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DEPARTMENT OF CLINICAL LABORATORY DIAGNOSTICS**

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DRUG INFLUENCE ON LABORATORY INDICES

MANUAL ON CLINICAL LABORATORY DIAGNOSTICS

for foreign students of medical and pharmaceutical
higher schools and colleges

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The book contains a brief information laboratory diagnosis of human conditions, evaluation of efficiency and safety of medicines, the impact of drugs on the results of clinical analyses.

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Introduction

The aim of the manual is presentation of a brief information on laboratory diagnosis of human conditions and changes of clinical laboratory indices under the action of drugs. It is focused on assisting the future pharmacist to assess the efficiency and safety of drug use, to cover the problems of the drug influence on the results of clinical tests.

The manual gives definitions of concepts, standards, as well as the sets of test problems.

References at the end of the book aims to facilitate the task of the learner's search for additional sources covering research methods, reagents, equipment, and other details that go beyond the standard curriculum in clinical laboratory diagnostics.

Abbreviations

AH – arterial hypertension

AlAt – alanine aminotransferase

ARF – acute renal failure

BS – biliary System

CL – cholelithiasis

CRF – chronic Renal Failure

CI – colour index of blood (hemoglobin value)

Da – daltons (kDa – kilodaltons)

DD – duodenum

Dg – drug

df – drug field

ESR – erythrocyte Sedimentation Rate

f – female

GCS – glucocorticosteroids

g – gramm

GIT – gastrointestinal Tract

hr – hour

Hb – hemoglobin

HCl – hydrochloric acid

Hp – helicobacter pylori (seu campilobacter) – microbe, etiologic factor of peptic ulcer of the stomach and duodenum

Ht – hematocrit

i/m – intramuscularly

i/v – intravenously

IACE – inhibitors of angiotensin - converting enzyme

IP – the shift index (in the leukocyte count)

L – litre

m – male, masculine

mL – millilitre

mln – a million

MW – molecular weight

NSAIDs – non-steroidal anti-inflammatory drug

NaOH – sodium hydroxide

PNL – polynuclear Leukocyte

pH – pH value (parametrum Hydrogenium) – negative logarithm (lg) the concentration of hydrogen ions

RBC – red Blood Cell (erythrocyte)

sc – subcutaneously

u – unit (titr. u – titration unit)

UrS – urinary system

vf – viewing field

WBC – white Blood Cell (leukocyte)

\angle – comes from ...

$>$ – more

\geq – at least

\leq – max

$<$ – less than

$=$ – equal

\approx – approximately

Complete blood count

The standard clinical (general) blood test includes the assessment of the cytological structure of the capillary blood (taken from the pulp of the distal phalanx of the thumb IV), the values of hemoglobin, the colour index, the erythrocyte sedimentation rate, the blood clotting time and duration of the (capillary) bleeding (Table 1).

The cytological study is done by the method of light microscopy with the help of a blood smear stained with azure–eosin dyes, the hemoglobin level is studied by the colorimetric method. The erythrocyte sedimentation rate and the blood clotting time (according to Sukharev) are estimate day observation of the behaviour of blood in a glass capillary, and the bleeding time (according to Duke) it examined by observation of the capillary bleeding from the puncture of tip IV thumb to the depth of 3–4 mm.

Table 1

*The composition and normal parameters of the clinical analysis
peripheral blood of a healthy adult*

<i>Factor</i>	<i>Gender</i>	<i>The range of fluctuations, the dimension of the parameter</i>
Erythrocytes (RBC)	m	$4.0-5.1 \times 10^{12}/L$
	f	$3.7-4.7 \times 10^{12}/L$
Hemoglobin (Hb)	m	132–164 g/L
	f	115–145 g/L
Colour index (Hb value)	m, f	0.86–1.05 (1.10) units
Reticulocytes (RET)	m, f	0.2–1.2 % (an average of 0.5 – 1.0%)
Erythrocyte sedimentation rate (ESR)	m	1–10 mm/hr
	f	2–15 mm/hr
Trombocytes (PLT)	m, f	$180-320 \times 10^9/L$
Leukocytes (White Blood Cells): – myelocytes – metamyelocytes – neutrophils: banded (BN) segmented (SN) – basophils – eosinophil granulocytes – lymphocytes – monocytes	m, f	$4.0-8.8 \times 10^9/\mu$ (an average of $6-8 \times 10^9/L$) absent absent (or less than 1%) 1–6 % – $0.04-0.3 \times 10^9/L$ 46 (47) – 72% – $2.0-5.5 \times 10^9/L$ 0–1% – $0-0.065 \times 10^9/L$ 0.5–5% – $0.2-0.3 \times 10^9/L$ 19–37% – $1.2-3.0 \times 10^9/L$ 3–1% – $0.09-0.6 \times 10^9/L$
Blood clotting time (according to Sukharev)		Lower limit = 0.5–2 min; upper limit = 3–5 min.
Bleeding time	m, f	≤4 min. (according to Duke), ≤8 min/ (according to Ive)

Basic concepts in physiology and pathology of the blood, assessment criteria

Blood, *Lat.* haema, *Greek.* αἷμα (as tissue), sanguis (as liquid) – is a mixture of blood cell (40-45% by volume) in the plasma (50-60% of the blood volume), along with the lymph and the interstitial fluid it composed the bodys internal environment. The most important of the blood functions is transport (transfer of gases, nutrients, metabolic products, etc.).

Plasma, *Lat.* plasma [from the Greek. πλάσμα – something shaped, formed] – is the liquid component of the blood. The percentage of the plasma in the blood is 52-60%. It comprises amino acids, poly- and oligopeptides, hormones, enzymes, lipids, cholesterol, bilirubin, glucose, urea, electrolytes, etc. The specific gravity (density) of the plasma is 1.025–1.029 and depends mainly on the content of protein in it. The plasma proteins are albumins – 60%, globulins α , β , γ – 13%, 12%, 15% respectively, fibrinogen – 0.2–0.4%, pH 7.34–7.43. On average, 1 litre of the human plasma contains 900–910 g of water, 65–85 g of protein and 20 g of low molecular weight compounds.

Serum, *Lat.* serum – is the fibrinogen free plasma (after retraction of the clot).

Hematocrit (Ht), *Lat.* haematokritis [from al-Greek. αἷμα – blood, κριτός – index]. The blood is composed of two main components – plasma and formed elements suspended in it. In an adult human blood cells are about 40–48%, and the plasma – 52–60%. This relatio is called the hematocrit. Normally Ht is 44–46% in men and 41–43% in women.

Hemacyte, *Lat.* cytocomponenta [Greek. kytos, *Lat.* cytus – cell + componentum – component there are the following blood cells: red blood cells (RBC), platelets and leukocytes (white blood cells, WBC).

Erythrocyte, red blood cells (RBC), *Lat.* erythrocytus [Greek. erythros red + kytos – cell] – is a nuclear-free hemacyte containing a red pigment called hemoglobin. A red blood cell has the shape of a biconcave disk with the diameter of 7–8 microns (from 5.89 to 9.13 μm). In the human peripheral blood there are erythrocytes $4\text{--}5.1 \times 10^{12}/\text{L}$ in men and in women – $3.7\text{--}4.7 \times 10^{12}/\text{L}$. The synonymis: normocyte.

Polycythemia, *Lat.* erythrocytosis [Greek. erythros – red + kytos – cell + osis – long, often painful condition] – the content of red blood cells in the blood is $>5.5 \times 10^{12}/\text{L}$ in men and $>5.0 \times 10^{12}/\text{L}$ in women. Polycythemia is a consequence of the activation of erythropoiesis during oxygen starvation of tissues, accumulation of

carboxyhemoglobin when smoking, a consequence of the tumor process in the myeloid tissue, and dehydration from diarrhea, burns, administration of diuretics, etc.

Haemoglobinopathies – a disease caused by the presence in the blood of one or more abnormal hemoglobins.

Eritropenia, *Lat.* erythropenia [Greek. erythros – red + penia – poverty] – the content of red blood cells $<4.0 \times 10^{12}/L$ in men and $<3.7 \times 10^{12}/L$ in women. Eritropeniya – a consequence of reduced activity of erythropoiesis by hyperoxia in myeloid tumor tissue, as well as chronic blood loss, destruction (hemolysis) of red blood cells. Normally night erythrocyte destruction rate = $1/120$ germ erythrocyte population (bone marrow) or $7/120$ ($<10\%$) per week. Drop in the number of red blood cells per week $>10\%$ determined by the rapid destruction of cells, $<10\%$ – lack of erythropoiesis (bone marrow). State erythropoiesis reflect the number of reticulocytes, a color indicator, the size and shape of red blood cells.

Reticulocyte [Lat. reticulum – cell mesh + cytus] – young red blood cell containing a granular substance of the mesh (the remnants of the endoplasmic reticulum and RNA). In a normal blood – from 2 to 12 per 1000 reticulocytes or erythrocytes 0.2–1.2% (average of 0.5–1%) of the total number of erythrocytes in the blood.

Reticulocytosis, *Lat.* reticulocytosis – increase in the number of reticulocytes in the blood of $> 12/1000$ erythrocytes. The reason – the activation of erythropoiesis in blood loss (up to 3.0–4.0%), with aplastic anemia in remission, in hemolytic anemia, especially in times of crises (up to 20–60%).

Retikulopenia, *Lat.* reticulopenia – reducing the number of reticulocytes in blood $<2/1000$ erythrocytes. Cause – inhibition of erythropoiesis (vitamin B12 deficiency, folic acid, bone marrow aplasia, including as a result of ionizing radiation, cytotoxic coupon). Prognostically unfavorable sign.

Hemoglobin (Hb), *Lat.* haemoglobinum [Lat. haema – blood + globus – ball, Greek. protein] – the red pigment of red blood cells, consists of globin (one part) and heme (four parts). Globin – sulfur-containing protein, wherein amino acids 574 assembled in four pairs of identical circuits arranged. Heme ferroprotoporphirin. A healthy person has Hb Hb A 1 – $\alpha_2\beta_2$ (96–98%), Hb A2 – $\alpha_2\delta_2$ (2–3%) and Hb F – $\alpha_2\gamma_2$ (1–2%) – fetal Hb, which is replaced in the first days after birth for Hb A and completely disappears by the second year of life. In normal Hb = 130–160 g/L for men and 115 (120) – 140 g/L for women. The content of Hb levels below the physiological limit is called anemia, higher – polychromemia. Education Hb starts

during the conversion of basophilic normocytes polychromatic and ends at the reticulocyte stage.

Colour index of blood (hemoglobin value) (CI), *Lat.* index chromaticus [Lat. index figure, chromaticus – chromatic [Gk. chroma – colour, paint] – an indicator of the average content of Hb in a single red blood cell (E). The CI can be defined by the formula:

$$CI = 3 \times Hb \text{ (g/L)}$$

the first three digits of the number of red blood cells, expressed in millions/ml.

Normally, the CI = 0.86–1.05 (1.1). Can also be calculated MCH – the average mass of hemoglobin per red blood cell. $MCH = Hb \text{ (g/L)} / \text{number of erythrocytes in mln/mL}$. Normally MCH = 27–33.3 pg ($\leq 36\%$ of the weight of red blood cell).

Hyperchromia (for CI) – increase CI > 1.05 (1.1) – always combined with macrocytosis (increased volume of each red blood cell), because hemoglobin in a red blood cell may not be more than 36% of its mass. Hyperchromia, more often, can not compensate for the lack of hemoglobin (red blood cells) in a unit volume of blood, anemia is therefore natural.

Hypochromia (for CI) – reducing CI < 0.86 – a consequence of reducing the amount of iron in a single erythrocyte (iron deficiency or undigested serum iron), occurs when blood loss, diseases of the gastrointestinal tract, kidneys, liver, etc.

Anemia, *Lat.* anaemia [Lat. an – without + haema – blood] – decrease of hemoglobin (Hb) in blood < 115 (120) g/L: moderate anemia – 80 g/L, weight – 60 g/L, a very heavy < 60 g/L. Possible anemia:

1) pernicious [Lat. perniciosus dangerous, fatal] – anemia, which leads to death. The term legacy. The reason most often deficient in vitamin B₁₂ and folic acid;

2) sideroprive [Gk. sideros – iron + privus – stripped] – iron (hypochromic) anemia due to lack of serum iron – in diseases of the gastrointestinal tract, hemolysis, chronic blood loss, pregnancy, lead poisoning, in thalassemia and others;

3) sideroachrestic [Gk. sideros + a + chresis use] – anemia due to non-use (undigested) erythrocytes of iron present in the plasma in sufficient quantity (10.7–21.5 pmol/L – women, 14.3–26.0 pmol/L – male) ;

4) macrocytic (hyperchromic) – anemia associated with vitamin B₁₂ deficiency, is possible with the use of cytostatics, in acute radiation sickness;

5) normohromic – anemia with protein malnutrition, kidney disease, hypothyroidism, tuberculosis, taking Chloramphenicol, hydantoins, insecticide poisoning, hemolysis, acute blood loss, leukemia, cirrhosis of the liver.

Platelet, *Lat.* thrombocytus [Greek. thrombos – clot + kytos – hutch] – third, together with erythrocytes and leukocytes, hemocyte/cytoplasmic fragment giant cell bone marrow megakaryocyte; has dimensions of 1 to 3 microns, due to the presence of a large set of enzymes performs many functions: adhesive, retract, antiheparin, fibrinogen and tromboplastic, vasoconstriction, stimulating cell growth, etc.

In peripheral blood normally 180-320 thousand platelets in 1 ml; life of platelets in the blood = 5–8 days, daily updated 12–20% of the total weight of platelets.

In addition to mature azurophil platelets (90–95% of the mass) in healthy individuals can be (to 0.8%) of young platelets with a bluish hyalomere and sparse grit. Platelets with irregular outlines, dense granulomere referred to as the old (2.2–5.6%). Small or giant (up to 120 microns) platelets referred to as "forms of stimulation" (0.8–2.3%) and 0.2% of platelets may relate to "degenerate."

Thrombocytosis (thrombocythemia, high platelet count) – increase in the number of platelets in myeloproliferative disease (primary polycythemia, chronic myelogenous leukemia, chronic inflammatory diseases (tuberculosis, rheumatoid arthritis, sarcoidosis), granulomatosis, colitis, enteritis, splenectomy, and other neoplasms

Thrombocytopenia (low platelet count, platelet deficiency) [Greek. penia – poverty] – decrease in peripheral blood platelet count $<180 \times 10^9/L$ (<100 platelets / 1000 erythrocytes). Bleeding occurs typically when platelet counts $<50 \times 10^9/L$. Critical number of platelets (below which are natural bleeding = $30 \times 10^9/L$. Causes: decreased production of megakaryocytes, the strengthening of destruction. Operates at DIC, alcoholic cirrhosis of the liver with splenomegaly, with thrombocytopenic purpura disease, massive use of blood substitutes, transfusion of stored blood, uremia. Thrombocytopenia is possible using drugs such as aspirin and other nonsteroidal anti-inflammatory agents, cephalosporins, penicillins.

Trombocytopaty – reduced functional ability of platelets. The number of platelets while always $>70 \times 10^9/L$, and tolerance to heparin below normal (normal is about 135 seconds).

Leukocyte, *Lat.* leucocytus [Greek. leukos – white + kytos – cell] – a general term for white blood cells: basophils, eosinophils, neutrophils, lymphocytes,

monocytes. The number of leukocytes in the blood of normal human adults can individually be in the range $4.0\text{--}8.8 \times 10^9/\text{L}$, but in most cases it has – from 6 to $8 \times 10^9/\text{L}$ (6–8 thousand per 1 ml). The children in the normal number of white blood cells: up to 1 year – $6\text{--}16 \times 10^9/\text{L}$, 1–3 years – $9.2\text{--}13.8 \times 10^9/\text{L}$, 13–14 – $6\text{--}10^9/\text{L}$.

Depending on the ability to be colored paint "triatsid" Ehrlich white blood cell called neutrophils, eosinophils and basophils. They all contain in the cytoplasm stained on and referred to as "granulocytes". Granulocytes and monocytes are.

Leukocytosis – increase in the number of leukocytes in peripheral blood of adult $>9 \times 10^9/\text{L}$: Not sharply pronounced leukocytosis $>9 < 12 \times 10^9/\text{L}$, moderate leukocytosis $>12 < 25 \times 10^9/\text{L}$, pronounced leukocytosis $>25 < 40 \times 10^9/\text{L}$.

Leukemoid reaction, *Lat.* effectus leucaemicus [Lat. = Reaction similar to leukemia] – a condition characterized by an increase in the number of leukocytes in peripheral blood of $> 40 \times 10^9 / \text{L}$ without identifying with the blast forms blood cells. For verification of a very likely at this state of leukemia requires a bone marrow (bone marrow punctate) and / or follow-up study of blood. Leukocytosis occurs in the majority of infectious and inflammatory diseases, and sometimes – for bleeding, paroxysmal tachycardia. When infection is neutrophilic leukocytosis with a shift pattern of neutrophil (leukocyte) formula to the left – the index of the shift (IS) >0.08 . $\text{IS} = (\text{myelocytes} + \text{metamyelocytes} + \text{stab neutrophiles}) / \text{segmented neutrophiles}$. The normal segmented = 0.05–0.08.

Physiological leukocytosis: food, myogenic, emotional, pregnancy (within $9\text{--}12 \times 10^9/\text{L}$ – not more than 1.5 times the initial number of cells). Index offset with OK. Mechanisms: 1) Driving – redistributive (mobilization of white blood cells of the vascular edge pool and a pool of mature bone marrow), 2) of a product – myogenic.

Leukopenia [Greek. leukos – white + penia poverty] – reducing the number of leukocytes in peripheral blood $<6 \times 10^9/\text{L}$: mild terms – up to $4 \times 10^9/\text{L}$, expressed – up to $2 \times 10^9/\text{L}$, heavy – $<2 \times 10^9/\text{L}$.

Causes of leukopenia:

1. Oppression myelopoietic: chronic leukemias, metastatic tumors in the bone marrow, ionizing radiation, toxic effect of chemicals, drugs, hereditary neutropenia, systemic disease of connective tissue (systemic lupus erythematosus, rheumatoid arthritis), brucellosis, viral disease, AIDS.

2. Output delay of neutrophils from the bone marrow: acute leukemia, hypersplenism.

3. Enhanced destruction of white blood cells (with severe illnesses and diseases with auto-aggression, under the influence of chemotherapy).

4. The redistribution of white blood cells in the vascular system (shock, collapse, vomiting, eating, taking vagotropic drugs, alcoholism).

