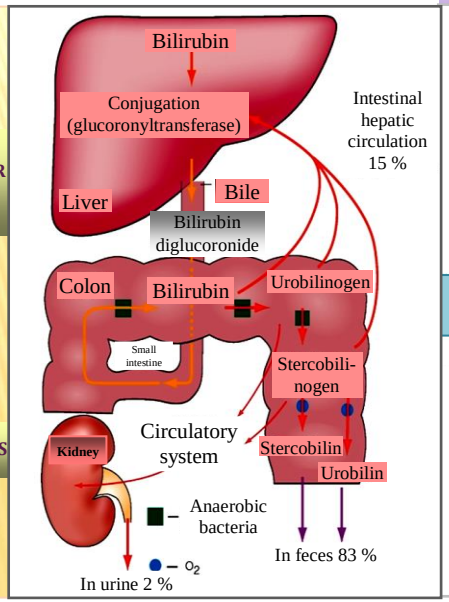
_____

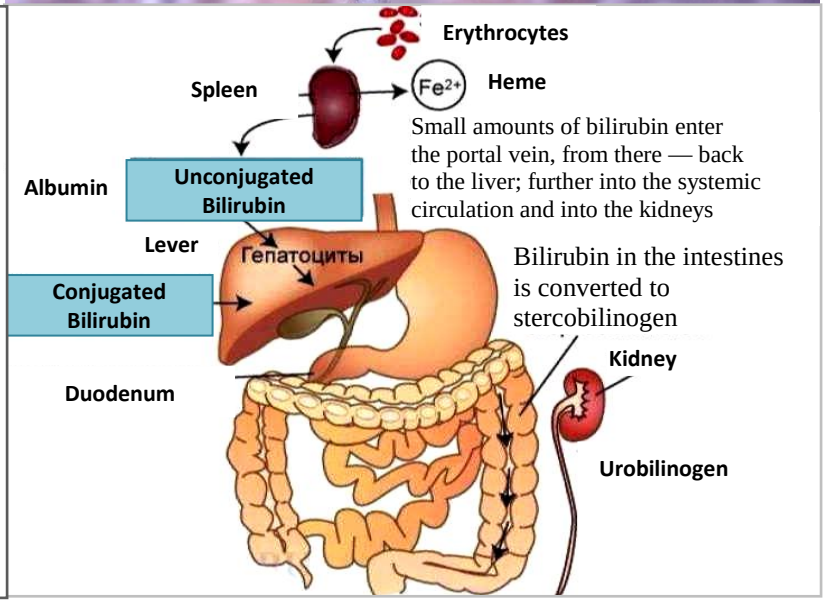
33. Fill in the Scheme.



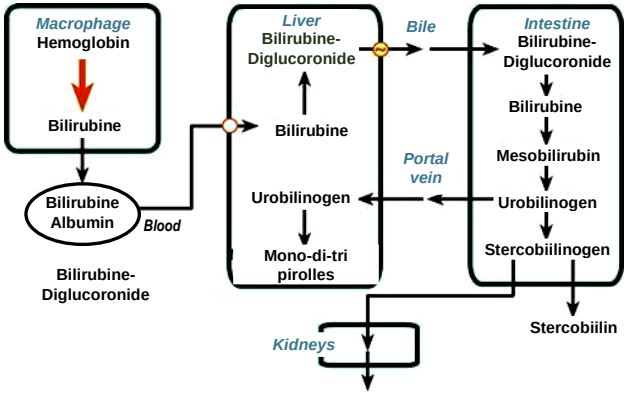




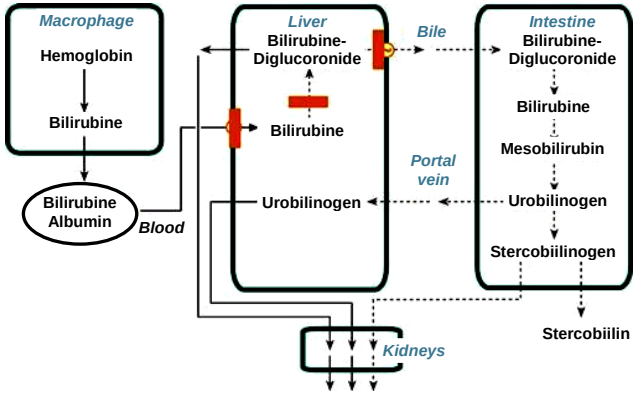




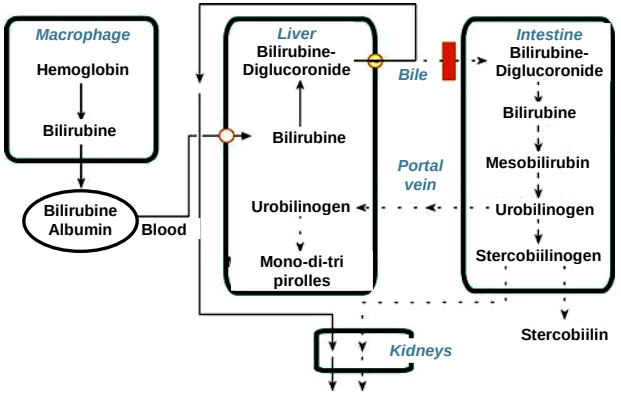
34. Study the development mechanisms of the main types of jaundice according to the presented schemes and fill in the table.



Pathogenesis of hemolytic jaundice



Pathogenesis of parenchymal jaundice



Pathogenesis of obstructive jaundice

Types of jaundice by pathogenesis

Type	Variants	Causes of occurrence
Suprahepatic	*Hemolysis due to increased red blood cell breakdown*	
	Shunt hyperbilirubinemia	
	Violation of the plasma transport of bilirubin	
Hepatic	*Parenchymal*	
	Cholestatic	
	Enzymatic	
Subhepatic		

35. Fill in the Table.

Differential diagnosis criteria for jaundice

Feature	Suprahepatic jaundice	Hepatic jaundice	Subhepatic jaundice
Biochemical blood test:			
Bilirubin content	↑ due to unconjugated (indirect)		
Activity of AlAT, AsAT			
Cholesterol level			
Alkaline phosphatase activity			
γ -GTP activity			
Urine			
Colour			
Urobilinogen content			
Sterkobilinogen content			
The content of bilirubin (direct)			
Feces			
Colour			
Sterkobilin content			

36. Fill in the Table.

The main manifestations of cholemic syndrome

Manifestations	Development Mechanism
Bradycardia and hypotension	_____ _____
General asthenia, irritability, drowsiness during the day and insomnia at night, headaches, increased fatigue	_____ _____
Itchy skin	_____ _____

37. Fill in the Scheme.

Cholestasis syndrome

Cholestasis is _____

Types of cholestasis:

intrahepatic

– _____

_____

– _____

_____

extrahepatic

Mechanism of development:

– _____

_____

_____

– _____

_____

– _____

_____

– _____

_____

– _____

_____

_____

The main manifestations:

– _____

_____

– _____

_____

– _____

_____

– _____

_____

– _____

_____

– _____

_____

– _____

_____

38. Fill in the Table.

The main manifestations of malnutrition syndrome

Violations	**Characteristics**
Protein metabolic disorders	_____
Carbohydrate metabolism	_____
Lipid metabolism	_____
Disruptions in the metabolism of hormones and biologically active substances	_____
Disorders of water-electrolyte metabolism	_____

39. Fill in the Table.

The main links in hemorrhagic syndrome pathogenesis			
_____ _____	_____ _____	_____ _____	_____ _____

40. Fill in the Scheme.

Portal hypertension is _____
_____

Types	**The main cause for the increase in the portal pressure** — _____ _____
intrahepatic: _____	**The main link of pathogenesis** — _____ _____
extrahepatic: – _____ _____ _____ – _____ _____	**Early compensatory response** — _____
	«+» value: _____ _____ _____
	«-» value: – _____ – _____ – _____

Clinical manifestations and mechanisms of their development:
1. _____
_____
2. _____
_____
3. _____

41. What is the essence of hepato-endocrine syndrome? _____
_____
_____
_____

42. Fill in the Scheme.

The main manifestations of hepato-cerebral insufficiency syndrome

1. _____
_____
_____
_____

2. _____
_____
_____
_____
_____

3. **Hepatic coma** is _____
_____

Variants of pathogenesis:
– _____
_____
_____
– _____
_____
_____

The basic mechanisms of development:
– _____
– _____
– _____
– _____
– _____

43. Fill in the Table.

Clinical and biochemical liver syndromes

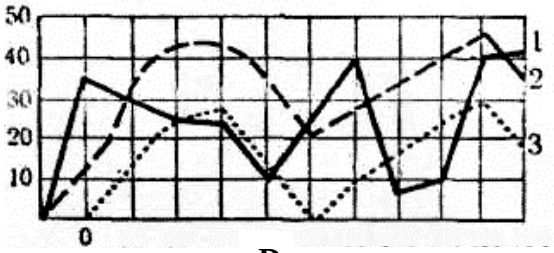
Syndrome	Characteristic
Cytolysis syndrome	_____
Cholestasis syndrome (excretory-biliary)	_____
Hepatocellular insufficiency syndrome	_____
Mesenchymal inflammatory syndrome	_____

PART 2. PRACTICAL WORK

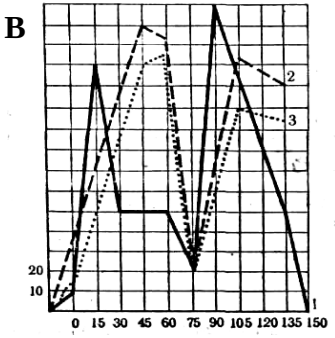
Work 1. DETERMINING THE TYPES OF GASTRIC SECRETION

Determine the types of gastric secretion of various patients using graphs A, B, C, D, E.

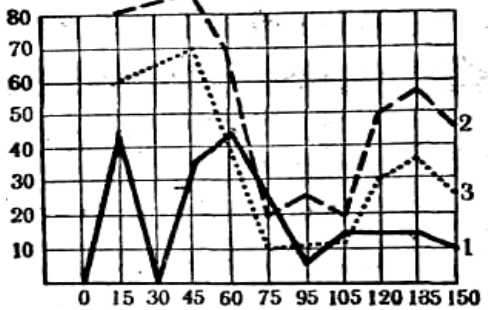
A



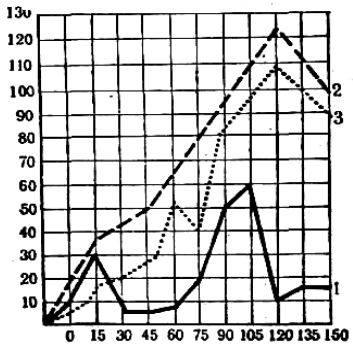
B



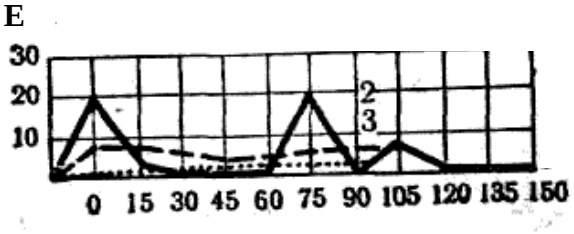
C



D



E



Ordinate axis — the amount of juice in milliliters, acidity in titration units. Abscissa axis — the time in minutes: under 10 min — on an empty stomach, 10–60 min — in mechanical irritation of the stomach, 60–150 min — in chemical irritation of the stomach.

Conclusion: specify the types of gastric secretion (graphs a, b, c, d, e):

A.: _____

B.: _____

C.: _____

D.: _____

E.: _____

Work 2. DETERMINATION OF DISORDERS OF ACID-PRODUCTIVE AND ACID-NEUTRALYZING FUNCTIONS OF THE STOMACH BASED ON GASTRIC pH-METRY DATA

The method for determining intragastric pH is a functional electrometric method. The pH probe has 3 electrodes: for determining the pH in the cardia, antrum and the body of the stomach. Evaluation of acid production and acid neutralization is carried out according to the parameters proposed by E.Y. Linar, Y.Y. Leja, presented in the Table.

Assessment of acid-forming and acid-neutralizing functions of the stomach

Assessment of acid production Fasting stomach body type	**pH**	**Acid neutralization assessment — antral pH probe data**	**pH**
Hyperacidity	< 1,5	Compensated state — the acidic secretion of the main glands is completely neutralized	> 5,0
		Partially compensated state	2,0–4,9
Normacidity, continuous acidification	1,5–2,0	Decompensated state — the acidic secretion of the main glands is not neutralized	< 2
Hypoacidity	2,1–5,9		
Anacidity	> 6,0		

An example of a conclusion: Partially compensated (by 1 pH unit) mid-acid stomach.
On the basis of digital data of intragastric pH-metry, determine the violation of secretion and neutralization of gastric juice in patients A, B.
Patient A: pH of the body of the stomach on an empty stomach is 1.5, in the antrum pH = 4.0.
Patient B: pH of the body of the stomach on an empty stomach is 1.3, in the antrum pH = 1.9.

***Conclusions*:**
Patient A: _____
_____

Patient B: _____
_____

Work 3. EXPERIMENTAL METHODS FOR STUDYING THE LIVER FUNCTIONS

1. Draw schemes of the operations.

Eck's fistula	Ekk–Pavlov fistula

Work 4. STUDYING THE METHOD OF EXPERIMENT "THE GENERAL TOXIC EFFECT OF BILE ON THE BODY", THE PROTOCOL OF THE RESEARCH AND MAKING CONCLUSIONS

1.5–2.0 ml of bile are injected into the frog's lymphatic bag located under the skin. A healthy animal serves as control. The observation data are given in the Table.