Leukocyte (WBC) formula, *Lat.* – formula leucocytorum [Lat. formula – model, image; leucocytus – leukocyte] – the ratio of certain types of white blood cells in% of the total actual number. Normally: basophils = 0–1%, lymphocytes = 18–40%, monocytes = 2–9%, stab neutrophils = 1.6% segmented neutrophils = 45–70%.

Lymphocyte, *Lat.* lymphocytus [Greek. lymph – "Spring Water", lymph + kytos – cell] – one of the nezernistyh forms of white blood cells. Name required a large number of lymphocytes in the lymph, and that at normal color formalin cytoplasmic granules is practically undetectable. "Lymphocyte" – a collective term for the cells are very similar in appearance, but with different functions. The best known of their function as effectors of the immune system, the predictors of delayed-type hypersensitivity reactions.

Lymphocytosis, *Lat.* lymphocytosis – an increase in the number of lymphocytes in the peripheral blood of >40% (relative) or >2800 per 1 ml (absolute lymphocytosis). Causes: drug use, asthma, whooping cough, infectious mononucleosis, hyperthyroidism, myxedema, lymphocytosis in typhoid fever and recurrent, tuberculosis, brucellosis – a favorable prognostic sign.

Lymphopenia [Greek. penia – poverty] – reduction in the number of lymphocytes in the peripheral blood <18% (relative) or <1200 in 1 ml (absolute lymphopenia). Reasons: inhibition of lymphopoiesis, the increase in the death of lymphocytes: purulent infections, sarcoidosis, systemic lupus erythematosus, AIDS, chronic renal failure, viral infections, radiation sickness, corticosteroids and alkylating drugs.

Monocyte, *Lat.* monocytus [Greek. mono – one + kytos cell] – the largest white blood cell (12–20 microns) with a compact core and a relatively wide border of the cytoplasm. Monocytes are not so much blood as in tissues where they may become specialized macrophages having immunoglobulin receptors and complement. In a normal peripheral blood monocytes = 2–9%.

Monoblast, *Lat.* monoblastus [Greek. blastus – sprout] – number of progenitor cells of monocytic size ≥ 20 mm.

Monocytosis [Greek. kytos – cell] – increase the number of monocytes in the peripheral blood of >10–11% (>800 cells in 1 mL) – in syphilis, tuberculosis,

brucellosis, protozoal infections, viral diseases (measles, mumps), scarlet fever, chlamydia, infectious endocarditis. With infectious mononucleosis number of monocytes in the midst of the disease may reach 40–50% (with leukocytosis and 20–25 thousand per 1 mL and lymphocytosis in the 50–70%).

Monocytopenia [Greek. penia – poverty] – reducing the number of monocytes in the peripheral blood <3% (<200 cells in 1 mL). The phenomenon of poorly studied in the clinic. Monocytopenia observed in aplastic anemia, systemic lupus erythematosus, rheumatoid arthritis, AIDS, after application of α -interferon and tumor necrosis factor.

Basofil, *Lat.* basophylus [Greek. basis – base + phylia – love, addiction] – a white blood cell, stain well with basic dyes. In a normal peripheral blood contains 0–1% basophils.

Basophilia – increase in the number of basophils in the blood. Observed in chronic myeloid leukemia, thyrotoxicosis, in the premenstrual period in women.

Granulocytes [*Lat.* granulum – grain + cytus – cell] – white blood cells that contain grit in the cytoplasm: basophils, eosinophils, neutrophils, monocytes. Synonym: myelocytes (meaning their bone marrow origin (Greek myelos – brain)).

Agranulocytosis – reducing the number of granulocytes in the blood to <500/mL.

Eosinophil, *Lat.* eosynophylus [Greek. Eos (pink) – goddess of the dawn; *Lat.* early, pink + Greek. phylia –love] – a white blood cell that contains a large number of granules, painted in yellow-red color. The cytoplasm of the large number of eosinophil granule little noticeable, slightly stained in blue. Normally, in the peripheral blood is 0–5% eosinophils (0–300 in 1 mL). The granules of eosinophils contain a large number of antihistaminic agents, antiparasitic alkaline protein, etc.

Eosinophilia – increase in the number of eosinophils in the peripheral blood of >5% ($>0.3 \times 10^9/L$). Takes place in the immediate type allergic reactions, helminths, in the stage of recovery from infectious diseases, and chronic pancreatitis, chlamydia, chronic myelogenous leukemia, systemic scleroderma, periarteritis nodosa, with antibiotics, sulfonamides, paraaminosalicylic acid (PASA).

Neutrophil, *Lat.* neutrophylus [*Lat.* neuter – of any one or the other side + Greek. phylia – love] – leukocyte perceiving and acidic (eosin) and basic (azure II) components of the dye (dyeing at Romanovsky). Cell size of 10–12 microns cytoplasm pale pink, grain – pink-blue or purple. Depending on the shape of the nucleus is isolated neutrophils: stab (belt-shaped core), segmented (separated into

individual core segments of varying size and shape). Average number of nuclear segments in neutrophils = 2–5. Neutrophils are a number of nuclear segments ≥ 8 –12 multisegmental called neutrophils or polynuclear leukocytes (PMNs). Funds are also young forms of neutrophils: metamielotsit and medullozell.

Neutrophil levels in normal:

stab = 1–6% (0.04 – $0.3 \times 10^9/L$)

segmented = 47–72% (2.0 – $5.5 \times 10^9/L$).

Neutrophil function: phagocytosis, production of peroxides.

Neutrocytosis (neutrophilia) – increase in the number of neutrophils (absolute or relative – as a % of the total number of white blood cells) – is observed in inflammatory processes of diverse etiology, after bleeding during pregnancy, after splenectomy, etc.

Neutropenia – reducing the number of neutrophils in the blood – the case of viral diseases (influenza, infectious hepatitis, chicken pox, polio), malaria, severe sepsis, disseminated tuberculosis, bone marrow hypoplasia, when receiving cytotoxic drugs, sulfonamides, amidopirina, reopirin, some antibiotics.

Pancytopenia [Greek. pan – all] – reducing the number of blood cells.

Erythrocyte sedimentation rate (ESR), *Lat.* velocitas haemaggregationis [Lat. velocitas – speed; haema – blood, aggregatio – formation of clusters] – property of blood cells (everyone, not just red blood cells, red blood cells but the overwhelming majority of blood cells) to aggregate and precipitate at the bottom of the container (vial), provided that incoagulable of the blood.

According to Stokes' law, the ESR is directly proportional to the square of the radius of the erythrocyte and the difference between the density of red blood cells and plasma, and inversely proportional to the viscosity of the plasma, ie, ESR depends on: 1) the number of red blood cells in 1 mL and size, 2) the protein composition of the plasma. The more high plasma protein (fibrinogen, globulins, proteins "acute phase of fair"), the higher the ESR.

Image ESR moderate – 25–35 mm/hr; pronounced >35 mm/hr (sometimes – 70–80 mm/hr).

ESR is increased in tumors, heart attack, hepatitis, cirrhosis of the liver, after blood loss, after taking non-steroidal anti-inflammatory drugs regularly increases in inflammatory processes. The increase in erythrocyte sedimentation rate requires a

"booster" of time (\approx a few days). Reducing ESR behind the rate of disappearance of the inflammatory process, so important assessment of the dynamics of ESR. Slowing ESR characteristic of polycythemia.

Drugs and blood pathology

The basic mechanisms of drug-induced anemia

Denaturation of hemoglobin straight: preparations of copper, lead, gold, chymotrypsin, aminophylline, aspirin, diphenhydramine, vitamins of B group, chlorates and even prednisone.

Denaturation of hemoglobin oxidant (through education and meth- and sulfohemoglobin): sulfonamides, sulfones, phenacetin, salicylate, chlorates, oxygen, methylene blue (neonates), nitrites and nitrates, resorcinol.

Hapten mechanism. With large doses of drugs are drugs adsorption on erythrocytes – opsonization ("enveloping"): penicillins, cephalosporins, tetracyclines.

Autoimmune mechanism – the formation of autoantibodies after prolonged use of drugs, such as alpha-methyldop.

Immune-complex mechanism – deposition (settling) anti-drug anti-bodies on the surface of red blood cells to form immune complexes, such as aspirin, leykeran, phenacetin, quinidine, rifampin, cefotaxime, 5-fluorouracil, isoniazid, thiazides.

Several mechanisms simultaneously: clonidine, streptomycin (hapten + autoimmune), etc.

Drugs used to stimulate erythropoiesis

Iron ferrous sulphate (lactate), Ferrum-Lek, ferkoven, ferbitol, zhektofer, ferrlecyt, ferroceron, Ferroplex, Aktiferrin, fenyuls, ferrogematogen, Sorbifer, vitrum, durules, Ferretab, ferro-Folgamma, Eritrea (epoetin beta), Eprex (epoetin alpha), hydroxocobalamin, cyanocobalamin (vitamin B12), Vitamaks, multi-tabs, multivita plus, duovit, ascorbic acid (vitamin C), folic acid (vitamin B₉), calcium fomenat-Ebewe, batilol.

Prescription of iron supplements

1) Determine the iron deficiency by the formula:

$$\text{Deficiency Fe, mg} = [\text{BW kg} \times 2.5] \times [16.5 - (1.3 \times \text{Hb g/dL})]$$

where Fe – is iron;

BW – is the body weight, kilograms,

Hb – is hemoglobin, g/dL.

Example: BW = 70 kg

Hb = 80 g/L = 8 g/dL

Deficiency Fe = $[70 \times 2.5] \times [16.5 - (1.3 \times 8)] = 1050.5$ mg.

Bear in mind that a daily dose of iron should not exceed 300-400 mg (hereinafter dose increasing sense!). The physiological need $\text{Fe}^{2+} = 20\text{--}30$ mg!

Take into account the dose of iron in standard packaging of the drug and calculate the required amount of the course and on the day.

Example. Ferrum Lek contains 1 vial (2 ml) for a intramuscular injection = 100 mg 0.1 tribasic iron complexed with maltose (1 mL = 50 mg). Hence the need for a course $1050.5 : 50 \approx 21$ mL. The drug can be introduced intramuscular at 6 days: Day 1 – 4 mL, 2nd – 4 mL, 3rd – 4 mL, 4th – 4 mL, 5-th – 4 mL, 2nd – 2 mL.

2) Exchange dose is calculated using the formula:

Dose of course Fe, mg = $\text{BW} \times (78 - 0.35 \text{ Hb g/L})$.

3) Exchange dose is calculated using the formula:

Dose course Fe, mg = $\text{BW} \times (100 - \text{Hb g/L}) \times 0.66$.

4) Exchange dose is calculated based on the basic tenet that it should not exceed 5 mg /kg/day – for adults, 5–8 mg/kg/day – (per os) for children up to 3 years or a maximum of 100 mg/day parenterally.

This completely saturates transferrin.

All calculations for iron are lawful if it comes to iron deficiency anemia, – at low serum iron (normal = 14.3–6.0 men, women = 10.7–21.5 mol/l. To replenish iron therapy is carried out for a further 12 months (physiological dose).

Prescription of vitamin B₁₂ and folic acid

Physiological daily requirement for vitamin B₁₂ = 10–15 micrograms. Formulations Vit. B₁₂ usually contain 50, 100, 200 and 500 micrograms. Dosing – thumb – from 50 to 500 mg 1 time in 2 days (most often – 200–400 mcg), premature babies – 30 mg/day in tech. 15 days. Doses of Vit. B₁₂ > 1000 mg cause toxic effects on proteins and their loss in the urine.

Physiological daily requirement of folic acid \approx 200 mg (adults), 25 mg (children 1–6 months). The use of drugs is justified in persons with impaired maturation megaloblasts. Absorption (in the duodenum) requires (and absorption vit. B₁₂) intrinsic factor Castle – specific glycoprotein produced by the gastric mucosa. Folic acid comprises para-aminobenzoic acid (PABA) and glutamic acid residues 2–3. PABA antagonist PAS causes a deficiency of folic acid. When folic acid deficiency, as vitamin B₁₂, developed megaloblastic (giperhromnaya!) anemia. The major difference is that when there is no shortage of folic acid reticulocytosis.

Dosage of folic acid is empiric: 1–5 – 10 mg/day.

Drugs that cause leukopoiesis depression most often

Nonsteroidal antiinflammatory drugs (aminopyrine, phenylbutadione), nitrogen, silver, mercury, bismuth compounds, alkylating agents, cytotoxic agents, aminoglycosides, chloramphenicol, neuroleptics (chlorpromazine, elenium, etc.), antihistamines (Table 2).

Table 2

Drugs that are recommended for leukopoiesis stimulation

<i>Drugs</i>	<i>Comment</i>
Amyfoscyn	
Batilol	
Methyluracyn	
Leycohen	
Fylgrasthym	
Molgramoctyn	
Pentoxyl	
Thymogen, thymosyn-alfa, thymostimulin,	
Sodium nucleynat	
Lenograsthym	

Drugs depressing the platelet function most often

Nonsteroidal anti-inflammatory agents; antiplatelet (ticlopidine, curantil, prostacyclin), anticoagulants, fibrinolytics (heparin, streptokinase, urokinase), antineoplastics (daunorubicin, etc.), cephalosporins, aminoglycosides, tetracyclines, chloramphenicol, lincosamides (lincomycin, clindamycin), ristomycin; antiviral agents (acyclovir, ganciclovir, vidarabine), cytotoxic agents (azathioprine, cyclophosphamide, etc.), steroids, furosemide, ethanol (Table 3,4,5).

Table 3

Anticoagulants, antiplatelet (antiaggregant) agents, fibrinolytic

<i>Medicinal product</i>	<i>Comment</i>
Antithrombin III (cybernin)	
Heparin	thrombin biosynthesis inhibitor, antithrombin III coenzyme
Low molecular weight heparins: dalteparin (fragmin) nadroparin (fraxiparine) reviparin (klivarin) certoparin, enoxaparin (clexane)	Xa, Va, VIIa, XIIa blocking agents
Calciparin	
Phenindione (fenilin), acenocoumarol, warfarin, ethyl biskumacetat (pelentan)	anticoagulants of indirect action – antagonists vit. K, , prothrombin inhibitors, f. VII, IX, X.
Pentoxifylline (trental, agapurin), clopidogrel, dipyridamole (curantil)	antiplatelet agents – adenosine receptor blockers, PDE blockers
Abciximab, ticlopidine (tiklid)	antiplatelet agents – GP II b / III a platelet membrane receptors blockers
Pirikarbat (anginin, parmidin)	bradykinin and kallikrein inhibitor – vazoprotektor
Escin (escusan)	vein tonic
Non-steroidal antiinflammatory agents (aspirin, indometacin, ndobufen (ibustrin), ibuprofen, diclofenac, ketoprofen, etc.)	inhibitors of platelet
Alteplase (actylase)	recombinant plasminogen activator
Plasminogen (profibrinolysin)	precursor of plasmin (fibrinolysin)
Streptokinase	plasminogen activator
Urokinase	serine protease – plasminogen activator
Sulofeksid (Vessel Due F)	a natural mixture of heparin fractions of small intestine of animals (80%), and dermatan sulfate (20%) – f. X activator, prostacyclin synthesis stimulant; lowers the concentration of fibrinogen in the blood and tissue plasminogen inhibitor

Table 4

Hemostatic agents

<i>Hemostatic agent</i>	<i>Mode of action</i>
Trombin	trombogen
Etamzilat sodium (dicynone)	activator formation of thromboplastin
Protamine sulfate	heparin antidote (multiplicity 1: 1)
Coagulation factor IX	antihemophilic factor B – plasma thromboplastin component
Menadione, fitomenadion	synthetic analogs of vitamin K. Vit. K activate special carboxylase that converts glutamic acid residues in

<i>Hemostatic agent</i>	<i>Mode of action</i>
	various proteins (prothrombin – f.II, proconvertin – f. VII, antihemophilic globulin – f. IX, trombotropin - f. X, protein C, S) in carboxyglutamic acid, which provides them with the binding of Ca^{2+} and activation (conformational change)
Aminocapronic (epsilon-aminocapronic) acid	fibrinolysis inhibitor, and especially plasminogen
Traneskamic acid (transamcha)	transition inhibitor of plasminogen to plasmin (fibrinolysin)
Aprotin (antagozan, gordox, contrycal, trasilol, transkolan)	polyvalent protease inhibitor plasma
Calcium supplements: calcium gluconate and chloride	auxiliary hemostatic agents
Beriplast, gelatin, Tachocomb	local styptics

Table 5

Hematologic side effects of different groups of drugs

<i>Drugs and their effects</i>	<i>Comments</i>
Penicillins: benzylpenicillin, bitsillinom, ampicillin, etc. – Thrombocytopenia, increased duration of bleeding/ – Leukopenia – Eosinophilia	The risk of severe forms. Allergization
Cephalosporins: I-cefazolin, cephalothin, cephalirin, cefadroxil, cephalixin; II-cefamandole, cefoxitin, cefotetan, cefuroxime, cefaclor; III-cefodizime, cefoperazone, cefotaxime, tsefpiramid; IV-cefepime, cefpirome: – Thrombocytopenia, increased duration of bleeding. – Neutropenia – Eosinophilia	Cephalosporins II and III-rd generations inhibit epoxide required for the conversion of vit. K to an active form (vit. K exist as gidrohinina, epoxide and quinone continuously into each other in this order) The maximum effect after 3 days of use Allergization
Carbapenems: meropenem-, thienyl-, primaksil-eosinophilia	Allergization
Monobaktamy: aztreonam: – eosinophilia – bleeding	Reduces prothrombin index
Macrolides / azalides (for intravenous): clarithromycin, oleandomycin: – eosinophilia – thrombosis	Allergization Phlebitis by bolus intravenous injection

<i>Drugs and their effects</i>	<i>Comments</i>
Aminoglycosides: amikacin, gentamicin, isepamitsin, kanamycin, netilmicin, sizomitsin, streptomycin, tobramycin: – anemia – leukopenia – thrombocytopenia	Granulocytopenia!
Tetracyclines: tetracycline, doxycycline, methacycline: – neutropenia – thrombocytopenia	Eosinophilia of neutropenia!
Lincosamides: lincomycin, clindamycin: – neutropenia – thrombocytopenia	Mostly eosinophilia of neutropenia!
Polymyxin: M, B, E: – thrombocytopenia	Rarely
Chloramphenicol (laevomycetin): – pancytopenia – anemia – thrombocytopenia – basophilopeniya	The drug is not recommended for children. By inhibiting microsomal enzymes of the liver, increases the toxicity of its own, and other drugs
Rifampycins: rifampycin, rifaximin – anemia – thrombocytopenia	Rarely Rarely
Ristomycin: – anemia – leukopenia (neutropenia) – thrombocytopenia – eosinophilia – basophilopenia	Rarely Chance of agranulocytosis Rarely
Spectinomycin: – anemia	Hemolysis of red blood cells!
Quinolones: grepafloksatsin, lomefloxacin, norfloxacin, ofloxacin, pefloxacin, fleroxacin, ciprofloxacin, enoxacin: – anemia – eosinophilia – thrombocytosis	Cause hemolysis in patients with deficiency of the enzyme G-6-PD
Glycopeptides vancomycin, teicoplanin: – eosinophilia – granulocytopenia	To 500 of 1 mL

<i>Drugs and their effects</i>	<i>Comments</i>
<p>Sulfonamides: sulfadimethoxine, sulfaguanidin (sulgin), sulfadimezin, sulfalen, sulfakarbamid (urosulfan), sulfamonometotoksin, sulfasalazine, sulfaetidol (etazol), ftalilsulfatiazol (ftalazol) and biseptol (sulfamethoxazole + trimethoprim):</p> <ul style="list-style-type: none"> – anemia – eosinophilia 	<p>Cause a relative deficiency of folic acid, especially in combination with trimethoprim. Cause hemolysis in patients with deficiency of G-6-PD. Cause the formation of sulfhemoglobine</p>
<p>Antiviral agents: vidarabine, acyclovir, ganciclovir:</p> <ul style="list-style-type: none"> – pancytopenia 	<p>Obscure</p>
<p>Drugs for treatment of AIDS: AZT, fosfopofomat:</p> <ul style="list-style-type: none"> – eritropeniya 	
<p>Antineoplastic: oxaliplatin, paclitaxel, pamidronic acid, etoposide, dactinomycin, daunorubicin, mitomycin, doxorubicin, epirubicin):</p> <ul style="list-style-type: none"> – anemia 	
<p>Cytotoxic agents: azathioprine, cyclophosphamide, methotrexate, altrepamin, amsacrine, vinorelbine, gemcitabine, docetaxel, irinotecan, mercaptopurine, raltitrexid, streptozocin, topotecan, fludarabina phosphate tsitarbin:</p> <ul style="list-style-type: none"> – Pancytopenia: erythro-leukopenia and thrombocytopenia. 	<p>Expressed leukopenia (to $<3.0 \times 10^9/L$)</p>
<p>Corticosteroids: prednisolone, triamcinolone, methylprednisolone, dexamethasone:</p> <ul style="list-style-type: none"> – polycythemia – neutrocytosis – thrombocytopenia – lymphopenia – eosinopenia – bazofilopeniya – monocytopeniya 	<p>Increase the yield of the depot neutrophils. Dexamethasone increases especially diapedesis, increases bleeding.</p> <p>The mechanism of lymphopenia is not clear (redistribution in the tissue, the depression?)</p>

<i>Drugs and their effects</i>	<i>Comments</i>
NSAID – primarily: aspirin, phenylbutazone, indomethacin, piroxicam: – anemia – thrombocytopenia, bleeding – acceleration of ESR – leukocytosis	Analgins cause hemolysis in patients with deficiency of G-6-PD. The clotting time was increased by 1.5-2 times, inhibits the trophic (for vascular endothelium) platelet function. Granulocytic
Alkylating agents: a) mustard: chlorbutin, cyclophosphamide, ifosfamide b) the derivatives of ethyleneimine: tiofosfamid, imifos, iftorbenzotef, fotrin; c) disulfonic acid derivatives: melosan, busulfan, melobromol; g) nitrosoureas: lomustine, carmustine, streptozocin, arazoza, fotemustine; e) products of different origin: procarbazine, dacarbazine, prospidin, carboplatin: – pancytopenia: erythromycin, leukopenia, thrombocytopenia	Cause cytolysis Group of medicines with high hematotoxicity
Gold preparations: aurofin, krizanol, aurotioglyukoz, aurothiomalate: – pancytopenia	Group of medicines with high hematotoxicity
Antituberculosis drugs: – eosinophilia – anemia – thrombocytopenia – neutropenia	Paraaminosalicylic acid Paraaminosalicylic acid Thioacetosone Thioacetosone
Antimalarial drugs: mefloquine, pyrimethamine, chloroquine (delagil), dapsone, metakelfin, proguanil (bigumal) – anemia – agranulocytosis – thrombocytopenia	Hemolysis
Uricosuric and urikozuricheskie drugs: allopurinol, probenecid, sulfinpyrazone: – Eritropeniya, thrombocytopenia, leukopenia	Probenecid – deficiency anemia in G-6-PD. Sulfinpyrazone – at high doses (>600 mg/day) inhibits platelet function. Allopurinol – an inhibitor of xanthine oxidase.
ACE inhibitors (all): – pancytopenia (observed)	Inhibiting the formation of ACE promotes accumulation of blood in one of the substrates for the synthesis of ACE, a negative regulator of hematopoiesis, peptide N-acetyl-lysyl-proline.

<i>Drugs and their effects</i>	<i>Comments</i>
Statins are: pravastatin, fluvastatin, cerivastatin, atorvastatin: – anemia – thrombocytopenia	Obscure pronounced: Mechanisms: inhibition of cholesterol synthesis (hemolysis), toxic-allergic cholestasis
Antidiabetic agents: a) bucarban, Manninen, gliquidone: – neutropenia – thrombocytopenia b) metformin, buformin: – anemia	Violate the absorption of vitamin B ₁₂
Antiepileptic drugs: primidone, ethosuximide, felbamate, phenytoin (phenytoin), valproic acid, carbamazepine (finlepsin), trimethadione, lamotrigine: – anemia – thrombocytopenia – eosinophilia – neutropenia – pancytopenia	Rarely Rarely (carbamazepine, valproic acid) Rarely (valproic acid, lamotrigine) Phelbamate
Neuroleptics: fluphenazine, espazin, droperidol, haloperidol, levopromazin, clozapine, trifluoperazine, thioproperazine, pericyazine, chlorprothixene, chlorpromazine (thorazine), pipotiazin: – anemia – pancytopenia – agranulocytosis – lymphopenia – thrombocytopenia	Hemolysis, bone marrow aplasia! Carbamazepine, clozapine Clozapine. Chlorpromazine Fluphenazine Fluphenazine, espazin – rarely
Antidepressants: amiksid, amitriptyline, paroxetine, desipramine, doxepin: – pancytopenia – anemia – neutrocytosis – neutropenia – eosinophilia (rarely)	Cause bone marrow aplasia Paroxetine (7.5 x 10 ⁹ /L)! It also stimulates polycythemia! Desipramine, mianserin Desipramine, doxepin, paroxetine, as well as temazepam and doxepin

<i>Drugs and their effects</i>	<i>Comments</i>
<p>Tranquilizers:</p> <p>a) diazepam (seduksen, relanium, sibazon, valium); elenium, librium, nozepam, tazepam, temazepam, lorazepam, medazepam (rudotel), phenazepam tofisopam (grandaxinum), gidazepam, alprozolam;</p> <p>b) meprobamate, skutamil, trioxazine; oksilidin; mebikar; amizil; Phenibutum:</p> <p>– anemia – thrombocytopenia – neutropenia</p>	<p>Mechanisms of gematotoxicity are not well understood.</p> <p>Meprabamat – rarely Rarely Rarely</p>
<p>Barbiturates: barbamil, etaminal, phenobarbital, amobarbital:</p> <p>– anemia – agranulocytosis – thrombocytopenia</p>	<p>Mechanisms of gematotoxicity are not well understood.</p>
<p>Benzodiazepines: nitrazepam, phenazepam, lorazepam, etc.</p> <p>– agranulocytosis</p>	<p>The inhibitory effect on many systems of the body, providing granulocytopoiesis</p>
<p>Nootropics: lucetham</p> <p>– bleeding</p>	<p>Inhibits platelet aggregation</p>
<p>Alpha-agonists: methyldopa (dopegit)</p> <p>– leukopenia</p>	
<p>Alpha-adrenergic blockers: prazosin</p> <p>– anemia</p>	
<p>Myotropic means: hydralazine</p> <p>– polycythemia – leukopenia</p>	<p>Mechanisms of gematotoxicity are not well understood.</p>
<p>Antiarrhythmic agents: disopyramide (ritmilen), procainamide, propafenone:</p> <p>– leukopenia</p>	
<p>Anticonvulsants, protivoepileptical means: levodopa, madopar:</p> <p>– anemia – thrombocytopenia – leukopenia</p>	<p>Mild, transient</p>
<p>Bile acid resins: cholestyramine, colestipol, pectin, kvantalan:</p> <p>– bleeding</p>	<p>Violate the absorption of vitamin K, folic acid</p>
<p>Antihistamines: diphenhydramine, suprastin, etc.:</p> <p>– eosinopenia – thrombocytopenia</p>	<p>Obscure Ketotifen (reversible effect)</p>

<i>Drugs and their effects</i>	<i>Comments</i>
Anthelmintics: praziquantel, levamisole: – eosinophilia – anemia – agranulocytosis – thrombocytopenia	
Calcium antagonists – nifedipine: – anemia	Inhibition of erythropoiesis (expressed obscure)
Nitrates and nitrites: nitroglycerin, sustak, etc.: – anemia	With prolonged use at high doses (> 20 nitroglycerin tablets / day).
Diuretics (saluretics)	

Note: Deficiency of G-6-PD clinically suspected in the development of hemolysis during routine infectious diseases, and laboratory – when it detects less than 10–20 formasan granules in one erythrocyte (L.A. Danilova, 2003). **Common urine analysis**

The main goals of clinical and pharmacological studies uronefrologicheskogo patient are:

- Diagnosis of clinical syndromes nephropathy;
- To establish the etiology of nephropathy;
- The establishment of the activity of pathological processes;
- Assessment of renal function and urinary system as a whole;
- Assessment of the effects of nephrotoxic drugs.

Complete urinalysis includes sections: macroscopic, biochemical, microscopic (cytology), and microbiology. Last goes beyond "urinalysis" and range of the first three chapters may vary in different laboratories (table 6).

Table 6

*The composition and normal parameters
of the standard common urine analysis*

<i>Parameter</i>	<i>Standard</i>
Quantity, mL	No (fixed volume delivered urine)
Transparency	Glassy
Color	Light yellow
Relative density, rel. units	1015–1025
pH reaction	Slightly acidic
Protein, g/L	No
Glucose	No
Ketone bodies (KET)	No
Reaction to the blood	Negative

<i>Parameter</i>	<i>Standard</i>
	The very few the very few
	The very few

Basic concepts in physiology and pathology of the urinary system

Kidney, *Lat.* ren, *Greek.* nephros – paired organ of urine formation (located in the spine, leg buds (veins, artery, ureter) resembles a sprig of plants that connects the kidney to the barrel).

Nephron, *Lat.* nephron – the structural and functional unit of the kidney. One nephron is a 20–40 capillaries gathered into a ball, surrounded by a capsule (Shymlanskaya-Bowman) of 2 sheets of epithelium. From the cavity between the sheets of the capsule is U-shaped tubule. The initial and final sections are convoluted tubule character, and the middle, connecting, – the form of a smooth bend (loop of Henle). Top-down and bottom-up departments wider connection. In the final section tubule and the renal glomerulus is located a juxtaglomerular apparatus (periarterial pad) – histological structure, which controls the biochemical composition of urine and blood. In the glomerulus is filtered blood serum – anything that has a MM <5–10 kDa (I.B. Mikhailov, 2001), formed provisionally ("primary"), urine (\approx 150–170 L/day). Tubule reabsorption occurs in the protein, water, etc. The result is a "secondary" urine.

Urine, [*Lat.* urina = *Greek.* uron, irrita = urine] – liquid separated by the kidneys, and its output to the outside through the urethra / ultrafiltration of plasma.

The quantity (volume) of urine, *Lat.* volumen (circuitus) urinae. In the conventional urinalysis does not matter, because patient brings its arbitrary amount.

In a healthy person the amount of morning urine \approx 150–200 mL, the daily volume = 1000–1800 (2000) mL.

Polyuria – the amount of urine daily dose of > 2000 mL (in extreme cases – up to 10.3 liters / day.).

Anuria – daily dose urine volume <50 mL.

Oliguria – a daily dose of urine volume <800 ml

The smell of urine, *Lat.* odor urinae – normally easy-specific, after settling due to the decomposition of urea by bacteria – a sharp ammoniac, with purulent processes – putrid; diabetes – sweet (at the expense of ketone bodies), pickled apples (acetone); in the elderly, after the use of valerian, menthol, alcohol, and horseradish, garlic, asparagus – a sharp smell of urine.

Urine color, *Lat.* color urinae – is a direct function of its density (specific gravity) and the presence in it urochroma. Normally – from straw yellow to deep yellow. Basically, straw-yellow urine gives stercobilin (oxidize in air stercobilinogen). Stercobilinogen invaded into the blood and then into the urine of hemorrhoidal veins, called "urobilinogen". Urobilinogen in the urine is normal almost there.

Hypohromuria – pale urine color – with low specific weight (<1012-1016).

Hyperhromuria – dark yellow urine – with a high specific gravity (> 1030).

Urine stained color:

Red – beets, red blood cells (the color "meat slops") santonine (in alkaline urine), urate, aminopyrine, a large amount of uric acid overdose of anticoagulants (red cells in the urine!)

Cherry – acetic acid (from the first minutes of poisoning her);

Brown-red – rifampicin (rare, but causes hemolysis!)

Pink – aspirin;

Dark brown – salol;

Bright yellow – santonine (acidic urine);

Dark yellow, orange – dehydration;

Greenish or golden yellow – the rhubarb;

Black – melanin, carbolic acid and its derivatives;

Pale – diuretics, alcohol;

Milky white – phosphates, lymph;

Brown (the color of dark beer) – bilirubin, urobilin, urate, phenol, cresol, bear ears; carbol;

Green or dirty blue – rotting urine (typhoid, cholera);

Dark – methyldopa (dopegit) – while standing urine.

Foaming, *Lat.* spumatio urinae – normally fresh urine foams slightly. The increase in foaming – with proteinuria bilirubinuria.

Transparency, *Lat.* perspicuitas urinae – fresh urine normally transparent.

Clouding of urine, *Lat.* opacitas urinae, determined mucin (mucus), white blood cells, fat droplets, as well as the decomposition of urine bacteria and precipitation of salts in the sludge (on standing urine or kidney stones). Thus, blurred urine caused urates, disappears when it is heated, phosphates – adding acetic acid oxalate – adding hydrochloric acid. Turbidity increases urine with heating if pus in the urine, phosphates, carbonates, is not affected by heat if the urine contains bacteria semen mucin.

Cellular elements, bacteria, slime can be removed by filtration, fat – urine mixing with ether or alcohol.

Density (specific gravity) of urine, *Lat.* densitas urinae. The normal density of primary urine ≈ 1.010 units., secondary ≈ 1015 – 1025 units. Urine density depends mainly on its content of urea. It falls $\approx 50\%$ dissolved solids. Urea – a non-toxic compound, the carbonic acid amide is complete ($\text{NH}_2\text{-CO-NH}_2$), formed in the liver during the hydrolysis of arginine (V.P. Komov, V.N. Shvedova, 2004).

The criteria for the density of urine are: a) The defrosting point (frozen) blood $\approx -0.87^\circ \text{C}$, and b) The density of blood plasma ≈ 1025 – 1029 units.

The density of urine is a criterion of concentration (nitrogen excretion) kidney function, may vary during the day from 1004 to 1045 units. It is sufficient if for a day at least one portion reaches a value ≥ 1015 .

Hyposthenuria – low specific gravity of urine – <1012 – 1015 units. (The defrosting urine point higher than the -0.87°C). Hyposthenuria occurs when diuretics (saluretics), and renal failure.

Hupersthenuria (baruria) – high urine specific gravity > 1030 units. (The defrosting urine point below the -0.87°C). Baruria takes place with abundant sweating, fever, intense release of the products of protein breakdown. She regularities in diabetes (≥ 1030 – 1040); while each 10 g/L of glucose in the urine (1%) increase in the proportion of 4 units. At every proteinuria 3.3 g/L of protein increases urine specific gravity by 1.

pH of urine – urine pH adult humans may range from 4.5 to 8.5, but in normal circumstances when the mixed feed pH 5.5–6.5 (average 6.0), i.e. slightly acid reaction of urine. Blood pH \approx 7.40 (7.35–7.45).

Aciduria – when consuming large amounts of meat, food rich in proteins. Aciduria – with hypokalemic alkalosis, with prolonged use saluretics, metabolic or respiratory acidosis of any origin (diabetes, rickets during the height of the disease, renal and cardiac failure, fasting, fever) in the use of drug-acids: aspirin, etc.

Alkaline urine – at long vegetarian diet, conditions involving metabolic or respiratory alkalosis, resorption of exudate and transudate, urinary tract infections caused by microorganisms that have urease (cleaves urea), in cases of poisoning by heavy metal salts, sulfonamides, in severe forms of glomerulonephritis and pyelonephritis, in renal tubular acidosis, with the introduction of sodium bicarbonate, use of alkaline mineral waters.

Sharply acidic reaction to the formation of a urine urate stones, alkaline reaction – phosphate. In an acidic environment is well propagated *E. coli*.

In an alkaline environment, more rapid destruction of leukocytes and erythrocytes in urine caught.

The protein in the urine – proteinuria (albuminuria). Investigated for urine protein should be transparent and slightly acidic. In case of severe acidification of the proteins in mochepriobretayut negative charge, making them difficult to deposition and definition. Normally, the amount of protein in urine is so small that is not determined by conventional sedimentation tests.

Daily urinary protein excretion is less than 50–150 mg. In the renal tubule reabsorbed protein with MW <4000 Da.

Origin of urinary protein:

- To quantify the main (normal) – Tamm-Horsfall protein secreted by cells of the thick ascending loop of Henle;

- Cell proteins desquamated tubular epithelium;

- Plasma proteins, filtered at the glomerulus and reabsorbed in the tubules.

The mechanism of development of proteinuria:

- Damage the glomeruli: the loss of their negative charge – increased intake of protein in the urine with a small MM: albumin, transferrin, α 1-antitrypsin, loss of

ability to retain macromolecular proteins in the blood: α 2-macroglobulin, immunoglobulin G, and others;

– The defeat of the proximal tubules of the nephrons – suffers reabsorption of proteins (proteinuria while usually small) – entering into the urine paraprotein in excess of the capacity of the tubules to reabsorption.

– "False proteinuria" – entering protein in urine due to inflammation, trauma, tumors, ureter, bladder, prostate, urethra.