Bile effect on the state of the nervous and cardiovascular systems

Time	Control	Experiment
1'	Spontaneous twitching of extremity muscles is not marked. Coordination of movements is preserved. HR — 40 per min	Periodic twitching of legs is observed. The muscular tone is not changed. Coordination of movements is preserved. The frog, being turned over on the back, returns to a normal position. HR — 43 per min
3'	The frog is sitting, under external stimuli its motor activity increases. The muscular tone is not changed. Coordination of movements is not impaired. HR — 42 per min	The frog is jumping, bumping at the chamber walls. The muscular tone is elevated, muscular contractions are periodically observed. Lying on the back, the frog cannot take the former position at once. HR — 30 per min
5'	The same condition. HR — 42 per min	Motor activity is reduced due to significant decrease of the muscular tone. The frog is motionless, listless, is lying, it cannot return to the initial position from the position on the back. HR — 35 per min
7'	The same condition. A pain stimulus action is accompanied by squeak and increase of motor activity. HR — 43 per min	The frog has not changed the position given to its body. It does not response to the action of a pain stimulus. HR — 30 per min

Make the conclusions, answer the following questions:

1. What syndrome arises in the animal that got parenteral bile injection? By what bile components is it caused? _____

_____

_____

2. What systems are impaired? Give their characteristics, possible development mechanisms _____

_____

_____

Work 5. STUDYING OF THE METHOD OF EXPERIMENT "THE EFFECT OF BILE ON THE TIME OF A MOTOR REFLEX IN THE FROG", THE PROTOCOL OF THE RESEARCH AND MAKING CONCLUSIONS

A decapitated frog is suspended by the mandible on the stand. In 5–10 min a leg of the frog is dipped into 0.2 % solution of hydrochloric acid. Using the metronome the time of the frog's motor response to irritation by the acid (it jerks the leg back) is taken. After several repeated irritations the average latent period of response (the number of metronome beats) is determined. After each immersion into the acid it is necessary to wash the leg with water carefully. Then 0.5–1.0 ml of bile are injected into the frog's lymphatic bag, in 15–20 min the experiment with irritating the leg with hydrochloric acid is repeated.

Bile effect on the time of a motor reflex in the frog

Reflex time by Turk, sec	
Before bile injection	**After bile injection**
2	7
1	9
3	8
2	10
average latent period	average latent period
2	8,5

Make the conclusions, answering the following questions:

What are the manifestations of bile effect on the nervous system? _____

_____

What are possible mechanisms of this action? _____

_____

Work 6. STUDYING THE METHOD OF EXPERIMENT "THE BILE EFFECT ON HEART RATE OF THE FROG", THE PROTOCOL OF THE RESEARCH AND MAKING THE CONCLUSIONS

An immobilized frog is attached to a plate with its abdomen upward, the thorax and the pericardium are open and the heart is exposed. The heart rate is counted. Then some drops of bile are applied to the frog's heart with the pipette in various concentrations: 1:10, 1:5, 1:2 and whole bile. After every application and repeated HR registration the heart is carefully washed with physiological solution.

Effect of bile in various concentrations on the frog's heart rate

Effect	Heart rate, beats/min
Reference value (before the effect)	43
Bile, dilution 1:10	40
Bile, dilution 1:5	30
Bile, dilution 1:2	5
Whole bile	Cardiac arrest

Analyze the results, make the conclusions and answer the following questions:

What is the character of the cardiac muscle response to application of bile? _____

_____

What is the mechanism of bile action on the cardiac muscle? _____

_____

Work 7. SITUATIONAL TASKS

№ 1

Patient B., 46 years, was admitted to clinic with the diagnosis "Suspected cancer of the pancreas". His body weight — 59 kg, the height being 179 cm; he had lost 14 kg of weight for the last year. Stool — 3–4 times a day, profuse. Meteorism. The tongue was coated, the appetite considerably decreased. There were no pains in the abdomen; the body temperature was in norm.

In the anamnesis: the patient has been abusing alcohol for 15-20 years; 10 years ago after a usual alcoholic excess he suffered acute pancreatitis (with hospitalization); after this there were 2–3 episodes of severe pains in the abdomen, but he didn't apply to the doctor, was not treated, didn't follow a diet, continued taking alcohol.

In the analyses made in the clinic: hyperglycemia — 20.6 mmol/l, glucosuria — 4 % (in diurnal diuresis of 3–4 l), marked steatorrhea, 5-fold reduction of the factor of maximum activity of tripsin as compared to the norm. The results of ultrasound examination and computer tomography of the pancreas: diffuse consolidation and inhomogeneity of the gland structure, the presence of calcificators there.

Questions:

1. Evaluate the functional state of the pancreas in the patient.
2. On the basis of the evaluation of the pancreas function give your suggestions regarding the pathological processes that have developed in the pancreas and their possible cause.
3. What additional examinations are required to confirm (or reject) the preliminary diagnosis in this patient with a greater degree of probability?
4. Can the suggested pathological processes develop in the pancreas independently on each other? Can they be interrelated in this case? If yes, what is their most probable sequence of occurrence?
5. What disease, to your opinion, does the patient suffer?
6. In what way can you explain such a considerable loss of weight of this patient lately?

№ 2

The patient with insufficient secretion of bile into a small intestine and marked steatorrhea developed multiple hemorrhages.

Question: Explain the possible mechanisms of interrelations of the above pathologic processes.

№ 3

For reproduction of experimental gastric ulcers, a ligature is applied to the pylorus preserving its passability (Sheia's method).

Question: What is the occurrence mechanism of gastric ulcer in applying the ligature?

Give the situations, when the human may develop ulcers with a similar pathogenesis.

№ 4

Three years later after a subtotal resection of the stomach the patient developed progressive anemia. The blood test revealed: erythrocyte count — 1.9×10^{12}/l, leukocyte count — 3×10^{9}/l, thrombocyte count — 100×10^{9}/l. In the smear: megalocytes, hypersegmentated neutrophiles.

Question: Is there any interrelation between the above blood pathology and stomach resection performed earlier? If yes, what does it mean?

№ 5

Patient K., 31 years, was delivered to clinic by an ambulance. On admission: passive, retarded, apathic, answers questions not always at once and adequately. The tongue is coated. The body temperature — 36.5 °C. Skin integuments and mucous membranes are of a yellowish color, there are teleangiectasias on the skin of the upper trunk, erythema of the palms is marked. The abdomen is enlarged due to ascites fluid that makes palpation of the liver difficult. Edemas of lower extremities are noted. The border of the left ventricle of the heart is slightly dilated. BP — 160/95 mm Hg, HR — 90 beats/min, the pulse is rhythmic.

The results of biochemical blood test: hyperbilirubinemia, hypoglycemia, hypoproteinemia, hypocholesterinemia, the urea content is decreased, the prothrombin index is reduced. The activity of AlAT and AsAT in blood is increased.

Questions:

1. What are the development mechanisms of teleangiectasias and persistent erythema of the palms in the patient? What other symptoms are caused by the same effect?
2. Specify the basic development causes of portal hypertension and ascites? What is the role of ascites in secondary impairments of the organism function?

3. Are there any laboratory symptoms of hepatic insufficiency? If yes, then what is their development mechanism?
4. How can you assess the state of consciousness in this patient?

№ 6

Specify the type of jaundice and give the conclusion.

Table 8

	Factor	Content	Norm
Blood	Bilirubin:		
	– indirect	51.3 mcmol/l	8.5–20.5 mcmol/l
	– direct	–	–
	Urobilin-(ogen)	++	–
	Stercobilin-(ogen)	+++	+
	Cholesterol	6.8 mcmol/l	3.1–5.2 mmol/l
	Bile acids	–	–
Urine	Bilirubin:	–	–
	Urobilin-(ogen)	++	–
	Stercobilin-(ogen)	+++	+
	Bile acids	–	–
	Color	saturated yellow	straw-yellow
Feces	Stercobilin	+++	+
	Fatty acids	–	–
	Bile acids	+	±
	Color	dark-brown	brown

Table 9

	Factor	Content	Norm
Blood	Bilirubin:	342.3 mcmol/l	
	– indirect	20.1 mcmol/l	8.5–20.5 mkmol/l
	– direct	322.2 mcmol/l	–
	Urobilin-(ogen)	–	–
	Stercobilin-(ogen)	–	+
	Cholesterol	14.2 mmol/l	3.1–5.2 mmol/l
	Bile acids	+++	–

	Factor	Content	Norm
Urine	Bilirubin: Urobilin-(ogen) Stercobilin-(ogen) Bile acids Color	+++ – – +++ dark beer	– – + – straw-yellow
Feces	Stercobilin Fatty acids Bile acids Color	– +++ – grey-white clay	+ – ± brown

Table 10

	Factor	Content	Norm
Blood	Bilirubin: – indirect – direct Urobilin-(ogen) Stercobilin-(ogen) Cholesterol Bile acids	150.7 mcmol/l 20.5 mcmol/l 130.2 mcmol/l ++ ++ 10.2 mmol/l ++	 8.5–20.5 mkmol/l – – + 3.1–5.2 mmol/l –
Urine	Bilirubin: Urobilin-(ogen) Stercobilin-(ogen) Bile acids Color	+ ++ ++ + dark beer	– – + – straw-yellow
	Factor	**Content**	**Norm**
Feces	Stercobilin Fatty acids Bile acids Color	± + ± light-brown	+ – ± brown

№ 7

Patient I. at the age of 20 suffered serum hepatitis. After discharge from the hospital he didn't apply to doctors for a number of years. Periodically he was troubled by pains in the right hypochondrium, nausea, malaise. By 28 years his weakness increased. There appeared marked signs of "meduza's head" on the anterior abdominal wall, often he had diarrhea, hemorrhagic bleedings. Palpation revealed splenomegaly, the liver extending 2 cm from the costal arch, its edge being uneven.

Question: What syndrome develops in the patient? Name its form

№ 8

There is a yellowish coloring of sclera and skin integuments, severe itching, general malaise, increased excitability in the patient; the urine is of a beer color, he has an acholic stool, bilirubinemia, cholacidemia, bilirubinuria.

Question: Give a full name of the syndrome developed in this patient.

№ 9

What syndrome is characterized by a yellowish coloring of sclera and skin, bilirubinemia, bilirubinuria? Specify the possible causes of its development.

№ 10

Patient A. was delivered to clinic by an ambulance with profuse epigastric bleeding. Three years ago he was diagnosed cirrhosis of the liver.

Question: The complication of what syndrome was epigastric bleeding?

Control questions

1. Experimental methods of studying the digestive system activity in norm and in pathology (I. N. Basov, I. P. Pavlov).
2. The impairment causes of the digestive system activity and basic signs of these impairments.
3. Digestion impairment in the oral cavity: principal causes and consequences of hypo- and hypersalivation, mastication impairments. Principal causes of dysphagia.
4. Basic manifestations of gastric dyspepsia: the disorders of appetite, nausea, belching, vomiting, pain syndrome. Causes of their development.
5. Interrelation of secretory and motor functional impairments of the stomach. Manifestations of hyper- and hypochlorohydria. Pathology of a pyloric reflex.
6. Gastric ulcer and duodenal ulcer. Development theories of ulcer. Modern concepts of etiology and pathogenesis of gastric ulcer. The role of *H. pylori* in pathogenesis of the diseases.
7. Impairments of intestinal secretory activity and absorption processes. Etiology, pathogenesis and clinical manifestations of syndromes of maldigestion and malabsorption.
8. Impairment mechanisms of motor intestinal function (diarrhea, constipation). Etiology, pathogenesis.
9. Intestinal autointoxication. Etiology, pathogenesis, manifestations.

10. Experimental methods of studying the liver functions (N. V. Ekk, E. S. London, I. P. Pavlov). Changes in the organism in the given interventions.
11. Basic etiologic factors of the liver damage. Basic syndromes in pathology of the liver and bile ducts.
12. The definition, etiology and pathogenesis of mechanical, parenchymatous and hemolytic forms of jaundice. Bilirubin exchange in various forms of jaundice.
13. The definition and basic syndromes of cholemia, acholia and hypercholia in jaundice of various forms.
14. The syndrome of portal hypertension. The definition, forms, clinical symptoms.
15. Pathogenetic characteristic of collateral and portocoval blood circulation in portal hypertension.
16. Pathogenesis of ascites in portal hypertension.
17. Hepatic insufficiency. The definition, etiology, pathogenesis, laboratory and clinical manifestations.
18. Hepatic coma. The definition, forms (bypass, hepatic-cellular). Pathogenesis.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 12).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins and Cotran Pathologic Basis of Disease. V. II / V. Kumar, A. K. Abbas, J. C. Aster. South Asia ed. India : Elsevier, 2015. 1391 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 2nd ed. 107 MB. NY : Appleton & Lange, 2000.

Teacher's signature: _____

LESSON 13. PATHOLOGICAL PHYSIOLOGY OF THE KIDNEYS

Date: «____» _____ 20__

Purpose of the Lesson: to study the causes, mechanisms of development and the main clinical manifestations of renal dysfunction. To characterize the typical forms of renal dysfunction.

Tasks:

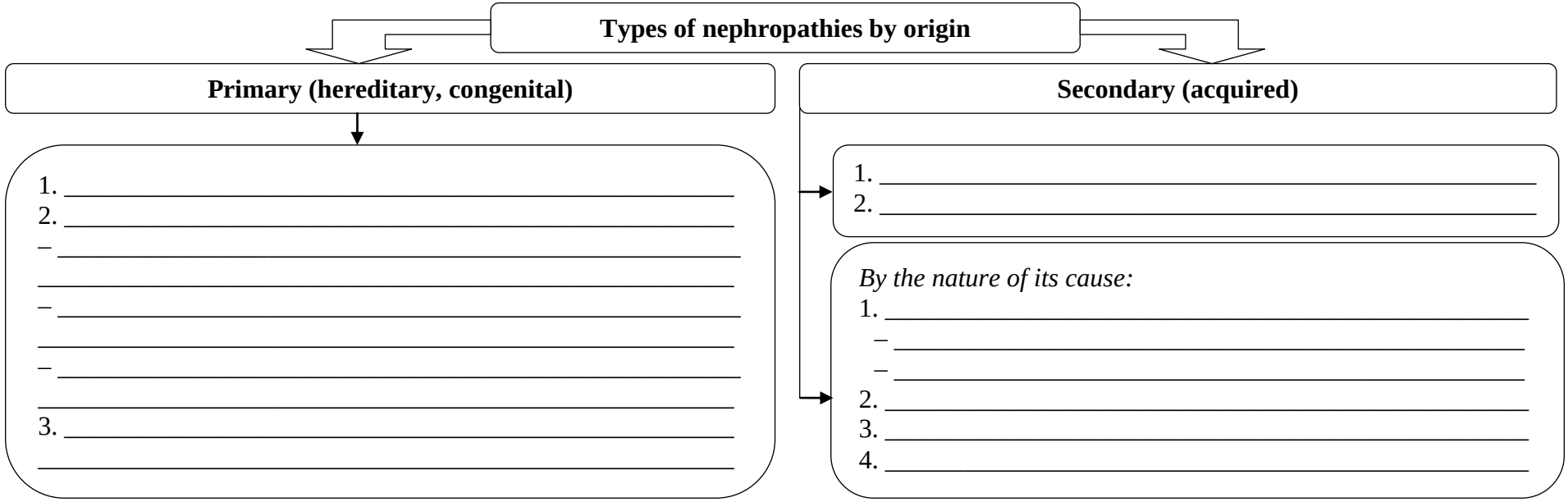
– To study some typical disorders of renal function in the experiment.