The levels of proteinuria:

microproteinuria – urine protein = 0.033–0.2 g/L (trace amount);

small proteinuria – urinary protein > 0.2 < 1.0 g/L;

moderate proteinuria – urinary protein > 1.0 < 3.5 g/L;

massive proteinuria – urine protein \geq 4.0 g/L. Liver albumin synthesis does not cover their loss. Develop low-protein edema (nephrotic syndrome!). Described in the urine protein excretion > 50 g/day. Multiple myeloma in the urine appears labile protein ("protein bodies") Bence-Jones (MM = 25–45 kDa). It is precipitated by heating the urine to 45–60°C. The same protein, as well as Waldenstrom's macroglobulin, hemoglobin and myoglobin (in small amounts, short) may occur during exercise, at least – heart failure, hypovolemia, and lordosis.

Provocateurs proteinuria are antibiotics, especially aminoglycosides, phenolphthalein, captopril, etc.

The term "albuminuria" is obsolete, because the urine is never allocated only albumin.

Glucose in the urine, Lat glycosuria – glycosuria.

Glucose is freely filtered at the glomerulus. Its concentration in the initial urine such as blood plasma, but in the proximal tubule reabsorption is almost full with the glucose transporter proteins. In the secondary healthy human urine containing glucose in such small amounts that the quality is not determined by conventional reactions. The daily excretion of urine glucose – from 10 to 500 mg. In normal human blood contains 3.9–5.8 mmol/L glucose (0.7–1.05 g/L) blood glucose threshold for renal = 8.5–10.0 mmol/L.

Causes of glycosuria: diabetes mellitus, hyperthyroidism, acromegaly, hypercortisolism, pancreatitis, traumatic brain injury, stroke, epilepsy, severe

infectious diseases, asphyxia, disease and syndrome of de Toni-Debre-Fanconi (aminoatsido-, phosphate-and glucosuria) defeat tubules salts heavy metals cleavage products tetracycline poisoning strychnine, morphine, chloroform.

False positive reaction for glucose can cause: aspirin, sulfonamides, streptomycin, cephaloridine, cephalothin, furazolidone, zinkofen, chloral hydrate.

Ketone bodies in urine, ketonuria [Lat. acetum – sour wine, vinegar – aliphatic ketone] – appearance in the urine (positive reaction) of ketone compounds: acetone, acetoacetate and beta-hydroxybutyric acid.

Ketone bodies are synthesized in the liver from fatty acids, carbohydrates, and certain amino acids. Used as an energy material cardiac and skeletal muscle, in part – by the kidneys, the brain.

Reasons ketonuria: Heavy diabetes, at least – starvation, carbohydrate-free diet, acute infections, fever. In children – vomiting and diarrhea. Ketonuria developing thyrotoxicosis, cushing's, poisoning by isopropanol (isopropyl alcohol)

The daily urinary excretion of ketone bodies = 20–50 mg, but in some portions of urine ketone bodies through quality rapid methods are not defined.

The reaction of the urine for blood – Hemoglobinuria, *Lat.* haemoglobinuria and myoglobinuria, *Lat.* myohaemoglobinuria. Chemical determination of hemoglobin in the urine is rare because microscopy sediment erythrocytes are detected in the cases where the response to the hemoglobin may be more negative. Urine investigated hemoglobin must be fresh, as on standing hemoglobin is oxidized to methemoglobin, which lacks pseudoperoxidase activity.

False negative reaction with hemoglobin possible infection MFR bacteria that produce a large amount of peroxidase in the presence of protein in urine, high levels of ascorbic acid, nitrites.

When hemoglobinuria urine long retains the red color, with myoglobinuria – quickly darkens and becomes fulvous-brown.

Bilirubin in urine – bilirubinuria, *Lat.* bilirubinuria – urinary excretion of bilirubin – perhaps when the content in the blood of direct bilirubin >0.01 – 0.02 g/L. Urine with bilirubinuria yellow, amber, yellow-brown in color, with shaking produced copious yellow foam.

In the urine can only go direct bilirubin. Indirect bilirubin can not pass through the kidney filter.

Reasons of bilirubinuria: parenchymal and mechanical jaundice.

The practical value of samples used for the determination of bilirubin in urine is reduced in the later stages of parenchymal and jaundice, where, despite the high levels of bilirubin in the blood, it can not be detected in the urine. It is believed that this is due to the formation of bilirubin III, monokonyugirovannogo covalently bound to albumin. Last is not filtered by the glomerulus and consequently does not appear in the urine.

Urobilinoids (urobilinogen, urobilin body or bile pigments) in the urine – urobilinuria. "Urobilinoids" – decomposition products of bilirubin in the intestine (mainly – stergobilinogen which oxidation air becomes stercobilin (urobilin). Normally urobilinoids in urine represented sterkobilinogena tracks (up to 4–6 mg/day), are not detected by conventional quality samples, if properly executed.

Reasons urobilinuria (sterkobilinurii): hepatitis, liver cirrhosis, hemolysis, bowel disease.

Urobilinuria mechanism – the weakening of the liver, or an excessive intake of urobilinogen from the intestines to the liver.

Epithelial cells in urine – epitheliuria – the presence in the urine sediment >3–5 epithelial cells in sight (in field of microscope). The most important is not the quantity but the nature of the desquamated cells (kidney, tumor, etc.).

Reasons epiteliuria: tubular necrosis, nephritis, amyloidosis. Renal epithelium attach importance only in the presence of protein in the urine, cylinders and blood cells or detecting signs of protein or fatty degeneration. In a normal healthy person in the urine 0...3 epithelial cells within the field of microscope.

White blood cells in urine – Leukocyturia, *Lat.* leucocyturia – content in the urine sediment >10 white blood cells per field of microscope, or >2000 (4000) in 1 mL or >2000000 / daily urine.

Levels of leykocyturia:

- Slight – 10–20 leukocytes in field of microscope;
- Moderate – 20–60 leukocytes in field of microscope;
- Solid piuria >60 white blood cells in the field of microscope ("Completely" in all fields of view).

More often than in normal white blood cells in the urine 0–2 in field of microscope by males and 5 field of microscope by women. White blood cells are lysed easily, so the urine should be examined fresh (hot).

Reasons of leikocyturia:

Urinary system infection (pyelonephritis, tuberculosis, chlamydia, gonorrhea, etc.).

Erythroцитess in the urine – hematuria, *Lat.* haematuria – the presence in the urine of >1000 red blood cells in 1 mL or >1 million / daily urine.

Levels of hematuria:

– Gross hematuria, *Lat.* macrohaematuria – the presence in the urine sediment >12 red blood cells in the field of microscope (urine becomes red or brownish-red shade);

– Microscopic hematuria, *Lat.* microhaematuria – the presence in the urine sediment <7–12 erythrocytes in sight.

The urine with a low density and high pH erythrocytes rapidly lose hemoglobin and appear as a single or dual-rings (altered, leached erythrocytes).

In healthy human urine sediment erythrocytes either not detected or determined in Preparation 1–2 pieces.

The causes of hematuria: Kidney: glomerulonephritis, renal vascular thrombosis, renal tuberculosis, drug nephropathy, etc.; extrarenal: kidney stones, tumors, trauma, thrombocytopathia, an overdose of anticoagulants.

cylindruria – appearance in the urine sediment cylinders – curing products of proteins in the renal tubules or identify them in quantities of >50–100 in 1 mL of urine.

Isolated hyaline cylinders, waxy, grainy, false (cylindroids).

Hyaline casts [Gk. hyalos – glass] are present in the urine of a healthy person (<50–100 per 1 mL) consist of only precipitated Tamm-Horsfall protein, which is absent in the plasma, secreted by the renal tubules.

In glomerulonephritis major role in the formation of the cylinder begins to play filterable serum albumin.

Waxy casts – are similar in color to the wax; protein in them is tight.

Granular casts – hyaline and waxy cylinders covered with decaying leukocytes, erythrocytes and epithelial – evidence of serious damage to the kidneys.

False casts (cylindroids) – cylinders leukocyte, erythrocyte, epithelial, pigment, of mucus, etc.

All types of cylinders (casts) are well identified and long remain only in acidic urine. Epithelial cylinders are found in heavy metal poisoning, ethylene glycol; pigment – with the transfusion of incompatible blood, poisoning hematotropic substances.

Blennuria [Greek. blennos – slime + uron – urine] – urinary excretion of mucus – broken white blood cells and epithelial cells. Actually Slime – mucin in the urine almost does not contain.

Blennuria has no independent significance. To a large extent depend on the conditions of storage of urine and its pH.

The crystals in the urine: urates, oxalates, phosphates, rare (cystine, leucine, tyrosine, fat, bilirubin, hematin etc.).

Urates – stones, consisting of uric acid and urate ammonium.

Abundant and early loss in the urinary sediment of uric acid crystals in gout is not observed (deposition goes to the fabric!), and for conditions involving the collapse of the diseased tissue and acidic urine (renal failure), urine pH = 5.5–6.0. The growth of urate stones can strengthen ACE inhibitors.

Oxalates – calcium oxalate crystals. Identified in the use of foods rich in oxalic acid (tomatoes, spinach, apples, cranberries), and ethylene glycol poisoning, urinary pH = 5.1–5.9. Oxalaturia degree proportional to the extent of the inflammatory process.

Phosphates – calcium phosphate crystals. Detected in the urine with a pH \geq 6.5.

In the genesis of kidney stones – stone disease (nephrolithiasis) are: inflammation in the urinary tract, high urinary concentrations of salts, the presence of a template for stone formation and metabolic disorders.

Bacteriological examination can complement urine analysis.

Fresh urine contains a small amount of bacteria that are washed from the exterior of the genitals, the urethra. Bacterioscopic method is applicable only to fresh

urine. In a constant urine bacteria manage to propagate. Especially a lot of urine is *E. coli* and coccal flora. On pyelonephritis should think if urine taken from a bladder catheter, contains >50–100 thousands of bacteria in 1 ml.

In practice, often resort to indirect methods for evaluating the degree of bacteriuria – by adding to the urine of sulfanilic acid and alpha naphthylamine, or by the addition of trifeniltetrasolin chloride. When the content of 1 ml of urine > 100.000 microbial cells is loss of red sludge.

The most important diagnostic importance is possible seeding the patient from the urine of tubercle bacilli, gonococcus, the elements of hydatid cysts, etc.

Drugs and pathology of the urinary system

Basic mechanisms of nephrotoxicity of drugs

Nephrotoxic drugs, or "drug nephropathy" – directly or indirectly through the immune response damaging effects of drugs on AIM, and, above all, on glomerular and tubular kidney machine. The term "nephropathy" less wide than the "nephrotoxicity". It is a generic with respect to only four pathological states:

- Acute glomerulonephritis,
- Rapidly progressive glomerulonephritis,
- Chronic glomerulonephritis,
- Nephrotoxicity syndrome.

The most important syndromes of nephrotoxicity:

- Capillary and tubular necrosis;
- Nephritic;
- Nephrotic;
- Renal failure (from mild to uremia);
- Renal hypertension;
- Stone disease and urinary tract obstruction;
- Nephrogenic diabetes insipidus.

The major symptoms of nephrotoxicity:

- Gipostenuriya;

- Proteinuria;
- Hematuria;
- Leykotsituriya;
- Hyperuricemia;
- Dysfunction of the bladder (urinary incontinence, acute urinary retention);
- Changes in pH, color, transparency of urine;
- Azotemia.

Among the well-known (as described in the manuals of clinical pharmacology) mechanisms of side effects of drugs in development are the main direct nephrotoxicity (necrosis!) or immune responses mediated through damage to the glomeruli and tubules of the kidney, at least – of the lower urinary tract.

Nephrotoxicity of the individual drugs

Kidney disease have a more than 20% of patients with drug allergies when applying:

- Antibiotics,
- Sulfonamides,
- Pirazolan derivatives
- Phenothiazines,
- Preparations of gold,
- Serums and vaccines.

They usually occur after 2 weeks of treatment in the form of proteinuria, microscopic hematuria, leukocyturia.

Immune damage to the kidneys are mainly immunocomplex character with the deposition of IgG, M in the glomeruli and the development of cytotoxic effects. Symmetrical cortical necrosis of the kidney is the result of allergic shock with thrombosis of renal capillaries, with the development of oliguria and anuria.

"Analgesic nephropathy" develops in 10–15 years of systemic administration of analgesics. Manifested by polyuria, nocturia, renal colic, chronic renal failure, anemia. The mechanism of "analgesic nephropathy" – change veins – renal ischemia

– acute necrosis with a separation capillary tips of the papillae – ureteral obstruction. Further developing chronic renal failure, hypertension, increased liver (60%) and spleen (in 20% of cases). "Analgesic nephropathy" in recent years in the form of whole epidemics marked when taking salicylates [Zmushko E.I., Belozyorov E.C., 2001].

The overall renal failure can cause more than 70 drugs: sulfonamides, antibiotics, anticoagulants, X-ray contrast agents.

The drug glomerulonephritis can occur with prolonged treatment with hydralazine, cephalosporins, antidepressants (paroxetine), polyene antibiotics (nystatin, levorin, natamycin, amphotericin). Well known for a high degree of nephrotoxicity of aminoglycosides (gentamicin, streptomycin, etc.), amphotericin B, polymyxin. However, each antibiotic in one way or another nephrotoxic. In general, the defeat of MBC in second place after neurological disorders among all the toxic effects of antibiotics. Kidney damage ascertained in 20% of patients treated with streptomycin. Chlorotetracycline 30% of patients causes symptoms of renal diabetes. Even low-toxicity penicillins in 7—10% of patients with lower density of urine, causing a small proteinuria, hematuria. Hematuria provoke some second-line drugs, cytotoxic drugs, overdose of vitamins A and E.

With the combination of antibiotics and sulfonamides with corticosteroids is highly probable candidiasis urinary system

Barbiturates may cause oliguria and even anuria. This is due to the enhanced production of antidiuretic hormone (stimulation of the hypothalamic-pituitary their activity). Additionally, renal disease barbiturates in urine excretion decreases by less than 50%.

Tranquilizers, atropine reduced bladder contractile activity and undesirable in prostate cancer.

Aminoglycoside nephrotoxicity seen after 4–7 days of treatment (kanamycin, gentamicin): proteinuria, hematuria, cylindruria; oliguria. Proteinuria is characterized by the appearance of protein in the urine of MW >60<150 kDa. Histopathological changes in the kidneys – from malnutrition to necrosis of glomeruli and tubules. When creatinine clearance by 25% nephrotoxicity of aminoglycosides appears natural. The decrease in creatinine clearance by 50% – the basis for the cancellation of an aminoglycoside.

Nephrotoxicity of polymyxin polypeptide is determined by their structure. Neuro- and nephrotoxicity – side effects which are the main applications of these

limiters antibiotics in the clinic. Symptoms of toxic damage to the kidneys polymyxins: proteinuria, hematuria, cylindruria (after 1–2 weeks of treatment), azotemia. Kidney disease associated mechanism (like aminoglycosides) with a high concentration of antibiotic in urine (5–15 times higher than in blood when administered intramuscularly). Changes usually disappear within 7–10 days after discontinuation.

Symptoms are similar to those of nephrotoxicity of *vancomycin* and aminoglycosides with polymyxin.

Isoniazid is a major component of all the schemes of anti-TB therapy. Ganglioplegicheskoe effect of the drug determines the occurrence of urinary retention in patients with BPH.

Sulfa drugs can cause a range of side effects (hematologic, neuro-psychiatric, etc.). Renal dysfunction ($\approx 5\%$ of cases), usually clinically mild (pain, fever), but violations of urine sediment – significant: proteinuria, cylindruria, hematuria, the presence of sulfate crystals. Number recent increases downwards as urine density increases. Means of struggle – increase urine output to 2 liters / day and alkalization of urine (up to 12 g/day of soda), and the use of sulfonamides are excreted slowly.

Nephrotoxicity of *nitrofurans* disputable because they create for the treatment of urinary concentration (50–500 ug/mL) in 10–100 times higher than in blood. Formulations nevertheless readily soluble in urine and do not violate the morphological and functional properties of the kidneys.

It should be noted that long-term use of nitrofurans, although reversible, but inhibited spermatogenesis [G. Panaitescu, E. Popescu, 1976].

Non-steroidal anti-inflammatory drugs cause a small proteinuria, microhematuria, cylindruria. The mechanism of this action – degeneration of the epithelium of glomeruli and tubules. This is evidenced by the appearance of secondary urine protein with MW 100 kDa. Phenylbutazone inhibits tubular reabsorption and contributes to the delay in the body of water, salts, excretion of other drugs. It should be emphasized that the clinical edema in patients receiving butadiona appear at a delay in the body of >6.5 liters of water.

Phenacetin. The reason for its nephrotoxic action – interstitial nephritis (long-term use of the drug) as a result of toxic and allergic effects on the glomeruli and tubules, loss of potassium and create conditions for the development of urinary tract infection. Symptoms: polyuria, reduction in the density of urine, hematuria, leukocyturia, azotemia, decreased glomerular filtration and tubular reabsorption,

anemia metrorrhagias, withdrawal syndrome in children – inhibition of phenacetin glykuroniltransferazy and bilirubin-I deposition in the gray matter of the cerebral cortex and cerebellum.

Gold salts. Used in the treatment of rheumatoid arthritis ("treatment of disease of unknown etiology unknown drug action"). Nephrotoxic drugs is seen in 50% of patients: proteinuria, microscopic hematuria, coagulation necrosis of the tubules.

Glucocorticosteroids. Side effects of their multifaceted. Of renal function may occur: glycosuria (steroid diabetes), sodium retention, water, increased excretion of potassium and calcium, azotemia. There are cases of steroid bilateral necrosis of the kidneys.

Alpha-methyldopa (dopegit) is a decarboxylase inhibitor, fermenting, the 5-hydroxytryptophan to serotonin. Causes an increase in renal tubule reabsorption of sodium. Thiazide diuretics attenuate this effect dopegita.

Phenolphthalein can cause a small proteinuria. Furthermore, it stains alkaline urine (feces and alkaline) in red (phenolphthalein color change depending on the pH of the solution is well known in chemistry!) And simulates this haematuria (hemorrhoids).

Cytostatics, causing massive damage to white blood cells and the release of large amounts of uric acid, may provoke the development of nephrolithiasis, gout attacks, cause proteinuria cylindruria.

Antivirals – rimantadine, deytiforin, adapromin – can cause urinary retention, acyclovir, farmatsiklovir, valacyclovir – called when the on / in a formation of urinary crystals.

Diuretics are actively influence the processes of ion and mass transfer in the tubules, causing eye irritation and damage. Thiazide diuretics sometimes provoke an attack of gout.

Nitroimidazoles (metronidazole, tinidazole, ornidazole increase diuresis, as partially block receptors of angiotensin II.

Ammonium chloride and calcium chloride previously widely used as "acid-diuretics." Their main disadvantage — provoking hyperchloraemic development of acidosis.

Nephrotoxicity inherent antiarrhythmic, psychotropic drugs, anticoagulants, but in reality, it develops later in the damaging effect of these tools on the heart, nervous system, blood, and moves them to the back of nephrotoxicity.

The principles of prevention of drug nephrotoxicity

The principles of prevention of nephropathy:

- The rejection of foods containing allergens obligate: coffee, cocoa, chocolate, honey, nuts, citrus fruits, eggs, and meat, fish, crabs, shrimp, caviar, smoked, canned, digestible carbohydrates;
- Exclusion of polypharmacy, rational pharmacotherapy;
- To limit the use of antibiotics and antimicrobial agents for viral colds;
- Careful use of drugs with a small period of clinical use (being in the pharmacy network);
- Exclusion of drug released from the expiry date.

Special "renoprotective" no money, but studies have shown a positive effect on renal function in diseases of the connective tissue of drugs such as enalapril and magnerot.

At which developed nephrotoxicity should use the principles of antidotal therapy, including the use of drugs – inducers of microsomal oxidation: phenobarbital (reducing the effects of coumarin drugs, anticoagulants, cardiac glycosides, griseofulvin), rifampicin, diphenhydramine, phenylbutazone, carbamazepine, diazepam. Diuresis is expedient to hold at about 1500 mL/day.

Derivation barbiturates enhanced by applying alkalinizing agents, such as soda. Caffeine and other purine derivatives (theophylline, theobromine) increase urine output, and it is not about their inhibitory effect on tubular reabsorption of water, characteristic of most "classical" plasma protein that facilitates the production of water in the interstitium, blood vessels and kidneys. Caffeine intensifies the production of antidiuretic hormone (ADH), but this effect develops late and is not a determining factor in its effect on the diuresis.

Reduce the pH of urine (urine becomes acidic!), ascorbic acid, calcium chloride, ammonium chloride, arginine chloride, sulfur-containing amino acids.

In acidic urine output better LS-base: quinidine, morphine, codeine, etc., in neutral and alkaline – LS-acids: salicylates, nalidoxie acid, barbiturates, diakarb etc.

The reaction of the urine is shifted to the alkaline side in pregnant women, which should be considered when assigning them drugs

In an acidic environment are active:

- Trimethoprim,
- Novobiocin,
- Penicillin,
- Nitrofurans.

In alkaline chart:

- Streptomycin
- Gentamicin
- Neomycin,
- Erythromycin,
- Sulfonamides,
- Nalidoxic acid.

Stool analysis (stool sample)

Medicinal lesions of the gastrointestinal tract (GIT) occupy one of the leading medication side effects. In most cases the drug when administered orally irritate mucous membranes of the gastrointestinal tract. NSAIDs (Nonsteroidal AntiInflammatory Drugs) can cause stomach and intestinal bleeding, potassium chloride – perforation of the small bowel, antibiotics – disbiotsenez, antispasmodics – gastrointestinal dysmotility.

Feces, *Lat.* faex, faeces, copros, excrementum [*Lat.* faex = litter, sediment; *Lat.* faeces – feces; *Greek.* copros – feces; *Lat.* excrementum – feces, sewage (feces, urine, sputum, lochia, menstrual blood)] – stool; *Lat.* sedes – the seat of a chair, stool.

Defecation, *Lat.* defaecatio [*Lat.* = Purification] – a natural act of removing feces; urge to defecate occurs when the pressure in the rectum \approx 40–50 mm height of water, at which 30% of healthy people are defecation 1 time/day, 60% – 1–3 times/day, and 10% – 1 times in 2 days.

Constipation, *Lat.* constipatio (obstipatio) – chronic delay stool > 48 hours and / or hard stools / <100 g of solid stool/day, which requires more time and effort to the act of defecation, often accompanied by pain and / or incomplete bowel movement.

Coprostasia, *Lat.* coprostasis – calories in the form of hard rounded lumps, defecation difficult.

Diarrhea, *Lat.* diarrhoea [Greek. = Diarrhea] – stool >3 times/day. or a one-time allocation of liquid stool or chair weighing >300 g/day. in patients treated with moderate amounts of plant food / increase in water in the stool.

The composition of feces: water = 75–80%, a solid residue = 20–25%. Half of the solid residue is occupied bacteria (90% of them are dead), the rest – the remnants of food, gastrointestinal secretions.

Polyfaecalia, *Lat.* faeculentia – allocation for the day more than 500 g of feces.

Shaped stool – cylindrical shape of feces and dense texture (consistency).

Liquid mushy stool – contains water >80–85%; **hard stool** – contains water <50%. **"Sheep" stool** – fragmented, dense feces. **Ribbon stool** (the pencil) – a consequence of prolonged spasm of the sigmoid colon and rectum or obstacles in the rectum.

Stool color – "normal" – from light yellow to dark brown. Depends on the presence of stercobilin, food pigments.

Plant pigments (chlorophyll) contained in the sorrel, spinach and others give greenish feces, black currants – black or reddish, beets – first pink, then reddish, blueberry, chocolate, as well as preparations of bismuth and iron stained stool in black; rhubarb, senna – a yellow-brown, pork – a reddish, beef – in black and brown, Purgenum fecal pH>7.0 – a reddish (normal stool pH = 6.0–8.0 (7.0) barium sulfate determines the white or light yellow color of feces.

Yellow or golden color children's stool – a consequence of presence of bilirubin (no deficit microflora transforming bilirubin in stercobilin). When you restore only to the stage of bilirubin biliverdin cal turns green.

"Clay" (acholeic, discolored) stool – the result of deficiency of bile into the intestinal lumen.

Whitish shaped stool – amylorrhoea – the result of the presence of undigested starch in the feces of the enzymatic deficiency of the pancreas (amylase).

Bloody stool (red color!) indicates bleeding from the rectum (hemorrhoids) or (rarely) the outpouring of more than 1 liter of blood from the upstream parts of the intestine.

Stool of the "crimson" (blackberry) jelly, *Lat.* faex «rubi gelatinosi» observed in volvulus, accompanied by bloating and tenesmus – futile painful impulses (in the stool).

Blood in stool samples determined with benzidine (blue-green coloring!) or headache tablets (purple coloring!). The last test is less sensitive.

Black, similar to tar stool – melaena [Greek. melas black + haima, *Lat.* haema blood] – feces as a black adhesive mass or black streaks – result effusion at least 60 mL and not more than 1 liter of blood in the esophagus, stomach, duodenum. Black feces determined by the formation of iron sulfate.

Lienteria [Greek. leios sleek + enteron gut] – diarrhea with undigested particles in the stool.

Creatorrhoea [*Lat.* creatura creature, creature (man, animal) + Greek. During rheo] – allocation of the faeces products related to animal tissues / allocation of feces with a lot of poorly digested or undigested muscle fibers – the result of achylia, failure of the excretory function of the pancreas.

Steatorrhea [Greek. stear fat, tallow + rhoe for] – fat excretion in feces >7 g/day. (in 5 portions daily stool and dietary intake of at least 100 grams of fat) – when sprue failure excretory function of liver, pancreas, at least – an enzymatic activity of the intestine. Detected in the stool fat particles. Steatorrhea moderate – stands out in the night of fat >7<15 g, expressed >15<35 g, heavy >35 severity of steatorrhea in lesions of the liver corresponds to the degree of jaundice.

The stools have a kind of "rice water" in cholera, "pea soup" – in typhoid fever.

The smell of feces, *Lat.* odor faecis – depends on the presence of fecal indole, skatole, phenol, cresol and other products of bacterial decomposition of protein. With a large number of proteins in the diet sharp smell of feces, in putrid processes – fetid (ammonia), and fermentation dyspepsia (evolution of CO₂) – sour. Fasting feces almost odorless.

Mucus in stool – normally barely noticeable. Accumulations of mucus found in inflammatory processes in the gut.

In the stool should not be animalculines, helminths (including their eggs and fragments).

Stoll newborn – meconium [Gk. mekonion = juice] – the first 2–3 days. After 8–10 hours after birth, there is a first defecation, feces looks unformed thick, viscous mass of dark green, acidic, odorless, 70–100 g/day.

Stool healthy child who is breastfed – shapeless, mushy, golden yellow, turning green in the air, the smell of sour (acidic pH) contains bilirubin, a large amount of fatty acids, a little bit of mucus, white blood cells, neutral fat, 40–60 g/day, 2–3 times/day.

Stool healthy child who is bottle-fed – unformed, thick, pale yellow, the air does not turn green, pH neutral or slightly alkaline.

Gastrointestinal microflora

The upper portion of the small intestine (duodenum and small intestine) is practically sterile. They may be a small number of lactobacilli, streptococci and veylonella. In the ileum (3/5 of the lower small intestine) is contained in 1 mL of the chyme to 10^6 of *E. coli* and anaerobic bacteria. In the colon, revealed more than 400 species of bacteria in the amount of 10^{11} – 10^{12} /mL of feces. However, the individual composition of the microflora of the colon in humans is determined by eight or nine associations of anaerobic and facultative – anaerobic microorganisms, including main:

- Bifidobacteria – 10^8 – 10^9 /g,
- Lactobacilli – 10^6 – 10^8 /g,
- Escherichia (*E. coli*) – 10^6 – 10^8 /g,
- Enterococcus – 10^5 – 10^6 /g,
- Peptostreptococcus – 10^5 – 10^6 /g of feces.

By pathogenic (saprophytic) microflora of the large intestine include:

- Bacteroides – 10^7 – 10^{11} /g,
- Peptococcus – 10^5 – 10^6 /g,
- Streptococcus – 10^4 – 10^5 /g,
- Clostridium $\approx 10^3$ /g,

– Molds $\approx 10^2$ /g, and a small number of staphylococci, Candida, Proteus, Klebsiella, etc.

Depending on the nature of nutrition, lifestyle, the environment can be detected in the feces of small (up to 100 in 1 g of feces), the number of "transient" species of micro-organisms: non-fermentative Gram-negative rods, flavobacterium, pseudomonas, atsinetobakter etc.

The colonization of microbes sterile intestine begins in the first days after birth. The composition of the intestinal microflora changes dramatically after weaning. In adults, as already mentioned, it is also deeply individual that requires a great deal of caution in carrying out various "treatments" dysbacterioses, imbalance indigenous (local) of the intestinal microflora.

The physiological role of the intestinal microflora

1. Production of enzymes involved in the digestion of proteins, fats, carbohydrates, nucleic acids, cholesterol metabolism, absorption of calcium, iron, vitamin D.

2. Synthesis of some essential amino acids, vitamins, K.

3. Block settlement intestinal pathogenic and conditionally pathogenic microflora (competition for dietary factors and receptors binding, production of antibiotic compounds: reuterin, plantaritsin, lactocidine, laktolin, colicin; production of acetic and lactic acids, preventing the proliferation of *Proteus*, *Clostridium*, *Shigella*, *Salmonella*, etc., participation in the development of exopolysaccharide glycocalyx – a protective film on the mucous membrane of the intestine).

4. Detoxification of xenobiotics (the processes of hydrolysis and reduction).

5. Stimulation of interferon, lysozyme, etc.

Dysbacteriosis or disbiocenesis – qualitative and quantitative violation of the natural intestinal flora.

Degree of dysbiosis:

I – reduction in the number of bifidobacteria and lactobacilli in the order of 1–2. Clinic: loss of appetite, bloating, constipation, irregular coloration of feces.

II – in the presence of one type of stool conditionally pathogenic microorganisms ($<10^5/\text{g}$) or association ($10^3\text{--}10^4/\text{d}$), the occurrence of *E. coli* or *laktobacillus* with altered enzymatic properties. Clinic: indigestion, changes in odor, color, feces, etc.

III – the presence of bacteria in the feces stateally in high titers. Clinic: transient bacteremia (fever, symptoms of intoxication), persistent diarrhea, intestinal colic, bacteriuria.

The composition of the microflora of feces requires bacterial inoculation test. Smear-differentiated: *Mycobacterium tuberculosis*, non-pathogenic flora iodophilic in

amyloidosis, fermentative dyspepsia, as well as the animalcules: amoeba dysentery, intestinal amoeba balantidium E., E. Giardia, Trichomonas, fungi of the genus Candida, helminth eggs, larvae of roundworms, tapeworms, or segments of their body completely: hepatic, Siberian, the lancet fluke, tapeworm wide, dwarf tapeworm, roundworm, pinworm, whipworm, an intestinal ugritsa, echinococcus, alveococcus, unarmed tapeworm, schistosoma.

Drugs that can cause diarrhea

– Laxatives: salt, phenolphthalein, castor oil and petrolatum, rhubarb root, buckthorn bark, senna leaves, mukofalk;

– Antacids containing magnesium salts;

– Means comprising a potassium salt;

– Artificial sugar: sorbitol, mannitol – increase the volume of water in the stool!

– Cephalosporins, clindamycin, lincomycin, ampicillin, and others – dysbiosis!

– Antiarrhythmic drugs: quinidine, propranolol, procainamide, aymaline, cardiac glycosides – a damaging effect on the epithelium of the digestive tract!

– Indirect anticoagulants (vitamin K antagonists) warfarin, sinkumar, pelentan – effect on the micro!

– Chenodeoxycholic acid (henofalk) and cholagogue – increased motility of the digestive tract!

– Sympatholytics: guanetidin (izobarin), reserpine;

– Imidazoline receptor agonists: rilminedin;

– Alpha-2-adrenostimulatory: methyl dopa;

– Thyroid hormone drugs: levothyroxine sodium, liothyronine, thyreocombum – stimulation of GI motility!

– Iodide.

Laxative effect is also: aloe juice, agar-agar, sea cabbage, flaxseed, boltings (siftings), vegetable oils: almond, olive.

Antidiarrheal agents

- Antispasmodics: papaverine, drotaverine (no-schpa), meteospazmil, mebeverin;
- Anticholinergics atropine, platifillin extract of belladonna;
- Mu receptor agonists: loperamide (Imodium), as well as opioids: morphine, promedol, fentanyl;
- Octreotide (Sandostatin) – a synthetic analogue of somatostatin (antisecretory action!)
- Enzymes: pancreatin, pankreoflet, zimopleks, betaine (atsidin-pepsin) abomin, panzinorm, festal, mezim forte, pankurmen, enzistal;
- Defoamers: Espumizan (dimethicone);
- Astringents: Tannakomp (albumins tannin 0.5 + lactate etakridina 0.05);
- Chelators: carbol, karbolong, mikrosorb-P enterosorb, cholestyramine, Polyphedanum, enterokat-M lignasorb, white clay, smectite, Neointestopan (attapulgit);
- Indigenous (autochthonous, private) microflora correctors, or BTA – "biotherapeutic agents":
 - a) products containing bifidobacteria: bifidum, Bifidobacterium bakterin forte, bifikol, bifidin, bifilong, bifilin, bifatsid, bifiform;
 - b) preparations containing lactobacilli: laktobakterin, biofruktolakt, atsilak, Acipol, Biobakton, primadofilyus;
 - c) preparations containing colibacteria: colibacterin;
 - d) milk biologics: bifilakt, Rostock, Rostock 1, Vitalakt, Biolakt, bi-forms;
- "Selective decontamination agent":
 - a) bacteriophages: amount proteus, staphylococcus, pseudomonas, klebsielesny, piobakteriofag, intestibakteriofag;
 - b) eubiotics: baktisubtil (flonivin-BS), Linex, enterol, hilak fort biosporin, sporobakterin, Pamba;
 - c) antibiotics: intestopan, hlorhinaldola (Kwesi, efungil) nitroksolin (5-NOC), entero-sediv, nifuroxazide, itetriks, meksaza, meksaform; furadonin, ertsefuril; blacks

(nevigramon), metronidazole (trihopol, flags); sulfasalazine, ftalilsulfatiazol (ftalazol), mesalazine (Salofalk) polymyxin M sulfate, gentamicin.

Antihelminthic drugs

Group 1 – for the treatment of nematodes (roundworms invasions)

- Levamisole (Dekaris)
- Mebenazol (Vermoxum)
- Albendazole (nemozol)
- Pyrantel pemoat,
- Pervin embonate,
- Piperazine
- Befeny hydroxynoaftoat (naftamon)
- Karbendatsim (medamin)
- Diethylcarbamazine (ditrozin).

Group 2 – for the treatment of trematode infection (invasions flat articulate extra intestinal worms)

- Cloxyl
- Prakzivantel (Biltritsid).

Group 3 – the treatment of cestodoses (invasions flatworms)

- Niclosamide (Fenasal)
- Aminoakrihin
- Filiksan

Group 4 – means of spread-spectrum activity:

- Prakzivantel (Biltritsid).

Sputum analysis

Sputum [Lat. sputum – spit] – bronchial secretions, "spat" (clears throat), or obtained by suction devices at the person in the pathology of the respiratory tract.

"Normal" sputum can not be!

The structure of sputum analysis

1. Number (per day): a small, moderate, high, very high.

2. Colour:

colourless (vitreous)

yellow (yellow)

green

yellow-green

red (pink, bloody)

"rusty" (brown)

"crimson or "currant jelly "

chocolate (brown)

white-grey

dirty grey

"creamy" (white)

black.

3. Smell:

no (no odour) or weak

unpleasant

fetid (putrid)

cadaveric (nauseous)

specific

4. Consistency:

viscous, thick, liquid

5. Stickiness:

mild, moderate, severe

6. Foaming:

No (not foam), the weak, high

7. Lamination:

one -, two -, three-layer

8. Character (gross composition):

slimy, putrid, bloody, serous, mixed.

Microscopy:**9. Epithelium:**

flat – single, a lot;

cylinder – single, a lot;

alveolar macrophages – a bit much;

siderophage – availability;

dust cells – availability;

menophage – availability;

neoplastic (abnormal) cells – the availability.

10. White blood cells:

neutrophils – a little, a moderate amount, a lot;

eosinophils – a little, a moderate amount, a lot;

lymphocytes – individual, a lot;

basophils – availability;

monocytes – presence.

11. Red blood cells:

erythrocytes – isolated, moderate amount, a lot.

12. Fiber formation:

Kurshman spiral – a little, a moderate amount, a lot;

elastic fibers ("normal") – presence;
elastic fibers staghorn – availability;
calcified elastic fibers – availability;
fibrinous fibers (filaments of fibrin convolution) – presence;
diphtheria film – availability;
necrotic lung slices – presence.