– To solve the situational tasks. Control test.

PART 1. WORKING WITH TRAINING MATERIALS

1. Give the definition of "nephropathy": _____
_____
_____

2. Fill in the Scheme.



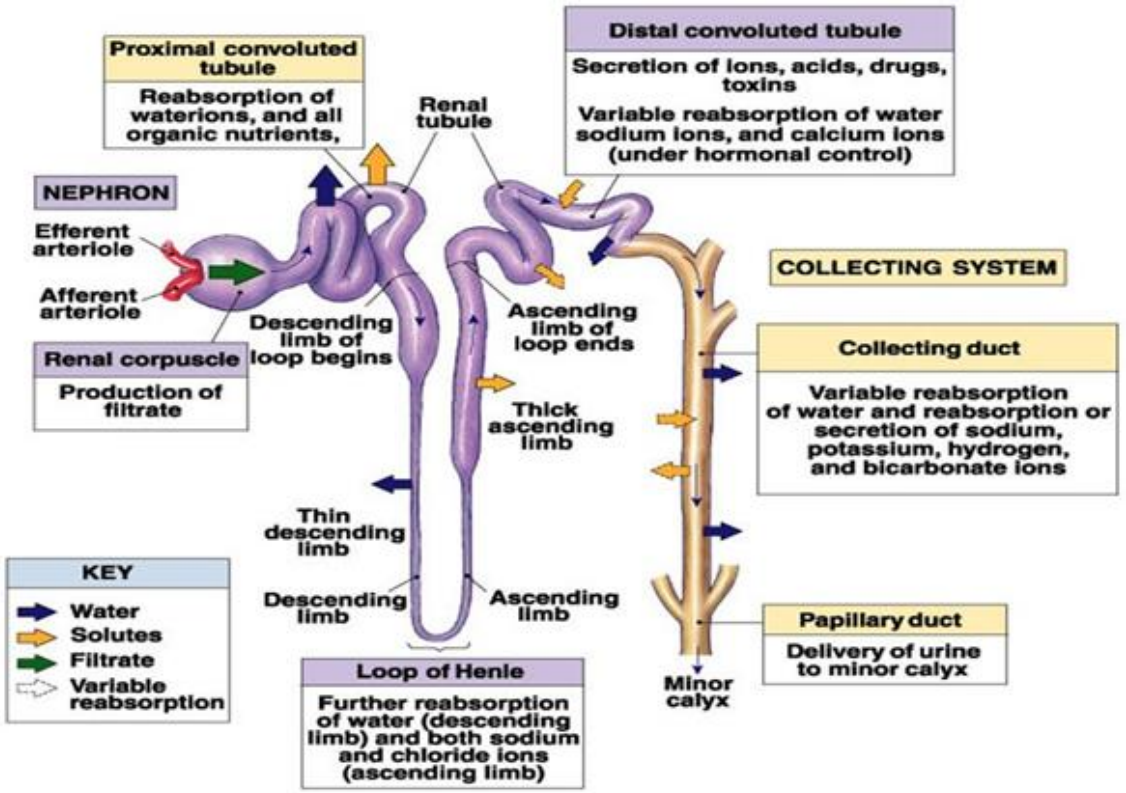


Fig. 1. Nephron components and functions

3. Fill in the Table.

The main pathogenetic groups of renal pathology

Group	Examples of pathology

4. Fill in the Scheme.

The main clinical manifestations of the renal pathology

Minor renal syndromes	***Major renal syndromes***	***Non-specific manifestations***
1. _____ 2. _____ 3. _____	1. _____ 2. _____ 3. _____	_____ _____ _____

5. Study the normal process of urine formation according to the presented figure 2 and indicate on the diagram the main processes, the disorder of which will lead to the urine formation impairment.

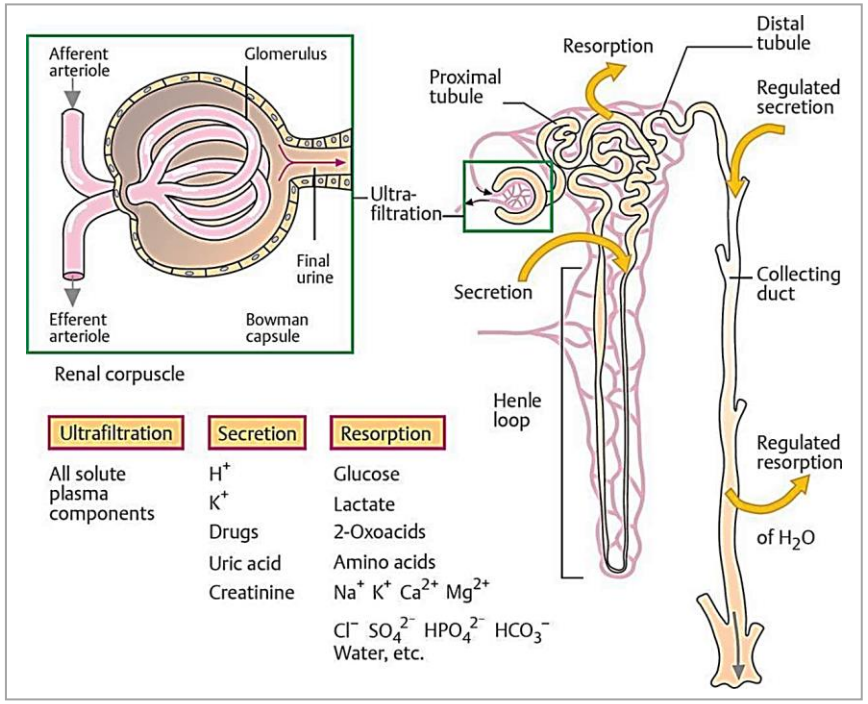


Fig. 2. Urine formation process

Urinary disorders occur as a result of impairment of:

_____
_____

_____
_____

_____
_____

_____
_____

_____
_____

6. Fill in the Scheme.

The glomerular filtration rate depends on:

permeability of the glomerular filter

_____

_____

effective filtration pressure (EFP) level

EFP = $P_{hydrostat.}$ – ($P_{oncot.}$ + $P_{intracaps.}$)

EFP = _____ = _____ mmHg

Glomerular filtration disorders:

decreased glomerular filtration

1. ↓**$P_{hydrostat.}$** less _____

_____

_____

2. ↑**$P_{oncot.}$** more _____

_____

_____

3. ↑**$P_{intracaps.}$** more_____

_____

_____

4. _____

_____

5. _____

_____

6. _____

_____

increased glomerular filtration

1. ↑**$P_{hydrostat.}$** _____

_____

2. ↓**$P_{oncot.}$** _____

_____

3. _____

_____

4. _____

_____

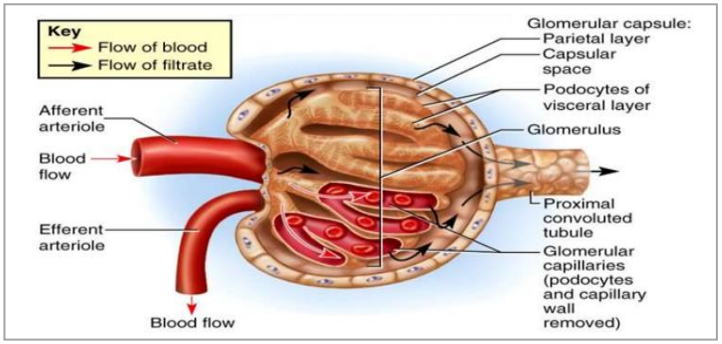


Fig. 3. Glomerular filtration

7. Study the normal reabsorption process according to the presented picture 4 and fill in the Scheme.

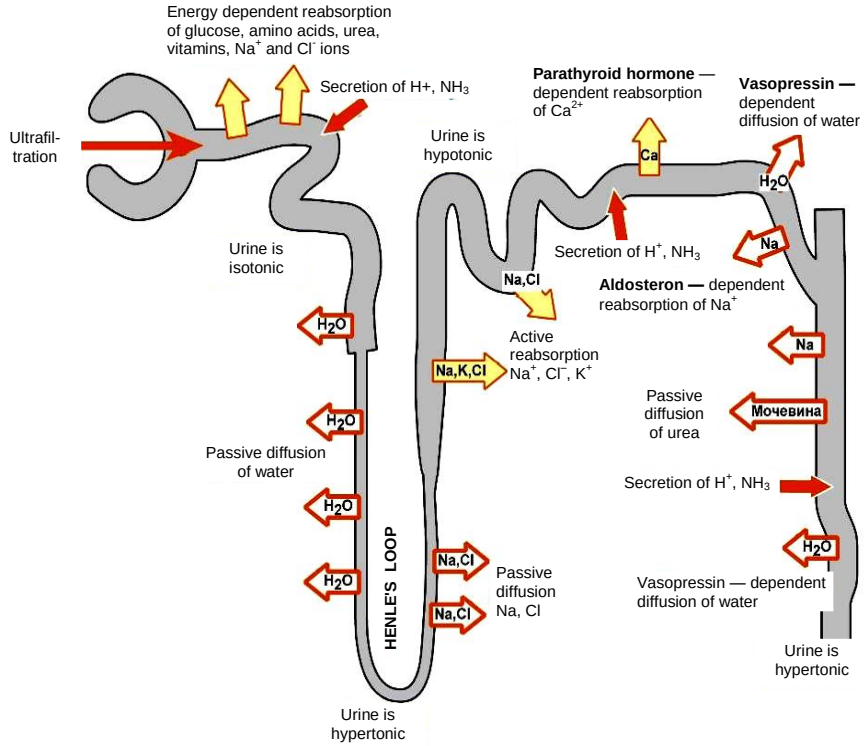


Fig. 4. Reabsorption process

Disorders of the processes of reabsorption, excretion and secretion in the tubules

Tubulopathy

By etiology:

– _____

– _____

The main causes:

– _____

_____

– _____

_____

– _____

_____

– _____

_____

Depending on the localization of the defect:

proximal

Reabsorption disorder:

_____

_____

_____

_____

_____

_____

_____

_____

distal

Reabsorption disorder

Na^+

K^+

Mg^{2+}

Ca^{2+}

H_2O

8. Fill in the Scheme.

Manifestations of various types of renal pathology

Renal syndromes (urinary syndrome)

– _____

– _____

– _____

– _____

Extrarenal syndromes

– _____

– _____

– _____

– _____

9. Fill in the Table.

Changes in the amount of urine (diuresis)

Changes	The amount of urine per day	Causes
Polyuria	_____ _____	– _____ – _____ – _____ – _____ – _____ – _____ – _____
Oliguria	_____ _____	– _____ – _____ – _____ – _____ – _____
Anuria	_____ _____	– _____ – _____ – _____ – _____

10. Fill in the Table.

Normal relative (specific) urine gravity and its possible changes

Changes	Relative urine gravity	It appears when
Normostenuria	_____	_____
Hypersthenuria	_____	_____
Hypostenuria	_____	_____
Isostenuria	_____	_____

11. Fill in the Table.

Changes in the qualitative composition of urine

Changes	Definition	Types, characteristics
Proteinuria	_____	By the amount of detected protein: – _____ – _____ – _____ According to the qualitative composition of the detected protein: – _____ – _____ By biological value: – _____ – _____ By the level of the damage: – _____ _____ – _____ _____ – _____ _____
Hematuria (erythrocyturia)	_____	By severity: – _____ – _____ By the origin of erythrocytes: – _____ – _____
Leukocyturia	_____	_____

Changes	Definition	Types, characteristics
Cylindruria	_____ _____ _____ _____ _____	Types of cylinders: – _____ – _____ – _____ – _____
Glucosuria	_____ _____ _____ _____ _____	By origin: – _____ – _____ a) _____ b) _____
Epitheliuria	_____ _____ _____	_____ _____ _____
Crystalluria	_____ _____ _____	_____ _____ _____

12. Fill in the Table.

Changes in the rhythm of urination

Type of change	Definition	Causes
Pollakiuria	_____	_____
Ollakiuria	_____	_____
Nocturia	_____	_____

13. Give the definition of “nephritis” _____
_____
_____

14. Fill in the Scheme.

Acute diffuse glomerulonephritis

Etiology:

– infectious factors: _____

– non-infectious factors: _____

Pathogenesis:

Immune mechanisms:

Types, characteristics:

– _____

_____

– _____

_____

– _____

_____

Non-immune mechanisms:

Types, characteristics:

– _____

_____

_____

– _____

_____

_____

Clinical manifestations:

_____

(name the syndrome)

Manifestations: _____

_____

_____

(name the syndrome)

Mechanism: _____

_____

_____

(name the syndrome)

Mechanism: _____

_____

Forms:

_____

Complications: _____

_____

_____

_____

_____

15. Fill in the Scheme.

Chronic diffuse glomerulonephritis

Etiology:

– infectious factors: _____

– non-infections factors: _____

Pathogenesis:

Immune mechanisms:

_____

_____

_____

Non-immune mechanisms:

_____

_____

_____

Forms:

_____ (about _____ %)

_____ (about _____ %)

_____ (about _____ %)

_____ (about _____ %)

Clinical manifestations:

_____

_____

_____

Complications:

– at hypertensive form: _____

– at nephrosclerotic form: _____

16. Fill in the Scheme.

Pyelonephritis

Definition:

_____
_____

Etiology:

Nature: _____
Pathogens: _____
Ways of infection: _____
Risk factors: _____

Classification by its clinical course:

Acute

Clinical manifestations: _____
_____
_____
Outcome:
_____
_____

Chronic

Clinical manifestations: _____
_____
_____
Outcome:
_____
_____

17. Complete the definition. ***Nephrotic syndrome*** is a symptom complex that develops in renal pathology and is characterized by:

– _____
– _____
– _____
– _____
– _____

18. Fill in the Scheme.

Nephrotic syndrome

Etiology:

Primary nephrotic syndrome ▼ _____

Secondary nephrotic syndrome ▼ _____

Pathogenesis:

▼

The main pathogenetic links: _____

Manifestations and development mechanisms:

▼

Manifestations	**Development mechanisms**
Proteinuria	_____
Hypoproteinemia, dysproteinemia	_____
Edema	Hypoproteinemia → ↓ of colloidal-osmotic pressure → _____ → Hypovolemia → ↑_____ → _____ → hypernatremia → stimulation of ADH secretion → _____ → ↑ hypoproteinemia
Hyperlipidemia	
Hypercoagulation	_____
Infection attachment	
Hypocalcemia	

19. Fill in the Scheme.

Acute renal failure (ARF)

Etiology:

Prerenal causes	***Renal causes***	***Post-renal causes***
_____ _____ _____ _____ _____ _____	*– ischemic acute tubular necrosis:* _____ *– nephrotoxic acute tubular necrosis:* _____ *– myorenal syndrome:* _____	_____ _____ _____ _____ _____ _____

Pathogenesis:

The main pathogenetic link: _____

Development stages and manifestations

Stage	Terms	Manifestations

Clinically ARF is manifested by

Manifestations	Mechanisms, characteristics
Water-electrolyte metabolism disorders	
Azotemia	
Acidosis	
Heart rhythm disorders	
Infectious complications	

Death in ARF most often occurs from _____

20. Fill in the Scheme.

Chronic renal failure (CRF)

Etiology *(most common causes):*_____

Pathogenesis *(basic mechanisms):*_____
_____

Stages:
- ***Preuremic:*** _____
- ***Uremia*** is _____

The basis of uremia — azotemia — is _____
_____

Types of azotemia:
- – _____
- – _____

Etiology of uremia: _____

Uremia pathogenesis: _____
_____

Clinical manifestations of uremia

Disorders	Characteristics
Of the central nervous system	
Dystrophic disorders	
Gastrointestinal disorders	
Cardiovascular disorders	
Respiratory system disorders	
Disorders in the blood system	
Bone disorders	
Metabolic disorders	
ABS violations	
Water-electrolyte metabolism disorders	

PART 2. PRACTICAL PART

Work 1. STUDY OF THE MECHANISMS OF DIURESIS DISTURBANCE IN EXPERIMENT

Under morphine-ether anesthesia, the dog's abdominal cavity is opened and the ureters are carefully isolated. In the upper third, we incise them and insert glass cannulas connected to two urine-diverting glass tubes into the proximal sections. A cannula with a rubber tube and a clamp is inserted into the distal segment of one of the ureters, the other distal segment is tied with a ligature. We put a ligature on the urethral orifice. We separate the common carotid, femoral arteries and jugular vein. A cannula connected to a manometer is inserted into the carotid artery to register the arterial blood pressure. A cannula with a rubber tube and a clamp is placed into the femoral artery. A cannula is inserted into the jugular vein, connected by a tube with a graduated cylinder, and the system is filled with saline. We bring ligatures under the highlighted sciatic nerve and one of the renal arteries and veins.

Experiment 1. Change in diuresis at the hydremia

We determine the initial level of diuresis by counting the number of drops of urine excreted in 3 minutes by each kidney. Into the jugular vein we inject 300–400 ml of saline (38–40 °C) and measure the diuresis again. At the same time, we register blood pressure.

Experiment 2. Changes in diuresis in hyperglycemia

Having determined the initial level of diuresis, a 40 % glucose solution (1 ml/kg of body weight) is injected into the jugular vein. After 5 minutes, we measure the urine output by the number of drops of urine.

Experiment 3. Changes in diuresis in acute blood loss.

After preliminary measurement of diuresis we release 50–100 ml of blood from the femoral artery. We determine the diuresis, register the arterial pressure.

Experiment 4. Hormonal influences on diuresis

A 0.1 % solution of adrenaline (0.02 ml/kg of body weight) is injected into the jugular vein. After 3–5 minutes, we measure the diuresis and register the arterial pressure.

Experiment 5. Reflex anuria during distension of the bladder

Through a cannula with a rubber tube and a clamp inserted into the distal part of one of the ureters, we use a syringe to stretch the walls of the bladder with air. We determine the diuresis before and after stretching the bladder.

Experiment 6. Reflex oliguria in painful stimulation of the sciatic nerve

We put electrodes on the separated sciatic nerve and irritate it with electrical impulses from the electrical stimulator. We study the change in diuresis, register blood pressure.

Experiment 7. Changes in diuresis in renal ischemia

We squeeze one of the renal arteries with a ligature for 1–2 minutes. After collecting a small amount of urine from the ischemic kidney, we put a test for the presence of protein in the urine. After that, 200 ml of saline (38–40 °C), tinted with 2 ml of 5 % indigo carmine solution, is injected into the jugular vein. We register the time of appearance of paint in urine, secreted by intact and ischemic kidneys.

The results of the experiments are presented in the Table.

Changes in diuresis and arterial blood pressure in a number of typical renal dysfunctions

№	Pathological influence	Diuresis, drops/min				BP, mmHg	
		Left kidney		Right kidney			
		Before	after	before	after	before	after
1	Hydremia	6	8	5	9	130/60	145/65
2	Hyperglycemia	5	9	6	10	125/65	130/75
3	Acute blood loss	6	2	6	2	130/60	95/75
4	Intravenous injection of 0.1 % epinephrine	5	2	5	3	120/65	150/80
5	Bladder distension	6	1	7	0	125/60	140/65
6	Sciatic nerve irritation	7	3	6	3	130/60	150/85
7	Ischemia of the kidney	6	2	5	6	125/60	140/80
Test for protein in urine from ischemic kidney							+++
Time of appearance of colored urine				intact kidney			2 min
				ischemic kidney			5 min

Answer the questions:

1. Explain the mechanism of diuresis change in hydremia, hyperglycemia. _____

_____

2. Explain the mechanism of diuresis change in acute blood loss, with intravenous injection of adrenaline. _____

_____

3. Explain the mechanism of anuria development during distension of the bladder. _____

_____

4. Explain the mechanism of development of pain oliguria. _____

_____

5. Explain the mechanism of diuresis change in renal ischemia. _____

_____

6. Why is there protein in the urine sample from the ischemic kidney? What type of proteinuria develops in this case? _____

_____

_____

7. Why is the time of appearance of paint in urine different for intact and ischemic kidney? _____

_____

Work 2. SOLVING SITUATIONAL TASKS

№ 1

Patient B., 10 years, complains of general weakness, headaches, reduced appetite, thirst. In the anamnesis — frequent quinsy. The clinical-laboratory examination revealed physical development retardation, pale, dry and deciduous integuments. BP — 130/90 mm Hg. The blood test showed a slightly expressed anemia. Urea of blood — 8.9 mmol/l. Diurnal urine — 6–8 times a day, night urination takes place. Urine is straw-colored, transparent, of an acid reaction, relative density fluctuation is 1.009–1.017, protein — 0.2 g/l. In the deposit: a small amount of epithelium, leukocytes — 0–2 in the field of vision, erythrocytes, hyalinous cylinders — single in the preparation. Glomerular filtration rate by insulin — 50 ml/min.

Questions:

1. Are there any signs of renal insufficiency in the patient?
2. Is the nocturia in the patient?
3. Have there been obtained any data suggesting pollakiuria?

№ 2

Patient P., 39 years, was admitted to the renal center in a severe precomatous condition: there was marked weakness, apathy, the pain in muscles and joints, itching, the ammoniac smell from the mouth. It is found out, that she has been suffering from renal diseases since 26 years. Objectively determined are: edemas on the feet, face and congested enlarged liver. BP — 190/120 mm Hg. Residual blood nitrogen — 148 mmol/l. Glomerular filtration by endogenous creatinine — 12.0 ml/min. Zimnitsky test: in diurnal diuresis of 360 ml the fluctuation of relative density is 1.003–1.007.

Questions:

1. What type of renal insufficiency and what stage are there in the patient?
2. Are there any signs of uremia in the patient?
3. Due to what substances has the residual blood nitrogen increased?

№ 3

In patient Z., 26 years, soon after she had suffered the flu, appeared aggravated edemas, olyguria, proteinuria, hematuria. The anamnesis made it possible to establish, that edemas, proteinuria, headache had been observed in the patient for several previous years.

The clinical-laboratory examination revealed: residual blood nitrogen — 57 mmol/l, urea — 16.6 mmol/l, plasma creatinine — 200 mcmol/l. Glomerular filtration by endogenous creatinine — 28 ml/min. Zimnitsky test: fluctuations of relative urine density — 1.003–1.008 in diurnal diuresis — 350 ml.

Questions:

1. What type and what stage of renal insufficiency are there in the patient?
2. How can you explain the decrease of glomerular filtration in this type of insufficiency?

№ 4

Patient F., 26 years, was delivered to hospital with profuse gastric bleeding in a severe condition. BP — 80/60 mm Hg. The patient excretes 160–180 ml of urine a day. Residual blood nitrogen — 62 mmol/l, blood urea — 36 mmol/l, creatinine — 260 mcmol/l.

Questions:

1. What type and what stage of renal insufficiency are there in the patient?
2. How can you explain the reduction of diuresis in the patient?

№ 5

After overcooling the patient, 24 years, acquired a sharp disease. Complains of general weakness, edema of the face, headache, breathlessness on the slightest exertion.

The urine analysis: a red-brown color, turbulent, acid reaction, protein — 1.2 g/l, glucose is absent. In the deposit: epithelium in a moderate amount, leukocytes — 3–8, erythrocytes — 20–40–100, cylinders hyalinous — 0–2 in the field of vision, urates, uric acid. Zimnitsky test: urine relative density — 1.012–1.031 in diurnal diuresis of 780 ml. Endogenous creatinine clearance — 56 ml/min.

Questions:

1. What pathological components of urine are revealed in the patient?
2. What features testify to the impairment of filtration ability of the kidneys?
3. What is a possible impairment mechanism of the kidneys filtration ability in this case?
4. Are there any features testifying to the impairment of the kidneys concentration ability?

№ 6

Patient K., 3 years, complains of early fatigue, constant feeling of hunger and thirst. No objective changes on the part of internal organs are present.

Zimnitsky test: relative density fluctuations of urine — 1.020–1.038 in diurnal diuresis of 3 l. Daily excretion of glucose with urine is 1.2 g, the degree of glucosuria being identical in diurnal and nocturnal portions. Blood glucose — 3 mmol/l. The Glycemic curve on sugar loading or introduction of insulin is normal. While examining a brother, 1.5 years, a permanent glucosuria is also revealed.

Question: What renal function is also impaired and what is a possible mechanism of glucosuria in this case?

Control questions

1. General etiology and pathogenesis of renal function disorders.
2. Mechanisms of glomerular filtration, proximal and distal reabsorption, tubular secretion and excretion disorders.
3. Clinical manifestations of renal dysfunction. Changes in diuresis and urine composition. Urinary syndrome: hematuria, hemoglobinuria, proteinuria, cylindruria, anuria, oliguria, polyuria, hypostenuria, isostenuria. The reasons and mechanisms of their development. Pathological constituents of urine of renal and extrarenal origin.

4. General symptoms in kidney disease.

5. The concept of glomerulopathies. Diffuse glomerulonephritis (etiology, pathogenesis and clinical manifestations).

6. Nephrotic syndrome.

7. Acute renal failure. Its types, etiology, pathogenesis, stages, clinical manifestations, outcomes. Changes in the volume and composition of blood and urine.

8. Chronic renal failure. Etiology, pathogenesis, stages, clinical manifestations. The concept of azotemia and uremia. The main clinical manifestations of uremia.

9. Causes and mechanisms of kidney stones and nephrolithiasis formation.

10. Changes in the tissues of the dentoalveolar system in chronic renal failure.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 13).

2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.

3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.

5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.

6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.

7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.

8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.

9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 14. FINAL LESSON ON THE COVERED TOPICS OF THE SECTION "PATHOPHYSIOLOGY OF ORGANS AND SYSTEMS OF THE ORGANISM". SOLVING SITUATIONAL PROBLEMS. COLLOQUIUM

Date: «____» _____ 20__

The purpose of the Lesson: to consolidate and evaluate the knowledge gained in lectures and practical classes on issues of specific pathophysiology, studied in lessons No. 8-13. (etiology, pathogenesis, pathogenesis of the main clinical manifestations). Colloquium.

Tasks: colloquium format — solving situational problems reflecting to the content of topics No. 8–13 with assignment of a grade.

Control questions: see lessons No 8–13 of this practical manual.

Teacher's signature: _____

LESSON 15. PATHOLOGICAL PHYSIOLOGY OF THE ENDOCRINE SYSTEM

Date: «____» _____ 20___

The purpose of the Lesson: to study general etiology and pathogenesis of endocrinopathies; typical impairment forms of some endocrine glands.

Tasks:

– To get acquainted with typical impairment forms of some endocrine glands on the basis of materials presented on slides, tables and figures on the topic.

– Solving the situational tasks.

– Control test.