13. Crystals:

Charcot-Leyden – a little, a moderate amount, a lot;
cholesterol – availability;
fatty acids (cork Dietrich) – presence;
hematoidin – presence.

14. Foreign bodies – presence.

Bacterioscopy:

15. BC (Koch's bacillus) – not detected, detected.

16. Other bacteria – not detected, detected:

pneumococci catarrhal (*Bacillus influenzae*)

pneumococci (diplococci) Frenkel-Vekselbauma

pnevmobacillus Friedlander

Pfeiffer bacillus

streptococci

klebsiela

stafililococci

pseudomonas aeruginosa

colon bacillus

Loeffler bacillus.

17. Fungi:

Candida, Aspergillus, actinomycetes, Cryptococcus.

18. Elementary:

trichomonas.

19. Helminths:

ascaris, echinococcus.

Number of sputum – cough volume:

meager number of sputum – some spitting 1–5 mL;

moderate – 50–100 mL/day.;

large – 200–300 mL/day.;

very large (copious) > 300 mL/day.

Colour — depend on the composition (structures character) sputum:

– Colourless – glassy, slimy, transparent. The basic cell structure – lymphocytes, squamous epithelium;

– Yellowish – muco-purulent. Yellow sputum eosinophils attached;

– Green – purulent. Green sputum neutrophils attach to, or rather, the decay products of the enzyme zhelezoporfirinovoy verdoperoksidazy neutrophils;

– Red – bloody. The red color of sputum give fresh red blood cells;

– "Rusty" – with lobar pneumonia – color gives a breakdown product of hemoglobin – hematin;

– White ("creamy") – in the presence of a large number of lymph sputum, white sputum millers;

– Black sputum gives coal dust, etc.

In describing the complex composition of sputum taken the predominant substrate is put in last place: purulent mucus, slizito-purulent, muco-purulent, bloody, etc.

The smell. Freshly isolated sputum is usually odorless. Bad smell sputum becomes prolonged standing, in putrid and purulent processes in the lung (gangrene,

abscess, bronchiectasis). Specific odors have phlegm when taking alcohol, antibiotics (the smell of mold), in cases of poisoning with acetic acid (violet odor), SM: valerian, marshmallow, anise, corvalolum, camphor, etc.

Consistency of sputum – density, viscosity. Sputum may be viscous (lots of mucus), thick (many form elements and epithelium), liquid (whey lot in sputum).

Stickiness of sputum. The more sputum fibrin, the greater its tackiness. Sticky mucus sticks to the slide, to the walls of the tubes (bowl).

Frothy. The more sputum protein (serum), the more it foams. Frothy sputum creates a big obstacle for ventilation.

The layering of sputum. Mucous expectoration – single-layer, the decay of tissue (gangrene of the lung, bronchiectasis) sputum three-layer: the bottom layer – pus (detritus), medium – the liquid portion, the upper – foam, phlegm-layer (upper layer – the serous fluid, pus bottom) – abscess, lobar pneumonia.

Components (substrates) of the sputum

- Mucus and sweaty plasma;
- Blood cells, airway epithelium, detritus;
- Bacteria and special inclusions.

Mucus – a product of the mucous glands of the upper respiratory tract. The mucous sputum in acute bronchitis, bronchial asthma resolution, acute respiratory infections, inhaled irritants airways.

Detritus [Lat. detritus = beaten] — the remains of the destroyed cells, tissues.

Charcot-Leyden crystals, *Lat.* crystalles Charcot-Leydeni – brilliant colorless diamond-shaped formation – a breakdown product of eosinophils – have a diagnostic value of bronchial asthma, allergic processes in the airways.

Lenses (lentils) Koch, *Lat.* lenticulae Kochi – melon seed body greenish-yellow colour, composed of detritus, tubercle bacilli and elastic fibers – a product of the collapse of the lung (in cavernous pulmonary tuberculosis).

Corks (particles) Dietrich, *Lat.* particulae Dietrichi – purulent plugs – lumps of whitish or yellowish-gray color, the size of a pin head with a fetid odor, composed of detritus, bacteria, crystals of fatty acids appear bronchiectasis, gangrene of the lung.

Kurshman Spirals, *Lat.* spirae Kurchmanni – spirally twisted transparent, whitish fibers, which are usually in the middle of a brilliant central thread is visible, can be covered with Charcot-Leyden crystals and eosinophils – pathognomonic for asthma – muco-protein casts spasm of bronchial tubes.

Cholesterol crystals – formed by the decay of zhiropererozhdennyh cells in sputum retention cavities (alveoli) and placed on a background of detritus, found in tuberculosis, abscesses, hydatid cyst, lung cancer.

Flat epithelium – deskvamat mucous membranes of the mouth, nose, throat, epiglottis, vocal cords. It is determined by the amount of saliva, mucus trapped in.

Columnar epithelium – deskvamat the mucous membranes of the trachea and bronchi. Found in the sputum in large quantities at an acute attack of asthma, acute bronchitis.

The alveolar epithelium (alveolar macrophages) – appear in the sputum in pneumonia, silicosis. Macrophages containing hemosiderin appear pulmonary infarction, hemoptysis in patients with left ventricular failure.

Microorganisms – smear-defined only when their content is not less than 10⁶ microbial cells in 1 ml of sputum.

Streptococci [Gk. streptos curved, kokkos grain] – the chain of spherical bacteria, characteristic of the sputum in suppuration in the lungs, at least for bronchitis, pneumonia, are not sensitive to aminoglycosides (only in combination with penicillin!).

Friedlander diplobacillus (pneumococcus) – pathogens of lobar pneumonia are resistant to aminoglycosides.

Mycobacterium Koch – TB germs.

Staphylococci [Gk. staphyle – bunch] – clusters of cocci, in hospitals is often detected *Staphylococcus aureus* – the causative agent of purulent processes.

Haemophilus bacteria, *Lat.* *Haemophilus influenzae* – short rods (“Lictor’s rods”) – cause acute respiratory disease. *Influenza bacillus* highlights chloramphenicol acetyltransferase and destroys chloramphenicol.

Pseudomonas aeruginosa, *Lat.* *Bacterium pyocyaneum* seu *Pseudomonas aeruginosa* – the causative agent of green festering. Antipseudomonas aeruginosa activity exhibit: inhibitor-protected penicillin, amoxycillin / clavulanate, ampicillin / salbaktam, ticarcillin / clavulanate, piperacillin / tazobactam, a combination of the

two penicillins (ampicillin, oxacillin +). By pseudomonas activity of drugs can be located as follows (in ascending order): carbenicillin < ticarcillin = azlocillin < piperacillin. But they are destroyed metitsilinazoy therefore combined with aminoglycosides II–III generations or ciprofloxacin (but not in the same syringe!).

Microorganisms from the eponymous names: Escherichia coli (E. coli Bacterium coli), Klebsiella pneumoniae, Moraxella catarrhalis.

Beta-lactamase activity staphylococcus, klebsiella, E. coli. They inactivate penicillin, ampicillin, cephalosporins.

Against most germs that cause of respiratory quinolones are effective generation III ("respiratory" difluorochinoines) sparfloxacin, levofloxacin, and macrolides: azithromycin and other fluoroquinolin II-generation ineffective against streptococci, pneumatic, enterococci, mycoplasma, chlamydia, spirochetes, Listeria and most anaerobes.

Sometimes resort to estimate the pH of sputum. It varies in a wide range – from 5.0 to 9.0. Typically, the reaction is slightly alkaline mucus. This should be considered when selecting drugs. Sputum becomes acidic either by decomposition or by admixing thereto gastric contents.

Antitussives

Centrally acting drugs:

– Codeine and drugs containing it: kodterpin, panadein, perdolan; neokodion (codeine kamfosulfonat + sulfogvayakol + Grindel thick extract);

– Containing folkodein (a derivative of morphine)

– Biokaliptol, geksapnevmin;

Non-narcotic central action:

– Glaucine, dimemorfan, okseladin, pentoxyverin,

peripheral actions:

– Levodropronizin, prenoksidiazin (libeksin)

Mucolytics, expectorants (clears throat):

– Dorniza alpha – deoxyribonuclease I – mucolytic;

– Acetylcysteine – mucolytic;

- Ambroksol – a metabolite of bromhexine – mucolytic;
- Bromgexine – mucolytic;
- Solvin expectorant (bromgexine + pseudoephedrine) – mucolytic;
- Karbotsistein – mucolytic;
- Mesna – mucolytic;
- Tonzilgon (marshmallow root + chamomile flowers + horsetail + yarrow leaves + walnut + dandelion + oak bark);
- Pulmeks (Peru balsam + camphor + eucalyptus and rosemary oils);
- Fees (herbs) № 1, 2, 4;
- Rosemary;
- An extract of licorice root;
- Tussamag (liquid extract of thyme)
- Thymine (a mixture of extracts of the root of the primrose (primula) and the root of Pimpinella aniseturn);
- Sinupret (gentian root powder + primula flowers + verbena + sorrel flowers + elderberry);
- Mukaltin (extract of the herb marshmallow + sodium bicarbonate);
- Bronhosan (bromhexine + menthol + oil of fennel, anise, marjoram, peppermint, eucalyptus);
- Bronhikum drops (tincture of herbs thyme, quebracho, Saponaria) bronhikum elixir (Grindel tincture of herbs, roots wildflowers, primrose root, bark quebracho, thyme)
- Doctor MOM solution (eucalyptus oil + menthol + camphor + methyl salicylate);
- Zedeks (bromgexine + dextromethorphan + ammonium chloride + menthol);
- Karmolis (menthol + oil of thyme, anise, Chinese Cinnamomi, clove, lemon, lavender angustifolia, broadleaf lavender, citronella, sage, nutmeg oil);
- Terpon (Turpin + essential oils of Siberian pine, nyauli, eucalyptus);

- Pektussin (menthol + eucalyptus (eucalyptol));
- Pertussin (extracts of thyme, cumin + potassium bromide);
- Stoptussin (butamirata citrate + guaifenesin);
- Trisolvin (ambroksol + guaifenesin + theophylline);
- Altaleks (a blend of essential oils of lemon balm, peppermint, fennel, nutmeg, cloves, thyme, pine needles, aniseed, eucalyptus, sage, cinnamon and lavender);
- Protiazin expectorant (guaifenesin + promethazine + extract of ipecac);
- Mukodeks (bromgexine + dextromethorphan + chlorphenamine).

Drugs that cause affection of the respiratory system

1. Drugs, tranquilizers, sedatives, barbiturates, anti-histamine funds - cause relaxation of the respiratory muscles to the development of pulmonary hypoventilation.

2. Diakarb, ethacrynic acid - cause violations of water-electrolyte and acid-base so9stoyaniya.

3. Respiratory analeptic agents - cause hyperventilation, respiratory muscle fatigue.

4. Medicines (large group) causing asthmatic symptoms (bronchospasm, airway obstruction phlegm), including the expense of allergic reactions:

- beta blockers, anticholinergics, sympatholytics;
- chymotrypsin;
- non-steroidal anti-inflammatory drugs;
- iodo, bromo, procainamide;
- antibiotics, sulfonamides.

Danger Inhalation of mineral oils, which, in contrast to the plant, do not expectorate (suppress the cough reflex!), Inhibit the activity of the ciliary epithelium, are absorbed by macrophages and cause chronic inflammation.

Morphine, nitrofurans, aspirin can, although rarely, cause a respiratory distress syndrome.

Cytotoxic agents, corticosteroids can cause aggravation of purulent processes in the lungs, or cause them. Immunosuppressive action has chloramphenicol.

Allergic drug-induced bronchial accompanied by phlegm, characteristic of asthma (eosinophils, Kurshmana spirals, Charcot-Leyden crystals).

When the dosage pneumonia (PAS, sulfonamides, antibiotics) in the sputum appear streaks of blood, a large number of eosinophils.

Drug asthma often occurs in people who work in the production of drugs and involved in their implementation.

Analysis of the gastric juice

Gastric juice succus gastricus (stomach contents) - The Secret of the stomach, colorless liquid acidic, extracted from the stomach by probing (in the last decade, only multiple moment (fractional)) - aspiration method with a thin probe - a rubber tube length 100-150cm, external diameter of 4-5mm and 2-3mm internal. At intervals of 15 minutes produced 5 aspirates [Lat. aspiratio - sucking, breathing] - on an empty stomach and 4 after stimulation of gastric acid secretion (histamine, pentagastrin, insulin). Determine in each batch volume (ml) of juice, its acidity (in microtiter units - ml of 0.1% solution NaOH), calculated flow rate of hydrochloric acid hour.

Probe only reliable method juice at pH <2.1. At pH >2.1 method underestimates the numbers of acidity.

The composition of the gastric juice

Water, about 0.5% hydrochloric acid, little (less active) lipase enzyme; gastromukoprotein (Castle intrinsic factor), mucin – total mukoproteidov to 8 g/L protein – to 3 g/L; mukoproteazy – to 7 g/L; protease pepsin, renin, cathepsins, gelatinase, parapepsiny, chloride salts of potassium, sodium, ammonium phosphates, sulfates, creatinine, glucose, adenozyfosfornye acid, food debris, desquamated epithelium, uric acid, ammonia, urea.

Number of the gastric juice:

fasting 0–180 mL (mostly = 0–50 mL);

after the test meal: I phase secretion 50–100 ml, II phase 50–150 ml, per day 2–3 L gastric juice.

The smell of gastric juice – is absent or slightly sour, putrid at rotting food proteins (decay of cancer of the stomach, pyloric stenosis); sour in hypo- and anacidic gastric juice through fermentation products (oil, acetic acid, lactic acid).

Color of gastric juice – colorless. Stained gastric contents regurgitant bile, blood.

Slime – a small amount. Mucin - mukoproteinov complex, protects the gastric mucosa from the damaging effects of HCl, pepsin. Gastromukoprotein (intrinsic factor Castle) is required for the intestinal absorption of vitamin B12, folic acid.

Gastric acidity

Hydrochloric acid (HCl) is produced by parietal cells of the stomach, creating the optimum pH for protein foods, preparing them to hydrolysis, is involved in the hormonal excitation major glands of the stomach and endocrine secretion of the pancreas is one of the regulators of motility of the stomach and colon, has a bactericidal effect.

Physiological stimulant of acid in the stomach is the hormone gastrin, produced in the antrum (pylorus) of the stomach. Specific stimulator of gastric acid is histamine. They provide the basal secretion of gastric juice to 50 mL/hr to 200 mL/hr in the sample with the maximum stimulation (histamine).

Normoacidity, *Lat.* normo(a)ciditas – basal gastric pH = 1.6–2.0, stimulated = 1.21–1.8.

Hypoacidity, *Lat.* hypo(a)ciditas – reduced gastric acidity: pH>2.1<6.0.

Hyperacidity, *Lat.* hyperaciditas - increased acidity of gastric juice: basal pH<1.6, stimulated pH <1.2.

Anacidity, *Lat.* anaciditas – the absence of acid in the stomach, the gastric juice in the appearance of lactic acid bacteria, lactic acid; pH> 6.0.

Total acidity – the sum of all factors acid which may be in the stomach: the free and bound hydrochloric acid, acidic phosphates, organic acid: lactic acid, butyric acid, acetic acid, carbonic. Determined by titration with 0.1% solution of phenolphthalein in the presence of NaOH (to pink coloration.) The normal basal total acidity = 40–60 titration units. (Ml of 0.1% solution of NaOH), with maximal stimulation titer = 100–120 titr. u.

Free hydrochloric acid – the main part of acidic stomach contents - that part HCl, which is contained in the stomach in the form of dissociated hydrogen ions and

chlorine. Determined by titration with NaOH in the presence of dimetilamidoazobenzola (up to color "salmon" – orange-yellow) or Congo red (in the presence of free HCl Congo red piece of paper turns blue.) Normally, the basal level of free hydrochloric acid titer = 20–40 titr. u., after maximal stimulation = 90–110 titr. u.

Related hydrochloric acid – part HCl, chemically bound to the proteins of the gastric juice. Determined using the indicator alizarinsulfonovokislogo sodium. Becomes purple after neutralization of acidic valences bound except HCl. Normally, the amount of HCl increases associated with the accumulation of protein products in the stomach (food, decaying tumors, inflammation).

Debit hour hydrochloric acid (determined only when receiving all time portions gastric juice) – gross amount of HCl, isolated stomach per unit time (hour). Preference is given to debit-hour total acidity.

The formula for calculating flow rates HCl:

$$1) D = V_1 \times E_1 \times 0,0365 + V_2 \times E_2 \times 0,0365 + \dots,$$

where D is debit of HCl (mg), V – volume of a portion of the gastric juice (ml)
E – concentration of HCl (in titr. u) 0.0365 – number of milligrams in 1 mL of HCl gastric juice at a concentration of 1 its titr. u.

$$2) D = V_1 \times E / 1000 + V_2 \times E_2 / 1000 + \dots,$$

where D – debit HCl in mmoles.

Normally, the total flow rate of HCl: basal secretion = 1.5–5.5 mmol/hr, with maximum stimulation = 18–26 mmol/hr.

Pepsin, *Greek*. peptikos – peptogenic – the main enzyme that breaks down protein. Normally, the "power hour" of pepsin in gastric juice after breakfast cabbage = 21–45 mg/L (basal secretion = 10–40 mg/hr, max = 90–160 mg/hour). Activated at pH = 1.5–2.65. Uropepsin – normal = 38–96 mg/day. Debit-hour on an empty stomach = 2.3 mg.

Significance of study has elements of gastric mucus (leukocytes, erythrocytes, epithelial), the presence of yeasts, undigested tissue, tumor cells. But they quickly lysed juice.

In the treatment of acid-related diseases of the esophagus, stomach and duodenum are two major problems:

1) securing intragastric $\text{pH} > 3.0$ for 18 hours a day for 2-4 weeks;

2) eradication (removal) of *H. pylori*. *Helicobacter helicobacter pylori* (HP) are open in 1983 (described 9 types) – S-shaped gram-negative curved rod with 4–6 flagella to one end produces a urease, catalase, lipase, phospholipase, cytokines, is capable of adhesion to epithelial cells stomach, HP, mainly type 1, concentrating near the intercellular gaps - places the output of urea decomposes to ammonia last (which protects the HP from the action of gastric juice), destroys the gastric mucus and damages the epithelium, causing inflammation. HP expressed on their membrane antigens that are close to human, particularly, to antigens of group I-blood, which forms a high resistance vital HP in humans. For HP "optimal" $\text{pH} = 4.0\text{--}8.0$, with a $\text{pH} < 3.5$ HP is non active.

Methods for detection HP: cytological, urease, histological, immunological.