PART 1. WORK WITH TRAINING MATERIALS

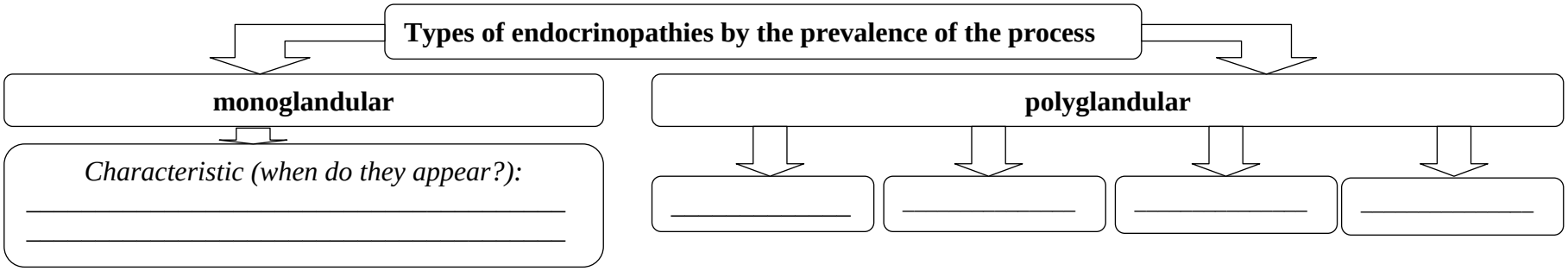
1. Give the definition of "endocrinopathy": _____
_____

2. Fill in the Table.

Types of endocrinopathies

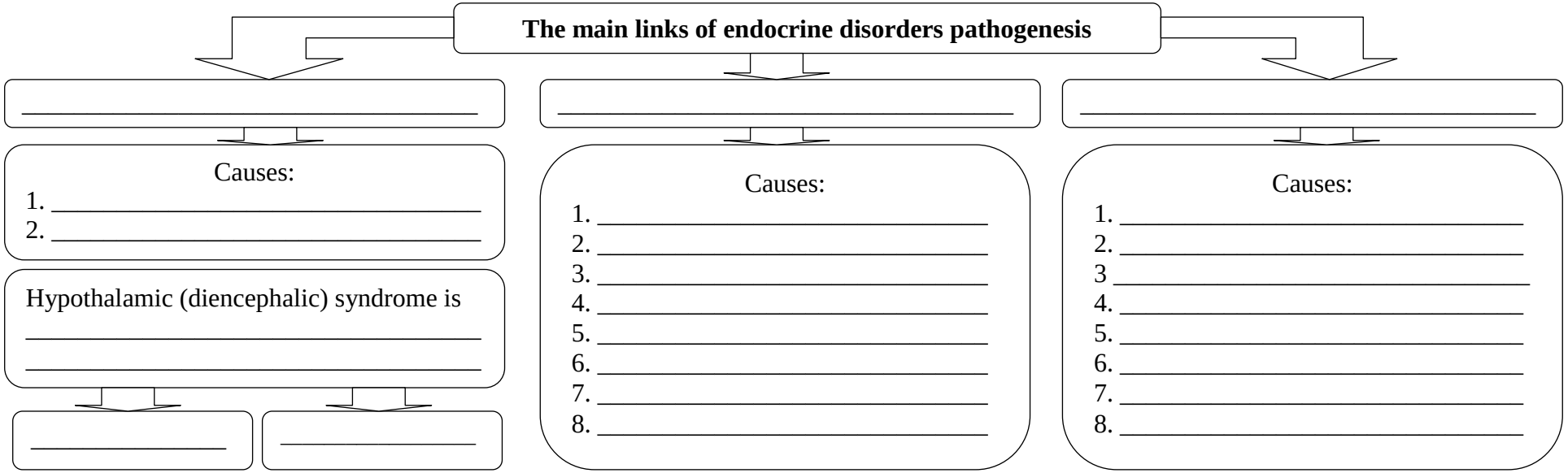
Classification principle	Characteristic
Gland incretory activity	1. _____ 2. _____ 3. _____
Process prevalence	1. _____ 2. _____
Gland lesion scale	1. _____ 2. _____ 3. _____
Changes in hormone production by the gland or peripheral effect violation	1. _____ 2. _____ 3. _____
Damage level	1. _____ 2. _____

3. Fill in the Scheme.



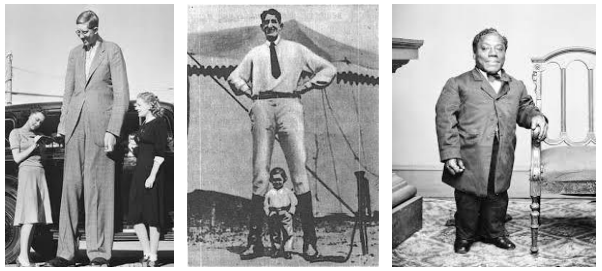
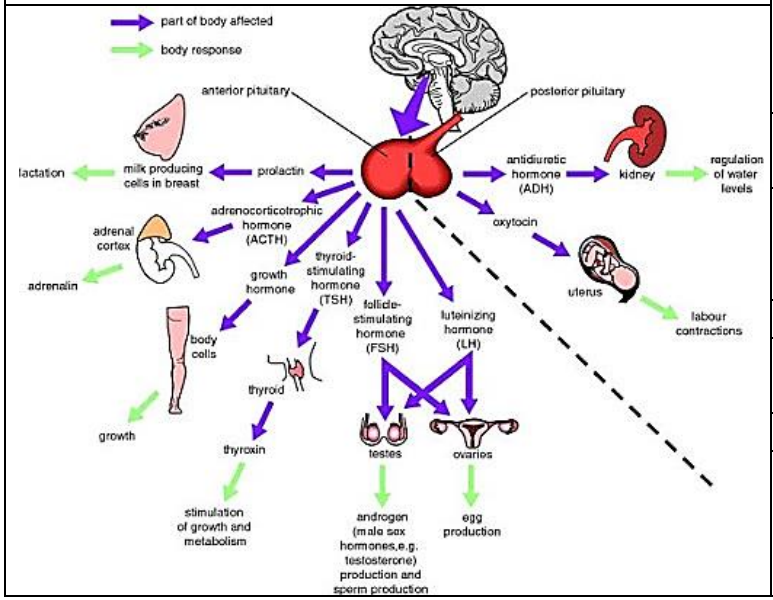
4. List the main etiological factors of endocrine disorders: _____

5. Fill in the Scheme.



6. Fill in the Table.

Violations of hypothalamic-pituitary system functions

<table>
<tr><th colspan="2">Hypofunction</th><th>Hypofunction</th></tr>
<tr><th>Total</th><th>Partial</th><th>Partial</th></tr>
<tr><td>Simmonds disease
(panhypopituitarism, pituitary cachexia)</td><td>Hypothalamic-pituitary dwarfism (nanism)</td><td>Gigantism</td></tr>
<tr><td>Deficit of _____</td><td>Deficit of_____</td><td>Hyperproduction of_____</td></tr>
<tr><td>Sheehan Syndrome</td><td>Hypothalamic-pituitary hypogonadism</td><td>Acromegaly</td></tr>
<tr><td>In whom does it develop?
_____
Predisposing factor is:
_____
_____
_____</td><td>Deficit of_____
Manifestations:
– in boys and youths _____
_____
– in adult men _____
_____
– in girls _____
_____</td><td>Hyperproduction of_____
  </td></tr>
<tr><td rowspan="3"> 
</td><td>Adiposogenital dystrophy (Frelich disease)</td><td>Pituitary (true) premature sexual development syndrome</td></tr>
<tr><td>Violations of hormonal homeostasis:
_____</td><td>Premature excessive secretion_____
_____</td></tr>
<tr><td>Neuroendocrine (pituitary) obesity
Deficit of_____</td><td>Itsenko-Cushing's Disease
Hyperproduction of_____</td></tr>
<tr><td></td><td>Hypothalamic-pituitary (hypocorticism)
Deficit of_____
_____</td><td>Hypothalamic-pituitary hyperthyroidism
Hyperproduction of_____
_____</td></tr>
</table>

7. Fill in the Table.

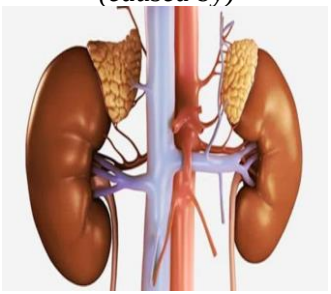
Disorders of the hypothalamic-neurohypophysial system

Characteristic	Diabetes insipidus	Inadequate ADH Secretion Syndrome (Parkhon Syndrome)
As a result of what does it develop? (deficiency / hyperproduction of ADH)	_____	_____
Pathogenesis	_____	_____
Manifestations	_____	_____

8. Fill in the Table.

Adrenal dysfunction

<table>
<tr><th colspan="2">Hypofunction</th><th colspan="2">Hyperfunction</th></tr>
<tr><td colspan="2">Acute adrenal insufficiency</td><td colspan="2">Hyperfunction of adrenal zona GLOMERULOSA</td></tr>
<tr><td colspan="2">Acute adrenal insufficiency is _____
_____
Causes:
1. _____
2. _____</td><td>Primary hyperaldosteronism (Conn Syndrome)
Causes:
_____
_____</td><td>Secondary hyperaldosteronism
Causes:
_____
_____</td></tr>
<tr><td colspan="2">Chronic adrenal cortex insufficiency</td><td colspan="2">Hyperfunction of adrenal zona FASCICULATA</td></tr>
<tr><td>Primary
_____
_____
(caused by)</td><td>Secondary
_____
_____
_____
(caused by)</td><td colspan="2">Itsenko-Cushing's Syndrome
Itsenko-Cushing's Syndrome is characterized by _____
_____</td></tr>
<tr><td colspan="2">Addison's Disease (Bronze Disease)</td><td colspan="2">Hyperfunction of adrenal zona RETICULARIS</td></tr>
<tr><td colspan="2">Causes:
1. Primary form _____
_____
2. Secondary form _____
_____
3. Iatrogenic form _____
_____</td><td colspan="2">Adrenogenital syndrome</td></tr>
<tr><td colspan="2"></td><td>Congenital
Forms:
1. _____
2. _____
3. _____</td><td>Acquired
_____
_____
_____</td></tr>
<tr><td colspan="2"></td><td colspan="2">Hyperfunction of the adrenal MEDULLA</td></tr>
<tr><td colspan="2"></td><td colspan="2">Causes: _____</td></tr>
</table>



9. Fill in the Scheme.

Thyroid Disorders

Hypothyroid states

Hypothyroidism is _____
_____

Types of hypothyroidism and the level of TTH:
1. _____
2. _____
3. _____
4. _____

Clinical forms:
– _____
– _____

Hyperthyroid states

_____

_____

_____

_____

_____

Type	Etiology	Level of TTH
Primary		
Secondary		
Tertiary		

10. Fill in the Scheme.

Parathyroid Disorders

Hypoparathyroid conditions

_____
_____
_____

_____
_____
_____

Hyperparathyroid conditions

_____
_____
_____

_____
_____
_____

_____
_____
_____

_____
_____
_____

11. Fill in the Scheme.

Pancreatic disorder

Diabetes mellitus

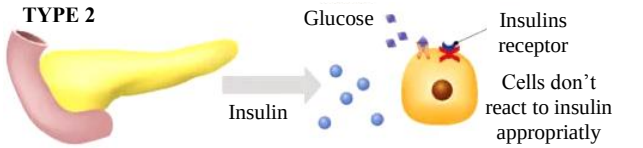
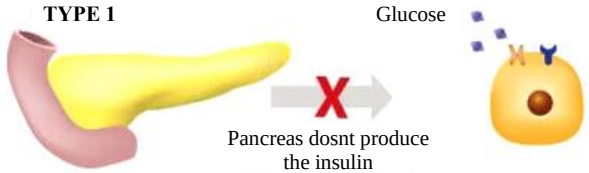
Primary

Secondary

_____ _____ _____

12. Fill in the Table.

Comparative characteristics of diabetes mellitus type 1 and 2

Characteristic	**1 type ( )**	**2 type ( )**
Prevalence		
Age		
Etiology	– _____ – _____ – _____ – _____ – _____	_____ _____ 
Predisposing factors	- _____ - _____ 	– _____ – _____ – _____ – _____ – _____ – _____
Pathogenesis *(what is in the basis)*	_____	_____
Clinical manifestations	_____ _____	_____ _____

13. Fill in the Table.

Complications of Diabetes

Acute complications	*Coma*	_____ _____ _____
Long-term complications	*Macroangiopathy*	_____ _____ _____ _____
	Microangiopathy	_____ _____ _____ _____
	Neuropathy	_____ _____ _____ _____

PART 2. PRACTICAL PART

Work 1. SOLVING SITUATIONAL TASKS

№ 1

Patient K., 37 years, was admitted to clinic with complaints of severe palpitation, weakness, sweating, irritability, anxiety, sleep impairment, decrease of workability. On examination of the patient the following was revealed: intense glitter of the eyes, exophthalm; tremor, subfebrilititis; an increase of T_3, T_4in the blood, total iodine and iodine bound with protein; the content of residual nitrogen in the urine is increased; basic metabolism is increased.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of this disease?

№ 2

Patient I., 27 years, complains of headache, thirst, frequent and profuse urination, diurnal diuresis — 6.5 l. On examination: the pulse — 72 beats/min, BP — 135/98 mm Hg. The following is revealed in the patient: the relative density of urine — 1.009; sugar in urine is absent. In the plasma: sodium — 140 mmol/l, potassium — 4.3 mmol/l.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of this disease?

№ 3

Patient M. was admitted to clinic with complaints of terminal paralyses, sensation of parasthesia, increased thirst. The examination of the patient revealed: BP — 160/110 mm Hg, hypokalemia, diurnal urine excretion — 6 l, the content of aldosterone in the urine is increased.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of this disease?
3. Why is this disease, unlike secondary hyperaldesteronism, characterized by polyuria and not by an edematous syndrome?

№ 4

Patient I., 41 years, was admitted to clinic. 2 years ago she suffered a severe flue. She complains of the absence of appetite, frequent headaches, listlessness, sleepiness. The examination of the patient revealed: sharp exhaustion, elderly air; BP — 100/80 mm Hg; a decreased content of follitropin, 17-keto-steroids in urine; tropin, somatotropin and corticotropin are absent in blood.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of this disease?

№ 5

Patient Z., 25 years, was admitted to clinic with complaints of growing whiskers and beard, impairment of a menstrual cycle. The examination revealed: the skin is thin and dry, expressed obesity of the trunk; BP — 150/95 mm Hg. The ultrasound examination findings: bilateral hypertrophy of adrenal glands. The level of ACTH if 1.8-fold increased.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of this disease?
3. List the main clinical forms of this disease.
4. What form of the disease is in this patient?

№ 6

Patient I., 26 years, was admitted to clinic in an unconscious state. According to her husband, after the flue the patient developed thirst, loss of weight, poor appetite, pains in the abdomen, weakness, head ache.

On the eve she developed a pain in the abdomen, recurrent vomiting, and confused consciousness. On examination: the consciousness is absent, respiration of Kussmaul, acetone smell from the mouth, signs of dehydration — the skin is dry, pale, cold, the tongue is coated with a brown film. The pulse — 120 beats/min; of slight filling and tension; BP — 95/60 mm Hg. The abdomen is soft, tenderless; the blood sugar level — 21 mmol/l, hyperketonemia, pH of the blood — 7.0.

Questions:

1. What disease can be suggested?
2. Characterize the state of the patient on admission.
3. What pathogenesis of hyperketonemia is in this pathology?
4. List the main pathogenesis components of a coma in this pathology?

№ 7

Patient K., 45 years, was admitted to clinic with complaints of general weakness, difficulty while walking, a creepy feeling on movement, pain in the abdomen, diarrhea, thinning, absence of appetite, nausea, pains in the back. On examination it was revealed: on X-ray film — diffuse osteoporosis; the level of inorganic phosphorus in the blood is reduced, the calcium content in the blood is increased; hematuria, albuminuria, hypercalciuria, hyperphosphaturia.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of the disease?