The degree of contamination of the gastric mucosa HP:

cytologic method:

1 level – Weak (+) – 20 HP in microscope field;

2 level – Moderate (+ +) – 20–40 HP in microscope field ;

3 level – High (+ + +) > 40 HP in microscope field ;

urease method:

1 level – Minor infection (+) – crimson staining the gel carrier appears at the end of the day (if later! – The test is negative);

2 level – Mild infection (+ +) – the indicator changes color in 2-3 hours;

3 level – Significant infections (+ + +) – raspberry staining gel carrier occurs within 1 hour.

The method for determination of the intragastric pH – pH-metry

The method is based on measuring the electromotive force (EMF) generated between two electrodes placed in the solution where H^+ ions are present. The electrodes are mounted in a slim stomach tube. One pair of electrodes placed in the pyloric region (here produced bicarbonate, mucus), a second pair – in the body of the stomach – Housing electrodes (here parietal glands produce HCl !).

According to the testimony of body electrodes emit five initial states (G.E. Roytberg, A.V. Strutynsky, 1999):

- 1 – stomach is strongly acidic, pH 0.9–1.9;
- 2 – middling acidic stomach, pH = 2.0–2.9;
- 3 – bland acidic stomach pH 3.0–4.9;
- 4 – slightly acidic stomach pH 5.0–6.9;
- 5 – alkaline stomach pH 7.0–8.9.

The reaction gastric secretory apparatus in response to the use of stimulants is evaluated as normal – pH 1.2–2.0; hyperacidic – pH<1.2; hypoacidic – pH 2.1–3.5, weak – pH 3.6–5.9; anacidic (aclorhydrate) or lack of response – pH \geq 6.0.

When used atropin hyperacidic state test – administered 1 mL of 0.1% atropine (by drop infusion):

- 1) pH changes (increases) by more than 0.5 units. – A symptom of the complete unresponsiveness of vagal stomach;
- 2) the pH is increased by 0.5–1 units. – Slight positive test;
- 3) increased by 1.0–2.0 pH units. – Moderately positive test;
- 4) the pH is increased to \geq 4.0 units. – Strongly positive test.

Determination of the gastric acid-saturation reaction

- 1. When acid-preserved features antrum it in both phases is neutral or slightly alkaline pH.
- 2. If you violate alkalizing ability antrum and excess acid production in the stomach develops "decompensated state sour stomach": low pH in the antrum and body (table 7,8).

Table 7

Stimulants of the gastric secretion

<i>Medicinal product</i>	<i>Comment</i>
Histamine	.
Pentagastrin	.
Insulin	
Metylaxanthines: Caffeine; Theophylline;	

<i>Medicinal product</i>	<i>Comment</i>
Aminophylline (theophylline, aminophylline = + ethylene); choline theophyllinate	
Beta-blockers: propranolol and others	
Reserpine	
Acetylcholinesterase inhibitors: Physostigmine; Neostigmine Methilsulfate (Proserine) Galantamine; Pyridostigmine bromide; Amiridin	
Vitamin B ₅ (vitamin PP, nicotinic acid)	
Vitamin B ₆ (pyridoxine)	Promotes the exchange of amino acids, energy processes in cells.

Table 8

Inhibitors of the gastric secretion

<i>Medicinal product</i>	<i>Comment</i>
H ₂ receptor inhibitors histamine: Cimetidine (120 synonyms); Ranitidine (Zantac); Famotidine (Kvamatel); Nizatidine (Axsid); Roxatidine (Roxane).	
Inhibitors of proton pump inhibitors (H ⁺ – K ⁺ – Adenosine triphosphatases) Omeprazole; Esomeprazole; lansoprazole; Rabeprazole; Pantoprazole.	
M-anticholinergics (M-cholinergic receptor blockers): Atropine; Pirenzepine (gastrosepin) Telenzepine;	

<i>Medicinal product</i>	<i>Comment</i>
Metocinium iodide (metacin).	
Synthetic peptides with antiseecretory: Dalargin;	
Octreotide (Sandostatin).	
Antacids: Sodium alexitol (actal); Sodium bicarbonate; Aluminum phosphate (Fosfalyugel); Algedrat (aluminum hydroxide - Rivofarm); Magnesium hydroxide; Hydrotalcite (taltsid); Simaldrat (Gelusil); Almazilat (simagel, megalak almasilat); Megalak; Almagel (Maalox); Tisacid; Gastal; Almagel A; Anacid kompozitum; Andrews Liver Salt; Magaldrate (magalfil); Alyugel (alprogel); Vikair; Vikalin; Bismofalk; Gastralyugel; Gestid; Digel;	

<i>Medicinal product</i>	<i>Comment</i>
Rennie; Karbaldrat (alyugastrin); Mil-pairs; Regla-PH; Topalkan; Sucralfate (Venter); Bekarbon	
Bismuth preparations: Bismuth subsalicylate; Bismuth tri dicitrate; De-Nol; Bevisal	
Diacarb	
Calcium antagonists: Amlodipine (Norvasc) Isradipine (Lomir); Lacidipine (latsipil); Nisoldipine (siskor); Nitrendipine (nitrepin); Valium (foridon).	
NSAIDs: Voltaren, indomethacin, aspirin, paracetamol, etc.	Reduce the product HCl, and the alkalizing ability of the stomach, leading to a deficiency of prostaglandin E ₁ .
Misoprostol (Cytotec)	Synthetic analogue of prostaglandin E ₁ . Inhibits basal and stimulated gastric acid secretion overnight, HCl; enhances the formation of mucus and bicarbonate. Reduce the production of pepsin (basal, but not stimulated by histamine!).
Carbenoxolone (bioral, duogastron)	Chemically pure glitsirritinovaya acid extracted from licorice root. The drug is known as an instrument for the topical treatment of stomatitis, reduces the rate of exfoliation of mucosal and thereby increases the production of mucin and bicarbonate, reduces the release of hydrolases. Agent for the treatment of drug-related gastric ulcers on the background of low gastric secretory parameters.

***Recommendations of the Maastricht Conference (2000) on the eradication of
Helicobacter pylori***

Home – triple circuit line 1 - days:

1) proton pump inhibitors × 2 time a day or

ranitidine bismuth citrate $\times 2$ time a day

2) Clarithromycin 500 mg $\times 2$ time a day

3) Metronidazole 500 mg $\times 2$ time a day or

Amoxicillin 1000 mg $\times 2$ time a day

In the absence of scarring ulcers - circuit kvadriterapii

– *Eradication therapy Line 2 – 7 days:*

1) proton pump inhibitors $\times 2$ time a day

2) Preparations of Bismuth 120 mg $\times 4$ time a day

3) Tetracycline 2 g/day

4) Metronidazole 1.5 g/day

Analysis of the duodenal contents

Duodenal content – variable composition zhelchesoderzhaschy chyme duodenal ulcer (DU), obtained by duodenal probe - a rubber tube 1.5 m long with a metal olive tree at the end. The tube has three labels: the first - at the level of 40-45 cm from the olive tree, which corresponds to the distance from the tip of the tooth to the cardiac portion of the stomach, the second – at 70 cm (the entrance to the gatekeeper), the third – at 90 cm from the olive tree, which corresponds to Distance from the tip of the tooth to the KDP. (table 9)

Duodenal contents include bile secrets pancreas and duodenum, small amounts of gastric juice.

Liver produces bile rate of about 10 mL/kg body weight / day, a maximum of 2 L/day, average = 0.6–1 L/day. Bile is composed of 80% water and 20% of solutes, are \approx 65% – cholic acid, 4% – cholesterol, 20% – phospholipids 4–5% – proteins, 0.3% conjugated bilirubin, other – vitamins, hormones , enzymes, drugs, etc.

Phases of the biliary excretion

Phase I – from the moment of getting the probe into the duodenum to the infusion of money into it holetsistokineticheskogo. It is recommended to trace the biliary excretion in this phase for 20–30 minutes. In a healthy person during this time receive 20–35 mL of bile, ie \approx 1 mL/min. Current phase hyposecretion – bile <0.5 mL/min; hypersecretion >1.5 mL/min. Hypersecretion in the I-th phase

characteristic postcholecystectomical states hyposecretion – for obstruction of extrahepatic large rotok.

Phase II – closed sphincter of Oddi – from the introduction of the stimulus until the new light colored bile. Length phase = 2–6 (3–5) minutes. If bile is not >10–15 minutes – a sign of the sphincter of Oddi spasm.

Phase III – cystic reflex latency period - from the beginning of the appearance of light bile ducts until dark gallbladder bile. The normal duration of the phase of 3-4 min, during which time stands 3–5 mL light bile. In foreign literature, this portion is referred to as bile (serving) A. A portion of the CIS called all the bile obtained before activation of the cystic reflex.

Phase IV – cystic (bile B) – is characterized by the release of 20-50 ml dark brown viscous bile flowing from the gall bladder. The duration of this phase is normal = 20–30 min, 25–45 mL allocated bile. Initially, the rate of release of bile \approx 4 mL/min, and then decreases. Exact Phase IV study (time, speed and expiration bemsya received bile) in the clinic recognized as the most important aspect of duodenal intubation. Said end of phase IV bile appearance similar color in the portions A. If there is no reflection cystic >30 min, antispasmodics administered, and then re holetsistokineticheskoe means. If still no dark bile, talk about "disabled" gallbladder.

Phase V – a portion of C – light bile outflow (of hepatic ducts). It is collected for 25–30 min. To check whether a fully contracted gallbladder, it is recommended to re-enter this phase holetsistokinetiki (table 9).

Cholecystic kinetic medicines used during duodenal intubation

– Magnesium sulphate, 30–50 mL of 33% sterile solution heated; administered for 7 min;

– Sorbitol, 50 ml of a 10% solution – cholecystokinin (Sweden – not in the CIS) – intravenous 1 ampoule (75 units).

Table 9

The structure of the duodenal contents

<i>Factor</i>	<i>Portion</i>	<i>Comment</i>
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<i>Factor</i>	<i>Portion</i>			<i>Comment</i>
	<i>A</i>	<i>B</i>	<i>C</i>	
Colour	Golden-yellow	Olive, brown	Golden-yellow	
Transparency	Full	Full	Full	
Body	Slightly viscous	Viscous	Slightly viscous	
Specific gravity, units	1007–1015	1016–1034	1007–1010	Specific gravity
pH, units	7.0 – 7.5	6.5 – 7.3	7.5 – 8.2	
Bilirubin, mmol/L	343 – 428	256.5–769.7	343 – 428	
Cholesterol, mmol/L	1.04 – 2.08	5.2 – 10.4	1.04 – 2.08	
Parasite	No	No	No	In pathology possible: ascaris eggs, liver and catliver flukes, the larvae ugritsa, vegetative forms of giardia and other

Interpretation of cell elements comprising bile difficult because they can enter the duodenum from the stomach, mouth, respiratory. Having them together with crystals of cholesterol, bilirubin in the lump of mucus indicates the biliary origin of the clot. Interpretation of duodenal contents is only possible if you use the correct technology duodenal intubation procedure.

Some concepts of the physiology and pathology of the biliary excretion

Gallstone (cholelithiasis) disease (GSD) – Cholelithiasis, *Lat.* cholelithiasis – a disease characterized by the development of the gall bladder and (rarely) in the bile duct stones. Gallstones occur in 10% of men, but only 10% of them (in turn) is developing gall stones. Clinic: pain in the right upper quadrant until the biliary colic, fever, nausea, vomiting, leukocytosis.

Bile acids – are synthesized by the liver ≈ 0.5 g/day - the end products of cholesterol metabolism. In bile detected mainly bile glycocholic and taurocholic acid. Normally cholate in a portion B = 12-33 mg/l, in a portion C = 3.9-6.3 mg/l. Bile acids up to 3-5 times/day pass through the circle of the enterohepatic circulation, replacing the consequent need for their secretion of 15-17 g/day. Increase in blood levels of bile acids causes hemolysis. The toxicity of bile acids depends on their degree of lipophilicity to hepatotoxicity include acid: chenodeoxycholic, lithocholic, deoxycholic. Chenodeoxycholic synthesized in the liver from cholesterol. Deoxycholic and lithocholic formed in the intestine by the action of bacteria of the primary (secondary bile acids). With the influence of bile acids bind hepatocyte

apoptosis, and the development of autoimmune reactions against hepatocytes and bile ducts.

Cholate-cholesterol index or index litogenoti (IL) – the ratio of the content of bile in the gallbladder bile acids, cholesterol. Normally, the HHI = 25. An increase indicates an increase in bile lithogenicity ie of the increased tendency to cholelithiasis.

Cholestasis – reduction of revenues in the duodenum of bile due to violation of its formation and / or excretion.

The pathological process that causes cholestasis can be located at any level of biliary system – from the sinusoidal membrane of hepatocytes to duodenal (faterova) papilla. In cholestasis decreases tubular current bile, the rate of hepatic excretion of water, organic anions (bilirubin, bile acids), bile builds up in the hepatocytes and biliary tract, the blood retained components of bile (bilirubin, bile acids, and lipids). Prolonged cholestasis (months – years) leads to the development of biliary cirrhosis (shrinkage) of the liver.

The etiology of cholestasis: drugs, viruses, alcohol, etc.

Markers of severe chronic cholestasis are xanthomas around the eyes, in the palmar creases, under the breasts, neck, chest or back. Xanthoma formation precedes hypercholesterolemia than 450 mg/dL (>28 mmol/L) for ≥ 3 months. The resulting cholestasis steatoreya corresponds to the degree of jaundice. Stool color is a reliable indicator of cholestasis. When extrahepatic cholestasis expulsion of bile acids and bilirubin in the blood starts in 36 hours. After about 2 weeks of cholestasis degree of morphological and functional changes peaks. When the duration of cholestatic jaundice = 3–5 years developed severe hepatocellular insufficiency.

Lack of bile acids in the intestine causes malabsorption of vitamins A, D, K, E (and the corresponding clinical picture).

Enterohepatic circulation – multiple (2–5) reabsorption from the intestine into the blood of some pairs of compounds and glucuronides. Related to their ability to hydrolyze and intestinal bacterial enzymes and transformed into lipid-soluble substances.

Biotransformation of drugs – drugs conversion in the body into metabolites which in the first stage have more or less equal to the pharmacological activity compared with that of the starting compound, and the second step are converted into water-soluble (polar) conjugates are readily excreted from the body (urine, bile, sweat). Process drug biotransformation 90–95% occurs in the liver. Preparations with

a high hepatic clearance extracted hepatocytes depending on blood flow velocity intrahepatic, metabolism of drugs with low hepatic clearance depends primarily on the rate of protein binding activity is determined and of the liver. Microsomal biotransformation occurs in the liver microsomes. Conjugation with glucuronic acid is also influenced by microsomal enzymes. Nemikrosomalnaya liver biotransformation addition takes place in the kidneys, blood plasma and some other organs (in the intestinal wall) (Table 7).

Table 10

Drugs affecting the activity of liver microsomal enzymes

<i>Inhibitors (antiferments)</i>	<i>Inducing substances</i>
Chloramphenicol (Laevomycetin) Tetracycline Erythromycin Cimetidine Amiodarone Indomethacin Chlorpromazine (Aminazin))	

Gall stones – concrements in the biliary system with a diameter ≥ 2 mm:

- Cholesterol stones – white or yellowish, soft and easy to crumble, and often have an admixture of calcium carbonate;
- Pigment stones – small sized fragile section in black color composed mainly of bilirubin and lime;
- Calcium stones – bizarre, composed of carbonate, calcium bilirubinate and others;
- Mixed stones – cholesterol-pigment-lime – are the most common – different shapes, colors, layered.

Liver toxicity (hepatotoxicity) of drugs

Hepatotoxicity of drugs – the ability of drugs, directly or indirectly damage the liver.

Substances are direct protoplasmic poisons, tissue damage, liver damage in these cases is similar to that of viral hepatitis (cytostatics, immunosuppressive agents, salicylates, tetracycline etc.).

Substances with an indirect mechanism of action cause competitive inhibition of specific metabolic processes in the liver without significant damage to other organs, causing cholestatic hepatitis, intrahepatic cholestasis, hepatotoxicity. Mechanisms for the implementation of liver toxicity: immune, enzymopaticheskie toxic-allergic. When toxic-allergic lesions plays a major role sensitization of the organism to the drug. Clinically toxic-allergic hepatitis occur as cholestatic. Time of occurrence of hepatotoxicity is not dependent on the duration of treatment. It may develop after the first taking drugs or after 6–12 months of starting treatment. Removal of the drug leads to recovery, less toxic manifestations of hepatitis progresses.

There are more than 1,000 drugs that can cause drug-induced hepatitis, steatosis (fatty, cholestatic), chemically induced hyperplasia of the liver tissue (table 11). The mechanisms of drug hepatotoxicity are poorly understood. There is no generally accepted classification.

Table 11

Hepatotoxic drugs

<i>Medicinal product</i>	<i>Character of liver damage</i>	<i>The leading mechanism. Comments</i>
Phenothiazines: Chlorpromazine (Aminazine), fluphenazine, etc.		
Anti-TB drugs: a) Ftivazide, Isoniazide Rifampicin PASA b) Ethionamide Pyrazinamide c) Prothionamide Ethambutol Streptomycin		
Antidiabetic drugs – derivatives of sulfonyleureas: Tolbutamide, Carbutamide (bucarban) Glibenclamide (maninil), etc.		
Merkazolil, potassium iodide		
Propanolol		
Tetracycline		

<i>Medicinal product</i>	<i>Character of liver damage</i>	<i>The leading mechanism. Comments</i>
Paracetamol (has 413 synonyms)		
Aspirin		
Heavy metal salts Valproic acid		
Allopurinol Hydralazine, Phenylbutazone, Phenytoin		
Chinidin (quinidin)		
Thiazides; Erythromycin		
Indomethacin; Cimetidine		
Proserin Physostigmine		
Preperations of calcium		
Narcotic analgesics		
Amiodarone		
Cytotoxic agents: Cyclophosphamide, Methotrexate, Azathioprine, Mercaptopurine		
Androgens; Gestagens		
Anabolic steroids: Methandrostenolone Metilandrostandiol, Etiestrenol, Nandrolone decanoate (Retabolil) etc.		
Estrogens: Estradiol, Premarin, Ethinyl estradiol, Diethylstilbestrol, Sinestrol etc.		
Cephalosporins; Lincosamides: Lincomycin, Clindamycin		
Laevomycetin		
Nitrofurantoin (furadonin)		
Clozil		
Polyene antibiotics: Nystatin, Levorin, Natamycin,		

<i>Medicinal product</i>	<i>Character of liver damage</i>	<i>The leading mechanism. Comments</i>
Amfotertsin B Mikogeptin		
Imidazole derivatives: Ketoconazole, Miconazole, Chlotrimazole		
Vitamin D (overdose)		
Vitamin E (overdose)		
Halothane; Alcohol; Phosphorus		
Sulfanilamides		
Statins		
Antidepressant medications		

All drugs undergoing hepatic glucuronidation reaction, capable of long-term use, overdose, glucuronidase fermentopathy cause hyperbilirubinemia and cholestatic hepatitis (liver toxicity).