№ 8

In patient D., 43 years, the computer tomography revealed the enlargement of the hypophysis dimensions, on ultrasound examination — a bilateral enlargement of adrenal glands with hyperplasia of the cortical layer. The state on admission: obesity, «moon-like» face, gyrsutism, purple scars on the skin of the hips, BP — 190/95 mm Hg, blood glucose content — 18.9 mmol/l, glucozuria.

Questions:

1. The function of what endocrine gland is impaired in the patient?
2. What is the name of the disease?
3. The clinic pictures of patient U. and patient D. being the same, the ultrasound examination of patient U. revealed hyperplasia of one adrenal gland and a low level of ACTH in the blood. What is the name of the disease in patient U.?
4. Why was a low blood level of ACTH revealed in patient U.?

№ 9

Patient B., 36 years, was admitted to clinic in an unconscious state. When at home, the patient developed a psychic and motor excitation followed by a loss of consciousness. According to neighbors, the patient had been suffering from diabetes mellitus for many years, was treated with insulin and ate irregularly due to constant business trips.

On examination: consciousness is absent, the skin is wet, twitching of face muscles is noted, the pupils are dilated; respiration rate — 32 resp./min, pulse — 70 per min, rhythmic, BP — 130/80 mm Hg; blood glucose level — 2.45 mmol/l.

Question: What is the name of the state developed in the patient?

№ 10

A woman, 30 years, after a massive loss of blood during deliveries followed in 2 hours by hemotransfusion, developed a progressive thinning, atrophy of skeletal muscles, dystrophic changes of the skin, loss of hair and teeth, hypotrophy of internal organs, decrease of body temperature. On admission it was revealed: BP — 95/55 mm Hg; blood glucose level — 3.75 mmol/l.

Question: What pathology is characterized by specified manifestations?

№ 11

Patient A., 26 years, applied to the doctor with complaints of general weakness, headaches, changing of the appearance, enlargement of hands and feet. His shoe size enlarged from 39 to 42 within 2 years.

Objectively: the enlargement of the face features is marked (massive superciliary and cheek arches, a large nose, lips). A barrel-shaped chest, clavicles are thickened; hands and feet are enlarged in size. No essential changes on the part of internal organs are revealed. The pulse — 70 per min, BP — 150/90 mm Hg.

Questions:

1. On the excess or insufficiency of what hormone are similar changes marked?
2. What is this disease called, what is its etiology?

№ 12

Patient K., 14 years, was admitted with complaints of early fatigue, poor appetite, nausea, darkening of the skin.

The parents associate her disease with scarlet fever she has suffered half for a year ago, when early fatigue, listlessness, apathy, decrease of appetite appeared. She eats with pleasure only salty food. Lately the parents noted darkening of the skin integuments.

Objectively: Marked asthenia is noted. BP — 95/55 mm Hg. Muscular strength is attenuated. The skin is swarthy, of a golden-brown color, some pigmentation being more intense on the neck, face, hands. There is a dark fringe on the mucous membrane of the gums. No substantial deviations from the norm on the part of internal organs are present.

Questions:

1. What endocrine pathology is characterized by these symptoms?
2. Explain the development mechanism of hyperpigmentation of the skin.
3. Explain the development mechanism of arterial hypotension in this case.

4. How can you explain the preference of salty food by the child?
5. What diet should be recommended to the patient: rich in salts of sodium or potassium?

№ 13

Patient A., 37 years, was admitted to clinic with complaints of listlessness, sleepiness, depressed mood, poor memory, frequent headaches, constipation, impairment of the menstrual cycle. For the last half a year she gained much weight despite poor appetite. She constantly feels cold. The examination revealed: the patient with signs of moderate obesity, the face is puffy, amimic, the lids are edematous, movements are flaccid. The pulse — 54 beats per min. The body temperature — 35.4 ºC. The basic metabolism is reduced by 27 %. The blood cholesterol content — 6.8 mmol/l; glucose level — 3.9 mmol/l.

Question: What pathology of the endocrine system can be suggested?

№ 14

Patient K., 48 years has been suffering from bronchial asthma for 30 years. The complex treatment of asthma used preparations of glucocorticoids, further on the patient took them independently for several years. During this time obesity developed. BP became elevated up to 190/110 mm Hg. Some days after he discontinued the preparation by himself there appeared sharp weakness, his appetite disappeared, diarrhea appeared. Due to the presence of these symptoms he was delivered to hospital.

On examination: the patient of middle height, obesity with predominant fat deposit in the area of the face and abdomen, the extremities being thin. There are purple strips of tension on the abdomen, much acne on the face and back. BP — 70/50 mm Hg, blood glucose level — 2.7 mmol/l.

Questions:

1. What pathology of the endocrine system can be suggested?
2. Why did hypotension and hypoglycemia develop after discontinuation of glucocorticoids?

№ 15

Patient V., 39 years, was hospitalized to the neurosurgical department by the first aid after he fell flat on his back trying to get up at night.

On examination: the patient is not contacted, profuse cold perspiration, clonic spasms, asymmetry of the face, tendon reflexes are increased, Babinski symptom is positive. In the reception ward a subarachnoidal hemorrhage was suggested. The severity of the patient's condition increased: convulsions, hyperreflexia started to come into ascending paresis of muscles, areflexia, the respiration rhythm was impaired. To prevent the involvement of the brain stem the patient was perfused 40 ml of 10 % solution of glucose and started a droplet injection of mannitol, giving an unexpectedly positive effect that disappeared and recovered on additional injection of glucose. After a massive infusion of glucose, the patient recovered his consciousness. According to his words, he was having such attacks for the last year, they occurred after physical exertion or emotional stresses, the severity of stresses becoming gradually worse. At first they showed as shivering, weakness, dizziness, sweating and feeling of hunger; during the last 2 months the attacks were accompanied by a short-term loss of consciousness.

Question: What is your suggested diagnosis?

№ 16

Patient Sh., 52 years, soon after strumectomy, felt muscular spasms of hands, numbness of the face. The spasms recurred 2-3 times during a day.

On examination: the general condition is satisfactory. The pulse — 76 per min, BP — 110/70 mm Hg. No pathologic changes in the internal organs are revealed. Positive symptoms of Khvosteck and Trusso.

Question: What complication occurred after strumectomy?

№ 17

What symptoms are characteristic of diabetic ketoacidosis (A) and hypoglycemic state (B):

1) pain in the abdomen;
2) nausea;
3) vomiting;
4) feeling of hunger;
5) absence of appetite;
6) disorientation;
7) anxiety;
8) shivering;
9) apathy;
10) indifference;
11) dryness of the skin;
12) wetness of the skin;
13) usual respiration;
14) deep respiration;
15) the skin and muscles are flabby;
16) pupils are narrowed;
17) pupils are dilated;
18) tachycardia;
19) arterial hypotension;
20) hypo-, areflexia;
21) hyperketonemia;
22) hyperglycemia;
23) acetonuria;
24) hypoglycemia;
25) alkaline blood reservoir is normal;
26) alkaline blood reservoir is decreased.

Control questions

1. Etiology and pathogenesis of endocrinopathies. Principles of their classification. Main principles of treatment.
2. The notion of intra-uterine endocrinopathy. Peculiarities of functional integration of homologous endocrine organs of the maternal organism and the fetus.
3. Total (Simmonds disease) and partial hypofunction of adenohypophysis (hypophyseal nannism, infantilism), clinical manifestations.
4. Hyperfunction of the adenohypophysis: hypophyseal giantism, acromegally, disease of Itsenko–Cushing, clinical manifestations.
5. The pathology of a posterior lobe of the hypophysis: signs of hypo-and hypersecretions of vasopressin.
6. The thyroid gland pathology, its forms, pathogenesis, clinical manifestations.
7. The parathyroid glands pathology, its forms, pathogenesis, clinical manifestations.
8. Hypofunction of the cortical substance of adrenal glands. Acute and chronic insufficiency of adrenal glands, etiology, pathogenesis, clinical manifestations.
9. Hyper- and dysfunction of the cortical and medulla substance of adrenal glands. Syndrome of Itsenko-Cushing, primary and secondary hyperaldosteronism, adreno-genital syndrome, pheochromocytoma, clinical manifestations.
10. Diabetes of the Ist and IInd type, their etiology, pathogenesis, clinical manifestations. Mechanisms of hyperglycemia and glycozuria. Manifestations of the impairment of target organs in diabetes.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 15).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

LESSON 16. PATHOLOGICAL PHYSIOLOGY OF THE NERVOUS SYSTEM

Date: «____» _____ 20__

The purpose of the Lesson: to study the causes, mechanisms and main clinical manifestations of disorders of sensory and locomotor functions of the body in case of damage to various parts of the nervous system.

Tasks:

– To study the causes, development mechanisms and clinical manifestations of disorders of locomotor functions in case of damage to the pyramidal and extrapyramidal systems based on the materials presented in educational videos.

– To study the manifestations of disturbances in the sensory and locomotor functions of the body in case of damage to the anterior and posterior roots of the spinal cord in the experiment.

– Solving the situational tasks.

– Control test.

PART 1. WORKING WITH THE TRAINING MATERIALS

1. Fill in the scheme:

Typical forms of disorders in the nervous system

_____ _____ _____

_____ _____ _____

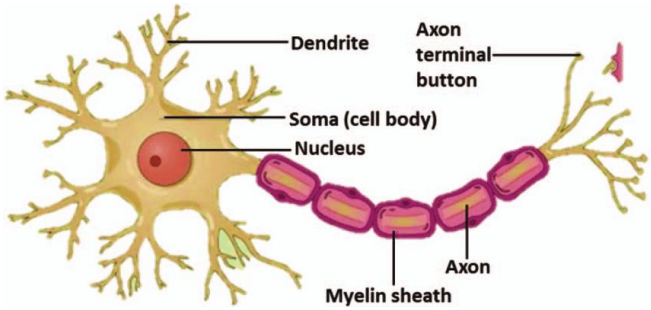
_____ _____ _____

_____

_____

_____

_____



2. Fill in the Table.

Types of neurogenic sensitivity disorders

Depending on the level of damage	▪ _____ ▪ _____ ▪ _____
Depending on the disturbance in the perception of irritant intensity	▪ complete loss of sensitivity — _____ ▪ decrease in sensitivity — _____ ▪ increase in sensitivity — _____
Violation of the adequacy of sensation (dysesthesia)	▪ perversion of sensitivity — _____ ▪ sensation of the action of many stimuli when exposed to one factor — _____ _____ ▪ excessive pain — _____ the appearance of several sensations when one sensory organ is irritated, as a result of irradiation of excitation from the nervous structures of one sensory system to another _____ ▪ perception of non-painful effects as pain — _____
By the volume of sensitivity loss	▪ _____ ▪ _____
Depending on the nature and type of the lost sensitivity	▪ _____ ▪ _____ ▪ _____ ▪ _____ ▪ _____ ▪ _____ ▪ _____ ▪ _____

3. Give the definition of “phase states”:_____
_____
_____

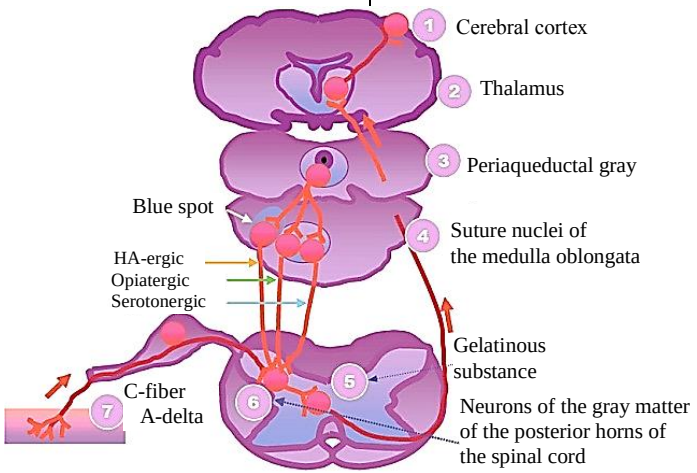
4. Fill in the Table.

Phase states of the nervous system

Phase state	Characteristic
equalizing	
	little or no reaction to strong stimuli; maintaining or increasing reaction to mild stimuli
narcotic	
inhibitory	
	negative reactions develop in response to positive stimuli

5. Fill in the Table.

Nociceptive and antinociceptive systems

Nociceptive system		Antinociceptive system	
Levels of formation of pain feelings	**Are represented by**	**Neurogenic mechanisms**	**Humoral mechanisms (systems)**
Receptor apparatus	▪ _____ ▪ _____ ▪ _____	_____	▪ _____ ▪ _____ ▪ _____ ▪ _____
Conductor apparatus	_____		
Central apparatus	_____		

6. Fill in the Table.

Comparative characteristics of epicritic and protopathic pain

Properties	Epicritical	Protopathic
Synonyms		
Type of irritant by strength		
Source of irritant		
Pain character according to subjective sensation		
Duration		
Localization accuracy		
Development of adaptation		

7. Fill in the Table.

Classification of hypokinesias

By severity	▪ _____ ▪ _____
By prevalence	▪ paralysis or paresis of one limb — _____ ▪ paralysis or paresis of both arms or both legs — _____ ▪ paralysis or paresis of the left or right side of the body — _____ ▪ paralysis or paresis of three limbs — _____ ▪ paralysis or paresis of the arms and legs — _____
By changes in muscle tone	▪ _____ ▪ _____ ▪ _____
By predominantly affected nerve structures	▪ _____ ▪ _____ ▪ _____ ▪ _____

8. Fill in the Table.

Comparative characteristics of central and peripheral paralysis

Characteristic	Central	Peripheral
Localization of the damage	_____ _____	_____ _____
Active movements		
Muscle tone		
Reflexes	_____	_____
Pathological reflexes	_____	_____
Synkinesia		
Amyotrophy		

9. Fill in the Table.

Classification of hyperkinesias

By localization of the damaged structures	▪ _____ ▪ _____ ▪ _____
By the prevalence of the process	▪ _____ ▪ _____

10. Fill in the Table.

Types of seizures

Characteristic	Tonic	Clonic
The essence	_____ _____	_____ _____
The functional basis of which hyperkinesis	_____	_____

11. Fill in the Table.

Types of tremor

Characteristic	**Parkinsonian**	**Intentional**
Causes	_____ _____ _____	_____ _____ _____
When observed (at rest / during voluntary movement)	_____ _____ _____	_____ _____ _____

PART 2. PRACTICAL PART

Work 1. STUDY OF ETIOLOGY, PATHOGENESIS AND CLINICAL MANIFESTATIONS OF DISORDERS OF THE NERVOUS SYSTEM FUNCTIONS BASED ON MATERIALS OF EDUCATIONAL VIDEOS

a) mechanisms and clinical forms of spastic and flaccid paralysis;
b) pathogenetic treatment of some hereditary extrapyramidal diseases.

Make conclusions based on the materials of the videos by answering the questions:

1. What is the manifestation of the motor function disorder with damage to the nervous system? _____
_____

2. Damage to which parts (structures) of the nervous system leads to central (spastic) and peripheral (flaccid) paralysis? _____
_____

3. How does muscle tone, tendon and periosteal reflexes, the state of muscle trophism change in spastic and flaccid paralysis? _____
_____

4. Why do tendon and periosteal reflexes increase in spastic paralysis, but they are absent in flaccid paralysis? _____
_____

5. What type of paralysis is characterized by the presence of pathological reflexes? _____
_____

Conclusions (*determine the symptom complex typical for spastic (central) and flaccid (peripheral) paralysis*): _____
_____
_____
_____

Work 2. THE STUDY OF MOTOR REACTION DISORDERS DURING THE INTERCUT OF THE ANTERIOR AND POSTERIOR SPINAL ROOTS IN A FROG

We fix the frog on the board with its back up. We cut the skin of the back from the fourth vertebra to the caudal part and deepen the incision to the spinous processes of the vertebrae. We separate the muscles adjacent to them so that the vertebral arches are exposed. The arches are removed with scissors from the third to the fifth vertebrae. Now we can see the spinal cord with its membranes, which we carefully cut and reveal the roots of the spinal cord. Cut the back (sensitive) roots on the right and the anterior (motor) roots on the left.

If you pinch the right hind foot, then no reaction is found (Fig. 1). If you pinch the hind foot on the side with the anterior roots cut (Fig. 2), then there will be no reaction due to the shutdown of the motor roots, but contraction of the right foot is detected.

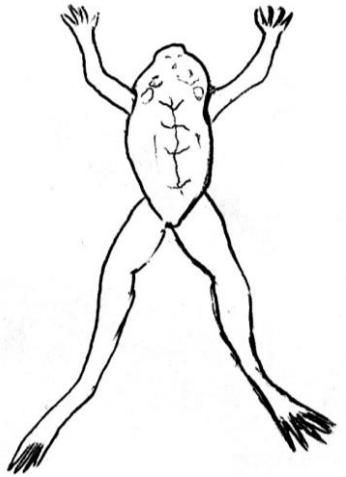


Fig. 1. Lack of response to irritation

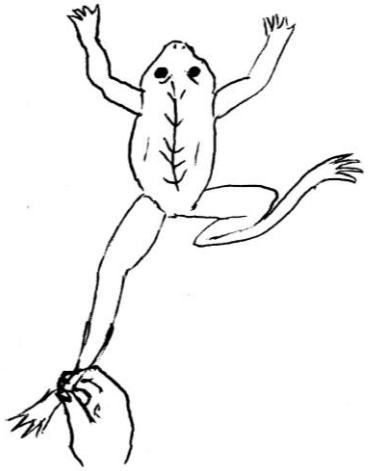


Fig. 2. Contraction of the right leg

Answer the questions:

1. What types of sensitivity are impaired during transection of the posterior roots of the spinal cord, and why did the frog have a lack of a motor response to irritation of this leg (Fig. 1)?_____
_____

2. Why does a frog with cut anterior roots of the spinal cord have no motor response in response to the irritation of the leg on this side, but there is a motor response of the leg on the side where the posterior roots of the spinal cord are cut (Fig. 2)? _____
_____
_____

3. What type of paralysis is observed when the anterior roots of the spinal cord are transected? _____
_____

Work 3. SOLVING SITUATIONAL TASKS

№ 1

Patient E, 28 years, was admitted to the neurological clinic with complaints for slight (fine) tremor of extremities and the head at rest. Mimics and jests are absent. She stares at one point. Voluntary movements are made slowly. The speech fades away and turns into unclear bubbling. The patient moves as a mannequin, making small steps without the appropriate movements of the trunk and arms, is depressed, becomes tired quickly. When walking, the tremor is considerably decreased unless it disappears.

Questions:

1. What syndrome (disease) developed in the patient?
2. Explain the underlying mechanisms.
3. Name the type of tremor.

№ 2

There are observed quick arrhythmic involuntary movements of extremities and the trunk in patient D., 7 years. He grimaces, smacking his lips, often shows the tongue. The muscular tone of extremities is decreased.

Questions:

1. What is the described syndrome called?
2. What brain structures are impaired?

№ 3

In patient K., 53 years, active movements of the left leg are absent; the tone of the leg extensors is increased. The knee and ankle reflexes on the left are higher than those on the right, abdominal reflexes on the right are absent. Pathological Babinski's reflex is produced on the left. From the level of nipples downwards the sensitivity to pain and temperature is lost, on the left is lost a tactile, muscular-articular and vibration sensitivity.

Questions:

1. With the impairment of what structures of the nervous system is the described semiology associated?
2. What is the name of such a syndrome?
3. Explain the pathogenesis of the above symptoms.

№ 4

Patient L., 62 years, complains of extremely early fatigue (asthenia). On examination there was revealed scanned speech, horizontal nystagmus, staggering ("drunken") gait, instability in Romberg's test. Co-adjoining movements (asynergy) are absent, the muscles of extremities are hypotonic. A constant tremor and swaying of the trunk and extremities are noted (astasia). The coordination of movements is impaired (ataxia).

Question: Prove your suggested diagnosis.

№ 5

Patient K., treated in the neurological clinic, is noted to have lost the pain and temperature sensitivity in the lower part of the body and the muscular-articular feeling in the right leg.

Question: What can be said regarding the syndrome and mechanism of its origin?

№ 6

A girl, 10 years, applied to the doctor with complaints of a constant involuntary twitching of the right eye lid.

Questions:

1. Name the type of pathology.
2. What are the possible mechanisms of its origin?

№ 7

A patient of 55 years applied to the doctor with complaints of restriction of active movements in the left arm and leg. On examination of the patient the restriction of voluntary movements in the specified extremities is marked. The muscular tone and periosteal reflexes of the specified extremities are increased.

Questions:

1. Name the impairment form of the movement function.
2. Explain the mechanism of muscular tone elevation and hyperreflexia of impaired extremities.

№ 8

A patient of 60 years applied to the doctor with complaints of rigidity of movements, a mask-like face, amimicity, finger tremor as "rolling pills". The tremor disappears on performing movements.

Questions:

1. Name the type of pathology.
2. What are the possible mechanisms of its origin?

№ 9

A patient of 50 years applied to the doctor with complaints of restriction of voluntary movements in the left arm and leg. A year before he had suffered cerebral hemorrhage. On examination his left arm is flexed and abducted to the trunk, his left leg is sharply straightened. The muscular tone and periosteal reflexes of the specified extremities are increased. There are pathologic reflexes.

Questions:

1. What can you say regarding the available impairments?
2. What is the mechanism of their origin?

№ 10

In a girl of 12 years, after she had suffered an infectious disease, appeared clonic spasms of various intensity that constantly change the place of their localization. As a result of alternately twitching movements of the arms, head and trunk the adaptive reactions of the organism are sharply restricted.

Question: Name the type of hyperkinesis and specify the possible mechanisms of its origin.

№ 11

After the impairment of cerebral circulation in patient T., 56 years, he developed a spastic muscular contraction of the right arm and right leg. The muscular tone of these extremities is increased. Voluntary movements of these extremities are impossible, and tendon and periosteal reflexes are increased. Muscular atrophy is not noted.

Questions:

1. Specify the form of akinesia in this patient.
2. Explain the mechanism of muscular tone elevation, tendon and periosteal reflexes.

№ 12

A patient of 58 years applied to the doctor complaining that some tremor occurred on brining a glass of water to the mouth, on an attempt to take some thing from the table or shelf; tremor swings increasing on approaching to the target.

Questions:

1. Name the type of hyperkinesis and possible mechanisms of its origin.
2. What is the difference between manifestations of intentional tremor and Parkinsonial one?

№ 13

A patient of 30 years applied to the doctor complaining that after a trauma of the back surface of the right hip, active movements in this extremity became sharply restricted, muscular atrophy of the leg appeared. On examination, alongside with muscular atrophy, the absence of the Achilles tendon reflex is noted.

Question: Name the impairment form of the motor function of the nervous system and specify its possible mechanism.

№ 14

In the patient treated in the neurological clinic occurred a spasm of a 3-minute duration with the first phase of tonic generalized and second phase of clonic generalized spasms.

Question: Name the form of spasms.

№ 15

On admission to clinic patient Ch., 23 years, a post-graduate of the university, presented multiple complaints of: bad sleep, irritability, tearfulness, absence of appetite, unstable mood, headaches.

Objectively: the somatic status is without deviations from the norm. The anamnesis revealed that specified on admission phenomena had been developing for the last 10 months. During this period the patient suffered a rather difficult situation: a failed marriage and the necessity to leave for a place of appointment (she didn't want to do something because she was not sure in her abilities as well as she was afraid to lose the connection with her husband). While staying in the department she constantly made faults with the personnel, demanded special attention. After every meal vomiting occurred (often in the presence of patients and personnel).

Questions:

1. What is the origin of a symptomatic complex developing in the patient?
2. In what type of HNA do similar impairments develop more often?

№ 16

Patient C., 42 years, was brought up in the family, the main task of which was to achieve a success in life and position in the society. He studied with great difficulty. Under the demand of his parents he tried to be a top schoolboy paying much effort. After school (by wish of his parents) he entered the institute. The studies at the institute demanded even more efforts. He studied much, sometimes at night. On graduation from the institute he started working at a plant as a shift master. As soon as the post of the chief of the shop became vacant, he applied for it, though the profile of the shop did not correspond to his acquired specialty. Besides, by that time his management experience was not sufficient. Having become the chief of the shop he faced great problems. The shop under his management stopped performing the production tasks, it resulted in reprimands and critics on the part of the administration and the collective of the shop.

It is in this period that he developed head aches, painful sensations in the heart area, sleeplessness, irritability, early fatigue, his workability sharply decreased.

Objectively: BP — 170/90 mm Hg, pulse — 90 beats per minute, Focal neurological symptoms were not revealed.

Questions:

1. What was the cause of appearing pains in the heart area, tachycardia and arterial hypertension?
2. What form of nervous system pathology developed in this patient?

Control questions

1. General etiology and pathogenesis of nervous system disorders.
2. Protective, restorative and compensatory processes in the nervous system. The concept of "protective inhibition", its role in pathology.
3. Neurogenic disorders of sensitivity, their types, mechanisms and clinical manifestations.
4. Brown-Séquard syndrome. The mechanism of origin and its manifestation.
5. Neurogenic disorders of locomotor function. Hypokinetic states: paresis and paralysis, their mechanisms and characteristics.
6. Hyperkinesia. Definition. Types of hyperkinesis.
7. Convulsive states, types of seizures and their pathogenesis.
8. Dysfunctions of the autonomic nervous system, their types and mechanisms.
9. Disorders of higher nervous activity, neuroses. The value of the types of higher nervous activity in the development of neuroses. Causes of neuroses, their characteristics, principles of therapy.
10. Experimental models of neuroses (I. P. Pavlov, M. K. Petrova). The principles of neurosis therapy.
11. Pain. Definition, biological significance. Pain syndrome pathogenesis. Antinociceptive system and its characteristics.
12. The concept of nervous trophism and neurogenic dystrophies. The standard form of neurogenic dystrophies (A. D. Speransky). The role of neurogenic dystrophies in the pathogenesis of diseases.
13. Modern ideas about the mechanisms of the trophic influence of the nervous system on tissues and organs and the development of neurogenic dystrophies. The concept of trophogens and pathotrophogens.

RECOMMENDED LITERATURE

Basic

1. EAMC (http://etest.bsmu.by/ → Courses → For Students with Training in English → General Medicine → Pathological Physiology → Lesson 16).
2. *Pathophysiology* : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. V. Krishtal [et al.] ; ed. by N. V. Krishtal, V. A. Mikhnev. Kyiv : AUS Medicine Publishing, 2017. 656 p.
3. *Kumar, V.* Robbins Basic Pathlogy / V. Kumar, A. K. Abbas, J. C. Aster. 10th ed. Canada : Elsevier, 2018. 952 p.

Additional

4. *General* and clinical pathophysiology : textbook for students of higher educational institutions, of IV th level of accreditation / A. V. Kubyshkin [et al.] ; ed. by A. V. Kubyshkin, A. I. Gozhenko. 2nd ed. Vinnytsya : Nova Knyha Publishers, 2016. 656 p.
5. *Litvitsky, P. F.* Pathophysiology : textbook for students / P. F. Litvitsky, S. V. Pirozhkov, E. B. Tezikov. Moscow : GEOTAR-Media, 2016. 432 p.
6. *Simeonova, N. K.* Pathophysiology : textbook for students of higher medical educational institutions of the III–IV accreditation levels / N. K. Simeonova ; ed. by V. A. Mikhnev. 2nd ed. Kyiv : AUS Medicine Publishing, 2015. 544 p.
7. *Gozhenko, A. I.* Pathophysiology / A. I. Gozhenko, I. P. Gurkalova. Odessa : The Odessa State Medical University, 2005. 325 p.
8. *Mufson, M. A.* Pathophysiology : PreTest Self-Assessment & Review / M. A. Mufson, C. A. Heck, S. M. Nesler. 3th ed. Chicago : Medical Publishing Division, 2002. 268 p.
9. *McPhee, S. J.* Pathophysiology of Disease : An Introduction to Clinical Medicine [Electronic resource] / S. J. McPhee. 8nd ed. NY : McGraw-Hill Education, 2019.

Teacher's signature: _____

PROTECTION OF ABSTRACT

Date: «____» _____ 20___

The purpose of the lesson: to depen and systematize the theoretical knowledge gained in the "Pathological physiology" while preparing the abstract. Writing the abstract allows the students to improvetheir ability to search the necessary information and to be well orientated in the modern scientific literature.

A credit lesson is carried out in the form ***of defense the abstract*** by student.