*Drugs with the hepatoprotective effect
affecting production of bile, its flow and composition*

Hepatoprotectors – drugs have a protective effect on hepatocytes, impaired liver function to: reduce cytolysis, inflammation, cholestasis, hepatocellular failure, strengthen regeneration and proliferation of hepatocytes, increases metabolic reactions: non-synthetic (oxidation, reduction, hydrolysis) and synthetic (conjugation of glucuronic acid, methyl groups, glycine, glutathione, sulfates, etc.) to increase the level of endogenous tocopherols hepatocyte cytochrome P-450, inhibit the formation of free radicals (oxygen, chlorine, nitrogen) increase glycogen deposition; lithogenicity reduce bile, etc. (table 12). Ursodioksiholevaya acid replaces toxic bile acids from enteropathic circulation, has a choleretic effect, reduces the surface of hepatocyte antigens HLA I class (block autoimmune reactions), embedded in the membrane of hepatocytes (straight gepatoprotection).

Set hepatic relatively small. From some of these abandoned in recent years because established their unwanted effects. This refers to the Liv-52, vitamin E, tioktanu. On the positive effects of levamisole, delagila can count only in the presence of allergic hepatitis syndrome, and a positive effect of essentielle - with synthetic reactions of liver failure. The use of phenobarbital, rifampicin treatment itching requires high doses and thus, caution.

Table 12

Hepatoprotectors

<i>Drugs</i>	<i>Comments</i>
Lipoic acid	
Heptral (ademethionine)	
Riboxinum, Ethimidazol	
Potassium orotate	
Chloroquine (delahil)	
Ursodeoxycholic acid	
<i>Vegetable hepatoprotectors:</i> Hepobene, Legalon (Carsil, Filibinin) Biligin, Felling Rozinol, Gepatofalk, Tykveol. <i>Synthetic hepatoprotectors:</i> Holinohlorid, Lecithin Phospholipids, Methionine Essentiale, Ziksorin, Katerhen.	

Cholagogic drugs

Cholagogic drugs, *Lat.* cholagoga [Greek. chole – gall + agogos – caller] – a group of drugs contributing to an increase in the number of bile into the duodenum:

a) cholesecretica (choleretica) – drugs that promote bile production: digidrohlevaya acid allohol, holenzim; cikvalon, nicodin, xafenamid, helichrysum extracts, corn stigmas, rose, barberry;

b) cholekinetica – drugs that promote zhelcheottoku: magnesium sulfate, sorbitol, mannitol, xylitol;

c) cholespasmolytics – cholespasmodic drugs: atropine, papaverine, drotaverine, No-Spa, Euphyllinum olimetin, holagol, platifillin.

Drugs for dissolution of gallstones (litholitics)

Litholytic drugs:

- Ursodeoxycholic acid (ursosan, ursofalk);
- Chenodeoxycholic acid (henosan, henofalk, henohol).

Ursodeoxycholic Acid – tertiary bile acid, normally produced in the intestine and liver is 0.1–0.5% of the total pool of bile acids is non-toxic, as hydrophilic. Drug safety and efficacy is proven (for cholesterol stones). The mechanism of action:

1) displaces toxic bile acids from the enterohepatic circulation by competitive inhibition of absorption in the ileum;

2) embedded in the membrane of hepatocytes, providing a cytoprotective effect;

3) decreases the production of antigens on the surface of hepatocytes HLA I-class preventing immune responses;

4) has a choleretic effect by holecapaticeskogo shunt – the return of bile acids from the sinusoidal membrane tubules through the peribiliary plexus.

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Appendix

Tests

Blood count

1. Blood count of patient A., 40 years: erythrocytes = $4.38 \times 10^{12}/L$, hemoglobin = 120 g/L, color index = 0.85, platelets = $320 \times 10^9/L$, WBC = $150 \times 10^9/L$, basophils = 0.5% = 1%, eosinophils, myelocytes = 1%, young neutrophils = 4%, stab neutrophils = 7%, segmented neutrophils = 69.5%, lymphocytes = 15%, monocytes = 2%. ESR = 26 mm/hr.

This analysis reflects:

- a) classic inflammatory process
- b) the toxic effects of macrolides
- c) the toxic effects of penicillin
- d) an overdose of an ACE inhibitor

2. Blood count of patient B., 36 years: erythrocytes = $1.6 \times 10^{12}/L$, hemoglobin = 52 g/L, color index = 0.98, platelets = $40 \times 10^9/L$, WBC = $2.5 \times 10^9/L$, basophils = 0%, eosinophils = 0.5%, neutrophils stab = 4%, segmented neutrophils = 36.5%, lymphocytes = 51%, monocytes = 8%. ESR = 42 mm/hr.

This analysis reflects:

- a) a deficiency of vitamin B₁₂
- b) the toxic effects of glucocorticosteroids
- c) the toxicity of cytostatics
- d) the inflammatory process

3. Blood count of patient V., 28 years: erythrocytes = $4.7 \times 10^{12}/L$, hemoglobin = 138 g/L, color index = 1.02, reticulocytes = 0.4%, platelets = $310 \times 10^9/L$, WBC = $6.8 \times 10^9/L$, white blood cells: neutrophils stab = 2%, segmented = 63%, eosinophils = 2%, basophils = 1%, lymphocytes = 25%, monocytes = 8%. ESR = 6 mm/hr. Clotting time by Sukharev = 3 min. Duration haemorrhage by Duque = 2 min.

This analysis reflects:

- a) normal blood
- b) an overdose of heparin
- c) an overdose of tetracyclines
- d) toxicity novokainamida

4. In the appointment of diuretics should be expected:

- a) the development of anemia
- b) an increase in hematocrit
- c) leukopenia
- d) leukocytosis

5. Cytostatic agents (cyclophosphamide, azathioprine, and others) cause:

- a) only leukopenia
- b) only eritropeniya
- c) only thrombocytopenia
- d) pancytopenia

6. Thrombocytopenia can be caused by:

- a) Indomethacin
- b) Ftalazol
- c) Heparin
- d) Vikasol

7. Tetracycline cause:

- a) agranulocytosis
- b) eosinopenia
- c) eosinophilia
- d) leukocytosis

8. Which vitamin is necessary to appoint a newborn if the mother during pregnancy has received indirect anticoagulants:

- a) K;
- b) A;
- c) E;
- d) B₁₂

9. To stimulate of leukopoiesis use:

- a) metiluracyl
- b) filgrastim
- c) levamisole
- d) phenylbutazone

10. By hematostatic medications include:

- a) calciparin
- b) pentoxifylline
- c) aminocaproic acid
- d) sodium etamzilat

11. Agents for the treatment of iron deficiency anemia are:

- a) durules
- b) cyanocobalamin
- c) folic acid
- d) jektofer

12. As used heparin antagonist:

- a) protamine sulfate
- b) aprotin
- c) calcium chloride
- d) vikasol

Urine analysis

1. The density of the urine is greatly enhanced when:

- a) glycosuria
- b) leukocyturia
- c) proteinuria
- d) hematuria

2. Pink color of the urine can cause:

- a) rhubarb
- b) aspirin
- c) dopegit
- d) alcohol

3. Low specific gravity of urine can cause:

- a) diuretics
- b) cardiac glycosides
- c) aspirin
- g) diphenhydramine

4. pH of the urine reduce:

- a) sulfonamides
- b) aspirin
- c) thiazide diuretics,
- d) caffeine

5. Reduce contractility of the bladder and undesirable in prostate cancer:

- a) barbiturates
- b) tranquilizers
- c) aminoglycosides
- d) nitrofurans

6. Glycosuria may be due to the drug administration:

- a) glucocorticosteroids
- b) nonsteroidal anti-inflammatory drugs
- c) diuretics
- d) anabolic hormones

7. What is the most likely cause of hematuria in the analysis of urine: number – 80 mL, color – bloody, transparency – muddy, specific gravity – 1.019, reaction - weakly acidic, protein – 0.33 g/L, the reaction to the blood + +, epithelium: flat = 7–8 in field of microscope, kidney = 3.2 in field of microscope, WBC = 14–16 in field of microscope, red blood cells – fresh, cover the entire field of view, the cylinders – no, slime + +, bacteria 70000 in 1 mL, lot of oxalates:

- a) acute glomerulonephritis
- b) urolithiasis
- c) intake of atropine
- d) intake of nitrofurans

8. The smallest nephrotoxic effect has:

- a) erythromycin
- b) gentamicin
- c) streptomycin

d) penicillin

9. Nephrotoxicity have the most:

a) aminoglycosides

b) non-steroidal anti-inflammatory drugs

c) sulfonamides

g) barbiturates

Stool analysis

1. In the treatment of helminthiasis with praksivantel may be justified to add:

- a) erythromycin
- b) prednisone
- c) diazolin
- d) multivitamins

2. The optimal treatment for ascariasis is:

- a) levamisole
- b) [chlorsil](#)
- c) fenasal
- d) metronidazole

3. Diarrhea can cause:

- a) mannitol
- b) reserpine
- c) morphine
- d) [espumizan](#)

4. Antidiarrhoeal effect have

- a) [espumizan](#)
- b) reserpine
- b) morphine
- g) [warfarin](#)

Sputum analysis

Which processes can be characterized by phlegm in the analyzes?

1. Macroscopic examination of sputum

1. Amount per day 20 to 100 ml
2. Color – colorless, sometimes white and gray
3. Smell – no
4. Consistency – viscous
5. Stickiness – weak
6. Foaming – no
7. Lamination – single-layer
8. Character – a slimy

Microscopic examination of sputum

9. Epithelium: flat – single, cylindrical – a lot of dust cells – [isolated alveolar macrophages in the preparation – individual](#)

10. White blood cells:

neutrophils – to 10 in field of microscope

eosinophils – single in field of microscope

lymphocytes – single in field of microscope

11. Red blood cells – 5 red blood cells / 1000 of leukocytes

12. Fiber formation -- are not found

13. Crystal formation – are not found

Direct microscopic examination of sputum

[VK](#) – not found

Revealed catarrhal pneumococci.

Possible reasons are:

a) lobar pneumonia

- b) bronchoalveolitis
- c) pulmonary tuberculosis
- d) acute bronchitis

2. Macroscopic examination of sputum

- 1. Amount per day – 100 ml
- 2. Color – yellowish (xantic)
- 3. Smell – no
- 4. Consistency – viscous and sometimes – semi-liquid
- 5. Stickiness – weak
- 6. Foaming – no
- 7. Lamination - single-layer
- 8. Character – mucous

Microscopic examination of sputum

9. Epithelium:

flat – a little

cylinder – a lot

alveolar macrophages – a little

10. White blood cells:

neutrophils – to 10 in field of microscope

eosinophils – a lot (the main part of leukocytes)

lymphocytes – single in field of microscope

basophils – single in preparation

11. Red blood cells – up to 20 red blood cells / 1000 of leukocytes

12. Kurshman spirals – single in field of microscope

The threads of fibrin – **single** in a preparation

13. Charcot-Leyden crystals – small clusters throughout a preparation

Bacterioscopic examination of sputum

VC, other microorganisms - are not found

Possible reasons are:

- a) lobar pneumonia
- b) bronchial asthma
- c) the use of heparin
- d) aspirin

3. Macroscopic examination of sputum

- 1. Amount per day - 300 ml
- 2. Color – yellow-green mixed with blood
- 3. Smell – nasty
- 4. Consistency – thick
- 5. Stickiness – weak
- 6. Foaming – weak
- 7. Lamination – a three-layer
- 8. Character – mixed (**bloody-muco-purulent**)

Microscopic examination of sputum

9. Epithelium:

flat – a lot

cylinder – a lot

alveolar macrophages – a little

dust cells – **single** in field of microscope

atypical cells – are not found

10. White blood cells:

Neutrophils – 50–70 in field of microscope

eosinophils – single in field of microscope

lymphocytes – single in field of microscope

11. Red blood cells – 10–20 red blood cells / 1000 leukocytes

12. Kurshman spirals – not found

Elastic fibers – **single** in preparation

13. Charcot-Leyden crystals – are not found

Corks Dietrich – revealed

Direct microscopic examination of sputum

VK – not found

Identified bacilli Pfeiffer, candides.

Possible reasons are:

- a) lobar pneumonia
- b) a lung abscess
- c) the use of heparin
- d) the use of tetracycline

4. Macroscopic examination of sputum

- 1. Quantity per day – up to 100 mL
- 2. Color – yellow-green
- 3. The smell – no, sometimes a little edgy
- 4. Consistency – viscous
- 5. Stickiness – weak

6. Foaming – weak

7. Lamination – single-layer

8. Character – mixed (mucopurulent)

Microscopic examination of sputum

9. Epithelium:

flat – a little

cylinder – a lot

alveolar macrophages – large aggregations

10. White blood cells:

Neutrophils – 50–60 in field of microscope

eosinophils – **single** in field of microscope

lymphocytes – **single** in field of microscope

monocytes – **single** in preparation

11. Red blood cells – 20–25 / 1000 leukocytes

12. Fiber formation – not identified

13. Crystals – not identified

Direct microscopic examination of sputum

VK – not found

Identified bacilles of Pfeiffer, **pneumobacilles** of Friedlander.

Possible reasons are:

a) asthma

b) the use of heparin

c) the use of nystatin

g) acute pneumonia

5. Macroscopic examination of sputum

1. Quantity per day – up to 100 mL
2. Color – "rusty", occasionally yellow-green
3. Smell – a small, blurred
4. Consistency – viscous and sometimes – semi-liquid
5. Stickiness – moderate
6. Foaming – weak
7. Lamination – single-layer
8. Character – mixed (muco-purulent and bloody)

Microscopic examination of sputum

9. Epithelium:

flat – a little

cylinder – a lot

alveolar macrophages – large aggregations

10. White blood cells:

Neutrophils – 40–70 in field of microscope

eosinophils – small clusters throughout the all preparation

lymphocytes – [single](#)

basophils – [single](#)

11. Red blood cells – 40–60 / 1000 leukocytes

12. Fiber formation – not identified

13. Charcot-Leyden crystals – single in field of microscope

Direct microscopic examination of sputum

[VC](#) – no

Identified [diplococcus](#) of Friedlander.

Possible reasons are:

- a) asthma
- b) the use of heparin
- c) lobar pneumonia
- d) the use of ambroxol

6. By expectorant drugs reflex action includes all except:

- a) ambroxol
- b) ipecac
- c) thermopsis
- d) the root of polygala (milkwort)

7. Sodium cromoglycate (Intal) disease:

- a) bronchodilation
- b) airway obstruction
- c) the stabilization of mast cell
- d) colliquation of sputum

Analysis of the gastric juice

1. Antacids optimal administration:

- a) to the food
- b) during a meal
- c) an hour and three hours after meal
- d) regardless of mealtime

2. By the development of encephalopathy in patients with kidney disease can cause long-term use:

- a) magnesium oxide
- b) sodium hydrogencarbonate
- c) aluminum hydroxide
- d) magnesium trisilicate

3. Treatment for stomach ulcers caused by aspirin and flowing against the low acidity of gastric juice, the drug of choice should be considered:

- a) [misoprostol](#)
- b) [carbenoxalon](#)
- c) cimetidine
- d) omeprazole

4. Assess the following analysis of the gastric juice:

<i>Portion, time (minutes)</i>	<i>Quantity (mL)</i>	<i>Acidity</i>	
		<i>total</i>	<i>free</i>
fasting	30	32	10
15	10	40	20
30	30	40	30
45	30	35	20
After the introduction of caffeine by gavage			

<i>Portion, time (minutes)</i>	<i>Quantity (mL)</i>	<i>Acidity</i>	
		<i>total</i>	<i>free</i>
15	65	54	38
30	50	85	60
60	40	68	48

Microscopy: colorless, mucus – a little white blood cells up to 10 in field of microscope, squamous epithelium – 3–5 in field of microscope.

Possible conclusions:

- a) normocidity
- b) hypercidity
- c) hyipocidityt

5. Stimulant of gastric secretion are:

- a) ranitidine
- b) lansoprazole
- c) insulin
- d) caffeine

6. Gastric acid secretion inhibitors are:

- a) ranitidine
- b) lansoprazole
- c) dalargin
- d) insulin

Analysis of the duodenal contents

1. Hepatotoxicity most pronounced in:

- a) chlorpromazine
- b) propranolol
- c) aspirin
- d) metilandrostandiol

2. Two-thirds of all drug-induced hepatitis caused:

- a) phenothiazines
- b) TB drugs
- c) anti-diabetic drugs
- d) beta adrenoblocker

3. Direct damage to hepatocytes (cytolysis) cause

- a) chloramphenicol
- b) [chloxyl](#)
- c) alcohol
- d) statins

4. Lack of bile acids in the intestine causes malabsorption of vitamins

- a) B₁₂
- b) A
- c) D
- d) K

5. **Non-microsomal** biotransformation of drugs are:

- a) only in the liver
- b) only in the kidney
- c) only in the blood plasma
- d) in the liver, kidneys, plasma, gut wall

6. Drugs of cholesecretica (choleretica) group include:

- a) ursodeoxycholic acid
- b) dehydrocholic acid
- c) drotaverine
- d) **oxafenamid**

7. Ursodeoxycholic acid is effective in the treatment of gallstones:

- a) cholesterol
- b) pigment
- c) calcium
- d) was mixed

8. The main side effect of nonsteroidal anti-inflammatory drugs are:

- a) hepatotoxic
- b) gastrotoxic
- c) nephrotoxic
- d) hematotoxic

Answers

<i>Blood count</i>	<i>Urine analysis</i>	<i>Stool analysis</i>	<i>Sputum analysis</i>	<i>Analysis of the gastric juice</i>	<i>Analysis of the duodenal contents</i>
1. a	1. a	1. c	1. d	1. c	1. a
2. c	2. b	2. a	2. b	2. c	2. b
3. a	3. a	3. a, b	3. b	3. b	3. b, c
4. b	4. b, c	4. a, c	4. d	4. a	4. b, c, d
5. d	5. b		5. c	5. c, d	5. d
6. a	6. a		6. a	6. a, b, c	6. b, d
7. c	7. b		7. c		7. a
8. a	8. d				8. b
9. a, b	9. a				
10. c, d					
11. a, d					
12. a					