Abstract writing

The structure of the abstract includes:

• **Title page** (a sample title page is presented in the appendix);

• **A table of contents** indicating the work plan, which should contain an introduction, the name of the main sections (subsections) of the work, a conclusion, a list of used literature;

• **Introduction** which defines the purpose and objectives of the study, its relevance, theoretical and practical significance, the basic questions studied, as well as not fully disclosed questions on the topic under study, the object and subject of the study are determined, and statistical methods, if applicable, are indicated;

• **The main text** which reveals the main content of the plan. The text should contain at least two sections (subsections are allowed);

• **Conclusion** where evidence is formed on the basis of the content of the material studied by the author;

• **List of used literature and other sources**. Literature is drawn up in accordance with the requirements of GOST 7.1-2003 "Bibliographic record. Bibliographic description. General requirements and compilation rules". References to the literature are printed inside the article in square brackets after the quotation according to the alphabetical order declared in the list of references. The number of references in the work should be at least ten.

The text of the work should be printed on one side of a white sheet of A4 paper (orientation — portrait) at 1.5 intervals, in Times New Roman font, size 14 (cover sheet — 16 font). Each page of text and applications should have margins: left — 30 mm, right — 10 mm, top and bottom 15 mm. The first line indent (paragraph indent) is 1.25 cm. Do not do hyphenation. All pages exept the title one are numbered at the bottom center. Abstract volume: not less than 15 pages. **The student's signature is placed** on the last page of the abstract.

When writing the abstact **copyright requirements must be followed**. A plagiarism check report must be attached to the abstract. It may be done of the following sites: https://www.text.ru or https://www.antiplagiat.ru (the uniqueness of the work (introduction, main part and conclusion) should be at least 60 %).

The abstract should be drawn up according to the requirements.

The abstract is protected by a short (6–8 min) presentation to the audience on the topic of work and answers to questions. When speaking, the use of multimedia devices (projector, computer, TV) is allowed.

Early defense of the abstract is possible at one of the practical classes during the semester, if the work is performed in accordance with all the requirements presented and the content of the abstract corresponds to the topic of the practical class.

Selection of the topic of the abstract

The topics of the abstract are determined by the requirements of the curriculum, the program for the study of the discipline "Pathological physiology" at the Belarusian State Medical University, they cover sections intended for self-study. The student may choose the topic of the abstract by himself agreeing it with the teacher.

Topic of abstracts

1. Impaired absorption of food carbohydrates, disaccharidase deficiency. Violation of the synthesis, deposition and splitting of glycogen, the transport of carbohydrates in the cell and their assimilation. Galactosemia. Fructosuria. Pentosuria. Glycogenosis.
2. Hypoglycemic conditions, their types and mechanisms. Pathogenesis of hypoglycemic coma and its manifestations.
3. Hyperglycemic conditions: classification, etiology. Pathogenic consequences of acute and chronic hyperglycemia.
4. Hyperglycemic coma. The role of protein glycosylation in pathology.
5. Experimental models of diabetes mellitus.
6. Etiology and pathogenesis of type 1 diabetes mellitus. The role of viruses and autoimmune processes in the damage of beta cells.
7. Etiology and pathogenesis of type 2 diabetes mellitus. Mechanisms of decreased sensitivity of B cells to glucose. Insulin resistance, its types and mechanisms.
8. The role of heredity in the development of type 2 diabetes mellitus. The role of destruction of heterocellular zones and disturbance of paracrine influences in pancreatic islets.
9. Absolute and relative insulin deficiency in diabetes mellitus. Pathogenesis of secondary diabetes mellitus in endocrine diseases.
10. Pathogenesis of ketoacidosis, ketoacidotic coma, hyperosmolar coma. Hypoglycemic coma.
11. Diabetogens: types, pathogenic effect. Immunopathological mechanisms of type I insulin-dependent diabetes mellitus.
12. Metabolic disorders in diabetes mellitus: pathogenesis and manifestations of disorders of protein, lipid, water-electrolyte metabolism in diabetes mellitus.
13. Pathogenesis of polyuria, cachexia, obesity, secondary immunodeficiency in various forms of diabetes mellitus.
14. Chronic complications of diabetes mellitus. Pathogenesis and manifestations of diabetic microangiopathy and macroangiopathy.
15. Pathophysiology of appetite disorders. Neurogenic anorexia and bulimia and their mechanisms.
16. Acute renal failure. Etiology, pathogenesis, main manifestations, stages.
17. Chronic renal failure. Etiology, pathogenesis, stages, main manifestations.
18. Metabolic disorders in chronic renal failure. Uremia.
19. Diffuse glomerulonephritis. Etiology and pathogenesis, main manifestations. Pathological changes in the urine with glomerulonephritis.
20. Comparative characteristics of nephrotic and nephritic syndromes.
21. Etiology, pathogenesis, main manifestations of nephrotic syndrome, the role of immunopathological mechanisms.

22. Pathogenesis of the most common signs of digestive disorders (pain, dysphagia, belching, heartburn, vomiting, diarrhea).
23. Disorders of digestion in the mouth and esophagus. The role of nervous mechanisms in the pathogenesis of diseases of the digestive system.
24. Disorders of digestion in the stomach. Disorders of gastric secretion and motility.
25. Etiology and pathogenesis of gastritis and peptic ulcer disease. Role of infection, autoimmune mechanisms, stress and other risk factors.
26. Disorders of digestion in the duodenum. Duodenal insufficiency syndrome, etiology, pathogenesis, experimental modeling.
27. Pancreatitis, etiology, pathogenesis, mechanisms of manifestation. Violations of the exocrine function of the pancreas.
28. Intestinal obstruction. Types. Pathogenesis.
29. Dysbacteriosis. Causes and consequences of dysbiosis.
30. Consequences of removing various parts of the gastrointestinal tract; pathophysiology of the operated stomach. Compensatory and restorative processes in the digestive system.
31. Malabsorption. Disorders of cavity and parietal digestion in the small intestine.
32. Absorption, their mechanisms. Intestinal enzymopathies. Dysbiosis.
33. Features of digestive disorders in children.
34. Liver failure. Types. The causes. Violations of the basic functions of the liver in acute liver failure.
35. Hepatic coma: etiology and pathogenesis.
36. Disorders of protein, lipid, carbohydrate, water-salt metabolism, acid-base balance, metabolism of vitamins and microelements in chronic liver failure.
37. Pathophysiological bases of differential diagnosis of jaundice.
38. Peculiarities of etiology, pathogenesis and manifestations of jaundice in newborns and premature babies.
39. Kernicterus and its pathogenesis.
40. Pathogenesis and manifestations of the main syndromes in acute viral hepatitis (cytolytic, mesenchymal-inflammatory, icteric, cholestatic, etc.). The role of immunopathological factors in hepatitis.
41. Characteristics of the Crigler–Nayard, Gilbert, Dabin–Johnson syndromes.
42. Liver cirrhosis: etiology, pathogenesis, types, outcomes.
43. Portal hypertension. Etiology, pathogenesis of manifestations.
44. Features of the etiology and pathogenesis of cirrhosis in children.
45. Non-alcoholic fatty liver disease.
46. Respiratory failure: types, etiology, respiratory parameters. Mechanisms of ventilation, diffusion and perfusion disorders.
47. Compensatory and adaptive processes in the external respiration system in case of damage to its individual links.
48. Pathological breathing and its difference from shortness of breath. Types of pathological respiration, their pathogenesis.
49. Ventilation respiratory failure of the obstructive type: causes of development, violation of the gas composition of the blood.
50. Chronic obstructive pulmonary disease, types. Causes and mechanisms of development of obstructive syndrome.
51. Ventilation respiratory failure of the restrictive type, causes of development, violation of the gas composition of the blood.

52. Disorders of the metabolic functions of the lungs. Violation of the surfactant system.

53. Asphyxia: etiology and pathogenesis, blood gas disturbances, periods of acute asphyxia. "False asphyxia" in violation of nasal breathing, its consequences. "Asphyxia of newborns" and its consequences.

54. Atelectasis. Types, etiology, pathogenesis. Features of the mechanisms of formation of various types of atelectasis. Modeling of atelectasis.

55. Pneumothorax. Types, etiology, pathogenesis of various types of pneumothorax. Modeling pneumothorax. Features of pneumothorax in young children. Mechanisms of sanogenic action of therapeutic pneumothorax.

56. Emphysema as a component of chronic obstructive pulmonary disease. Formation mechanisms, a key link in the pathogenesis of various types of emphysema. Pathogenesis of respiratory disorders and blood gas composition, pathogenesis of obstruction in emphysema.

57. Bronchial asthma. Allergic and non-allergic forms of bronchial asthma. The pathogenesis of respiratory failure in emphysema and bronchial asthma.

58. Pathogenesis of respiratory failure in pneumonia. Features of the etiology and pathogenesis of interstitial pneumonia. Pneumonia in premature babies and babies born by cesarean section, their pathogenesis.

59. Pulmonary edema, types. Etiology and pathogenesis of cardiogenic, pulmonogenic and nephrogenic pulmonary edema. Pathophysiological basis of emergency care for pulmonary edema.

60. Etiology and pathogenesis of respiratory distress syndrome in adults and newborns.

61. Urgent compensatory-adaptive mechanisms in case of myocardial hyperfunction (mechanisms of Starling, Bowdich, Hill, an increase in the rate of diastolic relaxation with an increase in contractile function, positive inotropic and chronotropic effects of catecholamines).

62. Consequences of myocardial hyperfunction. Comparative characteristics of isotonic and isometric hyperfunction and its consequences. The concept of tonogenic and myogenic dilation.

63. Reasons for development, especially intracardiac and general hemodynamics in various types of heart failure. Molecular bases (ionic and energetic) of the pathogenesis of heart failure.

64. Myocardial hypertrophy: etiology, pathogenesis, stages. Structural, biochemical and functional features of the myocardium at various stages of the development of hypertrophy.

65. Metabolic disorders in the myocardium in IHD. Reperfusion phenomenon. Consequences of ischemic heart disease. Pre- and post-conditioning.

66. Coronary spasm of peripheral origin. Characteristics of intercoronary, cardiocoronary and viscerocoronary reflexes.

67. Myocardial infarction. Pathogenesis of complications of myocardial infarction (cardiogenic shock, postinfarction arrhythmias, aneurysms and cardiac tamponade, pulmonary edema, immune complications).

68. Complex violations of the heart rhythm (flutter and fibrillation of the atria and ventricles). Features of the etiology and pathogenesis of atrial fibrillation. Violations of cardiac contractility and general hemodynamics in complex cardiac arrhythmias.

69. Cardiac fibrillation and defibrillation. Causes and mechanisms of development. The concept of artificial pacemakers.

70. Vascular circulatory failure. Definition of the concept, etiology, pathogenesis, types. General compensatory and adaptive mechanisms.

71. Collapse. Etiology, pathogenesis, differences from shock. Hypotensive syndrome as a manifestation of sympatho-adrenal insufficiency. Orthostatic collapse.

72. Symptomatic (secondary) hypertension and mechanisms of their development.
73. Experimental models of hypertension.
74. Clinical manifestations of hypertension. The concept of a hypertensive crisis. Relationship between arterial hypertension and atherosclerosis.
75. Stages and general links of shock pathogenesis. Differences in the pathogenesis of certain types of shock (traumatic, hypovolemic, anaphylactic, septic, cardiogenic, etc.).
76. Hemodynamics and metabolic disorders in shock. Importance of microcirculation disturbance and systemic action of cell damage mediators.
77. Bleeding and hemorrhage. Etiology, pathogenesis, types. Consequences, urgent and long-term compensatory and adaptive mechanisms.
78. Polycythemia. Etiology, pathogenesis. Types of polycythemias, their differences. Features of the etiology and pathogenesis of polycythemia vera and erythromyelosis. Hemodynamic disorders in polycythemia.
79. Disorders of iron metabolism in the body (iron depot, daily requirement and transport). Disorders in the body associated with impaired iron metabolism.
80. Sideroblastic anemias. Hemochromatosis, etiology, pathogenesis, types.
81. Erythrocytopathies, general characteristics. Hereditary microspherocytosis: hereditary defect, mechanism and localization of hemolysis, blood picture.
82. Hemoglobinopathies, types, prevalence, etiology and pathogenesis. The crisis nature of the course of hemoglobinopathies.
83. Acquired hemolytic anemias. Types, etiology, pathogenesis. The role of immunopathological factors in the pathogenesis of hemolytic anemias.
84. Industrial poisons as etiological factors of anemias.
85. The role of autoimmune mechanisms in the occurrence of aplastic anemias. Features of the etiology and pathogenesis of Fanconi anemia in children.
86. Vasopathies: types, etiology, pathogenesis.
87. The role of autoimmune factors in the etiology and pathogenesis of endocrine diseases. Autoimmune endocrinopathies.
88. Disturbances of lipid metabolism in endocrine diseases. Types, etiology, pathogenesis.
89. Disorders of arterial blood pressure in endocrine diseases. Types, etiology, pathogenesis.
90. Disorders of water and electrolyte metabolism in endocrine diseases. Types, etiology, pathogenesis.
91. Disorders of carbohydrate metabolism in endocrine diseases. Types, etiology, pathogenesis.
92. Hypophysectomy. The consequences of removing the pituitary gland, depending on age. Disorders associated with impaired activity of the adenohypophysis.
93. Pathology of the thymus as an endocrine gland and an organ of immunogenesis. Types of disorders, etiology, pathogenesis, manifestations. Role in immunopathology. Neonatal thymectomy, its consequences.
94. The role of maternal endocrinopathies in the formation of intrauterine development pathology. The role of transplacental transfer of immunoglobulins in the pathogenesis of fetal immune endocrinopathies.
95. Information neuroses: pathophysiological aspects.

The student gets a permission to take an exam if he/she:

1. Attended all practical classes (if there are any missed classes it is necessary to work out them in accordance with the applicable requirements).
2. Attended all lectures (if there are missed lectures it is necessary to rework them in accordance with the applicable requirements).
3. Prepared and defended the abstract.
4. All the topics in the workbook are signed by the teacher.

Abstract topic: _____

_____

The teacher's signature: _____

Sample title page of the abstract

Ministry of Health of the Republic of Belarus

Belarusian State Medical University

Department of Pathological Physiology

ESSAY

The topic: **“EXPERIMENTAL MODELS OF DIABETES MELLITUS”**

Performed:
3rd year student
Faculty of General Medicine
Group 6301
Ivanov Ivan Ivanovich

Scientific adviser:
MD, Professor
Vismont F.I.

CONTENT

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